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# EEG correlates of well-being and wearable EEG

Cédric Cannard

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# THÈSE

En vue de l'obtention du  
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Présentée et soutenue par  
**Cédric CANNARD**

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**Corrélat EEG du bien-être et EEG portable**

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Thèse dirigée par  
**Arnaud DELORME**

Jury

M. Michel LE VAN QUYEN, Rapporteur  
M. Pascal BENQUET, Rapporteur  
M. Pier-Giorgio ZANONE, Examineur  
Mme Nathalie GEORGE, Examinatrice  
M. Arnaud DELORME, Directeur de thèse



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## Résumé en Français

Au cours des 30 dernières années, nous avons observé des déclinés dramatiques de la santé mentale et du bien-être dans le monde, avec près de 450 millions de personnes souffrant actuellement de troubles mentaux, tandis que les disparités d'accès aux soins mentaux continuent d'augmenter. L'objectif principal de cette thèse est l'identification de méthodes nouvelles et rentables pour mesurer le bien-être et son évolution au cours du temps. Combiner mesures subjectives et objectives (physiologiques) est crucial pour atteindre cet objectif. Le bien-être module la structure et la fonction du cerveau tout au long de la vie, qui, à son tour, module les niveaux de bien-être. Cependant, notre compréhension de cette relation bidirectionnelle est incomplète. Les progrès technologiques récents ont conduit au développement de systèmes électroencéphalographiques (EEG) portables économiques qui offrent un temps de préparation rapide et qui facilitent l'acquisition de données EEG sur des échantillons larges et diversifiés. Ces derniers permettent l'utilisation de méthodes statistiques robustes qui facilitent la prédiction de variables indépendantes (e.g., bien-être), l'identification de tendances et de médiateurs, et augmentent la puissance statistique. Dans la première étude de ce projet, nous avons validé la capacité d'une échelle subjective rapide à mesurer les dimensions principales du bien-être (hédonique, eudaimonique, physique) sur 1615 sujets qui ont participé à un sondage en ligne. Tandis que les systèmes EEG à bas coût et à basse densité présentent des défis techniques importants (e.g., baisse de la qualité du signal, résolution spatiale basse, limitation du nombre d'algorithmes de traitement de données qui peuvent être utilisés), nous avons montré qu'un tel système pouvait être utilisé pour acquérir des mesures EEG spectrales (domaine fréquentiel) pertinentes pour l'étude du bien-être (étude 2). Dans une 3<sup>ème</sup> étude, nous avons utilisé les outils validés dans les études 1 et 2 et validé une méthode de prétraitement du signal automatique (rejet d'artéfacts) afin d'examiner les corrélats EEG du bien-être sur un grand échantillon ( $N = 353$ ). Un marqueur EEG potentiel du bien-être (associé à l'âge) est présenté, une asymétrie interhémisphérique de puissance spectrale alpha (8-13 Hz) dans les régions temporopariétales. Nous présentons nos interprétations de ces résultats et discutons les limites liées à ces études, les directions futures, et les implications éthiques pour ce domaine de recherche de manière plus large. Les applications cliniques et expérimentales à long terme contribueront, espérons-le, à une amélioration du bien-être et de la prévention des troubles mentaux dans la population générale, et à une réduction des disparités d'accès aux soins mentaux dans le monde.



## **Abstract**

Over the past 30 years, we have seen dramatic declines in mental health and wellbeing around the world, with almost 450 million people currently suffering from mental disorders, while disparities in access to mental care continue to increase. This thesis' main objective is the identification of novel and affordable methods to measure well-being and its evolution over time. Combining subjective and objective (physiological) measures is crucial to achieving this goal. Well-being modulates brain structure and function throughout life, which, in turn, modulates levels of well-being. However, our understanding of this bidirectional relationship is incomplete. In the first study of this project, we validated the ability of a quick subjective scale to measure the main dimensions of well-being (hedonic, eudaimonic, physical) on 1,615 subjects who participated in an online survey. Recent advances in technology have led to the development of low-cost, portable, and wireless electroencephalographic (EEG) systems that offer fast set-up time and facilitate the acquisition of EEG data on large and diverse samples. In turn, these large datasets allow the use of robust statistical methods (e.g., linear models) that facilitate the identification of trends, mediators (e.g., co-variables), and the prediction of independent variables (e.g., well-being). While low-cost, low-density EEG systems present significant technical challenges (e.g., lower signal quality, lower spatial resolution, limitation of the number of data processing algorithms that can be used), we have shown that such a system could be used to acquire spectral (frequency domain) EEG measurements relevant to the study of well-being (Study 2). In Study 3, we used the tools validated in Studies 1 and 2 and validated an automatic signal preprocessing method (artifact rejection) to examine the EEG correlates of well-being in a large sample ( $N = 353$ ). A potential EEG marker of well-being (associated with age) is presented, an interhemispheric asymmetry of alpha spectral power (8-13 Hz) in the temporoparietal regions. We present our interpretations of these results and discuss the limitations of these studies, future directions, and ethical implications for this area of research more broadly. Long-term clinical and experimental applications will hopefully contribute to improved well-being and the prevention of mental disorders in the general population and reduce disparities in access to mental care around the world.



## Résumé substantiel en Français

Au cours des 30 dernières années, nous avons observé des déclinés dramatiques de la santé mentale et du bien-être dans le monde, avec près de 450 millions de personnes souffrant actuellement de troubles mentaux (Patel *et al.*, 2018; Global Health Data Exchange, 2019), tandis que les inégalités d'accès aux soins mentaux continuent d'augmenter (Saxena *et al.*, 2007; World Health Organization, 2021). Les dégradations de la santé mentale commencent très tôt (14 ans, pouvant conduire au suicide) et sont liées à des réductions d'environ 10-20 ans d'espérance de vie (United Nation, 2020). L'objectif principal de cette thèse est l'identification de méthodes nouvelles, mobiles, et économiques pour évaluer, prédire, et améliorer le bien-être dans la société. Les applications de cet axe de recherche contribueront, espérons-le, à réduire la prévalence des troubles mentaux (e.g., le stress chronique, les troubles anxieux, la dépression, les troubles psychiatriques) et les disparités d'accès aux soins mentaux dans le monde.

Le concept de « bien-être » est un concept évolutif et multidimensionnel qui englobe les dimensions hédonique (i.e., affect positif et négatif), eudaimonique (i.e., avoir un objectif de vie, épanouissement, autonomie), physique (e.g., santé, qualité de sommeil, comorbidités), et sociale (e.g., sentiment de connexion avec autrui, relations positives; Ryff, 1989; Ryan and Deci, 2001; Maslow, 2013). Le bien-être détermine comment nous nous sentons, pensons et agissons dans le monde et dans notre vie quotidienne. Par exemple, des études suggèrent que les personnes qui déclarent elles-mêmes des niveaux de bien-être faible sont à risque d'épisodes dépressifs ultérieurs (e.g., Keyes, Dhingra and Simoes, 2010). Les échelles rapides subjectives sont de plus en plus utilisées pour capturer rapidement les éléments clés relatifs au bien-être mental et physique (Derogatis and Melisaratos, 1983; Faustman and Overall, 1999; Østergaard *et al.*, 2014). Elles peuvent en effet recueillir avec précision des caractéristiques psychologiques qui nécessitaient auparavant de longs questionnaires et des techniques d'évaluation psychométrique plus avancées (Idler and Kasl, 1991; Idler and Benyamini, 1997; Bath, 1999; Menec, Chipperfield and Perry, 1999). Les échelles rapides subjectives reposent sur les capacités métacognitives de l'individu. Malgré les limites que cela peut impliquer (e.g., réponses de complaisance), cela représente des caractéristiques psychologiques importantes que l'on peut manquer avec des questionnaires qui ont des critères prédéfinis (Nartova-Bochaver, Donat and Rüprich, 2019). Par exemple, cela permet à chaque individu de peser l'importance de chaque élément pour eux-mêmes. Ces échelles sont rapides à administrer à la fois chez les populations cliniques et non cliniques, et

peuvent être facilement mises en œuvre en ligne ou en conjonction avec des mesures physiologiques telles que l'électroencéphalographie (EEG).

La première étude de ce projet visait à valider une échelle rapide de bien-être, the *Arizona Integrative Outcome Scale (AIOS)* ; Bell *et al.*, 2004), sur un échantillon large et diversifié. Nous avons collecté l'AIOS (versions 24h et 1 mois) et d'autres valeurs de bien-être à l'aide d'échelles et questionnaires validés sur 1 615 personnes. Ces personnes ont participé à un sondage en ligne sur une période d'un an. Dans une première analyse transversale, nous avons observé une validité convergente élevée entre les deux formes d'AIOS ( $r(1463) = .71$ ,  $CI [0.59, 0.67]$ ,  $p < 0.01$ ) et que les scores d'AIOS étaient significativement associés aux dimensions hédonique, eudaimonique et physique du bien-être ( $F(1442) = 292$ ,  $R^2 \text{ ajusté} = 0.446$ ,  $p < 0.0001$ ). Le modèle linéaire multiple a indiqué que ces trois dimensions expliquaient 44.6% de la variance des scores AIOS, une valeur élevée en psychologie pour un concept complexe et abstrait comme le bien-être. La dimension sociale, l'âge, le sexe, l'origine ethnique et le niveau d'éducation n'étaient pas prédicteurs des scores d'AIOS dans ce groupe. Un second modèle linéaire multiple a montré que les scores d'AIOS étaient positivement corrélés aux traits de personnalité ( $t = 8.8$ ,  $p\text{-corrigée} < 0.001$ ), au sentiment de connexion avec la nature ( $t = 3.5$ ,  $p\text{-corrigée} < 0.001$ ), au niveau d'activité physique (pendant les loisirs, mais pas au travail ;  $t = 3$ ,  $p\text{-corrigée} < 0.05$ ) et au sentiment d'importance de la religion/spiritualité ( $t = 2.9$ ,  $p\text{-corrigée} < 0.05$ ).

Une analyse longitudinale sur les individus qui avaient complété l'enquête avant et après une intervention en ligne visant à améliorer le bien-être et le développement personnel a indiqué une fiabilité *test-retest* moyenne ( $r(398) = .36$ ,  $CI [0.21, 0.44]$ ,  $p < 0.01$ ) et une amélioration du bien-être suite à l'intervention (*Wilcoxon signed-rank*  $z = 3.8$ ,  $p < 0.0001$ ). Ceci était le cas en présence et en absence de trouble mental actuel ou passé (e.g., dépression, anxiété, dépendance).

La santé mentale et le bien-être individuel influencent la structure et la fonction du cerveau tout au long de la vie, ce qui à son tour affecte les niveaux de bien-être. Cependant, notre compréhension des dynamiques entre le bien-être et la fonction cérébrale est encore incomplète à ce jour (e.g., Dolcos, Moore and Katsumi, 2018). Le cerveau humain est un système complexe. Malgré l'apparence de stabilité sur de longues périodes, le cerveau est dans un état de changement perpétuel (i.e., plasticité cérébrale) et présente à la fois une activité spontanée (i.e., il génère sa propre activité interne) et ouverte (i.e., il échange de l'information avec le monde extérieur et se

calibre sur le contexte spatio-temporel; Buzsaki, 2006). Une difficulté dans l'étude de la fonction cérébrale est qu'elle est organisée à plusieurs échelles spatiales et temporelles et qu'elle présente des dynamiques à la fois linéaires (e.g., processus *bottom-up* et *top-down*) et non-linéaires (e.g., boucles inhibitrices/excitatrices *feedback/feedforward*; Buzsaki, 2006; Nunez and Srinivasan, 2006). L'observation isolée d'un seul neurone, d'un circuit local ou d'une région corticale ignore le fait que chaque niveau est un système complexe local intégré d'un système complexe global (Buzsaki, 2006).

Les méthodes telles que l'EEG intracrânien sont nécessaires pour mieux comprendre les mécanismes électrophysiologiques complexes se produisant au niveau du neurone ou du circuit local. Les technologies de neuroimagerie non-invasives telles que l'imagerie par résonance magnétique fonctionnelle (IRMf), la magnétoencéphalographie (MEG), ou la tomographie par émission de positrons (TEP) offrent chacune des avantages et différents types d'informations sur l'activité et les fonctions cérébrales. Cependant, ces technologies sont extrêmement coûteuses et nécessitent du personnel et de la maintenance ainsi que l'immobilisation des participants, facteurs qui limitent fortement leurs applications. L'électroencéphalographie (EEG) mesure les champs électriques moyens à la surface du scalp - générés par des courants postsynaptiques de populations synchrones de neurones - qui contiennent des informations multidimensionnelles utiles (i.e., espace, temps, fréquence, temps-fréquence). L'EEG est plus abordable financièrement, requiert très peu de maintenance, moins d'expertise pour l'acquisition des données en milieu clinique, et offre plus de mobilité aux participants. Bien que la résolution spatiale de l'EEG soit faible (surtout pour les sources profondes), la résolution temporelle est très élevée, procurant de l'information temporelle cruciale à l'étude des étapes de traitement rapide et l'activité oscillatoire du cerveau (Luck, 2014). Le signal EEG est utile pour comprendre les processus cérébraux locaux et globaux associés à des états neuropsychologiques complexes tels que la cognition, l'émotion et le bien-être.

L'équipement EEG scientifique de haute qualité reste coûteux (généralement entre 20 000 et 100 000 €), le temps de préparation et d'acquisition des données est relativement long (plusieurs heures pour la plupart des expériences), et la mobilité des participants est limitée par les câbles des électrodes. Ces contraintes impactent les populations qui peuvent être étudiées, la conception du paradigme expérimental, et les applications à long terme visant à étudier le cerveau en milieu plus écologique. En conséquence, la plupart des études EEG sont menées sur de petits



échantillons peu représentatifs de la population générale et inadéquats pour évaluer les différences interindividuelles ou examiner les interactions entre plusieurs variables (e.g., les changements EEG associés à l'âge ou au genre). En conséquence, une grande partie des études en neuroscience a une puissance statistique faible (~8-31%), menant à la surestimation de la taille de l'effet (avec peu de chance qu'un résultat significatif reflète un effet réel), et une faible reproductibilité des résultats (Button, 2013).

Le progrès technologique des dernières décennies a conduit au développement de technologies EEG portables légères et économiques qui adressent ces problèmes en offrant des temps de préparation réduits et une mobilité augmentée pour les participants (e.g., Badcock *et al.*, 2015; Krigolson *et al.*, 2017). Ces systèmes portables facilitent donc la collecte de données EEG sur des populations nombreuses et diversifiées en augmentant l'accès à des populations difficiles à étudier avec les systèmes conventionnels comme les enfants, les personnes âgées et les patients (e.g., Hashemi *et al.*, 2016). Ces grandes bases de données peuvent être analysées à l'aide de méthodes statistiques robustes (e.g., Pernet *et al.*, 2011; Pernet, Wilcox and Rousselet, 2013) ou d'algorithmes de *machine learning* (e.g., Marcus *et al.*, 2011; Golmohammadi *et al.*, 2019) facilitant l'identification de médiateurs susceptibles d'aider chaque individu à améliorer son bien-être ou la détection d'un trouble mental avant que les symptômes ne deviennent graves et difficiles à traiter (e.g., Dea *et al.*, 2019; Gemein *et al.*, 2020).

De plus, avec leur mobilité accrue et les innovations récentes du traitement du signal (i.e., extraction des artefacts tels que les mouvements des yeux ou de la tête, des tensions musculaires du visage et du cou, des pertes de contact des électrodes, etc.), ces technologies permettent l'étude du cerveau et du comportement dans des contextes plus écologiques (e.g., Bjork *et al.*, 2004; Debener *et al.*, 2012; Bozkurt and Coskun, 2014; Hu *et al.*, 2015; Jebelli, Hwang and Lee, 2017; Neale *et al.*, 2017). A long terme, ces systèmes portables permettront l'étude du cerveau en monde réel (e.g., détection de somnolence au volant avant l'occurrence d'un accident), l'utilisation d'interfaces cerveau-machine non-invasives (e.g., contrôle de bras robotiques ou systèmes de communications/transportation pour patients paralysés ou handicapés qui fonctionnent seulement avec électrodes intracérébrales actuellement), ou de thérapies cognitives et comportementales de type *neurofeedback* (e.g., Askamp and van Putten, 2014; Miralles *et al.*, 2015; Wolpaw *et al.*, 2018).

Cependant, malgré tous ces points positifs, ces applications présentent des limites significatives incluant la méthode de référencement, une résolution spatiale faible (peu d'électrodes), les positions des électrodes sur la tête, la résolution du signal, et l'augmentation des artefacts contaminant le signal suite à la plus grande mobilité des participants. Ainsi, le deuxième objectif de ce projet était de tester si un système EEG portable à bas coût et de faible densité (4 électrodes) pouvait mesurer des caractéristiques neuronales pertinentes et fiables pour l'étude du bien-être.

Les potentiels évoqués (*event-related potentials* ; *ERP* ; *i.e.*, domaine temporel) sont surtout utiles pour répondre aux questions sur les processus neuronaux de traitement d'un stimulus artificiel et se concentrent sur des signaux spécifiques qui doivent être faciles à isoler (e.g., P300 ; Luck, 2014). Les bandes de fréquences et les oscillations cérébrales (*i.e.*, domaine fréquentiel ou spectre de puissance) mesurées au « repos » ou durant des tâches sont fonctionnellement associées aux processus cognitifs (activité spontanée). Les oscillations alpha (8-13 Hz) présentent des propriétés fonctionnelles clés nécessaires aux processus cognitifs et attentionnels de base tels que l'inhibition, la synchronisation neuronale, ou l'allocation de ressources corticales vers les régions impliquées dans la tâche (Laufs *et al.*, 2003, 2006; Oakes, 2004; Klimesch, Sauseng and Hanslmayr, 2007; Mathewson *et al.*, 2011; Scheeringa *et al.*, 2012). De plus, elles présentent des propriétés de cohérence globales (*i.e.*, synchronisation de phase) et peuvent être mesurées sur tous les sites d'enregistrement (Nunez, Wingeier and Silberstein, 2001; Nunez and Srinivasan, 2006). Les oscillations alpha (et leurs caractéristiques) sont donc particulièrement intéressantes pour cette ligne de recherche.

L'asymétrie alpha frontale (AAF ; aussi appelée l'asymétrie EEG) fait référence à la différence interhémisphérique relative en puissance spectrale alpha entre les régions frontales droite et gauche. L'AAF a été historiquement utilisée comme index neurophysiologique pour étudier les processus cognitifs, émotionnels et attentionnels des participants, ainsi que la neuropathologie et la santé mentale (Davidson, 1998, 1998; Coan and Allen, 2003, 2004; Harmon-Jones, Gable and Peterson, 2010; Allen and Reznik, 2015). Parce que les oscillations alpha sont connues pour inhiber fonctionnellement l'activité corticale régionale (Laufs *et al.*, 2003, 2006; Mathewson *et al.*, 2011; Oakes, 2004; Scheeringa *et al.*, 2012), une augmentation en puissance alpha dans une région est généralement associée à une réduction de l'activité corticale dans la même région (ou une diminution de l'allocation des ressources pour cette région). Ainsi, une puissance alpha relativement plus grande dans la région frontale droite que dans la région frontale gauche est

associée à une activité corticale relativement supérieure à gauche qu'à droite (corrélation inverse). Une plus grande activation frontale gauche par rapport à celle de droite est liée aux processus de motivation d'approche et des émotions à valence positive (comportements d'addiction ou risques extrêmes), et vice-versa pour l'asymétrie inverse (i.e., dépression, anxiété, apathie, isolation). L'AAF peut être examinée à la fois en réponse à un stimulus (i.e., ERP) ou en tant que trait au repos (i.e., EEG continu, spontané). Le trait AAF est mieux adapté pour évaluer l'état de santé mentale général et prédire la santé mentale future (Allen, Coan and Nazarian, 2004; Hagemann *et al.*, 2005; Allen and Reznik, 2015).

L'AAF est soupçonnée de refléter les processus neuronaux des systèmes de contrôle exécutif du réseau frontopariétal (Grimshaw and Carmel, 2014), qui comprend des zones temporopariétales (TP; Vossel, Geng and Fink, 2013). De plus, différents types d'anxiété sont associés à une asymétrie alpha dans les régions frontales et TP (Heller *et al.*, 1997; Engels *et al.*, 2007; Mathersul *et al.*, 2008; Müller *et al.*, 2015). D'autres publications suggèrent que l'asymétrie frontale reflète le traitement affectif tandis que l'asymétrie postérieure reflète les exigences cognitives d'une tâche et que l'asymétrie peut aller dans des directions opposées entre ces deux régions (Davidson, 1998). Nous faisons donc l'hypothèse que l'asymétrie alpha dans les régions frontales et TP représente un marqueur potentiel du bien-être, en capturant les processus neuronaux de réponse et de régulation émotionnelle participant au bien-être (motivation d'approche et d'évitement et les processus cognitifs sous-jacents). Cette mesure est particulièrement prometteuse puisque les oscillations alpha peuvent être mesurées sur tous les sites du scalp (pratique pour les systèmes EEG à faible densité) et impliquent des traitements du signal très simples et rapides (i.e., spectre de puissance), et serait donc facilement utilisable en milieu clinique.

Bien que l'ensemble de la littérature sur l'asymétrie EEG soit robuste, des non-répliques et des résultats contradictoires dus à des raisons méthodologiques ont été soulignés (méthode de référence, sélection des électrodes d'intérêt, techniques de traitement du signal, méthodes statistiques, petits échantillons, etc.). L'impact des différences interindividuelles en activité alpha a été particulièrement mis en évidence. Une grande partie de la population présente des oscillations alpha en dehors de la bande de fréquence traditionnelle (e.g., 7 ou 14 Hz). En outre, différentes associations ont été observées entre les fréquences inférieures (8-10.5 Hz) et supérieures (11-13 Hz) de la bande alpha, suggérant différentes sources ou processus sous-jacents contenus dans la même bande de fréquence (Nunez and Srinivasan, 2006).

La fréquence alpha individuelle (FAI) fait référence à la fréquence alpha dominante au sein de la bande alpha. La FAI peut être estimée pour chaque individu en utilisant la fréquence alpha de pic (FAP ; fréquence dans la bande alpha avec la puissance maximale) ou le centre de gravité alpha (CGA ; l'ensemble de la distribution spectrale est prise en compte et les limites inférieure et supérieure de la bande sont estimées individuellement pour chaque individu). Le CGA traite mieux les distributions spectrales alpha ambiguës qui apparaissent naturellement chez certains individus et protège donc mieux contre des différences interindividuelles (Corcoran *et al.*, 2017). Chez l'adulte, une FAI inférieure à 8 Hz est considérée comme anormale (sauf chez le sujet âgé), parfois même associée à une diminution de l'excitation corticale (Portnova *et al.*, 2020) ou à une lésion cérébrale traumatique (Angelakis *et al.*, 2004; Angelakis, Lubar and Stathopoulou, 2004). Une FAI élevée (plus proche de 13 Hz) est associée à des performances cognitives plus élevées (Rathee *et al.*, 2020).

Nous présentons donc ici l'hypothèse que la FAI pourrait représenter un marqueur robuste de bien-être, en reflétant des processus cognitifs impliqués dans le bien-être (e.g., prise de décision, sélection d'un but, inhibition des distractions lors de l'exécution d'une tâche, régulation des émotions). Nous faisons également l'hypothèse que le calcul de l'asymétrie alpha sur la FAI serait robuste aux différences interindividuelles et représenterait donc une estimation plus fiable que l'asymétrie traditionnelle (i.e., bande alpha moyenne).

L'asymétrie alpha et la FAI pourraient donc être bien adaptées pour mesurer et prédire le bien-être en milieu clinique (e.g., mesure de patients à distance ou dans le confort de leur maison, prédiction de réponse aux antidépresseurs, etc.). De plus, ces deux mesures sont relativement simples à interpréter pour un clinicien sans connaissance EEG approfondie.

Ainsi, la deuxième étude de ce projet de thèse a testé la faisabilité de la collecte de données EEG (en moins de 5 minutes) à l'aide d'un appareil EEG portable à bas coût, dans le but d'estimer des mesures spectrales pertinentes pour l'étude du bien-être (asymétrie alpha et FAI). Le MUSE (InterAxon Inc., au prix de ~177 €) possède deux canaux EEG actifs secs frontaux et deux pour la région temporopariétale (TP). Il a été validé pour le domaine temporel (i.e., ERP ; Krigolson *et al.*, 2017) et utilisé dans de nombreuses études récentes (Hashemi *et al.*, 2016; Krigolson, Williams and Colino, 2017; Papakostas *et al.*, 2017; Amores *et al.*, 2018; Cochrane *et al.*, 2018; Arsalan *et al.*, 2019; Asif, Majid and Anwar, 2019; Qu *et al.*, 2020; Herman, Ciechanowski and

Przegalińska, 2021; Hunkin, King and Zajac, 2021; Krigolson et al., 2021). Cependant, à notre connaissance, il n'a pas été validé pour l'analyse EEG dans le domaine fréquentiel.

Bien que plusieurs publications récentes ont utilisé des systèmes portables à faible coût pour l'étude de l'asymétrie EEG, elles n'ont pas évalué la validité du signal (Peng, Majoe and Kaegi-Trachsel, 2011; Hu *et al.*, 2015; Hashemi *et al.*, 2016; Jebelli, Hwang and Lee, 2017; Wu *et al.*, 2017; Zhao *et al.*, 2017; Hwang *et al.*, 2018; Jebelli *et al.*, 2018; Umar Saeed *et al.*, 2018; Cao *et al.*, 2019; Arpaia *et al.*, 2020; Park, Han and Im, 2020; Saeed *et al.*, 2020; Apicella *et al.*, 2021). Or, il s'agit d'un élément essentiel car une mauvaise estimation du spectre de puissance peut se produire en raison du montage ou de la méthode de référencement utilisés (Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017). Le MUSE semble bien adapté à ces mesures car elles sont généralement mesurées sur les régions frontales et postérieures (bilatéralement). La référence par défaut de MUSE est l'électrode Fpz, située entre les deux électrodes frontales, ce qui est robuste pour enregistrer le signal et réduire le bruit, mais potentiellement problématique pour les mesures d'asymétrie frontale.

Ainsi, nous avons comparé les données spectrales du MUSE à celles obtenues avec un système BIOSEMI Active Two à 64 canaux (pointe de la technologie utilisant du gel électroconducteur pour améliorer l'impédance du signal entre la peau et les électrodes). Les résultats ont montré que les canaux frontaux du MUSE devaient être re-référencés aux canaux temporo-pariétaux (TP) pour discriminer la puissance alpha entre les conditions yeux fermés/ouverts (*Yuen t-test et 95% high-density intervals; N = 37*). Les canaux TP n'ont pas nécessité de re-référencement. En utilisant la condition yeux fermés uniquement pour les analyses ultérieures, nous avons constaté que la densité spectrale de puissance était fortement corrélée (corrélations robustes de Spearman) entre les deux systèmes dans les bandes de fréquences delta (1-3 Hz), thêta (3-7 Hz), alpha (8-13 Hz), et bêta (14-30 Hz), et plus faiblement dans la fréquence gamma (31-100 Hz). L'asymétrie alpha et la FAI étaient significativement corrélées (sauf lorsque l'asymétrie était calculée sur la FAI au lieu de la bande alpha moyenne). Cette étude (Cannard *et al.*, 2021) a montré que le MUSE pourrait être utilisé pour enregistrer facilement, rapidement, et de manière fiable ces mesures spectrales.

Dans la troisième étude, nous avons utilisé le MUSE et l'échelle AIOS pour évaluer si le bien-être multidimensionnel était associé à l'asymétrie alpha ou à la FAI sur 353 individus pendant

qu'ils comptaient leurs cycles respiratoires (les yeux fermés pendant 2 minutes). Nous avons validé une méthode automatique de prétraitement des données disponible dans le logiciel EEGLAB (i.e., *artifact subspace reconstruction*) sur 150 fichiers EEG sélectionnés aléatoirement, afin de traiter le reste des données automatiquement. La performance obtenue avec les meilleurs paramètres testés correspondait à 84% de sensibilité (i.e., taux de vrais positifs) and 89% de spécificité (i.e., taux de faux négatifs).

Contrairement aux attentes, le bien-être était associé à une asymétrie alpha dans les zones temporopariétales ( $F(228) = 8.5$ ;  $R^2 = 0.036$ ;  $p < 0.05$ ) mais pas frontales ( $p > 0.05$ ). Un bien-être élevé était lié à une augmentation relative de puissance alpha dans la zone TP gauche par rapport à la droite. De plus, cette asymétrie alpha TP semble modulée par les fréquences plus basses de la bande alpha (8-10.5 Hz) et était associée à l'âge ( $F(216) = 30$ ;  $R^2 = 0.188$ ;  $p < 0.05$ ). L'âge était linéairement et positivement associé aux niveaux de bien-être et à une puissance alpha temporopariétale relativement plus élevée à gauche qu'à droite. Aucune association n'a été observée entre le bien-être et la FAI, ou le genre.

Dans le contexte de la dépression, l'asymétrie frontale pourrait être associée à un risque de dépression associé à la réponse physiologique émotionnelle (même après rémission ; Davidson, 1998; Stewart *et al.*, 2010), tandis que l'asymétrie TP refléterait les fonctions exécutives impliquées dans la régulation émotionnelle et l'inhibition de ruminations mentales à valence émotionnelle (Stewart *et al.*, 2010). Étant donné que l'asymétrie TP peut être prédictive de la réponse aux antidépresseurs (Bruder *et al.*, 2001, 2008), les antidépresseurs pourraient affecter ces processus cognitifs plus que les processus affectifs. Les processus TP pourraient refléter des changements plus plastiques des processus cognitifs associés à la parole intérieure, aux ruminations et à l'attention (trait à plus court terme). Par conséquent, l'asymétrie alpha frontale pourrait être un meilleur marqueur EEG pour prédire le risque de dépression à long terme, tandis que l'asymétrie alpha temporopariétale (postérieure) pourrait être mieux adaptée aux applications thérapeutiques (e.g., *neurofeedback* ou neuromodulation en accompagnement au traitement).

Des études de localisation de source et EEG-fMRI simultané ont montré que l'asymétrie alpha frontale reflétait les processus de contrôle exécutif du système dorsal du réseau frontopariétal (Grimshaw *and* Carmel, 2014). Ce système, comprenant le sulcus intrapariétal et les champs visuels frontaux, module l'allocation *top-down* de ressources attentionnelles pour la planification

des saccades, l'orientation spatiale et la mémoire de travail visuelle (Vossel *et al.*, 2013). Cependant, le système ventral, comprenant la jonction temporopariétale et le cortex frontal ventral, est impliqué dans la détection de stimuli non-attendus (non-prédits) et entraîne le transfert d'attention nécessaire à leur traitement (Vossel *et al.*, 2013). Ce système, latéralisé à l'hémisphère droit, montre une activité asymétrique durant la réorientation attentionnelle, le traitement de stimuli déviant rare, et la réponse à des cibles valides vs. invalides (Corbetta and Shulman, 2002; Corbetta, Patel and Shulman, 2008; Doricchi *et al.*, 2010). La jonction temporopariétale a également une fonction de filtrage de distracteurs non-importants durant des états d'attention soutenue, et de modulation d'activité neurale entre différents réseaux. Cette structure est également impliquée dans les processus de cognition sociale et de théorie de l'esprit (Vossel *et al.*, 2013).

Bien que ces interprétations soient conformes à la littérature, elles sont basées sur l'hypothèse que l'EEG de repos reflète la variable de trait (c'est-à-dire les processus et l'activité cérébrale à long terme associés à des traits tels que l'anatomie du cerveau, la connectivité, l'âge, le genre, les traits de personnalité, etc.). Il a été suggéré que, pendant le repos, 60% de l'activité mesurée est influencée par la variable trait et 40% est influencée par la variable d'état (Hagemann *et al.*, 2002). Les segments EEG de cette étude étant très courts, nos résultats reflètent potentiellement la variable d'état de manière dominante (i.e., tâche expérimentale). Cependant, ceci n'expliquerait pas la corrélation avec les niveaux de bien-être et d'âge.

Notre tâche expérimentale consistait à focaliser l'attention sur la respiration, détecter le vagabondage de l'esprit (i.e., distractions mentales) et à rediriger l'attention sur la respiration. L'asymétrie alpha temporopariétale pourrait refléter les processus attentionnels associés à cette tâche et au système ventral du réseau frontopariétal, tandis que la FAA pourrait mieux refléter l'activité du système dorsal (en particulier dans les études utilisant des stimuli visuels ou une croix de fixation visuelle engageant les systèmes spatiaux et visuomoteurs, et les saccades visuelles). Dans le contexte de l'anxiété, cette hypothèse serait en accord avec les résultats suggérant que l'AAF est associée à l'activation physiologique anxieuse (recrutement des systèmes impliqués dans une forte réponse émotionnelle en cas de stress ou de panique), et l'asymétrie TP est associée à une appréhension anxieuse (inquiétude, ruminations mentales négatives ; Heller *et al.*, 1997; Mathersul *et al.*, 2008). Cette dernière étant corrélée à une augmentation sélective de l'activité pariétale droite chez les participants anxieux uniquement lors

d'une tâche narrative émotionnelle (impliquant la parole intérieure), mais pas au repos (Mathersul *et al.*, 2008).

Ainsi, dans cette étude, nous avons peut-être plus capturé les processus cognitifs qu'émotionnels associés au bien-être, i.e. allocation de l'attention sur la tâche, détection de distractions (ruminations mentales, discours intérieur, vagabondage de l'esprit), régulation de l'émotion, et réallocation de l'attention sur la tâche. Par conséquent, une puissance alpha plus importante dans la zone TP gauche pourrait refléter une plus grande capacité à inhiber ces distractions mentales chez les individus rapportant un bien-être plus élevé, tandis que les individus rapportant un bien-être plus bas seraient plus distraits par leurs pensées négatives et leurs ruminations (anxiété, inquiétude).

La dynamique asymétrique entre ces systèmes frontaux et TP semble aller dans des directions différentes, un phénomène décrit précédemment (e.g., Davidson *et al.*, 1988) et pourrait refléter des processus dynamiques d'inhibition intercorticale distants (entre hémisphères et entre régions frontales et postérieures) qui devraient être étudiés plus en détail à l'aide de systèmes à haute densité. Bien que le bien-être n'était pas associé à des asymétries spectrales dans d'autres bandes de fréquences (delta, thêta, bêta), une analyse exploratoire (voir Annexe 2) suggère qu'il existe des interactions asymétriques entre différentes bandes de fréquences au niveau local (pour delta, thêta, alpha et bêta), et que seulement l'asymétrie alpha semble interagir au niveau global (correlation négative entre les régions frontales et temporopariétales). Ce résultat pourrait refléter les propriétés de cohérence locale et globale des oscillations alpha soulignées par Nunez *et al.* (2001), suspectées de refléter la connectivité fonctionnelle ou l'inhibition inter-hémisphérique.

Des études futures sont nécessaires pour éclaircir ces points. Par exemple, si la cross-corrélation de la phase des oscillations est inverse entre ces deux régions, ces mécanismes pourraient refléter les retards de conduction des potentiels d'action dus à la distance entre ces deux régions (Nunez, Wingeier and Silberstein, 2001). Ensuite, il pourrait être possible de déterminer quelle région module ou inhibe l'autre en premier. Une activité asymétrique aberrante pourrait correspondre à une réaction inhibitrice en chaîne qui compromettrait l'équilibre nécessaire à la régulation des émotions et des ruminations mentales. Par exemple, l'inhibition de la région A (e.g., région TP droite) sur la région B (e.g., région frontale gauche) augmente, entraînant une réduction de



l'inhibition de la région B sur la région A, augmentant l'inhibition de la région B de manière extrême. Ce type d'analyse nécessiterait des données EEG à haute densité et des méthodes à haute résolution spatiale pour comprendre avec précision ces dynamiques spatio-temporelles, locales-globales (e.g., *spline Laplacien*, *individual component analysis*, ou *eLORETA*; Makeig *et al.*, 1996; Pascual-Marqui *et al.*, 1999; Nunez, Wingeier and Silberstein, 2001; Delorme and Makeig, 2004).

Parallèlement, nous avons construit des électrodes électrocardiographiques (ECG) qui se connectent au port auxiliaire du MUSE et s'attachent au poignet des participants (électrodes jetables contenant du gel électroconductif). Les signaux EEG et ECG sont ensuite synchronisés temporellement, et les interactions entre l'EEG et l'ECG peuvent être facilement importés dans EEGLAB pour analyse à l'aide du *plugin* développé pour cette étude (voir Annexe 1). Nous avons enregistré EEG et ECG simultanément sur 60 participants au cours de ce projet. Bien que ces données n'aient pas encore été analysées, les interactions entre les signaux simultanés EEG et ECG pourraient être une mesure prometteuse du bien-être, ou augmenter la précision de la détection de bien-être en combinant ces deux mesures physiologiques. La variabilité de la fréquence cardiaque (VFC, i.e. la variation des intervalles de temps entre les battements cardiaques) est déjà utilisée pour prédire les résultats futurs pour la santé (Tsuji *et al.*, 1994; Dekker *et al.*, 1997; Shaffer, McCraty and Zerr, 2014). Une VFC réduite reflète une capacité de régulation réduite du corps à s'adapter et à répondre à des stressseurs, et est en corrélation avec l'apparition de la maladie et la mortalité (Dekker *et al.*, 1997; Beauchaine, 2001). La VFC peut être utilisée pour étudier le bien-être (Geisler 2010), pour supprimer les artefacts ECG des données EEG (Nakamura and Shibasaki, 1987), pour améliorer les performances de détection de pathologies en combinant les informations de l'EEG et de l'ECG (Valderrama *et al.*, 2012), ou pour évaluer les interactions entre le cœur et l'activité cérébrale et la dynamique de ces deux systèmes complexes (e.g., Jurysta *et al.*, 2003; McCraty and Zayas, 2014).

Pour que les applications en milieu naturel soient possibles, des points techniques doivent être résolus, tels que le traitement des artefacts EEG en temps réel et de manière robuste (en particulier les artefacts associés à une mobilité importante de l'utilisateur), l'identification et la prise en compte des différences interindividuelles, et la prise en compte des stimuli environnementaux non-contrôlés. De plus, le confort et l'esthétique de ces technologies doivent encore progresser pour qu'elles soient, un jour, intégrées dans des environnements naturels. Pour

finir, le développement d'une réglementation éthique et protectrice de ces neurotechnologies et de leurs applications à long-terme sont de haute importance.

En résumé, ce projet de thèse a démontré la faisabilité de l'utilisation de mesures rapides et économiques pour étudier les corrélats cérébraux du bien-être dans des échantillons larges et diversifiés. Nos résultats reflètent potentiellement un marqueur quantitatif de processus attentionnels important pour le bien-être et la santé mentale. Bien que des limites subsistent, nous présentons ici des méthodes et des solutions potentielles pour la prévention et le traitement de troubles mentaux à bas coûts et à l'échelle mondiale. Les progrès dans ce domaine aideront à mieux comprendre les mécanismes neuronaux sous-jacents de la cognition et de la régulation des émotions en lien avec le bien-être, et à trouver des marqueurs EEG pertinents.

A long terme, ces avancées faciliteront l'étude EEG dans des environnements de plus en plus écologiques et abordable financièrement (e.g., milieu clinique, maison du patient, etc.). Par conséquent, les applications incluent : 1) le suivi de la santé mentale des patients à distance et en continu (Biondi *et al.*, 2021); 2) le développement d'interfaces cerveau-machines qui permettent aux individus de restaurer ou de récupérer des capacités de mouvement ou de communication (Aflalo *et al.*, 2015; Makin, Moses and Chang, 2020; Willett *et al.*, 2021) ; 3) des protocoles de neurofeedback pouvant aider les individus à entraîner leurs états mentaux et processus cérébraux (Angelakis *et al.*, 2007; Quaedflieg *et al.*, 2016; Brandmeyer & Delorme, 2020a); 4) des études dyadiques (Lachat *et al.*, 2012; Liao *et al.*, 2015; Verdière, Dehais & Roy, 2019; Anaya, Vallorani & Pérez-Edgar, 2021); 5) ou la mise en œuvre de thérapies de neuromodulation (e.g., stimulation transcrânienne électrique à courant continu, stimulation magnétique transcrânienne, stimulation ultrasonore focalisée) pouvant être supervisées à distance tandis que les patients restent dans le confort de leur domicile (Kalu *et al.*, 2012; Sanguinetti *et al.*, 2020; Biondi *et al.*, 2021).



# Table of Contents

Part I .....	1
Chapter 1. Brain organization, dynamics, and mode of operation.....	3
1.1. Dynamic structures and connectivity of the brain.....	3
1.2. Local field potentials (LFP) .....	8
1.3. Cells, circuits, inhibition, and gating underlying brain oscillations .....	11
Chapter 2. Electroencephalography (EEG).....	17
2.1. What is EEG? .....	17
2.2. Why EEG?.....	21
2.3. EEG signals and main types of analyses.....	25
Chapter 3. Wearable EEG.....	31
3.1. EEG technology .....	31
3.2. Low-cost wearable EEG systems .....	35
Chapter 4. Well-being .....	47
4.1. The main dimensions of well-being .....	47
4.2. Stress and well-being.....	49
4.3. Predictors and mediators of well-being .....	51
4.4. Well-being and the brain.....	55
Part II.....	67
Chapter 5. Validating a quick scale to measure multidimensional well-being.....	69
5.1. Introduction.....	69
5.2. Methods .....	75
5.3. Results.....	86
5.4. Discussion .....	91

5.5. Conclusion.....	95
Chapter 6. Validating a low-cost wearable EEG headset for spectral analysis .....	97
6.1. Introduction.....	97
6.2. Methods.....	100
6.2.6. Statistics .....	105
6.3. Results.....	106
6.4. Discussion .....	114
6.5. Conclusion.....	117
Chapter 7. EEG asymmetry and well-being .....	119
7.1. Introduction.....	119
7.2. Methods.....	125
7.3. Results.....	131
7.4. Discussion .....	136
7.5. Conclusion.....	145
Part III.....	147
Chapter 8. Future directions related to the project.....	149
8.1. Experimental design.....	149
8.2. Automated removal of non-brain artifacts .....	150
8.3. Spatial and source distributions of alpha oscillations .....	152
8.4. Theta oscillations and well-being.....	155
8.5. Beta oscillations and well-being.....	156
8.6. Multimodal neuroimaging .....	156
Chapter 9. Future directions for the broader field of wearable EEG .....	159
9.1. Big data and machine learning.....	159
9.2. Brain-computer interfaces (BCI).....	163
9.3. Awareness, self-regulation, and neurofeedback.....	168

9.4. Wearable EEG and “real-world” applications .....	173
9.5. Other applications .....	180
9.6. Other limitations .....	181
General conclusion.....	189
Annexes .....	191
Annex 1: An EEGLAB plugin to import MUSE data.....	193
Annex 2: Asymmetric interactions between frequency bands .....	197
Annex 3: A hierarchical linear modelling of broad-band EEG power and well-being .....	199
References .....	203
Appendix A: List of publications and communications .....	255
Appendix B: Publications in published format .....	259



# Part I





# *Chapter 1. Brain organization, dynamics, and mode of operation*

This chapter introduces how the brain is organized, structured, and its general mode of operation. This chapter provides general context before introducing what electroencephalography (EEG) measures (next chapter).

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“Simple” systems are in balance and hard to perturb. The human brain is a “complex” system, in the sense that the whole (the brain) and its components (e.g., neurons) are both adaptive systems that form hierarchies and interact via non-linear dynamics by amplifying/damping feedback/feedforward loops. Despite the appearance of stability over long periods, the brain is in a state of perpetual change (i.e., entropy and evolution). It is both spontaneous (i.e., it generates its internal activity) and open (i.e, it can exchange information with the external world and calibrate itself to the spatiotemporal context). A fundamental problem in studying the brain derives from the fact that it is organized at multiple spatial and temporal scales. Examining a single neuron, small circuit, or region in isolation ignores the fact that each of these levels is a complex function of its lower-level components and, at the same time, is embedded in a large-scale organization (Buzsaki, 2006).

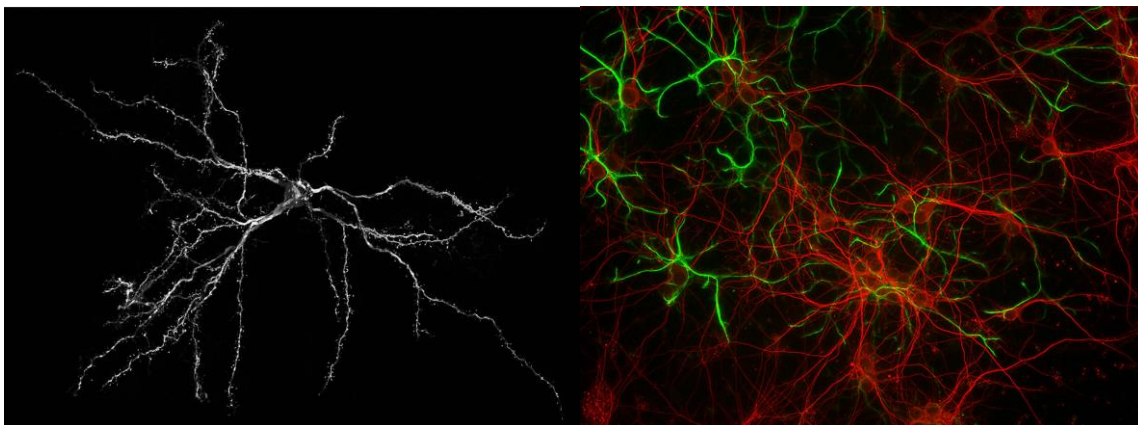
## *1.1. Dynamic structures and connectivity of the brain*

The brain’s structure, function, and connectivity have been studied by generations of brilliant minds (Cajal, 1959; Szentágothai, 1978; Nauta and Feirtag, 1979; Allman, 1999; Llinás, 2003). The human brain is estimated to have between 10 billion and 1 trillion neurons, and to have roughly 200 trillion connections between them in an average skull volume of 1.5 Litre (Williams and Herrup, 1988). It is divided into three primary structures: the brainstem, the cerebellum, and the cerebrum.

The brainstem is made of several substructures directly above the spinal cord that includes the medulla, the pons, and the midbrain, which relay signals between the spinal cord and higher brain centers. The cerebellum, which sits on top and to the back of the brainstem, has long been associated with the fine control of muscle movements (although also plays other roles in cognition).

The cerebrum is the largest part of the brain and is divided into two symmetrical hemispheres. Inner portions are referred to as the subcortical structures and include the thalamus, hypothalamus, hippocampal region, the basal ganglia, the olfactory bulb, and the limbic structures (Shariff, 1953; Lange, 1975; Pakkenberg and Gundersen, 1997). The thalamus, composed of two egg-shaped structures at the top and to the sides of the brainstem, integrates and relays all sensory inputs to the cortex (except for olfactory information). The outer portion is referred to as the cerebral cortex (also called the neocortex in mammals). It is a 2-5 mm thick, folded (gyri) spherical structure containing 15-31 billion neurons (gray matter), composed of five vertical layers of principal cells (e.g, pyramidal neurons; i.e., excitatory) and interneurons (i.e., inhibitory) called the cortical mini- and macro- columns (Rockel, Hiorns and Powell, 1980).

Neurons are “perhaps the most complicated cell type nature has created” (Buzsaki, 2006). The uniqueness of neurons is their ability to pass information to each other over long distances. They are treelike structures with various branching patterns (dendrites) that maximize the receptive surface area for connections from axons (nerve fibers) of other neurons (Figure 1, left).



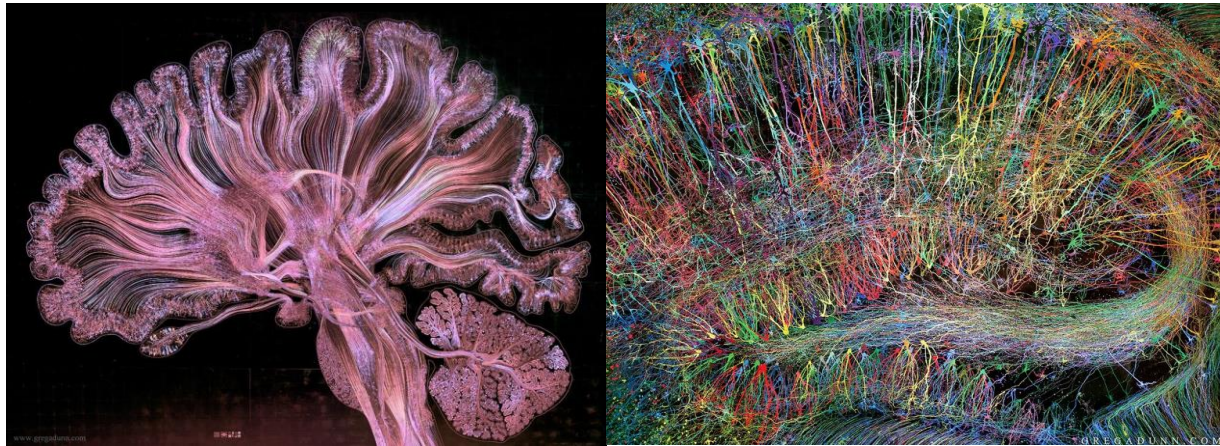
**Figure 1.** *Left:* Dendritic arborization of a neuron imaged with confocal and two-photon microscopy. Source: Bruno and Gastard (2010). *Right:* Cryopreserved slice of mouse cortex containing  $\geq 4$  million cells, illustrating the highly interconnected neurons (red) and astrocytes (green). Source: Lonza (2021).

Each dendrite is covered by numerous spines allowing them to create thousands of receptor sites called postsynaptic receptors. Axons emerge from the cell body (soma) and can reach tens of thousands of nearby and distant neurons, constituting the white matter (see Figure 2; Kalisman, Silberberg and Markram, 2005). The synapse is a thin gap between the membrane of each axon terminal (i.e., “bouton”) and the membrane of the dendrite of the target neuron serves as a chemical link enabling neuronal communication via neurotransmitters (Peters and Palay, 1996). 90% of connections are established between cortical pyramidal neurons which have 5,000-50,000 postsynaptic receiving sites.

While neurons vary in size, the number of connections and density, the general organization of the human cortex is remarkably homogeneous. Circuits and neuronal types that support the same functions and process similar information are strongly interconnected into local cortical modules (also termed clusters, assemblies, or systems) that form together the primary dynamical systems of the brain (e.g., motor, visual, auditory, somatosensory, olfactory). This is because the brain maps out adjacent relations of the environment most efficiently by minimizing the distance that axons must travel to connect the neurons that process the information from adjacent parts of the environment or body (e.g., retinotopic map or the somatosensory “homunculus”; Cherniak, 1995; Nakamura *et al.*, 1998; Weliky *et al.*, 2003; Fiser, Chiu and Weliky, 2004). Cortical modules, therefore, constitute local communication of a population of neurons capable of acting briefly as a single, cooperative structure, and constitute the most robust program in the cortex (Buzsáki, 2006).

However, no brain function could emerge from only local connectivity because communication between two distant modules (e.g., startle reflex requiring the quick synchrony of distant systems to adapt to a danger) would take too much time (a long “synaptic path length”; i.e., many synaptic contacts and interruptions). It is estimated that any neuron that can communicate with any other distant neuron within a second has as few as 6 synaptic contacts (even at the opposite side of the brain; Buzsáki, 2006). This maximal synaptic path length has been kept constant across animal species, despite the differences in brain sizes. It is suspected that this is the consequence of the spatiotemporal constraints of our environment that require the brain to integrate information from different systems and react in a finite time window despite the size of the brain, to survive (Buzsáki, 2006). The human brain has maintained a constant synaptic path despite the size increase during evolution by folding of the cortical surface (i.e., gyri and sulci, facilitating

communication between interconnected modules; see Figure 2, left; Kennedy *et al.*, 1998), by increasing dendritic density (Swadlow, 2000), and by increasing the number of intermediate- and long- range connections (Figure 2, left and right). The traveling velocity and pulse frequency of action potentials are accelerated by the myelination (up to 50 m/s compared to 0.3 m/s for thinner unmyelinated fibers). Furthermore, myelin also protects axons from conduction failure and reduces the cross-talk from neighboring axons. White matter occupies only 6% of cortical volume in small insectivores and ~40% in humans (Tomasch, 1954; Swadlow, 2000).



*Figure 2. Artistic representations of diffusion tensor imaging (DTI; Alexander et al., 2007) of cortical folding (i.e., gyri, left, external layers) and local-global connections (left and right). Source: Adunn (2021).*

However, transporting electrical pulses over long distances is metabolically expensive and prone to conduction delays: local synaptic delays (due to capacitive-resistive properties of single neurons) are typically in the 1-10 ms range, and global delays (due to action potential propagation along axons, even with myelin) range from ~10-30 ms between the most remote cortical regions. Furthermore, long-distance connections require more metabolic demand, glial maintenance, and larger vascular structures.

Hence, long-range connections represent a small fraction of neuronal connectivity that are limited to connecting primary sensory and action areas that require short time-scale synchrony. Most of the brain is organized in a hierarchy of multiple parallel circuits with overlapping short, intermediate, and long chains of neurons, with the oldest circuits (in evolution terms) at the bottom, and the most recent ones on top. These parallel layers are organized into highly interconnected scale-free networks (the neighbors of any given node are likely to be neighbors of each other) that display fractal patterns (a structure that looks the same at different scales;

Buzsáki, 2006). Thus, most nodes can be reached from every other node by short synaptic path lengths (i.e., a few synaptic contacts and limiting the number of long-range connections), reducing the local synaptic and global axonal conduction delays (Van Essen and Maunsell, 1983; Van Essen, Anderson and Felleman, 1992). The brain's arrangement therefore minimizes the volume of the axons required for interconnecting different areas (Stevens and Zador, 1998). Hence, despite the specialization of cortical systems, no precise physical boundaries exist to delineate them, and brain function results from the interaction of individual neurons at the local level and neuronal assemblies at the global level (Harth, 1993; Freeman, 2000; Nunez and Srinivasan, 2006).

According to the “neural Darwinism” view (Edelman, 1993; Ringo *et al.*, 1994; Sporns, 2013), this axon conduction delay limitation is what lead to the functional specialization or segregation of the brain into cortical systems within and between hemispheres (e.g., language is specialized to the left hemisphere; Perrone-Bertolotti *et al.*, 2014; Loevenbruck *et al.*, 2018).

Some interactions are more important than others, and the specific and unique patterns of input/output connectivity are the key to this functional segregation. While the precise connectivity patterns are still unknown, it is generally believed that environmental inputs ascend (feedforward) to higher areas (determined by layer 4), and connections that end in cortical layers other than layer 4 are considered to be descending (feedback).

Like other cells, neurons at rest need to maintain a voltage difference of between -55 and -80 millivolts (mV; with an average around -70 mV) by keeping a high concentration of potassium (K<sup>+</sup>) and chloride (Cl<sup>-</sup>) ions inside the cell, and sodium (Na<sup>+</sup>) and calcium (Ca<sup>2+</sup>) ions outside. However, neurons do not have reserves of nutrients. The brain is supplied by the highest density of blood vessels in the body and uses 20% of the body's blood-supplied oxygen and energy nutrients at every instant, even during sleep (Jessen and Mirsky, 1980; Chandra *et al.*, 2017). Because the brain quickly suffers damage from any disruption in blood supply (e.g., stroke), the cerebral circulatory system is autoregulated by the endothelial cells that constitute the blood-brain barrier. The blood-brain barrier also maintains the ion balance in the extracellular space required to keep neuronal membrane potentials in balance at rest, while restricting the passage of pathogens (Daneman and Prat, 2015).

Glial cells are also crucial for brain function and survival (Bartheld, Bahney and Herculano-Houzel, 2016; von Bartheld, 2018). Astrocytes (Figure 1, right) support the blood-brain barrier and the scarring (gliosis) of the brain during infections or injury (Freeman and Rowitch, 2013). Oligodendrocytes insulate the neurons' axons with myelination, which increases the conduction speed of action potentials (see section 1.3.; Baumann and Pham-Dinh, 2001; Bean, 2007). Damaged myelin results in degenerative disorders with serious disabilities (e.g., multiple sclerosis; Keegan *et al.*, 2002). Ependymal cells line the ventricular system to support the production of cerebrospinal fluid (CSF) and potentially neuroregeneration (Carlén *et al.*, 2009). Finally, the microglia maintains homeostasis and constitutes the main form of active immune defense of the central nervous system (Ginhoux *et al.*, 2013). Glial cells do not produce electrical potentials like neurons but they can propagate calcium ( $\text{Ca}^{2+}$ ) over long distances and release transmitters (called gliotransmitters) to modulate important brain functions (Fiacco, Agulhon and McCarthy, 2009). They also modulate synaptic transmission and couple multiple neurons and synapses into functional assemblies (Fields *et al.*, 2014). The glia supports the glymphatic system during sleep which eliminates neurotoxic waste that accumulates in the extracellular space (waste clearance), and might be responsible for major brain disorders when dysfunctional (e.g., Alzheimer's disease; Tsai *et al.*, 2021).

## 1.2. Local field potentials (LFP)

Most principal cells of the cortex (neurons) release excitatory neurotransmitters (i.e., glutamate). When glutamate released by the presynaptic neuron fixates on the postsynaptic receptors of the targeted neuron, it triggers a linear flow of  $\text{Na}^+$  ions entering through the postsynaptic membrane, which progressively decreases the voltage difference between the inside and outside of the postsynaptic membrane. When the neuron reaches a critical voltage difference, an avalanche of additional  $\text{Na}^+$  enters the membrane, leading to a sudden positive charge of 20 mV. This fast depolarization corresponds to the rising phase of the action potential (also called “spike”; Figure 3, left; Johnston and Wu, 1994). Because neurons can fire off hundreds of spikes per second, they need to relax and reset to avoid severe epileptic seizures if overstimulated. Once this peak voltage is reached, the voltage-dependent  $\text{Na}^+$  channels are inactivated, and the voltage-dependant  $\text{K}^+$  ion-channels are activated to quickly repolarize the cell by rapidly pumping  $\text{K}^+$

ions from the intracellular space and releasing it in the extracellular space (Johansson *et al.*, 2019). The falling phase of the action potential (Figure 3, left) corresponds to this fast repolarization. The whole process (depolarization-repolarization) takes about 1 ms and is the maximum firing rate limit of the neuron. Thus, neurons can transmit several hundred spikes per second at a maximum. The transfer of neuronal information via traveling action potentials is therefore an important limiting factor in the speed performance of neuronal networks.

The transfer of ions through the membrane channels generates electric potentials: excitatory postsynaptic potentials (EPSP, facilitating depolarization) or inhibitory postsynaptic potentials (IPSPs, from interneurons releasing GABA neurotransmitters that hyperpolarize the postsynaptic neuron). When the postsynaptic currents traverse the membrane from the extracellular space into the neuron, they are called “current sinks”, whereas when they go from the cell into the extracellular space, they are called “current sources” (Nunez and Srinivasan, 2006).

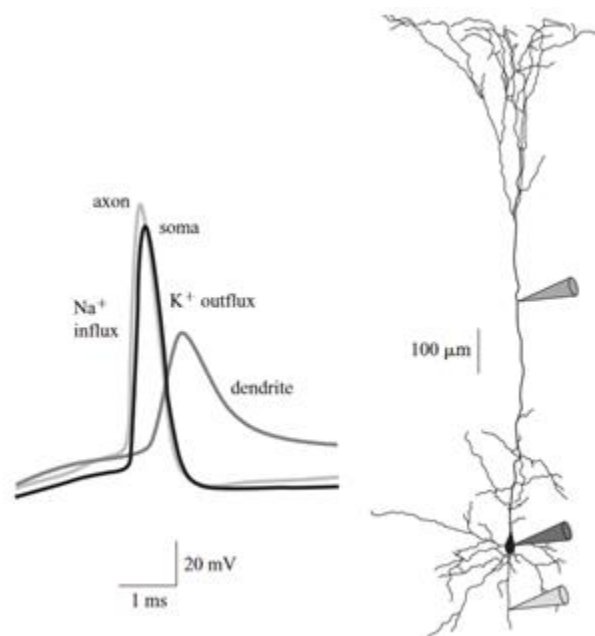


Figure 3. The action potential (or “spike”, **left**), triggered by ion exchanges across the neuron membrane ( $\text{Na}^+$  increase and  $\text{K}^+$  decrease), propagating from the dendrite to the axon (**right**). Recorded from the axon, soma, and dendrite in a layer 5 pyramidal neuron by patch pipettes. Source: Hausse (2000).

Excitatory currents (involving  $\text{Na}^+$  or  $\text{Ca}^{2+}$  ions) flow inwardly during depolarisation (from the activated excitatory postsynaptic site to the soma and axon of the neuron), and outwardly during



repolarization (away from the cell as ions return to the extracellular space). EPSPs, therefore, generate a negative voltage at the active sinks of the synapse due to the influx of Na<sup>+</sup> or Ca<sup>2+</sup> ions and positive current in the extracellular space at the passive source. Inhibitory loop currents (involving Cl<sup>-</sup> or K<sup>+</sup> ions) flow in the opposite direction. On the other hand, IPSPs generate positive current at the extracellular active source due to influx of Cl<sup>-</sup> or efflux of K<sup>+</sup> ions, and negative extracellular current at the passive sink (Nunez, Wingeier and Silberstein, 2001).

The extracellular space has a low resistance which acts as a passive low-pass filter (i.e., “shunting effect”) by attenuating more high-frequency events (action potentials) than slowly oscillating voltages (postsynaptic potentials). Thus, postsynaptic potentials have a smaller amplitude than action potentials but they propagate much farther in the extracellular space. Furthermore, they last longer (tens of ms) and have therefore a higher chance to overlap in time and synchronize compared to brief spikes. Finally, they occur much more than spikes because only a minority of neurons reach the depolarization threshold at any instant in time. As a consequence, action potentials barely contribute to the local field potential (LFP). Source currents from slow EPSPs and IPSPs of neighboring synchronized neurons flow through the extracellular space and sum to constitute the LFP (i.e., extracellular potentials; Buzsáki, 2006). It is important to note, however, that some active nonsynaptic properties of the neurons (e.g., subthreshold oscillations, afterpotentials, Ca<sup>2+</sup> spikes, and other intrinsic events) can also produce relatively long-lasting transmembrane events that can contribute to the LFP (Llinás, 1988).

In sum, LFPs (measured by intracranial macroelectrodes;) are the summed activity of neighboring neurons, propagating in the extracellular space (reflecting mostly the EPSPs and IPSPs). LFPs measured in this manner reflect the synaptic activity of tens to thousands of nearby neurons. Thus, LFPs reflect a weighted average of input signals emanating from the neurons in the area of the microelectrode. Note that this is only true for macroelectrodes (e.g., clinical SEEG electrodes) but not when they are combined with microwires that can record action potentials (i.e., spike-sorting studies; e.g., Elahian *et al.*, 2018).

When the electrode size increases, more and more neurons contribute to the measured electric fields, leading to a decrease in this LFP-spikes relationship (because of the larger number of neurons and combination of different electric fields; Buzsáki, 2006).

### *1.3. Cells, circuits, inhibition, and gating underlying brain oscillations*

No brain function would be possible with only excitatory connections as any input would trigger a chain reaction that would recruit all the other neurons and lead to population bursts and epileptic seizures. Brain circuits are characterized by phase-synchronized activity (i.e., coherence) and functional connectivity of populations of neurons that engage in common processes to select local inputs while integrating diverse external information streams (Siegel, Donner and Engel, 2012; Womelsdorf *et al.*, 2014). This rhythmic, resonant activity (i.e., oscillations) is based on precise neuronal structures (cellular, synaptic, local connectivity) and computational functions that give rise to specific activation signatures of operation (modulation of neuronal firing, spike output synchronization). The frequency of these signatures is therefore defined by the timescales and dynamics of cell-intrinsic conductances or synaptic mechanisms. At the core of these circuit dynamics are feedforward and feedback inhibition structures that operate (non-randomly) at specific time scales, leading to rhythmic activation patterns (Wang, 2010).

Feedforward inhibition (FFI) corresponds to the inhibition of the upstream postsynaptic neuron (Buzsaki and Eidelberg, 1981, 1982). Their activity strongly depends on the exact details of the connections, making the firing patterns of chains of inhibitory neurons hard to predict. For example, if an inhibitory neuron at the beginning of the chain is activated, it will prevent the target neuron from being active. If that neuron normally excites another inhibitory neuron, that inhibitory neuron will not inhibit the next interneuron, which will further inhibit the next neuron and so on. A small change in FFI may result in large repercussions for the network (i.e., nonlinearity). FFI provides a temporal filter of the circuits' input (Kepecs and Fishell, 2014) and is one of the most fundamental elements for information transfer in the brain. FFI allows the extraction of population-coded information while filtering out asynchronous inputs. The FFI system implements 3 main systems:

- 1) Frequency-specific filtering and modulation of postsynaptic sensitivity (gain control) through gamma frequencies, implemented by parvalbumin-positive (PV+) interneurons (fast-spiking GABAergic inhibitory cells), providing a fundamental regulation of the balance between excitation/inhibition of pyramidal neuron activity (Ferguson *and* Gao,

2018). This filtering property is tuned by the intrinsic properties (passive and active membrane) of the constituent cells that rhythmically pace the spike outputs (Womelsdorf *et al.*, 2014). Even when PV+ interneurons receive asynchronous inputs, they provide a rhythmic, resonant gamma input (30-80 Hz) to pyramidal neurons in superficial cortical layers (Sohal *et al.*, 2009; Patel and Joshi, 2013). The consequence is a layer-specific synchronized, rhythmic, resonant gamma input that switches pyramidal cells from a linear to multiplicative gain control, which is more robust against variations in input strength than a spike-threshold mechanism.

- 2) A thalamic, cell-specific (intrinsic) alpha (8-13 Hz) system that amplifies the transmission of attended sensory information. Thalamo-cortical projections are thought to originate from “relay-mode” cells that are inhibited by an intrinsic rhythmic system involving thalamic gap junction-coupled high-threshold (HT) bursting neurons (Lőrincz *et al.*, 2009). These thalamic HT cells can elicit excitatory spikes in interneurons in deep cortical layers (L4-6) to cause alpha rhythmic inhibition (Womelsdorf *et al.*, 2014). This thalamic alpha-generating system has been causally linked to electroencephalography (EEG) alpha oscillations measured on the scalp (Hughes *et al.*, 2011). However, this appears contradictory to empirical findings showing reduced local alpha activity when processing attended information (attention) and enhanced local cortical activity when these regions are idling or processing unattended information (see Section 4.4.2.). Furthermore, PV+ (thalamic) cells generate a gamma phase coherence between the thalamus and L4, which is thought to mediate long-range cortico-cortical interactions when processing attended stimuli (Womelsdorf *et al.*, 2014). This cross -layer and -frequency coupling might underly perceptual and working memory performance modulated by alpha-phase (Womelsdorf *et al.*, 2014).
- 3) In the absence of attention, a lack of this excitatory thalamic input causes a release of this inhibitory system (and gamma synchrony) in deep cortical layers (L4-6), generating local alpha-pulsing bursts that then cause a widespread inhibition of the vertical column (through postsynaptic potentials inhibition) to superficial cortical layers (Womelsdorf *et al.*, 2014). This supports why cortical alpha oscillations can easily be entrained by brain stimulation, unlike the thalamically-driven alpha rhythm (Helfrich *et al.*, 2014).

This FFI system, therefore, favors oscillatory inputs to principal cells by imposing a time constant (temporal structure) while excluding distracting asynchronous ones. This system could support “diverse biological functions that require the tuning of distant network modules to a common temporal processing mode” (Womelsdorf *et al.*, 2014).

Feedback inhibition (FBI) occurs when an interneuron’s firing rate increases in response to an increased firing rate from a principal neuron to reduce its output (Buzsáki and Chrobak, 1995). FBI is oscillatory and increases the temporal precision of spike-timing (sub-millisecond precision) by rapidly repolarizing the excitatory neuron, reducing its discharge probability (Pouille and Scanziani, 2001).

According to the dynamic pyramidal-interneuron gamma (PING) system, depolarization of pyramidal cells in superficial layers excite PV+ interneurons which then produce a GABAergic FBI of these pyramidal cells in the gamma frequencies ( $> 40$  Hz; Womelsdorf *et al.*, 2014). The exact frequency depends on the overall level of excitation that determines when and how fast pyramidal cells recover from inhibition to reactivate the interneurons. This inhibition provides reduced temporal variability, leading to an enhanced spike output in the presence of gamma rhythmic modulation even when the input is the same (Womelsdorf *et al.*, 2014). This system, therefore, provides higher probability for a spike and a more precise spike output, and selective routing of information (at the cortical column scale) by predicting which inputs are selected and which local groups of neurons communicate (gating). For example in V4 (visual cortex), the interneurons that are excited by principal cells phase-lock at later phases than them to produce FBI onto them (Vinck *et al.*, 2013). This led to stronger gamma-locking and higher firing rates for cells processing attended information than for cells processing irrelevant stimuli (or not processing the relevant stimulus).

Additionally, a computational function operating in the beta frequency band (15–30 Hz) combines the superficial PING FBI system with an intrinsic bursting-cell circuit in deep layers (cross-layer interaction; Kopell, Whittington and Kramer, 2011). The low-threshold spiking (LTS) cells (a subclass of Martinotti cells) typically implement dendritic inhibition of deep-layer burst neurons. When the superficial excitatory cells recover from the strong excitation associated with this PING FBI system, they excite these LTS cells, which then slows (“reset”) the deep-layer burst frequency (Womelsdorf *et al.*, 2014). The coupling of these two systems (PING + LTS) results

in a  $\sim 15$ -Hz oscillation (i.e., low-beta) that allows different inputs to remain segregated by different populations of pyramidal cells firing at different phases of low-beta oscillations (Womelsdorf *et al.*, 2014). Because the strong superficial-layer excitation from the PING FBI system would impose a selection of inputs, these cells firing at different phases in low-beta convey information from different parallel input streams. It is unclear whether this low-beta system underlies the 15-Hz oscillation measured at the scalp thought to index working memory maintenance, choice behavior, or long-range sensorimotor integration before decision making (Siegel, Donner and Engel, 2012). While PING alone provides selective and competitive gating, this beta system integrates diverse inputs and maintains them in a short-term memory buffer in the spiking activity of principal cells (Womelsdorf *et al.*, 2014).

These dynamic, context-dependent systems amplify or suppress inputs, and gate one specific input over many distinct ones while still integrating them through rhythmic activation. This context-specific gating of information seems to be mainly achieved by dendritic inhibition/disinhibition of pyramidal cells (“dendritic switches”; Lovett-Barron *et al.*, 2012; Palmer, Murayama and Larkum, 2012). For instance, in the hippocampal CA1 field, oriens lacunosum-moleculare (OLM) interneurons directly inhibit distal dendrites from the entorhinal cortex (i.e., sensory inputs) while indirectly disinhibiting proximal pyramidal cells that receive memory-related information from Schaffer collaterals CA3 (Womelsdorf *et al.*, 2014). This system favors the decoding of proximal memory-related inputs over distal sensory ones. OLM interneurons are activated by cholinergic inputs from the fimbria fornix and medial septum, modulate their firing in theta frequencies (3-7 Hz) and may support theta-gamma coupling in the hippocampus (Womelsdorf *et al.*, 2014). In brief, this OLM-cell-dependent and theta-rhythmic gate in the CA1 subfield could provide a dynamic system that parses information from different sources into distinct phases of the theta cycle (Womelsdorf *et al.*, 2014). Thus, this parsing/switching would functionally segregate sensory encoding (via entorhinal cortex) from memory retrieval (via CA3).

Lateral inhibition corresponds to the activation of a principal cell that in turn, excites an interneuron, which then inhibits surrounding excitatory neurons. If, for example, two principal cells sharing a common interneuron are excited by the same input, but the input to principal cell A is slightly stronger (or arrives faster) than the input to principal cell B, neuron A will indirectly inhibit neuron B. The initial difference in the inputs results in a large difference in the output.

This competitive asymmetric phenomenon increases the autonomy of neurons and is responsible for the necessary segregation of cortical systems, and is termed the “winner-take-all” mechanism.

In summary, the inhibitory interneuron system maintains the functional segregation of neighboring principal neurons and their temporal coordination by selectively hyperpolarizing (inhibiting) specific principal excitatory neurons. Hence, these oscillatory inhibitory interneuron systems are thought to be responsible for the balance necessary for cortical modules to function, for their temporal accuracy (Freund, 2003), and are critical for understanding how the EEG signal and oscillations are generated.



## *Chapter 2. Electroencephalography (EEG)*

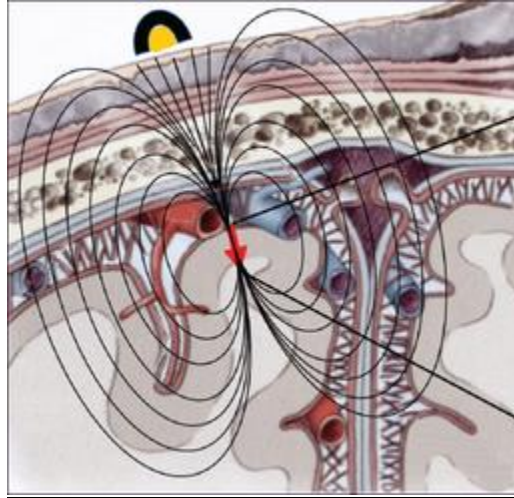
In this chapter, we describe what EEG is, why it is a relevant scientific tool to study cognition or neuropsychology, and the main approaches to analyze EEG data, with an emphasis on alpha oscillations, the signal of interest for this project.

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### *2.1. What is EEG?*

Local field potentials (LFP) and electroencephalography (EEG) are synonymous terms and are usually recorded by small-sized electrodes. However, for historic reasons, EEG typically refers to the “mean-field potentials” recorded at the surface of the scalp that reflect the summation of extracellular postsynaptic neuron potentials within large cortical areas that can propagate through the extracellular space, tissues, and skull (Figure 4). EEG, measuring the fields at the surface of the scalp, is, therefore, a spatially smoother version of the LFP (described in the previous section) resulting from large-scale synchrony of populations of neurons at different sites, and does not capture individual neuronal spiking activity. The measured “mean fields” mainly reflect the average, cooperative actions of interacting cortical neurons (Jirsa and Haken, 1997). Different current sources can produce identical electromagnetic fields on the scalp, and EPSPs and IPSPs can contribute to the scalp EEG with opposite polarity (see Figure 4). But broadly speaking, mean fields reflect the summation of extracellular postsynaptic neuron potentials within large cortical areas (1-6 cm<sup>2</sup>), against their “background” levels (Nunez and Srinivasan, 2006).





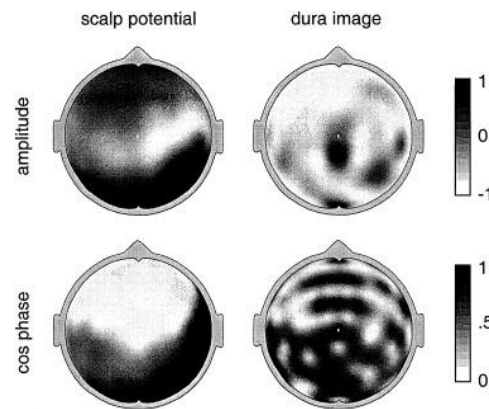
*Figure 4. EEG measures “mean fields” reflecting the summed extracellular postsynaptic potentials generated by transmembrane ion current in pyramidal neurons (cortical layers IV-V). The black ellipsoids represent the volume conduction of the currents between the source (red arrow) and the recording electrode at the surface of the scalp. Source: Beniczky and Schomer (2020).*

The “background synaptic action” refers to the synaptic current sources at the surface of cortical neurons at the millisecond scale, and is more of interest for intracranial EEG aiming to determine the local dynamics within cortical modules, and does not guarantee the observation of scalp surface potentials (Ombao *et al.*, 2016). Large potential differences occurring between deep and superficial layers of the cortex require a certain depth of synaptic action and enough source activity at low spatial frequencies for the sources to be active and synchronized in the centimeter scales (Petsche, Pockberger and Rappelsberger, 1984).

This “volume conduction effect” is the low-pass temporal filtering caused by the low resistivity of neuronal tissues to electrical current flow, the capacitive currents produced by the lipid cell membranes, and the distorting effects of glia, blood vessels, dura, skull, scalp muscles, and skin (see section 1.3.). As a consequence, action potential activity from single neurons (1 ms scale) is mainly absent in scalp activity. The resulting low spatial resolution of scalp EEG is what is referred to as the “inverse problem”, i.e., the difficulty in recovering locations and features of the mean-field sources based on the spatially averaged (and thus spatially distorted) activity that is recorded at the scalp.

The dura imaging method (or surface-Laplacian) is a useful approach that minimizes the volume conduction effects, by spatially filtering field potentials to focus on activity from sources within a few centimeters of the electrodes (see Figure 5; Nunez, Wingeier and Silberstein, 2001). This

spatial filter reduces global contributions relative to local contributions and provides a more accurate estimate of spatial sources of EEG scalp activity by eliminating most of the conduction effects.



*Figure 5. Scalp EEG reflects global distributions of activity (left column), compared to dura-imaging EEG that better captures local activity by filtering out the very low spatial frequencies associated with volume conduction (right column). The upper row corresponds to amplitude signal and the lower row to phase signal, at 10 Hz. Source: Nunez, Wingeier and Silberstein (2001).*

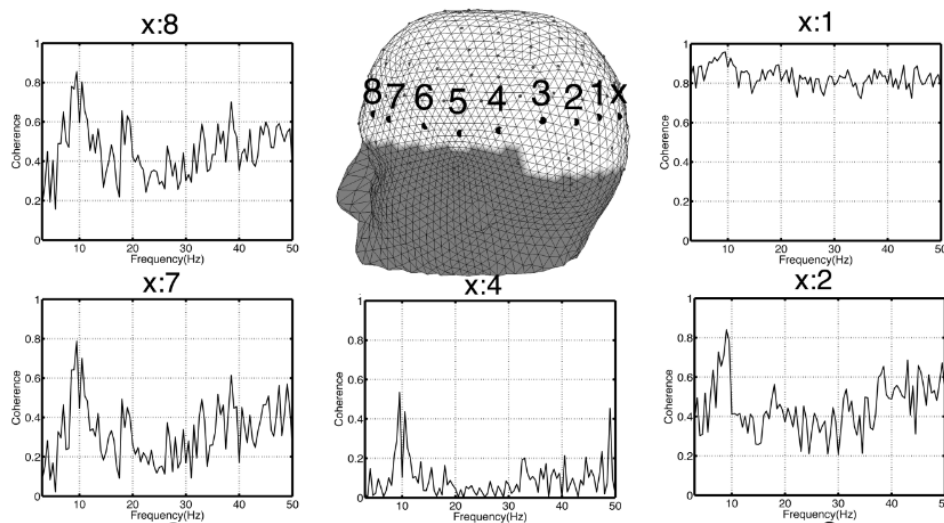
EEG recorded from the scalp measures therefore mostly the synaptic activity that occurs in the superficial layers of the cortex, and the contribution of deeper cortical layers is scaled down substantially (the contribution of neuronal activity from below the cortex is, in most cases, almost negligible). The amplitude of scalp EEG can largely vary because of variations in large-scale (centimeters) synchronization changes (with tangential direction). As a consequence, EEG researchers have termed large-amplitude increases and decreases “synchronization/desynchronization, respectively (Pfurtscheller and Lopes da Silva, 1999).

EEG synchrony refers to sources oscillating in phase and reflect the superposition of individual contributions to EEG, and desynchronization is associated with amplitude reduction of scalp EEG power (Pfurtscheller and Lopes da Silva, 1999; Nunez, 2000). However, synchronous activity can remain 180 degrees out of phase, leading to the cancelation of their contributions to EEG, and are therefore not measured by scalp EEG (Nunez, 2000).

EEG coherence is a measure of the phase consistency across epochs and frequencies (or at a specific frequency), between two electrodes, providing clues about local versus global dynamic behavior (Nunez and Srinivasan, 2006). It constitutes an important measure of functional connectivity (i.e., interactions between oscillating systems) and brain “binding” (how information

encoded by distinct brain circuits can be combined for perception, decision, and action to occur; Feldman, 2013). If the phase difference between two channels is constant across all the epochs, coherence is maximal (coefficient equals 1) and indicates a linear relationship between the two regions. Conversely, if the phase difference is random across epochs, the coherence will be minimal (coefficient equals 0), indicating no relationship between the two regions (Ombao *et al.*, 2016).

Volume conduction is associated with current spreading through the head, mixing and correlating the EEG signals at all frequencies, especially at short distances. Hence, coherence is generally independent of temporal frequency at short distances (Figure 6, right plots). Thus, a separation distance of  $\sim 10$  cm is recommended to measure coherence to minimize the volume conduction bias (Figure 6, middle).



*Figure 6. High scalp coherence at all frequencies between pairs of electrodes with short separation due to volume conduction effect that mixes activity at different frequencies (right plots). Coherence with electrodes over the temporal lobe (middle plot) shows moderate coherence, with coherence flooring close to zero for all frequencies except alpha power, indicating a very low volume conduction effect at this distance ( $\sim 10$  cm). At large separation (left plots), the volume conduction effect increases again slightly at long distances. Source: Nunez, Nunez and Srinivasan (2016).*

Thus, current sources generated at different times and places will have a much lower weight on scalp EEG, compared to synchronized signals over the cortical surface (Nunez and Srinivasan, 2006). “The magnitude of any scalp EEG signal is determined not only by the source strength but also by spatial properties of the source such as its size and synchrony.” (Nunez, Wingeier and Silberstein, 2001). As a result, the EEG recorded by a single electrode is a spatially smoothed version of the LFPs under a scalp surface on the order of  $10\text{ cm}^2$  and, which has (under most

conditions) little relationship with the specific spiking patterns of activity of the neurons that generate it (Nunez, 2000).

Other source-localization methods have also made significant advancements in addressing the low spatial resolution of EEG (Pascual-Marqui *et al.*, 1999; Zhukov, Weinstein and Johnson, 2000; Travis *et al.*, 2010; M. A. Jatoi *et al.*, 2014; Munsif Ali Jatoi *et al.*, 2014; Aoki *et al.*, 2015). Despite these advancements, the inverse problem remains difficult to resolve completely, which is why most EEG studies emphasize the significance of its temporal accuracy and focus on the time or frequency domains (see section 2.3.).

Hence, the superficial layers of the cortex are responsible for most of the electric fields measured on the scalp. Longer time-scale synaptic modulations ( $> 10$  ms scale) are associated with neuromodulators (neurotransmitters) and contribute to the mean-field potentials measured by scalp EEG. These global field modulations are thought to be the functional consequence of the brain's spatiotemporal constraints, requiring signals to propagate at a finite speed (Buzsaki, 2006; Nunez and Srinivasan, 2006). Thus, much of our conscious experience must involve, in some still unknown mechanism, the interaction of highly interconnected cortical neurons that communicate synchronously at a several-milliseconds scale. EEG has served as a key neuroimaging tool for the scientific study of human cognition, sleep, neurodegenerative disease, and brain disorders (Regan, 1989; Luck and Kappenman, 2011).

## 2.2. *Why EEG?*

### 2.2.1. **A brief comparison with other non-invasive neuroimaging methods**

Magnetoencephalography (MEG) measures the magnetic fields of the brain (Cohen, 1968). While electric currents (EEG) cannot propagate beyond the scalp, magnetic fields associated with each voltage change can and are less distorted by the skull (less volume conduction effects). Thus, MEG sensors do not need to be attached to the head, and the corresponding spatial resolution is slightly superior to that of EEG as the signal is not distorted by the skull and the scalp (Hämäläinen *et al.*, 1993). However, spatial resolution is not high enough to solve the inverse problem as in EEG. MEG signals predominantly reflect the intracellular currents (action potentials) and tangential dipoles generated in cortical fissures (versus extracellular currents with radial sources for EEG). MEG, therefore, provides different information on brain activity.

Magnetic fields generated by the brain have a very small magnitude (one hundred millionths to one billionth of the strength of Earth's magnetic field), so they can only be recorded using superconducting quantum interference devices (SQUID) that require the coils to be cooled down with liquid helium at  $-270^{\circ}\text{C}$  to operate (Hari and Salmelin, 2012). Thus, MEG is very bulky and expensive.

Since neurons require energy (oxygen and glucose) to discharge, when a large population of neurons are active at the same time, a large difference between oxygenated hemoglobin in the arterial blood (bringing nutrients to the neurons) and deoxygenated hemoglobin in the venous flow (evacuating used nutrients outside of the brain) is observed in the surrounding area. The resulting magnetic inhomogeneities are measured by the hydrogen atoms (representing tiny dipoles), termed the blood oxygenation level-dependent (BOLD) response, which is the basis of functional magnetic resonance imaging (fMRI; Ogawa *et al.*, 1990; Logothetis, 2003). This non-invasive method has been the leading tool in cognitive science research because of the detailed changes in brain response to perturbations it can detect. However, this method measures neuronal activity indirectly and misses many important components from both principal cells and inhibitory interneurons (e.g., EPSPs, IPSPs, action potentials and their propagation along the axons, release, binding, reuptake of neurotransmitters, etc.). Furthermore, how these processes relate to the BOLD signal has yet to be determined (e.g., excitation, inhibition, neurotransmitter release, etc.). Cognitive operations that are fundamentally different in the same structures can be generated with the same amount of energy, with no expected change in BOLD. Thus, while spatial resolution is highly increased, fMRI does not provide more information than EEG and MEG regarding the neuronal mechanisms. Finally, fMRI has not only a poor temporal resolution (dependent on the speed of blood flow) but is delayed  $\sim 0.5$  s after neuronal activation. This presents an important problem for evaluating the fast spatiotemporal nature of the cortical activity. Hence, fMRI cannot be used to understand the temporal sequence of neuronal activation, which is required to understand how information is processed.

Positron emission tomography (PET) provides useful information about the binding of specific chemicals and neurotransmitters in the brain (Maisey, 2005). Subjects are required to receive an injection of a very small amount of radioactive compound that accumulates in the brain and releases positrons (antimatter counterpart of the electron) as they decay. When they collide with electrons, they are both annihilated, and two photons are emitted in opposite directions and

detected by the sensors of the PET scanner. Their path is then reconstructed, indicating where it accumulated in the brain. Both the spatial and temporal resolutions of PET are inferior to fMRI.

A single MEG, PET, or fMRI device weighs several tons, has tremendous costs, and requires the subject's head to be immobilized for brain scanning as well as personnel and maintenance, making these methods not practical for the examination of behavior-generated brain changes in most laboratories, universities, or clinics. EEG is a more affordable and mobile technology, and its high temporal precision provides accurate temporal information that is useful for both clinicians and researchers (e.g., understanding processing steps of neural pathways contributing to perception to detect when and why they are dysfunctional). While the poor spatial resolution remains the more significant limitation of EEG for source localization purposes, it is possible to construct a smoothed map of the brain's electrical changes and obtain valuable spatiotemporal information on the states of the brain. Hemodynamic measures are limited to a resolution of several seconds because they rely on the BOLD response whereas EEG has a temporal resolution of less than 1 ms. This 1000-fold difference particularly highlights how valuable EEG can be for addressing many of the scientific questions that PET or fMRI cannot. It is important to note, however, that EEG does not directly measure activity from deep subcortical structures

### **2.2.2. The spatiotemporal context, calibration, and spontaneous activity of the brain**

A dynamical system cannot generate useful functions without adjusting its internal connectivity and activity to the external world, a process called “calibration”. The brain uses absolute time (e.g., date) and passage of time (i.e., duration) to calibrate our subjective experience and coordinate thoughts and activities. The experience of time is a linear (forward order of succession from past to future) and periodic (e.g., seasons, circadian rhythm), and is intricately tied to perception, causality, and prediction. Space has a similar distinction with position and distance, except that distance can have many directions in space (vector), whereas time only has one direction (scalar). By separating events in space and time (the spatiotemporal context), the brain can assess the consequences of past events and predict the most probable events to come and prepare for their occurrence. This ability significantly increases the chances of survival.

Our temporal perception is confined to a relatively short span from hundreds of milliseconds to tens of minutes and is best in the second range (corresponding to the duration of our basic

functions such as movement or speech). While events that are faster than the second range (e.g., 100 ms) may be used to update motor programs, they cannot be consciously perceived (Goodale et al., 1986). And periods longer than the hour range require body or environmental references such as hunger or sunlight changes (or time tracking from technology in modern times). Brain oscillations are thought to serve as a crucial internal metric for the calibration of neural systems.

Systems that can be perturbed from outside and incorporate external influences in their future behavior possess a remarkable capacity for learning and growth. Adaptation is the ability of the system to become optimized for a particular task as a result of external perturbation. If the statistical features of the environment reflect one particular pattern, the evolving brain should be able to adapt its internal structure (i.e., neuroplasticity, neurogenesis, synaptogenesis) so that its dynamics can predict most effectively the consequences of these external perturbations. In other words, the functional connectivity of the brain and the algorithms generated by such continuous modifications are derived from interactions with the body, the physical environment, and to a great extent, other beings. The outcome of this calibration/learning process is that, from experience, the brain can calculate the potential outcomes and convey this prediction to the effectors (e.g., the skeletal muscles). As a result, the effectors and perceptual sensors can be directed meaningfully and effectively.

The brain does not simply process incoming information from the environment, but also generates activity from within, independently of outside influences or perturbations (Llinás and Paré, 1991). This robust “spontaneous” activity is especially important in higher levels of the brain circuits that have less and less contact with sensory inputs. Interestingly, these spontaneous oscillations are present in all brains (not only in humans) and show the highest amplitude and regularity in the cerebral cortex when the brain is disengaged from the environment and body (e.g., during sleep; Buzsaki, 2006). In contrast, brain activity generally shows lower-amplitude rhythms and appears “desynchronized” during high activity (e.g., movement, decision making). As a result of these considerations, neurophysiologists have historically referred to spontaneous brain activity as the “resting state”.

Neuronal signals, therefore, have two fundamental appearances that involve different analysis methods: spontaneous oscillations (i.e., frequency domain or continuous EEG) and event-related potentials (ERP, i.e., time domain, also called “evoked response potential”). Both have varying

frequencies and evolve, but frequency and time cannot be mixed mathematically, leading to no concept of time in the frequency domain and vice versa. This phenomenon led to two main categories of analysis: the time (ERP) and the frequency (continuous) domains.

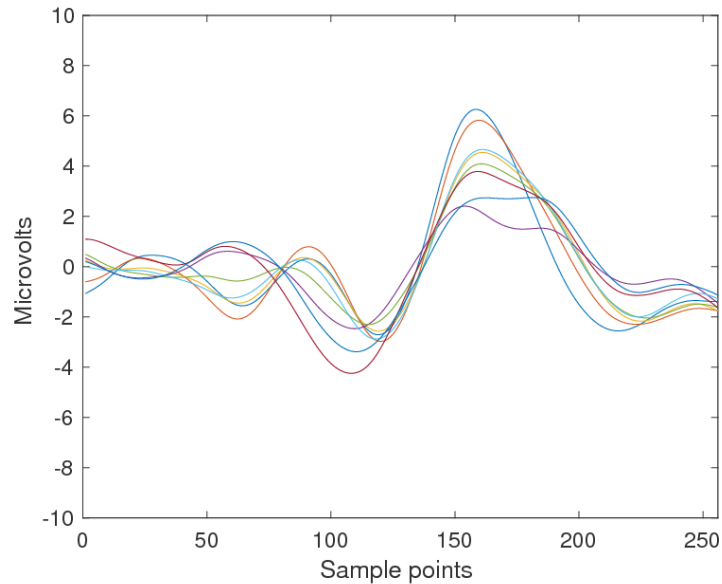
### *2.3. EEG signals and main types of analyses*

#### **2.3.1. Time-domain analyses**

Analyses in the time domain generally consist of temporal correlations. A stationary time series refers to a “random process whose statistical distribution is invariant over time”, and is considered weak when the mean and variance of the random process (e.g., EEG signal) are invariant to shifts in the time at which the sample was recorded (Ombao *et al.*, 2016). Low stationarity is assumed most of the time in resting-state EEG analysis (e.g., eyes closed, mental calculation, sleep), contrary to experiments using elicitation of cognitive and motor functions with the use of stimuli, which focus on nonstationarity (i.e., the statistics of the signal are directly associated with a specific event and the high stationarity of the pre-stimulus baseline).

ERP research is ubiquitous in the cognitive neuroscience literature (S. J. Luck, 2014). The ERP corresponds to the average over many trials (or “epochs”) of EEG response to several categories of stimulus, on the justification that only the signals relevant to the stimulus remain (the fluctuating noise-canceling itself out). ERPs typically consists of a waveform containing a series of characteristic peaks (positive or negative), typically occurring less than 1 second after the presentation of each stimulus (see Figure 7).





*Figure 7. Example of a positive event-related potential (ERP) occurring 150-200 ms after presentation of the stimulus at time 0 (i.e., fitting in the ERP category “P300/P3”), on 8 EEG channels. Source: Ramele, Villar and Santos (2018).*

Event-related potentials (ERPs; see Figure 7) “provide a continuous measure of processing between a stimulus and a response, making it possible to determine which stage or stages of processing are affected by a specific experimental manipulation.” (Luck, Woodman and Vogel, 2000; S. J. Luck, 2014). They have played a pivotal role in our understanding of the relationships between physical stimuli and brain activity (Luck and Kappenman, 2011), and have advanced our understanding of some mechanisms of cognition by isolating brain operations in subsystems such as attention, perception, working memory, or response selection (Luck, Woodman and Vogel, 2000). A strong advantage of ERPs is their ability to provide a real-time measure of the processing of a stimulus even in the absence of behavioral response (e.g., attended vs. ignored stimuli, or subliminal priming). ERPs have also been widely used in the study of cognitive disorders such as developmental dyslexia (Hämäläinen, Salminen and Leppänen, 2013), specific language impairment (McArthur and Bishop, 2004), psychiatric disorders (Park *et al.*, 2010), and autism (Čeponienė *et al.*, 2003), among others.

The main disadvantage of the ERP approach is the functional significance of the findings. The biophysical mechanisms underlying the ERP component or their consequence for neuronal processing cannot be drawn, without relying on a long chain of assumptions and inferences (S. J. Luck, 2014). Furthermore, the amplitude of ERPs is so small that many trials are typically

required to accurately measure them (50 to 100 trials per subject per condition). This implies finding participants open to volunteering hours of their time, which is hard and can be costly if studying large groups of participants. This is a significant limitation to the types of questions that can be approached with ERP experiments. Additionally, the spatial resolution of ERPs is undefined. “The voltage recorded at any given moment from a single electrode reflects the summed contributions from many different ERP generator sources, each of which reflects a different neurocognitive process. This makes it extremely difficult to isolate a single ERP component from the overall ERP waveform (S. J. Luck, 2014). Hence, ERP is only well-suited for addressing questions about which neurocognitive process is influenced by a given manipulation, and focusing either on specific components easy to isolate (e.g., the “lateralized readiness potential” in preparation of motor activity).

Autocorrelations used for ERP analysis (correlating the signal with itself) can also reveal repetitive components in the signal such as periodicity and resonance (VanRullen and Macdonald, 2012). Oscillations go in and out of phase when shifted in time. Thus, the autocorrelation function results in a periodic signal with a period identical to the original signal, which can reveal periodic components of that signal (e.g., a reverberation at 10 Hz in response to visual processing of luminance; Figure 8, A). Random noise, for example, does not autocorrelate and therefore does not result in a periodic signal. Correlations between two signals (cross-correlation) can also discriminate signals apart or assess their similarity. The correlation reaches a maximum when two signals have a similar shape and phase, and a minimum when they are out of phase. This method is very useful to detect a known reference signal within noise or the connectedness between neurons and its direction (with intracranial recordings).

### **2.3.2. Frequency domain**

EEG and MEG signals are complex waveforms that contain multiple simultaneous frequency components. The Fourier transform (Bracewell, 1989) allows the decomposition and separation of the waveforms into sinusoids of different frequencies, to distinguish the different frequencies and their respective amplitudes. The resulting Discrete Fourier Transform (DFT) is therefore a frequency domain conversion of the original input sequence, which represents the relative dominance of the various frequencies, called the power spectrum (spectra for plural). The signal is converted from the time domain into the frequency domain (Figure 8, B and C).

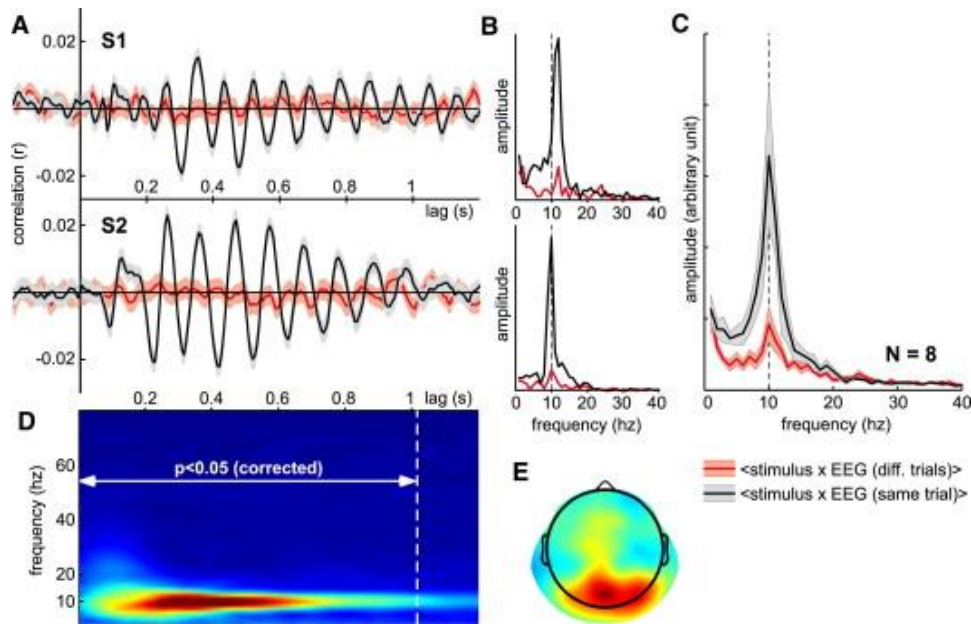


Figure 8. Resonant alpha oscillations in response to luminant visual stimuli. A: time-domain (i.e., cross-correlation of the signal). B and C: frequency domain (i.e., power spectra). D: Time-frequency representation of A over the group. E: Scalp topography representation of the effect showing the electrode sites where the effect was measured. Source: VanRullen and Macdonald (2012).

EEG systems and researchers use different spectral parameters that lead to different power amplitudes, making it harder to compare results across findings. The spectral analysis evaluates the statistical properties of the amplitude of multiple frequency bands. It can be a direct measure of interest or a step to assess the quality of the data in pre-processing steps (some frequencies are known to be associated with artifacts).

The Fourier transform is generally too slow to be practical for EEG analysis purposes (since EEG data have many channels and time points). The Fast Fourier Transform (FFT) solves this issue by factorizing the DFT matrix into a product of sparse factors, reducing the complexity of the calculation (Bendat and Piersol, 2011). While FFT provides a quick and easy assessment of the spectrum, it can be sensitive to noise and to nonstationarities that are very common in EEG signals (especially with wearable systems with electrodes disconnecting more frequently).

Power spectral density (PSD), calculated with the *pwelch* method (Stoica and Moses, 2005; Hayes, 2009), addresses these issues by smoothing the signal over non-systematic noise and normalizes the amplitude by the frequency resolution (homogenizing spectra amplitude across different spectral resolution used; Bendat and Piersol, 2011; Cohen, 2014). Finally, converting the power spectra to decibels (dB; i.e.,  $10 \cdot \log_{10}(\text{power})$ ) allows for comparison of effect sizes across

publications, relevant for interpretation and replication of findings, and can normalize the signal across electrodes and subjects (reducing large amplitude differences due to volume conduction effects for example; Smith *et al.*, 2017).

The power distribution of EEG signals typically follows an inverse power law relationship, or “ $1/f$  distribution” (i.e., an inverse relationship between amplitude and frequency; Barlow, 1993). While this might be the consequence of the scale-free organization of the brain organization (the long distribution tail might be the consequence of the dominant presence of modules; Albert and Barabási, 2002; see Chapter 1), the physiological bases for this inverse relationship between amplitude and frequency and most other salient characteristics of EEG are still unknown (Nunez, Wingeier and Silberstein, 2001), to our knowledge.

Frequency measures of the EEG signal are typically denoted in Hz (i.e., cycles/sec). The main frequency bands, defined based on their power spectra are termed: delta (<3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (>30 Hz). Some researchers have also identified the *mu* rhythm, corresponding to an “M” shape in the power spectrum distribution occurring in the alpha or beta frequencies, and is associated with motor-related activity (Pfurtscheller *et al.*, 2006).

Frequency bands have remained relatively constant throughout mammalian evolution even as the numbers of neurons and their connections have increased enormously (see section 1.1.), indicating that they represent crucial processes underlying important functions for adaptation and behavior (Buzsaki, 2006). While it is well established that EEG oscillations represent postsynaptic potentials of groups of cortical neurons, the physiological bases for oscillatory EEG behavior and the delineation of the main frequency bands remain poorly understood (Nunez, Wingeier and Silberstein, 2001).

### **2.3.3. Time-frequency domain**

While the frequency domain associated with spontaneous EEG activity is the focus of this thesis, it is important to briefly mention the time-frequency domain (e.g., “event-related spectral perturbation”, i.e., ERSP). Modern methods have been developed to examine how spectral and coherence information varies over short periods in response to a stimulus (combining the advantages of both time and frequency domains).

One approach uses short sliding time windows (e.g., 200 ms) and assumes stationarity over each window to calculate the spectra. Another approach, termed the Morlet Wavelet transform, estimates time-varying Fourier coefficients (Lachaux *et al.*, 2002). Phase-locked power in response to a stimulus can be calculated using the time average of the epochs and removing signals that are not phase-locked (corresponding to desynchronization and decrease in power).

These methods allow evaluating both the short-time activity from the time domain (ten-to-hundred ms range) and the slightly longer timescale of the frequency domain reflecting the oscillatory component of the signal (subsecond range; Bruns, 2004). An example of time-frequency analysis is the “steady-state evoked potentials” (SSEPs; Deng and Srinivasan, 2010), which can be evoked by flickering visual stimuli (steady-state visual evoked potentials; SSVEPs), auditory stimuli (steady-state auditory evoked potentials; SSAEPs), or somatosensory stimuli (steady-state somatosensory evoked potentials, SSSEPs). These methods provide high signal-to-noise (SNR) ratio by amplifying the brain signal of interest while reducing the weight of the background noise, and by minimizing broadband artifacts by focusing only on specific, narrow, frequency ranges (wavelet approach). They have therefore been used widely to study attention (e.g., Giabbiconi *et al.*, 2004) or to develop brain-computer interfaces (BCI; see section 9.2.).

The study of continuous (spontaneous) signals in the frequency domain corresponds to much longer time frames (seconds to minutes) and reflect oscillatory modulations of brain chemistry controlled by neuromodulators (Buzsaki, 2006).

## Chapter 3. Wearable EEG

*In this chapter, we discuss the EEG technologies, the minimum hardware requirements, the innovations that have led to the emergence of wearable EEG systems, list several examples of such systems, and discuss their advantages and disadvantages compared to traditional systems.*

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### 3.1. EEG technology

“The discovery of electroencephalography (EEG) in 1929 by the German psychiatrist Hans Berger was a historical breakthrough providing a new neurologic and psychiatric diagnostic tool at the time.” (Tudor, Tudor and Tudor, 2005). Figure 9 illustrates some of the first EEG systems developed. Over the past 50 years, major technological advancements have drastically changed EEG technology.

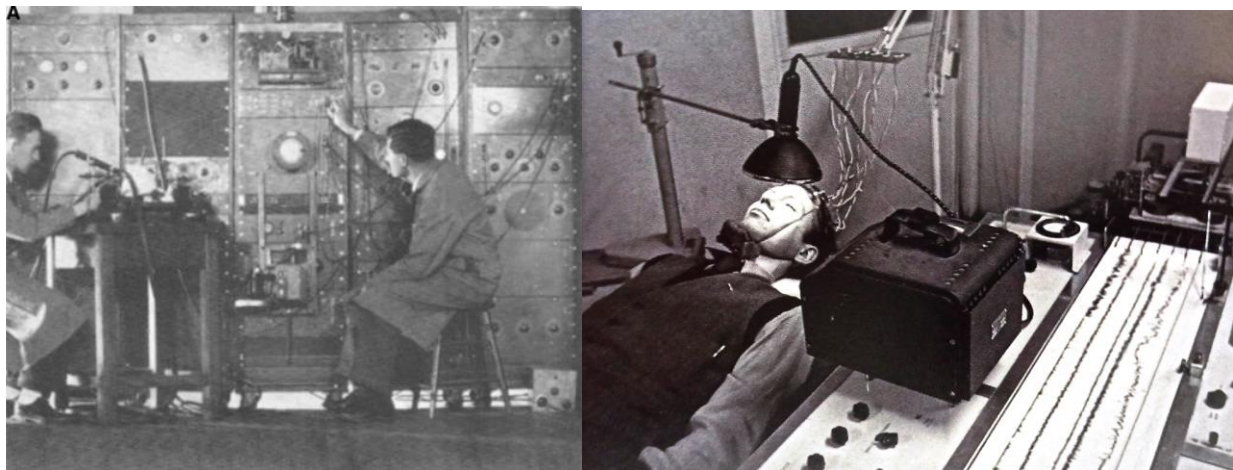


Figure 9. **Left:** Two pioneer neuroscientists working with an early EEG system at Harvard Medical School (1934). Source: Bernard Becker Medical Library, Washington University in St. Louis. **Right:** EEG recording of a participant in the 1950s while he is stimulated by a flashing light, taken at the Burden Neurological Institute at Bristol University. The EEG signal was traced by 2 thin pens on tape-recorded paper, and time-tracking was traced by a third pen at the top. Frequency analysis was done by hand using a caliper. Source: Hulton-Deutsch Collection/CORBIS.

### 3.1.1. EEG amplifier

While EEG is an analog signal (continuous in time), it is necessary to convert this analog signal into a digital signal (discrete in time) to be processed by the computer, a process called an analog-to-digital converter (ADC). In this process, the analog signal from each channel is assigned a digitized value that is proportional to the instantaneous amplitude. It is then converted from ADC to volts by the amplifier (Ombao *et al.*, 2016). The number of bits available to do this conversion corresponds to the signal resolution. Digitization must use a minimum resolution of 12 bits and be able to resolve the EEG down to 0.5 mV (Nuwer *et al.*, 1998).

Advancements in ADC technology have played an important role in wearable EEG technology because the signal sampling rate and the Nyquist limit are determined by the sampling rate of the ADC (Landau, 1967). The Nyquist limit refers to the minimum sampling rate required to be twice the value of the highest frequency of interest to avoid signal aliasing (i.e., under-sampled misrepresentation of high-frequencies). For example, a 100 Hz ADC sample rate is required to analyze EEG frequencies up to 50 Hz. While downsampling the signal is possible later in the preprocessing steps, aliasing cannot be undone because the necessary information for this procedure has been lost. Aliasing is generally avoided by integrating internal lowpass filters that eliminate the power at frequencies above the Nyquist limit (Landau, 1967). Internal highpass filters are also used to eliminate the EEG offsets and DC components to avoid saturation from internal electronic components of the system. Amplifiers without internal highpass are termed “DC-coupled” and are only preferred when very slow oscillations are of interest (e.g., slow cortical potentials in the study of movement preparation; Schmidt *et al.*, 2016). The signal bandwidth is the resulting frequency band with an amplitude attenuated by less than 3 decibels (dB) by the internal filters. ADC capacities have greatly increased with technological innovations over the years (e.g., 2000 samples per second), allowing scientists to study higher frequencies of EEG signals that were not accessible previously. A sampling rate of 200 Hz is generally required (although above 500 Hz is preferred; Nuwer *et al.*, 1998).

The amplifier input range (i.e., a maximum amplitude that can be recorded before saturation) depends on the output range (which relies on the power supply) and on the amplifier’s internal gain (i.e., the number of times the input signal is amplified). For EEG amplifiers, the input range must include not only the minimum and maximum values of brain electric field (tens of V range), but also those from other non-brain signals such as electromyography (EMG; i.e., from muscle

activity; tens of mV range), electrode offsets (tens of mV), and electroencephalography (EOG; i.e., ocular activity; hundreds of Volts; Harrison, 2007). If the input range is smaller than these signals, they will be clipped. This must be avoided for both brain and non-brain signals as the true signals may go undetected and can be consequently removed from the signal in the later preprocessing steps (if their signal features are altered). Typically, the minimum input range is 50 mV to avoid this issue.

Additionally, the input-referred noise (i.e., noise current produced by the amplifier's internal circuits) must remain below 1 microVolt ( $\mu\text{V}$ ), as to not affect the EEG signal that can have amplitudes as small as a few  $\mu\text{V}$  (Nuwer *et al.*, 1998).

The common-mode rejection ratio (CMRR) of the amplifier refers to the attenuation of common-mode voltage (i.e., the constant voltage for both positive and negative inputs) while amplifying the differential mode voltage (i.e., the voltage difference between positive and negative inputs). Thus, the CMRR amplifies the voltage difference between an electrode and the reference electrode, while attenuating artifacts like the power line noise that is recorded by both electrodes. The higher the CMRR, the better the amplifier can attenuate the common-mode signals. The minimum amplifier CMRR is considered to be 80dB attenuation of line noise (MettingVanRijn, Peper and Grimbergen, 1994).

The amplifier receives signals from electrodes with high impedance (especially from dry electrodes) and must not further attenuate the already weak signal amplitude (a few  $\mu\text{V}$ ) to avoid losing resolution. The amplitude can drop differently between electrodes depending on their impedance, decrease the CMRR and increase the noise (Kappenman and Luck, 2010). The amplifier must have a high “input impedance” (refers to the impedance of the input, whereas the electrode impedance is between the skin and the electrode) while maintaining the electrode impedance. The higher the input impedance of the amplifier, the better the signal in situations with high electrode impedance. Minimum input impedance generally corresponds to  $100\text{M}\Omega$  (i.e., a hundred times the electrode impedance), to keep the signal attenuation below 1% (MettingVanRijn, Peper and Grimbergen, 1994).



### 3.1.2. EEG electrodes

The electrode impedance (a measure of the opposition to the electric current due to resistance and reactance effects) present between the electrode and the skin is directly related to the performance of the electrode, and significantly affects EEG signal quality. Electrodes that are properly positioned with firm contact between the skin and the electrode can provide reliable levels of signal quality. Passive electrodes simply extend the connection from the conductive material to the equipment that captures, converts, and amplifies the signal. They are generally made of Ag/AgCl (silver/silver chloride) and require electroconductive (electrolytic) gel as a conductor between the scalp and the electrode. The biggest disadvantage of wet EEG systems is that they present long preparation times, requiring preparation of the skin, injection of the gel in each electrode site with a syringe, and cleaning of the electrodes at the end of each recording without damaging the sensitive materials (~30/45 minutes for a 64-channel system). Furthermore, participants need to wash their hair after the experiment, which can reduce motivation to participate in some individuals.

While great improvements have been made with the development of saline-soaked sponge electrodes held in place with flexible nets, they still require long preparation times and the speed of voltage change can still influence the amount of noise introduced into the signal (Laszlo *et al.*, 2014). Active electrodes have a pre-amplification module immediately after the conductive material (between the skin and the electrode) that amplifies the signal before additional noise is added. Active sensors generally consist of high-quality sintered stainless steel or Ag/AgCl and are perfectly suited for DC acquisition. Built-in active shielding allows recordings at high transition resistances (up to 500 kOhm) and allows the use of “dry” electrodes (no conductive gel required; Taheri, Knight and Smith, 1994).

While dry active electrodes have higher noise levels compared to wet active electrodes (Mathewson, Harrison and Kizuk, 2017), they can minimize ambient power-line interference as well as artifacts from cable movements, and have shown comparable performance (Nishimura, Tomita and Horiuchi, 1992; Alizadeh-Taheri, Smith and Knight, 1996; Fernandez and Pallas-Areny, 1996; Fonseca *et al.*, 2007). Their greatest advantage is that they significantly reduce preparation/cleaning time for experimenters, by removing the dependence on the conductive gel. More recently, solid-gel (silicon) electrodes have been developed and might offer a promising

middle ground by combining the advantages of both solid and wet electrode technology (Neuroelectronics, 2021b).

### *3.2. Low-cost wearable EEG systems*

Low-cost wearable technologies may offer several critical solutions for addressing health disparities (i.e., rising numbers of poor mental health, limited access to healthcare, rising healthcare costs) by providing cost-effective, scalable, real-time, and longitudinal monitoring of physiological data (Ghose *et al.*, 2012). With an increased capacity to acquire, share, process, store, retrieve, and apply machine-learning methods, wearable technologies may significantly improve our ability to tackle some of the major challenges of today’s society (Zheng *et al.*, 2014). Consumers can now access a wide array of wearable technologies that measure, monitor, and receive feedback from ongoing physiological activity. While the application of wearable technologies was previously limited to physiological measurements (e.g. heart rate, step-counter), recent advancements in EEG technology (see section 3.1.) have led to the development of low-cost wearable EEG systems. EEG data were traditionally transported to the computer’s hard drive using costly and fragile optic fibers, they can now be streamed wirelessly with WIFI or Bluetooth technology, and the data can be stored directly onto a cloud and accessed by anyone, anywhere (with collaborative access).

While research-grade wearable EEG systems can compete with research-grade stationary EEG systems (they often offer both wet or dry electrodes and similar hardware specifications), they are still very costly (>\$20,000), which greatly limits their access and use for clinicians, researchers, and other users. Here, “low-cost” wearable EEG systems refer to systems that cost less than \$2,000, and research-grade wearable systems above that value. Typically, low-cost systems have a significantly lower density (i.e., a few channels) compared to research-grade systems (>30 channels). Figure 10 illustrates a research-grade stationary system (left) and a research-grade wearable system (right). Some examples of low-cost wearable systems can be found in Figure 11 (upper row, left).



Figure 10. Illustration of the technological innovations in EEG technology. Left: High-density, research-grade, stationary 128-channel EEG system. Source: National Geographic (2009). Right: Wearable, wireless, 32-channel EEG system Source: Cognionics (2021).

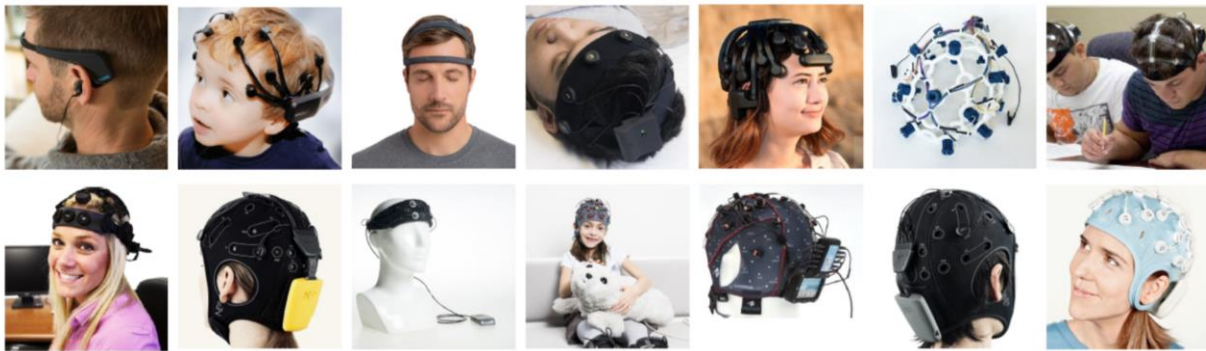


Figure 11. Top row (from left to right): Muse (interaxon), Epoc (Emotiv), Dreem (Rhythm), Sleep headband (Cognionics), Quick 30 (Cognionics), Ultracortex Mark IV (Open BCI), B-alert X10 (ABM). Bottom row (from left to right): DSI 1020 (Quasar), Enobio (Neuroelectrics), Octamon (Artini), g.Nautilus (g.tec), g.Nautilus EEG-fNIRS (g.tec), Starstim 8 and 32 (Neuroelectrics). Source: Cannard et al., (2020).

	Sensors	Price (\$)	Battery autonomy (h)	Connectivity / storage	Signal resolution (bits)	Sampling rate (Hz)	Weight (g)	Additional features	Auxiliary measures (EXG)	EEG	NF/BCI (included)	fNIRS	Neuroimaging	Audience and applications
<b>Muse (Interaxon)</b>	- 4 dry active electrodes (TP9, TP10, AF7, AF8); 2 silver and 2 conductive silicone rubber. - Reference on Fpz (DRL/DMS) - Adjustable headband (52 to 60 cm)	180	5	BLE	12	256	60	- Allows recording of raw EEG data directly on iPod, smartphone, or tablet - NF App - Allows to record data from multiple devices simultaneously on computer - Real-time impedance check - Triggers	- 6-axis motion-sensor - 1 input for custom physiological sensor - HR (Muse 2) - respiration (Muse 2)	X	X			For researchers and the public: home use, real-world recordings, attention/meditation training, relaxation, raw EEG recording, big data analyses, sleep research, BCI.
<b>EPOC+ (Emotiv)</b>	- 14 saline soaked felt pads (AF3, AF4, F3, F4, FC5, FC6, F7, F8, T7, T8, P7, P8, O1, O2) - CMS/DRL references (P3/P4) - Adjustable by pressure control	800	6	BLE	14/16	128/256	120	- Raw EEG data - Available detections of mental commands (neutral + up to 4 pretrained items per training profile), performance metrics (excitement, engagement, relaxation, interest, stress, focus), facial expressions (blink, wink L/R, surprise, frown, smile, clench, laugh, smirk) - Real-time impedance check	- 9-axis motion sensors	X	X			For researchers and the public: home use, real-world recordings, raw EEG recording, enhancing brain performance, 3D brain visualization, BCI.
<b>Dreem (Rythm)</b>	- 6 channels (4 frontal and 2 occipital) - 1 micro-amplifier - Adjustable headband - Reference electrodes on O1 and O2 (but flexible)	500	12	WiFi & BLE	24	250	120	- Sound is discreetly diffused to the inner ear via your forehead (using bone conduction technology). - Can connect to smartphone and iPod directly. - Sleep monitoring App that works without BLE and WiFi during sleep (data transferred later for report).	- 3-axis motion sensor - 2 pulse oximeters (respiration and HR)	X	X			Sleep monitoring, managing and improvement
<b>Sleep headband (Cognionics)</b>	- 2-8 active dry and semi dry electrodes (can be placed in any of 14 positions along the band).	4,5k	4	BLE/micro SD	24	250/1000	110	- Real-time impedance monitoring - Optional wireless triggers	- Optional add-on module for EXG	X	X			Sleep monitoring, managing and improvement
<b>Quick 20/30 (Cognionics)</b>	- 20/30 active dry and semi dry electrodes (10/20 system + 10 additional from 10/5 system) - Adjustable by pressure control	24k	8	BLE/micro SD	24	500/1000	610	- Real-time impedance monitoring - Raw EEG - Recording via microSD card possible	- 3-axis motion sensor - 2 optional EXG	X	X			Designed for real-world applications, BCIs.
<b>Ultracortex Mark IV (OpenBCI)</b>	- 8 (cyton board) or 16 (cyton + daisy boards) channels, with 35 possible different locations. - Passive gold cup electrodes using gel paste, or any standard electrode using adapter cables. - DRL, positive voltage supply (Vdd), and a negative voltage supply (Vss) - 3 different head sizes, and flexible structure	~ \$50/1,4k	?	BLE and WiFi	24	250/500		- Compatible with active and passive electrodes (adapters). - 3D printable - 30 sec to set up - Micro SD input for local storage - The prices correspond to the printable EEG headset with the OpenBCI boards. The headset can also be purchased printed but unassembled, or fully assembled for higher prices. Batteries are not included but represent a cost of around \$10.	- 3-axis motion sensor - optional EXG (EMG, ECG)	X	X			Raw EEG recording, BCI, NF, first 3D printable device.
<b>B-Alert X10/X20 (ABM)</b>	- 9 or 20 channels (frontal, central, parietal lobes), using a conductive cream - Fixed gain referenced to mastoids - 3 sensor strip sizes (S, M, L)	11,5k	12-24	BLE	16	256	11	- Ultra-low profile and comfortable fit allows for 8+ hour recording sessions - Patented real-time artifact decontamination - Software with classifications of cognitive states (for \$16.5k in total price) - setup: 10/20 mm	- 3-axis motion sensor - 1 EXG with the B-Alert X10; and 4 EXG for the B-alert X20 (EOG, ECG, EMG)	X	X			Raw EEG recording, BCI, cognitive assessment or training, performance enhancement, group studies, sleep studies, military studies
<b>DSI 10/20 (Quasar)</b>	- Up to 21 dry EEG electrodes (flat-ended finger electrodes) - Ground at Fpz and references on mastoids.	7k	24	BLE	16	300/600	500	- Patented shielding and circuit design reduce environmental noise - Mechanical design carefully controls contact pressure allowing comfortable wear all day - Internal storage (1 GB) - Impedance monitoring for each sensor - Cognitive states classification software	- Wireless belt that measures EKG, skin temperature, and 3D body acceleration and position - trigger inputs	X				Raw EEG recording, BCI and NF, cognitive states classification, real-world recordings.
<b>Enobio (Neuroelectrics)</b>	- 8/16/32 channels, using innovative solid-gel electrodes or dry electrodes - A disposable pregelled electrode or a cap can be used for CMS/DRL reference - Six different neoprene, flexible, head cap sizes	~ 4k/14k/20k	16/15/14	BLE	24	500	65	- 3D visualization real-time - Specific headcaps for children - microSD card for internal storage - compatible with TES and TMS - "Mickey Mouse" Headcap Cover for kids	- EOG/ECG	X				Researchers and clinicians: high quality raw EEG, high mobility, real-world studies, BCI and NF applications.
<b>OctaMon (Artinis)</b>	- 8-channels fNIRS headband	~ 17k	6	BLE		10	230	- 8x2 wavelengths: 760/850 (standard) - optode distance: 35 mm - no interference with EEG, EOG, ECG, EMG - TMSI packages: Octamon + EMG (2 channels or more), and Octamon + EEG (16 channels or more) - Real-time processing of fNIRS data in 3D	- Can be combined with external EEG and EXGs		X			Researchers and clinicians only: study of hemodynamic response with very high mobility, real-world studies, can be combined with other neuroimaging techniques, BCI, educational applications
<b>g.Nautilus (g-tec)</b>	- 8, 16, 32, 64 active, dry or gel-based EEG electrodes - GND and REF - flexible positioning of electrodes, 3 head sizes for both adults and children - 8 fNIRS channels, combined with EEG - Works with both dry and gel-based electrodes (8/16/32 channels) - flexible positioning of electrodes, 3 head sizes (including for kids)	from 5k	6-10	2.4 GHz ISM	24	250/500	<140	- Contactless charging of the battery - Waterproof - Allows simultaneous tDCS and TMS - Internal impedance check - 8 digital triggers - microSD (up to 2GB) - BCI software applications available	- 3-axis motion-sensor - 4 possible exg (ECG, EMG, EOG, GSR, limb movement, oxygen saturation, respiration effort and flow)	X		X		For researchers and clinicians only: high quality raw EEG, possible simultaneous EEG-fNIRS, and compatible with EEG-tDCS and EEG-TMS (with external equipment). Recording during physical activity, easy access to children and elderly, rehabilitation, real-world recordings, BCI.
<b>Starstim 8, R20, R32, (Neuroelectrics)</b>	- up to 20 or 32 electrodes with 39 possible locations - the Pistim hybrid electrodes allow for both EEG recording and TES (includes tDCS, tACS, tRNS) at the same site but not simultaneously. The gelrodes and sponstim electrodes allow for simultaneous EEG/TES, but at different sites - Multiple head cap sizes	~ 11k/29k/43k	4	WiFi	1 μA	1000	65	- Frequency stimulation: 0-250 Hz for tACS, and 0-500 Hz for tRNS. - ±15 V per electrode (30 V potential difference) - 2mA max current, 1 hour max duration of stimulation - Abortion possible at anytime - MRI compatible stimulation electrodes - Nube cloud platform allows scheduled stimulation from distance - can be combined with the OctaMon fNIRS	- 3-axis motion-sensor - ECG, EOG	X	X	X	X	For researchers and clinicians only: EEG recording, NF, simultaneous EEG and TES/fNIRS (all in one headset), BCIs, telemedicine, home-use, real-world recordings.

Table 1. This table lists a small selection of modern wearable EEG systems, both low-cost (< \$2,000) and research-grade (> \$2,000), their main hardware specifications, the provided features, and their intended applications and users. Source: Cannard et al., (2020).

An increasing number of research studies have now used low-cost wearable EEG headsets to study a wide array of fundamental research topics, including visual perception and auditory attention (Poythress *et al.*, 2008; Debener *et al.*, 2012; Wascher, Heppner and Hoffmann, 2014; Badcock *et al.*, 2015; Abujelala *et al.*, 2016; Maskeliunas *et al.*, 2016; Barham *et al.*, 2017; Krigolson *et al.*, 2017, 2021; Krigolson, Williams and Colino, 2017; Kuziek, Shienh and Mathewson, 2017; Williams *et al.*, 2020), emotions (Brouwer *et al.*, 2011; Brown, Grundlehner and Penders, 2011; Bashivan, Rish and Heisig, 2016; Jiang *et al.*, 2016, 2017; Zhao *et al.*, 2017), learning and memory (Berka, Daniel J. Levendowski, *et al.*, 2005; Berka *et al.*, 2007), and stress (Hu *et al.*, 2015; Ahn, Ku and Kim, 2019; Arpaia *et al.*, 2020).

### **3.2.1. Limitations of low-cost wearable systems**

An obvious concern with low-cost EEG systems is whether the hardware meets the minimum requirements (described in the previous section) necessary to achieve sufficient EEG signal quality (Picton *et al.*, 2000; Duvinage *et al.*, 2013). Increasingly more low-cost systems meet these hardware standards. Table 1 reviews some research-grade and low-cost wearable EEG systems that meet minimum hardware requirements and the features and applications provided by the manufacturers.

One common limitation of low-cost wearable EEG systems is the absence of software features to monitor the input impedance of the signal. This is important during the setup of the electrodes (and during the recording) to make adjustments to electrode contact before the recording to obtain as high quality as possible (since the input impedance is most affected by electrode impedance). Adjustments to improve electrode impedance include typically cleaning the skin with alcohol, applying the electroconductive gel, moving hair out of the contact area as much as possible. This is also important during the session to detect variations in impedance and make adjustments.

Impedance monitoring is generally provided by the research-grade systems by injecting a very faint artificial signal that is measured by each electrode. The common-mode sense (CMS) active electrode and the driven right leg (DRL) passive electrode form a feedback loop (both ideally placed in the center of the measuring electrodes) that drives the average potential of the common-mode voltage as close as possible to the ADC reference voltage. The CMS/DRL loop can provide

a 40 dB attenuation of power line signal, with the same impedance with a standard single ground electrode, and be used to cue the experimenter on the impedance quality of the signal. Furthermore, the return current passing through the DRL can be electronically limited to a certain threshold to protect the participant against the excessive flow of current due to amplifier or electrode defect. Hence, impedance monitoring is highly desirable, but often not provided by low-cost wearable systems.

The optimal number of recording channels generally depends on the objectives of the measurements. For example, ERPs or basic frequency components can be detected with only a few recording locations, whereas advanced source localization techniques require higher-density montages. This can be a significant limitation for ERP research since some ERP components are maximal or only detectable at specific scalp locations (S. J. Luck, 2014). While most low-cost wearable systems have only a few channels, these montages generally aim to follow the standard 10-20, 10-10, 10-5 electrode placement system (Oostenveld and Praamstra, 2001). Electrode and reference montages can be custom-made or modified to better address specific research questions (e.g., increased electrode density in the occipital region to study visual perception). Thus, the specific montage configuration must align with the targeted application and research question.

Event markers are crucial to ERP research to precisely extract epochs of data centered on the onset of events of interest. This allows the researcher to create event-related average waveforms for subsequent analysis (Luck and Kappenman, 2011). However, many low-cost manufacturers do not provide software development kits for the users (SDK; a set of program tools and code provided by hardware and software vendors to allow developers to build custom applications from them).

Hence, at least 3 electrodes are required to record EEG. “The amplifier ground (or DRL/CMS when available) electrode placed on the scalp (or sometimes on the neck) provides a reference voltage to the amplifier to prevent drift and facilitate better CMRR by serving as a reference for the differential amplifier (Nunez and Srinivasan, 2006). Other pairs of electrodes record the mean-field potentials by relying on the current passing through the circuit (bipolar recording) and are all recorded relative to the reference electrode. Thus, the choice of reference and electrode location greatly impacts what EEG signal is recorded and what sources are favored. However, while the location of the source is generally unknown before recording, the reference can be



changed offline after the data is recorded. The “average reference” method (or “common average reference”) is widely used in EEG research, has a good theoretical justification (Bertrand, Perrin and Pernier, 1985), and performs best with a large number of spherically distributed electrodes (e.g., 64, 128; Srinivasan, Nunez and Silberstein, 1998). However, the average reference method has a poor approximation of reference-independent potentials when working with a limited number of electrodes (Smith *et al.*, 2017).

The issue of the electrode reference and its impact on measures of frequency has been detailed (Davidson, Jackson and Larson, 2000; Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017; Yao *et al.*, 2019), and is of particular importance when considering low-density EEG montages. Referencing methods for EEG research include the infinity-reference (Yao, 2001), the current source density (CSD; or surface Laplacian) transformation (Smith *et al.*, 2017), in addition to the aforementioned average-reference (Allen, Coan and Nazarian, 2004). These methods, however, require a greater number of EEG channels than most low-cost systems provide (a minimum of 32 channels for the infinity reference and 64 for average reference). The average-reference requires equally spherical coverage over the whole head to be considered valid, and the CSD transformation might filter out patches of scalp activity between sensors where the scalp is under-sampled (Smith *et al.*, 2017). Thus, they cannot be used with the majority of low-cost wearable EEG systems. Another alternative method, referred to as the “residualization” procedure (Davidson, Jackson and Larson, 2000), is also not feasible with low-density montages as it requires a higher number of electrodes to properly correct for overall power. Cz-reference, although popular, greatly misestimates activity at the recording sites (Allen, Coan and Nazarian, 2004). While high-density systems are better suited for addressing specific research questions, investigators interested in conducting research using wearable systems can now find a diversity of high-end systems available today.

EEG signals from wearable systems streamed wirelessly via Bluetooth (and often lower quality Bluetooth) can lead to significant time lag artifacts as the result of brief disconnectivity during the online transfer of data (Krigolson *et al.*, 2017; Kotowski *et al.*, 2018). However, data is not lost, only delayed in time, and can therefore be reconstructed in the later preprocessing phase of analysis (e.g., Kotowski *et al.*, 2018). Some systems offer micro SD cards that store the data locally without requiring cables to maintain mobility but can only lead to offline analyses. Research-grade wearable systems use WIFI technology to stream the data more reliably. Bluetooth lag

artifacts are only a problem for analyses requiring time-locking of EEG data to markers with high temporal resolution as in ERP research, but not for continuous EEG focusing on the frequency domain.

Another significant potential limitation to most wearable systems (both low-cost and research-grade) is their increased vulnerability to EEG artifacts, by offering more movements to participants, and dry electrodes disconnecting more easily. The majority of scalp EEG is generated by biological artifacts (e.g., ocular artifacts, muscle artifacts, etc.). Environmental power line noise also contaminates the EEG signal (by capacitive coupling of body and electrode leads) and generally more so in low-cost wearable systems due to the lower performance of the amplifiers. However, line noise is localized to a specific frequency (e.g., 50 Hz for Europe and 60 Hz for the USA), and can therefore be relatively easily extracted from the signal using notch or lowpass filters (e.g., Cleanline, 2021).

### **3.2.2. Dealing with EEG artifacts**

Artifacts were traditionally removed by hand from the signal by researchers, which is time-consuming (which is not feasible when collecting large datasets as when using wearable EEG systems), and prone to subjective judgment errors when facing subtle artifacts that require a lot of expertise and knowledge. Subtle artifacts can be identified using raw waveforms, power spectra, and scalp topographies (e.g., muscle artifacts can be identified when the power spectrum does not follow the power-law distribution in higher frequencies and is located in the temporal areas, reflective of neck muscle activity).

Automated methods have been developed over the past couple of decades to remove non-brain artifacts from multichannel EEG data. The main initial approach was to use regression methods in the time or frequency domain on parallel EEG and EOG data. The spread of EOG artifacts in the EEG signal could be estimated. But these methods are problematic because regressing out eye artifacts requires subtracting relevant EEG signals or when a good regressing channel is not available for each artifact source, as in the case of muscle artifacts.” (Jung, Makeig, Westerfield, *et al.*, 2000; Schlögl *et al.*, 2007). Furthermore, regression methods cannot reconstruct the signal. This is possible with statistical thresholding methods (e.g., “Autoreject”, Jas *et al.*, 2017), but they require additional auxiliary channels, which is not convenient for wearable EEG applications that aim to quickly and easily record EEG data.



A popular approach to remove eye artifacts from multichannel EEG data is the principal component analysis (PCA), a mathematical algorithm that reduces the dimensionality of the data while retaining most of the variation in the dataset, by identifying directions (called principal components), along which the variation in the data is maximal. Each sample can be represented by relatively few principal components instead of thousands of variables, facilitating the detection of similarities and differences across samples, and which samples can be grouped or excluded (Ringnér, 2008). However, PCA does not completely separate eye artifacts from brain signals, especially when they have comparable amplitudes because it assumes that the components are uncorrelated in both spatial and temporal domains (Jung, Makeig, Humphries, *et al.*, 2000).

Independent component analysis (ICA), a widely used method, addresses these issues because the components are maximally statistically independent in one domain but not necessarily uncorrelated (Makeig *et al.*, 1996, 1997; Delorme and Makeig, 2004; Delorme, Sejnowski and Makeig, 2007). The rationale for ICA is that brain signal (both for EEG and fMRI) can be regarded as a linear combination of a smaller number of independent component sources (Beharelle and Small, 2016). Furthermore, classifier algorithms have now been implemented to automatically identify and reject the artifactual components without requiring the expertise and time to do it manually (Zou, Nathan and Jafari, 2016). The recent ICLabel EEGLAB plugin provides this feature using a large database of individual components (over 200,000 ICs from over 6000 EEG files) that were manually classified by EEG experts into 7 categories (“brain”, “muscle”, “eye”, “heart”, “line-noise”, “channel noise”, and “other”; Pion-Tonachini, Kreutz-Delgado and Makeig, 2019b, 2019a). The experimenters can select the confidence threshold used to reject artifactual components from the signal, for each category.

However, while ICA is very sensitive and reliably reconstructs the signal after removing non-brain artifactual components on high-density data and relatively long data files (i.e., several minutes), it does not perform as well on low-density montages and small data segments, and cannot be used in real-time because of the necessary computation. This is because it combines information from different channels and needs a certain amount of data to “learn” the patterns of the signal. Furthermore, it was suggested that ICA-based methods were “less effective in removing transient, non-biological artifacts such as abrupt impedance changes due to headset motions and were computationally expensive and generally for offline analyses” (Chang *et al.*, 2018). This limitation is especially important for real-time EEG monitoring applications that

require fast processing and protection against these types of artifacts that occur more frequently with wearable systems compared to traditional stationary ones.

The artifact subspace reconstruction (ASR) method is an automatic, online-capable, artifact removal method that can address these issues (Kothe and Jung 2016). The main difference with ICA is that it identifies and utilizes clean portions of data to determine thresholds for rejecting components. ASR detects what is considered an artifact-free “reference” (or baseline) within the data using PCA, computes statistics on it, and then detects artifactual sections that lie a few standard deviations away from this reference EEG using a sliding window. The segments containing artifacts can then be rejected (Euclidian method) or reconstructed (i.e., Riemannian method; Blum *et al.*, 2019) to keep the relevant part of the signal (i.e., brain signal), reducing data loss. ASR was compared to ICA performance and found to be a powerful approach for both offline data analysis and online real-time EEG applications such as clinical monitoring and brain-computer interfaces (BCI; Chang *et al.*, 2018). This method has been validated and used in many studies (e.g., (Mullen *et al.*, 2015; Artoni *et al.*, 2017; Chang *et al.*, 2018, 2019; Blum *et al.*, 2019; Blum, Mirkovic and Debener, 2019). Thus this method seems promising for EEG studies using low-cost, low-density, wearable EEG headsets, as in this thesis project, and for future use in real-world or -time situations (e.g., BCI).

### **3.2.3. Advantages of low-cost wearable EEG systems**

While research-grade stationary systems offer the best signal quality, they are very expensive, time-consuming to set up, do not provide mobility to participants, and can reduce the subjects’ motivation to participate in a study. Consequently, most EEG studies are conducted on very small samples (e.g., < 20 participants), leading to poor statistical power and misrepresentation of interindividual differences and of the general population (graduate students from the laboratory constitute sometimes the majority of the sample since they are easier to recruit).

Low-cost wearable EEG systems address these issues and offer promising ground-breaking applications for both fundamental and clinical research (see Chapter 9, and Cannard *et al.*, 2020). While these systems offer lower signal quality from the inferior hardware capacities compared to research-grade ones, they allow scientists to collect large amounts of data in a shorter time. By easing the comfort, simplicity, and time of recording sessions, wearable systems allow researchers and clinicians to gain better access to populations that were previously harder to

include in studies due to lengthy uncomfortable experimental conditions such as children (Badcock *et al.*, 2015) or elderly populations (Abbate, Avvenuti and Light, 2014; Dimitriadis *et al.*, 2016; Neale *et al.*, 2017, 2017; Tilley *et al.*, 2017).

Most EEG research studies do not reflect the overall population, which is the basis of statistical inference. Large samples better capture the overall human population and can identify trends within these populations that are not visible in small samples. For instance, they can highlight more accurately the mediator role of covariables (e.g., age, gender, personality trait, education, etc.) on spectral EEG (e.g., Hashemi *et al.*, 2016). Better access to all populations is crucial for the future of neuroscience to better understand how demographic differences affect EEG activity and to develop therapies that are more specific and better suited to each individual accordingly. Both structural (i.e. anatomical) and functional (i.e. brain activity) differences in brain activity have been observed across different categories of the population (e.g. children, elderly, mental disorders, etc.; Reiss *et al.*, 1996; Schlaggar *et al.*, 2002; Bjork *et al.*, 2004; Paus, 2005).

Note that there is a large remaining gap, between identifying interactions between EEG and individual characteristics at the group level, and at the subject level (the group level finding tends to smooth interindividual differences or to filter it out). But the remaining trends are still very informative on important questions such as “how does spectral power change with age in the different frequency bands?” (e.g., Davidson, 1988; Carrier *et al.*, 2001; Morgan *et al.*, 2005; Vysata *et al.*, 2014). Furthermore, novel findings indicated that individuals could be differentiated from simple measures of spectral power, with as short as 30 seconds of resting-state data, and that this was robust over time (i.e., weeks; da Silva Castanheira *et al.*, 2021).

Large datasets, along with advancements in data storage and computing capacity can, in turn, be used to develop sophisticated machine learning or deep learning methods that render the detection and classification of mental states increasingly reliable and accurate (Wu *et al.*, 2017; Dea *et al.*, 2019; Golmohammadi *et al.*, 2019; Pedroni, Bahreini and Langer, 2019; Gurve *et al.*, 2020). See section 9.1. for more detail on Big-data and machine learning (ML). Recent findings suggest that mental states detection and classification can even be reliably performed with a single-EEG channel (Umar Saeed *et al.*, 2018; Arpaia *et al.*, 2020; Mahmoodi *et al.*, 2021).

These systems are also very valuable for longitudinal applications by allowing to measure the same participants several times more easily. Such studies are useful to assess EEG changes over

time. Furthermore, these systems can be more easily combined with additional physiological measures such as electrocardiography (ECG) and galvanic skin response (GSR) to improve the efficacy of identifying unique mental states (see section 8.4.6.; Ahn, Ku and Kim, 2019).

Another strength is the potential to conduct research in more ecological environments and during mobility. Conventional studies in psychology and cognition systematically use highly controlled sterile environments, artificial stimuli, and fixed response options, to remove unknown biases and isolate as much as possible the brain processes of interest. However, these unnatural settings may inevitably lead to findings that are less ecologically valid in relation to real-world behavior and therefore our understanding of the brain and its complex mechanisms in its natural state. New technologies may provide solutions to this conundrum by offering more mobility to participants, wireless streaming of data, and online artifact correction. Furthermore, most of these systems include motion sensors that can help reject EEG artifacts or study EEG activity related to movements. The gyroscope indicates the orientation of an object in space (along the x-y-z axes) and the accelerometer measures the acceleration in space (along the same 3 axes). Their sampling rates are similar to those of EEG (see our plugin that synchronizes EEG and auxiliary signal data in Annexe 1).

While dealing with artifacts during movements still presents challenges today (see section 8.4.2.), data from wearable EEGs have now been collected on participants walking outdoors on the university campus (Debener *et al.*, 2012), in classrooms (Stevens, Galloway and Berka, 2007; Bozkurt and Coskun, 2014), in urban and green space environments (Aspinall *et al.*, 2015; Jebelli, Hwang and Lee, 2017; Neale *et al.*, 2017; Tilley *et al.*, 2017; Hwang *et al.*, 2018; Jebelli *et al.*, 2018), or in domestic and office settings (Hu *et al.*, 2015). Additionally, the capacity to easily share EEG data on clouds can significantly increase sample size, data sharing, and real-time EEG monitoring, opening a diversity of new groundbreaking applications (see Chapter 9).

This may significantly improve our ability to tackle some of the major challenges of today's society (Zheng *et al.*, 2014) such as improving health care access and monitoring (Ghose *et al.*, 2012). For example, an electrocardiograph (ECG) is the most widely adopted clinical tool to diagnose and assess the risk of arrhythmia (i.e. a very common type of cardiovascular disease that may indicate an increased risk of stroke or sudden cardiac death). During patients' hospital visits, however, arrhythmias may not be detected on standard resting ECG machines since the

condition may not be present at that moment in time. And while Holter-based (hospital) portable monitoring solutions offer 24-48 h ECG recording, they lack the capability of providing any real-time feedback for the thousands of heart beats they record, which must be tediously analyzed offline. ECG acquisition, display, feature extraction, and beat classification can be done by wearable and modern innovations (Oresko *et al.*, 2010). An alert can even be set to contact a medical center/care provider in the event of a potentially threatening or imminent health emergency (Kumar, Aggrawal and Gupta, 2012).

Furthermore, measuring patients' vital signs at-home may result in individualized treatment protocols that incorporate continuous, detailed information about the patients' ongoing physiological status without having to transport a patient, which can be detrimental and costly (Muse *et al.*, 2017). While the application of wearable technologies was previously focused on physiological measurements (e.g. heart rate, step-counter), equivalent applications are now possible with EEG (see Chapter 9 for more discussion on real-world applications of wearable EEG technologies). Furthermore, many modern wearable EEG headsets are now comfortable to wear and incorporate elegant designs and are becoming increasingly attractive for the general public, making these applications more and more realistic (Nijboer *et al.*, 2015). These topics are discussed in more detail in Chapter 9.

While low-cost wearable EEG systems face several challenges to match state-of-the-art research-grade stationary systems, some of them meet the minimum hardware requirements (see section 3.1.), and hold immense potential.

## *Chapter 4. Well-being*

*This chapter defines well-being, its main dimensions, the relation between chronic stress and well-being, some important predictors and mediators of well-being, and some brain correlates of well-being.*

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### *4.1. The main dimensions of well-being*

Well-being has been an important target of empirical, developmental, clinical, and humanistic psychology and attempts to elevate human functioning (Jahoda, 1958; Maslow, 1968; Bradburn, 1969; Diener, 1984; Jung, 1985; Deci and Ryan, 2008). The philosophical roots of what constitutes happiness and well-being date back to the first human civilizations (Adams, Lamberg-Karlovsky and Moran, 1974; Aristotle, Irwin and Fine, 1995; Aristotle, 2000). Two fundamental dimensions have long been highlighted: the hedonic approach, which focuses on happiness and positive affect, defining well-being in terms of pleasure attainment and pain avoidance (Kahneman, Diener and Schwarz, 1999); and the eudaimonic approach, which focuses on self-realization or actualizing one's human potential, defining well-being in terms of the degree to which a person is fully functioning (Ryff, 1989; Waterman, 1993). In ancient views, the hedonic dimension considered humans starting as an empty organism that gains its meaning according to social and cultural experiences that have a positive or negative valence, whereas the eudaimonic dimension viewed humans starting with a predefined nature and their goal is to identify it to fulfill their potential (Deci and Ryan, 2008). These two views have given rise to large research bodies that are in some areas divergent and others complementary (Ryan and Deci, 2001).

Assessment tools such as questionnaires and rating scales turn theoretical and philosophical constructs into psychometric properties (i.e, measures allowing statistical descriptions and inferences). Measurement instruments play an important role in research, clinical practice and health assessment, by quantifying bodily or psychological characteristics of the individuals (Portney and Watkins, 2009; Souza, Alexandre and Guirardello, 2017). The usefulness of measurement in clinical research or practice helps with decision-making and measuring progress

during rehabilitation. Clinicians and researchers use multi-items questionnaires and scales to measure well-being, mental health, diagnose disease, or measure change over time in any of these measures. Since well-being is highly subjective, psychologists have traditionally used self-report questionnaires and scales (Wiggins, 1973) to assess subjective happiness, life satisfaction, and positive affect (i.e., the hedonic dimension). Hence, subjective well-being refers to the psychologist's perspective of hedonic WB. This approach values metacognition by taking into account the individuals' capacity to evaluate for themselves the degree to which they experience a sense of wellness and life satisfaction (Diener *et al.*, 1999; Livingston, 2003; Dunlosky and Metcalfe, 2008). Thus, subjective WB includes the individuals' cognitive evaluation of their conditions (metacognition).

Most of the existing knowledge up until the '90s focused almost solely on the hedonic dimension of WB. To address this issue, the Ryff model of psychological well-being (Ryff, 1989) was developed and identified six overlapping, key eudaimonic components of well-being (Figure 12). Following a subjective self-report approach, the new measures probed: 1) purpose in life (the extent to which respondents felt their lives had meaning, purpose, and direction); 2) autonomy (whether they viewed themselves to be living in accord with their convictions); 3) personal growth (the extent to which they were making use of their talents and potential); 4) environmental mastery (how well they were managing their life situations); 5) positive relationships (the depth of connection they had in ties with significant others); 6) self-acceptance (the knowledge and acceptance they had of themselves, including awareness of personal limitations). The Ryff model was validated and used in many different sociocultural contexts (Clarke *et al.*, 2001; Kafka and Kozma, 2002; Cheng and Chan, 2005; Lindfors, Berntsson and Lundberg, 2006; van Dierendonck *et al.*, 2007; Abbott *et al.*, 2010), and led to numerous studies and interventions aiming at better understanding psychological well-being and improving the human condition (Ryff, 2014). This novel perspective even had larger implications by expanding the definition of health from an absence of illness to also the presence of "something positive" (Ryff and Singer, 1998). Most measures were focusing their evaluations on static local outcomes for improvements in negatively-valenced symptoms and signs (Otto *et al.*, 2010).

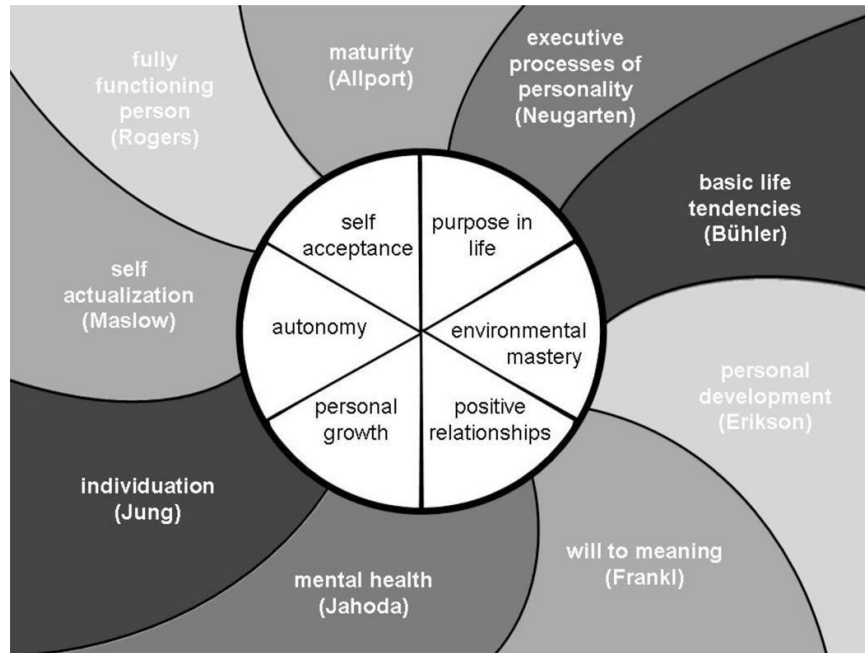


Figure 12. The 6-factor model of psychological well-being. Source: Ryff and Singer (2013).

#### 4.2. Stress and well-being

In absence of stress, there is a balance between the sympathetic and parasympathetic systems of the sympathetic nervous system (SNS), termed homeostasis (Cannon, 1929). However, stressful experiences are common throughout a human's life. Stress can be defined as a "state of threatened homeostasis or disharmony that must then be counteracted by an adaptive stress response, a complex array of physiologic and behavioral responses intended to re-establish homeostasis. The interacting hypothalamic-pituitary-adrenal (HPA) axis and the (SNS) are key regulatory centers with respective hormones that are influenced by a myriad of genetic, environmental, and developmental factors.

When a stressor occurs, the hypothalamus releases hormones that elicit the production of adrenocorticotrophic hormone (ACTH) from the posterior pituitary and the activation of the noradrenergic neurons of the locus coeruleus/norepinephrine (LC/NE) system in the brain (Tsigos and Chrousos, 2002). The ACTH then drives the production of cortisol from the adrenal cortex, whereas the LC/NE system is primarily responsible for the immediate "fight or flight". Under normal conditions, the production of CRH and ACTH fluctuate in a predictable circadian



cycle and are inhibited by high levels of blood cortisol via a negative feedback loop (Tsigos and Chrousos, 2002). Cortisol (and the general stress response) redirects cellular processes away from long-term metabolic processes and toward the immediate survival ones. The negative feedback loop is therefore designed to limit long-term exposure of tissues to these short-term catabolic and immunosuppressive actions (Tsigos and Chrousos, 2002). Excessive (trauma), prolonged (chronic stress), or inadequate activity of these systems leads to adverse health consequences (Wheaton, 1997; Tsigos and Chrousos, 2002).

Sources of acute stress are usually fairly obvious, but it is harder to identify the sources of chronic stress. There are four general categories of chronic stress: mental/emotional stress, sleep disorders, metabolic/glycemic dysregulation, and chronic inflammation (Wheaton, 1997). Grief, excitement, fear, anxiety, guilt, embarrassment all can trigger a robust HPA axis response. Also, events such as public speaking, performance evaluations, skydiving, or clinical appointments will drive up ACTH and cortisol in most individuals (Wheaton, 1997). Research has shown that the magnitude of the response and recovery to these stressors is based on the individual's perception rather than the stressors themselves (Bollini *et al.*, 2004). The four key factors that determine the magnitude of the HPA axis response to a mental/emotional stressor are its 1) novelty to the individual, 2) unpredictable nature, 3) threat to their person or ego, 4) sense of loss of control (Wheaton, 1997). Individual characteristics such as age, gender, hereditary predisposition, personality traits, and prenatal or early childhood experiences are also profoundly influential (Felitti *et al.*, 1998; Dong *et al.*, 2004).

“An implicit assumption of a high global well-being is that the individual can not only overcome stressors and negative affect but also flourish in his or her life course” (Fredrickson *et al.*, 2003). Resilience is the ability to bounce back or recover from stress and to show flexibility and adaptability to adverse life experiences (Tugade and Fredrickson, 2004; Smith *et al.*, 2008; Feder, Nestler and Charney, 2009), a key ability for long-term multidimensional well-being (Fredrickson *et al.*, 2003). Resilient individuals have been found to “use positive emotions to alleviate stress effects and show physiological differences in their ability to adapt to stress” (Tugade and Fredrickson, 2004; Otto *et al.*, 2010). Differences in adaptation to stress are associated with neural circuitry changes that, in turn, improve or reduce this adaptation capacity. The “broaden-and-build” model posits that positive emotions promote discovery of novel and creative actions, ideas, and social bonds, which in turn builds their physical, cognitive, social, and

psychological resources, “broadening their momentary thought-action repertoires” (Fredrickson, 1998, 2001). These resources serve as reserves that can be drawn on later to improve the odds of successful coping and survival. (Fredrickson, 2004). This model, influenced by positive psychology (Fredrickson, 2001), might explain the high covariance between the eudaimonic and hedonic dimensions (Waterman, Schwartz and Conti, 2008) despite the previous efforts to consider them as different dimensions of well-being with different psychometric properties.

### *4.3. Predictors and mediators of well-being*

A vast literature has evaluated how a variety of factors may mediate or modulate well-being over the past few decades.

Aging has been negatively associated with well-being in the later part of life through the decline in the sense of life purpose, autonomy, and personal growth (Ryff, 1989; Ryff and Keyes, 1995; Clarke *et al.*, 2000; Springer, Pudrovskaya and Hauser, 2011), whereas it is positively associated with progressing through the developmental tasks of adult life (Riediger and Freund, 2004; Ebner, Freund and Baltes, 2006). Realistic self-evaluation of aging predicts well-being, with individuals who feel younger than they are reporting higher well-being contrary to those who wish to be younger (Lachman *et al.*, 2008; Ward, 2010; Keyes and Westerhof, 2012).

Numerous individual trait differences have been investigated cross-sectional and longitudinal designs as mediators of well-being, including personality traits (often considered as heritable; Schmutte and Ryff, 1997; Staudinger, Fleeson and Baltes, 1999; Lucas and Diener, 2008), genetic predisposition (Keyes, Myers and Kendler, 2010), optimism (Ferguson and Goodwin, 2010), life management strategies (Freund, 2003), intentional activities (Sheldon and Lyubomirsky, 2006), empathy (Grühn *et al.*, 2008), emotional intelligence (Lopes, Salovey and Straus, 2003), and perceived independence (Abbott *et al.*, 2008).

Family role involvement promotes well-being (Ahrens and Ryff, 2006), whereas helping others seems to enhance purpose and self-acceptance more specifically (Greenfield, 2009; Schwartz *et al.*, 2009). Those who are consistently married have a well-being advantage compared to the

divorced, widowed, or never married, although single women score higher on autonomy and personal growth compared to married women (Bierman, Fazio and Milkie, 2006; Shapiro and Keyes, 2008). Parenting seems to enhance adult well-being, particularly if one's children are doing well (An and Cooney, 2006; Rothrauff and Cooney, 2008). Loss of a child in adulthood predicts impaired well-being decades later (Rogers *et al.*, 2008; Pudrovska, 2009), while loss of a parent in childhood predicts lower levels of multiple dimensions of adult well-being (Hailey Maier and Lachman, 2000). Adverse and stressful experiences in childhood compromise well-being through life (Shaw *et al.*, 2004; Greenfield and Marks, 2010), and parental warmth promotes well-being and a wide range of health and well-being outcomes (Pyatak *et al.*, 2014). Caring for an aging parent also reduces well-being, although less in women with high environmental mastery (Li, Seltzer and Greenberg, 1999).

Socioeconomic dimensions of WB have been extensively studied (Jurado and Perez-Mayo, 2012; Haq and Zia, 2013; Prilleltensky *et al.*, 2015). Education and employment are reliably associated with a lower likelihood of mental health problems and a higher likelihood of better physical health. Well-being is influenced by (and contributes to) career pursuit, income (Luhmann, Schimmack and Eid, 2011), and how work and family life interact (conflict between the two diminishes it, whereas positive overlaps support it). This component is affected by social roles and cultural differences (Keyes and Waterman, 2003; Carstensen *et al.*, 2011).

Well-being is significantly reduced by physical illnesses and disabilities (Schleicher *et al.*, 2005; Hickson *et al.*, 2008; Kashubeck-West and Meyer, 2008; Pusswald *et al.*, 2012), but having a life purpose can be protective against cognitive impairment, neuropathology, the risk for stroke, and myocardial infarction (Rafanelli *et al.*, 2012; Guidi *et al.*, 2013). Well-being is also strongly associated with physical health and health behaviors such as weight and the associated perceived discrimination (Carr and Friedman, 2005), physical activity (Hassmén, Koivula and Uutela, 2000; Edwards, Edwards and Basson, 2004; Svensson *et al.*, 2021), and sleep (Pilcher, Ginter and Sadowsky, 1997; Hamilton *et al.*, 2007). Higher well-being predicts better biological regulation as measured by the stress hormone, cortisol, and inflammation levels, or cardiovascular risk (Lindfors and Lundberg, 2002; Hayney *et al.*, 2003; Ryff, Singer and Dienberg Love, 2004). These relations were especially important when facing socioeconomic disadvantage or chronic conditions (Tsenkova *et al.*, 2007; Morozink *et al.*, 2010).

Meditation practice and training have been shown to improve well-being, response inhibition and self-regulation strategies, and to reduce stress and medical symptoms, as well as improvements in executive functions and emotion regulation (Carmody and Baer, 2008; Sahdra *et al.*, 2011; Brandmeyer and Delorme, 2016, 2020b). Additionally, intensive meditation training showed significantly greater telomerase activity and increased purpose in life outcomes (Jacobs *et al.*, 2011).

Well-being is also positively associated with connection with nature (Howell *et al.*, 2011; Russell *et al.*, 2013) and religious participation (related to higher levels of purpose and growth but lower levels of autonomy; Day, 2010).

Mental disorders are likely the strongest predictor, mediator, or outcome of low multidimensional well-being, including anxiety disorder, schizophrenia, major depression disorder (MDD), panic disorder, cyclothymia, agoraphobia, post-traumatic stress disorder (PTSD), or obsessive-compulsive disorder (Rafanelli *et al.*, 2000; Fava *et al.*, 2001; Keyes, 2002, 2005; Valiente, Cantero, *et al.*, 2011; Valiente, Provencio, *et al.*, 2011; Feder *et al.*, 2013). Before the COVID-19 pandemic, poor mental health was already a large and growing global problem, with 310 million (4.2%) suffering from depressive disorders, ~210 million (2.8%) people from major depressive disorders, and ~356 million (4.8%) from anxiety disorders in 2019 (Global Health Data Exchange, 2019). It is estimated that the global economy loses more than US\$ 1 trillion per year due to depression and anxiety (United Nation, 2020). Approximately 50% of all mental health conditions start by age 14 and can lead to suicide, the second leading cause of death in young people aged 15-29 (United Nation, 2020). People with severe mental conditions die 10-20 years earlier than the general population (United Nation, 2020). 76-85% of people with mental health conditions received no treatment in low- and middle-income countries (World Health Organization, 2021). Globally there is less than 1 mental health professional for every 10,000 people (United Nation, 2020).

During the COVID-19 pandemic, stress, social isolation, and violence in the family affect brain health and development in young children and adolescents (United Nation, 2020). Social isolation reduced physical activity and reduced intellectual stimulation increase the risk of cognitive decline and dementia in older adults (United Nation, 2020). Furthermore, mental health services had to reconvert their utilities to care for people with COVID-19, reducing the number of people

attending emergency mental health services (e.g., by 75% in Madrid). Mental health services had to adapt quickly to ensure the continuity of patients with severe conditions (e.g., transport to private clinics). Mental healthcare workers continued to work over the phone and home visits were organized for serious cases (United Nation, 2020).

A large study found that individuals who had low scores in multiple dimensions of well-being are at higher risk for a major depressive episode (Keyes, 2002). Only 16.6% of the population is thought to have perfect mental health, which corresponds to the presence of the positive and absence of the negative affect in all dimensions (Keyes, 2005). Psychiatric paradigms often define recovery as a reduction in symptoms or the absence of psychological distress. The presence of well-being is sometimes accompanied by reduced symptoms of these disorders. Moving beyond this formulation, studies in remitted patients with mood, anxiety, and panic disorders revealed significantly lower levels on multiple aspects of psychological well-being (Rafanelli *et al.*, 2000; Fava *et al.*, 2001).

Such findings clarify that complete recovery involves more than the reduction of distress; it must also include improvements in well-being, which in turn, highlights the need for therapeutic strategies focusing on positive outcomes (Fredrickson, 2004; Keyes, Dhingra and Simoes, 2010; Hou, Ng and Wan, 2014). The greatest advances have occurred in clinical intervention studies where improvements in well-being now constitute innovative new treatment targets needed to prevent relapse (Fava, Ruini and Belaise, 2007).

Multiple studies document long-term treatment benefits associated with well-being therapy (Fava *et al.*, 2004, 2005; Ruini and Fava, 2009). Other psychiatric interventions have employed measures of well-being to validate the effectiveness of diverse treatment programs (Hoen, Thelander and Worsley, 1997; Bell *et al.*, 2004; Hart *et al.*, 2005; Penn *et al.*, 2011). Studying well-being on non-clinical populations can be useful to provide estimates of optimal well-being to which clinical populations might aspire, and what factors might help each individual reach these targets (Milliar *et al.*, 2008; Ruini *et al.*, 2009). Interventions have been extrapolated beyond the clinic to school and workplace settings to enhance well-being to prevent mental illness and promote resilience (Ruini *et al.*, 2006; Milliar *et al.*, 2008).

Furthermore, changes in mental health can predict future mental illness, making it a useful tool to prevent and protect individuals from developing mental illness before the symptoms are serious (Keyes, Dhingra and Simoes, 2010).

#### *4.4. Well-being and the brain*

All these factors mediate not only well-being but also shape the structure and function of our brains throughout the lifespan, which in turn, can mediate well-being levels. While progress has been made recently regarding our understanding of the direct relationships between well-being and the brain, much is still unknown (Dolcos, Moore and Katsumi, 2018). By identifying brain correlates of well-being, wearable neurotechnologies will improve the detection, prediction, and treatment of poor mental health and low well-being, in an affordable manner.

##### **4.4.1. Functional Magnetic Resonance Imaging (fMRI) and well-being**

Structural MRI results indicated that psychological (eudaimonic) well-being is positively correlated with insular cortex volume (bilaterally), which is involved in many high-order functions (Lewis *et al.*, 2014). fMRI findings showed differences in amygdala activation in response to negative relative to neutral stimuli, corresponding to increased activation in people that were faster to evaluate negative information (van Reekum *et al.*, 2007). Interestingly, individuals with high well-being were slower to do this task and showed reduced activation, and increased ventral anterior cingulate cortex (vACC) activation. Another study showed that people with higher well-being and lower cortisol levels had sustained activity in the striatum and dorsolateral prefrontal cortex (dLPFC) while viewing positive stimuli (Heller *et al.*, 2013).

Together, these findings suggest that sustained engagement of reward circuitry during a positive event may underlie the phenomenology of well-being, and the regulation of the hypothalamo-pituitary-adrenal (HPA) axis (see section 4.2.; Smith and Vale, 2006). This goes along with a large body of literature on adaptation to stress and associated neural circuitry changes (Charney, 2004; Feder, Nestler and Charney, 2009; Stein, 2009).

While the gap remains in the neural mechanisms of well-being, there is a clear link between anxiety, depression, and low well-being, and the mechanisms of these mental disorders are much more understood thanks to animal studies implementing advanced invasive cellular, deep recording, optogenetics, pharmacological techniques.

For example, recent discoveries have highlighted the critical role of the lateral habenula (LHb) in regulating negatively motivated behavior in the context of depression and anxiety (e.g., Hu *et al.*, 2020). The LHb (“the brain's antireward centre”) receives information from the deep limbic and basal ganglia structures, and targets all midbrain neuromodulatory systems (i.e., noradrenergic, serotonergic, and dopaminergic) that then modulate both cortical and autonomous nervous systems (sympathetic and parasympathetic). Thus, the LHb is considered a “hub that integrates value-based, sensory and experience-dependent information to regulate various motivational, cognitive and motor processes” (Hu *et al.*, 2020). Its dysfunction is associated with psychiatric disorders and major depression.

Neural mechanisms underlying internal defensive states (i.e., fear activation or extinction) also seem crucial to understand anxiety. Fear and anxiety seem to be mediated by local microcircuits in the deep limbic regions (e.g., stria terminalis, lateral septum, ventral tegmental area, basolateral amygdala) and the prefrontal cortex, and brain-wide distributed network involving long-range projections (Tovote *et al.*, 2015). Inhibition of these circuits (that are known to also mediate positive and negative valence) dampens the fear and anxious response (Tovote *et al.*, 2015).

Importantly, these deep subcortical structures (limbic system, habenula complex) modulate the cortical areas involved in well-being (i.e., ACC, PCC, dLPFC) and inhibit the circuits underlying anxiety, both through dopaminergic modulation. This is confirmed by animal studies showing that DA inhibition increases anxiety, loss of motivation, anhedonia, helplessness, and other depressive-like behaviors. Similarly in Parkinson’s disease, DA agonists increase the quality of life and reduces anhedonia (e.g., Thobois *et al.*, 2013; Scheffer *et al.*, 2021).

#### **4.4.2. EEG: Alpha oscillations (context)**

Alpha oscillations are the dominant oscillatory feature of the EEG measured in a human brain, contained within the 8-13 Hz range for most individuals, and were the first EEG oscillations ever recorded in 1929 (Berger 1929). Their large amplitude is typically observed over posterior regions when the eyes are closed, but it can also be recorded across widespread scalp regions (Kellaway, 1979). Alpha rhythms are blocked (i.e., large reduction in amplitude) by eye-opening, drowsiness, and moderate-to-difficult mental tasks (Nunez, Wingeier and Silberstein, 2001).

Alpha oscillations were therefore initially considered by first researchers as an occipitoparietal rhythm due to the eyes closed/open phenomenon and considered it as a single phenomenon. However, alpha oscillations present both local and global dynamics, different activity between lower and upper alpha frequencies (Nunez, Wingeier and Silberstein, 2001), and large differences across individuals (Klimesch *et al.*, 1990; Klimesch, 1997, 1999).

Via its functional properties of inhibition and timing, alpha oscillations are thought to reflect the most basic cognitive and attentional processes (suppression and selection) that enable the ability to be consciously oriented in the spatiotemporal context. The rhythmic changes of alpha oscillations reflect the rhythmic changes in the synchronous activity of populations of neurons (Klimesch, 2012). “Phase-reset” (synchronous change in time and direction of phase) is a powerful mechanism for the timing of cortical processes (Klimesch, Sauseng and Hanslmayr, 2007).

Some sub-rhythms of the alpha range are widely distributed while others are more localized, with interactions with activity in other frequencies (Nunez, Wingeier and Silberstein, 2001). For example, spatially coherent global alpha dynamics increase during cognitive tasks for both upper theta (6.5 Hz; Figure 13, upper row) and upper alpha (10 Hz; Figure 13, lower row), whereas it decreases for lower-alpha. A decrease in upper alpha coherence (10-12 Hz) is also associated with decreased gamma coherence (38-40 Hz) in sensorimotor regions during movement preparation (Andrew and Pfurtscheller, 1996).

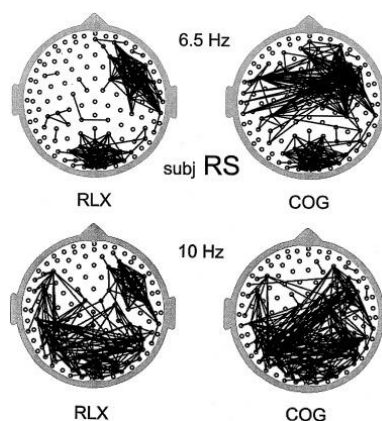


Figure 13. Dura image interelectrode coherence during relaxation (left) and a cognitive task (right) over 5 min (one subject). Lines show genuine interelectrode coherence at the 95% confidence interval (not affected by volume conduction) between electrode pairs excluding nearest neighbor electrodes. Coherence increased during the cognitive task for both upper theta (6.5 Hz; upper row) and upper alpha (10 Hz; lower row), whereas lower-alpha coherence decreased (not shown). Source: Nunez, Wingeier and Silberstein (2001).



### The individual alpha frequency (IAF)

The individual alpha frequency (IAF) refers to the dominant frequency within the alpha power distribution and is suspected (by some researchers) to reflect the dominant neural circuits that generate alpha oscillations (Klimesch, 1999; Corcoran *et al.*, 2017). Using the IAF to examine alpha activity is thought to better account for interindividual differences compared to the traditional, predefined, 8-13 Hz band because a large portion of individuals has alpha oscillations out of these bounds (W. Klimesch *et al.*, 1990; Klimesch, 1997, 1999; Haegens *et al.*, 2014; Mierau, Klimesch and Lefebvre, 2017). IAF estimates are considered a trait-like characteristic of the human EEG (Grandy *et al.*, 2013), have high heritability (Smit *et al.*, 2006), and have good test-retest reliability (Näpflin, Wildi and Sarnthein, 2007).

The IAF increases between 3 and 10 years old, while delta activity decreases up until 25-30 years of age (Niedermeyer, 1999), a time when myelination of cortico- cortical fibers is nearly complete (Courchesne, 1990). The IAF decreases with age (Klimesch, 1997; Hashemi *et al.*, 2016; Corcoran *et al.*, 2017; Finley *et al.*, 2020), or with hyperventilation and some drugs and alcohol (Kiloh, McComas and Osselton, 2013). In adults, a resting IAF lower than 8 Hz is considered abnormal (except for very old individuals; Nunez, Wingeier and Silberstein, 2001). Lower IAF values are associated with decreased cortical arousal (Portnova *et al.*, 2020) and traumatic brain injury (Angelakis, Lubar and Stathopoulou, 2004), whereas higher IAF is associated with cognitive performance (Rathee *et al.*, 2020). IAF can detect trait and state differences in cognitive preparedness and is affected by cognitive tasks (Angelakis *et al.*, 2004; Angelakis, Lubar and Stathopoulou, 2004).

The traditional approach to estimate IAF is to use the peak alpha frequency (PAF; frequency within the alpha band with the highest power). While this technique has been extensively used for the study of cognition (Klimesch, 1999; Angelakis *et al.*, 2004; Rathee *et al.*, 2020), it does not perform well with a portion of the population that have ambiguous alpha peaks, “split alpha peaks” (i.e., several peaks within the alpha band), or no alpha peak (see Figure 14; Anokhin and Vogel, 1996; Chiang *et al.*, 2008, 2011).

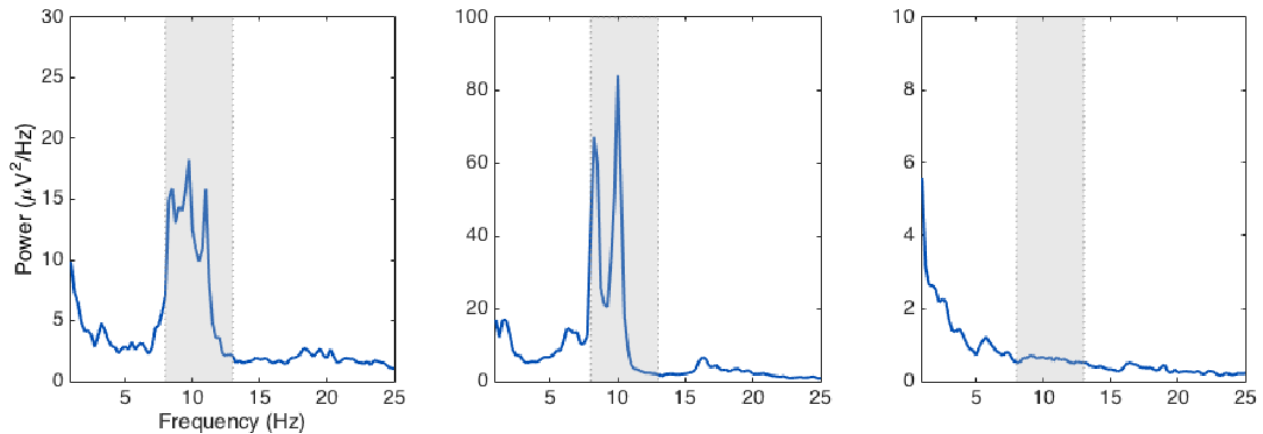


Figure 14. Illustration of ambiguous alpha peaks (left), “split” peaks (middle), and absent peaks (right). These problematic cases occur naturally in a large proportion of the population and lead to poor estimation of peak alpha frequency (PAF) for these individuals. Source: Corcoran *et al.* (2017).

Initial techniques to estimate the PAF relied on visual and manual inspection (Klimesch *et al.*, 1990) or cross-frequency assumptions (Klimesch *et al.*, 1998; Klimesch, 1999; Posthuma *et al.*, 2001). These methods were very time-consuming and prone to subjective judgment error. Novel automated methods have now been developed to avoid these limitations and implement a novel approach called the alpha center of gravity (CoG), which considers the shape of the whole alpha power distribution and is thought to provide a more accurate summary of the underlying alpha activity. The “channel-based method” (CRB; Goljahani *et al.*, 2012; Goljahani, Bisiacchi and Sparacino, 2014) is well suited for event-related EEG, whereas other statistical curve-fitting and clustering techniques are particularly adapted to IAF-estimation of continuous EEG data (Chiang *et al.*, 2008, 2011; Lodder and van Putten, 2011, 2013; Van Albada and Robinson, 2013; Corcoran *et al.*, 2017). These algorithms have been implemented in a fast, reliable, open-source toolbox operating in MATLAB and Python (Corcoran *et al.*, 2017), easing the fast estimation of this spectral measure on large datasets while reducing subjective judgment error of the experimenter.

### Local-global alpha dynamics

Local alpha may be partly but not fully isolated, with fractal dynamics at smaller spatial scales (e.g., down to the minicolumn scale; Nunez, Wingeier and Silberstein, 2001). While different modules do different things, they also interact to give rise to a “unified conscious scene and to

unify behaviors (they are integrated)” (Nunez, Wingeier and Silberstein, 2001). “Global alpha” refers to the widespread distribution of alpha power measured at all electrode sites over the scalp (see Figure 15; Florian, Andrew and Pfurtscheller, 1998; Nunez, Wingeier and Silberstein, 2001). The global alpha activity reflects high alpha coherence over large interelectrode distances (e.g., 10-25 cm) independent of volume conduction effects, in both resting state or cognitive tasks (see Figure 6 and Figure 13; Nunez, 2000).

Global alpha reduces in older individuals as well as in patients with neurological disorders (dominantly recorded in clinical settings) compared to healthy young people (Nunez, Wingeier and Silberstein, 2001). Global coherence increases with brain maturation in children and young adults (Srinivasan, 1999; Niedermeyer and Silva, 2020). Larger coherence amplitude was observed in the posterior area in children compared to young adults, whereas coherence in young adults shows lower amplitude and longer ranges between anterior and posterior areas (10-25 cm distances). “Raw” spectral amplitude alpha, therefore, better captures the global alpha dynamics that can be recorded at nearly all electrode sites, whereas higher-spatial resolution methods (e.g., dura image) better capture the local dynamics and processes (see Figure 5 and Figure 15).

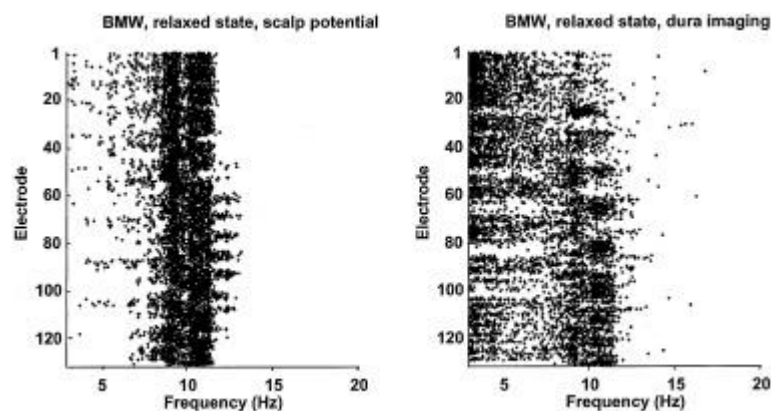


Figure 15. Illustration of global (widespread) alpha power recorded over all electrodes during rest (typical subject) with both scalp power (left) and dura image power (right). Source: Nunez, Wingeier and Silberstein (2001).

In sum, scalp alpha oscillations reflect the most basic cognitive and attentional processes, and to rely on large-scale processes (Hindriks, van Putten and Deco, 2014) supported by delayed network interactions (Cabral *et al.*, 2014), and to build on slower and more global inhibitory processes (Klimesch, Sauseng and Hanslmayr, 2007; Womelsdorf *et al.*, 2014), that may rely on

long-range cortico-cortical myelinated fibers (Nunez, Wingeier and Silberstein, 2001). These key functional properties are thought to reflect top-down, inhibitory processes that are necessary for cortical synchronization and timing of cortical processings required for any brain function (Laufs *et al.*, 2003; Oakes, 2004; Klimesch, Sauseng and Hanslmayr, 2007; Mathewson *et al.*, 2011; Klimesch, 2012; Scheeringa *et al.*, 2012). Global alpha may facilitate the synchronization of local rhythms across regions (Nunez, Wingeier and Silberstein, 2001). These global effects are suspected to influence local dynamics with top-down mechanisms (Nunez and Srinivasan, 1993), and are thought to involve intermediate- and long-range cortico-cortical interactions (Nunez, Wingeier and Silberstein, 2001).

Thus, different estimates of alpha activity can be obtained depending on the method used to measure it. Spatial filtering methods like the dura image will better reflect the combination of local dynamics contributing to the global dynamics, whereas traditional scalp amplitude measures will better capture the global coherent dynamics (see Figure 5 and Figure 15). Measuring alpha oscillations with scalp EEG amplitude signal focuses on the widespread alpha activity reflective mostly of global, coherent, synchronous activity measured at all electrode sites, that influences top-down local dynamics. Note also that longer epochs provide more stable estimates of global (widespread) alpha activity by masking short time fluctuations, and should be favored for scalp EEG analysis targeting these widespread alpha dynamics.

Scalp alpha EEG constitutes therefore a promising candidate for frequency analyses using low- and sparse-density EEG systems that cover only a few areas of the scalp (as long as local processes and spatial sources are not the purposes of the study).

#### **4.4.3. Alpha asymmetry**

A spectral measure that has been widely used to evaluate participants' attentional, motivational, and emotional processes is frontal alpha asymmetry (FAA, also called EEG asymmetry; (Davidson, 1988; Coan and Allen, 2003, 2004; Allen and Kline, 2004; Harmon-Jones, Gable and Peterson, 2010; Scherer and Ekman, 2014; Allen and Reznik, 2015; Smith *et al.*, 2017). FAA refers to the relative difference in alpha power (8-13 Hz) between the right and the left frontal regions.

Because alpha oscillations are known to functionally inhibit regional cortical activity (see the previous section; Oakes, 2004; Laufs *et al.*, 2006; Mathewson *et al.*, 2011; Scheeringa *et al.*, 2012), and asymmetries in alpha power have been observed between the two hemispheres, authors have

associated an increased alpha activity in one hemisphere with a decrease in brain activity or allocation of cortical resources in the same hemisphere (Davidson *et al.*, 1990; Cook *et al.*, 1998; Davidson, 1998; Allen and Kline, 2004). These observations have led to the emotional valence and motivational models of alpha asymmetry (Wheeler, Davidson and Tomarken, 1993; Tomarken and Davidson, 1994; Thibodeau, Jorgensen and Kim, 2006), where relatively greater left than right alpha power is associated with the relatively greater right than left cortical activity. In turn, greater activation of the left-frontal cortex relative to the right is related to approach motivation and emotions with positive valence (e.g., happiness, positive urgency), whereas greater activation of the right-frontal cortex relative to the left is associated with the brain processes related to avoidance motivation and negative emotional valence (e.g., depression, anxiety). These observations led to a large body of literature on the valence and motivational models of FAA (e.g., Coan and Allen, 2003, 2004; Allen and Kline, 2004; Thibodeau, Jorgensen and Kim, 2006; Harmon-Jones, Gable and Peterson, 2010; Allen and Reznik, 2015).

These models highlight that processes underlying approach motivation and positive affect are associated with relatively greater cortical activity in the left frontal area compared to the right, which in turn, is inversely correlated with alpha power (i.e., greater right than left alpha power in these areas). Inversely, emotional processes related to avoidance motivation and negative affect are associated with the relatively greater right than left frontal cortical activity (corresponding to the greater left than right frontal alpha power). Extreme approach-oriented traits and behaviors include for example positive urgency (i.e., the tendency towards rash action in response to extreme positive emotional states (Tomarken and Davidson, 1994), sensation-seeking (Santesso *et al.*, 2008), and high reward sensitivity (Pizzagalli *et al.*, 2005), whereas avoidance-related traits and behaviors include depression and anxiety (Thibodeau, Jorgensen and Kim, 2006; Allen and Reznik, 2015), shy temperament (Fox *et al.*, 1995), negative dispositional affect (Tomarken and Davidson, 1994), and poor regulation of negative emotions (Jackson *et al.*, 2003). These models align with the clinical literature showing that lesions in the left frontal area are associated with depression symptoms (Robinson and Price, 1982; Harmon-Jones, Gable and Peterson, 2010).

EEG asymmetry is considered to reflect the trait variable related to various psychological constructs and predictive of future emotional behavior or psychopathology when measured during rest (e.g., Wheeler, Davidson and Tomarken, 1993; Davidson, 1994; Sutton and Davidson,

1997; Hagemann *et al.*, 1999; Stewart *et al.*, 2010; Nusslock *et al.*, 2011; Papousek *et al.*, 2012), whereas it reflects the state variable when measured as an event-related response (e.g., Coan, Allen and Harmon-Jones, 2001; Harmon-Jones and Sigelman, 2001; Harmon-Jones, 2004). Some authors estimated that 60% of the variance in asymmetry measure within a resting session is due to traits influence, and the 40% to state influences (Hagemann *et al.*, 2002). The first approach aims to reduce state-related influences by reducing the situational variable (i.e., environmental factors that can unintentionally affect the results of a study; Coan, Allen and McKnight, 2006), whereas the second approach aims to increase them by eliciting emotions or states through the presentation of stimuli. In this study, we focus on the first approach, that is, the trait asymmetry related to subjective well-being levels.

Going one step further, investigators using EEG source-localization techniques (Laufs *et al.*, 2003; Pizzagalli *et al.*, 2005; Mantini *et al.*, 2007; Koslov *et al.*, 2011; Gable *et al.*, 2015; Smith, Cavanagh and Allen, 2018) found that frontal asymmetries originate from the dorsal frontoparietal network (dFPN), the inferior frontal gyrus, and the right dorsolateral prefrontal cortex (dlPFC; which is part of the dFPN). These results led them to suspect that frontal asymmetries reflect the integrity of the supervisory system, which is theorized to generate effortful constraint and self-control (Sutton and Davidson, 1997; Cacioppo, Tassinary and Berntson, 2007; Gable *et al.*, 2015). Gable and colleagues (2015) suspected that the alpha asymmetry is driven by the activity of this supervisory control system, supposedly located in the right frontal area (Gable *et al.*, 2015).

Frontal asymmetries may also reflect other associated executive control mechanisms, which play an essential role in allocating attention towards a goal and inhibiting interference from distractors (Corbetta, Patel and Shulman, 2008; Grimshaw and Carmel, 2014; Gable *et al.*, 2015). In this view, termed the asymmetric inhibition model, mechanisms in the left frontal cortex would inhibit negative distractors, whereas mechanisms in the right frontal cortex would inhibit positive distractors. Consequently, asymmetric aberrations in these systems result in bottom-up and top-down dysfunction, such as difficulty in disengaging attention from negative/avoidance-motivation information result in depression and anxiety (Eysenck *et al.*, 2007; Shackman *et al.*, 2009; Cisler and Koster, 2010; De Raedt and Koster, 2010; Engels *et al.*, 2010; Gotlib and Joormann, 2010; Kim *et al.*, 2012; Gable *et al.*, 2015), whereas difficulty in inhibiting

positive/approach-motivation distractors results in addiction and positive urgency behaviors (Bechara, 2005; Garavan and Hester, 2007; Goldstein and Volkow, 2011).

It is important to note the clear link between these processes and structures underlying alpha asymmetry and those highlighted in invasive studies examining the brain mechanisms of mental disorders (see beginning of this section 4.4.). Interestingly, these structures and networks (limbic system, prefrontal cortex, habenula complex) that lead to mental disorders when dysfunctioning show interhemispheric asymmetries (e.g., Ahumada-Galleguillos *et al.*, 2017; Gutiérrez-Ibáñez *et al.*, 2011; Bianco and Wilson, 2008), suggesting they are likely to be involved in generating EEG asymmetries.

Thus, multiple lines of research demonstrate that the mechanisms underlying alpha asymmetry measurements are highly implicated in processes that contribute to well-being (positive/negative affect, self-control, focused attention for conduction of daily tasks, capacity to fulfill one's potential and life goals, etc.). Only one study to our knowledge assessed the direct relationship between alpha asymmetry and well-being and found that participants reporting higher levels of both eudaimonic and hedonic well-being showed greater left than right frontal activation in response to emotional stimuli (Urry *et al.*, 2004). The authors suggested that the effect was driven by the eudaimonic dimension of well-being specifically.

EEG asymmetry seems like a good candidate measure for wearable EEG systems, as it involves very simple calculations (alpha power of the left channel subtracted from the right one) and just a few channels covering frontal regions of each hemisphere. Wearable EEG systems have been used extensively over the past few years to measure frontal asymmetry, suggesting this measure is well-suited for these technologies (Peng *et al.*, 2011; Hu *et al.*, 2015; Hashemi *et al.*, 2016; Jebelli, Hwang and Lee, 2017; Wu *et al.*, 2017; Zhao *et al.*, 2017; Hwang *et al.*, 2018; Umar Saeed *et al.*, 2018; Cao *et al.*, 2019; Arpaia *et al.*, 2020; Park, Han and Im, 2020; Saeed *et al.*, 2020; Apicella *et al.*, 2021).

To conclude this section on well-being and the brain, by identifying the neural correlates and predictors of well-being, as well as finding measures to capture changes in well-being, we will better understand the mechanisms that underlie higher levels of well-being, and in turn, develop promising interventions aiming at helping people live happier and more fulfilling lives (Dolcos, Moore and Katsumi, 2018). Attentional and inhibitory impairments are thought to be crucially

associated with an increased vulnerability to depressive episodes and cognitive vulnerability (De Raedt and Koster, 2010). Alpha asymmetry seems to play an essential role in understanding the neural networks underlying global top-down mechanisms involved in well-being, such as executive functions, attention, perception, and emotion regulation.





## Part II

## *Research goals of the thesis project: three studies*

- Validate a scale to rapidly measure multidimensional well-being, and use it to capture the main dimensions of well-being and associated predictor variables in a large sample (study 1: Chapter 5).
- Validate a low-cost wearable EEG system for collecting spectral signals relevant to the study of well-being, i.e., the individual alpha frequency and alpha asymmetry (study 2: Chapter 6).
- Validate an existing, open-source, automatic artifact rejection method to preprocess large EEG datasets collected with this wearable system (study 3: Chapter 7).
- Use all these methods to examine the EEG correlates of well-being in a large sample (study 3: Chapter 7).

# *Chapter 5. Validating a quick scale to measure multidimensional well-being*

*In this chapter, we test the feasibility of using a short visual scale to reliably capture multi-dimensional well-being in a large sample, and identify some predictors of well-being, in a large sample.*

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## *5.1. Introduction*

### **5.1.1. Objective vs. subjective measures**

Scientific reasoning can only be as strong as the measures. Essential components of psychometric properties include validity (the degree to which an instrument measures the construct it purports to measure), reliability (the degree to which the measurement is free from measurement error), responsiveness (the ability of an instrument to detect change over time in the construct to be measured), and interpretability (the degree to which one can assign qualitative meaning to an instrument's quantitative score).

The routine use of self-reported subjective measures and the quest for homogeneity across the well-being items have been suggested to lead to a lack of sensitivity on clinical outcomes, contrary to the clinimetric criteria used in conventional clinical measures (Ryff and Singer, 2013). Following these criticisms, efforts were made to make well-being scales more robust (Fava *et al.*, 1998; Tomba *et al.*, 2010; Tomba and Bech, 2012). For example, Fava and Colleagues developed a clinimetric, psychotherapeutic, interview version of the Ryff model (Fava and Tomba, 2009).

However, many authors highlighted that some psychometric self-rated scales often display relevant clinimetric properties and that clinimetrics measures do not always reflect the perceived well-being of the individual by using pre-selected items of physical and emotional health (e.g., the SF-36; Ware and Sherbourne, 1992). A variable can negatively affect one individuals' well-being, but not another (e.g., someone might experience chronic pain but still be happy because they are coping well with the pain). While clinimetrics are useful to differentiate sick from healthy

individuals, they do not take into account degrees of well-being by focusing on a diagnostic approach, that is the presence or absence of disease.

Thus, some authors suggested that they might be less efficient at assessing benefit/risk ratio compared to measures capturing the full scope of an individual's quality of life, which are also better suited for applications aiming at optimizing well-being in all individuals (Paterson, 1996; Paterson and Britten, 2000; Bell *et al.*, 2002). Furthermore, understanding well-being and its factors concern not only patients (reducing symptoms) but also non-patients (elevating or optimizing well-being).

### **5.1.2. Multi-items vs. single-item global scales/questionnaires**

Whole systems practices (e.g., traditional Chinese medicine, Ayurveda, naturopathy) focus on the whole person indicators of health, including the experienced global well-being (Bell *et al.*, 2003; Ritenbaugh *et al.*, 2003; Verhoef *et al.*, 2004, 2005; Otto *et al.*, 2010). In this approach, the roles of multiple subsystems are assessed concurrently and in relation to each other (symptom patterns, dynamics of symptom and illness change) providing an individualized, global measure, such as a change in global health or well-being status (Jonas and Chez, 2004; Koithan *et al.*, 2007; Otto *et al.*, 2010). Patients commonly report “non-specific” effects of treatment that are distinct from the targeted ones (e.g., pain relief), such as an increase in self-reported positive affect and global well-being (Bell *et al.*, 2002, 2003; Verhoef, Casebeer and Hilsden, 2002; Paterson and Britten, 2003; Verhoef *et al.*, 2004, 2006; Paterson, 2006; Paterson *et al.*, 2009). Well-being is now generally considered as a complex multidimensional construct that encompasses multiple dimensions and is defined as the experience (hedonic dimension) and function (eudaimonic dimension) of life (Bell *et al.*, 2004; Fredrickson and Losada, 2005; Waterman, Schwartz and Conti, 2008; Tuason, Güss and Boyd, 2021).

Long questionnaires can have negative effects on both response rates and the quality of those responses, especially towards the later parts of the surveys where participants seem to give very similar responses compared to the rest of the questionnaire (Herzog and Bachman, 1981; Eisele *et al.*, 2020). Similarly, designing questionnaires that are respondent-friendly (i.e., avoiding difficult questions) significantly improves response rates and quality (Dillman, Sinclair and Clark, 1993). Furthermore, multi-item questionnaires are considered by some researchers to limit the

individual's capacity to provide an accurate subjective response by providing only a few predefined response options to the participants.

Brief global rating scales are shorter versions of long questionnaires that summarize many items into fewer scales to provide a rapid assessment of the different dimensions. Brief rating scales address these issues and have been used for a long time in clinical research (Overall and Gorham, 1962; Marks and Mathews, 1979; Derogatis and Melisaratos, 1983; Morlan and Tan, 1998; Faustman and Overall, 1999; Østergaard *et al.*, 2014). Interestingly, many studies suggest that self-rated global health status is an even better predictor of mortality and health care needs, compared to traditional objective measures (e.g., physician examinations and assessments; Idler and Kasl, 1991; Idler and Benyamini, 1997; Bath, 1999; Menec, Chipperfield and Perry, 1999). Self-rated reports might reflect mediator variables that can be missed by multi-items scales (if not present in the response options), but not by the individual self-report. A global subjective self-report allows each individual to weigh the importance of each specific item or function for him/herself on quality of life scale. Subjective self-report might capture complex and unknown components of health relying on participants' metacognition (the ability to self-reflect and think about our thoughts; Flavell, 1979), which are not captured by questionnaires.

Furthermore, they are quick to administer in both clinically ill and non-clinical healthy populations. Reducing the participants' burden is especially relevant for populations that are harder to study like children, the elderly, and patients (Volpe and Dupaul, 2001; Briesch *et al.*, 2021). They also ease the tracking of overall well-being changes or intervention progress over time (longitudinal studies).

Disagreement still exists regarding whether multiple items should be monitored and assessed separately or jointly (e.g., composite indices). Keeping track of trends in many separate sub-components can be challenging for experimenters when there are too many indicators (Maasoumi and Yalonetzky, 2013). Furthermore, even when just a few dimensions are involved, one may be interested in computing measures of multidimensional WB that take into account the joint distribution of indicators in the population (Maasoumi and Yalonetzky, 2013).

Hence, brief global rating scales are well-suited for studying EEG correlates of well-being on large datasets when combined with wearable EEG systems, as well as for real-world applications (e.g., individuals can easily self-report from home in a few minutes compared to using a long

survey). Thus, they are of particular interest for interventions aiming at optimizing well-being or preventing negative outcomes using EEG tools (Baldwin *et al.*, 2002).

### **5.1.3. The Arizona integrative outcomes scale (AIOS)**

Bell *et al.* (2004) developed the AIOS, a global rating scale designed to rapidly capture the full picture of an individual's self-reported multidimensional well-being (Bell *et al.*, 2004), including the global sense of physical, social, psychological, affective, and spiritual well-being. It measures these dimensions jointly into a one-item visual, horizontally-displayed scale, over the past 24 hours (AIOS-24h) and the past month (AIOS-1m).

The AIOS was able to discriminate unhealthy individuals from healthy individuals in a rehabilitation outpatient clinic sample ( $N = 100$ ; Bell *et al.*, 2004, substudy 1). The AIOS correlated moderately and significantly with global health (and this association was stronger for the non-patients). The AIOS was inversely related to psychological distress measured by the Brief Symptom Inventory (BSI; Derogatis and Melisaratos, 1983) in undergraduate college students ( $N = 458$ ; Bell *et al.*, 2004, substudy 2). In another sample of undergraduate students ( $N = 62$ ; Bell *et al.*, 2004, substudy 3). The AIOS was positively associated with positive affect (20-item PANAS; Watson, Clark and Tellegen, 1988) and positive states of mind (PSOMS) and negatively associated with negative affect. The PSOMS measures “the individual's ability to achieve and appreciate positive experiences over the past 7 days, as a summation measuring focused attention, productivity, sharing, responsible caretaking, restful repose, sensuous nonsexual and sexual pleasure” (Bell *et al.*, 2004). Positive and negative affect and psychological distress explained 37% of the variance in AIOS-24h, and 57% of AIOS-1m, with PANAS as a stronger predictor. Additionally, Otto and colleagues (2010) found that positive and negative affect and physical health were correlated with the AIOS (Otto *et al.*, 2010).

Controls (*Pearson correlation*  $r = 0.64$ ) had a higher correlation between the AIOS 24-hour and 1-month forms than did the patients ( $r = 0.33$ ), indicating convergent validity for controls (stability of well-being over time), and capacity to measure improvement in the patients' condition over the previous 30 days in rehabilitation (i.e., large changes in well-being). Convergent validity was also indicated by a more recent study (Tuason, Güss and Boyd, 2021) that found a significant correlation ( $N = 1240$ ;  $r = .58$ ) between AIOS and another popular 8-item scale of

multidimensional well-being based on the biopsychosocial model of health (Engel, 1981; Diener *et al.*, 2010).

Another study (Paterson, 2006) showed the validity of the AIOS to measure self-concept (an important outcome for many interventions targeting people with long-term conditions) and that it was sensitive to changes in self-concept over time (sensitivity refers to the capacity to identify true positives, e.g., sick people correctly identified as sick). However, it lacked specificity (i.e., capacity to identify true negatives, e.g., healthy people correctly identified as healthy). Furthermore, an absence of ceiling effects was observed (Bell *et al.*, 2004), meaning the scale allows the potential for large degrees of improvement in self-rated well-being above and beyond the relative lack of diagnosed health problems (i.e., optimizing well-being in non-patient populations). Studies with larger and more diverse populations (especially with different age categories) would be instructive.

In summary, these cross-sectional studies showed that AIOS ratings were associated with several factors of well-being including psychological distress, overall health, positive and negative affect, positive states of the mind, and self-concept. Convergent and discriminant validity of the AIOS were indicated for health and emotional variables, suggesting that the AIOS is a reliable and rapid measure of global multidimensional well-being. However, these studies did not provide a detailed comprehensive evaluation of the different predictors of multidimensional well-being, and the capacity of AIOS to capture them (i.e., socioeconomic, psychological, physical, social, spiritual, etc.). While the capacity of the AIOS to capture the eudaimonic components of WB (e.g., life purpose and fulfillment) is implied by the psychological flourishing model (through the positive-to-negative affect ratio approach), it was not tested directly. Furthermore, all these studies are cross-sectional and did not include several time points necessary for test-retest reliability (except in Paterson, 2006, but in a small sample). This is necessary to determine if 1) the AIOS is reliable over time (i.e., test-retest reliability) and 2) the AIOS can detect improvements in well-being following intervention aiming at elevating well-being.



#### 5.1.4. Study goals and hypotheses

In this study, we aimed to:

- Validate the convergent and discriminant validity as well as test-retest reliability of the AIOS.
- Investigate whether the AIOS captures the main dimensions of well-being (hedonic, eudaimonic, physical, and social dimensions).
- Identify predictor variables of multidimensional well-being.

Based on the previous discussion, we hypothesize that:

- AIOS-24h and AIOS-1m will be significantly correlated, with a higher coefficient for healthy individuals relative to unhealthy ones, confirming convergent and discriminant validity of the scale underscored by Bell *et al.* (2004).
- AIOS-24h measured before and after the subjects participating in well-being interventions will be significantly correlated (indicating test-retest reliability) and measure improvements in well-being levels (measuring the efficacy of the intervention). We expect stronger improvements for unhealthy individuals compared to healthy ones (since well-being is more stable over time in healthy individuals).
- AIOS-24h will be associated with individual characteristics (i.e., age, gender, education, and ethnic origins), negatively with age, and positively with education (based on the literature).
- AIOS-24h captures the main dimensions of well-being (namely hedonic, eudaimonic, physical, and social dimensions), with hedonic and eudaimonic as the strongest predictors of self-reported multidimensional well-being.
- Multidimensional well-being will be associated with several predictor variables selected from the literature (i.e., connection with nature, meditation practice, religion/spirituality importance, physical activity, relationship status, personality, and creativity). These analyses are exploratory and aim to advance knowledge as to how multidimensional well-being can be elevated in future interventions.

## *5.2. Methods*

### **5.2.1. Participants**

The inclusion criteria were as follow: participants aged 18 years or older who could read and understand the consent form and complete the survey and tasks, and who had access to the survey online (during the COVID-19 pandemic). The exclusion criteria were as follows: people younger than 18 years of age, inability to understand the consent form or acute or chronic illness that precluded completion of measurements. Participants were recruited through the IONS webpage dedicated to the IONS Discovery Laboratory (IDL) research program, where potential workshop leaders learned about the opportunity. The IONS blog and newsletters were also distributed to community networks, previous workshop leaders, and conferences and meetings. All study activities were approved by the IONS Institutional Review Board (approval designation WAHH\_2018\_01).

### **5.2.2. Study Procedures**

Volunteers received a survey link to complete before their workshop or course. The survey could be completed on any computer with access to the internet. They entered their first name and date of birth to generate a random ID (and their information was not saved) to preserve participants' anonymity. Volunteers acknowledged that they read and understood the consent form and agreed to participate before continuing with the survey. They then completed a series of online self-report questionnaires (see below) in SurveyMonkey (SurveyMonkey, 2021).

After completing the pre-survey, participants engaged in their workshop or course. These events varied in duration (several days or weeks) and content (e.g., elevating well-being, meditation retreats, team cohesion training, personal development, and transformation). The post-survey was slightly shorter as it did not include individual characteristics questionnaires (e.g., demographical questions). Participants were advised to complete the survey as close as possible to the workshop's beginning and ending. Additionally, not all participants were invited to complete a post-survey for various reasons (e.g., part of an intervention not related to elevating well-being, being evaluated at our laboratory for physiology, or part of an intervention that was too short). Data from these participants before intervention were still used in cross-sectional analyses.

### 5.2.3. Measures

#### *Multidimensional well-being*

Multidimensional well-being was measured with the *Arizona Integrative Outcomes Scale (AIOS; Bell et al., 2004)*. Both time-frame forms (AIOS-24h and AIOS-1m) were used in this study. This single-item, horizontally-displayed, visual-analog self-rating scale. Participants are asked “Please reflect on your sense of well-being, taking into account your physical, mental, emotional, social, and spiritual condition over the past 24 hours. Please move the slider below to a point that summarizes your overall sense of well-being for the past 24 hours.” For the AIOS-1m version, “past 24 hours” was replaced with “past month”. The slider goes from 0-100 with 0 being corresponding to “Worst you have ever been” and 100 to “Best you’ve ever been.”

#### The hedonic dimension of well-being

The hedonic dimension of well-being was assessed using the *positive and negative affect schedule short form (I-PANAS-SF; Thompson, 2007)* which included 5 positive items (alert, inspired, determined, attentive, active) and 5 negative items (upset, hostile, ashamed, nervous, afraid). Participants were asked “This scale consists of several words that describe different feelings and emotions. Read each item and then select the appropriate answer next to that word. Indicate to what extent you have felt this way during the past few days.” Answers included “Very slightly or not at all” (score = 1), “A little” (score = 2), “Moderately” (score = 3), “Quite a bit” (score = 4), and “Extremely” (score = 5). The summed negative items were subtracted from the summed positive ones. Positive values, therefore, represent more positive affect over the past few days and negative values represent more negative affect over the past few days. These 10 items were selected from the original 20-item PANAS (Watson, Clark and Tellegen, 1988) and found to be psychometrically acceptable after being tested for cross-sample stability, internal reliability, temporal stability, cross-cultural factorial invariance, and convergent and criterion-related validities (Thompson, 2007).

#### *The physical dimension of well-being*

The physical dimension of well-being was assessed by a composite score calculated with: *Overall health - sleep disturbance - pain intensity*. Hence, negative scores reflect low physical WB and positive scores reflect high physical WB.

Sleep disturbance was measured by the *sleep quality scale (SQS)* (Cappelleri et al., 2009), a single-item visual rating scale measuring acute sleep or sleep quality during the past night before participation. Participants were asked, “How would you rate the quality of your sleep LAST NIGHT?” moving the slider for their response. The slider is anchored by “Best possible sleep” (0) and “Worst possible sleep” (10).

Pain intensity was measured using the *numeric pain rating scale (NPRS)* (Farrar et al., 2001), a similar horizontal visual rating scale. Participants are asked to report pain intensity in the past 24 hours on a slider from position 0 being “No pain” to position 10 being “Worst possible pain.” The NPRS is a reliable scale in terms of inter- or intra- rater repeatability and its ability to detect change (Bijur, Silver and Gallagher, 2001; Boonstra et al., 2008; Hawker et al., 2011).

Overall health was measured using the “single general self-rated health” question (*sGSRH*; DeSalvo et al., 2006), a single-item visual rating scale. Participants were asked, “In general, how would you rate your overall health?” which they rate as Poor (score = -3), Fair (score = -1), Good (score = 2), Very good (score = 3), or Excellent (score = 4). Individuals with “poor” self-rated health were previously found to have a 2-fold higher mortality risk than those reporting having an “excellent” overall health (DeSalvo et al., 2006). Furthermore, participants’ responses were previously found to maintain a strong association with mortality even after adjustment for key covariates such as functional status, depression, and comorbidity (DeSalvo et al., 2006).

Weight and height were collected (optional) to calculate the body mass index (BMI) to assess the reliability of the self-reported overall health measure. BMI is moderately correlated with more direct measures of body fat (Garrow and Webster, 1985; Freedman, Horlick and Berenson, 2013) and strongly correlated with various metabolic and disease outcomes (Flegal and Graubard, 2009; Freedman et al., 2009; Sun et al., 2010), and therefore reflects a robust index of overall health. It was calculated following standard procedure:  $BMI = (weight\ (lb) / height\ (in)^2) \times 703$ . A score of BMI < 18.5 is considered “Underweight” (score = -1), BMI between 18.5 and 24.9 is considered “Healthy weight” (score = 3), BMI between 25 and 29.9 is considered “Overweight” (score = -1), and BMI > 30 is considered “Obesity” (score = -3).

### *Eudaimonic dimension of well-being*

The eudaimonic dimension of well-being was measured by a composite score joining several eudaimonic components:

- Autonomy (referring to whether the individuals viewed themselves to be living in accord with their convictions) and purpose in life (the extent to which respondents felt their lives had meaning, purpose, and direction) were measured by one item of the 15-item *Cloninger self-transcendence subscale* (Cloninger, 1987). Participants were asked: “I think my natural responses now are usually consistent with my principles and long-term goals.” Participants answered with a 10-grades slider, anchored with “Definitely False” (score = 0) and “Definitely True” (score = 10).
- Environmental mastery (referring to how well they were managing their life situations) was assessed using a single-item visual analog scale that encompasses a comprehensive definition of socioeconomic status that is easily translatable across cultures (Adler and Ostrove, 1999). Participants were asked, “Please rate your access to material goods, money, friendship networks, healthcare, leisure time, or educational opportunities and your capacity or ability to direct or influence the behavior of others or the course of events below.” The slider goes from 0-100 with 0 being anchored by “I have no access” and 100 anchored by “I have unlimited”. This item does not include specific income values but rather is a subjective measure of a person’s access to resources. The question is based on the definition and recommendations of the Office of Behavioral and Social Sciences Research and National Institutes of Health.

“Environmental mastery” scores were divided by 10 to better fit the range and weight of the “autonomy/life purpose” ones. Eudaimonic well-being was then obtained by summing both measures.

### *The social dimension of well-being*

The social dimension of well-being was measured using the 1-item “Inclusion of the other in the self” (IOS; Aron, Aron and Smollan, 1992). This scale was developed to measure how close the respondent feels to another person or group. We used an adapted form with three graphical representations representing the Self and Other completely separated, partially, and completely

overlapped. The scale asks the participant: “Please move the slider below to the picture that best describes your relationship with other people. How interconnected are you with others? (Self = you; Others = other people)?” Participants move a slider to represent their answer on a sliding bar anchored by “Not at all” (score = 0) and “Completely” (score = 100). Higher scores represent greater subjective social well-being.

### Individual characteristics

Demographic characteristics including age, gender, education level (12 years = high school diploma), ethnic origins (categories included Native American, European, Native Pacific Islander, Asian, African, Middle-eastern, and Latinx or Hispanic), and relationship status were collected. The latter corresponds to “In a relationship” (Married, Domestic Partnership, Living with significant other, long-term significant other, etc.) or “Not in a relationship” (Single, Widowed, Divorced, Separated).

Personality traits (Eysenck, 1990; Rothbart, 2011; Segal, 2013) were evaluated using the 10-item “Brief five inventory” (BFI-10; Rammstedt, 2007) rating scale of personality traits. The BFI-10 scale was found to retain significant reliability and validity levels compared to the longer scales. Participants were asked “How well do the following statements describe your personality? I see myself as someone who...” and could respond: “Disagree strongly” (score = -2), “Disagree a little” (score = -1), “Neither agree nor disagree” (score = 0), “Agree a little” (score = 1), “Agree strongly” (Score = 2). The personality statements included: “Is reserved”, “Is generally trusting”, “Tends to be lazy”, “Is relaxed, handles stress well”, “Has few artistic interests”, “Is outgoing, sociable”, “Tends to find fault with others”, “Does a thorough job”, “Gets nervous easily”, “Has an active imagination”. These 10 statements correspond to the big five personality characteristics of extraversion, agreeableness, conscientiousness, neuroticism, and openness with two items per subscale. The summed negative traits were subtracted from the summed positive ones, meaning lower values represent dominantly negative traits, whereas higher values reflect dominantly positive traits.

Medical history was assessed by asking participants: “Have you ever been diagnosed with any of the following? [Please check all that apply]”. Responses included: “Major Depression”, “Anxiety Disorder (including phobia, panic, or OCD)”, “Bipolar Disorder”, “Mania”, “Psychosis or Schizophrenia”, “Addiction requiring treatment”, “Post-Traumatic Stress Disorder”, “Does not

apply". Participants that responded "Does not apply" were categorized as "Not diagnosed", and those that responded with any of the conditions (or several) were categorized as "Diagnosed". Then participants were "Are you currently being treated for a psychiatric condition?" to assess psychiatric status, with "Yes" or "No" as responses options. Finally, they were asked "Are you currently being followed by a health care provider for any health condition?" to assess their current health status. The aim was to determine whether the AIOS could discriminate between the categories of healthy/unhealthy individuals (as measured by these self-report questions).

### Predictor variables

Connection with nature was evaluated using a 1-item inclusion of nature in self scale (INS; Schultz, 2002). The INS test-retest correlations are very high after four weeks. Additionally, compared to other multiple-item scales, the INS scale is very accurate for measuring individual differences in connectedness with nature. We used an adapted form with three graphical representations representing the "self" and "nature" completely separated (score = 0, "not at all"), partially (score = 50), and completely overlapped (score = 100, "completely"). The instructions are: "Please move the slider below to the picture that best describes your relationship with the natural environment. How interconnected are you with nature? ("Self" = you; "Nature" = the environment)?" The item results with one score between 0 and 100, with 100 representing the highest connection with nature.

Meditation practice - Participants were asked, "Do you meditate?" Answer choices were "Yes" or "No". If yes, participants were asked "How often?" and could choose between: "4-11 times per year" (score = 1), "2-3 times per month" (score = 2), "Once a month" (score = 3), "1-2 times per week" (score = 4), "2-3 times per week" (score = 5), "3-4 times per week" (score = 6), "5-6 times per week" (score = 7), "Daily" (score = 8). Then they were asked "For how many years have you meditated?" and could enter a whole number. Meditation scores were then calculated by summing the two. If they did not respond or responded "No", they were given a score of 0.

Physical activity - was assessed using two short questionnaires (Gutiérrez-Fisac *et al.*, 2002; He and Baker, 2005). The first one concerned physical activity during leisure time. Participants were asked: "Describe your physical activity at leisure time. If the activities vary between summer and winter, try to give a mean estimate.". Participants could respond "Very light: almost no activity at all" (score = 1), "Light, e.g., walking, non-strenuous cycling or gardening approximately once

a week” (score = 2), “Moderate: regular activity at least once a week, (e.g., walking, bicycling, or gardening or walking to work) 10–30 min per day” (score = 3), “Active: regular activities more than once a week, e.g., intense walking or bicycling or sports” (score = 4), “Very active: strenuous activities several times a week” (score = 5). The second one concerned physical activity at work and the instructions were: “Describe your physical activity at work (even work at home, sick leave at home and studying, for instance in a university)”. Responses included “Very light, e.g., sitting at the computer most of the day or sitting at a desk” (score = 1), “Light, e.g., light industrial work, sales or office work that comprises light activities” (score = 2), “Moderate, e.g., cleaning, staffing at a kitchen or delivering mail on foot or by bicycle” (Score = 3), “Heavy, e.g., heavy industrial work, construction work or farming” (score = 4). Both scores were summed to obtain the physical activity variable. We chose not to include physical activity in the calculation of physical WB as physical activity during leisure and workplace can have opposite associations (e.g., Gutiérrez-Fisac *et al.*, 2002; He and Baker, 2005). Thus, it was examined as its own predictor variable.

Creativity was measured using a 1-item visual analog scale (custom made) asking participants “How creative do you consider yourself?”. Responses ranged from “Not at all creative” (score = 0) to “Very creative” (score = 100).

The importance of religion/spirituality was measured by asking participants “How important is your religious or spiritual involvement CURRENTLY?”. Responses ranged from “Not important” (score = 0) to “Very important” (score = 100).

#### **5.2.4. Statistical analyses**

No power analyses were done for this study, considering the large sample size. Cross-sectional analyses examined relationships between measures using unique survey records completed before the intervention only. These analyses included the test for convergent validity, as well as two linear regression models assessing relationships between multidimensional well-being and 1) different dimensions of well-being, and 2) different predictor variables. Pre-post intervention analyses examined test-retest reliability, and changes in well-being levels using records where surveys were completed before and after a workshop. These statistical analyses are described in more detail below.



### Convergent validity and test-retest reliability: Robust skipped correlations

This analysis was done using the Robust Correlation toolbox (Pernet, Wilcox and Rousselet, 2013) in MATLAB 2021a. The toolbox first tests for bivariate normality (i.e., tests the relationship between the two variables shows a normal distribution) using the Henze-Zirkler's Multivariate Normality Test (Henze and Zirkler, 1990) and then for variance homogeneity (to assess if the two variables tested have similar variance) using a 95% bootstrap *confidence interval* (CI). Different variance across variables indicate that significant correlations can be observed because of the heteroscedasticity rather than a true association (Wilcox, 1991; Wilcox and Muska, 2001). As is commonly observed in research (Micceri, 1989; Kupek, 2002; Schmidt, Germano and Milani, 2019), heteroscedasticity was found on most pairs of variables (i.e., data do not conform to normality). “*Skipped*” correlations present solutions to this issue, while accounting for bivariate outliers (Pernet, Wilcox and Rousselet, 2013; Wilcox, Rousselet and Pernet, 2018). Not addressing this issue can lead to poor control over the *type I error rate* (i.e., false-positive; Wilcox, 2012). Furthermore, *skipped Spearman correlations* are more conservative against false positives with large samples, even with normally distributed data (Pernet, Wilcox and Rousselet, 2013).

*Skipped correlations* were computed with the toolbox using the following steps: 1) identification of outliers with the minimum covariance determinant (MCD) estimator (i.e., a robust estimator of multivariate location and scatter; Rousseeuw, 1984; Hubert, Rousseeuw and Aelst, 2008), a projection technique (each data point is orthogonally projected onto lines joining them to the robust estimate of location), and the “box-plot rule” (relying on the interquartile range; Frigge, Hoaglin and Iglewicz, 1989; Carling, 2000); 2) *skipped Spearman’s correlations* and associated *t-values* are computed, taking into account the bivariate outliers; 3) to control for the *type I error rate* especially important in presence of heteroscedasticity that can lead to an incorrect estimate of the standard error), the data are then resampled and sorted, and the 2.5 and 97.5 percentiles are used to obtain the 95% *confidence interval* (CI). If the CI encompasses 0, then the null hypothesis of independence cannot be rejected. This method provides an alternative and more robust way to test the null hypothesis in presence of heteroscedasticity. (Wilcox, 2012; Pernet, Wilcox and Rousselet, 2013; Wilcox, Rousselet and Pernet, 2018).

*Degrees of freedom* are reported in parentheses after the *r correlation coefficients*. Rejections of *H0* at the 95% confidence level (i.e., significant correlations) are reported with *p-values* after the *r coefficients* and 95% *CI*. Bivariate outliers correspond to the red observations in the plots. The red line corresponds to the least square fit line, and the red shaded areas correspond to the 95% *CI*.

Skipped Spearman correlations were used to test convergent validity (between AIOS-24h and AIOS-1m on the pre-intervention sample), and test-retest reliability (between pre/post-AIOS-24 h on participants that completed both pre- and post- surveys).

*Pre/post changes in well-being levels: Wilcoxon signed-rank test*

For each variable, univariate normality was tested using the *Lilliefors test* (Lilliefors, 1967) with the *lillietest* MATLAB function. This test is based on the non-parametric *Kolmogorov-Smirnov test* that quantifies a distance between the variable sample distribution and the cumulative distribution function of a reference distribution, under the *null hypothesis (H0)* that the sample is drawn from the reference distribution (i.e. absence of difference with the normal distribution). With the *Lilliefors test*, the *H0* does not specify which normal distribution (i.e., expected value and variance of the distribution). Since the variables were paired and did not display normal distributions, pre/post changes were examined using the *Wilcoxon signed-rank test* (*signrank* function in MATLAB).

Pre/post changes in well-being levels were examined for three “healthy/unhealthy” groups discriminated by past: 1) diagnosis for a medical condition (absence/presence, respectively), 2) current treatment for a medical condition (absence, presence, respectively), and 3) current treatment for a psychiatric condition (absence, presence, respectively).

Since we do not have a control group in this study (i.e., a group of individuals doing the pre- and post- survey without intervention in between), we assessed (non-statistically) discriminant validity by comparing the pre/post changes between healthy and unhealthy individuals in each group, expecting unhealthy individuals to show larger changes between before and after the intervention (similar approach to Bell *et al.*, 2004).

### Robust linear regression models

Standard linear regressions use the *ordinary least-squares (OLS)* fitting method to compute the model parameters that relate the response data (also called dependent or outcome variable) to the predictor data (also called independent variables) with one or more coefficients. As a result, outliers have a large influence on the fit, because squaring the residuals magnifies the effects of these extreme data points. Similar to standard *Pearson* and *Spearman* correlations, models using standard *OLS* are based on the assumption that the observed responses come from a normal distribution of errors. If the distribution of errors is asymmetric or prone to outliers, model assumptions are invalid, and *beta* ( $\beta$ ) parameter estimates, *CI*s, and other computed statistics become unreliable.

“Robust” linear regressions use the *iteratively reweighted least-squares (IRLS)* method to automatically and iteratively calculate weights for each data point (Huber and Ronchetti, 2009). First, the algorithm assigns equal weight to each data point and estimates the  $\beta$  coefficients using the standard *OLS* method. Then, at each iteration, the algorithm computes the weights and gives lower weight to the points that are farther from the model predictions in the previous iteration. A low-quality data point (e.g., an outlier) is attributed less influence on the fit. Then, the  $\beta$  coefficients are computed using the *weighted least squares (WLS)* optimization (using these weights). The iterations stop when the values of the coefficient estimates converge within a specified tolerance. Thus, robust linear regressions are less sensitive to outliers (which are very common with self-report data) by down-weighting their impact on the fit of the model, therefore improving the fit (Huber and Ronchetti, 2009).

Each variable was tested for normality using *lillietests* (see above). Since data were not normally distributed and outliers were present in the data, robust linear regression models were generated in MATLAB 2021a using the *fitlm* package (*Tukey's bisquare* reweighting function; default tuning constant = 4.685). All models were tested for “*lack-of-fit*” first, using a degenerate model consisting of only a constant term. The *F-statistic* corresponds to an analysis of variance to test the significance of the model or the components in the model. The *p-value* for the *F-test* indicates whether the model is valid at the 95% confidence level (i.e.,  $p < 0.05$ ). A model can exhibit *lack-of-fit* when it fails to adequately describe the functional relationship between the predictor variables and the response variable. This can occur if large residuals result from fitting the model, or when

the data contain replicates (multiple observations with identical values). Replicates represent "pure error" because only random variation can cause differences between the observed response values. If the *p-value* for the *lack-of-fit* test is below the 5% confidence level, one can conclude that the model does not accurately fit the data (more terms or transformations may be needed). *F-statistics* and the associated *p-value* indicate a valid fit for the model and were reported in the far-right column of the tables. However, they do not inform on the relationship between the predictor and response variables. When the model is valid, the  $\beta$  *coefficients* and the associated *p-value* indicate for each variable whether they are significantly associated with the response variable. *The standard error (SE)* of the  $\beta$  *coefficients'* distributions are reported in parentheses next to the  $\beta$  *coefficients*. Each model regression equation follows the format: *Outcome*  $\sim$  *1* + *predictor1* + *predictor2* + *predictorX*. Additional summary statistics of the models include the number of observations (*N*), the *degrees of freedom (DF)*, the *root mean squared error (RMSE)*, the *F-statistic* and its associated *p-value*,  $R^2$  (for models with one predictor), *adjusted R<sup>2</sup>* (for multiple regression models).

#### *Multidimensional well-being and individual characteristics*

Since a multiple regression model assessing the relationship between multidimensional well-being (AIOS-24h) and individual characteristics showed a significant lack of fit (*F-test* for lack of fit  $p < 0.05$ ) indicating that the model could not accurately fit the data, they were assessed individually in four separate linear models (i.e., age, gender, education, ethnic origin).

#### *Multidimensional well-being and the main well-being dimensions*

One multiple regression model was computed to evaluate the associations between multidimensional well-being and the following dimensions of well-being: hedonic (i.e., positive and negative affect), eudaimonic (a composite measure of autonomy and environmental mastery), physical (overall health, sleep disturbance, and pain intensity), and social (sense of connection with other people) dimensions.

A *skipped Spearman correlation* was conducted to determine whether self-reported overall health was correlated with BMI values in individuals that reported height and weight, to test its reliability.

### *Multidimensional well-being and predictor variables*

One multiple regression model examined associations between multidimensional well-being and 8 predictor variables.

### *p-values and corrections for multiple comparisons*

Since we perform multiple tests on variables that are related to each other (same subjects or variables that may share similar information) in both skipped correlation and linear models, the risk of false positives increases with the number of tests (i.e., *type I error*). Thus, *Bonferroni correction for multiple comparisons* was used to assess significance. For instance, for 3 tests at the 95% confidence level, only *p-values* below 0.0167 are considered significant ( $5\% / 3 = 1.67\%$ ). For all statistical analyses,  $p < 0.05$  indicates significance at the 95% confidence level (corrected),  $p < 0.01$  indicates significance at the 99% confidence level (corrected), and  $p < 0.001$  indicates significance at the 99.9% confidence level (corrected).

## **5.3. Results**

### **5.3.1. Individual characteristics**

2647 individuals participated remotely in the online survey between November 19, 2020, and September 26, 2021, during the COVID-19 pandemic, reflecting a unique context. Of those entries, 1615 were unique pre-intervention records and 429 were unique post-intervention. Age ranged from 19 to 87 years old ( $Mean = 51.9$ ;  $SD = 13.2$ ), and education levels ranged from 9 to 30 years (12 years corresponding to high school diploma;  $Mean = 17$ ;  $SD = 3.2$ ). 83.9% were females, 15% males (1.1% missing). 73% reported living in the USA, 8% from Canada, 4.2% in the UK, 2.5% in Italy, 1.3% from Australia, and less than 1% from other countries. Ethnic origins were 76.2% European, 8.3% Mixed, 2.7% Asian, 1.5% African, 4.9% Hispanic/Latinx, 1.7% Native American, and 0.4% Pacific Islander.

34.4% had been previously diagnosed with either major depression, anxiety disorder, bipolar disorder, mania, psychosis or schizophrenia, addiction requiring treatment, post-traumatic stress disorder (PTSD), or several of these conditions. 35% were currently followed by a healthcare provider for a health condition, and 13.7% were currently being treated for a psychiatric condition.

The linear models examining the relationship between multidimensional well-being and age and education did not accurately fit the data (*lack of fit*  $p < 0.005$ ). While the fit was valid for the gender and ethnic origins, no associations were found between these variables and multidimensional well-being (see Figure 16).

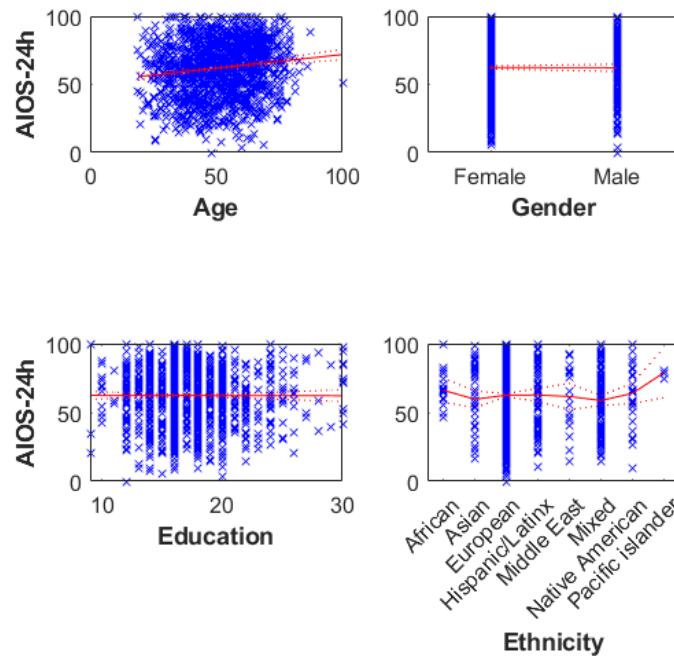


Figure 16. Robust linear regression models assessing the relationships between multidimensional well-being and individual characteristics. A lack-of-fit was found for the models with age and education ( $p < 0.0001$ ), indicating that these models did not accurately fit the data. The fit was valid for the models with gender and ethnicity but they did not show significant relationships with well-being ( $p = 0.29$  and  $p = 0.18$ , respectively).

### 5.3.2. Convergent validity

1512 participants completed both AIOS-24h and AIOS-1m. AIOS-24h was significantly correlated with AIOS-1m ( $r(1463) = .71$ ,  $CI [0.59, 0.67]$ ,  $p < 0.01$ ), indicating convergent validity of the AIOS scale (stronger convergence than the  $r=.64$  in Bell *et al.*, 2004). Mean AIOS-24h was 62.4 ( $SD = 19.1$ ) and mean AIOS-1m was 60.7 ( $SD = 21.3$ ).

### 5.3.3. Test-retest validity

401 participants completed both pre- and post- AIOS-24h. Pre-AIOS-24h was moderately and significantly correlated with post-AIOS-24h ( $r(398) = .36$ ,  $CI [0.21, 0.44]$ ,  $p < 0.01$ ), indicating moderate test-retest reliability.

### 5.3.4. Pre/post changes in multidimensional well-being

Well-being levels improved following intervention for all individuals except those who were currently taking treatment for a psychiatric condition ( $N = 65$ ,  $z = 1.5$ ,  $p > 0.05$ ). Individuals that experienced the strongest improvement in well-being were people not currently following a treatment for a psychiatric condition ( $N = 336$ ,  $z = 3.8$ ,  $p < 0.0001$ ) and with no past medical condition ( $N = 166$ ,  $z = 3.2$ ,  $p < 0.01$ ). These results are reported in Table 2.

**Table 2. Paired pre-post intervention changes in multidimensional well-being (AIOS-24h).**

Health group (N)	Pre Mean (SD)	Post Mean (SD)	Wilcoxon Signed-Rank Test <i>z, p-value</i>
No past medical diagnosis (235)	62.8 (20.3)	66.7 (20)	<b>2.6, &lt;0.05</b>
With past medical diagnosis (166)	57 (21.5)	63.2 (21.1)	<b>3.2, &lt;0.01</b>
No current medical treatment (236)	60.9 (20.5)	65 (20.2)	<b>2.9, &lt;0.01</b>
With current medical treatment (165)	59.7 (21.6)	65.6 (21)	<b>2.9, &lt;0.01</b>
No current treatment for a psychiatric condition (336)	61.3 (20.7)	66.2 (20)	<b>3.8, &lt;0.0001</b>
With current treatment for psychiatric condition (65)	55.6 (21.9)	60.4 (22.5)	1.5, >0.05

*The number of observations per health group (N) is reported in the 1st column. Mean pre- and post- AIOS-24h and standard deviation (SD) are reported in columns 2 and 3. Significant differences in pre/post changes assessed by the Wilcoxon signed-rank test are reported in bold in column 4.*

### 5.3.5. Well-being dimensions

Multidimensional well-being was significantly associated with all the dimensions except for the social one ( $p = 0.119$ ). In order of strength of association, it was significantly associated with the hedonic ( $t = 19.8$ ), the physical ( $t = 15$ ), and then with the eudaimonic ( $t = 3.4$ ) dimensions. As indicated by the  $\beta$  coefficients in Table 3, multidimensional well-being increases by 1.6 ( $SD = 0.08$ ) for every 1-unit increase in the hedonic dimension, by 1.5 ( $SD = 0.1$ ) for every 1-unit increase in the physical dimension, and 0.5 (0.15) for every 1-unit increase in the eudaimonic dimension. Together, these dimensions of well-being explained 44.6% of the variance in multidimensional

well-being ( $F(1442) = 292$ ,  $adjusted R^2 = 0.446$ ,  $p < 0.0001$ ). The whole multiple regression model is reported in Figure 17.

The self-reported overall health measure was significantly and moderately associated with BMI in participants that reported their height and weight ( $r(1006) = .29$ ,  $CI [0.19, 0.3]$ ,  $p < 0.01$ ), reinforcing the validity of this subjective measure of overall health.

**Table 3. Multidimensional well-being and the main dimensions of well-being**

Well-being dimensions	$\beta$ (SE)	$t$ -statistic, $p$ -value
(Intercept)	57.4 (2.26)	<b>25.3***</b>
Physical WB	1.5 (0.1)	<b>15***</b>
Hedonic WB	1.6 (0.08)	<b>19.8***</b>
Eudaimonic WB	0.5 (0.15)	<b>3.4**</b>
Social WB	0.3 (0.18)	1.6, 0.119

Column 1: Name of the predictor variables. Column 2: Unstandardized  $\beta$  coefficients for each variable and their distribution standard error (SE) in parentheses. Column 3:  $t$ -statistic and  $p$ -value for each variable (corrected for multiple comparisons with the Bonferroni method). Corrected  $p$ -values corresponded to 0.0125 at the 95% confidence level (reported with \*), 0.0025 at the 99% confidence level (reported with \*\*), and 0.00025 at the 99.9% confidence level (reported with \*\*\*).

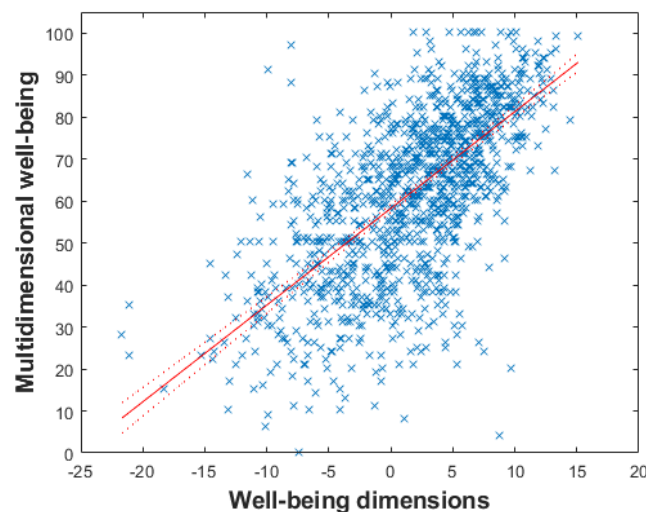


Figure 17. Multiple regression model examining associations between multidimensional well-being (i.e., AIOS-24h) and the main dimensions of well-being (i.e., hedonic, eudaimonic, physical, and social dimensions). The whole model explained 44.6% of the variance in multidimensional well-being ( $F(1442) = 292$ ,  $adjusted R^2 = 0.446$ ,  $p < 0.0001$ ).



### 5.3.6. Predictors/mediators of multidimensional well-being

Multidimensional well-being was significantly associated with connection with nature ( $t = 3.5$ , corrected  $p < 0.001$ ), religion/spirituality ( $t = 2.9$ , corrected  $p < 0.05$ ), physical activity during leisure ( $t = 3$ , corrected  $p < 0.05$ ), and personality trait ( $t = 8.8$ , corrected  $p < 0.001$ ).  $b$  coefficients indicated that multidimensional well-being increased by 1.8 ( $SD = 0.6$ ) for every 1-unit increase in physical activity during leisure, by 1 ( $SD = 0.1$ ) for every 1-unit increase in personality trait, by 1 ( $SD = 0.3$ ) for every 1-unit increase in connection with nature, and by 0.1 ( $SD = 0.03$ ) for every increase in religion/spirituality. Physical activity at work, meditation practice, relationship status, and reported creativity were not associated with multidimensional well-being in this sample. These results are reported in Table 4.

**Table 4. Multidimensional well-being and predictors of well-being**

Predictor variables	$\beta$ (SE)	$t$ -statistic, $p$ -value
(Intercept)	34.5 (3.7)	<b>9.2***</b>
Connection with nature	1.01 (0.3)	<b>3.5***</b>
Religion / Spirituality	0.1 (0.03)	<b>2.9*</b>
Physical activity (during leisure)	1.8 (0.6)	<b>3*</b>
Physical activity (at work)	0.2 (0.6)	0.3, $p = 0.722$
Meditation practice	0.06 (0.05)	1.4, $p = 0.168$
Relationship status (“not in a relationship” category)	-1.4 (1.2)	-1.2, $p = 0.227$
Personality trait	1.02 (0.1)	<b>8.8***</b>
Creativity	-0.001 (0.03)	-0.001, $p = 0.995$
<b><math>F(1100) = 20.8</math>, <math>RMSE = 18.7</math>, <math>adjusted R^2 = 0.125</math>, <math>p &lt; 0.0001</math></b>		

Column 1: Name of the predictor variables. Column 2: Unstandardized  $b$  coefficients for each variable and their distribution standard error in parentheses. Column 3:  $t$ -statistic and corrected  $p$ -value for each variable (Bonferroni correction for multiple comparisons). Corrected  $p$ -values equal 0.00625 at the 95% confidence level (reported with \*), 0.00125 at the 99% confidence level (reported with \*\*), and 0.000125 at the 99.9% confidence level (reported with \*\*\*). Exact  $p$ -values are reported when non-significant. Whole model statistics are reported in the bottom row and include:  $F$ -statistic with the error degree of freedom in parentheses, root mean squared error (RMSE), adjusted  $R^2$ , and the  $p$ -value for the model.

## 5.4. Discussion

This study aimed to evaluate whether multidimensional well-being could be assessed quickly and reliably on large samples along with EEG data collected with wearable systems.

### 5.4.1. Individual characteristics

We did not find associations between well-being levels and individual demographics. The absence of association with age is contrary to some previous research indicating that well-being decreases in later life with a reduction in life purpose and autonomy. This might be explained by the fact that the population studied here was intentionally seeking interventions aiming to elevate well-being and personal transformation, despite their age, suggesting that these older individuals do not correspond to the ones in the literature with loss of autonomy and purpose.

Future research should determine which interventions improve well-being most effectively in some individuals but not others, investigating other individual characteristics (e.g., personality traits). The main limit in this study regarding these research questions concerns the low sample diversity despite a large number of participants (83.9% females, 76.2% with European origins, and an average education corresponding to the Masters's level). The survey used in this study has now been translated into several other languages, which should increase diversity in future studies (along with online access).

### 5.4.2. Convergent validity

Convergent validity was reinforced by our findings on a large sample. The correlation coefficient ( $r = .71$ ) was higher than the one observed by Bell *et al.* (2004, i.e.,  $r = .64$ ), and Tuason, Güss and Boyd (2021, i.e.,  $r = .58$ ). This could be because the power is increased with the sample size of this study, or because of the robust statistical methods employed, or because well-being was more stable over the past month in this population compared to the ones in these two other studies.

### 5.4.3. Test-retest reliability

While previous authors did not validate the scale in terms of test-retest reliability, we found a significant correlation between pre-AIOS-24h and post-AIOS-24h over 401 people that completed the survey before and after the intervention. The correlation was significant,

indicating test-retest reliability of the scale, and moderate ( $r = .36$ ), indicating changes in well-being levels. This moderate correlation was expected as the interventions aimed at elevating well-being and personal transformation and development in these individuals, and likely affected individuals in different ways. This correlation coefficient is similar to the one obtained by Bell *et al.* (2004) when correlating AIOS-1m and AIOS-24h in patients following treatment over the past month ( $r = .33$ ).

#### **5.4.4. Discriminant validity**

While we did not have a control group in this study to assess discriminant validity of the AIOS (i.e., no group did pre- and post- survey with a placebo or no intervention between), the mean pre-AIOS-24h scores showed differences between healthy and unhealthy individuals ( $62.8 \pm 20.3$  for participants who were never diagnosed with a medical condition vs.  $57 \pm 21.5$  for those who did). This was also the case for people not currently taking treatment for a psychiatric condition vs. people who were (mean pre-AIOS-24h was  $61.3 \pm 20.7$  vs.  $55.6 \pm 21.9$ , respectively). However, the scale did not discriminate between well-being levels in the presence or absence of current medical treatment ( $60.9 \pm 20.5$  vs.  $59.7 \pm 21.6$ ). Note that we also found the subjective overall health measure to be significantly correlated in the body mass index (BMI), reinforcing the validity of this measure assessed with a 1-item self-report scale.

#### **5.4.5. Pre/post changes in well-being levels**

Multidimensional well-being was the most elevated by the interventions in individuals that did not have a current psychiatric condition but with a previous medical condition. Although individuals with no previous condition and with or without a current medical condition also showed significant improvements in well-being. The only group that did not report significant changes in multidimensional well-being were people currently treated for a psychiatric condition. This makes intuitive sense since these interventions are aimed to elevate well-being and improve self-transformation, which does not compare to the medical treatment that these individuals may require for their mental health. Future studies will elucidate whether some of these interventions did improve well-being in these individuals, but not others. These interventions can be used to improve well-being levels in both healthy and unhealthy populations.

#### **5.4.6. Well-being dimensions**

We observed that AIOS-24h can be used to capture, in one visual scale, the hedonic (positive/negative affect), the eudaimonic (life purpose, autonomy, and environmental mastery), and the physical (overall health, pain intensity, and sleep disturbance) dimensions of well-being. The social dimension (measured by the sense of connection with other people) was not associated with multidimensional well-being. This is likely because this study was conducted during the world COVID-19 pandemic, and that most people were isolated or confined in their homes.

Together, these three well-being dimensions explained 44.6% of the variance in multidimensional well-being. Tuason, Güss and Boyd (2021) reached 53% of the variance in AIOS using 11 variables. While one should be cautious when interpreting  $R^2$ , it can be considered a moderate-to-high effect size in humanities and social sciences (and especially with abstract variables as multidimensional well-being) since human behavior is hard to predict accurately (Cohen, 1977). However, an  $R^2$  of 44.6% also indicates that we might have missed some other important dimensions that contributed to the participants' multidimensional well-being (to get closer to 100% of the variance in well-being explained). It could also be because the measures used in this study to assess hedonic, eudaimonic, physical, and social WB lacked accuracy/consistency as they were also quick scales and questionnaires, designed to be easily completed by the participants. It could also be that subjective self-report is less stable across participants (large residuals), making it more difficult to obtain robust linear relationships compared to lengthy, multi-item measures. Data transformations were not explored in this study to keep interpretations of coefficients easier but they are often used to improve models' fit (Piepho, 2009).

#### **5.4.7. Predictors/mediators of multidimensional well-being**

In decreasing order of strength of association, multidimensional well-being was positively correlated with personality traits, connection with nature, physical activity during leisure, and religion/spirituality. Note that physical activity during leisure, but not at work, was associated with well-being, suggesting physical activity at work might represent a negative health outcome depending on the type of work and activity (e.g., if it is associated with chronic pain or injuries), whereas physical activity during leisure can be considered a positive predictor outcome. Contrary to expectation, meditation practice, relationship status, and creativity were not significantly associated with multidimensional well-being.

#### **5.4.8. AIOS-24h and longer-term well-being**

AIOS-24h (well-being over the past 24h) being associated with AIOS-1m (well-being over the past month) and with personality traits (considered to be highly heritable e.g., Lucas and Diener, 2008) suggest that the AIOS-24h can be used to capture longer-term (trait) well-being levels than just the past 24 hours. Future research should determine whether this is true correlating AIOS-24h with more trait variables (e.g., genetic predisposition, optimism, life management strategies, empathy, emotional intelligence, or perceived independence).

Additional health outcomes research should focus on developing systematic approaches to identifying these types of individualized needs and preferences and implementing the most appropriate, complementary interventions, which together may improve overall well-being and facilitate achieving very high scores on the AIOS.

#### **5.4.9. Limits**

##### *Positive bias in AIOS scores*

Note that the overall average pre-AIOS-24h score was 61.8 out of 100, and quartiles indicated that 25% of the scores were below 49, 50% below 64, and 75% below 77. This might indicate that people seeking these types of interventions coped well despite the stressful circumstances of the COVID-19 pandemic. Participating in these interventions indicates, in itself, a certain approach motivation as participants are seeking to elevate their well-being, whereas individuals with avoidance motivation withdraw and are harder to motivate to get better. However, it could also indicate that the scale is biased towards higher scores. Contrary to Bell *et al.* (2004), we observed a ceiling effect, with 17 individuals reporting well-being scores of 100 before the intervention, leaving no place for measurement of improvements following the intervention. Future studies should confirm or disprove this potential issue and compare scores of individuals not seeking an intervention with those who are to determine if the positive bias is due to motivation or a lack of accuracy from the scale. However, despite these limitations, this quick scale was able to measure the main dimensions of well-being, changes in well-being changes following interventions, and to discriminate between different health groups.

### Remote, subjective, brief self-report

Brief, subjective, self-report measures have many advantages (reduce participants' burden, increase motivation and attention, capture other dimensions that may be missed with preselected items, etc.), and be as accurate as conventional lengthy questionnaires or interviews (see Introduction). However, their reliability is harder to validate (e.g., internal consistency is not possible with a few items) and they are more prone to extreme, low-quality outlier responses. Whether this brief global scale is the most accurate measure of multidimensional well-being remains the subject of further research. Additionally, online survey completion is a recent, modern phenomenon. While it offers tremendous advantages for data collection, it remains to validate whether participants' responses are as reliable and accurate as in-person completion. Situational variables that can occur in the participant's home are uncontrollable and could seriously affect accuracy in the responses.

However, by combining the large samples they allow to access more easily with robust statistical methods that deal with the increased noise, they can be useful to measure well-being levels, discriminate between groups, capture different well-being dimensions, and measure well-being changes following interventions. It is encouraging that group differences emerged, even within this limitation.

Two recent short scales that seem to achieve a satisfying balance between psychometric properties and respondent burden are the “flourishing scale”, and the “Scale of Positive and Negative Experience” (Diener *et al.*, 2010; Hone, Jarden and Schofield, 2014; Schotanus-Dijkstra *et al.*, 2016). The former is a brief 8-item measure of psychological “flourishment” capturing self-perceived success in relationships, self-esteem, purpose, and optimism, whereas the latter is a 12-item brief scale of positive and negative feelings supposed to better capture a wider range of emotions and a longer period (over the past 4 weeks) compared to the PANAS used in Chapter 5.

### *5.5. Conclusion*

We validate the use of the AIOS to measure multidimensional well-being and the underlying dimensions (hedonic, eudaimonic, physical), assess associations with individual characteristics and predictor variables, and measure changes induced by well-being-targeted interventions.

Additional quantifiable robust measures (e.g., hormone levels, heart rate variability, electroencephalography) under controlled conditions would provide a more complete picture of individual well-being status.

## Chapter 6. Validating a low-cost wearable EEG headset for spectral analysis

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### 6.1. Introduction

#### 6.1.1. The MUSE

The MUSE (InterAxon Inc.) is a low-cost, off-the-shelf, wearable EEG headset that has two frontal and two temporoparietal (TP) dry active EEG channels. It has been validated for evoked-response potential (ERP) research (i.e., time-domain; Krigolson *et al.*, 2017) and used in many recent studies (Hashemi *et al.*, 2016; Krigolson, Williams and Colino, 2017; Papakostas *et al.*, 2017; Amores *et al.*, 2018; Cochrane *et al.*, 2018; Arsalan *et al.*, 2019; Asif, Majid and Anwar, 2019; Qu *et al.*, 2020; Herman, Ciechanowski and Przegalińska, 2021; Hunkin, King and Zajac, 2021; Krigolson *et al.*, 2021). However, to our knowledge, it has not yet been validated for frequency domain analysis (power spectra on continuous EEG data), with one study showing mixed results (Ratti *et al.*, 2017). In addition to assessing the validation of MUSE spectral measures, it is relevant to test if the MUSE could be used to estimate clinically- and research-relevant spectral measures, such as the frontal alpha asymmetry (FAA) and the individual alpha frequency (IAF). See sections 4.4.2. and 4.4.3. for more detail on these two spectral measures.

IAFs and FAA seem like promising candidate measures for wearable EEG systems, as they require simple calculations in the frequency domain and a few EEG channels covering the frontal regions of each hemisphere. While these measures have not been validated using these systems against research-grade EEG, wearable EEG systems have been used extensively over the past few years to measure frontal asymmetry, suggesting this measure is well-suited for these technologies (Peng, Majoe and Kaegi-Trachsel, 2011; Hashemi *et al.*, 2016; Jebelli, Hwang and Lee, 2017; Wu *et al.*, 2017; Hwang *et al.*, 2018; Jebelli *et al.*, 2018; Umar Saeed *et al.*, 2018; Cao *et al.*, 2019; Arpaia *et al.*, 2020; Saeed *et al.*, 2020). Wearable systems, when reliable, can offer advantages for researchers through easeful EEG data collection for over large samples, increased



access to populations that are hard to study with conventional systems (e.g., children, elderly, patients), reduced hardware and software costs, and facilitated EEG research in real-world environments by increasing subjects' mobility and streaming the data wirelessly (see section 9.4. and Cannard *et al.*, 2020). For example, both IAF and FAA are promising EEG measures for neurofeedback applications (Angelakis *et al.*, 2007; Quaedflieg *et al.*, 2016), which would benefit from mobile data collection.

However, there is still a lack of validation of the data collected by such devices and the interpretation of the results based on the literature based on conventional higher-density systems and different referencing methods (i.e., linked-mastoids or average reference). The reference method implemented for low-density wearable systems is of particular importance when considering measuring EEG asymmetry (Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017).

The present study tested whether the 4-channel wearable MUSE EEG system can quickly measure continuous EEG data with a maximum of 5-minute set-up and data collection time, that would yield quantifiable frequency components comparable to research-grade systems and if it can extract clinically relevant measures such as IAF and FAA.

### **6.1.2. Validating new EEG systems**

Once the minimum hardware requirements are met, signal validation is required to ensure that the EEG components of interest (e.g., raw waveform, ERP, power spectra) are captured accurately and reliably. This is generally done by comparing them with those obtained from conventional high-grade systems.

For example, Barham *et al.* (2017) showed that while significantly more trials are rejected from data acquired by these systems, the raw EEG waveforms captured were found to have a high degree of similarity with those measured by a clinical-grade system. Mayaud *et al.* (2013) compared the performance of six traditional EEG disc electrodes (i.e. electrodes made from silver metal and lead wires) with the electrodes provided by the Emotiv Epoc wearable headset and found no significant difference in performance between the two. Pinegger *et al.* (2016) evaluated three different commercially available EEG acquisition systems that differ in the type of electrode (gel-, water-, and dry-based), the amplifier technique, and the data transmission method. Every system was tested regarding three different aspects, namely technical, BCI effectiveness and efficiency (i.e. P300 detection, communication, and control), and user satisfaction (comfort). They

found that the water-based system had the lowest short circuit noise level, the hydrogel-based system had the highest P300 spelling accuracies, and the dry electrode system caused the least inconveniences. They concluded that building a reliable BCI was possible with all three systems (Pinegger *et al.*, 2016).

Other authors were able to validate low-cost wearable systems for ERP research. Kotowski *et al.* (2018) successfully measured differences in the early posterior negativity (EPN) component between neutral and emotional stimuli using the low-cost Emotiv Epoc+. Krigolson, Williams and Colino (2017) were able to reliably identify the N200, P300, and reward positivity ERP components with the Muse, an off-the-shelf low-cost wearable system. De Vos *et al.* (2014) revealed classification accuracies of P300 for both indoor (77%) and outdoor (69%) recording conditions. Other studies that have done so suggest that it is possible to collect data of sufficient quality for ERP analyses using such low-cost systems (e.g., Debener *et al.*, 2012; Duvinage *et al.*, 2013; Mayaud *et al.*, 2013; De Vos *et al.*, 2014; Badcock *et al.*, 2015; Maskeliunas *et al.*, 2016; Pinegger *et al.*, 2016; Barham *et al.*, 2017; Krigolson, Williams and Colino, 2017; Kuziek, Shienh and Mathewson, 2017; Kotowski *et al.*, 2018; Williams *et al.*, 2020).

### **6.1.3. Trait vs. state EEG**

While ERPs are useful to study EEG components associated with changes in brain state-related activity (as an outcome, in response to an event), resting-state EEG data is thought to provide information about individual traits (Allen, Coan and Nazarian, 2004). Trait EEG can be used to assess current or predict future psychopathological states such as the risk for depression (Smith *et al.*, 2017). Alpha oscillations have been historically measured as both a state and a trait to study constructs such as affect, cognition, or neuropsychology.

### **6.1.4. Referencing method**

The issue of the electrode reference and its impact on asymmetry scores has been detailed and is of high importance (Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017). The recommended referencing methods (i.e., average-referencing, current-source density) or the “residualization procedure” are not feasible with the low density of the Muse montage. The Muse frontal channels are located very close to the Fpz reference, potentially providing invalid asymmetry scores for the frontal channels, by not reflecting the same underlying cortical activity as in the literature.

Since frontal asymmetry estimated on linked-mastoids data are associated with the severity of current depression (Stewart *et al.*, 2010), we tested the validity of re-referencing the Muse frontal channels offline to TP9 and TP10 by comparing the resulting PSD and asymmetry scores to the ones obtained on averaged-referenced 64-channel Biosemi Active Two.

### **6.1.5. Study goals**

The present study aimed to test whether or not a low-cost, 4-channel wearable EEG system (The Muse EEG headset) could be used to quickly measure continuous EEG data that would yield observable and quantifiable frequency components similar to research-grade systems (a BIOSEMI Active 2 EEG system) such as power spectral density (PSD), IAF (PAF and CoG), and alpha asymmetry. Furthermore, one of the principal goals of this experiment was to develop a portable, efficient, and affordable method of measuring these spectral components for field and clinical research, making the trade-off between electrode location and ease of use worthwhile. As such, we deliberately collected a minimal amount of data. Our goal was for EEG setup and data collection to be completed in under 5 min.

## *6.2. Methods*

### **6.2.1. Participants**

Participants for this study were 40 English-speaking adults in the San Francisco Bay area. Exclusion criteria were: aged younger than 18 years old, unable to read, having an acute or chronic illness that interfered with the completion of the experiment, or being unable to sit on a chair for about 30 minutes. Participants had their EEG recorded with a 64-channel EEG system at the laboratory for another study (~2h session) and were asked if they wanted to volunteer a few more minutes of their time for an additional ~5 minutes EEG recording using the wearable headset. They were compensated only for their participation in the initial study. They gave informed consent, and the study was approved by the IONS Institutional Review Board.

### **6.2.2. EEG data collection procedures**

EEG data were collected with the active dry MUSE 1 (version 2016) at 256 Hz and a 64-channel gel-based BIOSEMI Active 2 system (BIOSEMI Inc.) at 512 Hz. Simultaneous recording of both systems was not possible due to their configurations. The MUSE data were recorded first, and then the BIOSEMI data about 30 minutes later, which corresponded to the time necessary to set

up the BIOSEMI equipment and optimize channel impedance). A comparison of the two systems' hardware specifications can be found in Table 5. For both systems, the participants' skin was cleaned with alcohol wipes at electrode sites before positioning the headband/head cap.

**MUSE** - A thin layer of water was applied to the dry electrodes with a sponge for both the frontal metallic sensor and the conductive silicone rubber mastoid sensors behind the ears to decrease the impedance and increase signal quality. The MindMonitor App (Clutterbuck, 2015) running on a Chromebook laptop was used to record the EEG signal and check electrode contact (a colored circle for each electrode was filled when the software deemed the connection acceptable). Visual examination of the raw EEG waveforms was also performed while participants were asked to generate eye blinks to provide an additional index of signal quality. The headset position was adjusted if the signal was judged too noisy by visual inspection of the data.

**BIOSEMI** - Highly conductive electrolytes SignaGel was injected into the electrode sites of the BIOSEMI head cap. BIOSEMI active electrode offsets were kept below offset 20 using the Actiview software.

**Table 5. Hardware specifications of each system**

	Biosemi Active Two	InteraXon MUSE
Electrode montage	64 wet active electrodes (10-20 system)	4 dry active electrodes (AF7, AF8, TP9, TP10) <sup>b</sup>
Sampling rate	512 Hz	256 Hz
Resolution	24 bits	12 bits
Active electrode system	Passive DRL and active CMS located around POz	Passive DRL and active CMS located at Fpz
Head sizes	3 different head cap sizes covering 54-62 cm	Adjustable headband, 52-60 cm range
Recording apparatus	Optic fiber and amplifier, MacBook Pro, Actiview Software	Bluetooth on a low-cost Chromebook, Mind Monitor App
Reference	Reference-free <sup>a</sup>	Fpz

<sup>a</sup> Data is reference-free at data collection time. A reference must be chosen when importing the data. Not choosing a reference led to a 40 dB loss of signal-to-noise (SNR) ratio.

<sup>b</sup> Approximate positions.

*MUSE and BIOSEMI* - Recordings were performed at the same location within the recording room, minimizing the differences in terms of potential electrical artifacts from the environment. One minute of data was recorded with eyes open gazing at the computer screen in front of them, and one minute was recorded with eyes closed. Half the participants did eyes open before eyes closed, and the other half did the reversed order to avoid carry-over effects. Participants were instructed to sit still on a chair, limit their movements, and focus their attention on their breath by counting each inhalation/exhalation cycle. In this manuscript, we only process eyes' closed data.

### **6.2.3. EEG data preprocessing**

We developed an EEGLAB plugin named *import\_muse* (see Annexe 1) to import the MUSE data into EEGLAB v2021.1 (Delorme and Makeig, 2004), integrated into MATLAB R2021 (The MathWorks, Inc.). BIOSEMI data were imported into EEGLAB using the BIOSIG plugin (v3.7.5). BIOSEMI data were downsampled to 256 Hz. Raw data were high-pass filtered with EEGLAB's linear non-causal Finite Impulse Response (FIR) filter of the FIRFILT (v2.4) plugin (filter order = 1129; transition bandwidth = 0.75 Hz; passband edge = 0.75 Hz; -6 dB cutoff frequency = 0.375 Hz). No low-pass filter was used to evaluate frequencies 1-100 Hz.

Files were inspected visually for abnormal channels (bad connection, impedance, very high noise, flat sections from disconnections, etc.) and artifactual segments (eye and muscle artifacts, high-frequency bursts, etc.). Artifactual regions and channels were manually rejected. MUSE data files with at least 1 visually abnormal channel were removed. If the BIOSEMI or the MUSE file was shorter than 45 s, the participant data was also excluded from further analysis. Using these criteria, three out of 40 data files were excluded (N = 37).

### **6.2.4. Reference method and montages**

Since the BIOSEMI (64-channel montage) does not include the MUSE TP9 and TP10 channels, we selected the closest channels, i.e. TP7 and TP8, to compare spectral data in the temporoparietal (TP) regions.

The default reference channel for the MUSE is Fpz which is close to the frontal channels AF7 and AF8 and may lead to biased spectral values at these channels. The FAA has been extensively calculated on frontal channels F7 and F8, with Cz-, mastoid-, or average- reference methods

(Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017). However, the average-reference (and more recently the current-source density or surface Laplacian transformations) was shown to be preferable (Smith *et al.*, 2017).

With 4 electrodes, an average reference (or CSD-transformation) is not meaningful for the MUSE system since it requires a whole-head (and spherical) electrode coverage. Hence, spectral measures were computed on MUSE frontal channels 1) referenced Fpz (default), 2) re-referenced to mastoids (i.e., TP9/TP10, termed the “*mastoid-ref montage*”), and 3) on the temporoparietal (TP) channels referenced to Fpz (default, termed “*Fpz-ref montage*”). Data obtained with these montages were compared to 1) BIOSEMI AF7 and AF8 referenced to mastoids (*mastoid-ref montage*), 2) TP7 and TP8 referenced to Fpz (*Fpz-ref montage*), and F7, F8, TP7, TP8 referenced to average (*average-ref montage*). Note that 1) and 2) were only tested in the first analysis only to determine which one was most accurate compared to BIOSEMI. Then, only the best referencing method for frontal channels was used for subsequent analyses.

The spectral measures described below were obtained for each system and montage. The measures from BIOSEMI *average-ref montage* were used as “optimal” spectral estimates and compared to MUSE estimates to determine whether they shared the same underlying neural activity and scalp distributions.

### **6.2.5. Power spectral density (PSD)**

Power spectral density (PSD) over frequencies 1-100 Hz was computed using the *pwelch* function in MATLAB 2021 (The MathWorks Inc.) for each EEG channel on 4-second *hamming* windows, with 50% overlap and 200% padding (better accounting for data discontinuity due to excluded artifactual regions). The mean was removed from PSD data, and they were converted to decibels ( $10 * \text{Log}_{10}(\text{power})$ ; Allen, Coan and Nazarian, 2004). Mean PSD was extracted for each frontal channel for each frequency band: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (>30 Hz). Then, the average between the two channels was used for analyses.

### **6.2.6. Individual alpha frequency (IAF)**

Both the peak alpha frequency (PAF) and the alpha center of gravity (CoG) were estimated using the open-source and automated *restingIAF* toolbox (v1.0.2; Corcoran *et al.*, 2017). The algorithm smoothes alpha power distribution with a Savitzky-Golay filter and uses curve-fitting and zero-

crossing methods to estimate the PAF and CoG for each EEG channel and subject. Since we use a low-density system, and that some individuals present alpha power outside of the traditional 8-13 Hz range (see section 4.4.2.), a minimum of 1 channel and a window of 7-14 Hz were selected in the toolbox parameters for IAF-estimation (all other parameters were kept at default values).

### 6.2.6. Alpha asymmetry

Based on the previous discussion (and section 4.4.2.), three methods were used to calculate alpha asymmetry (for both frontal and TP channels):

- Traditional asymmetry: difference in alpha power (averaged over the 8-13 Hz) band between the right and left channels averaged over the 8-13 Hz band (*mean\_alpha\_right - mean\_alpha\_left*).
- PAF-asymmetry. Same as above but on power at the peak alpha frequency (PAF).
- CoG-asymmetry. Same as above but on power at the alpha center of gravity (CoG).

### 6.2.7. Internal consistency reliability

The power spectrum of one large epoch is the exact representation of the frequency content of that EEG segment and is used for all main EEG results. However, one cannot estimate the statistical properties of the random process generating the EEG under the assumption of weak stationarity, which assumes that the mean and variance of the signal do not change over time (Bendat and Piersol, 2011). While this assumption of weak stationarity is generally valid in continuous EEG data, it is not in event-related signals where stimuli are presented and eliciting large changes in mean and variance (Ombao *et al.*, 2016). Nevertheless, the weak stationarity of continuous signal can be tested with internal consistency reliability by obtaining an estimate of mean and variance of EEG signal for several epochs of the data.

Previous research showed that reliable asymmetry values can be obtained with as little as 80 seconds of data, but internal consistency reliability should be reported when assessing asymmetry on less than 8 minutes of data (Towers and Allen, 2009). To confirm internal consistency reliability of the asymmetry measures with the different montage methods and with very short segments of data (45 seconds for the shortest file after data cleaning), mean alpha power and FAA (traditional method only) were also computed for each montage on eleven 4-s blocks of data (mean for each block). Internal consistency reliability of alpha PSD and FAA was evaluated using *Cronbach's standardized alpha* on the blocks of spectral data (Cronbach, 1951;

Schlegel, 2010). Similar to correlation coefficients, values  $>.8$  indicate high internal consistency reliability, and  $<.3$  indicate low internal consistency reliability).

### 6.2.6. *Statistics*

#### *Finding the best-referencing method for the frontal channels*

Since it is well established that alpha power increases when participants close their eyes (Berger, 1929), the PSD difference (frequencies 1-100 Hz) between eyes closed/open was used as a measure of each system's capacity to detect basic frequency components underlying physiological brain processes. The trimmed means of these differences were compared between the two systems using *Yuen t-statistics* (Yuen, 1974; Wilcox, 2005). Trimmed means are robust estimators of central tendency because they are less affected by outliers (e.g., measurement error or fixed effects), and therefore provide probability coverage for the *confidence intervals (CI)* and tighter control of the *type I error*.

Because EEG data are highly correlated across neighboring channels, time points, and frequencies (Pernet *et al.*, 2015), *p-values* were corrected to control for the *false discovery rate (FDR)*; Benjamini and Yekutieli, 2001). Significant frequencies are reported as a black bar at the bottom of the plots. Frequentist *CI*s only indicate if the observed values can be rejected by a (two-tailed) test with a given alpha. So a *95% CI* on a difference that includes 0 indicates that *H0* (the hypothesis of no effect) cannot be rejected with a 5% chance to be wrong in the long run (Pernet, 2017). Thus, classic *CI*s do not inform on the variation of the statistics (e.g., whether the mean difference varies between the two variables or not), but only about the hypothesis that the difference is 0 (Pernet, 2017). In contrast, *high-density intervals (HDI)*, computed using a Bayesian bootstrap (Rubin, 1981), give the actual probability coverage of the summary statistics (e.g., the mean difference varies between the two variables). Bayesian *HDI*s test *H1* (the hypothesis of a difference), so if the *HDI*s of each variable overlap (or if the *HDI* of the difference between the two variables always include 0), one can be more confident that there is no effect (rather than accepting *H0* without testing it; Pernet, 2017). While the *t-statistics* require correction for multiple comparisons because they are computed independently at each frequency (but frequencies are not independent), bayesian *HDI*s are only intended to provide the actual variation of the summary statistics. Thus, they only provide more confidence in the absence of a difference



observed with the *t*-statistics. In this study, 95% HDIs were used for the first analysis only. They were computed using code adapted from the LIMO-EEG toolbox (Pernet *et al.*, 2011) and correspond to the shaded intervals around the trimmed means.

### Comparing spectral measures from MUSE and BIOSEMI data

All other analyses of spectral measures were compared using the skipped Pearson correlations from the Robust Correlation MATLAB toolbox (Pernet, Wilcox and Rousselet, 2013). See section 5.2.4. (previous chapter) for more detail on skipped correlations. Bivariate outliers correspond to the red observations in the plots. The red line corresponds to the least square fit line, and the red shaded areas correspond to the 95% CI.

## 6.3. Results

### 6.3.1. Finding the best referencing method for the frontal channels

With the default Fpz-reference, the MUSE frontal channels did not discriminate the PSD between eyes open/closed conditions in the alpha frequencies (9-10.5 Hz;  $p < 0.05$  corrected for FDR), contrary to the average-referenced BIOSEMI (Figure 18, top panel). However, this difference became non-significant when the frontal channels were re-referenced offline to the temporoparietal (TP) channels (i.e., mastoids; see Figure 18, middle panel). The MUSE TP9 and TP10 channels referenced to Fpz discriminated activity between eyes closed/open conditions similar to those (TP7 and TP8) from average-referenced BIOSEMI (Figure 18, bottom panel). Since the 95% HDIs overlap, we can be more confident that there is no significant difference in terms of signal discriminability between the two systems.

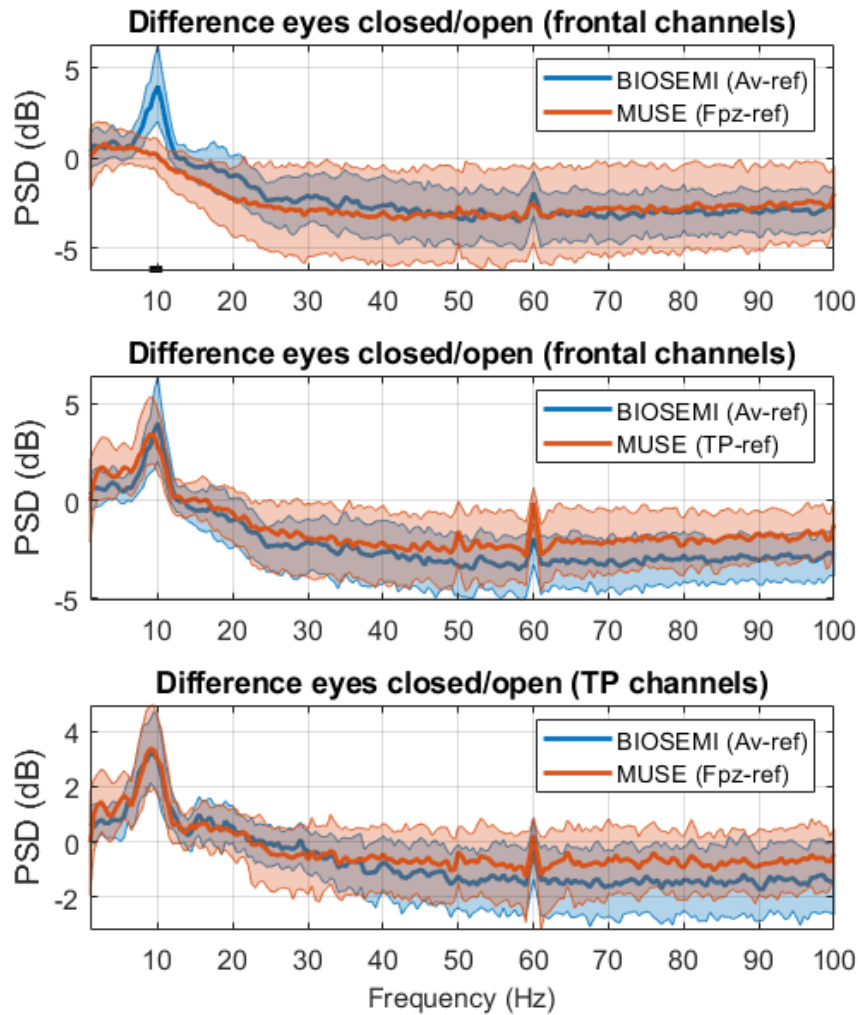


Figure 18. Comparison of power spectral density (PSD) difference between eyes closed/open conditions at frontal and temporoparietal (TP) channels ( $N = 37$ ), between the BIOSEMI and the MUSE. **Top panel** shows that the frontal channels of the MUSE Fpz-montage do not capture alpha power activity ( $p < 0.05$ , corrected for false discovery rate) compared to the BIOSEMI average-ref montage (same channels). **Middle panel** shows that this is corrected when the MUSE frontal channels are re-referenced offline to TP9 and TP10 (i.e., mastoid-ref montage). **Bottom panel** shows the temporoparietal channels (TP9/TP10) of the MUSE with the default Fpz reference capturing the whole PSD similarly to BIOSEMI (average-ref montage). **Notes:** Significance bars ( $p < 0.05$ ) are obtained using Yuen  $t$ -tests testing  $H_0$  at each frequency, corrected for false discovery rate (FDR). Thick lines are trimmed means of the power difference between eyes closed/open conditions. Shaded areas are 95% high-density intervals (HDI) testing  $H_1$  using a Bayesian bootstrap, confirming the absence of a difference when they overlap.

### 6.3.2. Spectral power in each frequency band (eyes closed only)

#### Mastoid-ref montage (frontal channels)

The averaged PSD of each frequency band was first compared between the BIOSEMI and the MUSE (*mastoid-ref montage* for both). All frequency bands were significantly correlated between at frontal channels: delta (1-3 Hz,  $r = .57^*$ , CI  $[0.32, 0.75]$ ), theta (3-7 Hz,  $r = .71^*$ , CI  $[0.48, 0.84]$ ), alpha (8-13 Hz,  $r = .88^*$ , CI  $[0.74, 0.94]$ ), beta (14-30 Hz,  $r = .80^*$ , CI  $[0.59, 0.91]$ ), and gamma ( $>30$  Hz,  $r = 0.51^*$ , CI  $[0.24, 0.70]$ ). These results are plotted in Figure 19.

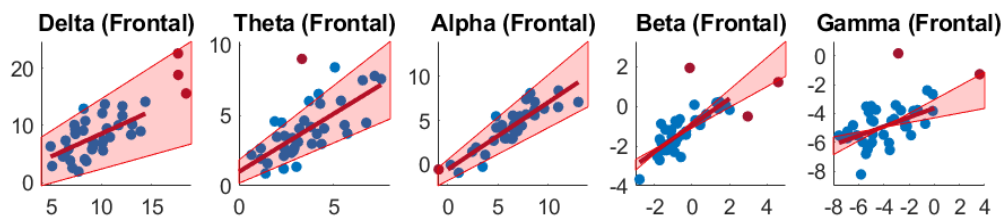


Figure 19. Correlations between BIOSEMI and MUSE (*mastoid-ref montage* for both) of mean power spectral density (PSD) for each frequency band, at frontal channels: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma ( $> 30$  Hz). All frequency bands were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The power spectral density (PSD) unit is deciBels ( $10^* \log_{10}(\mu V^2/Hz)$ ).

#### Fpz-ref montage (temporoparietal channels)

The averaged PSD of each frequency band from temporoparietal (TP) channels was compared between the BIOSEMI and the MUSE (*Fpz-ref montage* for both). All frequency bands were significantly correlated at TP channels: delta ( $r = .70^*$ , CI  $[0.50, 0.84]$ ), theta ( $r = .68^*$ , CI  $[0.46, 0.81]$ ), alpha ( $r = .88^*$ , CI  $[0.76, 0.94]$ ), beta ( $r = .75^*$ , CI  $[0.50, 0.88]$ ), and gamma ( $r = 0.53^*$ , CI  $[0.29, 0.67]$ ). These results are plotted in Figure 20.

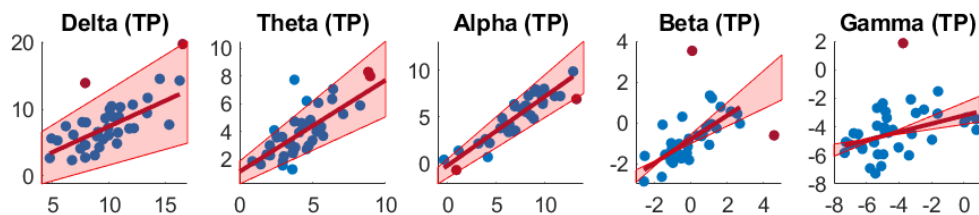


Figure 20. Correlations between BIOSEMI and MUSE (*mastoid-ref montage* for both) of mean power spectral density (PSD) for each frequency band, at temporoparietal (TP) channels: delta (1-3 Hz), theta (3-7 Hz), alpha

(8-13 Hz), beta (14-30 Hz), and gamma (> 30 Hz). All frequency bands were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The power spectral density (PSD) unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

Average-ref montage (frontal and temporoparietal channels)

The averaged PSD of each frequency band at frontal channels was then compared between the BIOSEMI *average-ref montage* and the MUSE *mastoid-ref montage*. All frequency bands were significantly correlated except the gamma band: delta ( $r = .53^*$ , CI  $[-0.20, 0.77]$ ), theta ( $r = .66^*$ , CI  $[-0.38, 0.82]$ ), alpha ( $r = .75^*$ , CI  $[-0.56, 0.88]$ ), beta ( $r = .60^*$ , CI  $[-0.34, 0.76]$ ), and gamma ( $r = 0.17$ , CI  $[-0.16, 0.48]$ ). These results are plotted in Figure 21.

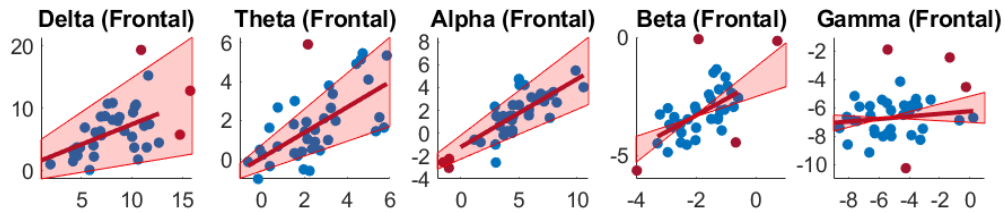


Figure 21. Correlations between BIOSEMI (*average-ref montage*) and MUSE (*mastoid-ref montage*) of mean power for each frequency band, at frontal channels: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (> 30 Hz). All frequency bands except gamma were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The power spectral density (PSD) unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

Correlations between frequency bands at temporoparietal (TP) channels from BIOSEMI *average-ref montage* and from MUSE *fpz-ref montage* are reported in Figure 22. Significant correlations were observed for all frequency bands: delta ( $r = .53^*$ , CI  $[-0.22, 0.75]$ ), theta ( $r = .56^*$ , CI  $[-0.27, 0.75]$ ), alpha ( $r = .80^*$ , CI  $[-0.58, 0.90]$ ), beta ( $r = .65^*$ , CI  $[-0.38, 0.81]$ ), and gamma ( $r = .34^*$ , CI  $[-0.02, 0.63]$ ).

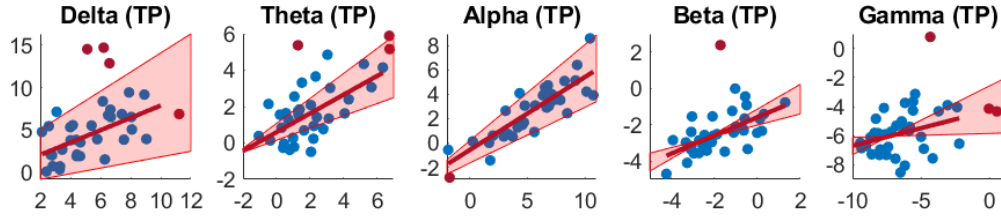


Figure 22. Correlations between BIOSEMI (average-ref montage) and MUSE (fpz-ref montage) of mean power for each frequency band, at temporoparietal (TP) channels: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (> 30 Hz). All frequency bands were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The power spectral density (PSD) unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

### 6.3.3. Individual alpha frequency (IAF)

#### Mastoid-ref (frontal channels) and Fpz-ref (temporoparietal channels) montages

IAFs at frontal channels estimated on BIOSEMI were significantly correlated with those obtained on MUSE using the same *mastoid-ref montage* (Figure 23, left), for both the PAF ( $r = .83^*$ , CI [0.58, 0.94]) and the CoG ( $r = .94^*$ , CI [0.85, 0.98]). However, frontal PAF could not be estimated on 4 BIOSEMI files and 11 MUSE files, whereas frontal CoG could not be estimated on 2 BIOSEMI files and 2 MUSE files. Correlations were also significant at temporoparietal (TP) channels (Figure 23, right), for both the PAF ( $r = .92^*$ , CI [0.78, 0.98]) and the CoG ( $r = .88^*$ , CI [0.73, 0.95]). The TP PAF could not be detected on 8 BIOSEMI files and 8 MUSE files, whereas the TP CoG could not be detected on 2 BIOSEMI files and 1 MUSE file.

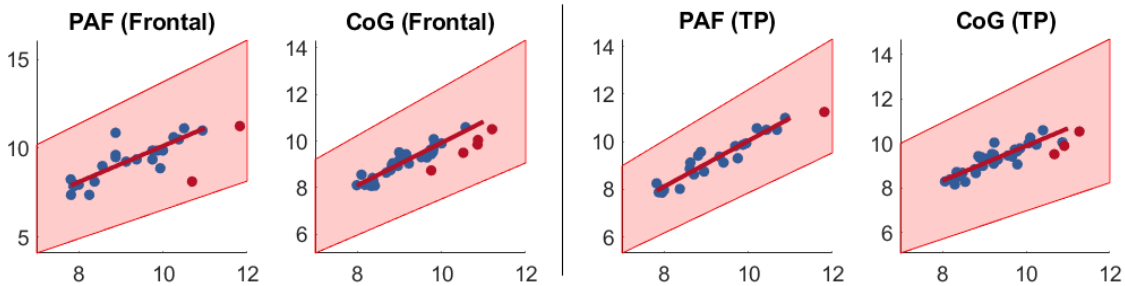


Figure 22. Correlations between BIOSEMI and MUSE (same mastoid-ref montage for both) of individual alpha frequency (IAF), at frontal (**left**) and temporoparietal (TP, **right**) channels. Both the peak alpha frequency (PAF) and the alpha center of gravity (CoG) were significantly correlated between the two systems, for both frontal and TP sites. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). Units are frequency bins (in Hz).

### Average-ref montage (frontal and temporoparietal channels)

Correlations between IAF for the BIOSEMI *average-ref montage* and the MUSE *mastoid-ref montage* were significant for frontal channels (Figure 23, left): PAF ( $r = .93^*$ , CI  $[0.78, 0.97]$ ) and CoG ( $r = .85^*$ , CI  $[0.69, 0.93]$ ). Note, however, that the automated algorithms could not detect the frontal PAF for 8 BIOSEMI files and 10 MUSE files. The frontal CoG was detected for all BIOSEMI files and undetected for 1 MUSE file. IAFs were also significantly correlated for TP channels (Figure 23, right): PAF ( $r = .93^*$ , CI  $[0.80, 0.98]$ ) and CoG ( $r = .86^*$ , CI  $[0.68, 0.95]$ ).

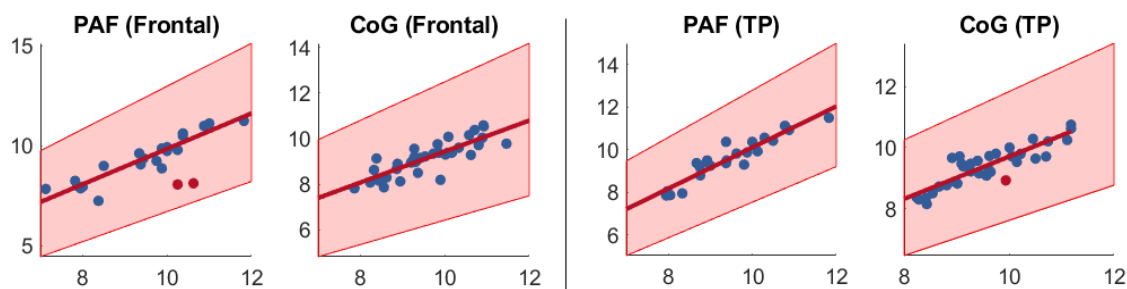


Figure 23. Correlations between BIOSEMI (*average-ref montage*) and MUSE (*mastoid-ref montage* for frontal channels and *fpz-ref montage* for TP channels) of individual alpha frequency (IAF), at frontal (**left**) and temporoparietal (TP, **right**) channels. Both the peak alpha frequency (PAF) and the alpha center of gravity (CoG) were significantly correlated between the two systems, at both frontal and TP sites. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). Units are frequency bins (in Hz).

### 6.3.4. Alpha asymmetry

#### Internal consistency reliability

The following Cronbach's alpha scores were obtained for frontal alpha power (.98 - BIOSEMI *average-ref montage*; .95 - MUSE *mastoid-ref montage*) and frontal alpha asymmetry (.67 - BIOSEMI *average-ref montage*; .76 - MUSE *mastoid-ref montage*).

#### Mastoid-ref montage (frontal channels)

Only the frontal alpha asymmetry (FAA) calculated with the traditional method (whole alpha band) was significantly correlated between BIOSEMI and MUSE with the same *mastoid-ref*

*montage*: traditional asymmetry ( $r = .76^*$ , CI  $[0.53, 0.89]$ ), PAF-asymmetry ( $r = .23$ , CI  $[-0.11, 0.53]$ ), CoG-asymmetry ( $r = 0.02$ , CI  $[-0.38, 0.48]$ ). These results are plotted in Figure 24.

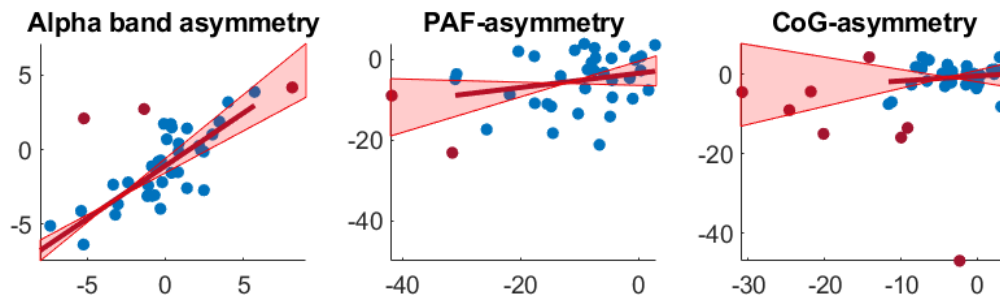


Figure 24. Comparison of frontal alpha asymmetry (FAA) measures from BIOSEMI and MUSE (*mastoid-ref montage*). Only FAA calculated with the traditional method (*i.e.*, whole alpha band) was significantly correlated between the two systems. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The asymmetry unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

#### Fpz-ref montage (temporoparietal channels)

Only the temporoparietal (TP) alpha asymmetry calculated with the traditional method (whole alpha band) was significantly correlated between BIOSEMI and MUSE with the same *mastoid-ref montage*: traditional asymmetry ( $r = .68^*$ , CI  $[0.43, 0.85]$ ), PAF-asymmetry ( $r = .18$ , CI  $[-0.20, 0.52]$ ), CoG-asymmetry ( $r = 0.20$ , CI  $[-0.19, 0.54]$ ). These results are plotted in Figure 25.

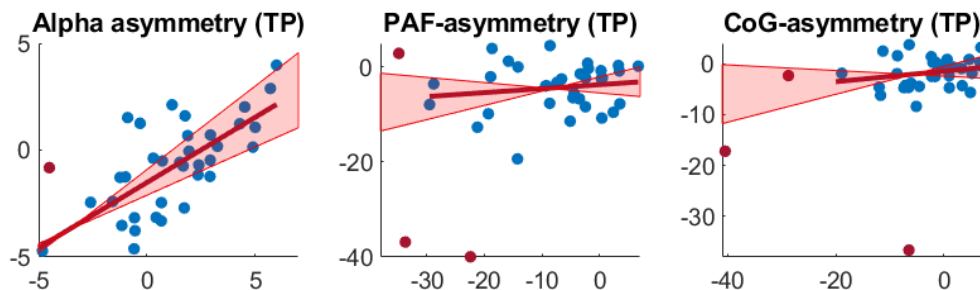


Figure 25. Comparison of temporoparietal (TP) alpha asymmetry measures from BIOSEMI and MUSE (*mastoid-ref montage*). Only asymmetry calculated with the traditional method (*i.e.*, whole alpha band) was significantly correlated. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The asymmetry unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).



Average-ref montage (frontal and temporoparietal channels)

Finally, alpha asymmetry measures were compared between the BIOSEMI *average-ref montage* and the MUSE *mastoid-ref montage*. FAA calculated on the average power over the whole alpha band (i.e., traditional method) was significantly correlated ( $r = .55^*$ , CI  $[0.20, 0.79]$ ). However, asymmetry scores calculated on power at the PAF ( $r = -0.07$ , CI  $[-0.38, 0.25]$ ) and at the CoG ( $r = .26$ , CI  $[-0.14, 0.63]$ ) were not significantly correlated. These results are reported in Figure 26.

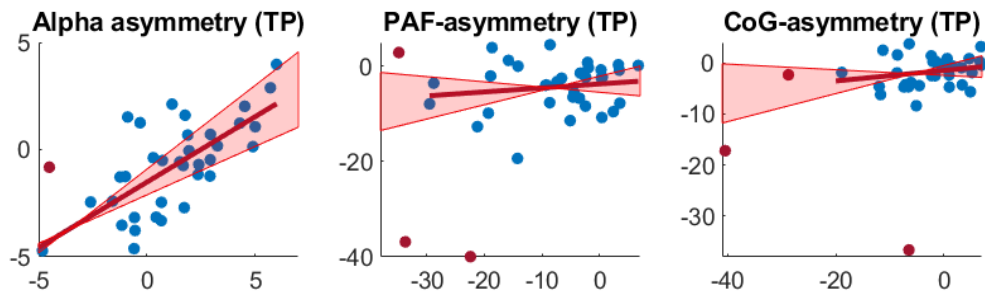


Figure 26. Comparison of frontal alpha asymmetry (FAA) measures from BIOSEMI (*average-ref*) and MUSE (*mastoid-ref montage*). Only asymmetry calculated with the traditional method (i.e., whole alpha band) was significantly correlated. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The asymmetry unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

Results were obtained for the temporoparietal (TP) alpha asymmetry compared between BIOSEMI *average-ref montage* and MUSE *Fpz-ref montage* (Figure 27): traditional method ( $r = .76$ ; CI  $[0.54, 0.88]$ ), PAF-asymmetry ( $r = .22$ , CI  $[-0.17, 0.55]$ ), CoG-asymmetry ( $r = .23$ , CI  $[-0.1, 0.49]$ ).

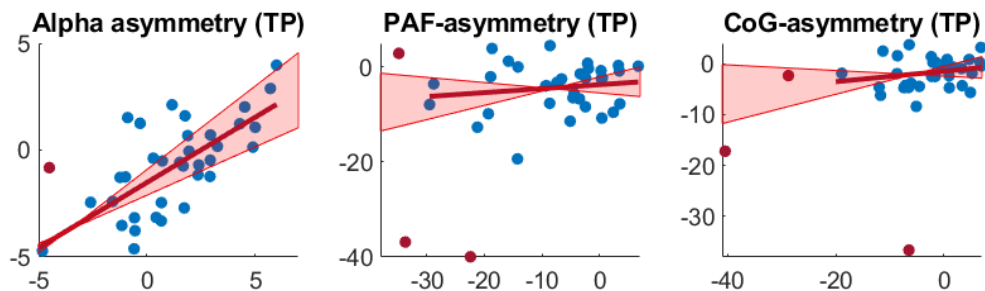


Figure 27. Comparison of temporoparietal (TP) alpha asymmetry between BIOSEMI (*average-ref*) and MUSE (*Fpz-ref montage*). Only asymmetry calculated with the traditional method (i.e., whole alpha band) was significantly correlated. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Spearman correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals (CI). The asymmetry unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).



## 6.4. Discussion

### 6.4.1. Results and interpretations

#### Validating the reference method

The MUSE frontal channels discriminated against power differences between eyes open/closed only when they were re-referenced to mastoids (TP9 and TP10 electrodes), especially in the alpha band. On the other hand, the TP channels did not require to be re-referenced offline and were left referenced to Fpz. The absence of difference in the *95% high-density intervals (HDI)* indicated with more confidence that the MUSE could discriminate spectral power between eyes open/closed similarly to the research-grade BIOSEMI. These reference montages (i.e., *mastoid-ref* for frontal channels and *Fpz-ref* for temporoparietal ones) were therefore used for subsequent validation of the MUSE.

#### Power in each frequency band

To further confirm that the MUSE could capture spectral content from each frequency band more accurately, we compared the spectral data directly between the two systems. Power in all frequency bands (i.e., delta, theta, alpha, beta, and gamma) from MUSE was similar to that of BIOSEMI, in all montage and electrodes, except in the gamma band ( $> 30$  Hz) for frontal channels when comparing MUSE *mastoid-ref montage* with BIOSEMI *average-ref montage*. These findings indicate that the wearable MUSE headset can reliably measure power spectral density in all frequency bands, but that caution should be taken when interpreting gamma oscillations recorded over frontal electrodes and their underlying sources. Note that similar caution should be taken regarding interpreting gamma power at TP channels, as the lower bound of the *95% confidence interval (CI)* is close to 0 (i.e., the null hypothesis of independence).

#### Individual alpha frequency (IAF)

IAFs estimated on MUSE data were strongly correlated with those from BIOSEMI data, for both estimation methods and both frontal and TP channels. Note, however, that the PAF was not detected by the automatic algorithms for more files than the CoG, especially on MUSE data, confirming the higher robustness of the CoG method compared to the PAF when facing ambiguous alpha peaks (see section 4.4.2.). While the automated IAF-estimation toolbox

performs best in high-density conditions by allowing to combine alpha activity across neighboring channels to improve detection performance (Corcoran *et al.*, 2017), it performed well on low- and sparse- density montages used in this study. Thus, the automated and open-source *restingIAF* plugin (Corcoran *et al.*, 2017) can be used on MUSE data (with frontal channels re-referenced offline to mastoids) to estimate the IAF on large datasets. And the CoG approach should be preferred over the PAF to better account for interindividual differences in alpha power distribution. Furthermore, interpretations can be made in line with the literature using the same EEG channels averaged to reference. However, the superior performance of the CoG method compared to the PAF method was apparent since it was able to find IAF in many more participants.

### Alpha asymmetry

Alpha asymmetry calculated with the traditional method (difference in alpha power averaged over the whole 8-13 Hz band) obtained from MUSE data (frontal and temporoparietal channels) were significantly correlated with those from BIOSEMI data for both *Fpz- mastoid- and average-reference montages*. However, asymmetry values calculated on the PAF and CoG frequencies were not correlated. These findings indicate that the MUSE can be used to measure frontal and TP alpha asymmetry (with the reference methods used in this study), and findings can be interpreted in line with previous findings obtained with the *average-ref montage*.

Previous research suggested that EEG asymmetry is influenced by different neural processes between the lower and the upper frequencies of the alpha band (Klimesch, 1997). Thus, while IAFs better account for interindividual differences and are associated with some cognitive processes (e.g., memory), they might reflect different underlying neural processes than those underlying alpha asymmetry (e.g., executive control, attention, emotion regulation). Thus, IAF-asymmetries might not be well-suited for asymmetry research.

The *restingIAF* toolbox also provides individualized lower and upper bounds of the alpha band. The alpha asymmetry calculated on the resulting individualized alpha range might be better suited to account for interindividual differences. Future studies should examine whether asymmetry measures obtained in this manner are more robust than the traditional method.

#### 6.4.2. Limitations and recommendations for future research

The main limitation of this study is the ~30 minutes difference between the two recordings (due to the preparation time for the BIOSEMI recording). Mental states may likely have changed between the two recordings. Previous research indicated that FAA during rest can vary ~60% from trait influences and 40% from state influences (Hagemann *et al.*, 2002), the former being the target measure in this study. While internal consistency reliability of asymmetry measures was relatively high, more variation and lower values were observed compared to the internal consistency reliability of the alpha power data (as in previous publications; Towers and Allen, 2009). This might explain the absence of correlation in the gamma frequencies when comparing MUSE *mastoid-ref montage* and BIOSEMI *average-ref montage*. Increasing the data length (e.g., 3 minutes of artifact-free data) might increase the trait influence by reducing the fluctuations due to state influences, and in turn, increase internal consistency reliability. We purposely used short segments to determine if they could be easily and reliably used in experimental and clinical conditions, but we did not compare different data lengths and their impact on these trait EEG measures. Future studies should compare asymmetry measures from a clinical system and a low-cost wearable system (as in this study) with longer data lengths to address this potential limitation. Ideally, both types of data should have been recorded simultaneously using markers to synchronize the data at the millisecond resolution. While no easy solution was found in this study, future research should aim to find a solution to address this limitation. However, correlations were still significant when comparing the MUSE and the BIOSEMI with different montages, suggesting trait spectral components were still captured.

Gamma oscillations from the MUSE frontal channels with *mastoid-ref montage* were not correlated to those from BIOSEMI *average-ref montage*. This is likely because these higher frequencies are prone to be contaminated with muscle artifacts, and that no advanced preprocessing cleaning method was used in this study since we aimed to keep data as raw as possible and remove as little data as possible considering the short data length. Future investigators using the MUSE headset might address this issue by collecting more data and using advanced preprocessing techniques to extract high-frequency artifacts from the data (e.g., independent component analysis or artifact subspace reconstruction; see section 3.2.2.). Another explanation might be that these frequencies may reflect activity from other brain processes when

referenced to average than those captured with the *mastoid-ref montage*. Thus, these frequencies should only be interpreted in the *mastoid-ref montage* context when using this system.

### 6.5. *Conclusion*

Our study validates the use of the low-cost MUSE headset for accurately and reliably measuring power spectral density, individual alpha frequency, and alpha asymmetry calculated with the traditional method. This system can help advance human neurophysiological monitoring techniques on large datasets using wearable neurotechnologies and increase the feasibility of their implementation into real-world applications.



## Chapter 7. EEG asymmetry and well-being

This Chapter uses the tools validated in the two previous chapters to examine the EEG correlates of well-being in a large sample.

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### 7.1. Introduction

#### 7.1.1. Context

For decades, frontal alpha asymmetry (FAA) has been a useful EEG measure to study emotion-related states and traits, motivation, temperament, cognitive control, and psychopathologies (see section 4.4.3.). Similarly, the individual alpha frequency (IAF) has been used for decades as an index to study cognition (see section 4.4.2.). We found that both measures can be reliably estimated using the low-cost, wearable MUSE EEG headset (see Chapter 6), and are promising measures for the study of multidimensional well-being that involves emotional and as well as cognitive functions (see Chapter 4).

While the literature on EEG asymmetry is sizable and robust, it is important to note that there have also been failed replications and contradictory results (e.g., Gotlib, 1998; Reid, Duke and Allen, 1998; Hagemann *et al.*, 1999; Müller *et al.*, 1999; Coan, Allen and Harmon-Jones, 2001; Gale *et al.*, 2001; Papousek and Schuster, 2002; Dennis and Solomon, 2010; Kop *et al.*, 2011; Koslov *et al.*, 2011; Quinn *et al.*, 2014; Meyer *et al.*, 2015; Arns *et al.*, 2016; Palmiero and Piccardi, 2017). These inconsistencies can be explained by heterogeneity in the experimental designs, EEG preprocessing techniques, and statistical approaches employed across investigators over the years (Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017). A summary of the main limitations of EEG asymmetry research and proposed solutions that were implemented in this study are now described.

### **7.1.2. Alpha asymmetry as a state vs. trait**

First, one limitation is that EEG asymmetry can reflect trait or state aspects and thus, designing experiments to highlight one over the other depending on the research question is essential. When measured during rest, EEG asymmetry is considered a trait variable related to various psychological constructs and predictive of future emotional behavior or psychopathology. When measured as an event-related response, it is considered a state variable reflecting the person's current emotional state (Allen, Coan and Nazarian, 2004; Hagemann *et al.*, 2005; Smith *et al.*, 2017). Some authors estimate that 60% of the variance in asymmetry measure within a resting session is due to trait influence, and the 40% to state influences (Hagemann *et al.*, 2002). Hence, the first approach aims to reduce the state influence during rest, whereas the second one aims to increase it using emotion-elicitation perturbations (Coan, Allen and McKnight, 2006). The present study focused on trait asymmetry related to subjective well-being levels.

### **7.1.3. Sample-specific characteristics**

Second, sample-specific characteristics (e.g., age, gender) have been shown to significantly influence EEG findings because of functional and anatomical differences (Klimesch, 1999; Sowell *et al.*, 2007; Hagemann *et al.*, 2008; Finley *et al.*, 2020). Many EEG asymmetry studies include participants of one gender to reduce this bias (Tomarken, Davidson and Henriques, 1990; Wheeler, Davidson and Tomarken, 1993; Jacobs and Snyder, 1996; Reid, Duke and Allen, 1998; Gale *et al.*, 2001; Dennis and Solomon, 2010; Mikolajczak *et al.*, 2010; Koslov *et al.*, 2011). However, this prevents investigators from examining gender as a potential mediator or moderator of asymmetry findings (MacKinnon *et al.*, 2013). There is a lack of consensus of the role gender plays in EEG asymmetry in the limited studies that have addressed this question (Veldhuizen, Jonkman and Poortvliet, 1993; Carrier *et al.*, 2001; Miller *et al.*, 2002; Otero *et al.*, 2003; Morgan *et al.*, 2005; Gasbarri *et al.*, 2006, 2007; Stewart *et al.*, 2010; Müller *et al.*, 2015). Similarly, the role age plays in EEG asymmetry is also not very well known. One solution to the lack of understanding of if and how demographic variables influence EEG asymmetry and well-being is to collect large and diversified datasets that better reflect the general population. A few studies with large samples found that age and gender mediate frontal asymmetry but that race or ethnicity or socioeconomic status did not (Stewart *et al.*, 2010; Gable *et al.*, 2015; Arns *et al.*, 2016)(Arns *et al.*, 2016; Gable *et al.*, 2015; Stewart *et al.*, 2010). However, these studies are rare

and hard to replicate because of the time and cost involved in recording EEG data on a large number of subjects with conventional systems (equipment cost, EEG preparations time, participants compensation for their time, equipment cleaning, etc.).

Wearable EEG technologies can address this issue by making the collection of large datasets of diversified and under-represented populations more feasible (see section 3.2.3.).

#### **7.1.4. Targeted components of the alpha band**

The third main limitation in EEG asymmetry research is the handling of alpha-band frequencies and bounds. The alpha band should not be considered as a single phenomenon because of interindividual differences in alpha power distribution, and frequency bounds (see Section 2.3.5; Klimesch *et al.*, 1990; Klimesch, 1997). Furthermore, differential changes (sometimes in opposing directions) within the same dataset have been observed between lower (8-10.5 Hz) and upper (11-13 Hz) frequencies, as well as between local and global properties (Klimesch, 1999; Nunez, Wingeier and Silberstein, 2001).

The individual alpha frequency (IAF), described in more detail in Section 2.3.5., is associated with cognitive constructs and better accounts for these interindividual differences. It has not been used to study well-being directly. While we suspected that asymmetry estimates calculated on the IAF might better account for interindividual differences (see section 4.4.2.), we found them to be unreliable in Chapter 6, at least when using the MUSE's montage. Thus, we evaluated the potential relationship between well-being and IAF, but not IAF-asymmetry in this study.

#### **7.1.5. Other frequencies than alpha**

The need to expand EEG asymmetry analyses to other frequency bands and areas of the brain has been expressed (e.g., Davidson, 1988, 1992; Ota, Toyoshima and Yamauchi, 1996; Ambrosini and Vallesi, 2016). Several studies have explored interactions between bands or other brain areas without a clear consensus on the findings (Sutton and Davidson, 1997; Hagemann *et al.*, 1999; Laufs *et al.*, 2006; Mathersul *et al.*, 2008; Müller *et al.*, 2015). Although it is likely that EEG frequency bands functionally interact with one another (Klimesch, 1999; Laufs *et al.*, 2006; Finley *et al.*, 2020), as far as we know, no robust literature is available to make reasonable interpretations about how alpha power may interact with other frequency bands, especially in the realm of EEG asymmetry (Smith *et al.*, 2017). While theta and beta oscillations are associated with well-being



and stress (see Section 8.4.4. and 8.4.5.), no asymmetry in these frequency bands (or others) have been robustly identified as a marker of well-being yet, to our knowledge. Therefore, this study includes asymmetry scores estimated on the delta (1-3 Hz), theta (4-7 Hz), and beta (14-30 Hz) frequency bands, for both frontal and TP sites.

#### **7.1.6. Limiting EEG asymmetry to the frontal areas**

The fourth limitation is the reduction of the study of EEG asymmetry phenomenon to only the frontal areas. It has been expressed for a long time that both anterior and posterior cortical regions show asymmetric activity patterns (Davidson, 1988, 1992). This is also reflected by studies showing that FAA obtained on data referenced with the current-source density (CSD) transformation (i.e., reflective of alpha power from local frontal sources only) correspond to a marker for depression risk, whereas FAA obtained on data referenced to mastoids or average (i.e., containing alpha power from distal, posterior cortical regions) correspond to a better marker of current depression severity (Stewart *et al.*, 2010).

Furthermore, expanding the analysis of alpha asymmetry to the temporoparietal (TP) regions seem particularly relevant since alpha asymmetries were source-localized to the frontoparietal network (FPN), which includes brain structures in both the frontal and the TP regions (see above; Vossel, Geng and Fink, 2013). Furthermore, different subtypes of anxiety disorders are differently associated with asymmetric activity in frontal and TP regions (Heller *et al.*, 1997; Engels *et al.*, 2007; Mathersul *et al.*, 2008; Müller *et al.*, 2015); Heller 1997; Mathersul 2008; Müller 2015). Together, these findings suggest that anxious arousal (physiological arousal and hyper-reactivity under conditions of panic) is associated with relatively greater right than left frontal activation, whereas anxious apprehension (involving worry and verbal ruminations; i.e., trait anxiety and generalized anxiety disorder) is linked to the opposite asymmetry in frontal area and asymmetry in the same direction in the TP area.

However, other findings suggested that TP asymmetry was less stable over time compared to frontal asymmetry (Müller *et al.*, 2015) and sometimes not associated with self-reported measures of affect and motivation (Sutton and Davidson, 1997). Other previous research suggested that frontal asymmetry is more associated with affective components, whereas posterior asymmetry is associated with the cognitive demands of the task, and their direction is generally not correlated, even sometimes anticorrelated (Davidson, 1988). In this study, we examine the

relationship between well-being and asymmetry in both frontal and TP regions and hypothesize that alpha asymmetry in both regions will be associated with well-being (with potentially a different direction).

#### **7.1.7. Limiting EEG asymmetry to the alpha oscillations**

The Fifth and last main limitation in EEG asymmetry research is the need to expand analyses to other frequency bands. Coherence in both alpha and theta oscillations has been highlighted during both relaxation and mental calculation (Nunez and Srinivasan, 2006). This widespread (global) phase coherence phenomenon increases in the upper frequencies of both alpha and theta bands while it simultaneously decreases in the lower frequencies (Wingeier, 2000; Nunez and Srinivasan, 2006). These findings go along with other findings indicating that global alpha and theta rhythms functionally interact during both relaxation and attentional tasks (Klimesch, 1999; Buzsaki, 2006; Laufs *et al.*, 2006).

Furthermore, theta power has been used to predict response to depression treatment in several studies (Knott *et al.*, 1996, 2000; Cook and Leuchter, 2001; Cook *et al.*, 2002; Bares *et al.*, 2008; Iosifescu *et al.*, 2009; Spronk *et al.*, 2011; Baskaran, Milev and McIntyre, 2012; Olbrich and Arns, 2013). Furthermore, theta power decreases while upper alpha power increases in several conditions (i.e., the early part of life until adulthood, in neurological disorders, and in the transition phase from awake to sleeping), whereas the direction of their relationship is opposite for the late part of the lifespan (Klimesch, 1999).

Similarly, alpha and beta spectral power have been found to interact (Laufs *et al.*, 2006; Hamid *et al.*, 2010), and both are associated with high levels of mental stress and depression (Hayashi *et al.*, 2009; Jena, 2015; Al-shargie *et al.*, 2016; Jun and Smitha, 2016; Díaz *et al.*, 2019; Al-Dabass, 2020; de Hemptinne *et al.*, 2021). More specifically, prefrontal beta power in lateral areas was found to be positively associated with depression and anxiety, whereas lateral beta power was negatively associated with mood (de Hemptinne *et al.*, 2021). The authors interpreted these results to be in line with the organization of the reward networks in the prefrontal cortex (PFC).

However, no robust literature is available to make specific interpretations about how alpha asymmetry interacts with other frequency bands, and whether asymmetries in other frequency bands could be associated with psychological constructs such as well-being. Thus, we aim to

bring light to this matter in this study and hypothesize that well-being will be associated with asymmetries in other frequency bands. This study includes asymmetry scores estimated on the delta (1-3 Hz), theta (4-7 Hz), and beta (14-30 Hz) frequency bands, for both frontal and TP sites. Since no previous research exists on this matter, we have no specific hypothesis concerning the direction of these potential associations.

#### **7.1.8. Study goals and hypotheses**

Considering the potential importance of alpha asymmetry as a physiological correlate in general, and for well-being specifically, the overall objective of this study was to determine whether a low-cost wearable EEG headset (the Muse by Interaxon) could be used to measure EEG correlates (CoG, EEG asymmetry) of well-being on a relatively large sample ( $N = 353$ ). The analyses were designed to address the main limitations of EEG asymmetry research addressed above.

The hypotheses for the study were as follows:

1. The wearable MUSE EEG headset can be used to examine associations between well-being and EEG spectral measures such as the IAF and the alpha asymmetry. We expect the IAF and FAA to be positively correlated with well-being.
2. Age and gender will be associated with both well-being and mean alpha asymmetry (predefined 8-13 Hz band).
3. Asymmetry scores estimated on sub-components of alpha oscillations (namely lower/upper alpha) will provide different correlations regarding the relationship between well-being and alpha asymmetry than those estimated on the predefined alpha band (8-13 Hz), by better accounting for different sources and mechanisms underlying alpha oscillations.
4. Well-being levels will be associated with alpha asymmetry in the TP regions and with EEG asymmetries in other frequency bands (namely theta, and beta).

## 7.2. Methods

### 7.2.1. Participants

353 participants were recruited from groups attending workshops focusing on well-being and personal development at the Earthrise Campus. Exclusion criteria: people younger than 18 years of age, inability to read or understand the consent form, acute or chronic illness precluding completion of measurements. Upon arrival at the research laboratory, participants were briefly interviewed by the research assistants to ensure they met the inclusion/exclusion criteria and were then allocated to a carrel where the following equipment was available for their participation: a wearable EEG headset, a Chromebook, and a pair of headphones. The settings allowed the recording of up to 9 participants simultaneously. Participants volunteered and were not compensated for participation. The study and the consent form were approved by the Institute of Noetic Sciences' institutional review board (IRB). All questionnaires were optional and anonymous.

### 7.2.2. Subjective and multidimensional well-being

Participants' multidimensional well-being was assessed on-site using the Arizona Integrative Outcomes Scale (AIOS; Bell *et al.*, 2004) in SurveyMonkey (SurveyMonkey, 2021). We confirmed the reliability, and validity of the AIOS at capturing multidimensional well-being and its main underlying components in Chapter 5. Only the 24h version of the AIOS was used in this study since we found that it was highly correlated with the 1-month form.

### 7.2.3. Electroencephalography (EEG)

#### Data collection

Once participants completed the survey, their EEG was recorded using InteraXon's Muse wearable EEG headband (version 2016), with a sampling rate of 256 Hz and 12-bits of data resolution. See Chapter 6 for more detail on the hardware specifications of the system, and its validation for measuring frequency domain EEG. Before positioning the headband on the subjects' heads, their skin was cleaned with alcohol swipes at electrode sites, and a thin layer of water was applied with a sponge to the electrodes to improve signal quality. EEG data were acquired on Chromebooks using the MindMonitor App (Clutterbuck, 2015) and were uploaded onto Dropbox at the end of the recording. Random unique identifiers were generated

automatically when participants signed the consent form digitally and used to link survey and EEG data. Impedance check was provided by the App (horseshoe symbol) and visually confirmed by the raw signal displayed on the screen in real-time.

EEG data were recorded while participants were instructed to focus their attention on their breath and count inhalation/exhalation cycles. They were instructed to bring their attention back to their breath and start counting again if they lost track of their count or noticed that their minds wandered. This task reduces EEG artifacts occurring naturally with eye movements. Most importantly, this task can later be implemented into practical translational and therapeutical applications aimed at increasing well-being levels through the modulation of alpha asymmetry and the underlying brain processes (Angelakis *et al.*, 2007; Sessa, 2007; Moynihan *et al.*, 2013; Doll *et al.*, 2016; Schmalzl *et al.*, 2018; Prpa *et al.*, 2020).

As shown in previous publications (Towers and Allen, 2009) and Chapter 6, satisfying internal consistency reliability of FAA can be obtained with as few as 45 s of data. Furthermore, a recent publication showed that individuals can robustly be “authenticated” using spectral EEG data obtained on segments as short as 30 s (and this was stable weeks later; da Silva Castanheira *et al.*, 2021). Thus, two minutes of EEG data were recorded for each participant. Raw data were made open-source, available at <https://www.doi.org/10.17605/OSF.IO/NQ7GA>.

### Data Preprocessing

Data preprocessing was done in *EEGLAB* version 2020.0 (Delorme & Makeig, 2004a) in *MATLAB* v2020a. EEG data were imported with the *muse\_monitor* plugin v3.2, low-pass filtered at 30 Hz (transition bandwidth 12.5 Hz; passband edge 50 Hz; cutoff frequency -6 dB 56.25 Hz; linear non-causal filter) to remove high-frequency artifacts, and high-passed filtered at 1 Hz (transition bandwidth 1 Hz; passband edge 1 Hz; cutoff frequency -6 dB 0.5 Hz; linear non-causal filter) to remove low-frequency drifts. 10-20 channel template locations from BESA spherical coordinates were used in *EEGLAB*. Following our findings reported in Chapter 6, frontal channels were re-referenced to TP9/TP10, while TP channels were left referenced to Fpz (manufacturer’s default).

No automated method tested on these data reliably removed bad channels from the MUSE signal. Thus, artifactual channels (with ~50% of data being noisy or artifactual) were manually tagged

and removed with a custom-made single-page figure displaying each channel's overall raw data, standard deviation, and power spectra (see Figure 28). Files with at least one bad channel were removed for analyses.

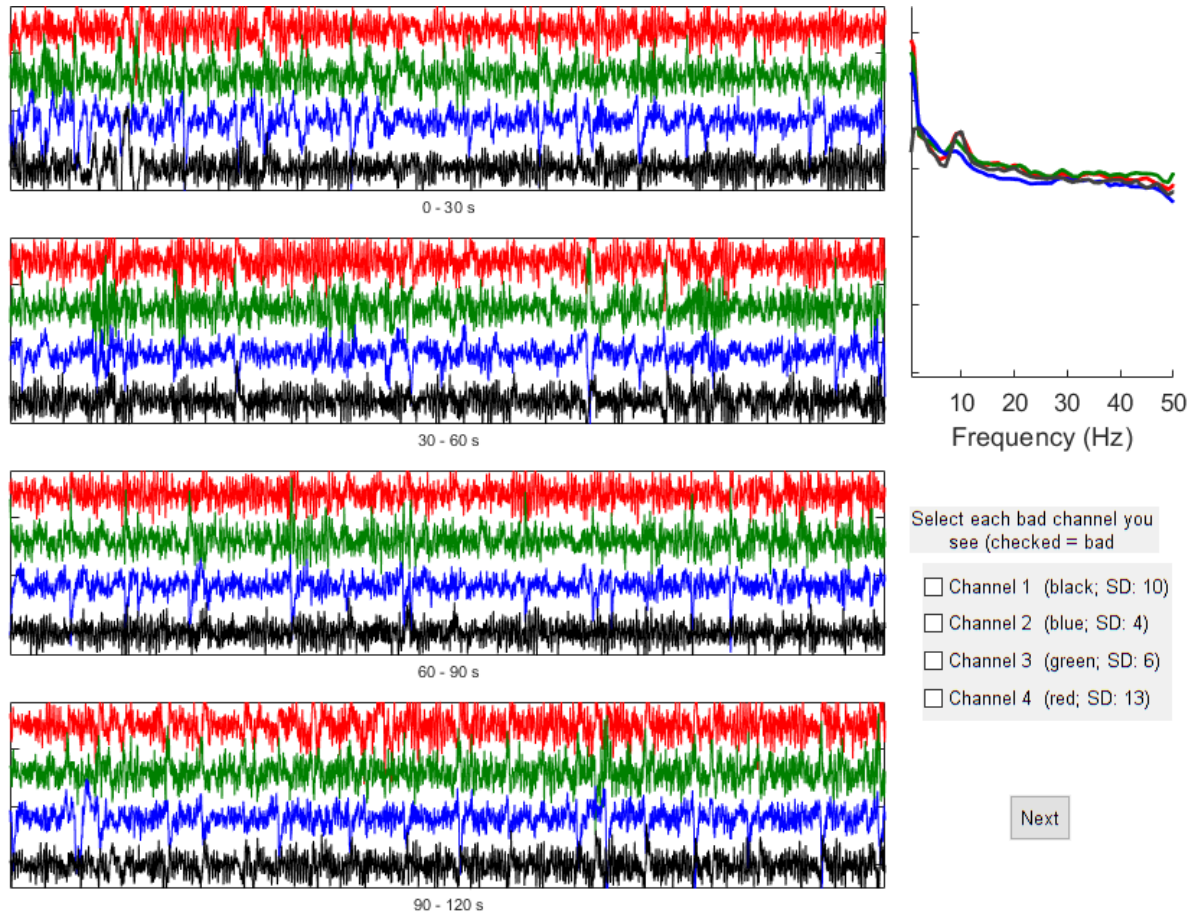


Figure 28. MATLAB function developed for the project to tag bad channels quickly over a large dataset. The left panel displays raw data (4 channels) in 30 s blocks, the top right plot shows the power spectra for each channel, and the bottom right plot provides the standard deviation and a check box to tag bad channels. This information is then saved in a structure variable to reject files with bad channels automatically over the whole sample.

We aimed to use the automated ASR algorithm (see section 3.2.2.), available in the open-source *clean\_rawdata* v2.2 EEGLAB plugin, to detect and remove non-brain artifacts on the large sample. Since it was never used on MUSE data before, we first cross-validated this method. The Riemannian method (reconstruction of the signal after removing artifacts to preserve the brain data of that section) did not perform well because it reconstructs the signal using a mixing matrix calculated on the reference data and then interpolates artifactual section based on the rest of the

EEG signal during that period. Since there are not enough channels without artifacts at the same period with 4 channels of only two different regions to create a good interpolation, this method could not be used. Thus, we used the Euclidean method, which rejects the detected artifactual segments instead of attempting to reconstruct them.

150 files (~half the sample) were randomly selected from the database to be cleaned manually first, and then automatically with the Euclidean method. Figure 29 shows an example of automatic artifact cleaning performed by the automatic method.

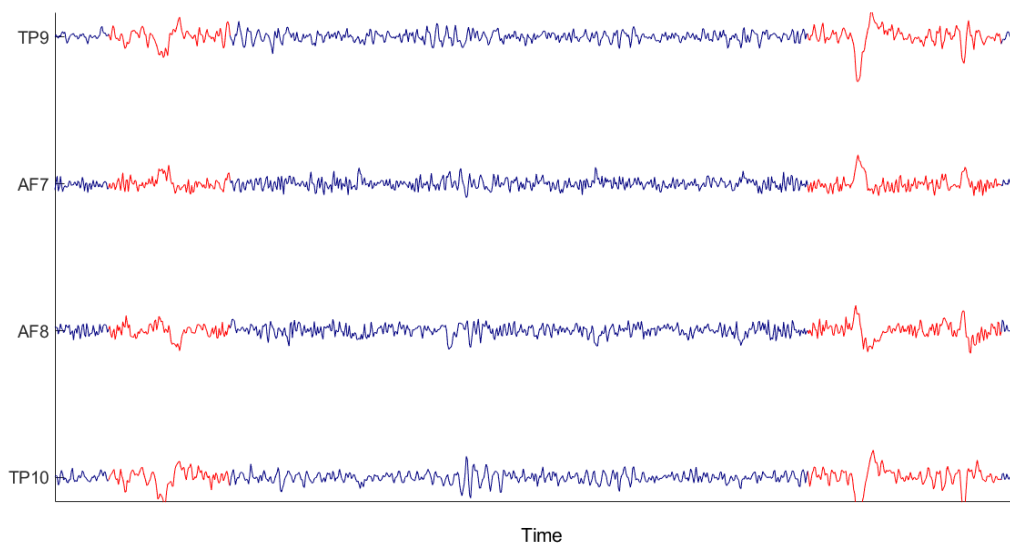


Figure 29. Illustration of artifact rejection performed by the automatic Euclidean method integrated into EEGLAB and cross-validated in this study, to preprocess a large dataset automatically.

Performance was calculated on each channel by comparing each sample as either true positive (bad sample correctly rejected), true negative (good sample correctly kept), false positive (good sample incorrectly rejected), or false negative (bad sample incorrectly kept). "Positive" and "negative" refer to presence or absence (see Figure 30). Then, the true positive rate (TPR, i.e., sensitivity) and the true negative rate (TNR, i.e., specificity or selectivity) were calculated for each channel with  $TPR = \text{true positives} / (\text{true positives} + \text{false negatives})$  and  $TNR = \text{true negatives} / (\text{true negatives} + \text{false positives})$ .

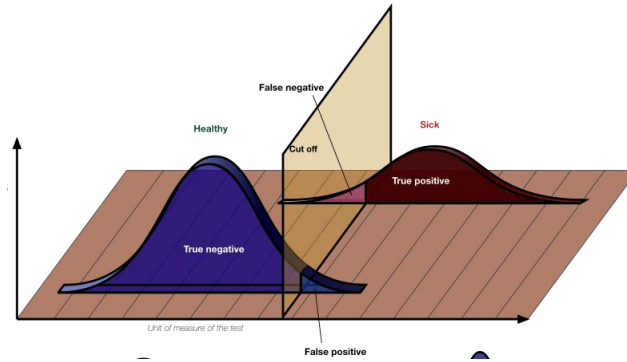


Figure 30. Representation of the true negative/true positive evaluation concept. Source: Maria (2021).

The average sensitivity and specificity were then calculated over all channels to obtain the overall performance of the automatic method compared to manual rejection. After testing different parameters, the best performance obtained showed 81% sensitivity and 83% specificity (settings: ‘burst\_criteria’ = 6, ‘window\_criteria’ = 0.3, ‘window\_tolerance’ =  $[-Inf\ 7]$ ). 50 additional datasets were randomly selected for cross-validation (reversed order, i.e., data were cleaned manually first and then compared to automated cleaning data), showing 84% sensitivity and 89% specificity. Since further increasing the sensitivity scores (i.e., removing more subtle artifacts) corresponded to a decrease in specificity (i.e., removing more non-artifactual data), these thresholds were considered most suited for this analysis. On average, this method removed an additional 11.4 seconds of data (+/- 23.0). Files with less than 60 s of remaining artifact-free data were not included in the analyses to preserve high internal consistency reliability and as much trait variable as possible (see Chapter 6 for more detail on this).

Note that these preprocessings were done on duplicated data that were averaged-referenced to a fifth zero-filled channel as it increased performance by homogenizing raw signal amplitude across channels. But because this average re-referencing method was not validated for this specific montage and is not recommended with less than 30 channels (Smith *et al.*, 2017), artifactual sections were removed from the original raw files and then re-processed as above. This step was only used to increase the performance of the EEGLAB plugin.

#### Power spectral density (PSD), individual alpha frequency (IAF), and EEG asymmetry

PSD was calculated using MATLAB’s *pwelch* function on 2-s *hamming* tapered windows (42.5 dB sidelobe attenuation) with 50% overlap (per guidelines; Allen, Coan and Nazarian, 2004; Smith *et al.*, 2017), since the *Welch* method smooths over non-systematic noise and is more robust



compared to the more popular *FFT* method that is more sensitive to noise and nonstationarities. PSD estimates were then converted to  $10 \cdot \log_{10}(\text{power})$  decibels (dB) as untransformed power values tend to be positively skewed due to individual differences in skull thickness that influence the signal amplitude (Allen, Coan and Nazarian, 2004).

The individual alpha frequency (IAF) was estimated only using the alpha center of gravity (CoG) using the automated, open-source *restingIAF* plugin (Corcoran *et al.*, 2017) since it provided the most robust estimates in our validation analyses reported in Chapter 6.

Alpha asymmetry scores were obtained on the alpha PSD averaged over the predefined band (8-13 Hz), averaged over the predefined lower (8-10.5 Hz) and upper (11-13 Hz) sub-bands. They were calculated following standard procedures by subtracting the alpha power of interest of the left channel from the right channel ( $\text{alpha\_power\_dB} - \text{alpha\_power\_dB}$ ). Positive scores, therefore, indicate greater alpha power in the right relative to the left electrode. Asymmetry scores were also obtained from the temporoparietal (TP) channels, as well as on the delta (1-3 Hz), theta (4-7 Hz), and beta (14-30) frequency bands. Gamma was not included due to the MUSE vulnerability to line noise and other non-brain artifacts that can occur in the high spectral frequencies, that are not accounted for by the cleaning method used in this study.

#### **7.2.4. Statistics**

Because of small portions of artifacts remaining in some EEG data after automatic preprocessing, robust least-squares regressions (Tukey's bisquare function; default tuning constant = 4.685) were used for statistical analysis to down-weight the residuals' influence on the model, using iterative reweighted least-squares (IRLS; Huber and Ronchetti, 2009). See more detail on robust linear regressions in Section 5.2.4.). Robust linear regression models were generated in MATLAB 2021a using MATLAB's *fitlm* package. All models were tested for lack of fit first using a degenerate model consisting of only a constant term (indicated by the F-statistics and associated p-value). The coefficient estimates are reported in the first column and indicate a significant linear relationship between the predictor and the outcome variables when p-values are present. Summary statistics of the models include the number of observations, the error degrees of freedom, the root mean squared error (RMSE),  $R^2$  (for models with one predictor), adjusted  $R^2$  (for models with multiple predictors).

### 7.3. Results

230 participants remained for analyses after preprocessing (83 with at least one bad channel and 36 with less than 60 s of artifact-free data; the data loss due to signal quality is discussed in the Discussion). They were aged from 22 to 80 years old (mean age was 55 +/- 13.4) and were 64.3% female, 28.7% males, and 7% "Other" or missing.

#### 7.3.1. Well-being and alpha asymmetry

No association was observed between multidimensional well-being and FAA (whole band; Table 6 and Figure 31). However, well-being was negatively correlated with temporoparietal (TP) alpha asymmetry scores (predefined 8-13 Hz band), reflecting greater cortical activity in the right TP area relative to the left is associated (assuming the inhibitory role of alpha oscillations on regional cortical activity; see Introduction). Detailed statistics are reported in Table 6 and an illustration of the results in the frequency and the scalp topography domain can be found in Figure 31, using the 20 participants with the highest well-being levels. The relationship between well-being and TP total alpha asymmetry scores appear to be driven more specifically by neural activity in the lower frequencies of the alpha band (8-10.5 Hz) because well-being was significantly correlated with lower alpha asymmetry but not with upper alpha asymmetry (see Table 7).

**Table 6. Well-being and alpha asymmetry (strict bounds at 8-13 Hz).**

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
Frontal $\alpha$ asymmetry	0.001 (0.002)	230 (228)	0.468	0.158	42.8***
TP $\alpha$ asymmetry	-0.007* (0.003)		0.808	0.036	8.51**

*p-values are reported with \* ( $p$ -value < 0.05; significance at the 95% level), \*\* ( $p$  < 0.01; significance at the 99% level, and \*\*\* ( $p$  < 0.001; significance at the 99.9% level).  $p$ -values on the F-statistic indicate whether the model fit is valid or not, and  $p$ -values on the coefficient estimate that the linear relationship between the predictor and the response variables is significant. The standard error (SE) of the  $\beta$  coefficients' distribution is reported in parentheses. Each simple linear model follows the equation: Response variable ~ 1 + predictor.*

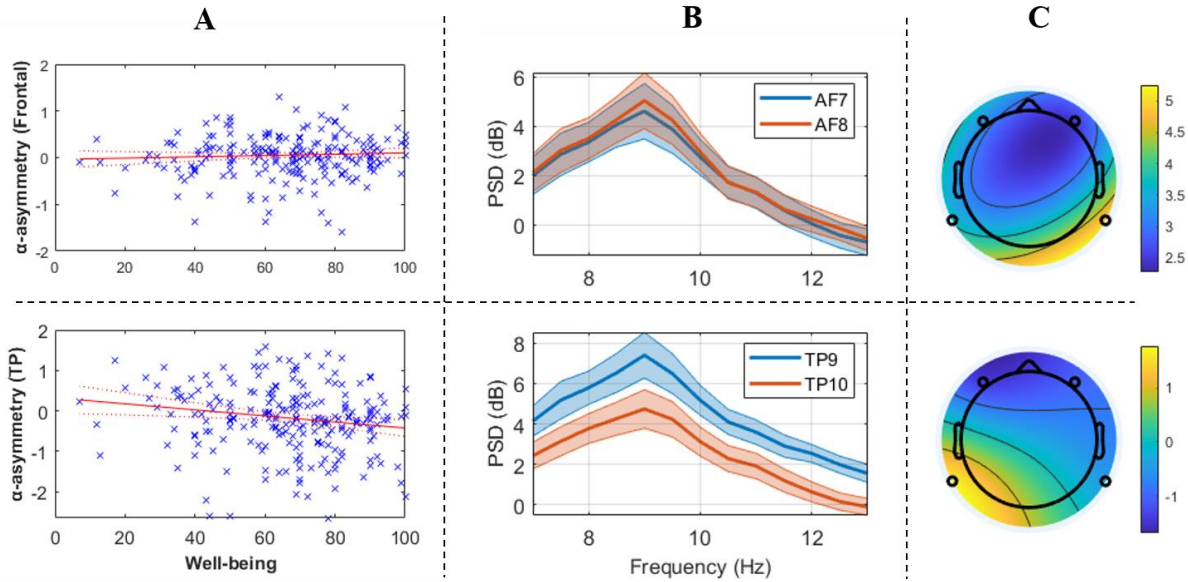


Figure 31. **Column A:** These linear regression models of well-being and mean alpha asymmetry (predefined 8-13 Hz band) show the absence of relationship at frontal channels (top) and the presence of one at temporoparietal (TP, bottom) channels. Higher well-being levels are associated with greater cortical activity in the right TP area relative to the left (assuming alpha inhibits regional cortical activity). **Column B:** Mean and standard error of the alpha power spectral density (PSD) from the 20 participants with highest reported well-being level at frontal (top) and TP (bottom) channels, illustrating the results reported in Panel A. **Column C:** Scalp topography of mean alpha PSD on a typical subject with low self-reported well-being (AIOS = 17; top) and high self-reported well-being (AIOS = 100; bottom), as an illustration of the effect reported in Panel A.

Table 7. Well-being and temporoparietal (TP) lower/upper alpha asymmetry.

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
Lower $\alpha$ -asymmetry (8-10.5 Hz)	-0.008* (0.003)	230 (228)	0.981	0.035	8.28**
Upper $\alpha$ -asymmetry (11-13 Hz)	-0.005 (0.003)		0.863	0.011	2.61

*p*-values are reported with \* (*p*-value < 0.05; significance at the 95% level), \*\* (*p* < 0.01; significance at the 99% level, and \*\*\* (*p* < 0.001; significance at the 99.9% level). *p*-values on the F-statistic indicate whether the model fit is valid or not, and *p*-values on the coefficient estimate that the linear relationship between the predictor and the response variables is significant. The standard error (SE) of the  $\beta$  coefficients' distribution is reported in parentheses. The multiple linear model follows the equation: Response variable  $\sim 1 + \text{predictor1} + \text{predictor2}$ .

### 7.3.2. Well-being, alpha asymmetry (predefined 8-13 Hz band), and covariates

Age was negatively correlated with alpha asymmetry calculated on the predefined 8-13 Hz band (meaning the older the individual, the greater cortical activity is in the right frontal and TP areas relative to the left ones) and positively correlated with subjective well-being levels (i.e., older age reflecting greater well-being score). However, gender was not associated the well-being or alpha asymmetry (Table 8 and Figure 32).

**Table 8. Well-being and alpha asymmetry, and covariates.**

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
<b><math>\alpha</math>-asymmetry (Frontal)</b>					
Age	-0.006* (0.002)	218 (216)	0.469	0.188	50***
Gender_Male	0.009 (0.071)	214 (212)	0.477	0.162	41***
<b><math>\alpha</math>-asymmetry (TP)</b>					
Age	-0.009* (0.004)	218 (216)	0.819	0.026	5.76*
Gender_Male	0.129 (0.123)	214 (212)	0.833	0.01	2.09
<b>Well-being</b>					
Age	0.258* (0.100)	218 (216)	19.7	0.031	7**
Gender_Male	0.68 (2.914)	214 (212)	19.7	0.003	0.56

*p*-values are reported with \* (*p*-value < 0.05; significance at the 95% level), \*\* (*p* < 0.01; significance at the 99% level), and \*\*\* (*p* < 0.001; significance at the 99.9% level). *p*-values on the F-statistic indicate whether the model fit is valid or not, and *p*-values on the coefficient estimate that the linear relationship between the predictor and the response variables is significant. The standard error (SE) of the  $\beta$  coefficients' distribution is reported in parentheses. Each simple linear model follows the equation: Response variable ~ 1 + predictor.

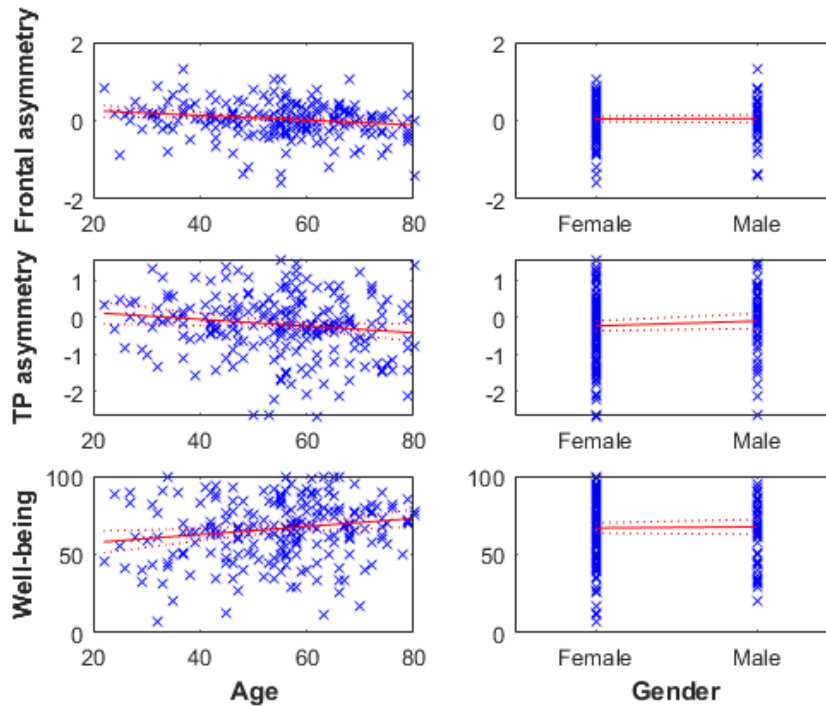


Figure 32. **Left:** Age is negatively associated with frontal (**top**) and TP (**middle**) alpha asymmetry scores, reflecting greater cortical activity in the right hemisphere relative to the left in older individuals. Age is positively associated with well-being levels (**bottom**). **Right:** Gender was not associated with any of the three variables.

### 7.3.3. Well-being and alpha center of gravity (CoG)

No linear relationships were observed between well-being and the CoG (Table 9), for both frontal and TP channels.

Table 9. Well-being and alpha center of gravity (CoG).

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model $R^2$	Model F-statistic
Frontal CoG	0.001 (0.004)	222 (220)	1.04	0.003	0.735
TP CoG	0.002 (0.003)		1.06	0.004	0.985

*p*-values are reported with \* (*p*-value < 0.05; significance at the 95% level), \*\* (*p* < 0.01; significance at the 99% level, and \*\*\* (*p* < 0.001; significance at the 99.9% level). *p*-values on the F-statistic indicate whether the model fit is valid or not, and *p*-values on the coefficient estimate that the linear relationship between the predictor and the response variables is significant. The standard error (SE) of the  $\beta$  coefficients' distribution is reported in parentheses. Each simple linear model follows the equation: Response variable  $\sim 1 +$  predictor.

### 7.3.4. Well-being and EEG asymmetry in other frequency bands

No associations were observed between well-being and EEG asymmetry in the delta (1-3 Hz), theta (3-7 Hz), or beta (14-30 Hz) frequency bands (Table 10, Figure 33).

**Table 10. Well-being and asymmetry in other frequency bands.**

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
<b>Frontal asymmetry</b>					
Delta (1-3 Hz)	0.001 (0.003)	230 (228)	0.99	0.0313	7.37**
Theta (3-7 Hz)	0.001 (0.002)		0.695	0.064	15.6***
Beta (14-30 Hz)	0.003 (0.003)		0.851	0.135	32.4***
<b>TP asymmetry</b>					
Delta (1-3 Hz)	0.001 (0.003)	230 (228)	1.03	0.001	0.029
Theta (3-7 Hz)	-0.003 (0.003)		0.775	0.006	1.36
Beta (14-30 Hz)	0.001 (0.003)		0.909	0.002	0.41

*p*-values are reported with \* (*p*-value < 0.05; significance at the 95% level), \*\* (*p* < 0.01; significance at the 99% level), and \*\*\* (*p* < 0.001; significance at the 99.9% level). *p*-values on the *F*-statistic indicate whether the model fit is valid or not, and *p*-values on the  $\beta$  coefficient estimate that the linear relationship between the predictor and the response variables is significant. The standard error (SE) of the  $\beta$  coefficients' distribution is reported in parentheses. The number of observations (*N*) and degrees of freedom (DF) are reported in column 3. Each simple linear model follows the equation: Response variable ~ 1 + predictor.

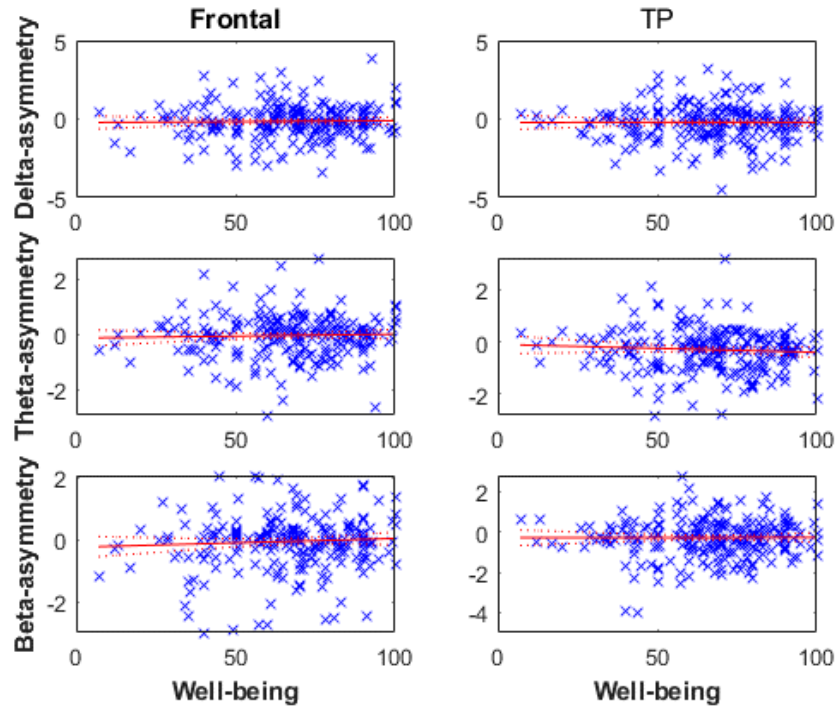


Figure 33. These linear regression models showed an absence of association between subjective well-being levels and PSD asymmetry in the Delta (1-3 Hz), Theta (3-7 Hz), and Beta (14-30 Hz) frequency bands. Note: Detailed statistics are reported in Table 10.

## 7.4. Discussion

### 7.4.1. Results summary

Contrary to the existing literature on the emotional valence and the motivational models of frontal EEG asymmetry, we found an absence of association between multidimensional well-being levels and FAA (whole band). However, well-being was negatively correlated with alpha asymmetry at the temporoparietal (TP) sites, reflecting greater cortical activity in the right TP area relative to the left (assuming the inhibitory role of alpha oscillations on regional cortical activity). Interestingly, the direction of the asymmetry is opposite to the one in the frontal areas in the literature of FAA. This effect appears to be driven more specifically by oscillatory activity in the lower frequencies of the alpha band (8-10.5 Hz), aligning with studies highlighting the inhibitory function of these lower frequencies (Oakes, 2004). Making the distinction between lower and upper frequencies of the alpha band seems therefore especially relevant for neurophysiological studies using source-localization or simultaneous EEG-fMRI techniques to

identify the intricate mechanisms involved in EEG asymmetry. Hence, while approach motivation and the related emotional processes are associated with relatively greater left than right frontal cortical activation, multidimensional well-being seems to be associated with asymmetric activation in the opposite direction in the TP areas, and specifically in the slower frequencies of the alpha range.

While CoG is associated with cognitive processes, we hypothesized that it would also be associated with multidimensional well-being. Contrary to our expectations, the alpha center of gravity (CoG; robust estimate of the IAF) did not show associations with well-being levels. The CoG may reflect other brain processes associated with cognition (e.g., memory) that are different from those involved with multidimensional well-being (e.g., emotion regulation, executive control). Future studies using advanced source localization methods and high-density EEG systems should elucidate the different sources and networks associated with the different sub-components of alpha oscillations (i.e., CoG, lower/upper alpha), and identify their different associations with cognitive and executive systems.

While some researchers suspected that gender was the main driver of frontal alpha asymmetry levels (Gale *et al.*, 2001; Dennis and Solomon, 2010; Mikolajczak *et al.*, 2010), it was not associated with well-being or alpha asymmetry measures (for both frontal and temporoparietal sites) in this sample. However, age was negatively correlated with alpha asymmetry scores of both regions (meaning that cortical activity is greater in the right areas relative to the left ones as age increases) and positively correlated with subjective well-being levels. This finding aligns with the well-being literature (e.g., Carstensen *et al.*, 2011), and supports a strong mediator role of age on the relationship between well-being and TP alpha asymmetry. Age is likely not the mechanism of change itself but may represent many underlying factors associated with brain changes and well-being (Kazdin, 2007). Thus, future studies using larger samples and higher density EEG data are necessary to better understand this meditation effect of age. Interestingly, age was negatively correlated with alpha asymmetry scores of both regions (meaning that cortical activity is greater in the right areas relative to the left ones as age increases) and positively correlated with subjective well-being levels. While the latter goes along with well-being literature (e.g., Carstensen *et al.*, 2011), the former goes against the literature where positive emotional valence and approach motivation is associated with relatively greater left than right frontal cortical activity. These findings suggest that alpha asymmetry behaves in the



opposite direction for the TP area, and confirm the mediator role of age on the relationship between well-being and TP alpha asymmetry. Age is likely not the mechanism of change itself but may represent many underlying factors associated with well-being and brain changes (Kazdin, 2007). While some researchers suspected that gender was the main driver of frontal alpha asymmetry levels (Gale *et al.*, 2001; Dennis and Solomon, 2010; Mikolajczak *et al.*, 2010), it was not associated with well-being or alpha asymmetry measures in this sample. Further studies are needed to elucidate further EEG asymmetry's relationship with age, gender, and other associated factors.

No associations were observed between subjective well-being and PSD asymmetry in the delta (1-3 Hz), theta (3-7 Hz), or beta (14-30 Hz) frequency bands, supporting the specificity of interhemispheric alpha asymmetry in the brain processes underlying well-being.

#### **7.4.2. Interpretations of the findings**

Despite these limitations, this study showed that it is feasible to use a low-cost, low-density wearable EEG system to examine the relationships between well-being and alpha asymmetry in a relatively large and diverse population.

Previous research suggested that asymmetries in the anterior regions are more closely associated with affective processing, whereas those in posterior regions are more related to cognitive processing (Davidson, 1988). For example, stimuli that differ in affective valence affect FAA in the absence of any influence on parietal alpha asymmetry, whereas tasks designed to differentially require verbal versus visuospatial processing produce changes in parietal and temporal asymmetry in the absence of any modifications in frontal asymmetry (Davidson, 1985). Not only frontal and posterior regions may have a different functional significance of hemispheric specialization, but they seem orthogonal to each other (i.e., asymmetric activation in one area is not correlated with one in the other region, or even sometimes anticorrelated; Davidson 1988). Davidson and Tomarken suggested that the functional significance of asymmetries in these regions differ and that the degree to which one hemisphere is relatively more activated than the other in the frontal region is relatively independent of activation asymmetry in the parietal region at the same moment in time (Davidson, 1988). However, this relation between activation asymmetries was suspected to differ in certain clinical populations (Davidson, 1985).

Similarly, different subtypes of anxiety disorders are differently associated with asymmetric activity in frontal and TP regions (Heller *et al.*, 1997; Nitschke *et al.*, 1999; Engels *et al.*, 2007; Mathersul *et al.*, 2008; Müller *et al.*, 2015). Greater left than right posterior alpha power is significantly predictive of antidepressant treatment response, whereas non-responders have shown the opposite asymmetric pattern in the frontal regions (Bruder *et al.*, 2001, 2008). Decreased left anterior activation associated with depression remains even after remission, suggesting frontal asymmetry patterns may be a state-independent marker that indexes risk for depression (Davidson, 1988). Conversely, other findings suggested that TP asymmetry might be less stable over time compared to frontal asymmetry (Müller *et al.*, 2015) and sometimes not associated with self-reported measures of affect and motivation (Sutton and Davidson, 1997).

Furthermore, anxious arousal (i.e., panic) is associated with only frontal asymmetry (greater right than left frontal activation), whereas anxious apprehension (i.e., trait anxiety and generalized anxiety disorder) is associated with both frontal (the reverse direction) and TP (same direction) asymmetry (greater activation in the right relative to the left hemisphere; (Mathersul *et al.*, 2008). Interestingly, anxious apprehension involves more worry and verbal ruminations whereas anxious arousal involves the physiological arousal and hyper-reactivity under conditions of panic, suggesting asymmetric activity in the TP area might be reflective of inner speech processes. Overt speech is associated with stronger activity in motor and sensory areas, associated with production (Broca's area in the frontal lobe) and processing (auditory, Wernicke's area, and associative regions in the temporoparietal areas) of one's speech, whereas inner speech involves different areas that are associated with inhibition of overt response (cingulate gyrus, left frontal gyrus), suggesting inner speech is a motor simulation of speech that include motor planning but exclude motor execution (Perrone-Bertolotti *et al.*, 2014; Loevenbruck *et al.*, 2018). Decreased activation of Heschl's gyrus (part of the temporal lobe containing the primary auditory cortex) and decreased activation of the left frontal gyrus was found during elicited inner-speech, whereas spontaneous inner speech (i.e., verbal ruminations or verbal mind wandering) is associated with increased activation of Heschl's gyrus and no association with the left frontal gyrus (Hurlburt *et al.*, 2016). Hence, the TP asymmetry associated with affect and anxiety might be associated with mental ruminations (involving inner speech), whereas frontal asymmetry might be more directly linked to affective and emotional processes directly. This was confirmed by Heller *et al.* (1997) that found a selective increase in right parietal activity in anxious

participants only during an emotional narrative task (involving verbal mechanisms) but not at rest.

This body of literature suggests that EEG asymmetry in the TP areas might reflect different processes that are indirectly associated with depression, affect, and motivation or that might be more state-related (e.g., negative mind wandering and inner speech) compared to frontal asymmetry that seems more stable over time and to better reflect affective and motivational processes.

Thus, alpha power picked up by posterior electrodes might reflect short-term current depression status and treatment response (therapeutic applications), whereas alpha power generated by frontal sources might better reflect traits and processes associated with the risk of depression (preventive applications). Frontal channels containing alpha activity from distal parietal and occipital sources might therefore reflect additional processes involved with current depression (and serve better as a rehabilitation tool), whereas alpha activity localized solely to the frontal areas would reflect the risk of future depression (and serve better as a predictor).

Additionally, “manipulations of emotion systematically affects asymmetries in the frontal leads, in the absence of any reliable effects in parietal asymmetry at the identical points in time. Conversely, data were described which illustrated the effects of cognitive task demands on parietal asymmetry in the absence of any effects on frontal recordings at the same moments in time.” (Davidson, 1988).

Depression is associated with a strategic attentional bias towards negative information and that this bias is stronger in individuals who habitually ruminate (Donaldson, Lam and Mathews, 2007; Peckham, McHugh and Otto, 2010). Parallel cognitive and affective phenomena associated with depression: discrepancies between perceived real and ideal self, increased affective response, self-attribution for negative events, and accurate self-reports. And these processes are modulated by self-focused attention and can maintain or exacerbate depression by affecting how an individual regularly tends to attend to its inner thoughts and feelings (Smith and Greenberg, 1981; Paelecke-Habermann, Pohl and Lepow, 2005). Since participants were instructed to count their breath-cycle with eyes closed in this study, we may have measured the state-related variable associated with this task, which contains some attentional (focus of the breath), cognitive processes (counting), with distractions from the objective when mental ruminations (often of

inner speech nature) occurred. These mechanisms may therefore reflect the trait variable (dispositional tendency to attend to one's inner thoughts and feelings) and explain the effects for this area in anxiety and depression. It may also reflect the general ability of individuals to do daily tasks (requiring attention and cognitive systems) and not get distracted and immersed in negative thoughts and ruminations (Donaldson, Lam and Mathews, 2007; Peckham, McHugh and Otto, 2010).

Additionally, findings from studies using source-localization methods may have brought light to this matter. They show that FAA is source-localized mainly to the dorsal system of the frontoparietal network (dFPN; 13). Functional magnetic resonance imagery (fMRI) showed that this system is organized bilaterally and comprises the intraparietal sulcus (IPS) and the frontal eye fields (FEF) of each hemisphere, and is thought to mediate top-down guided voluntary allocation of attention to locations or features (Vossel, Geng and Fink, 2013). Both IPS and FEF are active when attention is overtly or covertly oriented in space and are suspected to be the regions for the maintenance of spatial priority maps, saccade planning, and visual working memory. In contrast, the ventral system of the frontoparietal network (vFPN) comprises the temporoparietal junction (TPJ) and the ventral frontal cortex (VFC) and is associated with detecting unattended or unexpected stimuli and triggering shifts of attention (Vossel, Geng and Fink, 2013). It has been proposed that the ventral system is lateralized to the right hemisphere of the brain and exhibits asymmetric activity during attentional reorientation, the processing of rare deviant stimuli, and the response to valid vs. invalid cued targets (Corbetta and Shulman, 2002; Corbetta, Patel and Shulman, 2008; Doricchi *et al.*, 2010). The functional role of the TPJ also includes filtering irrelevant distractors during focused states of attention, modulating neural activity between various networks, and it has been implicated in social cognition and theory of mind (Vossel, Geng and Fink, 2013).

Hence, one might speculate that participants with lower subjective well-being were more likely to ruminate on negative thoughts or memories (associated with negative valence and a withdrawal motivation; Mason *et al.*, 2013; Smallwood and Andrews-Hanna, 2013) and less able to redirect their attention to their breath. This would decrease their capacity to detect negative thoughts and redirect their attention to their breath, corresponding to relatively greater left than right cortical activity in the TP area. On the other hand, participants with higher well-being would be more likely to engage in mind wandering with positive valence and more likely to

redirect their attention to their breath, which would correspond to greater right than left cortical activity in the TP area.

Furthermore, aging is associated with a positivity bias (referring to an “age-related trend that favors positive over negative stimuli in cognitive processing”; Reed and Carstensen, 2012), which could potentially explain the mediator role of age on TP alpha asymmetry and well-being. This phenomenon is thought to result from the fact that chronological age is inversely associated with actual and perceived time left in life, which drives differences in life goals (Reed and Carstensen, 2012).

CoG, typically associated with cognitive performance, was not associated with well-being levels, suggesting that the asymmetry was not largely affected by the cognitive component. The CoG was not associated with either well-being or alpha asymmetry (both frontal and TP areas).

Future studies using high-density systems and advanced source-localization methods are necessary to confirm or disprove these hypotheses; i.e., TP asymmetry better reflects brain processes associated with mental rumination and cognition, are generated in the dFPN (with a focus on the TPJ), and is more influenced by the state variable. On the other hand, FAA would be more associated with brain processes involved in affect, motivation, and visual attention, generated in the vFPN, and more influenced by the trait variable and more stable over time.

### **7.4.3. Limits**

There are several limitations of this study that should be considered when reviewing the results.

While the AIOS-24h was found to be associated with longer-term well-being levels (see Chapter 5), further validation is required to fully validate it as a measure of trait well-being.

While the asymmetry scores showed a relatively high internal reliability consistency and the MUSE signal was validated for ERP and continuous research (Chapter 6), 83 files had at least one bad channel and 36 had less than 60 s of remaining artifact-free data after preprocessing. This is a significant loss of data. The largest loss of data came from the presence of bad channels (considered bad when at least 50% of the channel was artifactual), likely due to the headband's flexibility that is prone to moving and disconnecting electrodes. Thus, future investigators could consider using the more recent Muse S that was developed for sleep studies. The Muse S is made

of a flexible fabric that can stretch and keep stronger pressure on the electrodes, preventing them from disconnecting as much. Furthermore, we recorded the data when participants already started the task with their eyes closed to reduce data cleaning over the large sample. Automatic cleaning performance would have likely been increased by adding a period before the task that includes obvious artifacts (e.g., asking participants to produce eye blinks and jaw clenching) to help the automatic method algorithms create a more robust baseline and therefore reject artifacts more efficiently. Thus, higher-grade and -density wearable EEG systems and longer recordings (at least 4 minutes of continuous data to ensure having at least 2 minutes of artifact-free data on a larger portion of the sample) are recommended for future studies to keep the advantages of wearable technologies to acquire large datasets without compromising data quantity and quality.

The automatic artifact rejection method tested and used in this study showed 81% sensitivity (true positive rate) and 83% specificity (true negative rate), suggesting some subtle artifacts may have remained in the datasets and potentially affected the results. While high-frequency artifacts were removed by the 30 Hz low pass, and main ocular artifacts were removed by the algorithm (artifacts with high amplitude are the easiest to detect automatically), slow frequency artifacts can be produced by slow eye movements, even with eyes closed. Frontal recording sites are especially sensitive to this type of ocular artifact. While large eye movements famously generate lateral dipoles that could completely interfere with asymmetry measures (they are used to identify and reject eye movement artifact using ICA for example; Delorme and Makeig, 2004), whether slow eye movements with eyes closed create the same typical artifact dipoles is unknown to our knowledge and can vary depending on the direction of the eye movements. These artifacts might not be easily detected by both data analysts and automated methods. Electrooculography (EOG) electrodes can help in this regard but were not included in the wearable EEG system we used, since they typically require to be taped to the skin near the eyes. However, these artifacts contaminate mainly slow frequency spectral content (e.g., delta and theta; Davidson, 1988) and should therefore not have influenced too much the frontal alpha asymmetry measures in this study (and should therefore not explain the absence of association with well-being). Furthermore, biased asymmetry scores would represent large outliers in the data that were accounted for by the robust regression models.

The Muse only has four channels. There are obvious benefits to having more EEG channels in terms of scalp distribution and data quality, which allow the use of advanced methods such as

independent component analysis (ICA) which can be used to remove subtle artifacts such as muscle activity, subtle eye movements, or channel noise (Makeig *et al.*, 1996; Delorme and Makeig, 2004). Furthermore, while we controlled for the potential reference issue using this system, a wearable headset with at least 30 channels would allow multiple referencing potentials (e.g., average or CSD) and ensure highly accurate asymmetry estimates. However, this study showed that it is feasible to use a low-cost, low-density wearable system to examine the relationships between well-being and alpha asymmetry in a relatively large and diverse population.

Linked-mastoids can contaminate alpha power in the frontal channels with the artifactual activity of opposing polarity from an occipital dipole (i.e., “alpha mirroring”; Hagemann, Naumann and Thayer, 2001). Thus, while the re-referencing method used in this study to obtain asymmetry scores that were correlated with conventional ones (F7/F8 averaged-referenced) compared to those using the Fpz-reference (see Chapter 6), it is possible that asymmetry scores in the frontal channels were contaminated by occipital alpha activity that was interfering with the alpha activity originating from frontal sources. However, Stewart and Colleagues (2010) found using advanced methods and a large sample that frontal asymmetry measured by CSD reference was associated with a trait-like marker of depression risk, whereas those obtained from average reference or linked-mastoids were found to be more strongly associated with the severity of current depression. Thus, frontal channels containing alpha activity from distal parietal and occipital sources might reflect processes involved with current depression (and serve better as a rehabilitation tool), whereas alpha activity localized solely to the frontal areas would reflect the risk of future depression (and serve better as a predictor). Similarly, alpha asymmetry solely captured in temporoparietal areas might reflect another dimension of depression.

Lastly, cross-sectional designs are always a limitation to consider. More sessions would be beneficial for the field to confirm the results and assess changes in both well-being and EEG asymmetry to evaluate the stability of this relationship over time.

## *7.5. Conclusion*

Overall, this study brings practical methodological information, challenges, and guidelines for conducting EEG research in large samples on well-being or related neuropsychological constructs, using wearable EEG technologies. Despite the limitations discussed, our findings bring novel knowledge that will help deepen our understanding of EEG asymmetries and their relations with well-being, the potential underlying neural networks and mechanisms, and the foreseeable long-term applications.





# Part III



## Chapter 8. Future directions related to the project

*This chapter discusses the short-term future directions, directly related to this project.*

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### 8.1. Experimental design

The first direction is to assess whether the MUSE can detect the typical association between FAA and affective and motivational measures (as in most of the literature) to confirm whether the absence of effect is due to the EEG recording system and referencing method (although we suspect it is not the case since other studies observed FAA effects with similar montages and we validated the measurements obtained with this system), or because multidimensional well-being encompasses other psychological constructs not associated with FAA, or if it is due to the experimental task (breath-counting instead of rest without instructions). Longer periods of data should be used (e.g., 8 1-m segments) to optimize internal consistency reliability, optimize data cleaning performance using more advanced methods (e.g., ICA), and increase influences from the trait variable while reducing state-related ones (e.g., inner speech, mind wandering, the current state during participation). Angelakis and colleagues (2007) proposed that “Traits are better reflected during post-task rest, whereas states are better reflected during initial resting baseline recordings.” Hence, one might better capture trait EEG asymmetry with several longer segments alternating between two types of task for example. Addressing these points will elucidate whether the effect in the TP alpha asymmetry is due to these factors associated with the short data length and the task, or with robust trait-related processes associated with multidimensional well-being.

Additionally, basal cortisol and depressed mood levels are highest during the fall and winter and lowest in spring (King *et al.*, 2000; Oyane *et al.*, 2008), and both are associated with relatively greater right than left frontal activity (Kalin *et al.*, 1998; Buss *et al.*, 2003). Like frontal asymmetry, higher basal cortisol is linked to personality traits (Schmidt, 1997) and anxious depression, and are modulated by genes and allostatic load (i.e., cost of chronically elevated endocrine or neural responses resulting from chronic stress associated with the HPA function

described in section 4.2.; e.g., Schulkin, Gold and McEwen, 1998). Similarly with circadian rhythms, basal cortisol levels and negative mood increase in the morning and decrease throughout the rest of the day, with the lowest levels at night (King *et al.*, 2000; McClung, 2013). Thus, future research might cluster participants per time of day and time of year to see if differences in FAA can be detected. In which case it would suggest that this variable should be taken into account when investigating EEG asymmetry. Alternatively, one might measure cortisol levels using simple, stress-free, non-invasive collection procedures of salivary cortisol (e.g., Vining *et al.*, 1983) and test direct correlations between the FAA, well-being, and time of day and year.

## 8.2. Automated removal of non-brain artifacts

Critiques have been made regarding the viability of wearable EEG headsets for conducting EEG research in non-laboratory or non-clinical settings (Cester *et al.*, 2008; Przegalinska *et al.*, 2018). EEG wearables systems will always face the challenges (that can exist in almost any data collection environment) of successfully collecting high fidelity EEG data acquisition. Real-time applications require the online detection of EEG markers for each individual, which can be largely biased by contamination of the data from non-brain artifacts. This is especially relevant since EEG data are more contaminated by artifacts and noise with wearable systems since participants have more mobility, and dry electrodes disconnect more easily and contain more noise (poorer impedance) than conventional wet electrodes.

Electromyogenic (EMG; i.e., electric signals associated with muscle activity) artifacts are the biggest threat to mobile EEG applications focusing on the frequency domain, because it is often subtle and hard to detect automatically, and can mask relevant brain signals. While some advanced methods have been developed to protect against them during offline analysis (e.g., ICA; see section 3.2.2.), they perform best on higher-density EEG montages and more data. No real-time automatic technique addresses this issue perfectly yet, to our knowledge.

The automated method employed in this study to preprocess 353 files achieved satisfying performance but missed some small artifacts and removed more data than manual cleaning on already short data files. However, ASR (Euclidean or the Riemannian method; see section 3.2.2.) should perform better on similar montage but longer data files (at least 4 minutes) and by adding

a period before the task where participants would be instructed to open and close their eyes, do slow eye movements, and clench their jaw to generate several different types of non-brain artifacts, to improve the accuracy of the “reference” data used to detect artifacts.

Some authors proposed that clean EEG data is not necessarily crucial when the sample size and several observations can reach large scales (i.e., big-data) since outliers can be dealt with efficiently and statistical power is increased (Meisler, Kahana and Ezzayat, 2019). Machine-learning (ML) algorithms (described in more detail in section 9.1.) might increase the reliability, accuracy, and variety of artifacts that can be corrected without losing the brain signal of interest (e.g., (Shao *et al.*, 2009; Barua and Begum, 2014; Radüntz *et al.*, 2017; Kang *et al.*, 2018; Golmohammadi *et al.*, 2019; Nejedly *et al.*, 2019; Pedroni, Bahreini and Langer, 2019). However, caution should be taken as they can also present biases, including sampling error, measurement error, multiple comparisons errors, or large inferential error (Kaplan 2014). These biases have greater implications on large datasets because they can magnify sampling or study design biases. Furthermore, these solutions can only be applied offline on large EEG data, but cannot be implemented in real-time for mobile or remote EEG applications, since the algorithms “learn” from an existing dataset.

Alternatively, some recent “simpler” methods have been developed specifically in the context of single-channel processing for wearable EEG applications, which may be promising for this field. For example, some researchers used a gaussian mixture model to improve the quality of EEG signals and a canonical correlation analysis decomposes the signals into different components (similar to PCA and ICA), followed by feature extraction and clustering to remove artifacts (Cao *et al.*, 2019). Other investigators implemented a discrete wavelet transformation (multi-resolution representation of signals and images that decomposes signals into multiscale representations) to reconstruct ocular artifacts and adaptive noise cancellation based on recursive least squares to remove them from the original data (additive noise interference used as a reference when adjusting coefficients automatically to achieve optimal results; Hu *et al.*, 2015). These approaches, along with other recent ones (Lan *et al.*, 2005; Lemm *et al.*, 2005; Dhindsa, 2017; Chavez *et al.*, 2018; Jebelli *et al.*, 2018; Mahmoodi *et al.*, 2021) are developed for real-time mobile EEG purposes and are therefore proposed to be more suitable for non-stationary EEG signals by providing fast computation and reliable artifact rejection and reconstruction on single-channels. These

algorithms are designed to detect small artifacts in the presence of high amplitude EEG, making it particularly useful for wearable EEG uses.

### *8.3. Spatial and source distributions of alpha oscillations*

While alpha activity reflects the large-scale synchronous activity of broad networks and can be recorded at all recording sites (and therefore a few sparse recording sites as with the low-cost system used in this study; see section 4.4.2.), the spatial differences and their meaning in terms of physiological and cognitive processes must be better understood.

Nunez and Colleagues (2016) showed that “split” alpha peaks (several spectral peaks in the alpha band distribution) have distinct spatial and source distributions over the scalp and that the choice of epoch length to calculate the spectra will either enhance or smooth this phenomenon (Nunez et al 2016). This is illustrated in Figure 34 where a resolution of 0.5 Hz (2 s window) reveals one peak below 10 Hz and one above (left), whereas a lower resolution of 1 Hz only highlights a single peak below 10 Hz (right). The higher the frequency resolution (one 60 s epoch without averaging), the more precision in the FFT is obtained, but no information about the statistical properties of the underlying random process is gained. To go further, the authors found that the two distinct peaks had distinct spatial distributions over the scalp, suggesting that they have different source distributions (Ombao *et al.*, 2016).

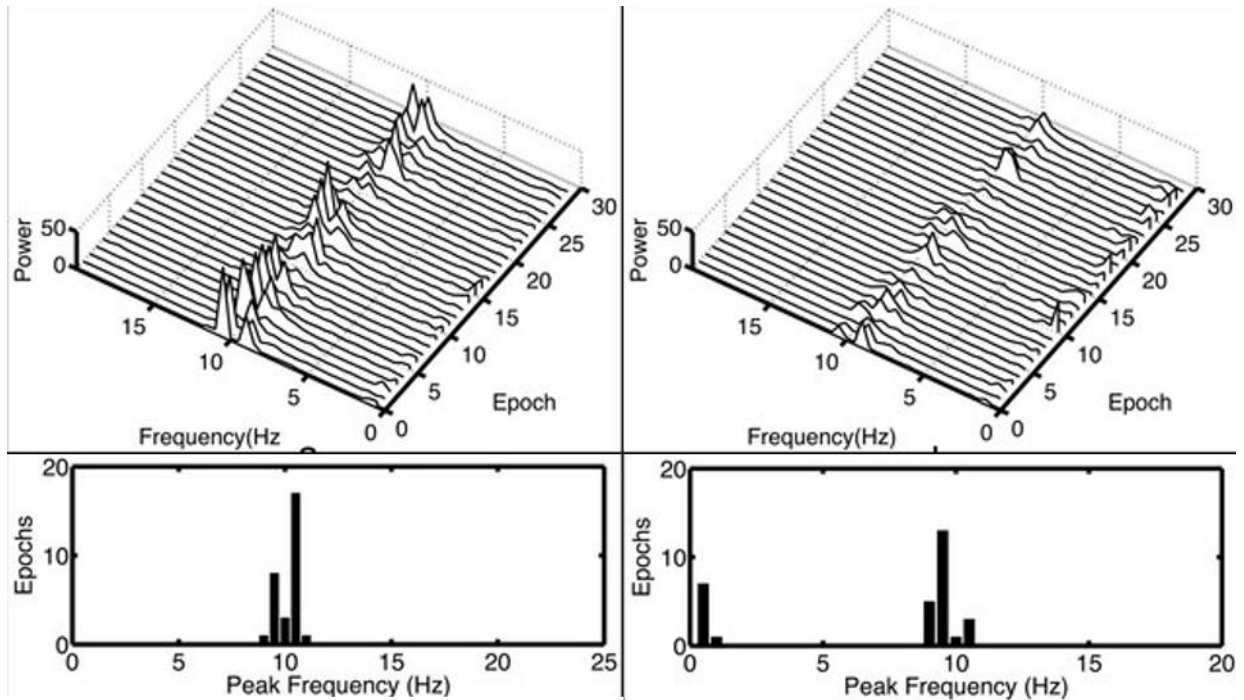


Figure 34. **Left:** power spectra (top) and IAF (bottom) of 30 2-sec epochs (0.5 Hz resolution) showing one peak below 10 Hz and one above. **Right:** power spectra (top) and IAF (bottom) calculated on 60 1-sec epochs (1 Hz resolution) showing only the peak below 10 Hz. Source: Nunez, Nunez and Srinivasan (2016).

Hence, the choice of the epoch length is crucial when calculating alpha power. Higher-resolution should be favored when examining the spatial distribution and resolution of alpha oscillations. We used the default 4 s window (high-frequency resolution) in this study to estimate the IAF, which better reflects global dynamics relative to local dynamics that fluctuate more (see section 4.4.2.). As a consequence, split peaks were enhanced, which may have led to the misestimation of peak alpha frequency (PAF) for some subjects in Chapters 6 and this chapter. While the alpha center of gravity (CoG) performed better in these situations, further research should determine what source(s) and processes this measure reflect, and if it misses important nuances between subcomponents of the band (e.g., lower and upper alpha frequencies) by assessing the IAF over the smoothed distribution over the whole alpha range (the *restingIAF* toolbox uses smoothing filters).

Similarly, future research should confirm whether asymmetry in frontal areas has different sources than that in the TP areas, or whether they have different phases but represent delayed conduction between the two areas. Coherence analyses could provide light to this question by determining whether left frontal activation precedes right TP activation, which inhibits the



contralateral hemisphere (which would correspond to the synchronized phase with a lag between the two areas). Future studies using high spatial and temporal resolution methods (e.g., surface Laplacian or EEG source-localization) should attempt to determine which subtypes of inhibition alpha oscillations reflect (see sections 1.3. and 4.4.2.). One may speculate that local alpha reflects feedback inhibition (interneuron's activity to reduce the increased activity of a principal cell in an oscillatory manner, increasing its spike timing) necessary for modules coherence at the local level, whereas global alpha may reflect lateral inhibition (activation of a principal cell targetting another interneuron) that can trigger chains of inhibitory/excitation reactions in a whole network. Interestingly, lateral inhibition shows competitive asymmetric phenomena that are responsible for the necessary segregation of cortical assemblies (i., winner-take-all mechanism). These lateral inhibitory dynamics may be the basis of alpha asymmetries, and dysfunctions in this system may explain the neuropathologies associated with abnormal asymmetries (see section 4.4.3.).

An exploratory analysis assessing interactions between asymmetries in different frequency bands (see Annexe 2) suggests that asymmetries in lower frequencies (delta, theta, and alpha) interact locally (within frontal and TP areas), whereas only alpha asymmetries interact with themselves between distant regions (frontal and TP areas). These findings go along with the literature described in section 4.4.2. on alpha coherence at both short and long distances, and reinforce the top-down regulatory role of alpha oscillations at the global level. Interventions implementing neurofeedback or neuromodulation techniques (described in more detail in sections 9.3. and 8.4.6., respectively) might be especially useful to re-establish the balance of these top-down inhibitory systems.

Future research should further elucidate the sources and distributions of alpha oscillations and asymmetries (including their sub-components) associated with well-being, as well as the asymmetric interactions with these other slow frequencies. This can only be done using high-density EEG recordings, and high-resolution methods such as the Spline-Laplacian or Dura image (see section 2.1. and 4.4.2.), current-source density (CSD) reference-free signal (Tenke *et al.*, 2011; Smith *et al.*, 2017), source separation as with ICA (see section 3.2.2.), or source-localization methods like eLoreta (Marqui 1999; Aoki 2015). The independent modulator analysis (IMA; Onton and Makeig, 2009a), implemented in EEGLAB, is a promising tool to advance this area of research, by identifying the nodes generating alpha oscillations measured at the scalp in

the source domain using ICA (Julie Onton and Makeig, 2009). Better understanding the interactions between subcomponents of alpha oscillations and sources in different states will be crucial for the accurate implementation of this spectral measure into interventions.

Simultaneous EEG-functional magnetic resonance imaging (fMRI) recordings (Allen, 2013), magnetoencephalography (Domschke et al., 2015; Onoda et al., 2007), source estimation (Pizzagalli et al., 2005; Smith, Cavanagh, & Allen, 2013), time-frequency analyses (Allen & Cohen, 2010), and scalp-level functional connectivity metrics may all be useful for revealing neural circuitry that contributes to alpha asymmetries and how subcomponents might be differentially involved in processes associated with well-being (Pizzagalli 2005; Smith 2018). Ultimately, a comprehensive model should examine EEG asymmetry as an indicator of both psychological and neural phenomena.

#### *8.4. Theta oscillations and well-being*

Aside from EEG asymmetry, theta power has been used to study depression and predict the antidepressant response (Baskaran, Milev and McIntyre, 2012; Olbrich and Arns, 2013). Theta power showed mixed associations with depression. While decreased theta band activity before treatment has been associated with treatment response (Knott *et al.*, 1996; Iosifescu *et al.*, 2009), increased theta power before treatment has also been associated with respondent/non-respondent differentiation (Knott *et al.*, 2000; Spronk *et al.*, 2011). Studies using low-resolution electromagnetic tomography analysis (LORETA) source-localized pre-treatment theta power positively associated with treatment response to the rostral ACC (rACC; Pizzagalli *et al.*, 2001; Mulert *et al.*, 2007; Korb *et al.*, 2009). This relation was later confirmed to be (Pizzagalli *et al.*, 2001, 2018). Theta cordance combines absolute and relative power (percentage relative to the total spectrum) and was suggested to better reflect regional cerebral perfusion than mean theta power (Leuchter *et al.*, 1994). It is less affected by demographic covariables or depression severity (Morgan *et al.*, 2005). Frontal theta cordance has been used to predict antidepressant treatment response in depressed patients with 77-88% accuracy (Cook and Leuchter, 2001; Cook *et al.*, 2002; Bares *et al.*, 2008). Theta cordance involves very simple computation resources (like alpha asymmetry) and should be considered in future research using wearable systems to study well-being. Similarly, cross-frequency analyses of asymmetry should be investigated.

### 8.5. *Beta oscillations and well-being*

Both alpha and beta power are associated with high and severe mental stress (Hayashi *et al.*, 2009; Jena, 2015; Al-shargie *et al.*, 2016; Jun and Smitha, 2016; Al-Dabass, 2020). Note that several of these studies use a nonlinear approach to study beta spectral power in relation to stress. Another study using an inter-channel frequency correlation approach suggested that stress and anxiety were more specifically associated with high-beta frequencies (22-30 Hz), rather than only the power activation of the beta frequency range (Díaz *et al.*, 2019). Other studies found alpha-beta ratios (Hamid *et al.*, 2010) and theta-beta ratios (Putman *et al.*, 2014) to be negatively associated with stress levels. While beta power seems like a good candidate to study stress and well-being, no consensus exists to our knowledge regarding the direction or the spatial location of these associations, or the underlying mechanisms. Some authors report positive correlations between stress and beta power, while others report negative relationships. A recent paper addresses these limitations. The authors observed positive correlations between prefrontal beta power and depression ( $r = 0.31$ ) and anxiety ( $r = 0.48$ ). Mood scores were negatively correlated with beta power in the lateral sites and positively correlated with beta power in the mesial areas. The authors suggested that the results were in line with the dichotomous organization of reward networks in the PFC (de Hemptinne *et al.*, 2021).

### 8.6. *Multimodal neuroimaging*

Future research might find more robust correlates of well-being by combining EEG with other physiological measures such as electrocardiography (ECG; Riera *et al.*, 2008; Ahn, Ku and Kim, 2019), eye-tracking (Soussou *et al.*, 2012), or galvanic skin response (GSR; Udovič ić *et al.*, 2017) that can easily be combined with wearable EEG systems.

Heart rate variability (HRV) is the change in the time intervals between adjacent heartbeats that may be used to predict future health outcomes (Tsuji *et al.*, 1994; Dekker *et al.*, 1997; Shaffer, McCraty and Zerr, 2014). Reduced HRV has been shown to correlate with disease onset and mortality as it reflects the reduced regulatory capacity of the body to adapt and respond to challenges like exercise or stressors (Dekker *et al.*, 1997; Beauchaine, 2001).

We built custom ECG electrodes that connect to the MUSE Auxiliary port and can be simply taped to the participants' wrist. Both EEG and ECG signals are then time-locked, meaning they are synchronized in time, and interactions between the EEG and the ECG can easily be analyzed without requiring offline synchronization. We recorded simultaneous EEG and ECG on 62 participants during this project using our custom-made ECG electrodes and the MUSE, which can be easily imported into EEGLAB using the plugin developed for this study (see Annexe 1). However, these data have not been analyzed yet. ECG signals can be used to evaluate the HRV correlates of well-being (Geisler *et al.*, 2010), to remove ECG artifacts from the EEG data (Nakamura and Shibasaki, 1987), to improve the performance of pathology detection by combining information from both EEG and ECG (Valderrama *et al.*, 2012), or to assess the interactions between the heart and the brain activity (e.g., Jurysta *et al.*, 2003; Kokonozi *et al.*, 2008; Valderrama *et al.*, 2012; Schiecke *et al.*, 2016; Raimondo *et al.*, 2017; Ramasamy and Varadan, 2017).

To go further, research-grade wearable EEG systems can now be combined with fNIRS (Kernel, 2021; Neuroelectronics, 2021d) or neuromodulation tools transcranial direct current stimulation (TDCS; Neuroelectronics, 2021b). Combining EEG and fNIRS will help better understand the interactions between the hemodynamic (BOLD) response and mean-field potentials, or improve the performance of EEG classification (Yin *et al.*, 2015). Neuromodulation techniques may be used to directly modulate specific networks such as the frontoparietal network (FPN), associated with processes underlying EEG asymmetry. For example, some clinical studies have shown that exciting the left dlPFC with transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS) improved depression symptoms (Kalu *et al.*, 2012). Conversely, excitation of the right dlPFC led to reductions in craving (Boggio *et al.*, 2008; Fregni *et al.*, 2008) and risky decision-making (Fecteau *et al.*, 2007), i.e., behaviors associated with difficulty in inhibiting extreme rewards with positive valence and urgency. Additionally, Sanguinetti *et al.* (2020) recently used novel transcranial focused ultrasound stimulation to target the right prefrontal cortex with higher resolution and depth than TMS or tDCS and successfully modulated mood and emotion regulation. By modulating both bottom-up and top-down systems, long-term solutions without side effects and at lower costs will emerge by helping patients self-control negative biases (Moser *et al.*, 2002; Hanslmayr *et al.*, 2011).

In the “open-loop” approach, currents are applied to the brain independently of the brain state. The biggest limitation for neuromodulation techniques is the state-dependency of the brain, i.e., neural populations are modulated differently depending on their current excitation states, leading sometimes to opposed effects than those desired (e.g., exciting instead of inhibiting a network because of an emotion the subject is experiencing at that moment). New advancements in this area should solve this issue (Metsomaa *et al.*, 2021). In the “closed-loop” approach, real-time EEG is used to assess the current states of brain regions and adjust the TDCS parameters accordingly. For example, the peak frequency of a given frequency band measured by EEG can be used to modify the stimulation frequency (the same can be done with phase but requires faster temporal resolution). Hence, a simultaneous EEG-TDCS headset can not only help better understand the mechanisms underlying specific cognitive processes and systems (via inhibition and excitation of neuronal populations) but also observe the effects on the EEG data that are recorded simultaneously.

## *Chapter 9. Future directions for the broader field of wearable EEG*

*This chapter discusses the current and future applications of wearable EEG technology in experimental, clinical, and “real-world” settings.*

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### *9.1. Big data and machine learning*

A majority of neuroimaging studies are conducted on small samples due to the cost and time-consuming nature of measuring EEG on large groups of participants. One main limitation for using wearable EEG systems in ecological environments or collecting large datasets used to be the need for fragile, costly optic fibers to stream the data or the advanced programming skills required to interface with the recording system to collect the raw data (using APIs from manufacturers). The lab streaming layer (LSL) is “a system for the unified collection of measurement time series in research experiments that handles both the networking, time-synchronization, (near-) real-time access as well as optionally the centralized collection, viewing and disk recording of the data.” (Lab Stream Layer, 2021). It is compatible with all the main programming languages and interfaces and is integrated into EEGLAB. This tool simplifies the acquisition and recording of EEG data from portable consumer devices by providing a single efficient interface, with applications in areas such as basic and behavioral research, prototyping, neurogaming, arts, and home-based applications. Such tools are actively being developed to help facilitate the recording and streaming of EEG data from consumer headsets that can be interfaced with a variety of programming languages and software packages, allowing for interchangeability across devices. Furthermore, recent advancements in cloud data storage and open-source platforms can lead to the availability of large datasets, reducing costs associated with data collection (purchase of equipment, financial compensations to subjects, salary of the person recording the data, repairs, etc.).

With larger data samples come more robust statistical inferences about the general population, as well as a better representation of the sociodemographic differences. Large datasets bring many advantages, such as capturing rare events, and implementing robust statistical methods that better account for outliers (e.g., IRLS, WLS). They can also reduce costs of investigation and time to evaluate research questions or record new participants (by answering different research questions with the same dataset).

The use of wearable EEG technology can help record patients that cannot attend specialized centers and facilitate access to more diverse populations and to larger samples, which improves the accuracy of the statistical inferences about the general population, and classification accuracy. For instance, Hashemi and colleagues (2016) recorded EEG data on 6029 subjects ranging from 18 to 88 years in age using the MUSE headset in a representative population of individuals completing the tasks in uncontrolled natural environments. They identified age-related shifts in EEG activity on a year-by-year scale, as well as how these changes differed between males and females.

Furthermore, the increasing availability of large, openly available datasets and advanced computational tools like machine learning (ML; Marcus *et al.*, 2011; Poldrack and Gorgolewski, 2014; Niso *et al.*, 2016) is propelling the field toward understanding the biological nature of individual traits and behavior, an overarching objective of neuroscience research ((Miller and Van Horn, 2007; Van Horn, Grafton and Miller, 2008). For example, in the clinical field of “pathology decoding” (diagnostic and prediction of pathology from EEG recordings using machine learning methods), Gemein *et al.* (2020) found differences in age and gender as a function of the evolution of pathology between the first and final clinical evaluations, using a sample of 3000 clinical EEG recordings (Figure 35; Gemein *et al.*, 2020).

Machine learning (ML) methods for automatic EEG classification are being developed to detect and predict pathologies such as epileptic seizures (Subasi, Kevric and Abdullah Canbaz, 2019), depression (Cai *et al.*, 2016), stroke (Giri *et al.*, 2016), or general abnormal EEG (López *et al.*, 2015; Roy, Kiral-Kornek and Harrer, 2019). They address limitations from traditional manual/visual evaluation that are time-consuming, require extensive training, present unclear criteria for decision making, and can be prone to subjective judgment errors. Automatic ML algorithms can support clinicians in making decisions regarding the presence or absence of

pathology, or help predict their future appearance, by identifying features that might be invisible with small samples or visual examination.

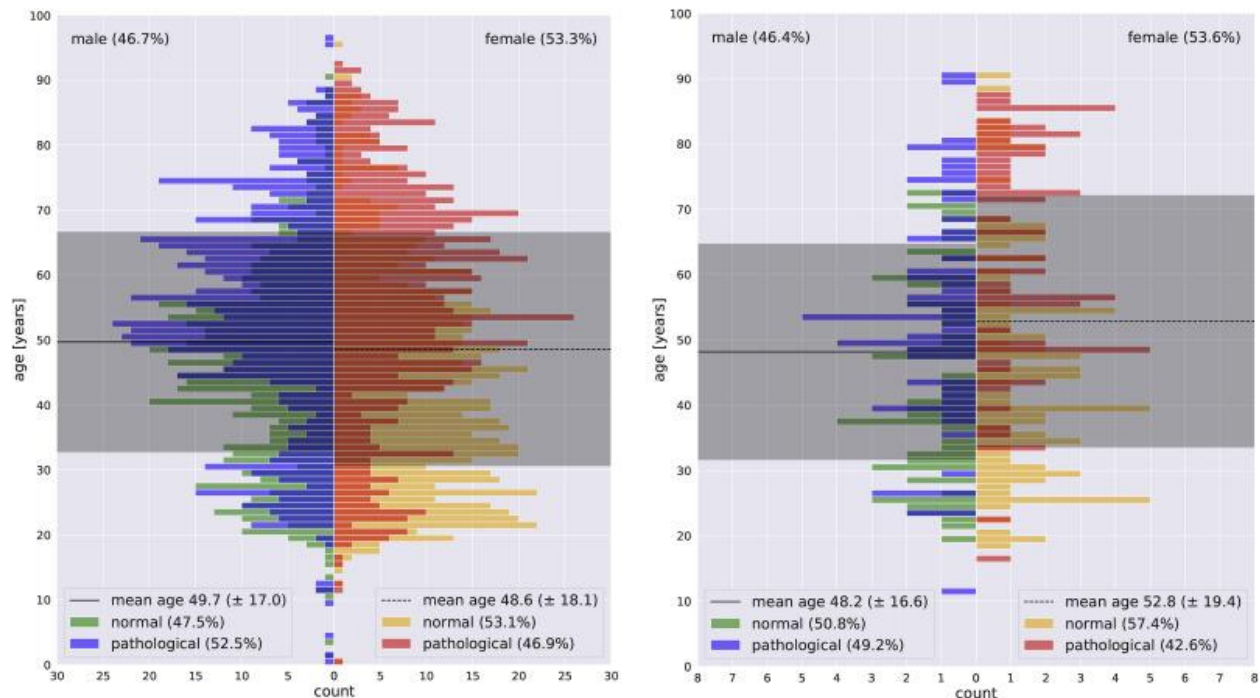


Figure 35. Examples of trends in EEG as a function of age and pathology can be highlighted using big data and machine-learning methods. These results show trends in the data, *i.e.*, mediator roles of covariables such as age and gender on the relationship between EEG and mental illness. This type of data clustering and identification of trends is not possible with small samples and is useful for mental illness detection applications to take into account interindividual differences. Source: (Gemein *et al.*, 2020).

There are two main ML approaches for EEG research. “Feature-based” and end-to-end (deep learning) decoding. The former is the most used historically in the clinical context, and consists of preselecting features in the EEG data for the detection of pathology (e.g., the specific frequency band of the power spectrum). This method is limited by the expertise of the experimenter and knowledge available in the literature, which can limit the quality of the results, but is easier to interpret and make decisions from these results. Feature-based ML methods include for example random forest (RF; Breiman, 2001), support vector machine (SVM; Boser, Guyon and Vapnik, 1992), Riemannian geometry (RG; Congedo, Barachant and Bhatia, 2017), or the auto-sklearn classifier (ASC; Feurer *et al.*, 2015).



Deep learning, “end-to-end” decoding has been more dominantly used in the research field such as computer vision (Krizhevsky, Sutskever and Hinton, 2017), speech recognition (Hinton *et al.*, 2012), and artificial neural networks (Craik, He and Contreras-Vidal, 2019; Roy *et al.*, 2019). This approach deals better with minimally processed data, and the algorithms learn features themselves, optimizing the feature extraction and classification. The advantage is that it can lead to unexpected features that were not anticipated, but can be a problem because it is a challenge to understand what they learned (the “black box” problem; Montavon, Samek and Müller, 2018). Convolutional neural networks (CNN or ConvNets) are neural networks using filters and weights to represent an organization in layers and interconnections inspired by the brain architecture (LeCun *et al.*, 1999). They are promising end-to-end decoding tools for EEG classification. For example, the 4-layer “Brain decode Deep4 ConvNet” (BD-Deep4; van Leeuwen *et al.*, 2019) has shown success for decoding motricity (movement preparation and execution; Schirrneister *et al.*, 2017), velocity, and speed decoding (Hammer *et al.*, 2013), and pathology (van Leeuwen *et al.*, 2019). Another example is the TCN (Bai, Kolter and Koltun, 2018), a CNN optimized for EEG decoding with a neural architecture search.

Both feature-based and deep learning decoding approaches present many groundbreaking advancements in personalized medicine and healthcare quality (Rajkomar *et al.*, 2018). Recent findings suggested that both approaches (including several ML methods from each approach) perform similarly in the range of 81-86% of accuracy at decoding EEG pathology (van Leeuwen *et al.*, 2019; Gemein *et al.*, 2020). Interestingly, they focused on similar features of the EEG data, that is delta and theta band power at temporal electrode locations (Gemein *et al.*, 2020). These big-data archives along with the use of robust ML and statistical methods might uncover, in the long term, robust patterns and trends in brain activity that have not been previously possible with smaller data sets.

However, the challenge is to identify individual differences using large group datasets (Dubois and Adolphs, 2016; Mišić and Sporns, 2016; Mars, Passingham and Jbabdi, 2018). Similar to fMRI research, recent findings suggest that EEG signals can be used to authenticate and differentiate individuals, corresponding to the human brain's “fingerprint” (Van De Ville *et al.*, 2021). While longer periods of signal show higher performance (frontoparietal-DMN driven), this was possible with very short segments of data (“bursts of identifiability”, visual-somatomotor driven). This was done using both advanced functional connectome and simpler spectral

measures. Another study indicated that differentiation of individuals could be achieved from the simple spatial distribution of spectral power, with as short as 30 seconds of resting-state data, and that this was robust over time (weeks later; da Silva Castanheira *et al.*, 2021). Individual connectomes were derived in all frequency bands from an amplitude envelope correlation approach, suggested to detect signal-coupling without phase coherence even among incoherent signals (Bruns *et al.*, 2000). These findings suggest that interindividual differences might be detected using these signal processing methods. This analysis was done using 158 participants from the OMEGA Open MEG Archives (Niso *et al.*, 2016). Interestingly, individual differentiability was not associated with demographics or data length in this study.

Similar to the anatomical brain atlases constructed from MRI data (e.g., the Julich-Brain Atlas; Amunts *et al.*, 2020), EEG atlases could be built in the near future, using large samples collected with wearable technologies, to obtain templates of “normal EEG” or “healthy EEG” for example.

In the case of the Hashemi (2006) study mentioned above, the groundbreaking component is that EEG data were self-recorded by the participants from their homes (InteraXon, 2021). The validity and value of such databases will depend on the signal quality being measured by users. Users lack basic training and experience in EEG recording movement artifacts and inaccurate electrode position (even if some Apps provide clear instructions and visual feedback about electrode impedance). As a consequence, a large portion of data is usually lost due to these low-quality recordings. Future advancements in artifact reconstruction might solve this issue (see Section 8.4.2.).

## 9.2. *Brain-computer interfaces (BCI)*

A brain-computer interface (BCI) is defined as “a system that records central nervous system (CNS) activity and translates it into artificial output that replaces, restores, enhances, supplements, or improves natural CNS outputs; it thereby modifies the interactions of the CNS with the rest of the body or with the external world.” (Wolpaw, Millán and Ramsey, 2020). The most used target for BCI applications is the detection of a particular pattern in EEG signal, following fast preprocessing and extraction of the feature (Nicolas-Alonso and Gomez-Gil, 2012). Thus, most non-invasive BCIs rely on the high temporal resolution of EEG. Furthermore, EEG-based BCIs hold the most potential for true wearable BCIs with its low-cost and accessibility

(Cohen and Gulbinaite, 2017). Features from EEG signals, often in the time domain (i.e., ERP components), are translated by the interface into commands that can replace, restore, enhance, supplement, or improve natural CNS outputs (see Figure 36).

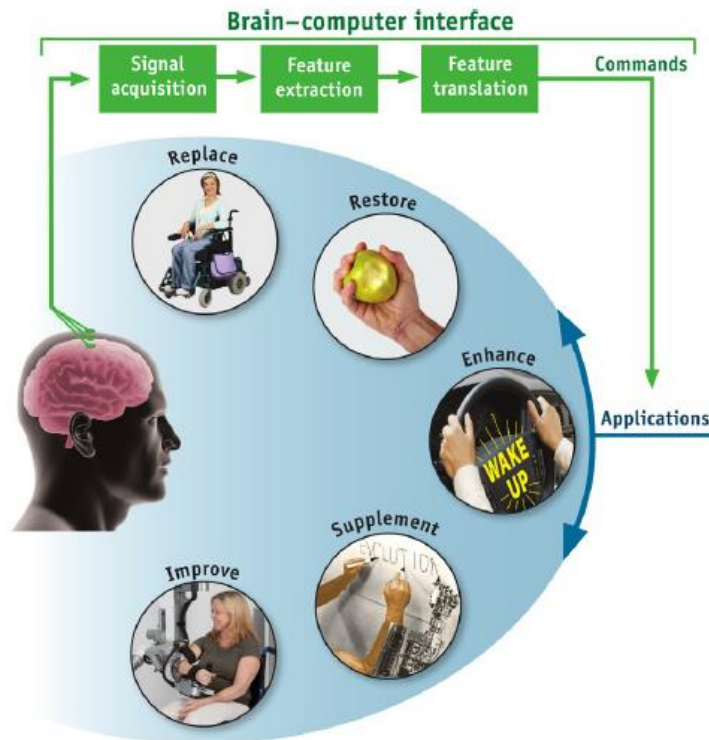


Figure 36. The five types of uses of a brain-computer interface (BCI): replace, restore, enhance, supplement, or improve, central nervous systems outputs (e.g., movement, communication). Source: (Wolpaw, Millán and Ramsey, 2020).

The four typical EEG patterns used in BCI systems include the P3 (used generally for bi-directional communication BCIs), the mu (i.e. 8-12 Hz) and beta (i.e. 18-26 Hz) rhythms (usually used for sensorimotor BCIs), and the steady-state visual evoked potentials (SSVEP; visual BCIs). For bidirectional BCIs, a decoder translates recorded EEG signals into motor commands and an encoder delivers sensory information from the environment to the brain creating a closed-loop system (Boi *et al.*, 2016).

BCIs can be used to facilitate linguistic communication, with the most renowned BCI paradigm being the P3/P300 speller dating back to 1988 (Farwell and Donchin, 1988; Mellinger *et al.*, 2004; Cipresso *et al.*, 2012). Other BCIs allow the patients to navigate text, to control a cursor

on a computer screen, browse forward and backward or use bookmarks (Kübler *et al.*, 2005; Krusienski *et al.*, 2007; Fruitet, McFarland and Wolpaw, 2010; Mugler *et al.*, 2010).

Under certain circumstances, patients can regain partial if not all of the lost motor control if provided effective rehabilitation. Motor-imagery-based BCI (Curran and Stokes, 2003) have been used as a means of providing patients real-time visual feedback of limb movement (corresponding to the injured limb) through a representative simulation on a computer screen. BCI protocols host the potential to accelerate rehabilitation through repeated reactivation of the underlying neural pathways (Pfurtscheller *et al.*, 2006; Güneysu and Akin, 2013). A difficult and frequent obstacle present in patient rehabilitation involves maintaining the necessary levels of motivation to remain persistent during repetitive and demanding physical tasks. BCI rehabilitation paradigms may improve patients' sense of well-being and motivation by providing more entertaining and engaging interfaces (e.g. video games) as opposed to more traditional clinical/medical settings.

When rehabilitation is not possible, prosthetic control can still provide improved mobility assistance, while promising research on BCI-controlled wheelchair movements may soon be an option for patients with paralysis (Carlson and Millan, 2013). The complex control commands required for robotic prosthetic limbs or exoskeletons have evaded BCI scientists for the last few decades. However, recent advancements have overcome several key limitations (McFarland, Sarnacki and Wolpaw, 2010). BCI patients are now capable of moving prostheses with increasing accuracy, flexibility (Clement, Bugler and Oliver, 2011), and affordability with the advancements in 3-D printing technology (Sullivan, Oh and Taylor, 2017).

Some simple versions of BCI (prototypes) use simple features like eye-blinks or the breath, which cannot be used by patients with paralysis (e.g. late-stage ALS, high-level spinal cord injury, stroke/aphasia, autism, severe cerebral palsy). A recent study developed a way to allow locked-in amyotrophic lateral sclerosis patients (ALS, a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord leading to paralysis) to remotely control a humanoid robot using their EEG activity (Spataro *et al.*, 2017). Their findings show that three out of four subjects were able to control the robot so that he could speak, move and act for them. While medical treatments are still required to be found to reverse neurodegeneration, BCIs can provide some autonomy to these patients.

In clinical settings, BCIs are typically integrated into bulky external devices (Shih, Krusienski and Wolpaw, 2012), and the main goal of BCI is to support these patients with severe motor and sensory deficits for their daily lives (outside of the laboratory), requiring wireless, battery-powered, portable systems, and to process EEG signal in real-time to detect ERPs and provide a fast output (Sullivan, Delorme and Luo, 2012). Some wearable EEG systems were shown to accurately measure ERPs during mismatch negativity tasks (Badcock *et al.*, 2015), during an auditory oddball task (Mayaud *et al.*, 2013; Barham *et al.*, 2017), or during visual oddball and reward-learning tasks (Krigolson *et al.*, 2017), depending on the ERP of interest. Thus, wearable EEG systems make daily BCI applications possible by addressing the limits of bulky medical systems.

While only a limited number of studies have integrated functional near-infrared spectroscopy (fNIRS) for BCI applications (Coyle, Ward and Markham, 2007; Aranyi, Charles and Cavazza, 2015) an increasing number of researchers are developing hybrid P300-based BCI interfaces via simultaneous fNIRS and EEG (Coyle, Ward and Markham, 2007; Pfurtscheller *et al.*, 2010; Fazli *et al.*, 2012; Liu *et al.*, 2013; Blokland *et al.*, 2014; Kaiser *et al.*, 2014; Khan, Hong and Hong, 2014; Tomita *et al.*, 2014; Yin *et al.*, 2015; Buccino, Keles and Omurtag, 2016). These studies show that simultaneous measurements of fNIRS and EEG can significantly improve the classification accuracy of brain signals, improve user performance, and may serve to be a viable multimodal imaging technique suitable for future BCI applications. fNIRS provides similar advantages as fMRI by focusing on the BOLD response (see section 2.2.) but is more affordable and less bulky. While its spatial resolution is much lower than fMRI, some new systems show tremendous progress on this level while keeping the mobility of the fNIRS technology, by using high-density hexagonal tile modules (e.g., (GowerLab, 2021; Kernel, 2021).

The main limitation with ERP-based BCI using low-cost wearable systems is the reliance on stimuli and the lack of control over them. In the laboratory, triggers are produced and controlled by the experimental paradigm and stimulation program, whereas many manufacturers of wearable EEG systems do not offer this feature since they sell their software for a specific purpose. Furthermore, even with the feature, this limitation will persist in real-world applications (discussed later in section 9.4.2.) where stimuli can originate from the environment upon which the experimenter or developer has no control. These stimuli might greatly interfere with both the online monitoring of EEG activity and the decoding-encoding algorithms of BCI systems

designed to detect predefined features in the signal (e.g., a P300 will hardly be detected if there are other conflicting stimuli occurring at the same period). Combining wearable EEG with other (time-locked) sensors might solve this issue. For example, smart glasses (for visual stimuli) and smart headphones (for auditory stimuli) might encode triggers in the EEG signal when specific stimuli are detected and recognized using online feature-based algorithms. However, no algorithm is capable of such performance (accuracy and speed) to solve this issue at the millisecond accuracy.

While this may be solved in the next decade, BCIs based on the frequency domain might be more promising, since the millisecond accuracy is not necessary when looking at spectral data over several seconds or minutes, and the features of interest might be less affected by such events (average spectra over a period). Computing spectra used to take time and bulky computers, which would lead to large lags in the BCI output and no mobility. With recent advancements in computation speed using small components that can be embedded in wearable systems, BCIs can also use frequency signals (Tonin *et al.*, 2012). For example, posterior steady-state evoked potentials (SSEP) in the alpha band associated with covert attention to spatial locations in the visual field can be used as a control signal for BCI (Kelly *et al.*, 2005). This is also the case for spontaneous alpha activity modulated by spatial attention (van Gerven and Jensen, 2009). Shifting and maintenance of attention generate different patterns of posterior (i.e., occipito-parietal) alpha oscillations and distributions that can be used in BCI (Rihs, Michel and Thut, 2007, 2009). These shifts were successfully decoded and classified, and the performance correlates with the strength of resting-state alpha power (Treder *et al.*, 2011).

While these studies were done offline, others showed that it was possible online, i.e. in real-time (Bahramisharif *et al.*, 2010; Tonin *et al.*, 2013). Posterior alpha activity is now established as a reliable control signal for continuous online BCIs (Horschig *et al.*, 2015). Continuous online BCIs are crucial for real-world BCI applications needed by these patients. Furthermore, these authors showed that shifts in covert spatial attention can be picked up at the single-trial level, which is crucial for the consistent performance of a BCI (whereas ERPs are not always visible and can require an average over many trials).

Posterior alpha oscillations might constitute a promising feature for BCIs because it is more protective against muscle artifacts compared to motor imagery for example (Neuper *et al.* 2006).

While ocular artifacts will greatly affect posterior alpha and bias BCI classification (Jensen *et al.*, 2011), they are much easier to extract than muscle artifacts (see Section 8.4.2.). Furthermore, motor-imagery-BCIs have only been shown successfully in a few conditions and require training participants (to accurately visualize movements mentally), which is not the case with alpha activity associated with covert attention (Wolpaw and McFarland, 2004). Alpha activity associated with covert attention can be used for useful BCI applications such as the control of objects or a cursor on a screen (Bahramisharif *et al.*, 2010).

Note that intracranial BCIs address these issues to a much greater level (with higher spatial and temporal resolution, as well as not being affected by artifacts inside the brain) and show groundbreaking results. For example, Willett *et al.* (2021) were able to translate intended handwriting movements from intracranial signals in the motor cortex into text in a patient with hand paralysis from spinal cord injury. Using a recurrent neural network decoding approach, the patient was able to “type” 90 characters per minute with 94.1% accuracy in real-time, and 99% accuracy offline with an additional autocorrect feature. Such performance has never been reached before and is comparable to smartphone typing speed (115 characters per minute). The authors propose that while most BCI research attempts to restore gross motor skills (e.g., reaching, grasping, point and click with computer cursor; (Hochberg *et al.*, 2012; Aflalo *et al.*, 2015; Bouton *et al.*, 2016; Ajiboye *et al.*, 2017; Pandarinath *et al.*, 2017), fast and complex dexterity (e.g., handwriting or touch typing) might enable faster rates of communication.

While intracranial BCI interfaces will certainly become the new “pacemaker” of tomorrow for the disabled with the constant improvements in this field, they are invasive and not realistic for healthy individuals (requiring craniotomy). Hence, wearable EEG technologies should be more suited for the general population, and patients once they match the performance of intracranial BCIs.

### *9.3. Awareness, self-regulation, and neurofeedback*

Chronic stress has strong repercussions on both the individual’s psychological and physical systems, and is associated with unhealthy behaviors that contribute to morbidity and mortality such as obesity, sleep deprivation, attention deficit, mood disorders, grey matter atrophy in the

brain, or substance abuse, to name a few (Sapolsky, 1996; Dallman *et al.*, 2003; Duman and Monteggia, 2006; Juster, McEwen and Lupien, 2009; Jackson, Knight and Rafferty, 2010; Miller, Chen and Parker, 2011).

Better understanding the brain processes associated with stress and self-regulation, as well as predictor variables that mediate both well-being and brain changes will be valuable for therapies and interventions aiming to elevate well-being or reduce depression and anxiety. Xu *et al.* (2018) found that positive-psychology interventions (PPI) increased not only subjective well-being and relief in depression but also left frontal asymmetry scores. Positive reappraisals techniques are PPI that train the participants to recognize the negative pattern that their thoughts have taken using meta-awareness and to cognitively reframe them as more positive, increasing the sense of well-being in the long term. Kim, Cornwell and Kim (2012) found that positive reappraisals showed an increase in metabolic activity in the left dlPFC, caudate, and cingulate regions. Self-regulation is a skill that can be trained to improve cognitive function and the parasympathetic system, as well as a wide range of clinical outcomes, by providing a daily tool to individuals to detect and monitor the occurrence and effects of chronic stress on their mental and physical health (Lehrer *et al.*, 2003; Alabdulgader, 2012; McCraty and Zayas, 2014).

Meditation encompasses several ancient self-regulation practices, and can greatly improve stress-related outcomes (Goyal *et al.*, 2014; Brandmeyer and Delorme, 2016, 2020b; Brandmeyer, Delorme and Wahbeh, 2019). A popular form of meditation practice is the focus of attention onto an object (e.g., mantra, beads counting, breath focus) and the monitoring of mind-wandering thoughts (i.e., distractor), to then reallocate attention to the object. Targeting the underlying neural processes and systems with NF can help users become aware of repetitive negative thoughts occurring daily, and reshape them towards positive ones. Meditation techniques include focused breathing exercises that help to directly regulate the cardiovascular system (Steinhubl *et al.*, 2015), negative mood, stress, pain, anxiety, and mind wandering (Zeidan *et al.*, 2010; Bhasin *et al.*, 2013; Prinsloo *et al.*, 2013; Steinhubl *et al.*, 2015; Brandmeyer and Delorme, 2020b). Moreover, meditation practices were found to increase regional brain gray matter density (Hölzel *et al.*, 2011). Moynihan *et al.* (2013) found that mindfulness-based stress reduction produced significant improvements in executive and immune functions, as well as increases in left-lateralized frontal alpha power.



Neurofeedback (NF) refers to the monitoring of neural activity in real-time using technology (electrophysiological sensors) to facilitate self-regulation of a targeted brain activity that was previously found to be associated with a mental state or behavior of interest (“operant conditioning”; Hammond, 2007; Sitaram *et al.*, 2017). NF originated in the late 1960s: “People can be taught to voluntarily control their alpha rhythms. This can be used to send messages in Morse code when an electroencephalogram pattern is used as part of a computer program. Such procedures may help to explain the mechanisms by which the alpha rhythm is blocked or unblocked.” (Dewan, 1967). However, many of the difficulties faced by the pioneers of BCI and NF (Dewan, 1967; Vidal, 1977) have been solved only recently with modern technological advancements. Several EEG measures have been used for neurofeedback research, including power spectra, functional connectivity, or other spatiotemporal patterns of EEG activity (Sitaram *et al.*, 2017).

NF has now been implemented in a large number of studies assessing its effectiveness as an alternative or complementary treatment of a myriad of conditions including epilepsy (Sterman and Egner, 2006), attention-deficit hyperactivity disorder (ADHD; Gevensleben *et al.*, 2009; Arns, Heinrich and Strehl, 2014), anxiety (Hammond, 2005), alcoholism (Saxby and Peniston, 1995), posttraumatic stress disorder (PTSD; Kluetsch *et al.*, 2014; Kolk *et al.*, 2016), mild head injuries (Byers, 1995), learning disabilities (Fernandez *et al.*, 2003), stroke (Shindo *et al.*, 2011), depression (Hammond, 2005), autistic spectrum disorder (Coben, Linden and Myers, 2009), tinnitus (i.e., chronic ear ringing that significantly interferes with daily tasks; Dohrmann *et al.*, 2007), recurrent migraine headaches (Walker, 2011), etc. Furthermore, NF can present interesting applications for healthy populations as well, by enhancing well-being (Kluetsch *et al.*, 2014), memory, attention, cognitive performance (Zoefel, Huster and Herrmann, 2011; Nan *et al.*, 2012; Wang and Hsieh, 2013), or peak performance (Hammond, 2007).

A few studies have investigated fMRI-neurofeedback and suggested it was possible (Wang, Mantini and Gillebert, 2018). The regular endogenous manipulation of one’s EEG activity through NF can improve both the targeted behavior and the associated symptoms, as well as longer-term changes in grey and white matter (i.e., brain plasticity; Sitaram *et al.*, 2017). Brain self-regulation is associated with structures including the thalamus and the dorsolateral prefrontal (dlPFC), posterior parietal and occipital cortices in neurofeedback control, and the dorsal and ventral striatum, anterior cingulate cortex (ACC), and anterior insula in

neurofeedback reward processing (Sitaram *et al.*, 2017). Some authors even suggested that NF could slow down neurodegeneration (i.e., neuronal death associated with aging or diseases like Alzheimer's disease or Parkinson's disease; Hölzel *et al.*, 2011). However, the bulkiness and costs of MRI equipment make it much less transferable to real-world applications.

Meditation-based NF can help users become aware of their emotions that are associated with many psychological conditions (e.g., anxiety, depression), and can help overcome them (Brandmeyer and Delorme, 2013, 2016; Mooneyham and Schooler, 2013). NF might increase the efficacy of interventions using positive reappraisal or meditation strategies by helping individuals detect negative thoughts (if the EEG markers are reliably classified) to then self-modulate their brain networks associated with the targeted neural processes (Linden, 2014; Brandmeyer and Delorme, 2020a). This might be especially true for individuals with social withdrawal, anhedonia (i.e., inability to experience pleasure from activities usually found enjoyable), and apathy (i.e., feeling indifferent or lacking emotion, often a sign of depression or misuse of alcohol or drugs) that cannot find the motivation or even the intention to get better and participate in interventions with clinicians. Note that these behaviors are all associated with greater right than left frontal alpha asymmetry, which would therefore potentially constitute a good target for NF training in these individuals. Allen, Harmon-Jones and Cavender (2001) found that increasing right frontal activity relative to the left using frontal asymmetry neurofeedback led to decreased positive affect. Angelakis *et al.* (2007) improved cognitive processing speed and executive function of elderly individuals using peak alpha frequency as a neurofeedback index.

By combining neural and physiological measures such as EEG and HRV (see section 8.4.6.) it is possible to develop NF paradigms aimed at improving measures related to anxiety, stress, emotions, cognition, and performance (Thompson and Thompson, 1998; Shaw, Zaichkowsky and Wilson, 2012; Gruzelier, 2014). Given that some NF protocols are already considered a first line of treatment for children with ADHD (Gevensleben *et al.*, 2009; Arns, Heinrich and Strehl, 2014), new NF protocols may soon be available as treatment options for stress management and the associated physical outcomes.

Wearable EEG technologies offer the benefits of EEG-NF while maintaining comfort, mobility, fast computation algorithms, high temporal resolution, and affordability (Cannard *et al.*, 2020). Other recent innovations include for example the development of assistive robots that provide

NF training sessions to elevate user engagement and motivation (Tsiakas *et al.*, 2017), or musical NF that might be particularly suited for art and educational purposes (Kovacevic *et al.*, 2015; Grandchamp and Delorme, 2016). Technological industries now offer products (wearable hardware and softwares accessible on phones) that can process EEG data in real-time and provide neurofeedback applications directly in the hands of consumers from home (Sullivan, Deiss and Cauwenberghs, 2007; Hu *et al.*, 2015; Hashemi *et al.*, 2016). Kovacevic *et al.* (2015) recorded 523 subjects with the same wearable EEG system in a collective and immersive neurofeedback science-art installation. They found that the participants' EEG baseline activity predicted subsequent NF training, indicating the existence of a state-dependence effect in learning ability during NF. The brain data recorded by NF Applications available on smartphones/tablets is currently aggregating some of the largest EEG databases in history (Hashemi *et al.*, 2016).

However, this body of literature must be considered with caution. These systems are often marketed to consumers as forms of cognitive enhancement and entertainment (Sandford, 2009) and may present potential dangers, as they do not involve professional supervision. Not only do appropriate methods need to be employed, but more transparency on the algorithms that are being used by these private software companies must be enforced so researchers can validate their use. Furthermore, no robust consensus exists in randomized controlled trials examining the efficacy of NF in clinical settings. This is due to the large differences in study design, the difficulty of identifying responders, the heterogeneity in the studied populations, differential influence of feedback, reward, and experimental instructions, or the sense of agency and self-control (Sitaram *et al.*, 2017). Some critics go as far as suggesting that NF works only via placebo but indicate that well-controlled experiments are feasible and “indispensable to elucidate how this contentious intervention promotes adaptive brain activity and desired behavior” (Thibault, Lifshitz and Raz, 2017). Additionally, neurofeedback results provided by these smartphone Apps as the algorithms used to generate these values are company trade-secret. It is therefore unknown what type of EEG activity they are targeting for the NF they provide, and often these algorithms have not been validated.

Nevertheless, while these questions require more research, NF training is a promising alternative and complementary treatment for many conditions treated with medications that are costly and present negative side effects for a large portion of the population (e.g., antidepressants; Ferguson, 2001; Cascade, Kalali and Kennedy, 2009). Such brain modulation can present useful

therapies of brain disorders associated with abnormal cortical rhythms, and support the use of NF as a non-invasive tool for establishing a causal link between rhythmic cortical activities and their functions.

#### *9.4. Wearable EEG and “real-world” applications*

The applications described below can be used either offline using traditional methods on data recorded with wearable EEG systems or online (real-time) using cloud-based recording methods (e.g., Cassani, Banville and Falk, 2015; Lab Stream Layer, 2021).

##### **9.4.1. Virtual Reality (VR)**

The accelerating development of increasingly sophisticated virtual reality (VR) platforms is now advancing our ability to study the brain and cognition in environments that simulate the ecological conditions of natural environments while staying in a controlled laboratory setting. Wearable EEGs have been combined with VR in a range of studies investigating the cognitive processes underlying (simulated) driving conditions such as alertness, vigilance, reaction time, fatigue, and drowsiness of automobile drivers in simulations (Brown, Johnson and Milavetz, 2013; Wascher, Heppner and Hoffmann, 2014; Armanfard *et al.*, 2016; Foong, Ang and Quek, 2017; Wang and Phyo Wai, 2017). This combination allows for the development of new closed-loop systems that may be integrated into the technology of newly manufactured vehicles in the near future. This technology holds the potential to ensure safer driving performances through the incorporation of features such as feedback alarms (Berka, Daniel J Levendowski, *et al.*, 2005), emergency braking predictions based on EEG signatures (Haufe *et al.*, 2011), red and yellow stop lights distinctions (Bayliss and Ballard, 2000), or the control of virtual cars (Zhao, Zhang and Cichocki, 2009). While the continued use of standard research-grade equipment is more appropriate when studying specific neural mechanisms and processes implicated in VR environments, these findings can later be used to inform models applied to real-world investigations implementing wearable EEG technologies.

Video-game-NF was found to improve symptoms associated with ADHD and anxiety, by making it more interactive and enjoyable (deBeus and Kaiser, 2011; Muñoz *et al.*, 2015; Schoneveld *et al.*, 2016; Perales and Amengual, 2017). The Neuroscape center for translational neuroscience at the University of California, San Francisco has developed multiple popular video games that

implement NF such as the “NeuroRacer”, “Meditrain”, the “Ace”, or the “Beep seeker”, to name a few. These applications are ready for use with a traditional monitor screen as well as in 3D VR environments (Desai *et al.*, 2014). Combining VR with NF training was suggested to successfully enhance attention (Cho *et al.*, 2002) and learning (Hubbard, Sipolins and Zhou, 2017), by providing better motivation through immersion (Lécuyer *et al.*, 2008). For instance, a multimodal interface prototype allowed participants to be suspended in the air by a harness, immersed in a 3D VR environment, controlling their “flight experience” using a wearable EEG (Perusquía-Hernández *et al.*, 2016).

#### **9.4.2. Real-world settings**

##### *Clinical environments*

In clinical settings, the feasibility of wearable neurotechnologies for real-world applications have been tested with advanced Alzheimer’s disease (AD) patients in a nursing home (Abbate, Avvenuti and Light, 2014), in Parkinson’s disease (PD) patients during a walking task (wearable fNIRS; Nieuwhof 2016), or in expert vs novice surgeons to assess stress levels during simulated operations (Maddox *et al.*, 2015).

##### *Educative and artistic environments*

Cultivating and enhancing creativity within the domains of science and education is another potential avenue whereby these technologies may help to facilitate improved and engaging educational opportunities while educating the next generation of future neuroscientists in a more engaged and interactive way. BCIs have now been developed to create music using devices such as the Emotiv Epoc (Levicán *et al.*, 2017) and the ‘Encephalophone’ system (Deuel *et al.*, 2017), as well as visualize music performance (T. Mullen *et al.*, 2015; Grandchamp and Delorme, 2016). For example, Grandchamp and Delorme (2016) developed the ‘Brainarium’, a portable planetarium dome on which the real-time EEG data is recorded from a subject and directly projected as vibrant and colorful multimedia content. These types of applications demonstrate the growing importance of the art and its contribution to the sciences in ways that have been overlooked for the last several decades (Andujar *et al.*, 2015). The ‘Unicorn Education Kit’ contains 8 wearable EEG headsets and software that allows professors to easily teach BCI technology to students, for \$13,168 at the time of writing. The kit is designed to teach a class of

up to 40 students (in groups of 5) during the beginning of a school term, and let them take the system to their home during the second half of the term to further learn the technology and principles of BCI. Students can learn how to assemble EEG electrodes, calibrate the system, run a P300 speller, interface with a robot, send commands to other applications, and develop their own BCI application using the API. For younger children, a 3-D printed wearable EEG system with cat ears connected to a spherical moving robot was developed to make the process more entertaining and engaging (Unicorn, 2021).

### Physical activity

While sedentarity is considered a high-risk factor for health, the benefits of physical activity have been extensively documented in the scientific literature (Tremblay *et al.*, 2010; de Rezende *et al.*, 2014). Several studies have shown that regular sport-based activities produced neuro-angiogenesis (i.e. creation of new blood vessels) and neurogenesis (i.e. creation of new neurons) in the brain (Fabel *et al.*, 2003; Olson *et al.*, 2006; Pereira *et al.*, 2007). While most of the studies on exercise assess pre/post measures, a lack of research studying the neural mechanisms taking place during the practice of exercise is due to the reduced mobility imposed by cables and the artifacts produced by the participants' movements.

With the development of wearable neurotechnologies, researchers have been able to study EEG activity during attentional tasks while walking outdoors (Debener *et al.*, 2012; Aspinall *et al.*, 2015), or riding a stationary bike (Scanlon *et al.*, 2017). Some expert athletes train their whole life to develop self-regulation techniques to keep a steady performance under stress and muscular fatigue. Some researchers were able to record EEG data from expert archers to study their relaxation capacities under stress and muscular activity (Lee, 2009), while others have accelerated the training of archers, golf players, and rifle marksmen using NF strategies (Berka *et al.*, 2010).

However, the challenge of dealing with EEG artifacts related to movements is most important for these applications (see section 8.4.2.). When these limitations are overcome, studying the brain of individuals while they are doing a physical activity will bring precious information on the effects and mechanisms of physical activity on the brain, which may have an important impact on both sports science (e.g. training strategies) and medical applications. Such studies could compare the long-term effects of different types and intensity of physical activity on different cognitive measures and various populations.

## Sleep

Poor sleep quality concerns one-third of the adult population (Roth, Roehrs and Pies, 2007), has been linked to many clinical and medical conditions such as depression and pain (Giron *et al.*, 2002), and is costly for both the individuals and society (i.e. lost productivity, sleep medication, etc.). The deleterious effects of chronic sleep deprivation and the associated outcomes have potentially dangerous and expensive consequences as a result of impaired neuropsychological functions for individuals at work, at home, and on the roads (Pilcher and Huffcutt, 1996; Dongen *et al.*, 2003). In addition, long-term health-related concerns include increased risk for metabolic and cardiovascular diseases (Cappuccio *et al.*, 2011), as well as an overall decrease in the immune system (Bryant, Trinder and Curtis, 2004). Research shows that 90% of the American population is using a technological device (e.g. television, laptop, or smartphone) in the hour preceding sleep, which disrupts the natural melatonin production and circadian rhythms necessary for good sleep quality (Gradisar *et al.*, 2013; Mortazavi *et al.*, 2018). “Night shifts” (i.e., blue light filters) now implemented in most computers and phones do not seem to solve the problem (Nagare, Plitnick and Figueiro, 2019; Duraccio *et al.*, 2021)

Some wearable technologies developed in the last decades (e.g. wristbands, mobile apps, smart pillows) target sleep quality monitoring but do not focus on interventions supporting a healthier sleep or making use of sleep cognition (Ravichandran *et al.*, 2017; Bianchi, 2018). Some wearable EEG headbands are more suited than others for sleep application by including soft flexible fabrics that are more comfortable and better prevent electrodes from disconnecting and focus the electrode coverage of frontal areas to limit artifacts (e.g., MUSE S by InteraXon, or the Dreem headband; Dreem, 2021; InteraXon, 2021). Only a limited number of sleep studies have been conducted using wearable EEG systems to our knowledge with mixed results (Berka *et al.*, 2007; Onton, Kang and Coleman, 2016; Debellemanni *et al.*, 2018; Liang and Chapa Martell, 2018). This is because of the large difficulty to obtain quality signals (pressure from the head-on posterior and lateral electrodes, movements, etc.). The challenge is even more difficult for patients suffering from pathological conditions such as Alzheimer’s disease (AD; Abbate, Avvenuti and Light, 2014).

In the long term, advancements in this area might provide complementary or alternative pro tools to improve sleep quality in the individuals’ home, using wearable neurotechnologies. A

closed-loop system could detect when sleep is disrupted and modulate the appropriate networks to prevent the individual from waking up. Some of these wearable neurotechnologies may allow for closed-loop auditory stimulation to modulate brain oscillations at the right moment by using a classification of sleep cycles (Chambon *et al.*, 2018; Debellemaniere *et al.*, 2018), enhancing sleep quality at night (Arnal *et al.*, 2017). To go further, a team from MIT media labs developed the first sleep BCI, an interactive interface named 'Dormio' (Haar Horowitz *et al.*, 2018). When the user enters the hypnagogic sleep stage (associated with high creativity), EEG and motor signals detect it and trigger an auditory feedback response provided by a robot located next to the sleeping user. The sound makes the user more aware of being in that state and extends the duration of the semi-lucid hypnagogic period, enhancing his/her creativity. Semantics can be used instead of a sound to influence the dreams of the users. Neuromodulation methods have been explored in sleep studies, such as attempting to increase awareness in dreams with gamma tDCS during rapid eye movement (REM) sleep (Voss *et al.*, 2014) or transcranial magnetic stimulation (TMS; Massimini, Tononi and Huber, 2009). The most sophisticated wearable EEG systems, therefore, present a promising future for sleep research, management, and monitoring.

### EEG-assisted driving

New research may lead to the first 'prevention systems' which uses real-time data recorded from a pilot or driver's brain that would enable the detection of mind wandering, the loss of attention, and/or drowsiness and could provide auditory, tactile, or visual feedback cue to the driver to avoid an accident (Healey and Picard, 2005; Akbar *et al.*, 2017; Wei *et al.*, 2018). Several studies have also examined the possibility of such EEG interfaces in real-life driving situations to identify an EEG marker of an individual's intention to brake or to turn at an intersection (Zhang *et al.*, 2015; Chavarriaga *et al.*, 2018; Martínez, Hernández and Antelis, 2018).

While these findings are groundbreaking, the machine learning methods used by these BCI systems still need to be improved to further reduce the margin of error. Only a 0% error rate will make these applications feasible to avoid accidents. Chavarriaga *et al.* (2018) suggested that combining EEG features with other physiological measures (e.g., eye tracking, ECG, EMG) as well as other car sensors (smart cars) might help improve the performance of such interfaces.



### Real-world applications

In the long term, BCI applications using wearable neurotechnologies are aimed to be delivered in “home-based” settings. Home-based applications are key as they can facilitate accessible and high-quality treatment options, reduce commute times, reduce the volume of consultations at clinics, increase the quality and quantity of patient information collected by healthcare professionals, and improve longitudinal measures of care quality.

Some preliminary studies have tested the feasibility of home-based EEG. Askamp and van Putten (2014) reported that 33% of Dutch neurologists use home EEG recordings collected with wearable systems in the context of epilepsy research and that patients are generally satisfied with the 24h home EEG procedure they use. While they report this type of application is not necessarily useful for the initial diagnosis after the first seizure, they indicated that mobile EEG can be largely useful in better understanding unclear paroxysms (i.e., sudden epileptic seizure event) that occur unexpectedly when the patients are at home (Askamp and van Putten, 2014). Wolpaw *et al.* (2018) had BCI placed in the home of 27 patients with advanced amyotrophic lateral sclerosis (ALS; i.e., break down of nerve cells supplying leading to the loss of muscle function), trained their caregivers to use them, and collected the data via the internet. They evaluated the benefits, burden, and quality of life with periodic visits over up to 18 months. They reported that only 33% completed the study and used the BCI for communication purposes. 12 could not continue due to death or rapid disease progression, and 6 because of decreased interest. They observed rare technical problems, low burden, and no improvements in quality of life (Wolpaw *et al.*, 2018).

Other limitations to these applications include poor signal quality and electrode contact, assistance in the interpretation of EEG, and motivation of the patients. Motivation generally relies on the efficacy of the technology (speed and accuracy), comfort and design, and of the system that facilitates its wear over long periods at home or in public (Askamp and van Putten, 2014; Käthner *et al.*, 2017). As discussed in previous sections, tremendous improvements are being made in the field with the constant improvements in signal acquisition and classification (for performance) as well as more elegant and comfortable systems (e.g., Muse S). Companies specialized in mobile neurology diagnostic devices are developing potential solutions for epilepsy using mobile and continuous EEG recording, smart clothing, smartphone application, and cloud

platforms (Valenza *et al.*, 2015). In a study by Valenza *et al.* (2015), they used wearable textile technology to characterize depressive states in bipolar patients during their normal daily activity.

“Neuro-phones” (phone-based BCI applications) have also been developed to enable practical and affordable everyday use, by allowing EEG signals to interface with mobile phone applications despite paralysis using wireless EEG headsets (Campbell *et al.*, 2010; Wang, Wang and Jung, 2011; Kumar, Aggrawal and Gupta, 2012; Stopczynski *et al.*, 2014; Debener *et al.*, 2015).

Another growing field is the development of Smart houses (Lee *et al.*, 2013). Numerous intelligent devices, embedded into the home environment, can provide the resident with both movement assistance (e.g. intelligent bed, intelligent wheelchair, and robotic hoist for effortless transfer of the user between bed and wheelchair), and 24-h health monitoring. They are therefore particularly relevant for elderly and disabled populations, as it helps restore independence and autonomy. However, these devices lack methods for decoding the intentions of disabled residents, which may be solved through the integration of wearable EEG headsets (Lee *et al.*, 2013; Hintermüller *et al.*, 2015; Miralles *et al.*, 2015; Käthner *et al.*, 2017). Measuring patients’ vital signs at home may result in higher quality, individualized treatment protocols that incorporate continuous, detailed information about the patients’ ongoing physiological status (Muse *et al.*, 2017). A variety of prototypes and commercial products have been recently developed that provide real-time health data directly to the user or the medical center/professional physician and can alert an individual or care provider in the event of a potentially threatening or imminent health emergency (Kumar, Aggrawal and Gupta, 2012).

Home-based BCI systems, once the limitations are addressed, may help support the autonomy and independence of patients with disabilities or paralysis, improve early detection of certain medical conditions, monitor progression of symptoms and effects of treatment remotely, sleep quality, and ultimately, provide large-scale longitudinal data on the effects of aging in the brain and body (Light, Li and Abbate, 2011). Furthermore, patients or elderly with low autonomy can gain better access to information as well as access applications that train mindfulness and stress-reduction techniques and can improve secondary symptoms (Gray, 2017).

Some advanced wearable neurotechnologies such as those developed by Neuroelectrics could also be very valuable for home-based use as they enable simultaneous EEG recording and brain stimulation (Dutta and Nitsche, 2013; Helfrich *et al.*, 2016), which was found to improve

neurorehabilitation effects by training motor function and learning processes (Gandiga, Hummel and Cohen, 2006). These technological advancements present valuable applications for many clinical conditions such as epilepsy, depression, or Parkinson’s disease (PD), to name a few. The Starstim (wearable system combining EEG and tDCS) is now approved for medical use and complies with the European legislation for clinical research (e.g. depression, pain, addiction, stroke). The NUBE Cloud Service and Neuroelectrics Instrument Controller (NIC; (Neuroelectrics, 2021a) provides a telemedicine platform, wherein clinicians and researchers can prepare general stimulation protocols, schedule the stimulation sessions for patients, confirm whether the sessions have been executed or not, and create pre/post-stimulation questionnaires (Aguilar Domingo, 2015). Remote (supervised) neurofeedback or neuromodulation protocols can therefore be accessible at a low cost while patients are in the comfort of their homes, reducing the logistics required to transport patients to the hospital and the clinical equipment (Biondi *et al.*, 2021).

### 9.5. *Other applications*

A new interesting area of research that emerged from the development of wearable neurotechnologies and wireless data streaming is dyadic EEG research, i.e. recording several individuals simultaneously. Dyadic EEG can be useful to better understand interindividual interactions, such as behavioral synchrony during social interactions (Anaya, Vallorani and Pérez-Edgar, 2021), action planning in the social context in children (Liao *et al.*, 2015), “brain-to-brain entrainment” (i.e. interbrain synchronization) during speech (Pérez, Carreiras and Duñabeitia, 2017), joint attention (i.e., one person follows another’s gaze onto an object leading to both individuals’ attention focused on the same object playing an important role in social interactions; (Lachat *et al.*, 2012), cooperation between workers and its role on safety and performance (Verdière, Dehais and Roy, 2019), cooperation vs competition between individuals facing (simulated) mortality threats (Zhou *et al.*, 2021), infant-mother EEG interactions (Krzczkowski, Lieshout and Schmidt, 2020), group dynamics and team cohesion (Stevens *et al.*, 2010, 2012, 2013).

Other secondary real-world applications include neuromarketing (i.e., the measurement of EEG signal to gain insight into customer’s motivations, preferences, and decisions to inform

marketing and product development; (Cartocci *et al.*, 2018; Ramsøy *et al.*, 2018; Vences, Díaz-Campo and Rosales, 2020), and neuroaesthetics (i.e., the science studying the biological underpinnings of aesthetic experience; (Cheung *et al.*, 2019; Cartocci *et al.*, 2021).

## 9.6. *Other limitations*

We already discussed the main limitations for real-world EEG applications, i.e. the problem of EEG artifacts (section 8.4.2), the potential bias of big data analysis on noisy signals (section 9.1.), the challenge of tracking uncontrolled stimuli from the environment (section 9.2.).

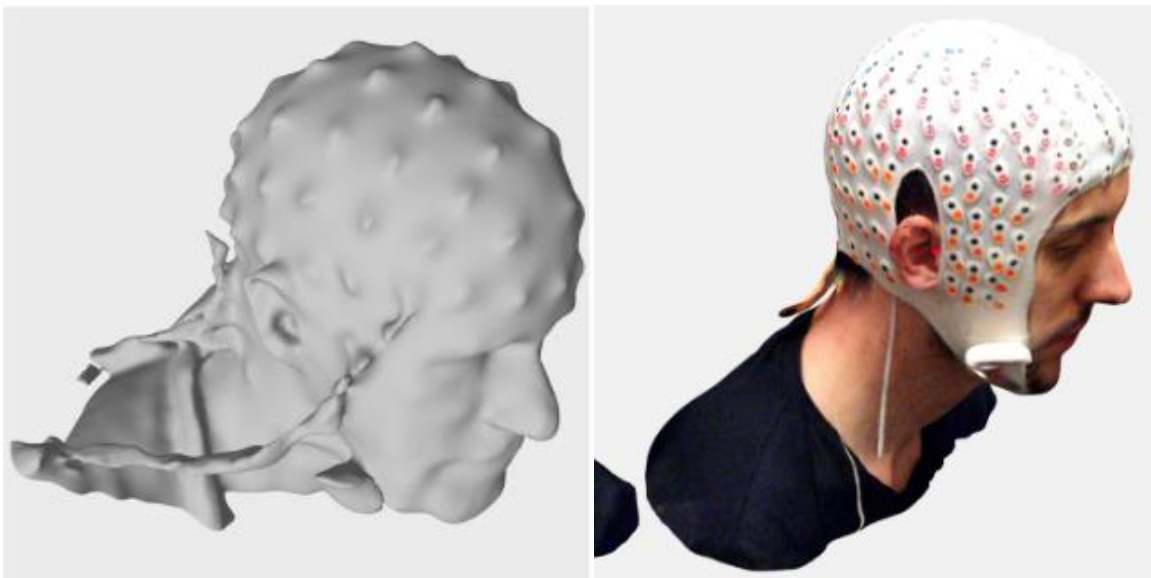
### 9.6.1. **Interindividual differences**

An important remaining limitation to these applications is to integrate individual differences from individual characteristics (e.g., age, brain anatomy, skull thickness) and from electrode positioning that can slightly differ across subjects (or across sessions with the same subjects). Addressing these issues is crucial to gain accuracy at the subject level at detecting specific mental states and providing the corresponding therapy successfully.

#### *Electrode positioning*

While a majority of NF and BCI systems require a minimal level of experience and knowledge to effectively acquire quality data and the targeted EEG correlates that have specific scalp distribution (see section 2.3.5.). While misplacing electrodes is most concerning for high-resolution applications such as source localization (Dalal *et al.*, 2014; Shirazi and Huang, 2019), ensuring the proper application of wearable technologies is also essential, especially if users are going to place their EEG systems on their head as for real-world applications. Manuals and tutorials provided in the documentation are generally not sufficient to cover the complexities of measuring, analyzing, and interpreting physiological data (let alone factoring in potential confounds and placebo effects that can interfere with the proper use of the technology). Misplaced electrodes even occur in laboratories with traditional preparation methods using the traditional nose (i.e., the lowest point between the nose and forehead) and ear (i.e., the intersection between the helix and the tragus of the ear) fiducial landmarks. This problem is likely exacerbated by wearable systems that have only a few electrodes that can be positioned quickly and easily at the wrong location.

One innovative existing solution is to obtain a quick 3-D head image that captures both the head fiducials and electrode positions (after electrodes are placed on the head) using a structure sensor camera that can be attached to a tablet or a phone (e.g., Structure, 2021) and can be used with an App on a phone or tablet (e.g., the itseez3d, 2021, has shown the best results for this EEG application; Clausner, Dalal and Crespo-García, 2017). These scans can be imported into EEGLAB using the *get\_chanlocs* plugin (Lee, 2021). Then, a low-resolution 3D head image can be previewed to check the overall quality of the scan (Figure 37, left), and once a satisfying image is obtained, the high-resolution model is obtained (Figure 37, right). Then the plugin locates the exact 3-D electrode positions from the 3-D scanned head image.



*Figure 37. Illustration of the 3D head image captured by a structure sensor camera and imported into EEGLAB with the *get\_chanlocs* plugin to obtain accurate electrode locations and their accurate relation to nose and ear fiducials. Note: a different participant and scan are illustrated here. Source: Lee (2021).*

This process can be done in under 1 minute. Future improvements will allow the use of 3D head scans to fit subject structural MR images and better account for volume conduction effects, gyri orientation, and other anatomical features that may affect each individual's EEG differently. This is especially crucial for neuromodulation applications that require high spatial accuracy (Mosayebi-Samani *et al.*, 2021), but also for BCI and neurofeedback applications since the mean-field potentials measured with EEG are greatly affected by these factors, and no solution currently exists to address this issue. One can imagine a wearable EEG toolkit that includes a 3D head scan feature, warns the user if the electrodes are not placed correctly, and directs the

user in which direction they should be adjusted (similar to the already existing impedance monitoring feature for electrode contact with the scalp; see section 3.1.).

Additionally, variability in electrode types, location, software, file formats, or interfaces constitutes a barrier in attempting to combine big databases across a range of sources. Research resource identifiers (RRID; e.g., SciCrunch, 2021) may help resolve this limitation by offering a platform to search for this information. Unlike more general search engines, they provide extensive access to a focused set of resources relevant to their communities and provide access to content that can be hard to find using standard web search engines. Users can also add their data to the platform. Furthermore, the brain imaging data structure (BIDS) is used more and more across modalities (e.g., EEG, fMRI), homogenizing the way neuroimaging data are organized and stored. Tools (e.g., BIDS-EEG integrated into EEGLAB; Pernet *et al.*, 2019; Delorme *et al.*, 2021) allow researchers to automatically convert their data into the BIDS format, greatly facilitating data sharing within and between laboratories, reuse of datasets knowing what the conditions, files, and markers correspond to, and most importantly replication of findings. Furthermore, the BIDS EEGLAB plugin allows the importation of large datasets into the software and to process and analyze them automatically.

### *Self-calibration protocols (SCP)*

Matching an individual's EEG signal to a normalized one over large samples loses accuracy and the specificity necessary for reliable and accurate individualized NF or BCI. The self-calibration protocols (SCP) can address this issue (Karydis *et al.*, 2015b, 2015a; Karydis, Foster and Mershin, 2016). The SCP establishes a baseline EEG activity of the user to obtain results that are specifically adapted to that signal. The SCP consists of a series of short assessments (tasks) on a PC, tablet, or phone while the EEG is recorded (before the actual experimental task or EEG application). The goal is to discriminate between the targeted state (e.g., pain sensation, positive emotion, perceived mind wandering) from the other non-targeted states, using the user's feedback. The user self-classifies his/her states using annotations on the device, guided by the task instructions. Then, semi-supervised machine learning algorithms can be used to train accurate, individualized classifiers.

The authors of this approach claim that relying on specific EEG correlates predefined using previous research (e.g., alpha asymmetry, or increased beta power at an electrode site) is no

longer necessary. Understanding the impact of individual characteristics such as age or gender would no longer be necessary by such an approach. However, this approach depends solely on the subject's feedback and might not reflect the targeted mental states and underlying EEG correlates because meta-awareness accuracy is not guaranteed (Kringelbach and Berridge, 2009; Polychroni, Hedman and Terhune, 2020), especially if participants are not motivated to do the task or have a hard time focusing their attention to do the task (as in clinical settings with patients with apathy, anhedonia, or ADHD for example). One approach that seems more reliable would be to use the same SCP but still target EEG correlates identified on large populations, but rendering them more accurate for each individual with the SCP. The algorithms can then be adjusted to provide neurofeedback, BCI, or neuromodulation for each individual while accounting for these factors. Other factors could be added once they are robustly identified, such as age and gender.

Furthermore, this approach may address the state-dependence problem highlighted in neuromodulation research (Metsomaa *et al.*, 2021; Mosayebi-Samani *et al.*, 2021). This concept refers to the stimulation of an area that can either excite or inhibit that region depending on the current state and activity of the network in that region. For example, if the person was presented with a positive-valence image, the neural networks processing emotion might be in a state of excitation or hyperpolarization (if inhibited) that will make it easier or harder to modulate them. The opposite effect can even be obtained (e.g., inhibiting when trying to excite). Progress has been made in this area for neuromodulation applications (Metsomaa *et al.*, 2021). Future developments are required to take this phenomenon into account for BCI and neurofeedback applications as well.

Once these intricacies are better understood, these technologies could be integrated into efficient methods and toolkits that might be useful for therapies aiming at tackling large societal problems such as depression. Furthermore, these improvements will help assess personalized benefits of interventions for each individual (as opposed to assessing how an intervention helps a large group), and identify why they might not help certain individuals.

### **9.6.2. Comfort and design**

A major limitation to the daily integration of wearables remains the feasibility of people feeling comfortable wearing such devices in public spaces. Mayaud *et al.* (2013) found that performance

and ‘level of comfort’ decreased after long periods of recording using low-cost wearable headsets (i.e. between 2 and 3 hours of use). Furthermore, populations such as the elderly often prefer simple, loose, and comfortable clothing, making the necessary placement of tight-fitting wearable devices close to the body difficult (Abbate, Avvenuti and Light, 2014).

However, Abbate, Avvenuti and Light (2014) showed in a study with Alzheimer’s disease (AD) patients, that a few simple modifications to the placement of the wearable EEG system, its color, and how it is integrated with clothing significantly improved its usability and acceptance, especially in the elderly population. While great improvements in design, weight, and comfort are under active development, wearable neurotechnologies will eventually need to diversify their designs to satisfy cultural differences, characteristics, and sensitivities, while maintaining the specific electrode locations required to target the right EEG correlates and the corresponding scalp spatial distributions.

New technologies developed by companies that offer innovative solutions such as the production of smart clothing that incorporates biometric sensors embedded into the material (see section 9.4.2.; Valenza *et al.*, 2015) are promising. However, more research will be necessary to establish and ensure high SNR as well as comfort to users.

A promising recent innovation is the development of transparent “in-ear EEG” (or ear-EEG) systems that provide microelectrodes in the ear canal (i.e. Goverdovsky *et al.*, 2016; Nakamura *et al.*, 2017) or the “cEEGrids”, a flex-printed C-shaped 10-channel grid that can be placed around the outer ear on the scalp (Bleichner *et al.*, 2015; Bleichner and Debener, 2017). These systems are capable of extracting relevant focal temporal features such as the P300, presenting promising innovative solutions and applications for augmenting hearing technology or BCI systems (Christensen *et al.*, 2018). The electrode location is the same as the MUSE TP channels used in this study, suggesting these systems would be well-suited to measure temporoparietal alpha asymmetry and well-being.

Grids with many channels will be particularly groundbreaking in the years to come because of the triangulation capacity they offer (as with intracerebral tetrodes or microelectromechanical system (MEMS)-based recording). They are very small and their geometrical distribution (3D arrays) provides a better spatiotemporal representation and estimation of neuronal connectivity (Wise and Najafi, 1991). Additionally, the chips they contain can amplify, filter, compute real-



time signal processing, and carry microstimulations at the recording site (Olsson and Wise, 2005; Olsson *et al.*, 2005), paving the path for implantable brain-chip interfaces and neural prosthetic devices.

Technological improvements have gone as far as the development of sensors integrated into smart glasses (Vahabzadeh *et al.*, 2018), smart EEG-glasses (Jiang *et al.*, 2017), stick-on electronic tattoos (Zheng *et al.*, 2014), and chemical wearable sensors (Matzeu, Florea and Diamond, 2015), or EEG-hats with hair-separation (Kawana *et al.*, 2019, 2020).

### **9.6.3. Ethical and safety concerns**

The rapid advancements in the biomedical-tech sector present clear ethical concerns such as consent, data protection, and identity protection (Trimper, Root Wolpe and Rommelfanger, 2014). These concerns are especially important when new signal processing techniques can allow to “authenticate” or differentiate individuals based on short segments of EEG data (see section 9.1.). At present, there is no globally established legislation regulating informed consent, personal data protection, or guidelines to avoid psychological and physical effects associated with BCI/NF or brain stimulation technologies (Kubler *et al.*, 2006; Evans *et al.*, 2009; Haselager *et al.*, 2009; Jwa, 2015; Wurzman *et al.*, 2016; Coin, Mulder and Dubljević, 2020; Naufel and Klein, 2020; Jawad, 2021). While the research and clinical use of BCIs across the world is regulated by national laws and Institutional Review Boards (IRBs), the private and commercial use falls out of these legislations, allowing the potential for non-ethical practices and applications of the technology.

Furthermore, while these technologies are considered non-invasive, their use as therapeutic tools proves that they might also have detrimental brain modifications if misused (if they can improve some brain processes, they can also damage them). This is especially true for neuromodulation tools. Furthermore, the ease of engineering the relevant hardware, the decrease in costs, and the enthusiastic ‘do it yourself’ (DIY) culture interested in cognitive enhancement make exploring these ethical issues especially pressing (Jwa, 2015; Wurzman *et al.*, 2016). Having observed the public outrage and opposition to previous scientific and technological advancements, such as was seen with the cloning of Dolly the sheep, ethicists and scientists must work together to ensure that the technology is developed with the highest ethical standards and that the public is informed accordingly (Wolpe, 2006).

Recent findings suggest highlight concerns surrounding the potentially deleterious effects of chronic and long-term exposure to the radio (RF), Bluetooth, and WIFI frequencies on biological and brain systems. Detrimental effects are generally considered to be dependent on the distance and relative size of a given object, but also on the environmental parameters, and there may be additional interindividual differences in sensitivities to RF, making the assessment of these risks difficult (Krause *et al.*, 2006; Hung *et al.*, 2007; Croft *et al.*, 2010; Ishak *et al.*, 2011; Volkow *et al.*, 2011; Avendaño *et al.*, 2012; Balachandran *et al.*, 2012; Laudisi *et al.*, 2012; Megha *et al.*, 2012, 2015; Banaceur *et al.*, 2013; Kesari *et al.*, 2013; Shahin *et al.*, 2013; Mandalà *et al.*, 2014; Saili *et al.*, 2015; Mohan *et al.*, 2016; Othman *et al.*, 2017). Wearable neurotechnologies concentrate Bluetooth and Wifi energies in and around the area of the brain in larger amplitudes than has been studied previously (wireless intracerebral electrodes might be especially concerning). The potential for chronic exposure to RF frequencies resulting from daily use of EEG/BCI/NF technologies in the long term demands that future studies explore solutions for RF protection or alternative deliverance modalities.

While it is safe to say that a majority of wearable technologies are designed under the premise of improving health monitoring and outcomes, and or enhancing or regulating cognitive and emotional processing, these technologies also host tremendous power and potential to drastically influence the choices and actions of the users (i.e. how to breathe, eat, drink, exercise, work, sleep, shop, regulate emotions, etc.). The short-term reality is that the user is often in the illusion that the feedback provided is highly accurate, which can heavily influence the way of life of that user. This is seen heavily with companies claiming their device can “read the mind” of the users. This concern has been already occurring with personal genome testing provided by private companies (McGuire and Burke, 2008).

Additionally, by offering consumers a way to delegate the task of lifestyle management to the technology, such products could alter individual responsibility and self-regulation (Schüll, 2016). This concern is even greater regarding the potential for neuromodulation technologies (e.g. tDCS) becoming available to the public (Walsh, 2013; Jwa, 2015; Wurzman *et al.*, 2016). Following the advice of commercial applications wherein participants are instructed to actively modulate their brain with technologies such as tDCS without any validation or control, presents a major concern.

As lifestyle, health, and technology become increasingly integrated and interfaced, these devices must remain tools to support and assist human needs, and not replace them. With an increasing rate of reliance on our technology, human beings are increasingly vulnerable to the potential dangers and pitfalls of this reliance. When technology is used to enhance or assist a function, this function no longer needs to be accomplished by the body, further directing one's attention towards additive systems. For example, recall is often better for self-generated answers than for answers obtained from an external technological source (Pyke and LeFevre, 2011). This phenomenon of cognitive loss following the delegation of a mental task to technology might be hard to predict with real-world BCI integration. However, neurofeedback (considering the intended effects are reached and the limitations discussed are overcome) might be less affected by this risk, since it relies on self-regulation and only provides sensory support to the user (guiding the user to detect subtle mental states through feedback). As neurofeedback might help users become aware of detrimental thought patterns or emotional responses, it is also possible that BCIs might enhance natural abilities beyond their initial potential (e.g. a system detecting cues that are imperceptible to the awareness to warn from a danger, could potentially train the brain to detect these stimuli that were previously subliminal through reward-conditioning mechanisms. The brain is constantly evolving and aiming to improve the prediction of environmental perturbations).

Species knowledge used to be carried and orally transferred by the tribe members, leading to each individual possessing the whole species' knowledge. With the invention of books, computers, and the Internet, an ever-increasing portion of species knowledge has become externalized from individuals. For example, most people do not know how to build a car they drive or harvest electricity, because they do not need to (and cannot) possess all the species knowledge. This evolution has led to a vast distinction between species and individual knowledge. This increasing externalization of information into technology (instead of in the individual brain and memory) produces a constant increase in species knowledge linearly associated with a constant decrease in individual knowledge (Buzsaki, 2006).

One can argue that brain resources that are no longer necessary because they are supplemented by technology could be recruited for new abilities. If this is possible, future studies should focus on how to develop technologies that aim to produce long-term benefits (like neurofeedback).

However, as basic cognitive abilities are more and more delegated to technology over generations, these cognitive abilities might be hard to recover when the system fails.

### *General conclusion*

In this 3-year project, we validated the use of a quick scale to evaluate multidimensional well-being, identified predictors of well-being in a large sample, and observed improvements in well-being levels following interventions. We validated the use of a low-cost wearable EEG headset to measure EEG spectral measures and used it to study the EEG correlates of multidimensional well-being on a large sample. We found a potential EEG marker that could be used to monitor and predict well-being levels, or that could be implemented into neurofeedback or neuromodulation interventions if further research supports this finding and brings more light to the underlying mechanisms. We show that affordable wearable neurotechnologies can provide solutions to the global increase in poor mental health associated with limited access to healthcare and treatment for a majority. While significant limitations and challenges remain, these technologies might be used in the long term to detect and predict mental health outcomes, support brain-computer interface, neurofeedback, or neuromodulation applications in real world settings, and elevate global well-being at affordable costs and no side effects.



# Annexes

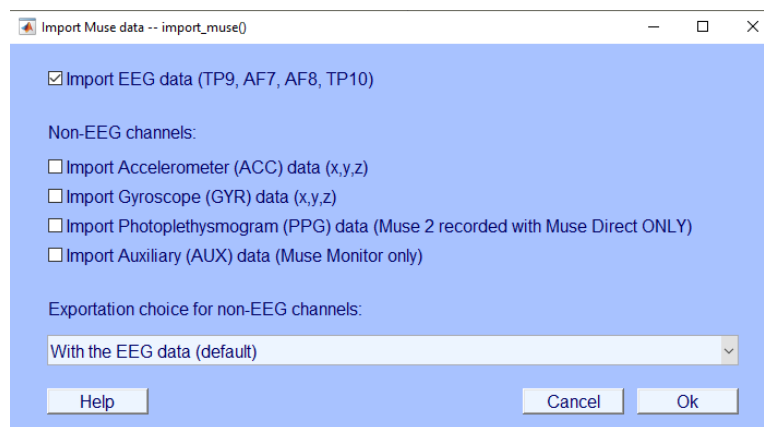


## *Annex 1: An EEGLAB plugin to import MUSE data*

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A new EEGLAB plugin named `import_muse` was developed to import EEG data collected with the wearable MUSE headset for this project (Cannard, 2021). This plugin functions in MATLAB and imports Muse .csv files recorded with either the Mind Monitor App (Clutterbuck 2021) or the Muse Direct IOS App (InteraXon 2021). It is compatible with different hardware models: Muse 1 (2014 and 2016), Muse 2, and Muse S.

Using either the graphical user interface (GUI) or the command lines, users can choose to import EEG, accelerometer (ACC), gyroscope (GYR), photoplethysmography (PPG), or auxiliary (AUX) data (Figure 38). They can also choose to have the non-EEG signals time-synchronized to the EEG data, for multimodal analyses (Figure 38).



*Figure 38. Graphical user interface (GUI) window when importing data recorded with the MUSE wearable systems. Users can select which data they wish to import for analysis, including EEG, accelerometer (ACC), gyroscope (GYR), photoplethysmography (PPG), or auxiliary (AUX).*

The plugin automatically detects which hardware was used to record the data and detects the sample rate for each signal (that is different). EEG data are converted to the EEGLAB format, so that users can access all the advanced EEGLAB tools and use them on the data recorded with MUSE, such as low- and high- pass filtering, re-referencing, automatic artifact removal techniques (e.g., ASR used in this study; Figure 39), power spectra (Figure 40), or robust statistical tools (e.g., LIMO-EEG, see Annexe 3).



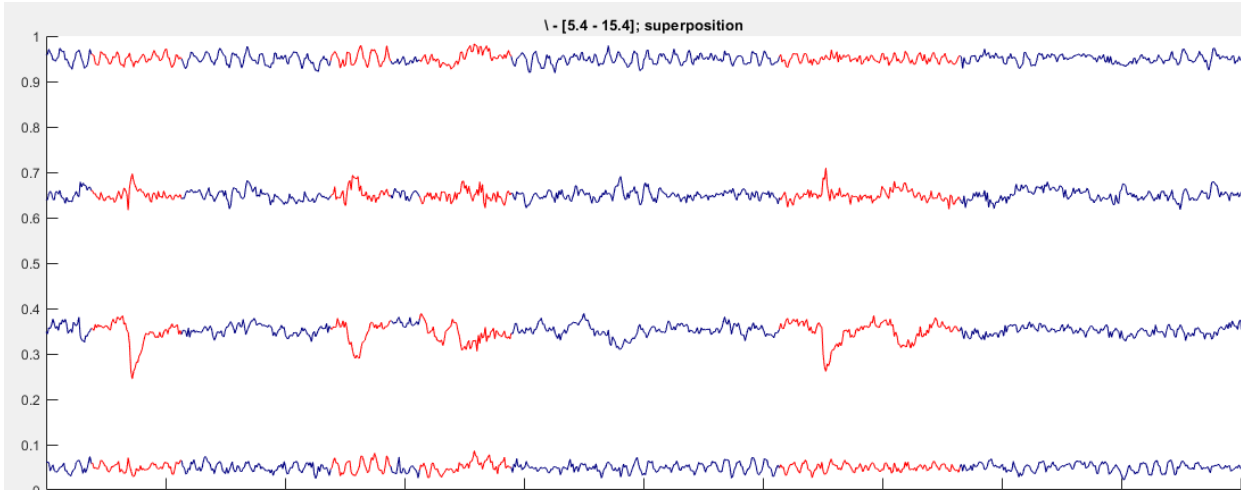


Figure 39. Illustration of the artifactual segments detected and removed by the EEGLAB `clean_rawdata` plugin, on EEG data recorded with a wearable MUSE headset.

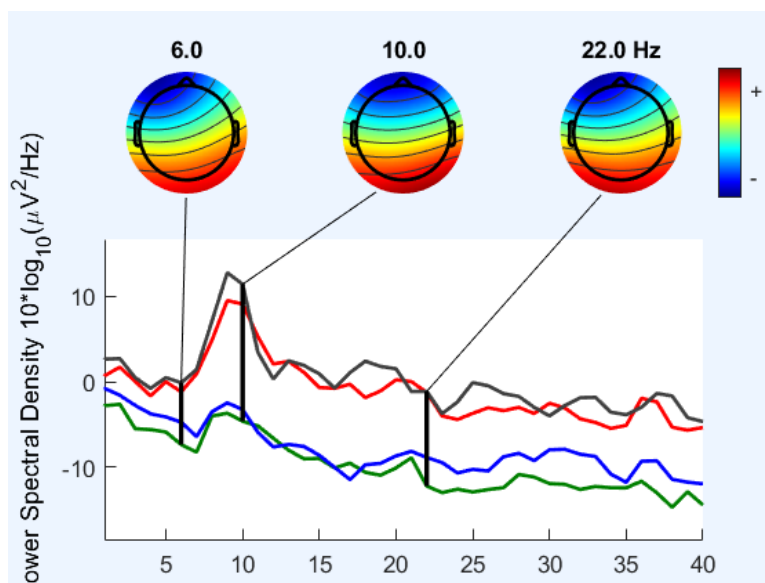


Figure 40. Power spectral density of EEG data recorded with the MUSE obtained with EEGLAB.

If users chose to synchronize the non-EEG signals with the EEG signals for multimodal (time-locked) analysis, these signals are resampled to match the EEG sample rate and converted to EEGLAB format. Figure 41 illustrates this feature with ECG data recorded by a custom electrode that connects to the auxiliary port of the MUSE, and Figure 42 with PPG signal recorded with a MUSE 2 or MUSE S (the PPG sensor was added in these recent models).

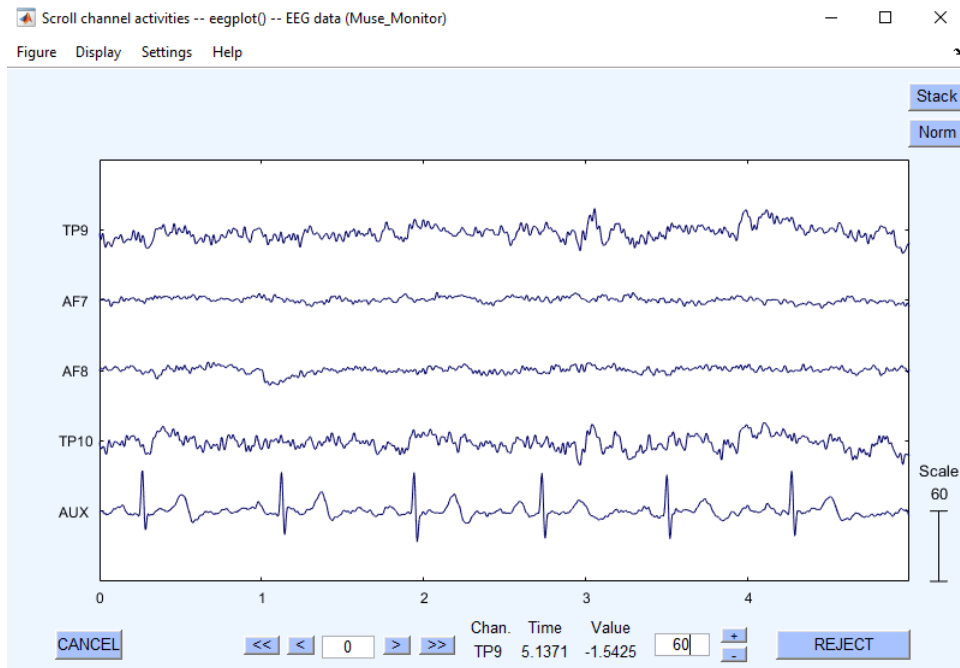


Figure 41. Plot of raw EEG and ECG data recorded with MUSE in EEGLAB. The ECG data was collected with a custom-made electrode that plugs into the auxiliary port, and time-synchronized to the EEG data for multimodal analysis

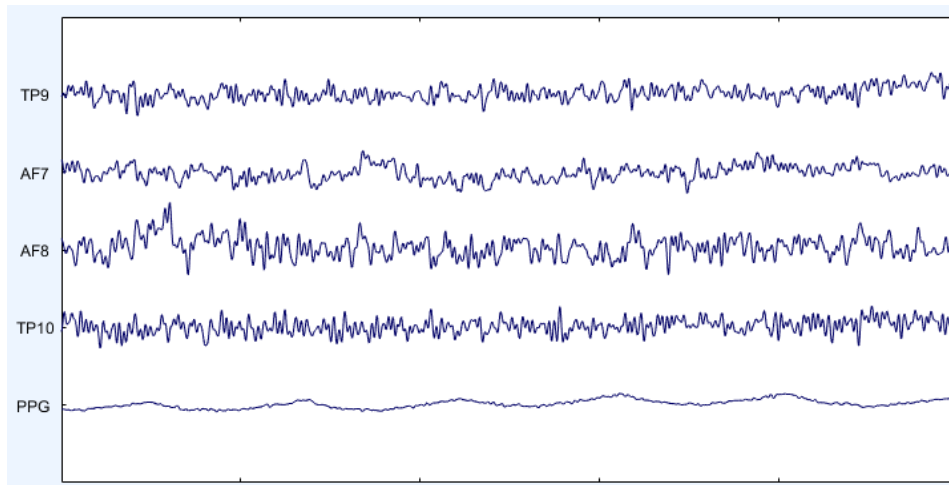


Figure 42. EEG and PPG data recorded with the MUSE S or MUSE 2, imported and time-locked by the `import_muse` EEGLAB plugin for analysis.

Note that non-EEG data (ACC, GYR, PPG, AUX) can also be exported as separate outputs (raw, untouched) for simpler physiological analyses (not time-locked to EEG), and are not illustrated here.



## Annex 2: Asymmetric interactions between frequency bands

Attempting to link EEG asymmetry not just to psychological constructs, but to other measures of neural function can identify potential mechanisms underlying EEG asymmetry and reveal more about the pathway from lateralized alpha power to psychological functioning (Smith et al 2017). Interactions between EEG asymmetries across different frequency bands were explored using *Skipped Spearman correlations* (see section 5.2.4. for more detail on the statistical methods) on the same data cleaned and used in Chapter 7 (N = 230). Only *p-values* corrected with the *Bonferroni* method for multiple comparisons to control for *Type 1 error* were considered as significant (see caption below Table 11 for more detail). Results are reported in Table 11.

**Table 11. Skipped Spearman correlations between EEG asymmetries across different frequency bands, for both frontal and temporoparietal (TP) regions.**

	Frontal delta	Frontal theta	Frontal alpha	Frontal beta	TP delta	TP theta	TP alpha	TP beta
Frontal delta	1							
Frontal theta	.68*	1						
Frontal alpha	.23*	.49*	1					
Frontal beta	.26*	.31*	.31*	1				
TP delta	.01	.03	.03	.01	1			
TP theta	.01	-.12	-.13	.01	.60*	1		
TP alpha	.07	.08	-.24*	-.03	.29*	.51*	1	
TP beta	.01	.05	-.08	-.07	.18*	.43*	.43*	1

Correlation coefficients from the skipped Spearman correlations are reported in the table (N = 230). Since 28 tests were done (asymmetries in theta, delta, alpha, beta, in both frontal and temporoparietal regions), corrected *p-value* was 0.0018 at 95% confidence level (\*), 0.00036 at the 99% confidence level (\*\*), and 3.5714e-05 at the 99.9% confidence level (\*\*\*)

We observed asymmetric associations across all bands in the same direction within frontal and TP areas (e.g., greater left than right theta power is associated with greater left than right power in alpha and beta frequencies), and an asymmetry in alpha frequencies in the opposite direction between frontal and TP areas (e.g., when alpha power increases in frontal left relative to frontal

right, it increases in the TP right relative to TP left). Note that the strongest correlations occurred locally between theta-delta and theta-alpha frequencies, suggesting the mechanisms underlying these asymmetric patterns may involve these frequencies specifically at the local level, whereas alpha oscillations may be involved in mechanisms underlying global (frontal-TP) asymmetries.

## *Annex 3: A hierarchical linear modelling of broad-band EEG power and well-being*

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An additional exploratory analysis was conducted to look at the data differently, using the advanced hierarchical linear modeling (HLM) provided by the EEGLAB LIMO-EEG plugin (Pernet *et al.*, 2011). This statistical tool tests for effects at all electrodes and frequency points, contrasting with traditional approaches that preselect features of interest based on the literature (e.g., alpha asymmetry, individual alpha frequency). While traditional analyses methods focus on averaged data over trials and subjects, this toolbox deals with both within- (1<sup>st</sup> level, i.e., single-trial analysis) and between- (2<sup>nd</sup> level, i.e., group level) subject variance.

Beta ( $\beta$ ) coefficients (or parameters) are estimated for each subject at each frequency point and each electrode independently (1<sup>st</sup> level), then the  $\beta$  coefficients are analyzed across subjects for robust statistical testing (2<sup>nd</sup> level). *Confidence intervals (CI)* are computed to test  $H1$  (the hypothesis of a difference) and corrections for multiple comparisons under  $H0$  (hypothesis of absence of a difference) are applied to control for the *Type 1 error* (i.e., false positives). The regression analysis employed consists in sampling with replacement 230 (number of subjects) matrices of frequency data (electrodes  $\times$  frequency bins). In other words, trial indices are sampled. The obtained regression  $\beta$  coefficients are then computed for each bootstrap and sorted in ascending order. For simple regressions, 599 bootstraps are performed to calculate the 95% *CI* (Wilcox, 2011).

We used the *weighted least square (WLS)* optimization method (1<sup>st</sup> level) to better account for outliers, and the maximum likelihood estimation method (Ward and Ahlquist, 2018) for correction for multiple comparison (the spatiotemporal correction was not possible with this montage). We found a significant association between well-being and beta power in the left frontal region (AF7 electrode), with a peak at 16 Hz (Figure 43). No covariate effect was found with age or gender.

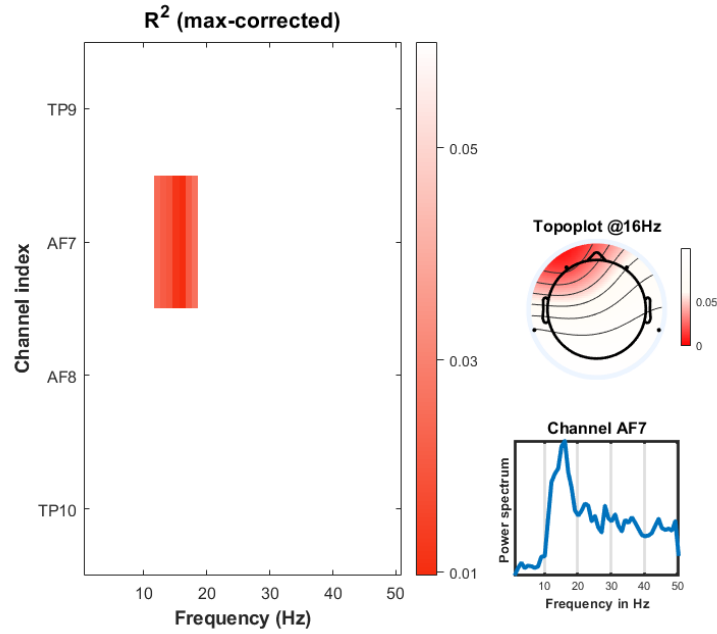


Figure 43. Associate between well-being and beta power in the left frontal region (AF7), with a peak at 16 Hz ( $p < 0.05$ , corrected for multiple comparisons with the maximum likelihood estimation method).

This finding goes along with some literature on stress, anxiety, and depression (Hamid *et al.*, 2010; Putman *et al.*, 2014; Jena, 2015; Jun and Smitha, 2016; Díaz *et al.*, 2019; de Hemptinne *et al.*, 2021).







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# Appendix A: List of publications and communications



## Publications

Patterson, J., Cannard, C., Bunney, William, E., Stein, Richard, A. (In review). Anticipation of pending pictures of unknown emotional valence - a pre-stimulus electroencephalography (EEG) study. *f1000 research*.

Cannard, C., Delorme, A., Wahbeh, H. (2021). Validating the wearable MUSE headset for EEG spectral analysis and Frontal Alpha Asymmetry. *2nd international workshop on Machine Learning for EEG Signal Processing (MLESP), in conjunction with the IEEE International Conference on Bioinformatics and Biomedicine (IEEE BIBM 2021)*.

Cannard, C., Delorme, A., Wahbeh, H. (2021). EEG correlates of well-being using a low-cost wearable system. *Frontiers in Human Neuroscience, section Brain-Computer Interface*.

Carpenter, L., Cannard, C., Wahbeh, H., & Radin, D. (2021). Psychophysical interactions with photons: Three exploratory studies with unexpected results. *Journal of the Society for Psychical Research, 85(1)*.

Delorme, A., Cannard, C., Radin, D., & Wahbeh, H. (2020). Accuracy and neural correlates of blinded mediumship compared to controls on an image classification task. *Brain and cognition, 146, 105638*.

Cannard, C., Brandmeyer, T., Wahbeh, H., & Delorme, A. (2020). Self-health monitoring and wearable neurotechnologies. *Chapter in Handbook of Clinical Neurology, Elsevier (Vol. 168, pp. 207-232)*.

Wahbeh, H., Cannard, C., Okonsky, J., & Delorme, A. (2019). A physiological examination of perceived incorporation during trance. *F1000 Research, 8*.

## Communications in International Conferences

A review of wearable EEG systems (2021). *EEGLAB workshop (virtual)*.

EEG correlates of well-being on a large sample, in the workshop session “The IONS Discovery Lab: a large-scale study of transformative practices” (2020). *The Science of Consciousness Conference (online; 2020)*.

A physiological examination of perceived incorporation during trance (2019). *The Science of Consciousness Conference, Interlaken, Switzerland*.





# Appendix B: Publications in published format

## Chapter 16

# Self-health monitoring and wearable neurotechnologies

CEDRIC CANNARD<sup>1,2</sup>, TRACY BRANDMEYER<sup>3</sup>, HELANÉ WAHBEH<sup>2</sup>, AND ARNAUD DELORME<sup>1,2,4\*</sup>

<sup>1</sup>*Centre de Recherche Cerveau et Cognition, Paul Sabatier University, Toulouse, France*

<sup>2</sup>*Institute of Noetic Sciences, Petaluma, CA, United States*

<sup>3</sup>*Osher Center for Integrative Medicine, University California San Francisco (UCSF), San Francisco, CA, United States*

<sup>4</sup>*Swartz Center for Computational Neuroscience, Institute of Neural Computation (INC), University of California San Diego, San Diego, CA, United States*

### Abstract

Brain-computer interfaces and wearable neurotechnologies are now used to measure real-time neural and physiologic signals from the human body and hold immense potential for advancements in medical diagnostics, prevention, and intervention. Given the future role that wearable neurotechnologies will likely serve in the health sector, a critical state-of-the-art assessment is necessary to gain a better understanding of their current strengths and limitations. In this chapter we present wearable electroencephalography systems that reflect groundbreaking innovations and improvements in real-time data collection and health monitoring. We focus on specifications reflecting technical advantages and disadvantages, discuss their use in fundamental and clinical research, their current applications, limitations, and future directions. While many methodological and ethical challenges remain, these systems host the potential to facilitate large-scale data collection far beyond the reach of traditional research laboratory settings.

### INTRODUCTION

Our society faces increasing health disparities, limited access to healthcare, and rising healthcare costs. Simultaneously, the technological sector has entered an era of bio- and neurotechnology producing wearable neurotechnologies that provide real-time and longitudinal monitoring of physiologic and neural activity and may present viable solutions to many of these issues (Ghose et al., 2012). Consumers can now access a wide array of wearable technologies that measure, monitor, and receive feedback from ongoing physiologic and neural activity. The information provided by wearable technologies has numerous overlapping applications. For example, measuring patients' vital signs at home may result in higher quality, individualized treatment protocols that incorporate continuous, detailed information about the

patients' ongoing physiologic status (Muse et al., 2017). A variety of prototypes and commercial products have been recently developed that provide real-time health data directly to the user or the medical center/professional physician, and can alert an individual or care provider in the event of a potentially threatening or imminent health emergency (Kumar et al., 2012). With an increasing capacity to acquire, share, process, store, retrieve, and apply big data methods, wearable technologies may significantly improve our ability to tackle some of the major challenges of today's society (Zheng et al., 2014).

While the application of wearable technologies was previously limited to physiologic measurements (e.g., heart rate, step counter), recent advancements in wireless electroencephalography (EEG; the measurement of neural electrical activity from electrodes placed on the

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\*Correspondence to: Arnaud Delorme, Swartz Center for Computational Neuroscience, Institute of Neural Computation (INC), University of California San Diego, San Diego, CA, United States. Tel: +1-858-405-7952, E-mail: adelorme@ucsd.edu

scalp) is now leading to the development of new applications. While wearable EEG technology faces a number of limitations and challenges to match state-of-the-art (SoA) research grade EEG equipment (e.g., number of electrodes and electrode locations, signal-to-noise ratio, and markers), they do hold immense potential, allowing direct interfacing between an individual's brain activity and a digital recording device in environments other than clinical and research infrastructures and at affordable prices for a wider part of the population. These devices will eventually allow us to train and target specific cognitive skill sets (Vernon et al., 2003), reinforce specific brain rhythms (Brandmeyer and Delorme, 2013), play video games (Schoneveld et al., 2016), and create art and music based on measured real-time neural activity (Grandchamp and Delorme, 2016).

EEG measurement reflects the cumulative electrical activity associated with the depolarization of cortical neurons, can reflect rhythmic and transient activity (Buzsáki, 2006), and facilitates analyses of neuroimaging data with very high temporal resolution. Brain oscillations reflect the postsynaptic potentials of neuronal populations, either in response to a stimulus from the environment (i.e., event-related potentials, ERP), or associated with mental states (e.g., sleep, coma, and cognitive activity). EEG scalp electrodes measure the electrical waves as they spread across the scalp (see Chapter 18 for more information on EEG). This rhythmic activity of the brain is then analyzed in the temporal domain (i.e., frequency domain), and most often within subbands of specific frequencies, customarily defined based on their spectral content such as  $\delta$  (<4 Hz),  $\theta$  (4–7 Hz),  $\alpha$  (8–13 Hz),  $\beta$  (14–30 Hz), and  $\gamma$  (>30 Hz). Frequency bands are believed to be functionally correlated with specific cognitive processes or with specific steps of processing depending on the location of their measurement or their latency within a specific process. The high temporal accuracy of EEG also provides precise temporal information about brain processing. EEG is also used clinically to diagnose and localize which steps in the brain's information processing pathways are malfunctioning (e.g., visual, auditory, and tactile processing).

The recent development of dry electrodes (Taheri et al., 1994) and wireless technologies have led to innovative wearable EEG systems, which offer quick and practical EEG data acquisition solutions (i.e., no gel, cleaning, or cables) and usually include real-time data preprocessing as well as correction for head movements. Several new systems are now fully portable, where data recordings can be stored directly on the device (i.e., microSD) or transmitted wirelessly to a smartphone (Stopczynski et al., 2014; Debener et al., 2015). As a result of these technological improvements, new possibilities in the domains of fundamental and clinical

research have now emerged. With features such as the lightweight portability, the ease of dry electrodes, and relatively fast set up times, well-designed wearable technologies enable access to populations that were previously harder to include in research laboratories settings.

By gaining access to wider range of populations, such as young children, the disabled, and elderly (Ramirez et al., 2015; Neale et al., 2017), neurotechnologies may enable longitudinal designs with larger sample-size studies (Kovacevic et al., 2015; Hashemi et al., 2016), and improve our ability to study the human brain in naturalistic settings (Debener et al., 2012). Many modern wearable EEG headsets are now comfortable to wear, incorporate elegant designs, and are becoming increasingly attractive for general public use (Nijboer et al., 2015). Innovative applications including practical, easy, and high fidelity at home recordings, have the potential to enable neurofeedback (NF) and brain-computer interface (BCI)-based cognitive interventions, applications, group studies (i.e., simultaneous recording of different participants), big data analyses, and more.

At present, wearable EEG technologies remain one of the most promising candidates for the real-world applications of self-health monitoring solutions (see Chapter 1 for more details on BCI principles, concepts, and domains). Recent innovations in wearable headset design enable the delivery of both transcranial current stimulation (TCS), functional near-infrared spectroscopy (fNIRS), in addition to the simultaneous combination of these methods with EEG (see Table 16.1). In the following chapter, we review several high-fidelity EEG wearable systems currently available (both consumer and research grade products), in addition to systems that combine EEG, TCS with fNIRS, or TCS. We then explore the different applications that already exist using wearable technologies and address the limitations, prospects, and precautions associated with such technologies.

## WEARABLE NEUROTECHNOLOGIES

In this section, we provide a list of both relatively low-cost (i.e., under a \$1000) and widely used (as of 2018) wearable EEG systems that are available for both fundamental and clinical research, NF, BCI, and home use-based applications. We also review a nonexhaustive list of less affordable (i.e., more than a \$1000) and more advanced systems that are destined for professionals who have access to funding and are interested in the applications using these systems. Excluded from this review are several single channel EEG devices—which are relatively limited based on today's standards (Picton et al., 2000; Luck, 2014)—or EEG devices that lacks significant technical or scientific evidence or were proven to provide poor signal quality (e.g., Emotiv

Table 16.1

This table reviews a range of different wearable headsets and their different features and specificities, going from low to high costs and functions. This table includes information about each device's sensors, sampling rate, connectivity type, and data resolution

Sensors	Price (\$)	Battery autonomy (h)	Connectivity/storage	Signal resolution (bits)	Sampling rate (Hz)	Weight (g)	Additional features	Auxiliary measures (EXG)	EEG	NF/BCI (included)	fNIRS	Neuromodulation	Audience and applications
Muse (Interaxon) <ul style="list-style-type: none"> <li>- Four dry active electrodes (TP9, TP10, AF7, AF8); two silver and two conductive silicone rubber</li> <li>- Reference on Fpz (DRL/DMS)</li> <li>- Adjustable headband (52–60cm)</li> </ul>	180	5	BLE	12	256	60	<ul style="list-style-type: none"> <li>- Allows recording of raw EEG data directly on iPod, smartphone, or tablet</li> <li>- NF App</li> <li>- Allows to record data from multiple devices simultaneously on computer</li> <li>- Real-time impedance check</li> <li>- Triggers</li> </ul>	<ul style="list-style-type: none"> <li>- 6-axis motion sensor</li> <li>- One input for custom physiologic sensor</li> <li>- HR (Muse 2)</li> <li>- Respiration (Muse 2)</li> </ul>	X	X			<i>For researchers and the public:</i> home use, real-world recordings, attention/meditation training, relaxation, raw EEG recording, big data analyses, sleep research, BCI
EPOC+ (Emotiv) <ul style="list-style-type: none"> <li>- 14 saline soaked felt pads (AF3, AF4, F3, F4, FC5, FC6, F7, F8, T7, T8, P7, P8, O1, O2)</li> <li>- CMS/DRL references (P3/P4)</li> <li>- Adjustable by pressure control</li> </ul>	800	6	BLE	14/16	128/256	120	<ul style="list-style-type: none"> <li>- Raw EEG data</li> <li>- Available detections of mental commands (neutral + up to four pretrained items per training profile), performance metrics (excitement, engagement, relaxation, interest, stress, focus), facial expressions (blink, wink L/R, surprise, frown, smile, clench, laugh, smirk)</li> <li>- Real-time impedance check</li> </ul>	<ul style="list-style-type: none"> <li>- 9-axis motion sensors</li> </ul>	X	X			<i>For researchers and the public:</i> home use, real-world recordings, raw EEG recording, enhancing brain performance, 3D brain visualization, BCI
Dreem (Rythm) <ul style="list-style-type: none"> <li>- Six channels (four frontal and two occipital)</li> <li>- One microamplifier</li> <li>- Adjustable headband</li> <li>- Reference electrodes on O1 and O2 (but flexible)</li> </ul>	500	12	Wi-Fi and BLE	24	250	120	<ul style="list-style-type: none"> <li>- Sound is discretely diffused to the inner ear via your forehead (using bone conduction technology)</li> <li>- Can connect to smartphone and iPod directly</li> <li>- Sleep monitoring App that works without BLE and Wi-Fi during sleep (data transferred later for report)</li> </ul>	<ul style="list-style-type: none"> <li>- 3-axis motion sensor</li> <li>- Two pulse oximeters (respiration and HR)</li> </ul>	X	X			Sleep monitoring, managing, and improvement
	4.5k	4	BLE/microSD	24	250/1000	110	<ul style="list-style-type: none"> <li>- Real-time impedance monitoring</li> </ul>		X	X			

Continued

Table 16.1

Continued

Sensors	Price (\$)	Battery autonomy (h)	Connectivity/storage	Signal resolution (bits)	Sampling rate (Hz)	Weight (g)	Additional features	Auxiliary measures (EXG)	EEG	NF/BCI (included)	fNIRS	Neuromodulation	Audience and applications
Sleep headband (Cognionics)							<ul style="list-style-type: none"> <li>– Optional wireless triggers</li> <li>– Raw EEG</li> <li>– Recording via microSD card possible</li> </ul>	<ul style="list-style-type: none"> <li>– Optional add-on module for EXG</li> </ul>					Sleep monitoring, managing, and improvement
Quick 20/30 (Cognionics)	24k	8	BLE/microSD	24	500/1000	610		<ul style="list-style-type: none"> <li>– 3-axis motion sensor</li> <li>– Two optional EXG</li> </ul>	X	X			Designed for real-world applications, BCIs
Ultracortex Mark IV (OpenBCI)	~850/1.4k	?	BLE and Wi-Fi	24	250/500		<ul style="list-style-type: none"> <li>– Compatible with active and passive electrodes (adapters)</li> <li>– 3D printable</li> <li>– 30 s to set up</li> <li>– microSD input for local storage</li> <li>– The prices correspond to the printable EEG headset with the OpenBCI boards. The headset can also be purchased printed but unassembled, or fully assembled for higher prices. Batteries are not included but represent a cost of around \$10</li> </ul>	<ul style="list-style-type: none"> <li>– 3-axis motion sensor</li> <li>– Optional EXG (EMG, ECG)</li> </ul>	X	X			Raw EEG recording, BCI, NF, first 3D printable device
B-Alert X10/X20 (ABM)	11.5k	12–24	BLE	16	256	11	<ul style="list-style-type: none"> <li>– Ultra-low profile and comfortable fit allows for 8+ hour recording sessions</li> <li>– Patented real-time artifact decontamination</li> <li>– Software with classifications of cognitive states (for \$16.5 k in total price)</li> <li>– Setup: 10/20 min</li> </ul>	<ul style="list-style-type: none"> <li>– 3-axis motion sensor</li> <li>– 1 EXG with the B-Alert X10; and 4 EXG for the B-Alert X20 (EOG, ECG, EMG)</li> </ul>	X	X			Raw EEG recording, BCI, cognitive assessment or training, performance enhancement, group studies, sleep studies, military studies

DSI 10/20 (Quasar)	<ul style="list-style-type: none"> <li>Up to 21 dry EEG electrodes (flat-ended finger electrodes)</li> <li>Ground at Fpz and references on mastoids</li> </ul>	7k	24	BLE	16	300/600	500	<ul style="list-style-type: none"> <li>Patented shielding and circuit design reduce environmental noise</li> <li>Mechanical design carefully controls contact pressure allowing comfortable wear all day</li> <li>Internal storage (1GB)</li> <li>Impedance monitoring for each sensor</li> <li>Cognitive states classification software</li> </ul>	<ul style="list-style-type: none"> <li>Wireless belt that measures EKG, skin temperature, and 3D body acceleration and position</li> <li>Trigger inputs</li> </ul>	X			Raw EEG recording, BCI and NF, cognitive states classification, real-world recordings
Enobio (Neuroelectronics)	<ul style="list-style-type: none"> <li>8/16/32 channels, using innovative solid-gel electrodes or dry electrodes</li> <li>A disposable pregelled electrode or a earclip can be used for CMS/DRL reference</li> <li>Six different neoprene, flexible, head cap sizes</li> </ul>	~4k/14k/20k	16/15/14	BLE	24	500	65	<ul style="list-style-type: none"> <li>3D visualization real time</li> <li>Specific headcaps for children</li> <li>MicroSD card for internal storage</li> <li>Compatible with TES and TMS</li> <li>"Mickey Mouse" Headcap Cover for kids</li> </ul>	<ul style="list-style-type: none"> <li>EOG/ECG</li> </ul>	X			<i>Researchers and clinicians:</i> high-quality raw EEG, high mobility, real-world studies, BCI, and NF applications
OctaMon (Artinis)	<ul style="list-style-type: none"> <li>8-channels fNIRS headband</li> </ul>	~17k	6	BLE		10	230	<ul style="list-style-type: none"> <li>8 × 2 wavelengths: 760/850 (standard)</li> <li>Optode distance: 35 mm</li> <li>No interference with EEG, EOG, ECG, EMG</li> <li>TMSI packages: Octamon+EMG (2 channels or more), and Octamon+EEG (16 channels or more)</li> <li>Real-time processing of fNIRS data in 3D</li> </ul>	<ul style="list-style-type: none"> <li>Can be combined with external EEG and EXGs</li> </ul>		X		<i>Researchers and clinicians only:</i> study of hemodynamic response with very high mobility, real-world studies, can be combined with other neuroimaging techniques, BCI, educational applications
g.Nautilus (g. tec)	<ul style="list-style-type: none"> <li>8, 16, 32, 64 active, dry, or gel-based EEG electrodes</li> <li>GND and REF</li> <li>Flexible positioning of electrodes, three head sizes for both adults and children</li> <li>8 fNIRS channels, combined with EEG</li> <li>Works with both dry and gel-based electrodes (8/16/32 channels)</li> <li>Flexible positioning of electrodes, three head sizes (including for kids)</li> </ul>	From 5k	6–10	2.4 GHz ISM	24	250/500	<140	<ul style="list-style-type: none"> <li>Contactless charging of the battery</li> <li>Waterproof</li> <li>Allows simultaneous tDCS and TMS</li> <li>Internal impedance check</li> <li>Eight digital triggers</li> <li>MicroSD (up to 2GB)</li> <li>BCI software applications available</li> </ul>	<ul style="list-style-type: none"> <li>3-axis motion sensor</li> <li>Four possible exg (ECG, EMG, EOG, GSR, limb movement, oxygen saturation, respiration effort, and flow)</li> </ul>	X	X		<i>For researchers and clinicians only:</i> high quality raw EEG, possible simultaneous EEG-fNIRS, and compatible with EEG-tDCS and EEG-TMS (with external equipment). Recording during physical activity, easy access to children and the elderly, rehabilitation, real-world recordings, BCI

*Continued*

Table 16.1

Continued

Sensors	Price (\$)	Battery autonomy (h)	Connectivity/storage	Signal resolution (bits)	Sampling rate (Hz)	Weight (g)	Additional features	Auxiliary measures (EXG)	EEG	NF/BCI (included)	fNIRS	Neuromodulation	Audience and applications
Starstim 8, R20, R32, (Neuroelectrics)	~11k/29k/43k	4	Wi-Fi	1 $\mu$ A	1000	65	<ul style="list-style-type: none"> <li>– Frequency stimulation: 0–250 Hz for tACS and 0–500 Hz for tRNS</li> <li>– <math>\pm 15</math> V per electrode (30 V potential difference)</li> <li>– 2 mA max current, 1 h max duration of stimulation</li> <li>– Abortion possible at any time</li> <li>– MRI compatible stimulation electrodes</li> <li>– Nube cloud platform allows scheduled stimulation from distance</li> <li>– Can be combined with the OctaMon fNIRS</li> </ul>	<ul style="list-style-type: none"> <li>– 3-axis motion sensor</li> <li>– ECG, EOG</li> </ul>	X	X	X	X	<p><i>For researchers and clinicians only:</i></p> <ul style="list-style-type: none"> <li>– EEG recording, NF, simultaneous EEG and TES/fNIRS (all in one headset), BCIs, telemedicine, home use, real-world recordings</li> </ul>

**Sensors:** EEG activity is typically recorded from the scalp using gel-based electrodes to achieve a high signal-to-noise ratio (SNR) between the source (the brain activity) and the measurement device (the electrode). Active electrodes contain individual microamplifiers which significantly improve the SNR and reduce application time. When passive electrodes are used, the skin must be properly prepared and abraded in order to achieve a high SNR. The main advantage of gel-based active electrodes is their high SNR. Disadvantages include high cost and relatively lengthy preparation and cleaning time. The recent development of dry electrodes (Taheri et al., 1994) along with wireless technologies have led to the development of innovative wearable EEG systems. While dry electrodes have an increased sensitivity to motion artifact, movement of cables, and electrostatic charges, they do not require extensive cap mounting time, skin abrasion, or hair washing.

**Sensor locations:** The international 10–20 system is an internationally recognized method to describe and apply the location of scalp electrodes for EEG (Klem et al., 1999). The 10–20 system is necessary for the comparison of brain data collected from different laboratories, which entails the comparison across subjects and populations, variations in equipment, and variations in the electrode montage. In the 10–20 system, each electrode placement site is labeled according to the corresponding topographical location on the scalp prefrontal (Pf), frontal (F), temporal (T), parietal (P), occipital (O), and central (C).

**Motion sensors:** To prevent the loss in signal quality, a majority of high-end wearables using dry electrode technology generally include motion sensors. The gyroscope indicates the orientation of an object in space (i.e., Along the 3-axis: X, Y, Z), and the accelerometer measures the acceleration (along the 3-axis as well). Their sampling rates are similar to those of EEG. This information can be used to reject artifacts in the data. However, motion sensors—especially gyroscopes—generally present a significant drain on battery power and may decrease battery life.

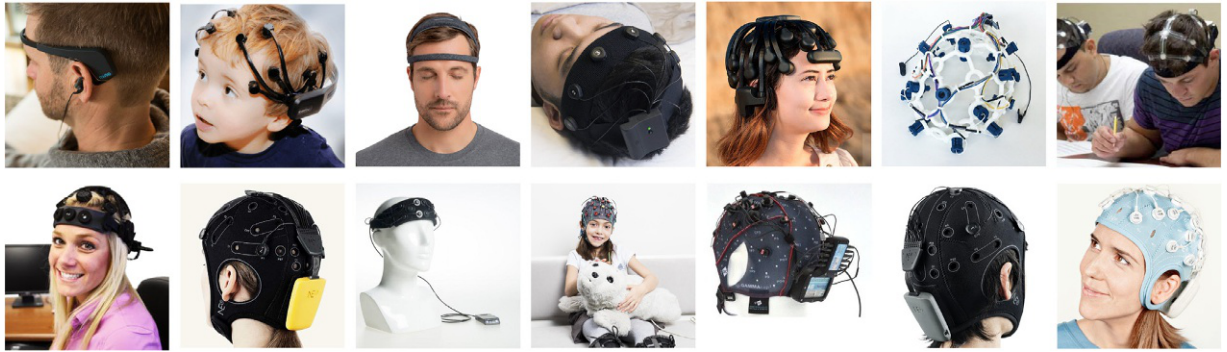
**Sampling rate:** Sampling rates generally vary from 128 Hz to 2048 kHz. Low cost EEG usually use multiplexing of a single analog to digital (AD) converter which scan each channels sequentially. So a 2048 kHz AD converter can convert 8 channels at 256 Hz sampling rate. Note that research systems usually have one AD converter per channel which not only allows for higher sampling rate but also ensures simultaneous acquisition of all channels (with the sequential solution, the acquisition time of each channel is slightly delayed for each channel which could potentially affect subsequent processing—although resampling techniques may be used to realign data collection time of each channel).

**Connectivity:** Bluetooth and Wi-Fi use the same band at 2.4 GHz (Wi-Fi may also use the 5.0 GHz frequency). Wi-Fi direct promises device-to-device transfer speeds of up to 250 MBPS, while Bluetooth 4.0 promises speeds similar to Bluetooth 3.0 of up to 25 MBPS. Bluetooth technology cannot transmit as much data as Wi-Fi.

**Sampling rate:** Sampling rates generally vary from 128 Hz to 2048 kHz. Low cost EEG usually use multiplexing of a single analog to digital (AD) converter which scan each channels sequentially. So a 2048 kHz AD converter can convert 8 channels at 256 Hz sampling rate. Note that research systems usually have one AD converter per channel which not only allows for higher sampling rate but also ensures simultaneous acquisition of all channels (with the sequential solution, the acquisition time of each channel is slightly delayed for each channel which could potentially affect subsequent processing—although resampling techniques may be used to realign data collection time of each channel).

**Data resolution (in bits):** It is generally accepted that EEG signal resolution does not go beyond 24 bits (due to environment and electric noise). However, this means that all systems acquiring less than 24 bits may lose important data, unless a dynamical gain mechanism is implemented to increase the range of possible values. Most low-cost wearable EEG system use 16-bit A/D (analog/digital) conversion resulting in some loss of data.





**Fig. 16.1.** Illustration of the wearable EEG headsets reviewed in [Table 16.1](#). *Top row (from left to right):* Muse (Interaxon), Epoc (Emotiv), Dreem (Rythm), Sleep headband (Cognionics), Quick 30 (Cognionics), Ultracortex, Mark IV (OpenBCI), B-Alert X10 (ABM). *Bottom row (from left to right):* DSI 10/20 (Quasar), Enobio (Neuroelectronics), Octamon (Artinis), g.Nautilus (g.tec), g. Nautilus EEG-fNIRS (g.tec), Starstim 8 and 32 (Neuroelectronics). Reproduced with permission.

Insight, Foc.us EEG Dev Kit, FocusBand, Imec, Neurosky Mindwave, and the two Kickstarter products: Melon and Melomind) ([Fig. 16.1](#)).

## APPLICATIONS

### Fundamental research

Over the past century, EEG studies have served as a key methodological tool for the scientific study of human cognition, sleep, neurodegenerative diseases, and brain disorders ([Regan, 1989](#); [Luck and Kappenman, 2011](#)). While traditional EEG laboratory recordings require lengthy application and recording procedures, several of these technical factors can be overcome by increasingly sophisticated lightweight, easy to setup wearable EEG headsets and headbands that implement wireless and dry electrode technologies and allow scientists to gain access to large volumes of raw data for research purposes.

However, it is important to note that several technical specifications are required to obtain good data quality when conducting both continuous EEG and event-related brain potential (ERP) research ([Picton et al., 2000](#); [Luck, 2014](#))—the type of electrode used, the minimum number of electrodes needed for meaningful interpretation, the importance of the scalp electrode locations (i.e., standard nomenclature of the 10/20 and 10/10 systems), interelectrode impedance, reference-electrode selection, and amplifier capabilities (e.g., number of bits available, the common-mode rejection ratio, or the amplifier gain). An obvious concern with low-cost EEG systems is whether the actual hardware meets the standards necessary to achieve sufficient EEG signal quality. As described in [Table 16.1](#), not all, but some wearable neurotechnological systems currently record the data at high-fidelity sampling rates (i.e., >256 Hz) and with high signal resolution (i.e., superior to 8 bits).

Regarding the argument for increased number of electrodes, as highlighted by [Picton et al. \(2000\)](#), “the optimal number of recording channels is not yet known. This number will depend on the spatial frequencies that are present in the scalp recordings ([Srinivasan et al., 1998](#)), provided that such frequencies are determined by the geometry of the intracerebral generators and not by errors in positioning the electrodes or modeling the impedances of the head” ([Picton et al., 2000](#)). To determine if wearable neurotechnologies meet such signal quality requirements, several studies have directly tested the signal quality of some advanced EEG wearable headsets (see [Table 16.1](#)) to directly determine whether they can provide data that reliably results in visible and statistically quantifiable ERP components.

[Krigolson et al. \(2017b\)](#) were able to reliably identify the N200, P300, and reward positivity ERP components with the Muse EEG headband in two 5-min experimental paradigms. [De Vos et al. \(2014\)](#) conducted a single-trial P300 classification with linear discriminant analysis and revealed high classification accuracies for both indoor (77%) and outdoor (69%) recording conditions. [Barham et al. \(2017\)](#) showed that while significantly more trials are rejected from data acquired by systems such as the Emotiv Epoc, the raw EEG waveforms captured were found to have a high degree of similarity to the corresponding waveforms measured with a SoA system (e.g., SynAmps). Similarly, [Mayaud et al. \(2013\)](#) compared the performance of six traditional EEG disc electrodes (i.e., electrodes made from silver metal and lead wires) with the electrodes provided by the Emotiv Epoc wearable headset, and found no significant difference in performance between the two. They did find, however, that performance and “level of comfort” decreased after long periods of recording using the wearable headset (i.e., between 2 and 3 h of use). [Pinegger et al. \(2016\)](#) evaluated three different commercially available EEG

acquisition systems that differ in the type of electrode (gel-, water-, and dry-based), the amplifier technique, and the data transmission method. Every system was tested regarding three different aspects, namely technical, BCI effectiveness and efficiency (i.e., P300 detection, communication, and control), and user satisfaction (comfort). They found that the water-based system had the lowest short-circuit noise level, the hydrogel-based system had the highest P300 spelling accuracies, and the dry electrode system caused the least inconveniences. They concluded that building a reliable BCI was possible with all evaluated systems and it is for the user to decide which system meets the given requirements best (Pinegger et al., 2016).

While these findings suggest that the hardware specifications of these wearable EEG systems are sufficient to conduct ERP studies successfully, some studies found that such low-cost wearable EEGs (e.g., Emotiv EPOC) showed poor performance compared to clinical-grade equipment (Duvinage et al., 2013). This highlights the importance of the methods employed by the experimenter. When thorough methods are employed, such as specific methods to increase the signal quality (i.e., clean hair, clean skin, a shielded environment, comfortable recording conditions), accurate results can be obtained. In fact, a fair number of studies have now used several different sophisticated low-cost wearable EEG headsets to study a wide array of fundamental topics such as visual and auditory attention and perception (Debener et al., 2012; Boutani and Ohsuga, 2013; Wascher et al., 2014; Badcock et al., 2015; Abujelala et al., 2016; Maskeliunas et al., 2016; Barham et al., 2017; Kuziek et al., 2017; Krigolson et al., 2017a, b), emotions (Peter et al., 2005; Brown et al., 2011; Bashivan et al., 2016; Jiang et al., 2016, 2017; Brouwer et al., 2017), learning, and memory (Berka et al., 2005a, 2007b).

Laboratory studies in psychology and cognition that have conducted research using artificial stimuli and fixed response options inevitably result in findings that are less ecologically valid in relation to real-world behavior. Advanced wearable EEG systems may facilitate a more accurate understanding of the human brain and its highly complex mechanisms occurring in natural settings. Data from wearable EEGs have now been collected on participants walking outdoors on university campuses (Debener et al., 2012) and in urban and green space environments (Aspinall et al., 2015; Neale et al., 2017; Tilley et al., 2017). Wearable EEG systems also facilitate an improved access to populations that were previously harder to include in studies due to lengthy uncomfortable experimental conditions, such as in studies with children (Badcock et al., 2015), in classrooms (Mohamed et al., 2020),

and with elderly populations (Abbate et al., 2014; Ramirez et al., 2015; Dimitriadis et al., 2016; Neale et al., 2017; Tilley et al., 2017).

There have been several critiques of the viability of wearable EEG headsets for conducting EEG research in nonlaboratory or nonclinical settings (Przegalinska et al., 2018). EEG wearables systems will always face the challenge (that can exist in almost any data collection environment) of successfully collecting high-fidelity EEG data. While EEG wearables allow for more mobility, they remain highly sensitive to movement artifacts. High-fidelity EEG data require individuals to limit all body and face movements as much as possible and will always present a challenge in signal analysis. More advanced machine-learning algorithms must be developed to increase the variety of artifacts that can be corrected in real time while not losing the signal of interest. Another considerable challenge involves the inability to directly control events occurring in the environment, while under laboratory settings, stimulus timing is the highly accurate mark of the occurrence of an experimental event. To our knowledge, no simple solutions have been found to mark the occurrence of natural events, except for the use of a synchronized video recording and then a manual synchronization offline. It is important to note that while some of these devices may offer a high signal-to-noise ratio (SNR) and waveform quality when thorough methods are applied, other technical aspects are equally important when recording EEG such as the number of electrodes and accurate electrode placement. Wearable EEG headsets often use dry electrodes that are practical; however, they are often reported to be less comfortable over long periods of time. Wearable headsets are equally sensitive to movement artifacts as SoA systems; they do not allow marker information and events to be directly embedded into the raw data, are often mishandled by users, and vary significantly in their advantages and disadvantages across devices (see Table 16.1). While these limits are important to keep in mind, some promising applications of advanced, low-cost wearable EEG systems have already emerged.

#### FROM VIRTUAL REALITY TO REAL-WORLD APPLICATIONS

The accelerating development of increasingly sophisticated virtual reality (VR) platforms is now advancing our ability to study real-world environment simulations in laboratory settings. VR is now being applied in neuroscience research and is also expanding the development of clinical interventions (Bohil et al., 2011) through the creation of immersive and highly controlled environments wherein the ecologic conditions of natural environments can be simulated. Wearable EEGs have

been combined with VR in a range of studies investigating the cognitive processes underlying (simulated) driving conditions such as alertness, vigilance, reaction time, fatigue, and drowsiness of automobile drivers in simulations (Johnson et al., 2011; Brown et al., 2013; Lin et al., 2014; Wascher et al., 2014; Armanfard et al., 2016; Foong et al., 2017; Wang and Phyo Wai, 2017). This combination allows for the development of new closed-loop systems that may be integrated into the technology of newly manufactured vehicles in the near future. This technology holds the potential to ensure safer driving performances through the incorporation of features such as feedback alarms (Berka et al., 2005b), emergency braking predictions based on EEG/ERP signatures (Haufe et al., 2011), red and yellow stop lights distinctions (Bayliss and Ballard, 2000), in addition to the control of a virtual car based on EEG activity (Zhao et al., 2009). While the continued use of standard research grade equipment is more appropriate when studying specific neural mechanisms and processes implicated in VR environments, these findings can later be used to inform models applied to real-world investigations implementing wearable EEG technologies.

Wearable EEG devices offers advantages such as increased freedom of movement for research participants, increased accessibility (i.e., low-cost equipment), and research that studies properties of locomotion (REF). However, often these technologies have yet to bring about a better understanding of brain processes than what has been shown by studies using the conventional golden standard (i.e., 64-channel research grade EEG equipment) that contain >32 electrodes and provide higher signal quality and SNR (e.g., gel-based systems). The application of wearable systems can be highlighted by new research that may lead to the first “prevention system,” which uses real-time data recorded from a pilot or driver’s brain that would enable the detection of mind wandering, loss of attention, and/or drowsiness and could provide an auditory, tactile, or visual feedback cue to the driver to avoid an accident (Healey and Picard, 2005; Akbar et al., 2017; Wei et al., 2018). Recently, new research (Zhang et al., 2015; Chavarriaga et al., 2018; Martínez et al., 2018) developed innovations in the EEG paradigms designed to study real-life driving situations that aimed to identify an EEG marker of an individual’s intention to brake or to turn at an intersection. While these findings are groundbreaking, the machine-learning methods used by these BCI systems still need to be improved to bring to the margin of error to zero. One way of compensating for changes in SNR while driving, as suggested by Chavarriaga et al. (2018), is the inclusion of additional physiologic measures, such as eye movements, the heart rate, or the electromyography (EMG) of the driver, as well as

contextual information gathered by in-car sensors, which will allow intelligent cars to provide timely and tailored assistance.

## SCIENCE AND EDUCATION

Cultivating and enhancing creativity within the domains of science and education are another potential avenue whereby these technologies may help to facilitate improved and engaged educational opportunities, while educating the next generation of neuroscientists in a more engaging and interactive way. Grandchamp and Delorme, 2016 developed the “Brainarium,” a portable planetarium dome on which the real-time EEG data is recorded from a subject and directly transformed to visually represent the real-time activity as vibrant and colorful multimedia content. Projects such as these demonstrate the growing importance of the art and its contribution toward the sciences in ways that have been overlooked for the last several decades (Andujar et al., 2015). BCIs have now been developed to create music using devices, such as the “Encephalophone” system (Deuel et al., 2017), as well as visualize music performances (Mullen et al., 2015).

## GROUP STUDIES AND BIG DATA

Wearable technologies also enable the simultaneous recording of multiple individuals, opening up new applications of EEG research for the study of group dynamics, team cohesion, or social synchronicity (Stevens et al., 2012, 2013). Big data research studies have the potential to revolutionize the way we investigate individual differences and differentiate commonalities in brain activity across subjects due to the power that a large participant sample size provides in distinguishing nuanced individual characteristics. A majority of neuroimaging studies is conducted on small samples due to the cost and time-consuming nature of measuring EEG on large groups of participants. With larger samples come more robust statistical inferences about the general population as well as a better representation of the sociodemographic differences. For instance, Hashemi et al. (2016) used the Interaxon wireless four-channel EEG headband to analyze the brain data (i.e., the participants were doing a NF mindfulness task such as a breath-focus exercise) of 6029 subjects ranging from 18 to 88 years in age and were able to identify subtle but robust age-related shifts in EEG activity (i.e., EEG power, peak frequencies, asymmetry measures between frontal and temporoparietal sites) on a year-by-year scale, as well as how these changes differed between males and females in a representative population of individuals completing the tasks in uncontrolled natural environments.

In another study, [Kovacevic et al. \(2015\)](#) recorded 523 subjects with the same wearable EEG system for 12h in a collective and immersive NF multimedia science-art installation. They found that the participants' EEG baseline activity predicted subsequent NF training, indicating the existence of a state-dependence effect in learning ability during NF.

The brain data recorded by NF applications available on smartphones/tablets is currently aggregating some of the largest EEG databases in history ([Hashemi et al., 2016](#)). These big data archives will allow for the development of new types of statistical analyses implemented via machine learning, and may highlight patterns and trends in brain activity that have not been previously possible with smaller datasets. The validity and value of such databases will depend on the signal quality being measured by users. Given that these users lack advanced training and experience in EEG, recording movement artifacts and placing electrode positions inaccurately (even though some Apps provide clear instructions and visual feedback about electrode impedance) are inevitable. As a consequence, a large portion of data is usually lost due to these low quality recordings. Furthermore, these devices measure the EEG from only a few electrodes and therefore lack the accuracy and value of a brain signal that is normally recorded from multiple sites on the scalp. As a consequence, the use of these databases is limited to small regions of the brain related to electrode placement (e.g., frontal and temporal for the Muse headband). In addition, the NF algorithms used by the smartphone Apps are the company's trade secrets (which have sometimes not been validated), making it impossible for researchers to know what brain mechanisms and activity were targeted to obtain these results.

In conclusion, sophisticated wearable neurotechnologies should be used by experienced EEG practitioners and reserved to real-world applications as they cannot yet replace SoA systems (e.g., gel-based electrodes) in controlled conditions for testing fundamental questions. Each device offers advantages and disadvantages compared to others, therefore researchers should determine which is best suited to their needs, taking into account all the features of the devices (i.e., sampling rate, electrode locations, SNRs, expected length of use, the availability of skilled labor for system setup and patient comfort). We recommend the collection of raw data and the development of customized NF codes instead of using the non-transparent programs provided by companies designing these devices.

### Clinical applications

One of the more significant clinical applications of wearable EEG involves the use of event-related potentials

(ERP), which reflect stereotypical changes in EEG activity evoked by environmental events. They have played a pivotal role in our understanding of the relationships between physical stimuli and brain activity ([Luck and Kappenman, 2011](#)) and have been widely used in the study of cognitive disorders such as developmental dyslexia ([Hämäläinen et al., 2013](#)), specific language impairment ([McArthur and Bishop, 2004](#)), psychiatric disorders ([Park et al., 2010](#)), and autism ([Čeponienė et al., 2003](#)) among others. The four main EEG patterns used in BCI systems include the P300 (i.e., positive brain oscillation occurring at 300ms), used generally for bidirectional communication BCIs, the  $\mu$  (i.e., 8–12 Hz) and  $\beta$  (i.e., 18–26 Hz) rhythms, usually used for sensorimotor BCIs, and the steady-state visual evoked potentials (SSVEPs), which correspond to the measured active visual focus (see [Chapters 7–11 and 14](#) for more details).

As described in section “[Fundamental research](#),” some wearable EEGs were shown to accurately measure certain types of ERPs, such as the P1/P100, N1/N100, P2/P200 assessed by their peak amplitude, latency, and mismatch negativity ([Badcock et al., 2015](#)) and the N2/N200 and P3/P300 assessed by latency and peak amplitude during an auditory oddball task ([Mayaud et al., 2013](#); [Barham et al., 2017](#)), assessed by classification accuracy ([Jijun et al., 2015](#)) and by a visual oddball task and a reward-learning task ([Krigolson et al., 2017b](#)).

As BCIs integrate the real-time analysis of ERPs ([Sullivan et al., 2012](#)), new potential applications emerge with the continuous improvement of wearable EEGs by maintaining this type of brainwave discrimination in real-world settings while the individuals are moving, by monitoring the events occurring in the environment, and by improving these neurotechnologies in terms of discreteness and design. For instance, early diagnosis of brain disorders by detecting specific EEG components and markers associated with a given disorder may be possible in the patient's home (e.g., unclear paroxysms in epileptic patients; [Askamp and van Putten, 2014](#); [Nunes et al., 2014](#)). [Hofmeijer et al. \(2018\)](#) were able to detect the cortical spreading depolarization producing detrimental effects in patients with traumatic brain injury and ischemic stroke. [Abbate et al. \(2014\)](#) tested the usability of wearable technologies (both physiologic and EEG activities) with elderly victims of advanced Alzheimer's disease (AD) in a nursing home. [Nieuwhof et al. \(2016\)](#) tested the feasibility of using a new portable and wireless fNIRS device to measure prefrontal cortex activity during different dual task walking protocols in Parkinson's disease (PD). [Billeci et al. \(2016\)](#) showed evidence of changes in neurophysiologic and autonomic response from the state of disengagement to the state of engagement of autistic children.



Maddox et al. (2015) measured brain activity for assessing concentration and stress levels during surgical simulator performance of laparoscopic tasks to determine if expert surgeons have different brain activity patterns compared to intermediate and novice surgeons.

### PHYSICAL ACTIVITY

While sedentary is considered a high-risk factor for health, the benefits of physical activity have been extensively documented in the scientific literature (Tremblay et al., 2010; de Rezende et al., 2014). Several studies have shown that regular sport-based activities produced neuroangiogenesis (i.e., creation of new blood vessels) and neurogenesis (i.e., creation of new neurons) in the brain (Fabel et al., 2003; Olson et al., 2006; Pereira et al., 2007). While most of the studies on exercise assess pre-/postmeasures, a lack of research studying the neural mechanisms taking place during the practice of exercise is due to the reduced mobility imposed by cables and the signal artifacts produced by the movements of the subjects. However, with the development of wearable technologies, researchers have now been able to study the electrical activity of the brain during exercise, during performance on attentional tasks while walking outdoors (Debener et al., 2012; Aspinall et al., 2015; Armanfard et al., 2016), walking on a treadmill (Lin et al., 2014), or riding a stationary bike (Scanlon et al., 2017). Some expert athletes train their whole life to develop relaxation techniques to keep a steady performance under stress and muscular fatigue. Some researchers were able to record EEG data from elite archers to study their relaxation capacities under stress and muscular activity (Lee, 2009), while others have accelerated the training of archers, golf players, and rifle marksman using NF strategies (Berka et al., 2010). Studying the brain of individuals while they are doing a physical activity will bring precious information on the effects and mechanisms of physical activity on the brain, which may have an important impact on both sports science (e.g., training strategies) and medical applications. In addition, longer recordings using wearable neurotechnologies would allow long-term assessment (i.e., from several days to several months or years) of a regular physical activity on the brain, as opposed to measuring only the pre- and postsession differences. Such studies could compare the long-term effects of different types of physical activity (e.g., weekly frequency of training sessions, interruptions, intensity, and nature of the exercise) on different types of populations. This would apply to clinical therapies as well.

### NEUROFEEDBACK

Stress has strong repercussions on both psychologic and physical systems. As a consequence, chronic stress was

shown to trigger unhealthy behaviors that contribute to morbidity and mortality (Jackson et al., 2010), such as depression, obesity, sleep deprivation, attention deficit, mood disorders, gray matter atrophy in the brain, or substance abuse, to name a few (Sapolsky, 1996; Dallman et al., 2003; Duman and Monteggia, 2006; Miller et al., 2011). However, meditation has been found to improve stress-related outcomes (Goyal et al., 2014). Meditation techniques include focused breathing exercises that help to directly regulate the cardiovascular system (Steinhubl et al., 2015), negative mood, stress, pain, anxiety, and mind wandering (Zeidan et al., 2010; Bhasin et al., 2013; Prinsloo et al., 2013; Brandmeyer and Delorme, 2016). Moreover, meditation practices were found to increase regional brain gray matter density (Hölzel et al., 2011). NF provides the possibility of endogenously manipulating brain activity as an independent variable, making it a powerful neuroscientific tool. NF training results in specific neural changes relevant to the trained brain circuit and the associated behavioral changes. These changes have been shown to last anywhere from hours to months after training and to correlate with changes in gray and white matter structure (Sitaram et al., 2017). Thus, by implementing meditation techniques, NF can help users become aware of their emotions or negative mind wandering (Brandmeyer and Delorme, 2013; Mooneyham and Schooler, 2013) that are associated with stress, and develop strategies to overcome them (Brandmeyer and Delorme, 2016), as well as slowing down the neurodegenerative process of neuronal structures (Hölzel et al., 2011). The demonstration of robust clinical effects remains a major hurdle in NF research. The results of randomized controlled trials in attention-deficit and hyperactivity disorder and stroke rehabilitation have been mixed, and have been affected by differences in study design, difficulty in identifying responders, and the scarcity of homogenous patient populations (Sitaram et al., 2017).

These benefits apply to cognition as well, as findings showed that NF increased memory, attention, and cognitive performance (Zoefel et al., 2011; Nan et al., 2012; Wang and Hsieh, 2013; Mishra and Gazzaley, 2015). Brainwave training provided by NF induces neuroplastic changes (Ros et al., 2010), suggesting important implications for therapies of brain disorders associated with abnormal cortical rhythms and supporting the use of NF as a noninvasive tool for establishing a causal link between rhythmic cortical activities and their functions. NF has been well investigated in the treatment of attention-deficit/hyperactivity disorder (ADHD) and has shown clinical efficacy (Gevensleben et al., 2009; Arns et al., 2014).

The sharp rise of computer processing capacity has solved many of the difficulties faced by the NF and

BCI pioneers of the 1970s (Dewan, 1967) and 1980s (Vidal, 1977). Some of the sophisticated software and hardware are now designed to process EEG data in real time (Hu et al., 2015), facilitating reliable NF and BCIs to consumers. Video games have been shown to be powerful NF companions. Research suggests that the combination of NF methods and video game interfaces significantly improves symptoms associated with conditions such as ADHD and anxiety (deBeus and Kaiser, 2011; Muñoz et al., 2015; Schoneveld et al., 2016; Perales and Amengual, 2017). In addition, some studies have combined NF, video games and VR to obtain more immersive results (Lécuyer et al., 2008). Musical NF paradigms are being developed as well, presenting an interesting alternative to other treatments by offering to users the ability to manipulate expressive parameters in music performances using their emotional state (Ramirez et al., 2015). However, these systems are now marketed to consumers as forms of cognitive enhancement and entertainment (Sandford, 2009) and may present potential dangers, as they do not involve professional supervision. Not only should appropriate methods be employed but more transparency in the algorithms that are being used by these private software companies must also be enforced so researchers can validate their use.

NF may also be coupled with other technologies to enhance its efficacy. The Neuroscape<sup>a</sup> center for translational neuroscience at the University of California, San Francisco has developed multiple games that implement NF, neuromodulation, and VR/AR such as the NeuroRacer, Meditrain, the Ace, or the Beep seeker to name a few. Neuroelectrics developed the Neurosurfer<sup>b</sup> software for advanced NF applications, offering for the first time the possibility of combining NF with brain stimulation (when combined with the Starstim device; Aguilar Domingo, 2015). Combined with VR, NF training may be used to enhance attention (Cho et al., 2002) and learning (Hubbard et al., 2017). In another experiment, a multimodal embodied interface was designed for 3D navigation as a modular wearable, with the user suspended in a harness that was directly controlled by the EEG activity of the user. This allows both physical and virtual displacement within an immersive virtual environment, allowing to simulate a flying experience (Perusquía-Hernández et al., 2016).

Heart rate variability (HRV) is the change in the time intervals between adjacent heartbeats that may be used to predict future health outcomes (Tsuji et al., 1994; Dekker et al., 1997; Shaffer et al., 2014). Reduced HRV has been shown to correlate with disease onset and mortality as it

reflects reduced regulatory capacity of the body to adaptively respond to challenges like exercise or stressors (Dekker et al., 1997; Beauchaine, 2001). Self-regulation techniques (Alabdulgader, 2012) were found to improve the cognitive function, the parasympathetic system, as well as a wide range of clinical outcomes (Lehrer et al., 2003; McCraty and Zayas, 2014). It can be enhanced by HRV feedback (McCraty et al., 2003), representing a therapeutic tool with a considerably reduced health care cost (Bedell and Kaszkin-Bettag, 2010). Several wearable headsets offer features that allow for the simultaneous recording of the heart rate, heart pressure, respiration, and EEG (see Table 16.1). By combining neural and physiologic measures, such as EEG and HRV (Steinhubl et al., 2015; Billeci et al., 2016), it is possible to develop NF paradigms aimed at improving measures related to anxiety, stress, emotions, cognition, and performance (Shaw et al., 2012; Thompson et al., 2013; Gruzelier et al., 2014). Given that some NF protocols are already considered a first line of treatment for children with ADHD (Gevensleben et al., 2009; Arns et al., 2014), new NF protocols may soon be available as treatment options for stress management and the associated physical outcomes.

## SLEEP

Poor sleep quality concerns one-third of the adult population (Roth et al., 2007) and has been linked to many clinical and medical conditions such as depression and pain (Giron et al., 2002), and has proven costly (i.e., lost productivity, health) for societies and individuals. The deleterious effects of chronic sleep deprivation and the associated outcomes have potentially dangerous and expensive consequences as a result of impaired neuropsychologic functions for individuals at work, at home, and on the roads (Pilcher and Huffcutt, 1996; Van Dongen et al., 2003). In addition, long-term health-related concerns include increased risk for metabolic and cardiovascular diseases (Cappuccio et al., 2011) as well as an overall decrease in immunity (Bryant et al., 2004). Research shows that 90% of the American population is using a technologic device (e.g., television, laptop, or smartphone) in the hour preceding sleep (Gradisar et al., 2013). Some wearable technologies developed in the last decades (e.g., wristbands, mobile apps, smart pillows) target monitoring of sleep quality, but do not focus on interventions supporting healthier sleep or making

<sup>a</sup><https://neuroscape.ucsf.edu/technology/>

<sup>b</sup><https://www.neuroelectrics.com/products/software/neurosurfer/>

use of sleep cognition (Ravichandran et al., 2017; Bianchi, 2018). While only a limited number of sleep studies have been conducted using wearable EEG systems (Berka et al., 2007a; Debellemaniere et al., 2018), recent advancements in neuroimaging research offer new ideas. These include the use of transcranial direct current stimulation (tDCS) in the gamma frequency band during rapid eye movement sleep to increase self-reflective awareness in dreams (Voss et al., 2014), the use of transcranial magnetic stimulation (TMS), and the use of pink noise to effectively manipulate sleep depth thereby increasing sleep efficiency (Suzuki et al., 1991; Massimini et al., 2009). Those findings could be implemented in BCI or NF applications with the help of wearable headsets such as the Starstim that allows simultaneous EEG and TCS (see Table 16.1). Some wearable EEG headbands that do not have electrodes behind the head and focus on frontal and temporoparietal brain activity offer the possibility to record EEG during sleep in the user's home environment (Onton et al., 2016; Debellemaniere et al., 2018, respectively). Although these studies are easy to perform with healthy individuals who are aware of the situation and make a conscious effort to limit their movements, it might prove more difficult for patients suffering from pathologic conditions such as AD (Abbate et al., 2014). Furthermore, some of these wearable neurotechnologies may allow for closed-loop auditory stimulation to modulate brain oscillations at the right moment by using a classification of sleep cycles (Chambon et al., 2018; Debellemaniere et al., 2018), enhancing sleep quality at night (Arnal et al., 2017). To go further, a team from MIT media labs developed the first sleep BCI, an interactive interface named "Dormio" (Haar Horowitz et al., 2018). When the user enters the hypnagogic sleep stage (associated with high creativity), EEG and motor signals detect it and trigger an auditory feedback response provided by a robot located next to the sleeping user. The sound makes the user more aware of being in that state and extends the duration of the semilucid hypnagogic period, enhancing his/her creativity. Semantics can be used instead of a sound to influence the dreams of the users. The most sophisticated wearable EEG systems, therefore, present a promising future for sleep research, management, and monitoring.

### BIOMEDICAL BCI

Modern BCI present a number of solutions for individuals with disabilities. Under certain circumstances, patients can regain partial if not all of the lost motor control if provided effective rehabilitation. Motor imagery-based BCI (Curran and Stokes, 2003) have been

used as a means of providing patients real-time visual feedback of limb movement (corresponding to the injured limb) through a representative simulation on a computer screen. BCI protocols host the potential to accelerate rehabilitation through repeated reactivation of the underlying neural pathways (Güneysu and Akin, 2013; Pfurtscheller et al., 2006; see Chapter 9). A difficult and frequent obstacle present in patient rehabilitation involves maintaining the necessary levels of motivation to remain persistent during repetitive and demanding physical tasks. NF and BCI rehabilitation paradigms may improve patients' sense of wellbeing and motivation by providing more entertaining and engaging interfaces (e.g., video games) as opposed to more traditional clinical/medical settings.

When rehabilitation is not possible, prosthetic control can still provide improved mobility assistance, and promising research on BCI-controlled wheelchair movements may soon be an option for patients with paralysis (Carlson and Millán, 2013; see Chapter 8). The complex control commands required for robotic prosthetic limbs or exoskeletons have evaded BCI scientists for the last few decades; however, recent systems have overcome several key limitations (McFarland et al., 2010). BCI patients are now capable of moving prostheses with increasing accuracy and flexibility (Clement et al., 2011), and prostheses have become more affordable (using 3D printing technology; Sullivan et al., 2017). An exciting new study developed a way to allow locked-in ALS patients (see Chapter 4) to remote control a humanoid robot using their EEG activity (Spataro et al., 2017). Their findings show that three out of four subjects were able to control the robot so that he could speak, move, and act for them. These technologies have tremendous potential for patients who are unable to engage with single-switch systems operated by movements such as eye blinks, or the breath (e.g., in late-stage ALS, high-level spinal cord injury, stroke/aphasia, autism, severe cerebral palsy; see Chapters 3–6). BCIs can also be used to facilitate linguistic communication, with the most renowned BCI paradigm being the P300 speller designed by Cipresso et al. (2012), Farwell and Donchin (1988), and Mellinger et al. (2004). Other BCIs allow the patients to navigate text, to control a cursor on a computer screen, browse forward and backward or use bookmarks (Kübler et al., 2005; Krusienski et al., 2007; Fruitet et al., 2010; Mugler et al., 2010). While only a limited number of studies have integrated fNIRS for BCI applications (Coyle et al., 2007; Aranyi et al., 2015) an increasing number of researchers are developing hybrid P300-based BCI interfaces via simultaneous fNIRS and EEG (Coyle et al., 2007; Pfurtscheller et al., 2010; Fazli et al., 2012; Liu et al., 2013; Blokland et al., 2014; Kaiser et al., 2014; Khan et al., 2014; Tomita et al., 2014; Yin et al., 2015;

Buccino et al., 2016). These studies show that simultaneous measurements of fNIRS and EEG can significantly improve accuracy of classification of brain signals, improve user performance, and may serve to be a viable multimodal imaging technique suitable for future BCI applications.

### REMOTE MONITORING AT HOME

BCI-based applications have now been effectively delivered in home-based settings (Askamp and van Putten, 2014; Käthner et al., 2017; Wolpaw et al., 2018), and have shed light on the potential for future clinical-based interventions. The “home-based” setting is key here as it can facilitate accessible and high-quality treatment options, reduce commute times, reduce the volume of consultations at clinics, increase the quality and quantity of patient information collected by healthcare professionals, and improve longitudinal measures of care quality. With increasing availability and integration of wearable EEG headsets, phone-based BCI applications have been developed to enable practical and affordable everyday use.

Neurophones are brain–mobile phone interfaces, which allow neural signals to drive mobile phone applications on the iPhone using wireless EEG headsets (Campbell et al., 2010; Wang et al., 2011; Kumar et al., 2012). Applications of NF devices in home-based settings could provide significant aid to patients with traumatic brain injuries, ADHD, and more, by improving motivation for engaging in treatment, as well as directly improving secondary symptoms through access to applications that train mindfulness and stress-reduction techniques (Gray, 2017). Advanced wearable EEG systems may help support the autonomy and independence of people with disabilities living at home, improve early detection of certain medical conditions, monitor sleep quality, and ultimately, provide large-scale longitudinal data on the effects of aging in the brain and body (Light et al., 2011). Companies specializing in mobile neurology diagnostic devices are developing potential solutions for epilepsy using mobile and continuous EEG recording, smart clothing, a smartphone application, and cloud platforms (Valenza et al., 2015). In the Netherlands, this type of home-based EEG applications are currently used in ~30% of hospitals for the treatment and monitoring of epileptic patients (Askamp and van Putten, 2014).

In a study by Valenza et al. (2015), they used wearable textile technology to characterize depressive states in bipolar patients during their normal daily activity. Some very advanced wearable neurotechnologies such as those developed by neuroelectrics could also be very valuable

for home-based use as they enable simultaneous EEG recording and brain stimulation (Dutta and Nitsche, 2013; Helfrich et al., 2016), which was found to improve neurorehabilitation effects by training motor function and learning processes (Gandiga et al., 2006). These technological advancements present valuable applications for many clinical conditions such as epilepsy, depression, or PD. The NUBE Cloud Service<sup>c</sup> from neuroelectrics provides a telemedicine platform, wherein clinicians and researchers can prepare general stimulation protocols, schedule the stimulation sessions for patients, confirm whether the sessions have been executed or not, and create pre-/poststimulation questionnaires. Clinicians can also remotely guide the stimulation sessions that patients can conduct by themselves from home. While Starstim is currently classified as an investigational device under US federal law, it is approved in Canada for medical use and complies with the European legislation for clinical research (e.g., depression, pain, addiction, stroke).

Another growing field is the development of Smart houses (Stefanov et al., 2004; Yin et al., 2015). Numerous intelligent devices, embedded into the home environment, can provide the resident with both movement assistance (e.g., intelligent bed, intelligent wheelchair, and robotic hoist for effortless transfer of the user between the bed and wheelchair), and 24-h health monitoring. They are therefore particularly relevant for elderly and disabled populations, as it helps restore independence and autonomy. However, these devices lack methods for decoding the intentions of disabled residents, which in the future may be solved through the integration of BCI and wearable headsets (Vaughan et al., 2006; Lee et al., 2013; Miralles et al., 2015).

## DISCUSSION

### Limits and possible solutions

While a majority of NF and BCI systems require a minimal level of experience and knowledge to effectively acquire quality data, misrepresentative findings and applications are always potential confounds to be taken into consideration when assessing the validity of scientific findings. Ensuring the proper application of wearable technologies is essential. Manuals and tutorials provided in the documentation are generally not sufficient to cover the complexities of measuring, analyzing, and interpreting physiologic data, let alone factoring in potential confounds and placebo effects that can interfere with the proper use of the technology. Furthermore, both structural (i.e., anatomical) and functional

<sup>c</sup><https://www.neuroelectrics.com/products/services/nube-stimulation/>



(i.e., brain activity) differences in brain activity have been observed across different categories of the population (e.g., children, the elderly, people with mental disorders) (Reiss et al., 1996; Schlaggar et al., 2002; Bjork et al., 2004; Paus, 2005). Moreover, no gold standard has been established regarding the choice of reference electrode(s), with the region of interest playing a key role when selecting the appropriate measures for obtaining good signal quality. Consequently, comparing different EEG systems remains a challenge. Future studies should aim to identify reference systems that could be standardized across protocols and headsets. In addition, the correct positioning of electrodes across the scalp is critical for applications involving neuromodulation, wherein cortical regions are selectively targeted and exert neuromodulatory effects (Villamar et al., 2013). Variability in electrode types, location, software, file formats, or interfaces constitute a barrier in attempting to combine big databases across a range of sources. The newly developed Research Resource Identifiers, such as SciCrunch,<sup>d</sup> may help resolve these issues, as they offer a platform, which enables straightforward searches of information pertaining to research studies implemented with specific types of technology, and contain user information about the device, signal quality, and the literature. Unlike more general search engines, they provide extensive access to a focused set of resources relevant to its communities and provide access to content that is traditionally “hidden” from web search engines. Users can also add their own data to the platform. Novel tools are actively being developed to help facilitate the recording and streaming of EEG data from consumer headsets that can be interfaced with a variety of programming languages and software packages, allowing for interchangeability across devices. The MuSAE lab is developing the MuSAE Lab EEG Server (MuLES<sup>e</sup>), an EEG acquisition and streaming server that aims to create a standard interface for portable EEG headsets to accelerate the development of BCI and of general EEG applications in novel contexts. Similarly, the Lab Streaming Layer (LSL<sup>f</sup>) from OpenBCI allows to synchronize streaming data for live analysis or recording via applications such as MATLAB. Successful, large studies could be conducted using these servers, with the open source data then available for future studies, limiting costs, and time spent collecting new data.

Another limitation regarding wearable devices pertains to the identification of event-related signal onset.

In laboratory settings, these triggers are produced by a controlled system or by the experimental paradigm whereas in real-life conditions these events can originate from the environment upon which the experimenter or developer has no control. While some companies provide features for markers and triggers that indicate the beginning and end of epochs in the data, several companies do not incorporate such features, making the analyses of data time consuming, a challenge when attempting to identify event-related activity. For studies comparing conditions across trials, it is crucial that these features are implemented in all wearable EEG devices. One solution (although not ideal) is the instruction for the subject to perform a small series of eye blinks at the beginning and end of each trial, as it is very easy to identify in the EEG signal. While this alternative is not sufficient for ERP type studies that require high temporal accuracy of the markers (i.e., in milliseconds), it highlights simple and novel methods that can be implemented for advancing wearable methodologies. While it is likely that significant challenges pertaining to the proper annotation of events that occur in real-life conditions will persist (i.e., the generators of such triggers), new and novel solutions are needed to address this critical shortcoming.

### The future of wearable neurotechnologies

A major limitation to the daily integration of wearables remains the feasibility of people feeling comfortable wearing such devices in public spaces. Abbate et al. (2014) showed that in a study with AD patients, a few simple modifications to the placement of the wearable EEG system, its color, and how it is integrated with clothing significantly improved its usability and acceptance, especially in the elderly population. While great improvements in design, weight, and comfort are under active development, wearable neurotechnologies will eventually need to diversify their designs to satisfy cultural differences, characteristics, and sensitivities. Furthermore, populations such as the elderly often prefer simple, loose, and comfortable clothing, making the necessary placement of tight fitting wearable devices close to the body difficult (Abbate et al., 2014). New technologies developed by companies that offer innovative solutions such as the production of smart clothing that incorporates biometric sensors embedded into the material (see section “Remote monitoring at home”;

<sup>d</sup><https://scicrunch.org/>

<sup>e</sup><http://musaelab.ca/news/mules-musae-lab-eeg-server-codes-up-on-github/>

<sup>f</sup><http://docs.openbci.com/3rd%20Party%20Software/04-LSL>

Valenza et al., 2015) are promising; however, more research will be necessary to establish and ensure high SNR as well as comfort to users.

Within the BCI domain, transparent EEG systems such as the “Ear-EEG” include both microelectrodes located in the ear canal (i.e., “in-ear EEG”) (Goverdovsky et al., 2016; Nakamura et al., 2017) as well as cEEGrids, a flex-printed C-shaped 10-channel grid that can be placed around the outer ear (Bleichner et al., 2015; Bleichner and Debener, 2017). The Ear-EEG is capable of extracting relevant focal temporal neural features such as the P300 ERP, presenting potential innovative solutions and applications for augmenting hearing technology (Fiedler et al., 2016; Christensen et al., 2018). Sensors are also being integrated into accessories such as smart glasses (Vahabzadeh et al., 2018), smart EEG-glasses (e.g., Jiang et al., 2017), stick-on electronic tattoos (Zheng et al., 2014), and chemical wearable sensors (Matzeu et al., 2015). Another feature necessary for the future of wearable neurotechnologies is the development of advanced machine-learning algorithms that monitor and correct artifacts in real time so that movement and muscular activities no longer interfere with the performance of BCI systems. To accomplish this, techniques must be developed that would allow for markers in the data, which would reflect the occurrence of uncontrolled events taking place in real-world environments, to build a better understanding of their impact on the brain and body activity. Given the rapid advancements in machine-learning techniques and analyses (see Chapter 23), in the not-so-far future we will most likely acquire a far more extensive knowledge and understanding of unknown EEG artifacts and the methods necessary to correct them (in real time) without losing the brain activity of interest (i.e., nonartifactual).

### Ethical and safety questions

The rapid advancements in the biomedical-tech sector present clear ethical questions such as consent, data protection, and identity (Trimper et al., 2014; see Chapter 25). At present, there is no legislation regulating informed consent and protecting personal data extracted via BCI, either therapeutically or outside clinical and research contexts. While the research and clinical use of BCIs across the world is regulated by national laws and Institutional Review Boards, the private and commercial use falls out of these legislations, allowing the potential for nonethical practices and applications of the technology. Furthermore, the noninvasive nature of these technologies, the ease of engineering the relevant hardware, and the enthusiastic “Do It Yourself” (DIY) culture interested in cognitive enhancement make exploring these ethical issues especially pressing.

Having observed the public outrage and opposition to previous scientific and technological advancements, such as was seen with the cloning of Dolly the sheep, ethicists, and scientists must work together to ensure that the technology is developed with the highest ethical standards and that the public is informed accordingly (Wolpe, 2006).

While it is safe to say that a majority of wearable technologies are designed under the premise of improving health monitoring and outcomes or enhancing or regulating cognitive and emotional processing, these technologies also host tremendous power and potential to drastically influence the choices and actions of the users (i.e., how to breathe, to eat, drink, exercise, work, sleep). The short-term reality is that the user is often under the illusion that the feedback provided is highly accurate, which can heavily influence the user’s way of life. This is seen heavily with companies claiming their device can “read the mind, thoughts or intentions” of the users. By offering consumers a way to simultaneously embrace and outsource the task of lifestyle management, one could imagine that such products both exemplify cultural ideals and short-circuit them for individual responsibility and self-regulation (Schüll, 2016). This concern is even greater with regard to the potential for electrical stimulation technologies (e.g., tDCS) becoming widely available to the public. Following the advice of commercial applications, wherein participants are instructed to actively modulate their brain with technologies such as tDCS without any validation or control, presents a major concern (Walsh, 2013). Ultimately, the companies depend on the engagement and participation of their customers, and thus it is the role of consumers to educate themselves and to exert the “consumer influence” over the quality and trajectory of future technologies.

As lifestyle, health, and technology become increasingly integrated and interfaced, it is crucial that these devices remain as tools to support and assist human needs. With an increasing rate of reliance on our technology, human beings are increasingly vulnerable to the potential dangers and pitfalls of this reliance. Furthermore, when something is used to enhance or assist a function, this function no longer needs to be accomplished by the body, further directing one’s attention toward additive systems (e.g., atrophied muscle after injury). This could potentially apply to the brain itself, given that too many cognitive functions were to be supported or replaced by technologies. On the other hand, it is also possible that the technological support could participate in training natural abilities beyond their initial potential (e.g., a system detecting normally imperceptible cues that warn of danger could train the brain to detect these stimuli). In addition, one can argue that the brain resources are no longer necessary because they are supplemented by technology that could be recruited for

new abilities (e.g., the invention of writing offered many new possibilities for human cognition). If this is possible, future studies should focus on how to develop technologies that aim to produce long-term benefits. For example, NF systems are used to help users train cognitive regulation (e.g., increased attention and improved emotion regulation).

Along with the development of new wearable technologies, concerns surrounding the potentially deleterious effects of radio frequencies (RF), cell phones (Pyrpasopoulou et al., 2004; Krause et al., 2006; Hung et al., 2007; Croft et al., 2010; Vecchio et al., 2010; Laudisi et al., 2012; Cassani et al., 2015; Mohan et al., 2016), bluetooth, and Wi-Fi frequencies (Balachandran et al., 2012; Banaceur et al., 2013; Mandalà et al., 2014; Sali et al., 2015; Othman et al., 2017) on the biologic systems also surface. Detrimental effects are generally considered to be dependent not only on the distance and relative size of a given object but also on the environmental parameters, and there may be additional interindividual differences in sensitivities to exposure, making the assessment of these risks difficult. However, research suggests that regular and long-term use of RF emitting devices (especially at close distance to the body) can have a negative impact on biologic systems, most notably on the brain (Ishak et al., 2011; Volkow et al., 2011; Avendaño et al., 2012; Megha et al., 2012, 2015; Atasoy et al., 2013; Kesari et al., 2013; Shahin et al., 2013). Wearable neurotechnologies concentrate RF energy from bluetooth and Wi-Fi in and around the area of the brain in larger amplitudes than has been studied previously. The potential for chronic exposure to RF frequencies resulting from daily BCI use demands that future studies explore solutions for RF protection or alternative deliverance modalities.

## CONCLUSION

Advancements in EEG wireless technology allow researchers and clinicians to study the brain easily, in natural environments, and with greater access to a wide range of the population (i.e., children, the elderly). While several new wireless devices enable the collection of data with both high temporal and spatial resolution (i.e., combined EEG and fNIRS, respectively), they also facilitate the simultaneous modulation of brain activity through the addition of stimulation sensors that administer TCS. At home use of wireless and wearable technologies has the potential to significantly reduce medical costs for both patients and medical centers in terms of both diagnosis and long-term treatment options. Online platforms now enable clinicians to arrange medical assessments and treatment interventions, such as EEG recordings or TCS therapeutic sessions for patients (e.g., epileptic or disabled patients) without ever

having to leave the comfort of their home. Advanced wearable neurotechnologies, such as the ones listed in Table 16.1, show recent improvements in terms of signal quality, sampling rate capacity, battery life, affordability, setup speed, implementation of manual triggers in the signal, data storage, comfort, and design. However, caution must be exercised when using these devices as they still encounter limits such as their sensitivity to movements, limited number of electrodes and their locations (i.e., limiting the variety of cognitive processes that can be studied), the lack of control regarding events occurring in the environment (when used in real-life settings), and the validity and reliability of the software- and phone-based applications that claim to train certain neural features but fail to provide transparency as to how they are designed (which are mainly due to proprietary reasons). We therefore suggest that these technologies are used primarily by informed and educated users for raw data acquisitions in nonordinary situations (e.g., real-life environments) and in a controlled manner. These technologies hold great potential for the home use of BCI and NF therapies by using simple and robust EEG features such as ERPs, frontal  $\theta$ , sensorimotor  $\mu$ , and occipital  $\alpha$  that have been accurately measured by advanced wearable EEG systems. With time, widely accessible wearable EEG technology and large-scale data collection will inevitably lead to an increased understanding of the brain and our abilities to interface with technology. By allowing patients to move, communicate, and create, these technologies aid not only in rehabilitation but also hold promise in aiding an individual's ability to regain a sense of wellbeing, autonomy, and independence. These technologies also present applications to the healthy population such as entertainment, art, education, and cognitive enhancement.

Major advancements in the technological sector combined with advanced data processing are bound to lead to an exciting and unpredictable future for wearable technologies. While these technological advancements host the potential for significantly improving the monitoring of one's health and in rehabilitation, mindful measures need to be taken to direct the evolution of wearable neurotechnologies toward positive applications serving the general interests of the public ethically.

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# Validating the wearable MUSE headset for EEG spectral analysis and Frontal Alpha Asymmetry\*

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Cédric Cannard

The Brain and Cognition Research  
Center (CerCo), CNRS, Paul Sabatier  
University, Toulouse, France

Institute of Noetic Sciences (IONS),  
Petaluma, USA

[ccannard@protonmail.com](mailto:ccannard@protonmail.com)

orcid: 0000-0002-6125-1175

Helané Wahbeh

Institute of Noetic Sciences (IONS),  
Petaluma, USA

[hwahbeh@noetic.org](mailto:hwahbeh@noetic.org)

orcid: 0000-0003-3650-4633

Arnaud Delorme

The Brain and Cognition Research  
Center (CerCo), CNRS, Paul Sabatier  
University, Toulouse, France

Swartz Center of Computational  
Neuroscience (SCCN), INC, UCSD, La  
Jolla, USA

Institute of Noetic Sciences (IONS),  
Petaluma, USA

[arnodelorme@gmail.com](mailto:arnodelorme@gmail.com)

orcid: 0000-0002-0799-3557

**Abstract**— EEG power spectral density (PSD), the individual alpha frequency (IAF) and the frontal alpha asymmetry (FAA) are all EEG spectral measures that have been widely used to evaluate cognitive and attentional processes in experimental and clinical settings, and that can be used for real-world applications (e.g., remote EEG monitoring, brain-computer interfaces, neurofeedback, neuromodulation, etc.). Potential applications remain limited by the high cost, low mobility, and long preparation times associated with high-density EEG recording systems. Low-density wearable systems address these issues and can increase access to larger and diversified samples. The present study tested whether a low-cost, 4-channel wearable EEG system (the MUSE) could be used to quickly measure continuous EEG data, yielding similar frequency components compared to a research-grade EEG system (the 64-channel BIOSEMI Active Two). MUSE data can be live-streamed using the Lab Stream Layer (LSL), and can therefore be implemented into real-world EEG monitoring, brain-computer interfaces (BCI), or neurofeedback applications. We compare the spectral measures from MUSE EEG data referenced to mastoids to those from BIOSEMI EEG data with two different references for validation (mastoids and average reference). A minimal amount of data was deliberately collected to test the feasibility for real-world applications (EEG setup and data collection being completed in under 5 min). We show that the MUSE can be used to examine power spectral density (PSD) in all frequency bands, the individual alpha frequency (IAF), and frontal alpha asymmetry (FAA). Furthermore, we observed satisfying internal consistency reliability in alpha power and asymmetry measures recorded with the MUSE. However, estimating asymmetry on the IAF did not yield significant advantages relative to the traditional method (average over the 8-13 Hz range). These findings should advance human neurophysiological monitoring using easily accessible wearable neurotechnologies in large samples and increase the feasibility of their implementation in real-world settings.

**Keywords**— wearable EEG, power spectral density (PSD), frequency domain, signal validation, frontal alpha asymmetry (FAA), individual alpha frequency (IAF).

## I. INTRODUCTION

The MUSE (InterAxon Inc.) is a low-cost, off-the-shelf, wearable EEG headset that has two frontal and two temporoparietal (TP) dry active EEG channels. It has been validated for event-related potential (ERP) research (i.e., time domain; [1]) and used in many recent studies [2]–[12]. The open-source Lab Streaming Layer (LSL) and MuSAE Lab EEG Server (MuLES) are acquisition and streaming servers that can be used to collect MUSE signals in real-time, facilitating its use for research, real-world EEG monitoring, brain-computer interfaces (BCI), or neurofeedback applications [13]. However, to our knowledge, the MUSE has not yet been validated for frequency domain analysis (i.e., power spectra on continuous EEG data), with one study showing mixed results [14]. In addition to assessing the validation of MUSE spectral measures, it is relevant to test if the MUSE could be used to estimate clinically- and research-relevant spectral measures, such as the frontal alpha asymmetry (FAA) and the individual alpha frequency (IAF).

Frontal alpha asymmetry (FAA; or frontal EEG asymmetry) refers to the relative difference in log alpha power (average over the 8-13 Hz range) between the right and the left frontal regions. This spectral measure has been widely used to evaluate participants' cognitive, emotional, and attentional processes, both as an event-related state response and as a trait during rest [15]–[20]. Because of the inhibitory role of alpha oscillations [21]–[24], relatively greater right than left alpha power is associated with relatively greater left than right cortical activity (inverse correlation). In turn, greater activation of the left frontal region relative to the right is related to approach motivation and emotions with positive valence (e.g., happiness, positive urgency), whereas the reverse is associated with brain processes underlying avoidance motivation and negative emotional valence (e.g., depression, anxiety, withdrawal). FAA is suspected to reflect neural processes of the executive control systems and has been source-localized to the frontoparietal network [20].

The individual alpha frequency (IAF) refers to the frequency within the alpha band with dominant spectral power [25]. It is associated with cognitive performance [26], considered a

trait-like characteristic of human EEG [27], has high heritability and test-retest reliability [28], [29], and better accounts for interindividual differences in alpha activity [25], [30]. It has been traditionally examined using the peak alpha frequency (PAF) approach, which takes the frequency with the highest alpha power within the alpha band [31]–[33]. However, it has been highlighted that this approach does not perform well in a large portion of the population (up to 44%) that displays absent, ambiguous, or “split” alpha peaks [25], [34]. The alpha center of gravity (CoG) is considered a more robust approach to calculate the IAF by considering the whole alpha power distribution [25].

The IAF may be used to estimate FAA. Since alpha power distribution can fall outside the traditional predefined range (8-13 Hz) for some individuals [33], asymmetry scores based on the IAF (instead of the traditional band) might better address interindividual differences and might therefore provide more accurate asymmetry indexes method for research and clinical applications [35], [36].

IAFs and FAA seem like promising candidate measures for wearable EEG systems, as they require simple calculations in the frequency domain and a few EEG channels covering the frontal regions of each hemisphere. While the acquisition of these measures has not been validated using low-cost wearable systems against research-grade ones, such systems have been used extensively over the past few years to measure FAA, suggesting this measure is well-suited for these technologies [2], [37]–[46]. Wearable systems, when reliable, can offer advantages for researchers through easeful EEG data collection over large samples, increased access to populations that are hard to study with conventional systems (e.g., children, elderly, patients), reduced hardware and software costs, and facilitated EEG research in real-world environments by increasing subjects’ mobility and streaming the data wirelessly [47].

However, there is still a lack of validation of the data collected by such devices and whether the obtained findings can be interpreted based on literature built on conventional systems that use different montages and referencing methods (and may therefore represent different spatial distributions ad sources). The reference method implemented for low-density wearable systems is of particular importance when measuring EEG asymmetry [48], [49]. Both IAF and FAA are promising EEG measures for neurofeedback applications [36], [50], which would benefit from mobile data collection.

The present study tested whether the 4-channel wearable MUSE EEG system can quickly measure continuous EEG data with a maximum of 5-minute setup and data collection time, which would yield quantifiable and clinically-relevant frequency components comparable to research-grade systems.

## II. METHODS

### A. Participants

Participants for this study were 40 English-speaking adults in the San Francisco Bay area. Exclusion criteria were: aged younger than 18 years old, unable to read, having an acute or chronic illness that interfered with the completion of the experiment, or being unable to sit on a chair for about 30

minutes. Participants had their EEG recorded with a 64-channel EEG system at the laboratory for another study (~2h session) and were asked if they wanted to volunteer a few more minutes of their time for an additional ~5 minutes EEG recording using the wearable headset. They were compensated only for their participation in the initial study. They gave informed consent, and the study was approved by the IONS Institutional Review Board.

### B. EEG data collection procedures

EEG data were collected with the active dry MUSE 1 (version 2016) at 256 Hz and a 64-channel gel-based BIOSEMI Active 2 system (BIOSEMI Inc.) at 512 Hz. Simultaneous recording of both systems was not possible due to their configurations. The MUSE data were recorded first, and then the BIOSEMI data about 30 minutes later, which corresponded to the time necessary to set up the equipment and optimize channel impedance. A comparison of the two systems’ hardware specifications can be found in Table 1. For both systems, the participants’ skin was cleaned with alcohol wipes at electrode sites before positioning the headband/head cap.

TABLE I. HARDWARE SPECIFICATIONS OF EACH SYSTEM

	Biosemi Active Two	InteraXon MUSE
<b>Electrode montage</b>	64 wet active electrodes (10-20 system)	4 dry active electrodes (AF7, AF8, TP9, TP10) <sup>b</sup>
<b>Sampling rate</b>	512 Hz	256 Hz
<b>Resolution</b>	24 bits	12 bits
<b>Active electrode system</b>	Passive DRL and active CMS located around POz	Passive DRL and active CMS located at Fpz
<b>Head sizes</b>	3 different head cap sizes covering 54-62 cm	Adjustable headband, 52-60 cm range
<b>Recording apparatus</b>	Optic fiber and amplifier, MacBook Pro, Actiview Software	Bluetooth on a low-cost Chromebook, Mind Monitor App
<b>Reference</b>	Reference-free <sup>a</sup>	Fpz

<sup>a</sup> Data is reference-free at data collection time. A reference must be chosen when importing the data. Not choosing a reference led to a 40 dB loss of signal-to-noise (SNR) ratio.

<sup>b</sup> Approximate positions.

*MUSE* - A thin layer of water was applied to the dry electrodes with a sponge for both the frontal metallic sensor and the conductive silicone rubber mastoid sensors behind the ears to decrease the impedance and increase signal quality. The MindMonitor App [51] running on a Chromebook laptop was used to record the EEG signal and check electrode contact (a colored circle for each electrode was filled when the software deemed the connection acceptable). Visual examination of the raw EEG waveforms was also performed while participants were asked to generate eye blinks to provide an additional index of signal quality. The headset position was adjusted if the signal was judged too noisy by visual inspection of the data.

*BIOSEMI* - Highly conductive electrolytes SignaGel was injected into the electrode sites of the BIOSEMI head cap. BIOSEMI active electrode offsets were kept below offset 20 using the Actiview software.

*MUSE and BIOSEMI* - Recordings were performed at the same location within the recording room, minimizing the differences in terms of potential electrical artifacts from the environment. One minute of data was recorded with eyes closed. Participants were instructed to sit still on a chair, limit their movements, and focus their attention on their breath by counting each inhalation/exhalation cycle.

### C. EEG data preprocessing

BIOSEMI data were imported into the EEGLAB processing software (v2021.1; [52]) using the BIOSIG plugin (v3.7.5). MUSE data were imported using the MUSEMonitor (v3.2) plugin of EEGLAB. BIOSEMI data were downsampled to 256 Hz. Raw data were high-pass filtered with EEGLAB's linear non-causal Finite Impulse Response (FIR) filter of the FIRFILT (v2.4) plugin (filter order = 1129; transition bandwidth = 0.75 Hz; passband edge = 0.75 Hz; -6 dB cutoff frequency = 0.375 Hz). No low-pass filter was used.

Files were inspected visually for abnormal channels (bad connection, impedance, very high noise, flat sections from disconnections, etc.) and artifactual segments (eye and muscle artifacts, high-frequency bursts, etc.). Artifactual regions and channels were manually rejected. MUSE data files with at least 1 visually abnormal channel were removed. If the BIOSEMI or the MUSE file was shorter than 45 s, the participant data were also excluded from further analysis. Using these criteria, three out of 40 data files were excluded.

The traditional method to compute frontal alpha asymmetry (FAA) is to subtract the mean log-transformed alpha power of the left channel (generally F7) from the right one (generally F8) on 64-channel EEG data [48], [49]. While average-referencing was shown to be preferable to estimate FAA [48], it is not meaningful with 4 electrodes since it requires a whole-head electrode coverage. The default reference channel for the MUSE is Fpz which is close to the frontal channels AF7 and AF8 and may lead to different spectral and asymmetry estimates than those obtained on conventional montages. Thus, the MUSE frontal channels (AF7 and AF8) were re-referenced to the TP9/TP10 mastoid electrodes (the two other channels available on the MUSE), termed in this study the “*mastoid-ref montage*”. This reference method has been widely used in the asymmetry literature (e.g., [48], [53]). Spectral estimates from BIOSEMI data were calculated on: 1) AF7-AF8 re-referenced to mastoids (to match the MUSE montage, i.e., “*mastoid-ref montage*”); and on 2) F7-F8 referenced to the average prior removal of the additional 62 channels (called “*average-ref montage*”, corresponding to the preferred montage for FAA analysis).

To assess if spectral measures obtained with the MUSE *mastoid-ref montage* are reliable and interpretable in terms of underlying neural activity, we tested whether they were comparable to those obtained with the BIOSEMI *mastoid-ref montage* (same montage) and the BIOSEMI *average-ref montage* (traditional montage).

### D. Power spectral density (PSD)

Power spectral density (PSD) was computed using the *pwelch* function in MATLAB 2021a (The MathWorks Inc., MA, United States) for each EEG channel on 4-second hamming

windows, with 50% overlap and 200% padding (taking into account data discontinuity due to excluded artifactual regions). PSD data were then converted to decibels ( $10 \cdot \log_{10}(\text{power})$ ) [49]. Mean PSD was extracted for each frontal channel for each frequency band: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (>30 Hz). Then, the average between the two channels was used for analyses.

### E. Individual alpha frequency (IAF)

Both the peak alpha frequency (PAF) and the alpha center of gravity (CoG) were estimated using the open-source and automated *restingIAF* toolbox (v1.0.2; [25]). This method uses curve-fitting algorithms, zero-crossing, and Savitzky-Golay Filter (SGF) smoothing techniques (same parameters as above for PSD estimation, a minimum of 1 required channel to estimate PAF and CoG, and the default values for the other parameters).

### F. Frontal alpha asymmetry

Three methods were used to calculate alpha asymmetry:

- *Traditional method*: the difference between the frontal channels on alpha power (in dB) averaged over the 8-13 Hz band ( $\text{mean\_alpha\_right} - \text{mean\_alpha\_left}$ ).
- *PAF-asymmetry*. Same as above but on power at the peak alpha frequency (PAF).
- *CoG-asymmetry*. Same as above but on power at the alpha center of gravity (CoG).

### G. Internal consistency reliability

Previous research showed that reliable asymmetry values could be obtained with as little as 80 seconds of data [54]. To confirm internal consistency reliability of the asymmetry measures with the different montage methods and with very short segments of data (45 seconds for the shortest file after data cleaning), mean alpha power and FAA (traditional method only) were also computed for each montage on eleven 4-s blocks of data (mean for each block). Internal consistency reliability of alpha PSD and FAA was evaluated using Cronbach's standardized alpha on the blocks of spectral data [55], [56]. Values  $>.8$  indicate high internal consistency reliability and  $<.3$  indicate low internal consistency reliability; [54].

### H. Statistics

All spectral measures were compared using the skipped Pearson correlation from the open-source Robust Correlation MATLAB toolbox [57]. Skipped Pearson correlations detect and remove bivariate outliers using the minimum covariance determinant (MCD) estimator, and better control for the type I error by accounting for their deletion when testing for significance, and by using bootstrapped 95% confidence intervals (CI; [57]–[59]). If the CI encompasses 0, then the null hypothesis ( $H_0$ ) of independence cannot be rejected. This approach is less sensitive to heteroscedasticity (i.e., change in the spread of the residuals over the range of measured values leading to biased results) and therefore, more robust against the type I error [57], [58]. Rejections of  $H_0$  at the 95% confidence level (i.e., significant correlations) are reported next to the skipped Pearson correlation  $r$  coefficient scores with \* (i.e.,  $p < 0.05$ ). Bivariate outliers correspond to the red observations in the plots. The red line

corresponds to the least square fit line, and the red shaded areas correspond to the 95% CI.

### III. RESULTS

#### A. Internal consistency reliability

The following Cronbach's alpha scores were obtained for frontal alpha power (.98 - BIOSEMI *average-ref montage*; .95 - MUSE *mastoid-ref montage*) and frontal alpha asymmetry (.67 - BIOSEMI *average-ref montage*; .76 - MUSE *mastoid-ref montage*).

#### B. Power spectral density (PSD) for each frequency band

The averaged PSD of each frequency band was first compared between the BIOSEMI *mastoid-ref montage* and the MUSE *mastoid-ref montage*. All frequency bands were significantly correlated between the two montages: delta (1-3 Hz,  $r = .59^*$ , CI [0.38, 0.75]), theta (3-7 Hz,  $r = .73^*$ , CI [0.55, 0.85]), alpha (8-13 Hz,  $r = .87^*$ , CI [0.77, 0.93]), beta (14-30 Hz,  $r = .84^*$ , CI [0.70, 0.91]), and gamma (>30 Hz,  $r = 0.48^*$ , CI [0.19, 0.69]). These results are plotted in Fig. 1.

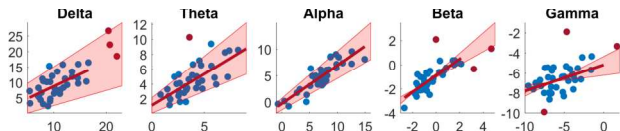


Fig. 1. Correlations between BIOSEMI (*mastoid-ref montage*) and MUSE (*mastoid-ref montage*) of mean power spectral density (PSD) for each frequency band: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (> 30 Hz). All frequency bands were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Pearson correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals. The power spectral density (PSD) unit is deciBels ( $10^* \log_{10}(\mu V^2/Hz)$ ).

Correlations between PSD estimates from MUSE *mastoid-ref montage* and those from BIOSEMI *average-ref montage* are reported in Fig. 2. Significant correlations were observed for the delta ( $r = .47^*$ , CI [0.19, 0.69]), the theta ( $r = .63^*$ , CI [0.43, 0.78]), the alpha ( $r = .80^*$ , CI [0.65, 0.90]), and the beta ( $r = .74^*$ , CI [0.58, 0.86]) bands. However, the correlation was not significant for the gamma band ( $r = .17$ , CI [-0.13, 0.50]).

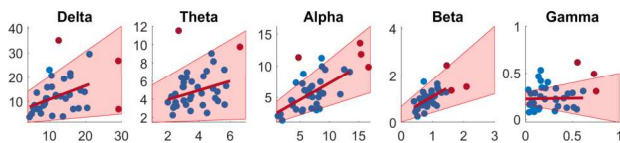


Fig. 2. Correlations between BIOSEMI (*average-ref montage*) and MUSE (*mastoid-ref montage*) of mean power spectral density (PSD) for each frequency band: delta (1-3 Hz), theta (3-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), and gamma (> 30 Hz). All frequency bands except gamma were significantly correlated. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Pearson correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals. The power spectral density (PSD) unit is deciBels ( $10^* \log_{10}(\mu V^2/Hz)$ ).

#### C. Individual alpha frequency (IAF)

IAFs estimated on BIOSEMI *mastoid-ref montage* were significantly correlated with those obtained on MUSE *mastoid-ref montage* (Fig. 3, left), for both PAF ( $r = .91^*$ , CI

[0.79, 0.97]) and CoG ( $r = .78^*$ , CI [0.64, 0.88]). However, PAF could not be estimated on 7 BIOSEMI files and 13 MUSE files. CoG could not be estimated on 5 BIOSEMI files and 4 MUSE files.

Correlations between IAF for the BIOSEMI *average-ref montage* and the MUSE *mastoid-ref montage* (Fig. 3, right) were also significant for both estimation methods: PAF ( $r = .95^*$ , CI [0.86, 0.98]) and CoG ( $r = .84^*$ , CI [0.69, 0.93]). However, the automated algorithms could not detect the PAF for 11 BIOSEMI files and 13 MUSE files, and the CoG for 6 5 BIOSEMI files and 4 MUSE files.

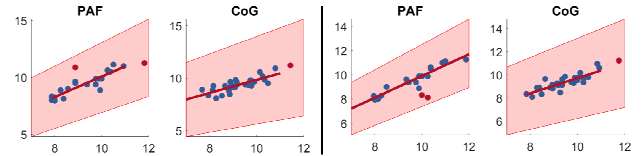


Fig. 3. Left: Correlations between BIOSEMI (*mastoid-ref montage*) and MUSE (*mastoid-ref montage*) of individual alpha frequency (IAF). Right: between BIOSEMI (*average-ref montage*) and MUSE (*mastoid-ref montage*). All estimates using both the peak alpha frequency (PAF) and the alpha center of gravity (CoG) were significantly correlated between the two systems and montages. Statistics are reported in the text of the Results section. Red dots are bivariate outliers accounted for by the skipped Pearson correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals. The power spectral density (PSD) unit is deciBels ( $10^* \log_{10}(\mu V^2/Hz)$ ).

#### D. Frontal alpha asymmetry (FAA)

The three methods to compute FAA were significantly correlated between BIOSEMI and MUSE with the same *mastoid-ref montage*: traditional asymmetry ( $r = .67^*$ , CI [0.40, 0.93]), PAF-asymmetry ( $r = .35^*$ , CI [0.7, 0.62]), CoG-asymmetry ( $r = 0.42^*$ , CI [0.05, 0.69]). These results are plotted in Fig. 4.

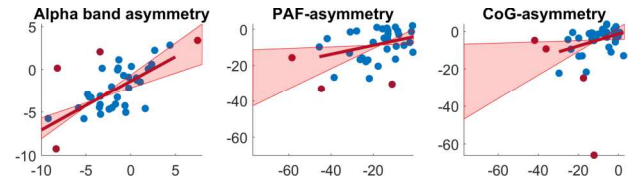


Fig. 4. Comparison of frontal alpha asymmetry measures from BIOSEMI *mastoid-ref montage* and MUSE *mastoid-ref montage*. The three forms of frontal alpha asymmetry were significantly correlated between the two systems. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Pearson correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals. The power spectral density (PSD) unit is deciBels ( $10^* \log_{10}(\mu V^2/Hz)$ ).

Finally, FAA measures were compared between the BIOSEMI *average-ref montage* and the MUSE *mastoid-ref montage* and are plotted in Fig. 5. FAA calculated on the average power over the whole alpha band (i.e., traditional method) was significantly correlated ( $r = .37^*$ , CI [0.06, 0.60]). However, asymmetry scores calculated on power at the PAF ( $r = .12$ , CI [-0.24, 0.44]) and at the CoG ( $r = .26$ , CI [-0.02, 0.55]) were not significantly correlated.



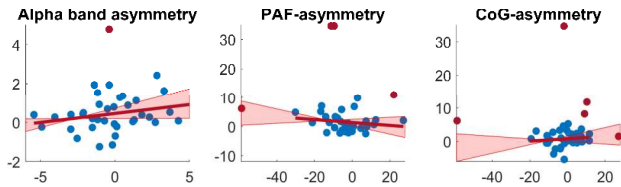


Fig. 5. Comparison of frontal alpha asymmetry measures from BIOSEMI average-ref montage and MUSE mastoid-ref montage. Alpha asymmetry calculated using the traditional method (on average power over the whole alpha band) was significantly correlated between the two systems. However, asymmetry scores calculated on the PAF and CoG power were not significantly correlated. Statistics are reported in the text. Red dots are bivariate outliers accounted for by the skipped Pearson correlations. The red line is the least-squares fit line. Shaded areas are the 95% confidence intervals. The power spectral density (PSD) unit is deciBels ( $10 \cdot \log_{10}(\mu V^2/Hz)$ ).

#### IV. DISCUSSION

##### A. Results and interpretations

When comparing MUSE *mastoid-ref montage* with BIOSEMI *mastoid-ref montage*, all spectral measures significantly correlated, indicating that this low-cost wearable EEG system can accurately capture these frequency components and that interpretations can be made in line with the literature using *mastoid-ref montages* (e.g., [53]). However, correlation coefficients and CIs indicate that the traditional method to calculate frontal alpha asymmetry is recommended compared to the PAF- and CoG- asymmetry methods.

When comparing MUSE *mastoid-ref montage* with BIOSEMI *average-ref montage*, PSD (in all frequencies below 30 Hz), IAF, and FAA (traditional method) were significantly correlated, indicating that the MUSE can be used to examine these measures and interpret the findings in line with the literature using the *average-ref montages* (i.e., F7 and F8 sites referenced to average). However, PAF- and CoG- asymmetry measures were not significantly correlated.

These latter findings may suggest that:

1. The automated toolbox used for IAF-estimation does not perform well on low-density sparse montages and is better suited for higher density montages (since it can use neighboring channels to improve detection performance; [25]). Channels referenced to average may have contained alpha spectral components from other channels that were not captured by the *mastoid-ref montage*. IAF measures (PAF and CoG) could not be estimated for some files, which could have reduced statistical power compared to the traditional measures. However, the superior performance of the CoG method compared to the PAF method was apparent since it was able to find the IAF in more participants.
2. The traditional asymmetry method is more robust and grounded in theory (independently of the montage). Previous research suggested that EEG asymmetry is influenced by different neural processes between the lower and the upper frequencies of the alpha band [33]. Thus, while IAFs better account for interindividual differences and are associated with some cognitive processes (e.g., memory), they might reflect different underlying neural processes than those underlying alpha asymmetry (e.g., executive control, attention, emotion

regulation). Thus, IAF-asymmetries might not be well-suited for asymmetry calculation.

##### B. Limitations

The first limitation of this study is the 30-minute difference between the two recordings. Mental states may likely have changed between the two recordings. However, correlations were still significant when comparing the MUSE and the BIOSEMI (except for gamma and IAF-asymmetries when compared to BIOSEMI *averaged-ref montage*), suggesting the main trait spectral components were still captured. Ideally, both types of data should have been recorded simultaneously using markers to synchronize the data at the millisecond resolution. While this was not possible for this study, future studies should aim to record both systems simultaneously.

Second, FAA during rest was previously estimated to vary ~60% from trait influence and 40% from state influences [60], the former being the target measure in this study. While internal consistency reliability of asymmetry measures was relatively high, more variation and lower values were observed compared to alpha power (as in previous publications; [54]). Increasing the data length (e.g., 3 minutes of artifact-free data) might increase the trait influence by reducing the fluctuations due to state influences, and in turn, increase internal consistency reliability. We purposely used short segments to determine if they could be easily and reliably used in experimental and clinical conditions, but we did not compare different data lengths and their impact on these EEG measures. Future studies should compare asymmetry measures from a clinical system and a low-cost wearable system (as in this study) with longer data lengths to address this potential limitation.

The absence of correlation in the higher frequencies (PSD > 30 Hz) when comparing MUSE with BIOSEMI *average-ref montage* but not *mastoid-ref montage* may suggest that these frequencies may reflect field potentials from other brain processes when referenced to average than those captured with the *mastoid-ref montage*. Thus, these frequencies should only be interpreted in the *mastoid-ref montage* context when using this system.

##### C. Recommendations for research and clinical MUSE recordings

Recommendations for using the MUSE in future clinical and experimental research are as follows:

- Eyes closed recordings of at least 1-minute corresponding to a total preparation and recording time of about 3 minutes (although longer segments should further increase the trait variable and internal consistency reliability).
- Cleaning the participants' skin with alcohol wipes and wetting the dry electrodes to reduce impedance (this is a general recommendation since we did not quantify the benefits here).
- Re-referencing the frontal channels to linked mastoid electrodes (i.e., TP9/TP10).
- Using measures found to be reliable with this system: PSD < 30 Hz, traditional FAA, and the IAF (in particular the CoG).

## V. CONCLUSION

Our study validates the use of the low-cost MUSE headset for accurately and reliably measuring PSD, IAFs, and FAA (calculated on the whole band). This system can help advance human neurophysiological monitoring techniques on large datasets using wearable neurotechnologies and increase the feasibility of their implementation into real-world applications.

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# Electroencephalography Correlates of Well-Being Using a Low-Cost Wearable System

Cédric Cannard<sup>1,2\*</sup>, Helané Wahbeh<sup>2</sup> and Arnaud Delorme<sup>1,2,3</sup>

<sup>1</sup> Centre de Recherche Cerveau et Cognition (CerCo), Centre National de la Recherche Scientifique (CNRS), Paul Sabatier University, Toulouse, France, <sup>2</sup> Institute of Noetic Sciences (IONS), Petaluma, CA, United States, <sup>3</sup> Swartz Center for Computational Neuroscience (SCCN), Institute of Neural Computation (INC), University of California, San Diego, San Diego, CA, United States

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### \*Correspondence:

Cédric Cannard  
ccannard@protonmail.com

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Electroencephalography (EEG) alpha asymmetry is thought to reflect crucial brain processes underlying executive control, motivation, and affect. It has been widely used in psychopathology and, more recently, in novel neuromodulation studies. However, inconsistencies remain in the field due to the lack of consensus in methodological approaches employed and the recurrent use of small samples. Wearable technologies ease the collection of large and diversified EEG datasets that better reflect the general population, allow longitudinal monitoring of individuals, and facilitate real-world experience sampling. We tested the feasibility of using a low-cost wearable headset to collect a relatively large EEG database ( $N = 230$ , 22–80 years old, 64.3% female), and an open-source automatic method to preprocess it. We then examined associations between well-being levels and the alpha center of gravity (CoG) as well as trait EEG asymmetries, in the frontal and temporoparietal (TP) areas. Robust linear regression models did not reveal an association between well-being and alpha (8–13 Hz) asymmetry in the frontal regions, nor with the CoG. However, well-being was associated with alpha asymmetry in the TP areas (i.e., corresponding to relatively less left than right TP cortical activity as well-being levels increased). This effect was driven by oscillatory activity in lower alpha frequencies (8–10.5 Hz), reinforcing the importance of dissociating sub-components of the alpha band when investigating alpha asymmetries. Age was correlated with both well-being and alpha asymmetry scores, but gender was not. Finally, EEG asymmetries in the other frequency bands were not associated with well-being, supporting the specific role of alpha asymmetries with the brain mechanisms underlying well-being levels. Interpretations, limitations, and recommendations for future studies are discussed. This paper presents novel methodological, experimental, and theoretical findings that help advance human neurophysiological monitoring techniques using wearable neurotechnologies and increase the feasibility of their implementation into real-world applications.

**Keywords:** wearable EEG, alpha asymmetry, frontal, temporoparietal, executive control, well-being, large sample analysis



## INTRODUCTION

### Well-Being

The question of what determines well-being has intrigued humans throughout recorded history and to this day remains a topic of significant interest and debate (Dodge et al., 2012; Alexandrova, 2015). The hedonic view of well-being focuses on the emotional dimension (i.e., positive and negative affect) to address this question. The eudaimonic perspective focuses on the sense of striving toward realizing one's potential or goals, a life purpose, and seeking personal growth (Ryan et al., 2008). Well-being is now understood as a multidimensional and dynamic construct encompassing both views and other new essential components such as mental and physical health, autonomy, social relationships, spirituality, self-acceptance (Keyes and Waterman, 2003; Ryff and Singer, 2013). Well-being can be mediated by numerous factors such as demographics (Keyes and Waterman, 2003; Carstensen et al., 2011), genetic predisposition (Keyes et al., 2010), personality traits (Lucas and Diener, 2008), income (Luhmann et al., 2011), exercise (Hassmén et al., 2000; Svensson et al., 2021), mindfulness meditation practice (Carmody and Baer, 2008), or connectedness with nature (Howell et al., 2011; Russell et al., 2013). These factors also shape the structure and function of our brains throughout the lifespan, with important implications for well-being levels. While progress has been made recently regarding our understanding of the relationships between well-being and the brain, much is still unknown (Dolcos et al., 2018). By identifying the neural correlates of well-being, we may better understand the mechanisms that underly higher levels of well-being, and in turn, develop promising interventions aiming at helping people live happier and more successful lives (Dolcos et al., 2018).

### Frontal Electroencephalographic Asymmetry

#### Definition and Calculation

For decades, frontal electroencephalographic (EEG) asymmetry has been a useful tool to study emotion-related states and traits, motivation, temperament, cognitive control, and psychopathologies (Coan and Allen, 2003, 2004; Allen et al., 2004; Harmon-Jones et al., 2010; Scherer and Ekman, 2014; Allen and Reznik, 2015; Smith et al., 2017). Frontal EEG asymmetry refers to a relative difference in alpha power spectral activity (8–13 Hz) between the left and right frontal regions of the brain. Because alpha oscillations are known to functionally inhibit regional cortical activity (Laufs et al., 2003, 2006; Oakes, 2004; Mathewson et al., 2011; Scheeringa et al., 2012; Grimshaw and Carmel, 2014), authors have associated an increased alpha activity with a decrease in brain activity or a decrease in allocation of cortical resources in the same region (Davidson, 1988; Davidson et al., 1990; Gevins et al., 1997; Cook et al., 1998; Allen et al., 2004). Thus, positive asymmetry scores (i.e., greater alpha power in the right frontal area relative to the left) are thought to reflect relatively lower right than left frontal cortical activity, and vice versa for a negative asymmetry score.

### The Main Models

Decades of work using the alpha asymmetry metric have led to emotional valence and motivation models (Allen et al., 2004; Harmon-Jones et al., 2010). These models highlight that approach motivation emotional processes are associated with relatively greater cortical activity in the left frontal area compared to the right, which in turn, is inversely correlated with alpha power (i.e., greater right than left alpha power in these areas). Inversely, emotional processes related to avoidance motivation and a negative valence are associated with relatively greater right than left frontal cortical activity (corresponding to greater left than right frontal alpha power). Extreme approach-oriented traits and behaviors include for example positive urgency (i.e., the tendency toward rash action in response to extreme positive emotional states (Tomarken and Davidson, 1994), sensation-seeking (Santesso et al., 2008), and high reward sensitivity (Pizzagalli et al., 2005), whereas avoidance-related traits and behaviors include depression and anxiety (Thibodeau et al., 2006), shy temperament (Fox et al., 1995), negative dispositional affect (Tomarken and Davidson, 1994), and poor regulation of negative emotions (Jackson et al., 2003). These models align with the clinical literature showing that lesions in the left frontal area are associated with depression symptoms (Robinson and Price, 1982; Harmon-Jones et al., 2010).

### The Underlying Brain Networks and Systems

Going one step further beyond these descriptive models, investigators using EEG source-localization techniques (Laufs et al., 2003; Pizzagalli et al., 2005; Mantini et al., 2007; Koslov et al., 2011; Gable et al., 2015; Smith et al., 2018) found that frontal asymmetries originate from the dorsal frontoparietal network (dFPN), the inferior frontal gyrus, and the right dorsolateral prefrontal cortex (dlPFC; which is part of the dFPN). These results led them to suspect that frontal asymmetries reflect the integrity of the supervisory system, which is theorized to generate effortful constraint and self-control (Sutton and Davidson, 1997; Cacioppo et al., 2007; Gable et al., 2015). Gable et al. (2015) suspected that the alpha asymmetry is driven by the activity of this supervisory control system, supposedly located in the right frontal area (Gable et al., 2015). Frontal asymmetries may also reflect other associated executive control mechanisms, which play an essential role in allocating attention toward a goal and inhibiting interference from distractors (Corbetta et al., 2008; Vossel et al., 2013; Grimshaw and Carmel, 2014; Gable et al., 2015). In this view, termed the asymmetric inhibition model, mechanisms in the left frontal cortex would inhibit negative distractors, whereas mechanisms in the right frontal cortex would inhibit positive distractors. Consequently, asymmetric aberrations in these systems result in bottom-up and top-down dysfunction, such as the difficulty in disengaging attention from negative/avoidance-motivation information AS in depression and anxiety (Eysenck et al., 2007; Shackman et al., 2009; Cisler and Koster, 2010; De Raedt and Koster, 2010; Engels et al., 2010; Gotlib and Joormann, 2010; Kim et al., 2012; Gable et al., 2015), whereas difficulty in inhibiting positive/approach-motivation distractors results in addiction and positive urgency behaviors (Bechara, 2005;

Garavan and Hester, 2007; Goldstein and Volkow, 2011). Thus, multiple lines of research demonstrate that the mechanisms underlying alpha asymmetry measurements are highly implicated in processes that contribute to well-being (positive/negative affect, capacity to fulfill one's potential and life goals, etc.).

## Limitations in Electroencephalographic Asymmetry Research

While the literature on EEG asymmetry is sizable and robust, it is important to note that there have also been failed replications and contradictory results (Gotlib, 1998; Reid et al., 1998; Hagemann et al., 1999; Müller et al., 1999; Coan et al., 2001; Gale et al., 2001; Papousek and Schuster, 2002; Dennis and Solomon, 2010; Stewart et al., 2010; Kop et al., 2011; Koslov et al., 2011; Quinn et al., 2014; Meyer et al., 2015; Arns et al., 2016; Palmiero and Piccardi, 2017; van der Vinne et al., 2017). These inconsistencies can be explained by the heterogeneity in the experimental designs, EEG preprocessing techniques, and statistical approaches employed across investigators over the years (Allen et al., 2004; Smith et al., 2017). A summary of the main limitations of EEG asymmetry research and proposed solutions that were implemented in this study are now described.

### Trait Versus State

One limitation is that EEG asymmetry can reflect trait or state aspects and thus, designing experiments to highlight one over the other depending on the research question is essential. When measured during rest, EEG asymmetry is considered a trait variable related to various psychological constructs and predictive of future emotional behavior or psychopathology (Wheeler et al., 1993; Davidson, 1994; Sutton and Davidson, 1997; Stewart et al., 2010; Nusslock et al., 2011; Papousek et al., 2012). When measured as an event-related response, it is considered a state variable reflecting the person's current emotional state (Coan et al., 2001; Harmon-Jones and Sigelman, 2001; Harmon-Jones, 2004). Some authors estimate that 60% of the variance in asymmetry measure within a resting session is due to trait influence, and the 40% to state influences (Hagemann et al., 2002). Hence, the first approach aims to reduce the state influence during rest, whereas the second one aims to increase it using emotion-elicitation perturbations (Coan et al., 2006). In this study, we focus on the trait variable and hypothesize that trait frontal alpha asymmetry will be associated with multidimensional well-being (since well-being is driven by both emotional valence and motivational components).

### Sample Characteristics

The second limitation to EEG asymmetry research is that sample-specific characteristics (e.g., age, gender) have been shown to significantly influence EEG findings because of functional and anatomical differences (Klimesch, 1999; Sowell et al., 2007; Hagemann et al., 2008; Finley et al., 2020). Many EEG asymmetry studies include participants of one gender to reduce this bias (Tomarken et al., 1990; Wheeler et al., 1993; Jacobs and Snyder, 1996; Reid et al., 1998; Gale et al., 2001; Dennis and Solomon, 2010; Mikolajczak et al., 2010; Koslov et al., 2011). However, this prevents investigators from examining gender as a potential

mediator or moderator of asymmetry findings (MacKinnon et al., 2013). There is a lack of consensus regarding the role gender plays in EEG asymmetry in the limited studies that have addressed this question (Veldhuizen et al., 1993; Carrier et al., 2001; Miller et al., 2002; Otero et al., 2003; Morgan et al., 2005; Gasbarri et al., 2006, 2007; Stewart et al., 2010; Kovacevic et al., 2015; Müller et al., 2015; Hashemi et al., 2016). Similarly, the role age plays in EEG asymmetry is also not very well known. One solution to the lack of understanding of if and how demographic variables influence EEG asymmetry and well-being is to collect large and diversified datasets that better reflect the general population. A few studies with large samples found that age and gender mediate frontal asymmetry but that ethnicity or socioeconomic status did not (Stewart et al., 2010; Gable et al., 2015; Arns et al., 2016). However, these studies are rare and hard to replicate because of the time and cost involved in recording EEG data on a large number of subjects with conventional systems (equipment cost, EEG preparations time, participants compensation for their time, equipment cleaning, etc.).

Wearable EEG technologies make the collection of large datasets of diversified and under-represented populations more feasible and offer promising new applications for both clinicians and researchers in the long term (Cannard et al., 2020). These applications include brain monitoring in naturalistic settings and in real-time (Hu et al., 2015; Jebelli et al., 2017), brain-computer interfaces (BCI; Park et al., 2020), neurofeedback interventions (Angelakis et al., 2007; Quaedflieg et al., 2016; Brandmeyer and Delorme, 2020a), neuromarketing (Cartocci et al., 2018; Ramsøy et al., 2018), or neuroaesthetics research (i.e., the science studying the biological underpinnings of aesthetic experience; Cheung et al., 2019; Cartocci et al., 2021). While these EEG systems can have inferior hardware capacities than conventional ones, recent technological and algorithmic advancements make the detection and measurement of mental states increasingly reliable (Wu et al., 2017), with as few as a single EEG channel (Umar Saeed et al., 2018; Arpaia et al., 2020; Mahmoodi et al., 2021). Additionally, these systems can easily combine other physiological measures such as electrocardiography (ECG) or galvanic skin response (GSR) to improve the efficacy of mental states detection (e.g., Ahn et al., 2019). Wearable EEG systems have been used extensively over the past few years to measure frontal asymmetry (Peng et al., 2011; Hu et al., 2015; Hashemi et al., 2016; Jebelli et al., 2017, 2018; Wu et al., 2017; Zhao et al., 2017; Hwang et al., 2018; Umar Saeed et al., 2018; Cao et al., 2019; Arpaia et al., 2020; Park et al., 2020; Saeed et al., 2020) and were used in this present study to enable the collection of a large dataset. Hence, in this study, we aim to evaluate the potential relationship between well-being, alpha asymmetry, and individual characteristics (namely age and gender) in a large sample, collected using a low-cost wearable EEG headset.

### Alpha Frequencies and Bounds

The third main limitation in EEG asymmetry research is the handling of alpha-band frequencies and bounds. The alpha band is dominantly considered as a single phenomenon in EEG asymmetry studies. However, previous evidence suggested that it should not. For instance, measuring alpha power spectral density

(PSD) on the traditionally *a priori*-defined bandwidth 8–13 Hz does not account well for interindividual differences because parts of the alpha power distribution fall outside this range for some individuals (Klimesch et al., 1990; Klimesch, 1997). Furthermore, differential changes in opposing directions within the same dataset have been observed between lower (8–10.5 Hz) and upper (11–13 Hz) alpha oscillations, as well as between local and global properties (Klimesch, 1999; Nunez et al., 2001; Nunez and Srinivasan, 2006).

The individual alpha frequency (IAF) refers to the dominant frequency within the alpha power distribution and is thought to reflect the dominant neural circuits that generate alpha oscillations. Because it varies within and across individuals, measuring alpha power on each individual's IAF better accounts for inter-individual variability (Klimesch, 1999; Haegens et al., 2014; Mierau et al., 2017). Individual alpha frequency estimates are considered a trait-like characteristic of the human EEG (Grandy et al., 2013), have high heritability (Smit et al., 2006), decrease with age (Klimesch, 1997; Corcoran et al., 2017; Finley et al., 2020), and have good test-retest reliability (Näpflin et al., 2007). Few studies have investigated EEG asymmetry using IAF estimates to our knowledge (Klimesch et al., 1998; Angelakis et al., 2004a; Vecchiato et al., 2012; Quaedflieg et al., 2015, 2016; Di Flumeri et al., 2016).

The first approach to estimate IAF is to use the peak alpha frequency (PAF; frequency within the alpha band with the highest power). While this technique has been extensively used for the study of cognition (Klimesch, 1999; Angelakis et al., 2004b; Rathee et al., 2020), it does not perform well with a portion of the population that have ambiguous alpha peaks, “split peaks” (i.e., several peaks within the alpha band), or no peak at all (Anokhin and Vogel, 1996; Chiang et al., 2008, 2011). A second approach called the alpha center of gravity (CoG) considers the shape of the alpha PSD distribution and is thought to provide a more accurate summary of the underlying alpha activity. Initial techniques to estimate IAFs relied on visual and manual inspection (Klimesch et al., 1990) or cross-frequency assumptions (Doppelmayer et al., 1998; Klimesch, 1999; Posthuma et al., 2001; Goljahani et al., 2012). These methods were very time-consuming and prone to subjective judgment error. Novel automated methods have now been developed to avoid these limitations. While the channel-based method (CRB; Goljahani et al., 2012, 2014) is better suited for event-related EEG asymmetry, other statistical curve-fitting and clustering techniques are particularly promising for IAF-estimation of resting EEG data (Chiang et al., 2008, 2011; Lodder and van Putten, 2011, 2013; Van Albada and Robinson, 2013; Corcoran et al., 2017). Corcoran et al. (2017) have implemented these algorithms into a fast, reliable, open-source toolbox operating in MATLAB and Python (Corcoran et al., 2017). This method seems suitable for large datasets with a relatively low signal-to-noise ratio (SNR) acquired with a wearable dry EEG system.

Hence, calculating alpha asymmetry scores on PSD estimated on the predefined alpha band (8–13 Hz), the lower (8–10.5 Hz) and upper (11–13 Hz) alpha sub-bands, and the CoG may help us understand more about the underlying mechanisms of alpha asymmetry. The present study incorporates these metrics to

evaluate differences in these measures and their relationship to well-being. We expect well-being to be positively correlated with CoG values, differently correlated with lower and upper alpha (no specific direction is hypothesized), and positively correlated with CoG-asymmetry (and we expect this association to be stronger than that with the traditional whole alpha band asymmetry, by better accounting for interindividual differences).

### Limiting Electroencephalographic Asymmetry to the Frontal Areas

The fourth limitation is the reduction of the study of EEG asymmetry phenomenon to only the frontal areas. It has been expressed for a long time that both anterior and posterior cortical regions show asymmetric activity patterns (Davidson, 1988, 1992). This is also reflected by studies showing that FAA obtained on data referenced with the current-source density (CSD) transformation (i.e., reflective of alpha power from local frontal sources only) correspond to a marker for depression risk, whereas FAA obtained on data referenced to mastoids or average (i.e., containing alpha power from distal, posterior cortical regions) correspond to a better marker of current depression severity (Stewart et al., 2010). Furthermore, expanding the analysis of alpha asymmetry to the temporoparietal (TP) regions seems particularly relevant since alpha asymmetries were source-localized to the frontoparietal network (FPN), which includes brain structures in both the frontal and the TP regions (see above; Vossel et al., 2013). Furthermore, different subtypes of anxiety disorders are differently associated with asymmetric activity in frontal and TP regions (Heller et al., 1997; Engels et al., 2007; Mathersul et al., 2008; Müller et al., 2015). Together, these findings suggest that anxious arousal (physiological arousal and hyper-reactivity under conditions of panic) is associated with relatively greater right than left frontal activation, whereas anxious apprehension (involving worry and verbal ruminations; i.e., trait anxiety and generalized anxiety disorder) is linked to the opposite asymmetry in frontal area and asymmetry in the same direction in the TP area. However, other findings suggested that TP asymmetry was less stable over time compared to frontal asymmetry (Müller et al., 2015) and sometimes not associated with self-reported measures of affect and motivation (Davidson et al., 1990). In this study, we examine the relationship between well-being and asymmetry in both frontal and TP regions and hypothesize that alpha asymmetry in both regions will be associated with well-being (with potentially a different direction).

### Limiting Electroencephalographic Asymmetry to the Alpha Oscillations

The Fifth and last main limitation in EEG asymmetry research is the need to expand analyses to other frequency bands. Coherence in both alpha and theta oscillations has been highlighted during both relaxation and mental calculation (Nunez and Srinivasan, 2006). This widespread (global) phase coherence phenomenon increases in the upper frequencies of both alpha and theta bands while it simultaneously decreases in the lower frequencies (Wingeier, 2000; Nunez and Srinivasan, 2006). These findings go along with other findings indicating that global alpha and theta rhythms functionally interact during both relaxation and



attentional tasks (Klimesch, 1999; Buzsáki, 2006; Laufs et al., 2006). Furthermore, theta power has been used to predict response to depression treatment in several studies (Knott et al., 1996, 2000; Cook and Leuchter, 2001; Cook et al., 2002; Bares et al., 2008; Iosifescu et al., 2009; Spronk et al., 2011; Baskaran et al., 2012; Olbrich and Arns, 2013). Furthermore, theta power decreases while upper alpha power increases in several conditions (i.e., the early part of life until adulthood, in neurological disorders, and the transition phase from awake to sleeping), whereas the direction of their relationship is opposite for the late part of the lifespan (Klimesch, 1999).

Similarly, alpha and beta spectral power have been found to interact (Laufs et al., 2006; Hamid et al., 2010), and both are associated with high levels of mental stress and depression (Hayashi et al., 2009; Alonso et al., 2015; Jena, 2015; Alshargie et al., 2016; Jun and Smitha, 2016; Díaz et al., 2019; Al-Dabass, 2020; de Hemptinne et al., 2021). More specifically, prefrontal beta power in lateral areas was found to be positively associated with depression and anxiety, whereas lateral beta power was negatively associated with mood (de Hemptinne et al., 2021). The authors interpreted these results to be in line with the organization of the reward networks in the prefrontal cortex (PFC).

However, no robust literature is available to make specific interpretations about how alpha asymmetry interacts with other frequency bands, and whether asymmetries in other frequency bands could be associated with psychological constructs such as well-being. Thus, we aim to bring light to this matter in this study and hypothesize that well-being will be associated with asymmetries in other frequency bands. This study includes asymmetry scores estimated on the delta (1–3 Hz), theta (4–7 Hz), and beta (14–30 Hz) frequency bands, for both frontal and TP sites. Since no previous research exists on this matter, we have no specific hypothesis concerning the direction of these potential associations.

### Summary of the Study Goals and Hypotheses

Considering the potential importance of alpha asymmetry as a physiological correlate in general, and for well-being specifically, the overall objective of this study was to determine whether a low-cost wearable EEG headset (the Muse by Interaxon) could be used to measure EEG correlates (CoG, EEG asymmetry) of well-being on a relatively large sample ( $N = 353$ ). The analyses were designed to address the main limitations of EEG asymmetry research addressed above. The hypotheses for the study were as follows:

1. Well-being will be positively associated with approach-motivation processes and positive valence of emotion, as reflected by relatively greater right than left alpha power. We hypothesize that this will be the case for both frontal and temporoparietal (TP) areas (although the direction might be different, based on the literature discussed).
2. Age and gender will be associated with both well-being and mean alpha asymmetry (predefined 8–13 Hz band).
3. The CoG will be positively correlated with well-being levels.

4. Asymmetry scores estimated on sub-components of alpha oscillations (namely lower/upper alpha and CoG) will provide stronger correlations regarding the relationship between well-being and alpha asymmetry than those estimated on the predefined alpha band (8–13 Hz), by better accounting for alpha source differences (lower/upper alpha) and interindividual differences (CoG).
5. Well-being levels will be associated with asymmetries in other frequency bands (namely delta, theta, and beta), although we do not have specific hypotheses regarding which bands and their directions.

## MATERIALS AND METHODS

### Participants

353 participants were recruited from groups attending workshops focusing on well-being and personal development at the Earthrise Campus. Exclusion criteria: people younger than 18 years of age, inability to read or understand the consent form, acute or chronic illness precluding completion of measurements. Upon arrival at the research laboratory, participants were briefly interviewed by the research assistants to ensure they met the inclusion/exclusion criteria and were then allocated to a carrel where the following equipment was available for their participation: a wearable EEG headset, a Chromebook, and a pair of headphones. The settings allowed the recording of up to 9 participants simultaneously. Participants volunteered and were not compensated for participation. The study and the consent form were approved by the Institute of Noetic Sciences' institutional review board (IRB). All questionnaires were optional and anonymous.

### Multidimensional Well-Being

Participants' multi-dimensional well-being was assessed on-site using the Arizona Integrative Outcomes Scale (AIOS; Bell et al., 2004) in SurveyMonkey<sup>1</sup>. The AIOS is a horizontally displayed scale that provides a quick and accurate assessment of the participants' self-rated global sense of physical, social, psychological, affective, and spiritual well-being over the past 24 h (Bell et al., 2004). The low anchor is "Worst you have ever been" (AIOS score = 0) and the high anchor is "Best you have ever been." (AIOS score = 100). The 24-h AIOS score was found to significantly reflect psychological well-being, global health, psychological distress, the positive and negative affect, and the positive states of mind, and was significantly correlated with the 1-month AIOS scores (Bell et al., 2004; Otto et al., 2010; Tuason et al., 2021). Furthermore, AIOS-24 h was found to be associated with personality traits (Wahbeh et al., 2021). While these findings suggest the AIOS-24 h reflects trait components of well-being, validation of this hypothesis requires further testing. The online survey included additional questionnaires that are not included in this study and are reported elsewhere (Wahbeh et al., 2021).

<sup>1</sup><https://www.surveymonkey.com/>

## EEG

### Data Collection

Once participants completed the survey, continuous EEG was recorded using InteraXon's Muse wearable EEG headband (version 2016). Electroencephalography data were recorded while participants were instructed to focus their attention on their breath and count inhalation/exhalation cycles. They were instructed to bring their attention back to their breath and start counting again if they lost track of their count or noticed their minds wandered. This task reduces EEG artifacts occurring naturally with eye movements. Most importantly, this task can later be implemented into practical translational and therapeutical applications aimed at increasing well-being levels through the modulation of alpha asymmetry and the underlying brain processes (Angelakis et al., 2007; Sessa, 2007; Moynihan et al., 2013; Doll et al., 2016; Schmalzl et al., 2018; Prpa et al., 2020). Electroencephalography data were with a sampling rate of 256 Hz and 12-bits of data resolution. This system has five active dry electrodes: two frontal silver (AF7 and AF8), two temporoparietal (TP) silicone electrodes (TP9 and TP10), and a reference electrode (FPz). Before positioning the headband on the subjects' heads, their skin was cleaned with alcohol swipes at electrode sites, and a thin layer of water was applied with a sponge to the electrodes to improve signal quality. EEG data were acquired on Chromebooks using the Muse Monitor App and were uploaded onto Dropbox at the end of the recording. Random unique identifiers were used to link survey and EEG data. Impedance check was provided by the App (horseshoe symbol) and visually confirmed by the raw signal displayed on the screen in real-time.

As shown in previous publications, good internal consistency reliability of frontal EEG asymmetry can be obtained with as few as 100 epochs, corresponding to one to 3 min of artifact-free recorded data [depending on window size; (Allen et al., 2004; Towers and Allen, 2009; Smith et al., 2017)]. Allen et al. (2004) found that the number of epochs used to estimate the asymmetry scores matters more than the number of minutes of data (Allen et al., 2004), with asymmetry scores estimated on 2 min of data showing similar consistency reliability than those obtained on 8 min of data. Furthermore, a recent publication showed that individuals can robustly be differentiated using spectral EEG data obtained on segments as short as 30 s (and this was stable weeks later; da Silva Castanheira et al., 2021). Thus, 2 min of EEG data were recorded for each participant. When less than 8 min of data is available, Allen et al. (2004) recommend reporting the internal consistency reliability and how many blocks were treated through the calculation of Cronbach's alpha (see below).

### Data Preprocessing

Data preprocessing was done in *EEGLAB* version 2020.0 (Delorme and Makeig, 2004) in *MATLAB* v2020a. EEG data were imported with the *muse\_monitor* plugin v3.2, low-pass filtered at 30 Hz (transition bandwidth 12.5 Hz; passband edge 50 Hz; cutoff frequency -6 dB 56.25 Hz; linear non-causal filter) to remove high-frequency artifacts, and high-passed filtered at 1 Hz (transition bandwidth 1 Hz; passband edge 1 Hz; cutoff

frequency -6 dB 0.5 Hz; linear non-causal filter) to remove low-frequency drifts. 10–20 channel template locations from BESA spherical coordinates were used in *EEGLAB*. Artifactual channels (with ~50% of data being noisy or artifactual) were manually tagged and removed with a custom-made single-page figure displaying each channel's overall raw data, standard deviation, and power spectra. Files with at least one bad channel were removed for analyses.

An existing automatic method to clean EEG artifacts over this large sample was cross-validated: 150 files were randomly selected from the database to be cleaned manually and automatically with *EEGLAB*'s *clean\_rawdata* plugin v2.2 (Euclidean method). Performance was calculated on each channel by comparing each sample as either true positive (TP, bad sample correctly rejected), true negative (TN, good sample correctly kept), false positive (FP, good sample incorrectly rejected), or false negative (FN, bad sample incorrectly kept). "Positive" and "negative" refer to presence or absence. Then, the true positive rate (TPR, i.e., sensitivity) and the true negative rate (TNR, i.e., specificity or selectivity) were calculated for each channel with:  $TPR = TP/(TP + FN)$  and  $TNR = TN/(TN + FP)$ . The average sensitivity and specificity were then calculated over all channels to obtain the overall performance of the automatic method compared to manual rejection. After testing different parameters, the best performance obtained showed 81% sensitivity and 83% specificity [settings: "*burst\_criteria*" = 6, "*window\_criteria*" = 0.3, "*window\_tolerance*" = "(-Inf 7)"]. 50 additional datasets were randomly selected for cross-validation, showing 84% sensitivity and 89% specificity. Since further increasing the sensitivity scores (i.e., removing more subtle artifacts) corresponded to a decrease in specificity (i.e., removing more non-artifactual data), these thresholds were considered most suited for this analysis. On average, this method removed an additional 11.4 s of data ( $\pm 23.0$ ). Thus, bad channels were manually tagged and data were cleaned using this automated method and parameters. Files with less than 60 s of remaining artifact-free data were removed for analysis.

Note that this was done on duplicated data that were averaged-referenced to a fifth zero-filled channel as it increased performance by homogenizing raw signal amplitude across channels. But because this average re-referencing method was not validated for this specific montage and is not recommended with less than 30 channels (Smith et al., 2017), artifactual sections were removed from the original raw files and then re-processed as above. The issue of the electrode reference and its impact on asymmetry scores has been detailed and is of high importance (Allen et al., 2004; Smith et al., 2017). The recommended referencing methods (i.e., average-referencing, current-source density transformation) or the "residualization procedure" are not feasible with the low density and sparse montage of the Muse headset. The frontal channels are located close to the Fpz reference, potentially providing invalid asymmetry scores for the frontal channels by not reflecting the same underlying cortical activity as in the literature. Since frontal asymmetry estimated on linked-mastoid data is associated with the severity of current depression (Stewart et al., 2010), frontal channels were

re-referenced to TP9/TP10. Temporoparietal channels were kept with the default Fpz reference.

### Power Spectral Density and Asymmetry Estimates

Power Spectral Density (PSD) was calculated using MATLAB's *pwelch* function on 1-s *hamming* tapered windows (42.5 dB sidelobe attenuation) with 50% overlap [per guidelines (Allen et al., 2004; Smith et al., 2017)], since the *pwelch* method smooths over non-systematic noise and is more robust compared to the more popular *fft* method that is more sensitive to noise and non-stationarities. Power spectra were then converted to  $10^* \log_{10}$  decibels (dB) as untransformed power values tend to be positively skewed due to individual differences in skull thickness that influence the signal amplitude (Allen et al., 2004).

The CoG was estimated for each channel using the automated, open-source method developed by Corcoran et al. (2017) which uses curve-fitting algorithms and a smoothing Savitzky-Golay Filter (SGF). This technique is thought to better account for interindividual variance and to be more reliable under low SNR conditions.

Asymmetry scores were obtained on the alpha PSD averaged over the predefined band (8–13 Hz), averaged over the predefined lower (8–10.5 Hz) and upper (11–13 Hz) sub-bands, and the individualized CoG.

They were calculated following standard procedures by subtracting the alpha power of interest of the left frontal channel from the right frontal channel ( $\alpha\_power\_dB\_AF8 - \alpha\_power\_dB\_AF7$ ). Positive scores, therefore, indicate greater alpha power in the right relative to the left electrode. Asymmetry scores were also obtained from the temporoparietal (TP) channels. Finally, asymmetry scores were also computed on the delta (1–3 Hz), theta (4–7 Hz), and beta (14–30) frequency bands. Gamma was not included due to the Muse's vulnerability to line noise in the high frequencies.

### Statistical Analyses

Robust linear regression models were generated in MATLAB 2021a using MATLAB's *fitlm* package. Because of small portions of artifacts remaining in some EEG data after automatic preprocessing, robust least-squares regressions (Tukey's bisquare function; default tuning constant = 4.685) were used for statistical analysis to down-weight the residuals' influence on the model, using iterative reweighted least-squares (IRLS; Huber and Ronchetti, 2009). All models were tested for lack of fit first using a degenerate model consisting of only a constant term. Reported *F*-statistics with a *p*-value, therefore, indicate a valid fit for the model but do not inform on the relationship between the dependent and independent variables. The Beta ( $\beta$ ) coefficient estimates and their standard error (SE) are reported in the first column and indicate a significant linear relationship between the predictor and the outcome variables when *p*-values are present. Summary statistics of the models include the number of observations, the error degrees of freedom, the root mean squared error (RMSE),  $R^2$  (for models with one predictor), adjusted  $R^2$  (for models with multiple predictors). Note that the descriptions below each table reporting the statistical results indicate whether the models were simple or multiple linear regressions (i.e., one or more predictor

variables). In sum, all models were simple linear models and one was a multiple linear model (the two variables being lower and upper alpha asymmetry). Finally, following recommendations (Allen et al., 2004), asymmetry scores were also calculated on eleven 4-s blocks (as opposed to the average alpha power over all blocks for the asymmetry measures) to validate the internal reliability consistency of alpha asymmetry scores obtained on these short file lengths, using Cronbach's alpha method, where a value below 0.2 indicates poor internal reliability consistency and greater than 0.8 a high internal reliability consistency (Cronbach, 1951).

## RESULTS

230 participants remained for analyses after preprocessing. 83 files contained at least one bad channel and 36 had less than 60 s of artifact-free data and were excluded from the analyses (the data loss due to signal quality is discussed in the Discussion). They were aged from 22 to 80 years old (mean age was  $55 \pm 13.4$ ) and were 64.3% female, 28.7% males, and 7% "Other" or missing. Cronbach's alpha scores indicated a high internal reliability consistency of the asymmetry scores estimated on both frontal (Cronbach  $\alpha = 0.95$ ) and temporoparietal (Cronbach  $\alpha = 0.82$ ) channels.

### Well-Being and Alpha Asymmetry (Predefined Frequency Bands)

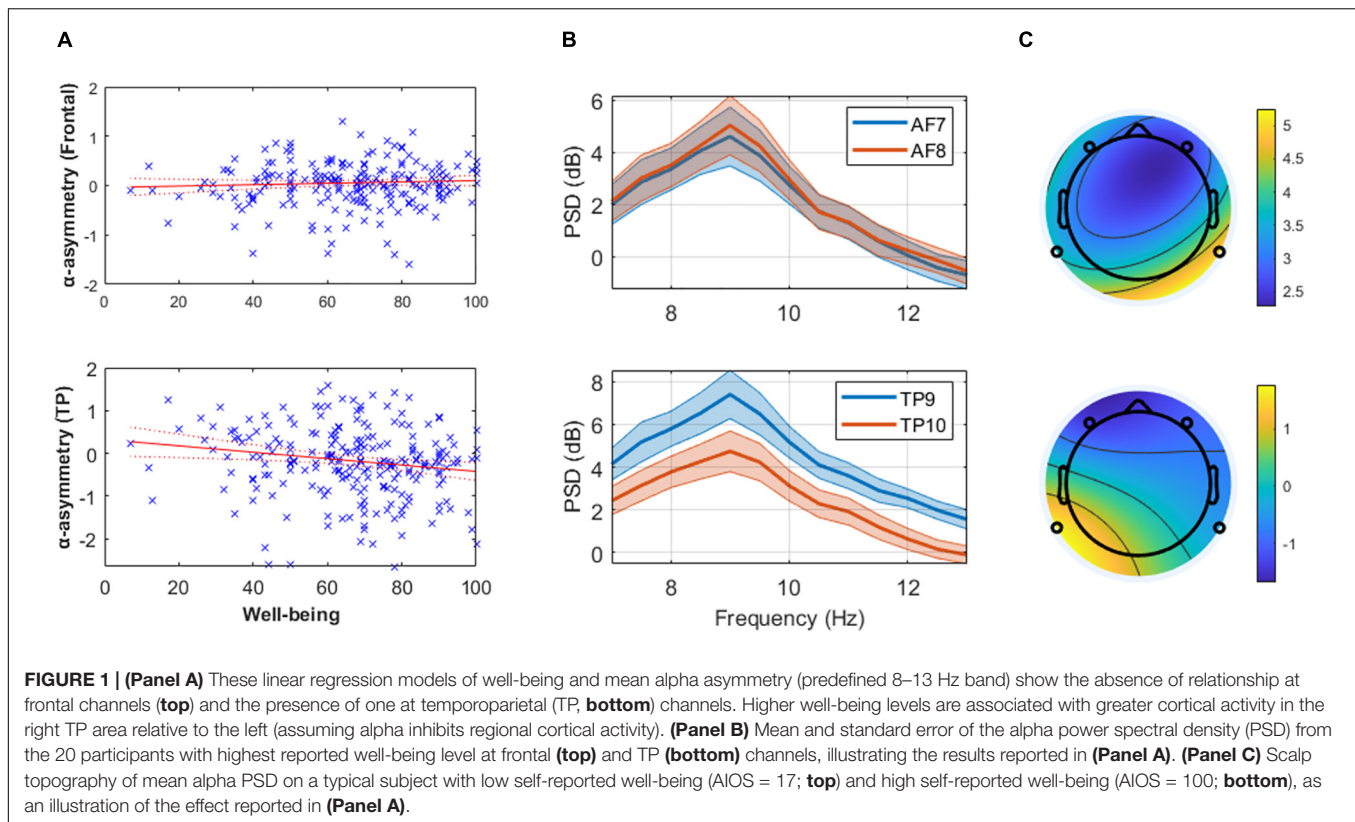
No association between subjective well-being levels and frontal alpha (predefined 8–13 Hz band) asymmetry was found (Figure 1 and Table 1). However, well-being was negatively correlated with TP alpha asymmetry scores (predefined 8–13 Hz band), reflecting greater cortical activity in the right TP area relative to the left is associated (assuming the inhibitory role of alpha oscillations on regional cortical activity; see Introduction). Detailed statistics are reported in Table 1 and an illustration of the results in the frequency and the scalp topography domain can be found in Figure 1, using the 20 participants with the highest well-being levels. The relationship between well-being and TP total alpha asymmetry scores appear to be driven more specifically by neural activity in the lower frequencies of the alpha band (8–10.5 Hz) because well-being was significantly correlated with

**TABLE 1** | Subjective well-being and alpha asymmetry (strict bounds at 8–13 Hz).

Predictor variable	$\beta$ (SE)	N (DF)	Model RMSE	Model $R^2$	Model F-statistic
Frontal $\alpha$ asymmetry	0.001 (0.002)	230 (228)	0.468	0.158	42.8***
TP $\alpha$ asymmetry	-0.007* (0.003)		0.808	0.036	8.51**

Column 2: *p*-values next to the Beta ( $\beta$ ) coefficients and their standard error (SE) indicate a significant association between the predictor and the response variable at 95% confidence level (\*), 99% confidence level (\*\*) and 99.9% confidence level (\*\*\*). Column 3: number of observations (N) and degrees of freedom (DF). Column 4–6: root mean square error (RMSE), R-squared, and F-statistic of the linear model. *p*-values next to F-statistic indicate a significant fit (see above for confidence levels). Each simple linear model follows the equation: Response variable  $\sim 1 +$  predictor.





**TABLE 2 |** Subjective well-being and temporoparietal (TP) lower/upper alpha asymmetry.

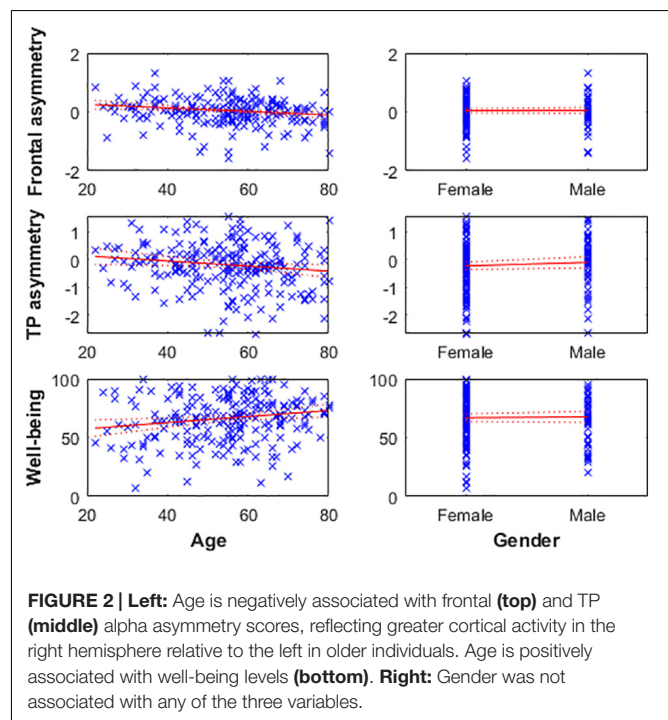
Predictor variable	Estimate (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
Lower $\alpha$ -asymmetry (8–10.5 Hz)	-0.008* (0.003)	230 (228)	0.981	0.035	8.28**
Upper $\alpha$ -asymmetry (11–13 Hz)	-0.005 (0.003)		0.863	0.011	2.61

Column 2:  $p$ -values next to the Beta ( $\beta$ ) coefficients and their standard error (SE) indicate a significant association between the predictor and the response variable at 95% confidence level (\*), 99% confidence level (\*\*) and 99.9% confidence level (\*\*\*). Column 3: number of observations (N) and degrees of freedom (DF). Column 4–6: root mean square error (RMSE), R-squared, and F-statistic of the linear model.  $p$ -values next to F-statistic indicate a significant fit (see above for confidence levels). The multiple linear model follows the equation: Response variable  $\sim 1 + \text{predictor1} + \text{predictor2}$ .

lower alpha asymmetry but not with upper alpha asymmetry (see **Table 2**).

## Well-Being, Alpha Asymmetry (Predefined 8–13 Hz Band), and Covariates

Age was negatively correlated with alpha asymmetry calculated on the predefined 8–13 Hz band (meaning the older the individual, the greater cortical activity is in the right frontal and TP areas relative to the left ones) and positively correlated with subjective well-being levels (i.e., older age



reflecting greater well-being score). However, gender was not associated with well-being or alpha asymmetry (**Figure 2** and **Table 3**).

**TABLE 3** | Subjective well-being and alpha asymmetry, and covariates.

Predictor variable	Estimate (SE)	N (DF)	Model RMSE	Model R <sup>2</sup>	Model F-statistic
<b>α-asymmetry (Frontal)</b>					
Age	-0.006* (0.002)	218 (216)	0.469	0.188	50***
Gender_Male	0.009 (0.071)	214 (212)	0.477	0.162	41***
<b>α-asymmetry (TP)</b>					
Age	-0.009* (0.004)	218 (216)	0.819	0.026	5.76*
Gender_Male	0.129 (0.123)	214 (212)	0.833	0.01	2.09
<b>Well-being</b>					
Age	0.258* (0.100)	218 (216)	19.7	0.031	7**
Gender_Male	0.68 (2.914)	214 (212)	19.7	0.003	0.56

Column 2: *p*-values next to the Beta ( $\beta$ ) coefficients and their standard error (SE) indicate a significant association between the predictor and the response variable at 95% confidence level (\*), 99% confidence level (\*\*), and 99.9% confidence level (\*\*\*). Column 3: number of observations (N) and degrees of freedom (DF). Column 4–6: root mean square error (RMSE), R-squared, and F-statistic of the linear model. *p*-values next to F-statistic indicate a significant fit (see above for confidence levels). Each simple linear model follows the equation: Response variable  $\sim 1 +$  predictor.

## Well-Being, Alpha Center of Gravity, and Center of Gravity-Asymmetry

No linear relationships were observed between well-being and the CoG (**Supplementary Table 2**), and between well-being and asymmetry scores calculated on the CoG (**Supplementary Table 3**), for both frontal and TP channels.

## Well-Being and EEG Asymmetry in the Other Frequency Bands

No associations were observed between well-being and EEG asymmetry in the delta (1–3 Hz), theta (3–7 Hz), or beta (14–30 Hz) frequency bands (**Supplementary Figure 1** and **Supplementary Table 1**).

## DISCUSSION

### Results Summary

Contrary to the existing literature on the emotional valence and the motivational models of frontal EEG asymmetry, we found an absence of association between multidimensional well-being levels and frontal alpha asymmetry (predefined 8–13 Hz band, 8–10.5 Hz, and CoG-asymmetry). However, well-being was negatively correlated with alpha asymmetry at the TP sites (predefined 8–13 Hz and 8–10.5 Hz bands, but not for CoG-asymmetry), reflecting greater cortical activity in the right TP area relative to the left (assuming the inhibitory role of alpha oscillations on regional cortical activity; see Introduction). Interestingly, the direction of the asymmetry is opposite to the one in the frontal areas in the literature of frontal alpha asymmetry. Hence, while approach motivation and the related emotional processes are associated with relatively greater left than right frontal cortical activation, multidimensional well-being seems to be associated with asymmetric activation in the opposite direction in the TP areas.

This effect appears to be driven more specifically by oscillatory activity in the lower frequencies of the alpha band (8–10.5 Hz),

aligning with studies highlighting the inhibitory function of these lower frequencies (Oakes, 2004). Making the distinction between lower and upper frequencies of the alpha band seems therefore especially relevant for neurophysiological studies using source-localization or simultaneous EEG-fMRI techniques to identify the intricate mechanisms involved in EEG asymmetry.

Contrary to our expectations, the CoG did not show associations with well-being levels. While CoG is associated with cognitive processes in the literature on the individual alpha frequency (IAF), we hypothesized that it would also be associated with self-reported well-being levels. However, the CoG may reflect other brain processes associated with cognition that are different than those involved with multidimensional well-being. Future studies using advanced source localization methods and high-density EEG systems should elucidate the different sources and networks associated with the different sub-components of alpha oscillations, and their associations with cognitive systems (i.e., PAF, CoG, lower/upper alpha).

While some researchers suspected that gender was the main driver of frontal alpha asymmetry levels (Gale et al., 2001; Dennis and Solomon, 2010; Mikolajczak et al., 2010), it was not associated with well-being or alpha asymmetry measures (for both frontal and temporoparietal sites) in this sample. However, age was negatively correlated with alpha asymmetry scores of both regions (meaning that cortical activity is greater in the right areas relative to the left ones as age increases) and positively correlated with subjective well-being levels. This finding aligns with the well-being literature (e.g., Carstensen et al., 2011), and supports a strong mediator role of age on the relationship between well-being and TP alpha asymmetry. Hence, the absence of a relationship between well-being and CoG-asymmetry might further indicate that there is a strong relationship between well-being, age, and alpha asymmetry in the TP area. Age is likely not the mechanism of change itself but may represent many underlying factors associated with brain changes and well-being (Kazdin, 2007). Thus, future studies using larger samples and higher density EEG data are necessary to confirm the accuracy of the asymmetry estimates obtained with this automated method, as well as to confirm or disprove the relationship between age, well-being, and alpha asymmetry in the TP area. If confirmed, the IAF-estimation method can be used to homogenize EEG asymmetry estimation procedures across investigators, and the specific interactions between these three variables should be further elucidated to determine the underlying mechanisms.

No associations were observed between subjective well-being and PSD asymmetry in the delta (1–3 Hz), theta (3–7 Hz), or beta (14–30 Hz) frequency bands (**Supplementary Figure 1** and **Supplementary Table 1**), supporting the specific role of alpha oscillations in the brain processes underlying well-being.

## Interpretations of the Results and Potential Mechanisms

Studies using source-localization methods found the alpha asymmetry to originate mainly from brain activity in the dorsal system of the frontoparietal network (FPN; 13). Functional magnetic resonance imagery (fMRI) showed that this system is organized bilaterally and comprises the intraparietal sulcus

(IPS) and the frontal eye fields (FEF) of each hemisphere, and is thought to mediate top-down guided voluntary allocation of attention to locations or features (Vossel et al., 2013). Both IPS and FEF are active when attention is overtly or covertly oriented in space and are suspected to be the regions for the maintenance of spatial priority maps, saccade planning, and visual working memory. In contrast, the ventral system comprises the temporoparietal junction (TPJ) and the ventral frontal cortex (VFC) and is associated with detecting unattended or unexpected stimuli and triggering shifts of attention (Vossel et al., 2013). It has been proposed that the ventral system is lateralized to the right hemisphere of the brain and exhibits asymmetric activity during attentional reorientation, the processing of rare deviant stimuli, and the response to valid vs. invalid cued targets (Corbetta and Shulman, 2002; Corbetta et al., 2008; Doricchi et al., 2010). The functional role of the TPJ also includes filtering irrelevant distractors during focused states of attention, modulating neural activity between various networks, and it has been implicated in social cognition and theory of mind (Vossel et al., 2013).

Hence, since our experimental task consisted of focusing attention on the breath, detecting mind-wandering thoughts (i.e., mental distractions), and reallocating attention to the goal, the TP alpha asymmetry may reflect these attentional processes and the underlying activity of the TPJ. Whereas, frontal alpha asymmetry may better reflect the dorsal system, as most studies use traditionally a cross-fixation task or resting-state condition with no focus of attention on any object. In line with these systems, one might speculate that participants with lower subjective well-being were more likely to ruminate on negative thoughts or memories (associated with negative valence and a withdrawal motivation; Mason et al., 2013; Smallwood and Andrews-Hanna, 2013) and less able to redirect their attention to their breath. This would decrease their capacity to detect negative thoughts and redirect their attention to their breath, corresponding to relatively greater left than right cortical activity in the TP area (positive TP asymmetry score). On the other hand, participants with higher well-being would be more likely to engage in mind wandering with positive valence and more likely to redirect their attention to their breath, which would correspond to greater cortical activity in the right TP area (negative TP asymmetry score). Another possibility is that alpha asymmetry in the TP regions might simply occur in opposite direction compared to the alpha asymmetry in the frontal areas (Davidson et al., 1990). Future studies using high-density systems and advanced source-localization methods are necessary to confirm or disprove this hypothesis.

## Limits and Recommendations

There are several limitations of this study that should be considered when reviewing the results.

While the AIOS-24h was found to be associated with longer-term well-being levels (i.e., reported well-being levels reflective of the past month and personality trait; see Methods), further validation is required to fully validate it as a measure of trait well-being.

While the asymmetry scores showed a relatively high internal reliability consistency and the Muse was validated for ERP research (Krigolson et al., 2017), 83 files had at least one bad channel and 36 had less than 60 s of remaining artifact-free data after preprocessing. This is a significant loss of data. The largest loss of data came from the presence of bad channels (considered bad when at least 50% of the channel was artifactual), likely due to the headband's flexibility that is prone to moving and disconnecting electrodes. Thus, future investigators could consider using the more recent Muse S that was developed for sleep studies. The Muse S is made of a flexible fabric that can stretch and keep stronger pressure on the electrodes, preventing them from disconnecting as much. Furthermore, we recorded the data when participants already started the task with their eyes closed to reduce data cleaning over the large sample. Automatic cleaning performance would have likely been increased by adding a period before the task that includes obvious artifacts (e.g., asking participants to produce eye blinks and jaw clenching) to help the automatic method algorithms create a more robust baseline and therefore reject artifacts more efficiently. Thus, higher-grade and -density wearable EEG systems and longer recordings (at least 4 min of continuous data to ensure having at least 2 min of artifact-free data on a larger portion of the sample) are recommended for future studies to keep the advantages of wearable technologies to acquire large datasets without compromising data quantity and quality.

The Muse has only four channels. There are obvious benefits to having more EEG channels in terms of scalp distribution and data quality, which allow the use of advanced methods such as independent component analysis (ICA) which can be used to remove subtle artifacts such as muscle activity, subtle eye movements, or channel noise (Makeig et al., 1996; Delorme and Makeig, 2004). Furthermore, while we controlled for the potential reference issue using this system, a wearable headset with at least 30 channels would allow multiple referencing methods (e.g., average or CSD) and ensure highly accurate asymmetry estimates. However, this study showed that it is feasible to use a low-cost, low-density wearable system to examine the relationships between well-being and alpha asymmetry in a relatively large and diverse population.

Alpha center of gravity (CoG) and therefore CoG-asymmetry is expected to better account for interindividual differences. The automated IAF-estimation toolbox used in this study was not able to detect the CoG for 8 subjects (see **Supplementary Tables 2, 3**). We wanted to ensure that the absence of association between well-being and TP asymmetry calculated on the CoG was not due to this small sample difference (8 subjects missing compared to models on predefined alpha bands). Thus, we removed these 8 subjects from the model assessing the association between well-being and TP-asymmetry (predefined 8–13 Hz band) to see if the effect disappeared as a consequence of these 8 subjects being removed. Results showed that the significant association was still present (see **Supplementary Table 4**). Hence, this absence of association between well-being and CoG-asymmetry is either due to:



- 1) poorer estimation of alpha activity by the automatic method compared to the predefined band since the method performs best with more neighboring EEG channels (and the Muse has only four sparse channels). Here, we fed the algorithm with 2 channels at a time to avoid alpha contamination from distal channels (to keep alpha activity from frontal and TP channels separate).
- 2) this method better accounting for interindividual differences, which would indicate that the main effect (TP asymmetry calculated on the predefined 8–13 Hz band) might be a consequence of the relationship between age, well-being, and related brain activity.

Lastly, cross-sectional designs are always a limitation to consider. More sessions would be beneficial for the field to confirm the results and assess changes in both well-being and EEG asymmetry to evaluate the stability of this relationship over time.

## Long Term Applications and Goals

Attentional and inhibitory impairments are thought to be crucially associated with an increased vulnerability to depressive episodes and cognitive vulnerability (De Raedt and Koster, 2010). Alpha asymmetry (both frontal and TP) seems to play an essential role in understanding the neural networks underlying executive functions, attention, emotion regulation, and well-being. A better understanding of these processes is crucial to improving general well-being levels via targeted interventions. For example, Xu et al. (2018) found that positive psychological interventions (PPIs) increased not only subjective well-being and relief in depression but also left frontal asymmetry scores (Xu et al., 2018). Kim et al. (2012) found that positive reappraisals (i.e., techniques to recognize the negative pattern that one's thoughts have taken using meta-awareness to cognitively reframe an event as more positive and therefore increase the sense of well-being) showed an increase in metabolic activity in the left dlPFC, caudate, and cingulate regions (Kim et al., 2012). Moynihan et al. (2013) found that mindfulness-based stress reduction produced significant changes in executive and immune functions, as well as in left frontal alpha asymmetry scores.

Neuroscientific tools such as neurofeedback (Linden, 2014; Brandmeyer and Delorme, 2020b) might increase these interventions' efficacy by targeting brain networks on the same occasion. For instance, Angelakis et al. (2007) improved cognitive processing speed and executive function of elderly individuals using PAF as a neurofeedback index (Angelakis et al., 2007). Allen et al. (2001) found that increasing right frontal activity relative to the left using frontal asymmetry neurofeedback led to decreased positive affect (Allen et al., 2001).

Furthermore, neuromodulation techniques may be used to directly modulate specific networks such as the FPN. For example, some clinical studies have shown that exciting the left dlPFC with transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS) improved depression symptoms (Kalu et al., 2012). Conversely, excitation of the right dlPFC led to reductions in craving (Boggio et al., 2008; Fregni et al., 2008) and risky decision-making (Fecteau et al., 2007), i.e., behaviors associated with difficulty in inhibiting

extreme rewards with positive valence. Additionally, Sanguinetti et al. (2020) recently used novel transcranial focused ultrasound stimulation to target the right prefrontal cortex with higher resolution and depth than TMS or tDCS and successfully modulated mood and emotion regulation. By modulating both bottom-up and top-down systems, long-term solutions without side effects and at lower costs will emerge by helping patients self-control negative biases (Moser et al., 2002; Hanslmayr et al., 2011).

Understanding the role of third variables on these mechanisms will help adapt these therapies to meet each individual's anatomy, physiology, and medical history, for more efficiency and safety. Once these intricacies are better understood, neuromodulation therapies might positively affect both the executive control and perceptive systems to decrease the propensity of depressive patients to focus on negative information and ruminative thought.

Finally, advancements in wearable technologies may allow care providers to monitor patients and apply neurofeedback or neuromodulation protocols at a low cost and remotely while patients are in the comfort of their homes (Cannard et al., 2020; Biondi et al., 2021).

## CONCLUSION

Overall, this study brings practical methodological information, challenges, and guidelines for conducting EEG research on large samples on well-being or related neuropsychological constructs, using wearable EEG technologies. Our findings bring novel knowledge that will help deepen our understanding of EEG asymmetries and their relations with well-being, the potential underlying neural networks and mechanisms, and the foreseeable long-term applications.

## DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: <https://osf.io/nq7ga/>.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institute of Noetic Sciences' Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

CC, HW, and AD made substantial contributions to the conception and design of the work, made substantial contributions to revising it critically for important intellectual content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. CC made a substantial contribution to the acquisition, analysis,

interpretation of data, and writing the work. HW and AD provided approval for the publication of the content. All authors contributed to the article and approved the submitted version.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fnhum.2021.745135/full#supplementary-material>

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