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Neural mechanisms underlying external distraction by unexpected environmental stimuli or by a secondary task: an intracranial EEG investigation

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Titre de la thèse

“Mécanismes neuronaux sous-jacents à la distraction externe par des stimuli environnementaux inattendus ou par une tâche secondaire: une investigation EEG intracrânienne”

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Résumé Détaillé

L'attention est un processus dynamique qui implique l'activité de différentes structures qui s'adaptent à la fois à nos besoins et au monde qui nous entoure. Son action débute au niveau de la perception, pour influencer la propagation des signaux relatifs à notre environnement depuis les régions sensorielles vers celles chargées des processus plus complexes. Elle agit également de manière descendante, depuis les zones responsables des fonctions cognitives dites supérieures pour adapter la prise d'information et le traitement de celle-ci en fonction des objectifs que l'individu se fixe, que ce soit à partir de ses souvenirs et expériences passées ou des contraintes du moment. La confrontation de cette double action ascendante et descendante aboutit à la stabilisation provisoire d'une dynamique cérébrale globale activant certaines aires du cerveau tout en désactivant d'autres régions, jusqu'à la production d'une réponse comportementale satisfaisante, qui conditionnera le comportement futur grâce aux informations obtenues sur l'efficacité de cette réponse.

Toutefois, ce schéma relativement idéal peut être dérouté dans le contexte d'une tâche, par des événements a priori non pertinents pour celle-ci, avec pour effet principal une déstabilisation de cette dynamique et une diminution des ressources cognitives disponibles pour cette tâche. L'objectif de cette thèse est d'étudier deux cas de figure fréquents amenant à une forme de déstabilisation de l'attention: les distractions environnementales et ce qu'il est convenu d'appeler le multitâche, c'est-à-dire la tentative de réaliser simultanément deux tâches.

Dans le cas des distractions provenant de l'environnement, mon travail s'attache à comprendre comment un stimulus naturaliste, du type de ceux auxquels nous pouvons tous être confrontés chaque jour, va interférer avec la dynamique neuronale optimale d'une tâche d'attention soutenue jusqu'à entraîner une baisse transitoire de la performance. Dans le cas du multitâche, mes recherches portent sur la manière dont cette même dynamique, lors de l'exécution de la même tâche d'attention soutenue, est parfois incompatible avec celle nécessaire à la réalisation d'une seconde tâche simultanée (une tâche de fluence verbale) au point de créer un effet de goulot d'étranglement cognitif qui force l'exécution séquentielle des deux tâches.

Ces deux études s'appuient sur des enregistrements de l'activité cérébrale humaine à très haute résolution spatiale et temporelle (millimètre/milliseconde) obtenus à partir d'électrodes placées directement dans le cerveau (électroencéphalographie intracérébrale, ou iEEG) lors de la phase d'exploration pré chirurgicale de patients épileptiques résistants aux médicaments. Nous avons enregistré ces patients lors d'une tâche expérimentale conçue spécialement pour mesurer des décrochages brefs de l'engagement attentionnel, de l'ordre de la seconde, la tâche BLAST (Bron/Lyon

Attention Stability Test), présentée de manière exhaustive dans ce document. Cette tâche a été réalisée dans trois conditions expérimentales : d'abord au calme sans distraction, puis à proximité immédiate d'un expérimentateur chargé de se conduire d'une manière distrayante (distractions « naturelles ») et/ou en situation de double-tâche, sous la contrainte de devoir chercher des noms de villes, d'animaux, de personnes commençant par une certaine lettre (tâche de fluence verbale).

La première originalité de ce travail est le recours à l'EEG intracérébrale : si de nombreuses études ont déjà été publiées sur l'effet des distractions et du multitâche sur l'attention, ces études ont privilégié des méthodes d'accès à l'activité cérébrale dites « non invasives » - telles que l'EEG, la MEG ou l'IRMf – qui ne permettent pas une étude fine de la dynamique spatio-temporelle du cerveau en action. Même si l'iEEG a certaines limitations bien connues, liées notamment au fait d'étudier le cerveau de patients souffrant d'une maladie neurologique sévère, la compétence de l'équipe d'accueil concernant la manipulation de ces signaux garantit que des conclusions générales peuvent être obtenues de ces signaux.

La deuxième particularité de ce travail est de s'approcher de situations réalistes : présence de l'expérimentateur à côté du participant, distractions communes liées à son comportement ... un nombre croissant d'études de neurosciences cognitives cherchent à étudier l'activité du cerveau humain dans des conditions rappelant la « vie quotidienne », afin de s'assurer que leurs conclusions s'étendent à la vie d'un être humain au-delà du cadre strict et limité d'une expérience menée dans un laboratoire. Ces études semblent indiquer que le cerveau humain est mieux adapté pour répondre à des scénarios complexes et enrichis qu'à des scénarios simplifiés. C'est un des autres avantages de l'iEEG que de bien s'adapter à des situations dont la valeur naturaliste est forte.

Dans ces conditions, l'étude de la situation de double-tâche révèle un certain nombre de populations neuronales cérébrales sources d'interférences directes et indirectes entre les deux tâches. Ces populations se distribuent dans les régions corticales suivantes : le gyrus/sulcus précentral, le cortex préfrontal dorsolatéral (dlPFC), le cortex temporal latéral (TLC), le cortex insulaire antérieur (AIC), le cortex cingulaire antérieur et l'aire motrice pré-supplémentaire (ACC/pre-SMA), et le cortex temporal basal (TBC).

L'analyse des performances comportementales montre clairement que l'exécution simultanée des deux tâches réduit les performances globales. Nos résultats en iEEG indiquent que les deux tâches nécessitent des ressources cognitives communes – c'est-à-dire l'activité simultanée des mêmes populations neuronales dans les régions précitées - qui ne peuvent être allouées en même temps, de sorte que le système exécutif force les deux tâches à être réalisées l'une après l'autre plutôt qu'en même temps, avec pour effet immédiat une diminution de la vitesse de réponse et une augmentation

du nombre d'erreurs. L'analyse précise de la dynamique de l'activation neuronale de ces régions révèle que les deux tâches sont « dynamiquement incompatibles » - c'est-à-dire que le profil temporel d'activation nécessaire à chacune, même s'il n'est pas parfaitement continu, ne laisse pas suffisamment de temps disponible au développement à celui de l'autre, et réciproquement. Ceci dit, l'interférence semble dans la majorité des cas davantage due à une incompatibilité entre deux stratégies plutôt qu'entre les tâches elles-mêmes : par exemple, la plupart des régions enregistrées – et notamment dans l'AIC et l'ACC, deux régions très impliquées dans le contrôle cognitif - l'activité neuronale est bien moindre pendant les essais les mieux réalisés – avec une réponse correcte et un temps de réaction court – que pendant les essais les moins bien réalisés. Ce résultat laisse penser que la tâche principale peut être réalisée avec la même efficacité en réduisant le contrôle cognitif et en libérant donc des ressources pour la seconde tâche. Dans le cas des autres régions, ces différences d'activité neuronale entre les essais les mieux et les moins bien réalisés est très révélatrice d'un changement de stratégie – abandon d'une stratégie d'encodage en mémoire verbal par exemple, lorsque celle-ci interfère avec la fluence verbale. Cela suggère que dans bien des cas, un changement subtil de stratégie cognitive permet de réduire les interférences entre deux tâches, même lorsque celles-ci ne sont pas automatisées. Ce type de changement de stratégie peut réduire l'effet de goulot d'étranglement au niveau central et l'incompatibilité dynamique entre les tâches. En conclusion, nous pensons qu'un contrôle cognitif excessif lors de l'exécution simultanée de deux tâches exigeantes peut nuire à leur exécution, et qu'il est possible d'obtenir une meilleure performance avec moins d'efforts.

L'étude sur l'effet des distractions environnementales révèle plusieurs populations neuronales recrutées spécifiquement pendant le traitement des distracteurs qui interfèrent avec le réseau nécessaire à la tâche BLAST. Dans la limite de notre échantillonnage spatiale, ces populations se trouvent dans trois régions principales : le cortex insulaire antérieur (AIC), le cortex cingulaire postérieur (PCC) et le cortex visuel extrastrié (EVC).

Après avoir analysé les résultats, nous avons remarqué que les distractions n'avaient pas un impact global sur la performance lors de la tâche prise dans son ensemble, mais plutôt de manière transitoire après chaque distraction. Une suractivation du système exécutif pourrait diminuer l'impact global des distractions sur le système attentionnel, pour maintenir la performance globale intacte. L'AIC et la PCC présentent des profils d'activité différents selon que les essais sont bien réussis ou non, ce qui suggère un effet de détournement des ressources cognitives limitées par les distracteurs menant à des réponses plus lentes, voire erronées. Le profil de réponse aux distracteurs de l'EVC suggère un effet d'ouverture par ces derniers du champ attentionnel visuel, qui devrait au contraire être resserré sur les stimuli présentés en champ visuel central pendant la tâche BLAST. L'un des effets des distracteurs

serait donc de forcer l'ouverture de l'attention, et d'empêcher de centrer les ressources sur la zone visuelle pertinente.

Ces deux études combinées révèlent donc que la distraction, qu'elle soit due à des stimuli extérieurs impromptus ou à une tâche secondaire, bouleverse les équilibres dynamiques fins nécessaires à la réalisation correcte d'une tâche exigeante sur le plan attentionnel. Mais ces bouleversements peuvent être limités grâce à des stratégies adaptées, en particulier grâce à une recherche du niveau de contrôle cognitif minimal pour réaliser correctement cette tâche. Il est fort probable – comme semblent l'indiquer clairement nos données – que nous exerçons généralement un contrôle cognitif exagéré par rapport aux demandes réelles des tâches que nous avons à mener, avec probablement une fatigue trop importante.

Mots Clés

Réseau exécutif; iEEG; SEEG; activité à haute fréquence; approche naturaliste; distraction; double tâche; embouteillage; sérialisation; dynamique incompatible; système de demande multiple; changement de stratégie; cortex insulaire antérieur.

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MAC-AULIFFE Diego

Title of the thesis

“Neural mechanisms underlying external distraction by unexpected environmental stimuli or by a secondary task: an intracranial EEG investigation”

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Abstract

In our everyday lives, efficiency and ease crucially depend on our ability to focus on what we are doing at any given time. From a neuropsychological point of view, it means that we are constantly "on-task", and that our brain always engages resources that are both necessarily and sufficient for the task at hand: at the neural level, this is characterized by a fine balance between activations and inhibitions to ensure that only perceptual, cognitive and motor processes relevant for the task are active, at the exclusion of any other. Yet, practically, such ideal patterns almost never occur because we are almost constantly distracted, most obviously by events in the environment around us, but also by spontaneous thoughts and fruitless attempts to perform several tasks at the same time.

This thesis tries to reveal the deep reasons why distraction has such a profound, detrimental effect on attention and performance. Why does performance drop when we try to perform two difficult attention-demanding tasks at the same time? Why is it so hard to stay on task in a noisy environment? Those questions have already been debated for years, and modelled in many ways, but no study so far had conducted the investigation at the deepest level of the fine neural dynamics that supports our ability to focus. We used the most precise recordings of a living human brain - intracranial EEG recordings with millisecond and milimetric resolution - to examine in two experiments how external distractions and multi-tasking interfere with the optimal dynamics of a demanding, continuous attention task, and we addressed those questions in naturalistic settings, in the context of a direct social interaction to ensure our conclusions extend to real-life situations.

We found that the tight balance between excitation and inhibition is disrupted in key regions supporting attention and executive control for short periods of time, at the subsecond level, but sufficiently to knock the network off-balance and impair performance. Altogether, our results provide explanations for many of the failures of attention of our modern lives and pave the way for new techniques to avoid them.

Keywords

Executive Network; iEEG; SEEG; High-Frequency Activity; Naturalistic Approach; Distraction; Dual-Tasking; Cortex; Bottleneck; Serialization; Incompatible Dynamics; Multiple Demand System; Change of Strategy; Anterior Insular Cortex.

Acknowledgements

As a personal reflection, I must say that doing the doctorate has been one of the most rewarding and enjoyable experiences of my life. I realized this by talking to a friend a few weeks ago, as we were eating our lunches to get back to work. Talking about our lives, future projects and the experience of being a PhD student, he asked me if I would ever do it all over again, and to his uneasiness and astonishment, I answered yes. In fact, I think it took me 2 seconds, 3 tops, to give my answer. Later I forgot about it, until after work, I headed for the tram station. I usually hum some stupid song, or make a schedule of what I should do at home, but sometimes I get lost in my thoughts. So I went through my answer again, and not only did I realize that I would be repeating my whole doctoral experience again, but I would be improving a lot of things which I think I had left undone. It may sound a bit crazy, but the truth is that if I had all the money and time in the world I would do another doctorate without hesitation, and the reason is clear: I like science.

I have always said I started doing science out of selfless passion. In Chile, being a physician is almost a way of solving your life: you secure a good job, get a good salary, and become an important member of society. The truth is that I did not need to be a scientist; and yet here I am, almost at the end of my road and ready to start a new stage as a postdoc, once again away from my homeland and my beloved ones. Yet, I am so happy and grateful for the opportunity, not only to learn from tremendously bright and resourceful people, but also to finally mature and become someone who can contribute something to humanity.

I want to start by thanking my tutor, Jean Philippe Lachaux, whom I consider not only a teacher but also a friend. I had the pleasure of spending 4 years and something by his side, and I realized that having him as my boss I hit the jackpot (he is probably one of the biggest reasons why I would do a PhD again). In spite of his frequent trips, and the fact that we could never agree on him coming to our house for dinner (which is still pending!), he never failed in his duty and always gave me help without hesitation. I promise that at some point I will learn to play ping-pong properly so that in the future, as they say in good Chilean, I will kick his ass (with kindness of course).

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of the lab, and of course, to our director, Olivier Bertrand, who has always been there to help or to deliver a simple hello in the mornings. I would also like to thank each of the members of Eduwell, but especially I would like to send a warm greeting to the whole group of irresponsible people with whom I have or had the pleasure of working: Florian, Mathilde, Adrien, Benjamin, and finally Benoit, who now receives the torch. Besides, I would like to thank all my masochist friends from the laboratory; from those who are still working at DYCOG, to those who have taken new paths: Jelle, Kristien, Stefano, Enrico, Oussama, Arnaud, Prisca, Cony, Laurie-Anne, Marta, Pauline, Hesham, Rapha, Rasa, Francesca, Mélodie, Nicole, Roxi, Mani, Judith... I hope, with all my heart that we meet again to have some beers and good laughs.

I also send a big hug to all the friends I made along the way. Thank you very much for being there in the moments of loneliness, of sorrow, of joy or of simple boredom, and for giving me a good laugh. Know that I treasure every good moment we spend in the depths of my heart, and wherever life takes us, you will always travel in my long-term memory.

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I want of course to thank my parents, Claudio and Mónica, and their infinite love and support. Know that the grandchildren will arrive... at some point. To my Soteli, who I miss very much and always think of her. To my sisters, Rosario and Maria Ignacia, who I would love to have here so that we could travel together, and go out to eat sushi and laugh at any nonsense. To my uncles, cousins, family and friends who, even if I make them lose their patience, always support me.

Finally, and most importantly, I want to thank my partner and sidekick, Mónica. Together we left our lives behind, and only came to France with our love. Here we grew, changed and improved together. We had good and bad times, like every couple, but we managed to move forward, and I can safely say that today I am a better man thanks to her. Thank you for your selfless and unconditional love, sweetie. I love you with all my <3.

There is some much to do

So wrapping up, you probably used a good chunk on the time available to you

If this is our one shot of life, there is no reason not to have fun, and to live as happily as possible

Bonus points if you make the life of people better. More bonus points if you help to build a galactic human empire

Do the things that make you feel good; you get to decide whatever this means for you

Optimistic Nihilism

Kurzgesagt – In a Nutshell

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Lexicon

Electroencephalography – Imaging – Visualization

HFA	→	High-Frequency Activity
HiBoP	→	Human Intracranial Brain Observations Player
iEEG	→	intracranial Electroencephalography
MRI	→	Magnetic Resonance Imaging
SEEG	→	Stereo-Electroencephalography

Tasks and Distractions

BLAST	→	Bron/Lyon Attention Stability Test
DIST	→	Distraction
DT	→	Dual-Task
PRP	→	Psychological Refractory Period
RSB	→	Response Selection Bottleneck
SOA	→	Stimulus Onset Asynchrony
ST	→	Single Task
VFT	→	Verbal Fluency Test

Frontal Locations

AIC	→	Anterior Insular Cortex
dFC	→	Dorsal Frontal Cortex
dIPFC	→	Dorsolateral Prefrontal Cortex
dmPFC	→	Dorsomedial Prefrontal Cortex
FEF	→	Frontal Eye Field
IFG	→	Inferior Frontal Gyrus
IFJ	→	Inferior Frontal Junction
IFS	→	Inferior Frontal Sulcus
LPFC	→	Lateral Prefrontal Cortex
MFG	→	Middle Frontal Gyrus
preSMA	→	Pre-Supplementary Motor Area
SFG	→	Superior Frontal Gyrus
SMA	→	Supplementary Motor Area
vFC	→	Ventral Frontal Cortex
vIPFC	→	Ventrolateral Prefrontal Cortex
vmPFC	→	Ventromedial Prefrontal Cortex

Networks

DAN	→	Dorsal Attention Network
DMN	→	Default Mode Network
MD	→	Multiple Demand System
VAN	→	Ventral Attention Network
WM	→	Working Memory

Parietal and Temporal Locations

BTC	→	Basal Temporal Cortex
IPL	→	Inferior Parietal Lobe
IPS	→	Intraparietal Sulcus
ITG	→	Inferior Temporal Gyrus
LTC	→	Lateral Temporal Cortex
MTG	→	Middle Temporal Gyrus
SPL	→	Superior Parietal Lobe
TPJ	→	Temporo-Parietal Junction

Occipital Locations

EVC	→	Extrastriatal Visual Cortex
FFA	→	Facial Fusiform Area
V1	→	Primary Visual Cortex
VWFA	→	Visual Word Form Area

Medial and Subcortical Locations

ACC	→	Anterior Cingulate Cortex
dSC	→	Superior Colliculus (deeper layers)
LGN	→	Lateral Geniculate Nucleus
MCC	→	Middle Cingulate Cortex
MGN	→	Medial Geniculate Nucleus
PCC	→	Posterior Cingulate Cortex
sSC	→	Superior Colliculus (superficial layers)

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Part I

GENERAL INTRODUCTION

” Behold a worthy sight, to which the God, turning his attention to his own work, may direct his gaze. Behold an equal thing, worthy of a God, a brave man matched in conflict with evil fortune.

– *Lucius Annaeus Seneca*

The human brain is constantly exposed to more sensory information than it can process. Attention focuses processing on the most relevant signals, as defined by current goals, habits and preferences. The factors defining priority, and the focus of attention, often contradict themselves and result in unstable attention, as it can be observed when an individual is distracted by salient, external events during an attention-demanding task, or when trying to perform two such tasks at the same time.

In this thesis, my main objective is to understand the mechanisms by which conflicting goals or stimuli might impair attention selection and lead to suboptimal performance, thanks to a detailed analysis of the disruption of the large-scale neural dynamics of a well-defined attention-demanding task. I will particularly study the interferences caused by multi-tasking and by external distractions, and their effects of the neural activity measured at high spatial and temporal resolution with intracranial electroencephalography (iEEG). All studies will be done in conditions as naturalistic as possible, so that their conclusions can directly be applied to real-life situations.

” *Any man who can drive safely while kissing a pretty girl is simply not giving the kiss the attention it deserves.*

– *Albert Einstein*

The human brain is able to compute only a limited amount of information from the surrounding world, due to a lack of processing power. This limits for instance the ability to perceive consciously several simultaneous stimuli in rivalry conditions, or in rapid succession, a phenomenon known as the attentional blink.¹ This lack of power is associated with a limited amount of cognitive resources,² which can be optimized by focusing them using attentional control. This would allow to perceive a target and to perform a goal-oriented decision as a task.³ Incoming stimuli therefore compete for attention, to gain access in some cases to cognitive resources. Some stimuli have intrinsic qualities that make them stand out from the rest, known as saliency.⁴ A stimulus with high saliency can attract attention automatically in a bottom-up way, and bypass attentional control. On the other hand, attentional control allows one to select a low saliency stimulus that is relevant for ongoing behavioral goals. Such control is implemented by higher cognitive areas capable of guiding attention in a top-down fashion.⁵

Allocating attention to an exogenous target involves several brain systems and networks, distributed in both cortical and subcortical areas.⁶⁻⁸ When attention focuses on an external stimulus, neural activity triggered by that stimulus ascends towards primary sensory areas, and then to sensory integration areas which build a more finished and abstract concept of the stimulus.⁸⁻¹⁰ Finally, this information reaches amodal areas located in frontal and parietal parts of the brain,¹¹ where it is evaluated with respect to the objectives, previous experiences and preferences of the individual, to reach a decision regarding the fate of that stimulus (*see Fig. 1*).¹² In classic stimulus-response paradigms, the process culminates with the motor execution according to task rules. The whole process can be seen as a classification procedure which ultimate goal is to save cognition for events that are important and optimize perception for ongoing goals.^{11,13} This procedure occurs practically in most daily life situations, such as reading a book without losing track of it.

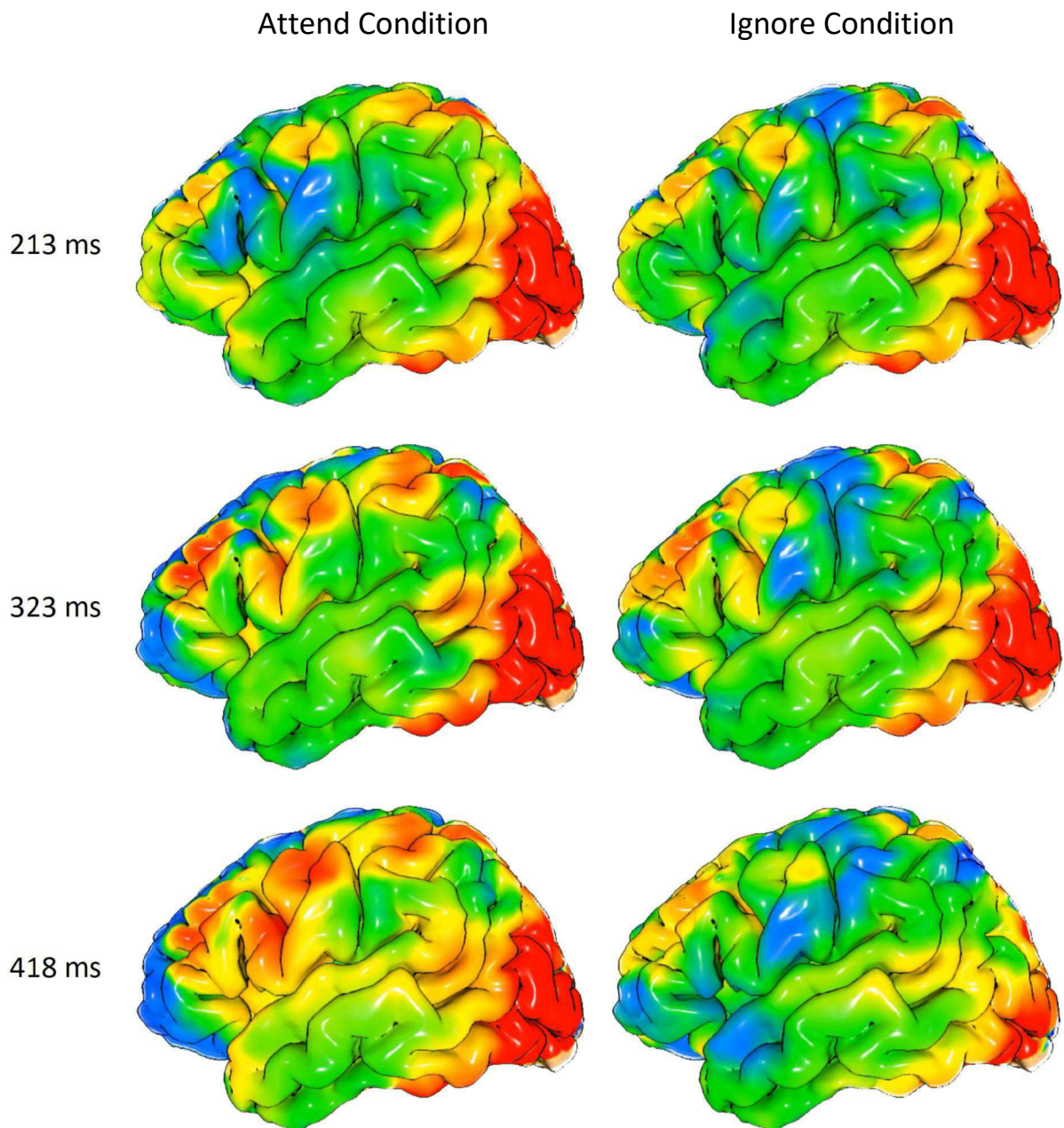


Figure 1: Endogenous attention orientation mixes with exogenous attention orientation. This image shows the cortical dynamic during an Attentive Reading Task, contrasting an attend condition on the left vs an ignore condition on the right at 213, 323 and 418 ms after the stimulus onset, with a divergent increase of activity in red in the attend condition after 300 ms. This helps to illustrate how exogenous and endogenous factors combine until the response selection process and motor execution. Finally, this whole process will be updated thanks to perceptual feedback due to online performance monitoring.

The orientation of attention is most often modelled through the action of two complementary networks, firstly conceptualized by Corbetta and Shulman¹¹ (see Fig. 2): a) the Ventral Attention Network (VAN), which allows the perception of relevant, or salient but irrelevant stimuli from the environment;¹⁴ b) the Dorsal Attention Network (DAN), which allows the selection of sensory stimuli based on goals and expectations, and links them to appropriate motor responses.^{14,15} Nowadays, it is widely accepted that both networks interact to determine where and to which target should be paid attention.¹⁶

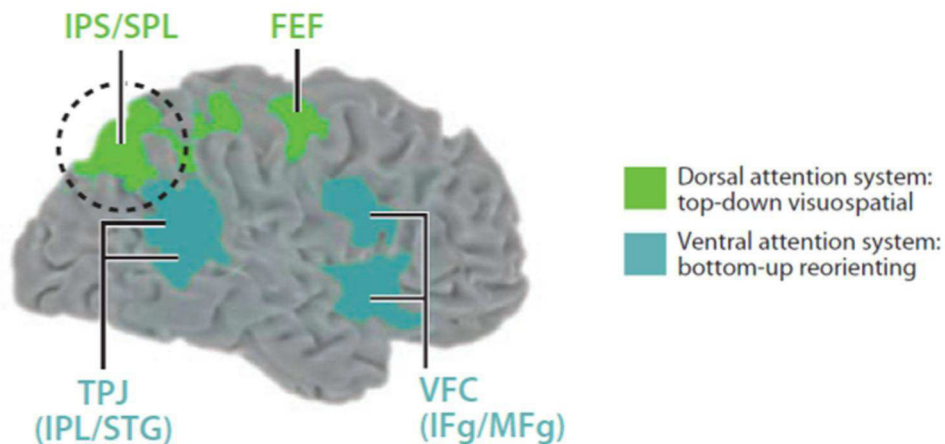


Figure 2: The Dorsal and Ventral Attention Networks. Taken from Petersen and Posner.¹⁴

The VAN comprises the Temporo-Parietal Junction (TPJ), and a large portion of the ventral Frontal Cortex (vFC) with the Inferior Frontal Junction (IFJ), composed in turn by the Middle and Inferior Frontal Gyri (MFG and IFG, respectively) (see Fig. 2).^{14,15} The VAN essentially responds to events and objects which lie outside of the current focus of attention, and which properties are not immediately relevant to ongoing behavioral goals.

The DAN comprises the Frontal Eye Field (FEF) in the dorsal and posterior frontal lobe, and an area close to the Intraparietal Sulcus (IPS), including the Superior Parietal Lobe (SPL) (see Fig. 2).¹⁴ In contrast to the VAN, the DAN mainly implements goal-driven attention,^{14,15} guiding perception through top-down signals through dynamic interactions with bottom-up information to implement rapid control over both overt and covert shifts of attention. It is crucially involved in standard attentional search, when specific targets must be found which match behavioral goals.

2.1 Searching for the Filter

The DAN plays a central role in filtering out stimuli that are irrelevant for the task-at-hand. Historically, several lines of arguments have been proposed to identify how this filtering process operates, and importantly, at which stage of sensory processing.

In broad terms, a first hypothesis, heralded by Broadbent,¹⁷ suggests that filtering occurs in the early stages of sensory processing, to discard elements which properties do not match target-defining properties (i.e. the specific timber of an instrument you're specifically listening to in an orchestra). Alternatively, a second view defended by Deutsch and Deutsch¹⁸ among others suggested that perception includes an early, automatic and parallel stage during which all stimuli are processed independent of their relevance for the task. That early analysis could not be "turned off". According to that view, attentional filtering would occur at later stages of processing, including for instance semantic analysis; which would allow a selection based on meaning, among other high-level properties, and not solely basic physical properties of the stimulus, as in the early selection model. Treisman¹⁹ then introduced a third possibility – or "thin" filter – in which irrelevant stimuli would not be blocked from the very start of sensory processing, but attenuated or weakened, in relation to their resemblance with task-relevant items: elements sharing some characteristics of the behavioral targets would be processed more extensively than very dissimilar stimuli.

In contrast with the previous views, which all suppose a common pool of resources shared by all incoming stimuli, Wickens²⁰ proposed that cognitive resources might in fact be parted into separate and independent reservoirs. The proposal predicts that it should be possible to process different stimuli simultaneously if they do not compete for the same reservoir of resources (e.g., visual and auditory stimuli), while stimuli of a same kind would interfere (e.g., only visual stimuli), and conflict with each other.²¹ This proposal has been refined by several authors, such as Young and Stanton²² who proposed that the size of these reservoirs might not be static, but change according to the features and demands of the task at hand.

2.2 Searching for a Target

The implementation of those ideas – and their relation to the DAN/VAN dichotomy – can be understood during the paradigmatic example of the visual search: searching for a predefined object among others. When searching for a target with particular features (e.g., a friend in a blue t-shirt and white cap), elements with physical characteristics markedly different from the target (e.g., people

wearing other colors) cause little or no delay to the search process.²³ This effect can be understood in the context of the Biased Competition Theory proposed by Desimone,²⁴ which proposes that visual processing can be biased by prioritizing certain features of an object (e.g., blue or white color) or an item (e.g., a T-shirt or a cap) over others, later influencing attention and cognitive processing.^{25,26} Within that model, attention would facilitate or inhibit any perceptual process flexibly through the DAN,^{27,28} so that the desired target could access into memory at the expense of irrelevant elements.²⁹

If the physical attributes of the target differ markedly from surrounding distractors, the search can be completed in a short time, regardless of the number of elements within the search array. The target is said to "pop-out" in a phenomenon known as "efficient search".^{30,31} However, when the target is characterized by a combination of features, rather than a single distinctive one (e.g. the same friend in a blue shirt and a white cap in the middle of a crowd of people wearing either blue shirts or white caps) the search becomes sequential with a one-by-one inspection of all items matching some aspects of the target, through voluntary attention shifts until the target is found.³² The search duration increases linearly with the number of elements in the search array, in a phenomenon known as inefficient search.^{30,31}

Efficient search would largely depend on a first stage of feature-level preattentive perception, mainly at the level of sensory cortices and adjacent areas, that would process all stimuli in parallel, while inefficient search would require a second sequential stage involving directed attention according to task demands,³⁰ and fronto-parietal areas of the DAN orienting network.^{33,34} According to this view, the fate of incoming stimuli would crucially depend on the interface between pre-attentive and attentive processing, which might mark a turning point in the entry to conscious awareness. Incidentally, a sensory stimulus could be processed and yet not be consciously perceived, before sequential top-down attentive processing.^{35,36}

A finer view of that turning point reveals that sensory features perceived pre-attentively by the primary visual area (color, brightness, motion, and edge orientation) are integrated into first- or second-order visual areas as feature maps.³⁷ Subsequently, this information is normalized and compiled pre-attentively in a "binding" parallel process, integrating into second-, third-, or fourth-order visual areas,³⁸ creating two-dimensional saliency maps.³⁹⁻⁴¹

This information would then interact with higher sensory, associative, and lower cognitive areas, to create a "priority map", which highlights those elements that stand out most intensely in the saliency maps because of intrinsic physical features (e.g. a shining cap),⁴¹ but also those that possess characteristics defining the ongoing behavioral targets (what needs to be found) based on signals descending from higher cognitive areas.⁴² Visual attention would spontaneously shift in space

according to the priority map, which implies that attention scan paths would be determined by a conjunction of bottom-up information and top-down signals.

If we consider a simple example, where an observer looks at someone jogging around a football field (see *Fig. 3*), the perceived information would first be processed automatically, leading to the perception of the colors of the subject's clothing and the background, their brightness, the speed at which the subject moves, and the spatial orientation of the surrounding objects. This information would be organized into specific feature maps, with each map providing important but discrete information about the scene. These feature maps would then be grouped into saliency maps, providing the observer with the ability to perceive the jogger's blue clothing and his speed against the background, standing out against other high saliency elements. Subsequently, this information would proceed from a pre-attentive to an attentive processing mechanism, organizing into a priority map that would contrast whether or not the perceived target matched the downstream control signal from higher cognitive areas (if the observer is trying to see whether he knows the person running, for instance).

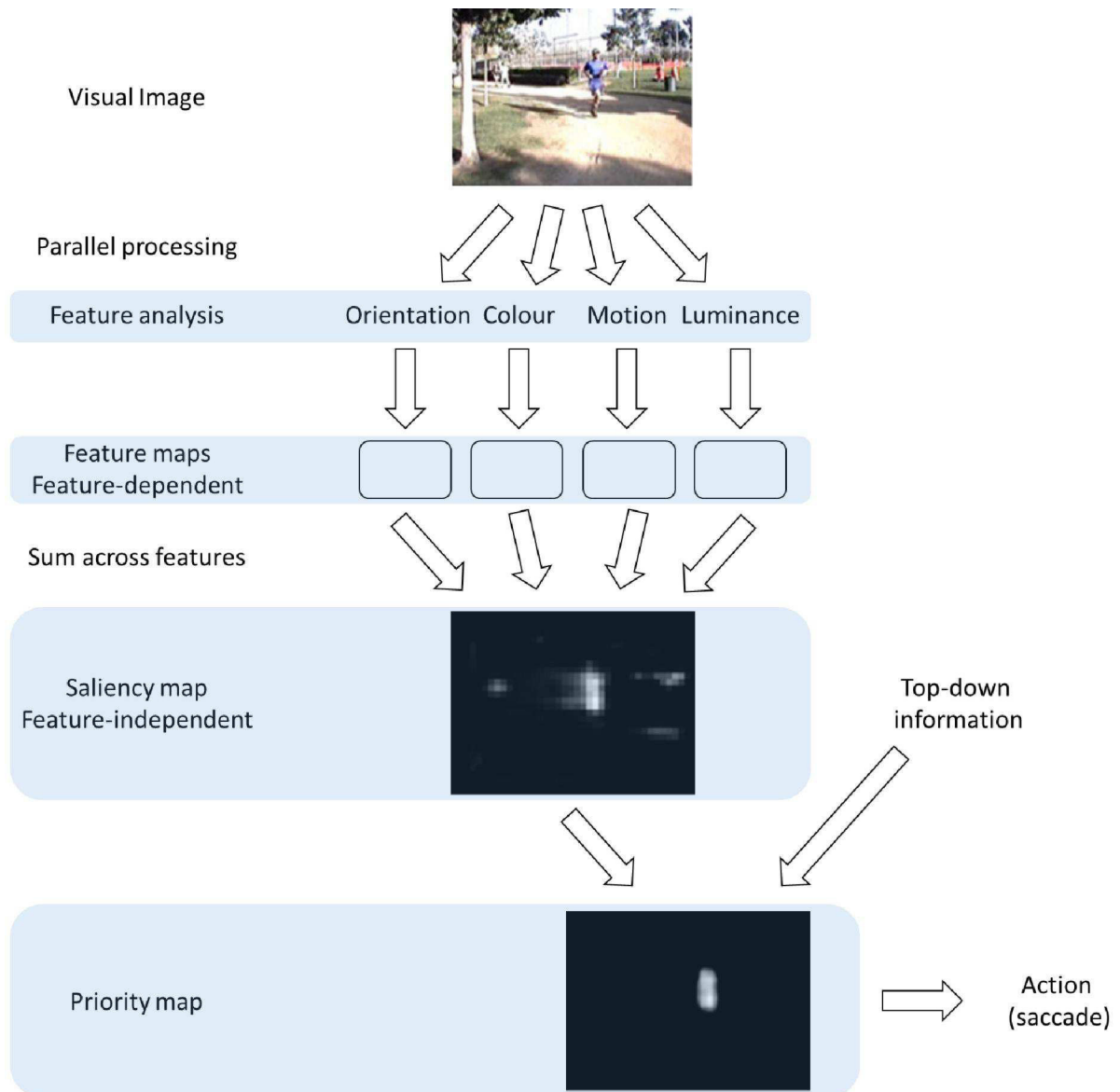


Figure 3: Major steps of the Visual Saliency Model. Visual information is analyzed in parallel at feature analysis and is used to detect noticeable locations at feature maps. Feature maps are then combined to make saliency maps. Then, they are combined with top-down information to make a priority map. Finally, a motor decision is taken (i.e. a saccade). Image based on Veale et al.⁴³

2.3 Attention and Eye-Movement

It follows that in most naturalistic conditions (i.e. with no explicit instructions to keep the gaze still), attention (in particular visual attention) and gaze are tightly coupled. Anatomical studies have revealed two visual pathways to control saccades, starting in the retina and ending in the extraocular muscles.^{45,46} The first route, known as the cortical pathway, enters information through the Primary Visual Cortex (V1) via relays in the Lateral Geniculate Nucleus (LGN) of the dorsal thalamus.^{45,46} According to the Dual Visual Stream model, V1 sends axons to higher visual areas such as V4 (part of the ventral visual stream) and IPS (part of the dorsal visual stream).^{6,47} V4 and IPS project fibers to the superficial layers of the Superior Colliculus (sSC) and the FEF, respectively, which then project fibers to the deeper layers of the Superior Colliculus (dSC).⁴⁸ From here, the information spreads to the brainstem, specifically to the eye movement control centers that manipulate the extraocular musculature.^{45,48,49} The second route, known as the subcortical pathway, begins in the retina and proceeds directly to the sSC, avoiding the LGN.⁵⁰ In these layers, the sSC not only receives fibers from this subcortical pathway, but also from primary visual areas such as V1,^{51,52} others of greater complexity such as V2 and V4, and from the middle (MTG) and posterior inferior temporal (ITG) gyri.^{53–55} Then, the sSC projects fibers through the Inferior Pulvinar towards the IPS,⁵⁶ continuing then to the dSC and FEF, or alternatively sending fibers towards the dSC through internal connections, finally arriving at the brainstem (*see Fig. 4*).

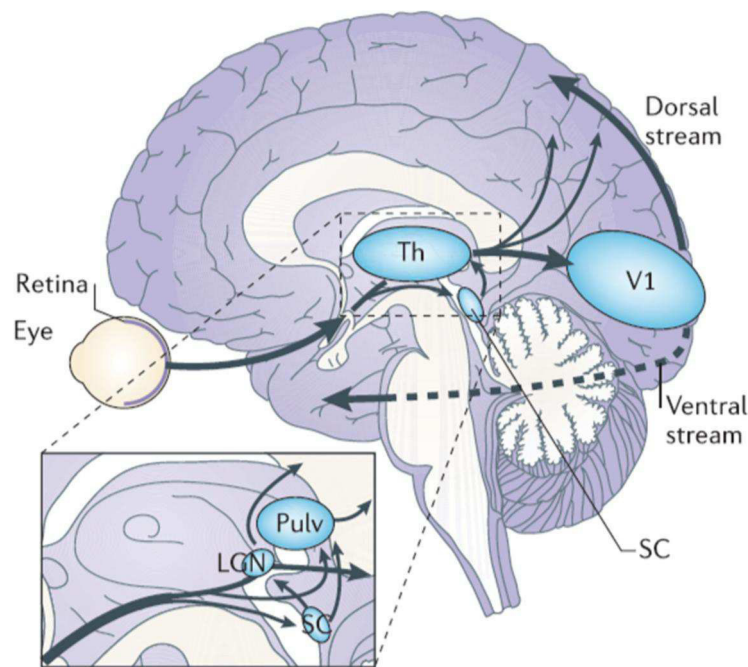


Figure 4: Cortical and subcortical pathways for vision. The majority of fibers (thick arrow) originate from the retina and projects to the primary V1 in the occipital lobe via LGN. From there, it divides into the dorsal and ventral visual streams. However, a minority of fibers originating in the retina take a direct route into sSC and IP, bypassing V1. Taken from Diederich et al.⁵⁷

Given the strong interplay between visual attention and gaze position, one should not be surprised by the fact that those areas are essential components of the cortical and subcortical pathways that can be functionally categorized as feature, saliency or priority maps (see Fig. 5). Whether any of these regions implements more a feature, a saliency or a priority maps can be subtle, but the decision can be based on the fact that local neural activity is solely dependent upon sensory information (feature detection) or upon the response which must be associated with the stimuli (goal-related activity). It follows that neurons of feature maps are expected to react to the specific visual features of a stimulus rather than its global saliency, or goal-related activity (i.e., related to top-down control). Using that criteria, feature maps have been found primarily in the LGN and in V1.⁵⁸⁻⁶¹

In contrast, neurons of a saliency map react selectively to the global saliency of a stimulus, rather than its specific visual features. They are not sensitive either to manipulation of the stimulus-goal relationship and must be organized along a bidimensional topographic map. These strict conditions are met mostly in the sSC and the Inferior Pulvinar of the subcortical pathway.⁶¹ The sSC activates

more intensively when the perceived information from a target matches the cognitive signal,⁶² but do not react strongly to particular visual features.^{63,64} The two regions seem to be related: neurons in the Inferior Pulvinar receive fibers from the sSC,⁶⁵ presenting a similar type of selective activity.⁶⁶

According to Veale and colleagues,⁴³ it is reasonable to think of the existence of a special type of priority map capable of detecting specific features and contrasting them with the cognitive signal, allowing active modulation (*see Fig. 5*). These "feature-specific priority maps" can be recognized as mid-level maps forming part of the cortical pathway, after areas that maintain feature and saliency maps, possibly involving V4 and IPS.⁴³ V4 receives fibers from lower visual areas, and would play a decisive role in selecting the next target to be pursued.^{67,68} It is strongly modulated downstream by the FEF,⁶⁹ highlighting behaviorally relevant stimuli,⁷⁰ transmitting this information to FEF and downstream regions. On the other hand, the IPS responds to the bottom-up information before the top-down signal, constantly interacting with FEF which responds first to the top-down signal and then to the bottom-up information.^{71,72} Priority maps would constitute a final output of that early sensory processing stage, in relation with top-down biasing signals: they would contain neurons that activate in response to global saliency and not selectively to specific visual features, and integrate this general information to mental goals. Areas that most likely fulfil this function are the FEF^{73,74} and the dSC.^{41,43}

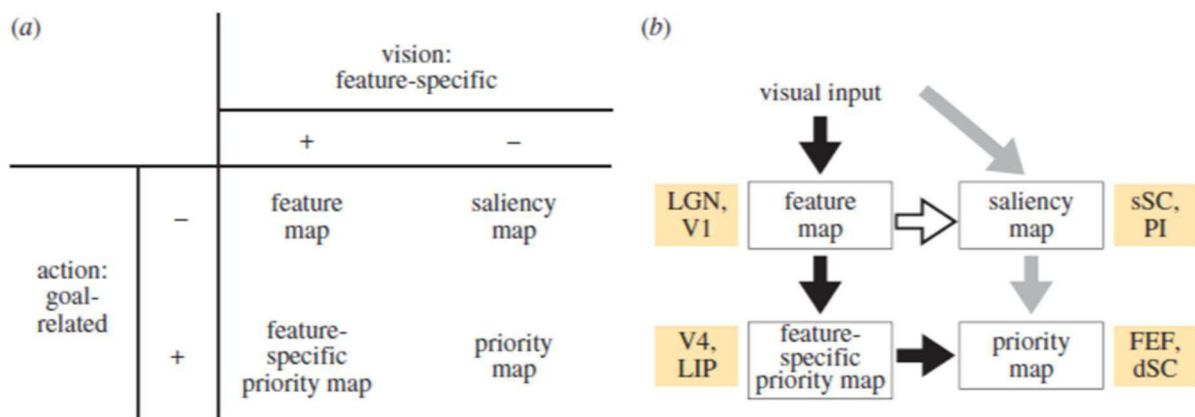


Figure 5: Possible routes for saliency computation. (a) Columns indicate recognition of visual features or not, and rows indicate if maps contain information about behavioral goals or not. (b) Cortical (black arrows) and subcortical (grey arrows) pathways. A white arrow indicates lack of clarity in transferred information from the initial to the following point. LIP in macaques is roughly the same area as IPS in human beings. PI mean Inferior Pulvinar. Taken from Veale et al.⁴³

Note that this architecture is mostly based on, and biased towards, the visual modality. Few studies have searched for saliency maps in relation to other sensory modalities, such as audition. In contrast to the visual system, the auditory system does not seem to have a common metric to define saliency. Although there are cases in which a sound really pops out, such as a fire alarm, in other cases separating someone's voice from the ambient noise already involves attention to separate targets from stimuli, which are not necessarily salient. This suggests that the interplay between a preattentive and an attentive stage of auditory processing, for instance, might not follow a more complex logic than for the visual modality.^{75,76}

In particular, it seems more difficult to define map-based models for ascending auditory information. Yet, a large number of models of auditory attention combining bottom-up and top-down processes have been proposed over the years, informed by numerous studies documenting neural modulation by attention⁷⁷ at several stages of the auditory pathways, in primary auditory areas, as well as in higher auditory areas.^{78,79}

These efforts have led to several models of auditory saliency. The earliest models were primarily inspired by the visual models,⁸⁰⁻⁸² but failed in most cases to capture essential aspects of the auditory modality. Later models based on the specificities of the auditory system operate on the premise that the system must determine whether a sequence of sounds comes from a single source and must be perceived as a single stream, or from multiple sources.^{83,84} According to Bregman, the auditory system performs internal processes in which it organizes complex sequences of auditory signals into coherent streams, corresponding to the source of each sound, forming an auditory stream analysis.⁸³ Attention would then stick to sounds of the same source, while ignoring intervening sounds of alternate sources.

The proposed architecture implies that the auditory system first segregates the sound sequence according to its features (based on continuity and discontinuity in intensity, frequency, time and orientation) simultaneously and pre-attentively. These features would thus integrate into streams sequentially,⁸⁵⁻⁸⁸ the question of whether this occurs in a pre-attentive way or not being still debated.⁸⁷⁻⁸⁹ As At the anatomical level, evidence suggest that pure and combined tone streams are already built up in the nuclei of the brainstem and in primary auditory areas, possibly in interaction with one another.^{90,91}

After that initial stage, streams would reach the "core" of the primary auditory cortex, where neural population would increase the contrast between the target and background streams using a specific mechanism of frequency-suppression, making it easier to focus on a sound of interest.^{90,91} These neurons would have a high attentional and contextual dependence,⁹² probably playing the role of a feature-specific priority map.

Auditory information would then be analyzed separately along the two main pathways of the dual auditory network.⁹³ One of these paths, called the antero-ventral stream, would provide a more abstract interpretation of the auditory information. Its lower sensory areas (the medial geniculate nucleus (MGN), the core and the IFG) would allow auditory switching between different streams depending on the features of the sound. In contrast, the second path, called postero-dorsal stream, would have the ability to direct attention towards a sound or speech anywhere in space. In addition, as for the visual modality, the MGN may possess a subcortical pathway capable of bypassing the auditory core, to interact directly with lower sensory areas such as the cerebellum or the caudate nucleus, and play a role in perceptual switching, detection of sound rhythmicity and novelty.⁹⁴⁻⁹⁶

2.4 Attention and Memory

Attention and memory closely interact with each other, for instance, when a subject realizes that some particular sensory elements are important for what he needs to do, the characteristics of those elements will be stored as a memory trace, which later serves as a template for the task at hand, guiding attention in a top-down fashion and influencing decision-making and behavior.^{97,98} Memory can be subdivided into several specific memory systems,⁹⁹⁻¹⁰³ most of which fall beyond the scope of this thesis; this section will primarily focus on working memory, and its modeling by Baddeley.¹⁰⁴

Baddeley' model describes a specific type of limited-capacity cognitive resource called working memory (WM),¹⁰⁴⁻¹⁰⁶ primarily used to encode and maintain items either drawn from the external environment¹⁰¹ or from long-term memory.^{107,108} WM serves as a dynamic workbench that allows the flexible use of information.¹⁰⁹

WM and attention strongly interact at the level of attentional templates, which characterize the properties of the items an individual should pay attention to and process in priority. This template represents in part the internal goals, previous experiences or preferences of each subject in relation to a particular objective or element. According to Monsell,¹¹⁰ a template is initially acquired through instruction or trial and error, thus the more one practices a task, or the more recent its execution, the easier it becomes to recall it again and activate it into WM.

Attention Templates must be thought in relation to the task-sets,¹¹¹⁻¹¹³ which function as "activation protocols" that guide how higher cognitive areas must modulate the attentional system and other associated networks downstream, in order to achieve a particular goal and update in real-time. With the task-set, templates serve as a guide capable of keeping a goal "in mind", allowing higher cognitive

areas to influence attentional orientation by sending a signal downstream that represents a preconceived idea,^{114,115} against which external information processing upstream must be compared.

Theories differentiate between two states of the task-set^{27,116,117}: an active one with a direct impact on attention, and another - accessory or passive - with no direct effect.¹¹⁶ An active template can behave in a flexible way, facilitating the target selection process²⁷ through different degrees of activation or suppression that varies according to the task demand.¹¹⁸⁻¹²⁰ This means that each template varies its degree of focus, without necessarily following an on/off mechanism. Additionally, upstream information that enters the WM can change the code of the neuronal population dedicated to maintaining active templates regardless of their relevance,^{121,122} behaving in a dynamic way that adapts to change over time.

Early attempts to localize task-sets found neural counterparts solely in the dorsolateral prefrontal cortex (dlPFC).^{123,124} However, more recent studies estimates that task-set are also maintained in the ventrolateral prefrontal cortex (vlPFC) towards the IFJ,¹²⁵⁻¹²⁷ with a variation related to sensory modality of the stimulus and memory trace.¹²⁸⁻¹³¹ Activity patterns in the lateral prefrontal cortex (LPFC) might contain and manipulate information related to templates currently in use, either in an active or passive state,^{123,124,132,133} and contribute to the behavioral performance of new or repeated tasks,¹³⁴ but the distribution of task-related memory content and task-sets might follow a gradient of abstraction, starting in sensory areas that reflect low-level features, ascending to prefrontal regions for more complex features and response-related content.¹³⁵

Yet, the management of templates goes beyond pure LPFC-related activity and extends to additional cognitive areas,¹³⁶ creating a collaborative network. The LPFC itself performs several different types of cognitive functions, such as managing attention reorientation conflicts between the upstream information and downstream signal, novel task-learning,¹³⁷ decision-making,¹³⁸ task switching,¹³⁹ and conflict resolution,¹⁴⁰ but beyond the LPFC, other frontal and prefrontal areas, such as the Premotor Cortex, Anterior Cingulate Cortex (ACC) and Anterior Insular Cortex (AIC) for instance, are consistently activated across a wide variety of these cognitive tasks when control is required in any non-automated task, and when control must be adjusted at task level rather than at trial level.¹⁴¹

As of today, there is still no consensus on how those areas organize into a coherent “executive network”. Yet, one general idea seems to be consensual about that network: it is the source of a top-down regulation of how external stimuli are processed; and feeds back information about performance for future adjustments on lower brain areas.^{14,15}

It is also widely accepted that top-down control is associated with ACC activation,^{14,15} which has even been postulated by some as a gatekeeper to consciousness.^{12,142} Most established is the fact that the dorsal ACC plays a key role in the executive system¹⁴³ and activates in relation to motivation and reward-based decision-making.¹⁴⁴ One particular aspect of motivation, the ability to stay on task and resist the urge to shift to an alternative,¹⁴⁵ has received a lot of interest by researchers interested in behavioral flexibility and implemented in computational models of the ACC.¹⁴⁶

The dorsal ACC constantly communicates with the AIC,¹⁴⁷ providing fast and efficient connectivity for top-down control. Both areas harbor a specific type of neurons called Von Economo neurons,¹⁴⁸ which are a specific type of brain cell found only in higher apes and humans, elephants and big-brained cetaceans. Although speculative, one popular idea is that those neurons are important computational components of self-regulation and willpower so developed in those species.

Nowadays, the most important debate is on whether the executive network follows a single or a dual organization. Proponents of the single organization, known as Unified Control Theory, propose that the dorsal ACC plays a leading role as a key area,^{149,150} while the dual organization, known as Dual Control Theory, favors a different view with two different and separate control networks, in which the role of the dorsal ACC is not so prominent.^{147,151}

According to the Unified Control Theory or Conflict Monitoring Theory, the dorsal ACC detects conflicts between incoming bottom-up information and top-down signals informing about behavioral goals, and makes the decision about whether the incoming signal should be processed further, with a report to the LPFC, which would in turn provide control over the orientation network, direct attention and influence perception.^{149,150,152,153} Within that framework, anterior parts of the LPFC would receive the instruction first from the dorsal ACC, actively maintain memory templates and goal representations in a rather abstract and amodal fashion, and then influence downwards,^{154,155} along a caudo-rostral hierarchical gradient, portions of the LPFC involved in more concrete representations of the task-set.^{156–158}

In contrast, the Dual Control Theory is reminiscent of other “dual-networks” such as the DAN/VAN network and suggests a division between a Fronto-Parietal network and a Cingulo-Opercular network.¹⁴¹ Both networks would work independently, but none of them could by itself establish a direct and constant communication with other cognitive areas: it is the interplay between the two networks that would implement a parallel control following a rapid-adaptive/set-maintenance model, constantly receiving external feedback.¹⁴⁷

The Fronto-Parietal network would comprise the dlPFC, the dorsal Frontal Cortex (dFC), the Middle Cingulate Cortex (MCC), the IPS, the Inferior Parietal Lobe (IPL) and the Precuneus (*see Fig. 6*).^{14,15} It would activate at task initiation, especially during the first presentation of a target or cue, during the switch to a new task, in response to errors and while adapting in real-time to task requirements.^{14,15}

In contrast, activity of the Cingulo-Opercular network would be stable during the task as long as the rules remain unchanged; it would most act as a background support for constant performance (an “energizer”).^{14,15} It includes the dorsal ACC, the medial Superior Frontal Cortex (msFC), the area around the AIC and frontal operculum (AIC/fo), the anterior prefrontal cortex and the Anterior Thalamus. Additionally, the cerebellum seems to act as a link between both control systems, carrying error information and triggering error related activity, making an indirect connection between the thalamus with the dlPFC and the IPL (*see Fig. 6*).¹⁴¹

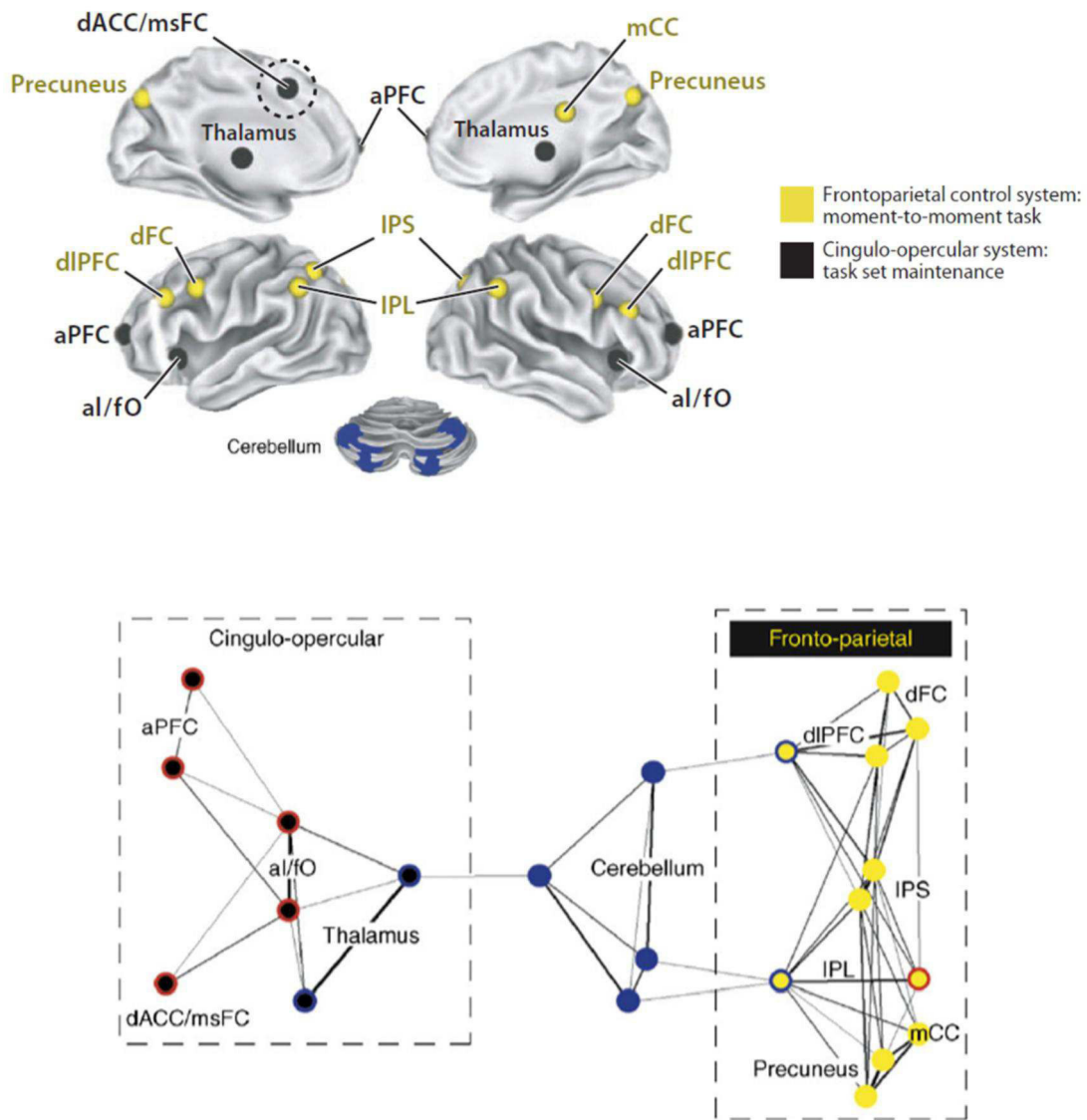


Figure 6: The Executive Network. Top half: Distinct cingulo-opercular (black) and fronto-parietal (yellow) control networks, in addition to cerebellar regions (blue circles) are shown on an inflated surface rendering of the human brain. Bottom half: Black lines indicate strong resting state functional connections between brain regions. The thickness of the lines indicates the relative connection strength. For each region (circle), the central color indicates to which network it belongs. The outer color indicates the predominant control signal type of each region (red = set-maintenance; blue = error-related and yellow = start cue-related). The cingulo-opercular and fronto-parietal networks are not directly connected to each other but each network is connected to the cerebellar error-network through regions that also carry error information (the Thalamus, dIPFC and IPL). Taken from Dosenbach et al. ¹⁴¹

Another influential theory proposes instead the existence of a Multiple Demand (MD) System (*see Fig. 7*),¹⁵⁹ which brings together a number of frontal and parietal areas into a general supramodal control system.^{160,161} Experimentally, all components of the MD system – the dIPFC (the Inferior Frontal Sulcus (IFS) and MFG), the AIC/fO, the precentral gyrus, the Supplementary Motor Area (SMA), the pre-Supplementary Motor Area (preSMA), the ACC and the IPS¹⁶² – are active during executive control processes.^{163,164} The network is conceptualized as a whole in which all components closely interact with each other and constantly exchange information. Its activity usually increases with the increasing difficulty of the task at hand,^{162,165} starting by recruiting parietal and frontal posterior regions, and then expanding to anterior regions as demand and complexity rises.^{160,166}

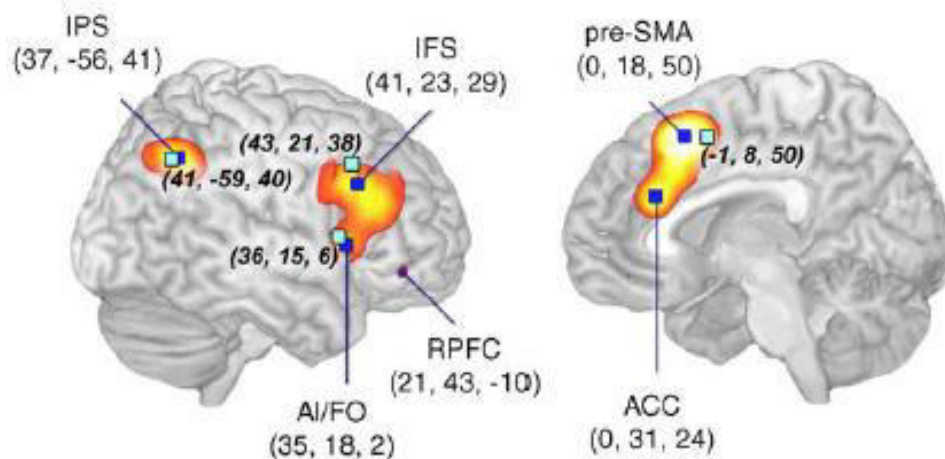


Figure 7: The Multiple Demand System. This system is responsible for managing goal-directed attention, as well as managing stimulus-directed attention when exogenous stimuli match endogenous objectives. Taken from Duncan et al.¹⁵⁹



The secret to multitasking is that it is not actually multitasking. It is just extreme focus and organization.

– Joss Whedon

Human beings are often inefficient at dividing their cognitive resources among multiple targets and performing multiple attention-demanding tasks, usually being able to execute only one task at a time. These limitations are central to a debate with broad social significance, such as the use of cell phones while driving, among other similar examples (see Fig. 8).

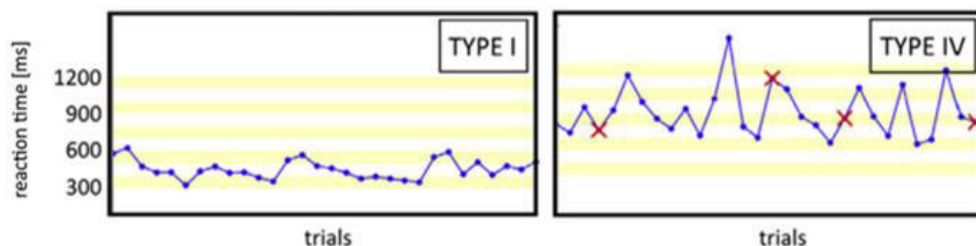


Figure 8: Comparison between an on-task and off-task performance. On the left panel, it is possible to observe the performance of a participant executing an attention-demanding task, with each blue dot signalling the response to a specific trial, with fast and accurate responses. On the right panel, it is possible to observe the performance of the same participant off-task, with slower and less accurate responses, forcing mistakes marked as red crosses. This probably happens because the participant engages in task-irrelevant cognitive processes. Taken from Petton et al (2019).¹⁶⁷

Early studies on divided attention videotaped subjects watching a basketball game while superimposed a hand-slapping game.¹⁶⁸ Subjects could successfully monitor one activity at a time while ignoring the other, but they had great difficulty trying to monitor both at once. Following these

results, the researchers hypothesized that the subjects would likely show an improvement in both task performance after practice.¹⁶⁸

Other seminal studies have used multi-tasking paradigms asking participants to read short stories while typing a dictated text.¹⁶⁹ The researchers compared and contrasted the latency and accuracy of performance in each of the three conditions (i.e., both tasks separately and both together). As expected, the initial performance of doing both tasks at the same time turned out to be quite poor compared to tasks alone. However, researchers tested subjects after practicing the two tasks 5 days a week for almost 85 weeks in total. Eventually, subjects showed an improvement in reading speed, reading comprehension, and increased recognition of written words during dictation. Subjects' performance on both tasks improved to the level of matching the performance of each task performed individually.¹⁶⁹

Additionally, the authors observed that when the dictated words were semantically related (e.g., rhymed or formed a sentence), the subjects did not notice that relationship before training, but did so after repeated practice.¹⁶⁹ These results suggest that controlled tasks could be automated, and liberate cognitive resources for high-level processes.

However, Pashler¹⁷⁰ claimed that no task can be fully automated, and always involve an intentional and conscious component involving high level cognitive processes and some level of control. According to Posner and Snyder,¹⁷¹ our limits in performing multiple tasks suggest that our ability for control is limited, opening up a completely different approach when studying divided attention.

Multitasking (MT) refers to situations when an individual performs two (or more) tasks involving the same cognitive processes at the same time.¹⁷⁰ This overlap prevents both tasks to be done independently of each other and with no interference, creating a situation of competition for shared limited resources.¹⁷² This notion is important because, instead of just indicating structural limitations (e.g., two tasks requiring activation of the same brain area), it also indicates functional limitations (e.g., two tasks requiring activation of the same brain function).¹⁷³ As an example, a structural limitation would occur when we try to drive a car and look at a map at the same time, while a functional limitation would occur when a phonological representation is used to encode heard words while reading sentences aloud.

The most studied experimental paradigms for MT are the Task Switching paradigm and the Dual-Task (DT) paradigm. Although both share similar features, they have led to quite separate lines of research (i.e., empirical and theoretical developments processed more or less separately).^{110,174} In the Task-Switching paradigm, the presentation of stimuli (i.e., S1 and S2) and their respective responses (i.e.,

R1 and R2) occur in a strictly sequential way (i.e., S1 - R1 - S2 - R2; or task 1 - task 2; or T1 - T2), whereas in a DT paradigm, the presentation of external stimuli occurs collectively before the response (i.e., S1 - S2 - R1 - R2) (see Fig. 9).

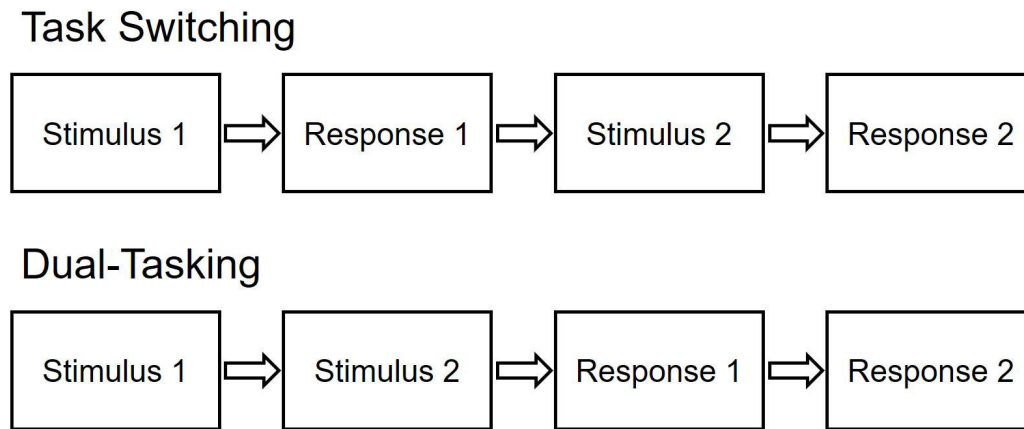


Figure 9: Comparison between Task-Switching and Dual-Tasking. As previously mentioned, in the Task-Switching the presentation of the stimuli and their respective responses occur in a strictly sequential way (i.e. stimulus-response), while in the DT paradigm, the presentation of external stimuli occurs before the response. Adapted from Strobach et al (2018).¹⁷⁴

3.1 Task Switching

In a Task Switching paradigm, subjects are usually presented with a stimulus that allows them to take more than one action (responses); they are asked to choose one of these actions, execute it and then continue with the following stimulus. For example, if a screen presents a letter next to a number (e.g. G7), the first task (or T1) would be to answer whether the letter is a vowel or consonant; then the second task (or T2) would be to answer whether the number is odd or even. In such circumstances, successful performance would require maintenance of the currently relevant task and careful selection of the response (T1), along with sufficient flexibility to update the task-set for the next task (T2).

When the performance of both single tasks (e.g., T1-T1-T1-T1 or T2-T2-T2-T2) is compared with both switched tasks (alternating tasks; e.g., T1-T2-T1-T2) and the difference between them is calculated, the resulting value is known as switch cost.¹⁷⁵ According to Roger and Monsell,¹¹¹ the switch cost reflects the time it takes for the cognitive system to reconfigure the current task-set and replace it

with the relevant parameters for the next task. It is important to mention that the concept of task-set in task-switching is lax and usually confused with the concept of attentional template, so we will be careful to use them under the definitions already provided.

Theoretically, switching between two tasks requires changing the attentional template (i.e., a full template reconfiguration), since the template applied in the previous trial is not necessarily valid for the next trial. In contrast, when the same task is maintained, no reconfiguration is needed, since the template applied in the previous trial is still valid for the following trial. Reconfiguring a template would lead the executive system to change the way systems are activated downstream, in a process called task-set reconfiguration.¹¹¹ This carries a reconfiguration cost, which can be reduced with enough preparation time before the target appears, for example by explicitly displaying a cue.¹⁷⁶ However, even with enough time, a small but consistent residual switch cost remains,¹³⁶ leading to the possibility that this process may have an inherent limitation associated with it.

Several studies have tried to manipulate the switch cost by creating mixed conditions, presenting trial sequences that allow both task repetition and switching within the same block (e.g., T1-T1-T2-T2). It then becomes possible to study repetitions and switches, and compare the settings at task-set level. Thus, subjects would not only need to switch activity between tasks, but would also need to maintain two passive templates at the same time in the WM.

However, when switches are mixed with repetitions in more complex ways (e.g., T1-T1-T2-T1-T2-T2), uncertainty increases. Therefore, part of the difficulty of mixed blocks would come from the lack of preparation that would affect all types of trials.¹⁷⁷ Even though performance would recover quickly after switching between tasks, responses would be slower than when executing only one task per block.^{136,177,178} Because repeated trials benefit more from predicted sequences than switched trials,¹⁷⁹ the sum of their individual performances would produce a "global" switch cost known as a mixing cost.¹⁸⁰

Another way to manipulate the switch cost is through voluntary task switching: executive control processes regulate what particular behavior should be carried out when there are multiple responses or tasks to choose from for a given stimulus.¹⁸¹ Using the example previously discussed (e.g., G7), it would become possible to answer whether the letter "G" corresponds to a vowel or a consonant using two different fingers of the left hand, as well as whether the number "7" is odd or even using two different fingers of the right hand.

Standard methods of task switching provide strict experimental control with factors such as setup time and transition, which allows for systematic investigation of parameters that influence switching

processes. In contrast, voluntary task switching swaps control for an environment in which task selection becomes a component of behavior. The main feature of voluntary task switching is that the task to be performed can be selected by the participant from trial to trial, without being imposed by the experimenter. This situation is interesting because it echoes experimental results showing that the switch cost increases more when subjects are forced to switch between targets driven by an external source than when they select them freely from "an internal source".¹⁸²

3.2 Dual-Tasking

During a DT paradigm, two consecutive stimuli (i.e., S1 and S2) traditionally occur. Early DT studies used a simplistic stimulus-response (S-R) structure,¹⁸³ while later studies proposed a more complex and more naturalistic DT paradigm with several possible responses for each stimulus.³ For example, an auditory stimulus could be one of two different sounds (i.e., S1 sounds like /yaya/ or /haha/) while a visual stimulus could present two different faces (i.e., S2 could be a male or female face). After choosing one of the possible responses for each stimulus (e.g., S1a and S2b), they must be executed as sequential motor tasks (i.e., R1a and R2b), by speaking aloud (i.e., /yaya/ for R1a) and by pressing a button (i.e., female face for R2b).

Both simple and complex DT paradigms require that participants perceive stimuli, either simultaneously or separated by a time interval, hold the information in memory, and chose a response among several while the two tasks keep going. In such designs, the processing of two simultaneous stimuli always comes with an associated cost, called DT cost. Although there is no clear explanation to justify its existence, the "dual task vs. single task" phenomenon correspond to a difference in performance between the two tasks performed individually (i.e., T1 or T2) vs. both combined (i.e., T1 and T2).¹⁶⁹ Results show that the performance of a single task is always be worse when it is executed in combination with another task than when it is executed alone.^{170,184}

It is widely accepted that the DT cost is due to a theoretical construct called the Psychological Refractory Period (PRP)³ which can be described as a cognitive limitation at a central, response selection (RS) stage,¹⁷⁰ when a response must be associated to the incoming stimulus (*see Fig. 10*).

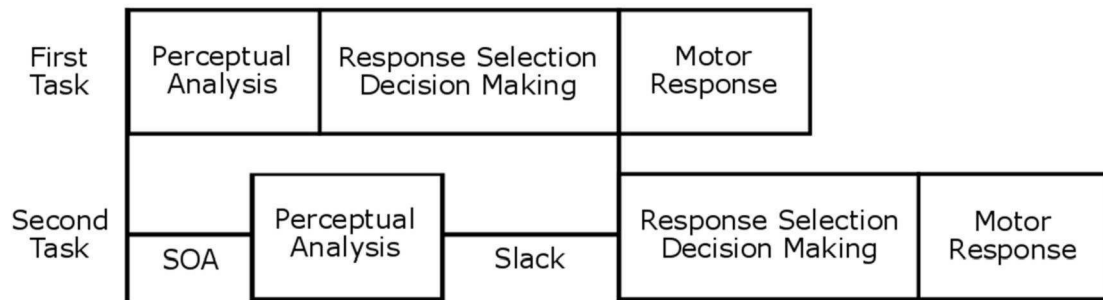


Figure 10: The PRP phenomenon. During this, both stimuli appear at the same or different times. The time difference between stimuli presentation is called SOA. After perceiving S1, information enters cognitive areas, allowing a RS1 and R1. Despite that S2 can be perceived overlapped with S1, RS2 experiences a delay or slack, delaying its R2 and affecting performance. Thus, RS2 cannot be completed before RS1. Taken from Pashler.³

That limitation would prevent tasks from proceeding at the same time, while the peripheral stages (i.e., perception and motor response) could occur in parallel. During DT, one of the tasks would keep the RS busy, forcing the other into a standby state until central resources are available again. As such, when two relevant stimuli are shown (i.e., S1 and S2) with a variable time separation known as Stimulus Onset Asynchrony (SOA),³ the cognitive processing of the first stimulus (i.e., RS1) would delay the cognitive processing of the second stimulus (i.e., RS2) and its response (i.e., R2) if the SOA is too short (see Fig. 10).

Since RS occurs in shared neuronal populations with limited resources, the task that is processed first (i.e., T1) would consume a large portion of those resources, preventing the processing of T2 and creating a Response Selection Bottleneck or RSB.^{3,170,185,186} This RSB would only allow one task to occur at one time due to its rigid single channel structure, operating as an "all or nothing" mechanism.^{187,188} Additionally, the longer the time required to complete RS1 (i.e., the higher the SOA between S1 and S2), the longer RS2 will be delayed. This would lead to a progressive deterioration of T2's performance without affecting T1's performance, resulting in the so-called PRP effect (see Fig. 10).³ Additionally, manipulating the difficulty of RS2 (e.g., varying S-R compatibility, number of alternatives per response, or number of repeat responses) can lead to an increase in overall processing time in T2, independent of SOA and RSB, resulting in an additive pattern on the effects of SOA (see Fig. 11).^{189,190}

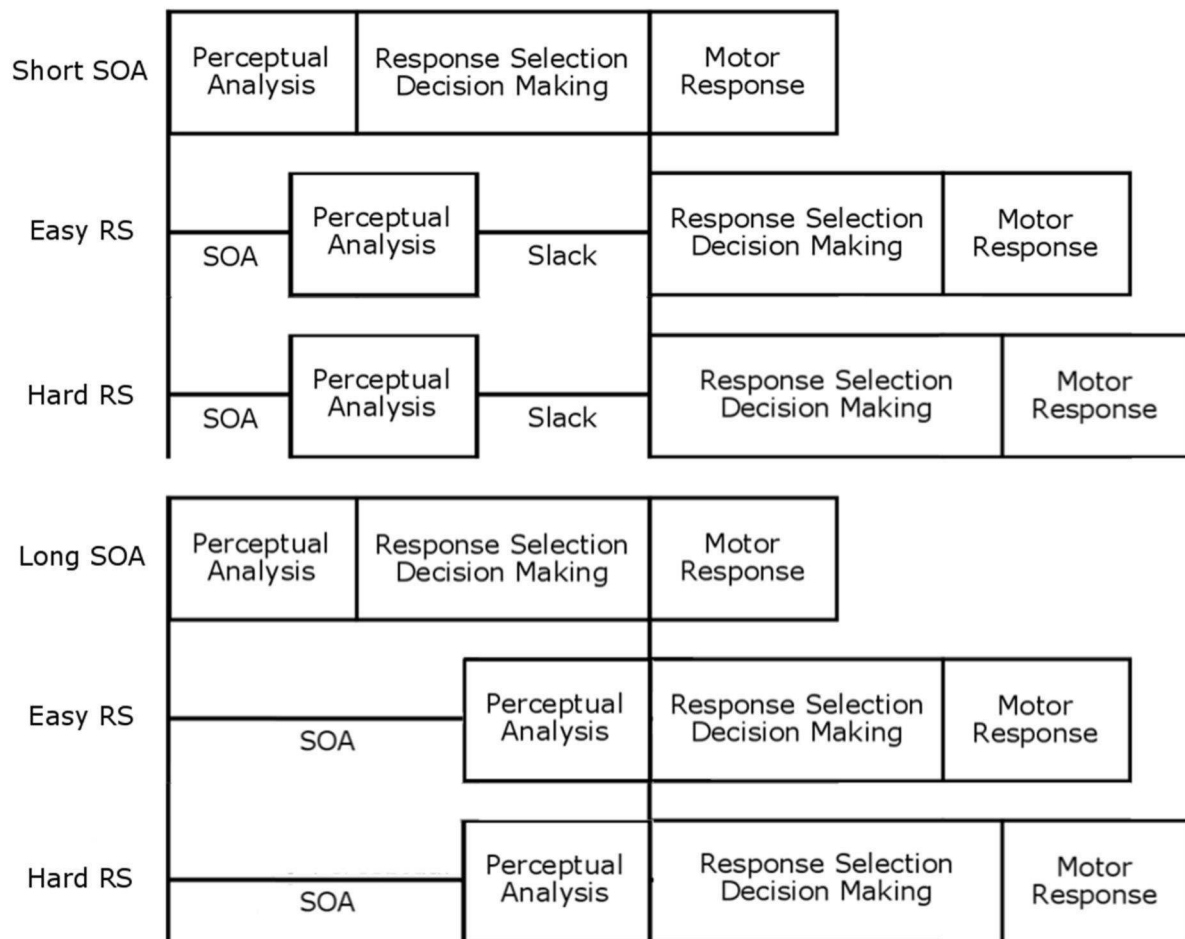


Figure 11: The additive effect of the RSB. The bottleneck is located at the response selection stages. Therefore, at short SOA an interruption emerges in the Task 2 chain before the response selection stage. An increase of the processing time in the RS2 stage leads to an increase of the processing time in Task 2 in the hard compared to the easy condition independently on SOA. This results in an additive pattern of the effects of SOA and difficulty on the response times in Task 2. Adapted from Schubert et al.¹⁹⁰

Alternatively, Schumacher and colleagues¹⁹¹ reported a sub-additive interaction in the overall processing time in T2, where manipulation of the difficulty of RS2 would lead to a smaller effect than mentioned above. They found that after a brief practice, the manipulation of S-R compatibility went from creating an additive effect to a sub-additive effect, finding a more important result when there is a shorter SOA than a longer one. They justified this finding by stating that the bottleneck is not located at the RS level, but at a later stage (i.e., at the motor response stage), so RS1 and RS2 can be

processed in parallel. In this way and during a short SOA, an increase in T2 difficulty (i.e., an increase in RS2) would be absorbed by the cognitive motor delay, while at a long SOA there would be no cognitive delay, so the increase in RS2 difficulty would only increase T2 processing time (see Fig. 12).

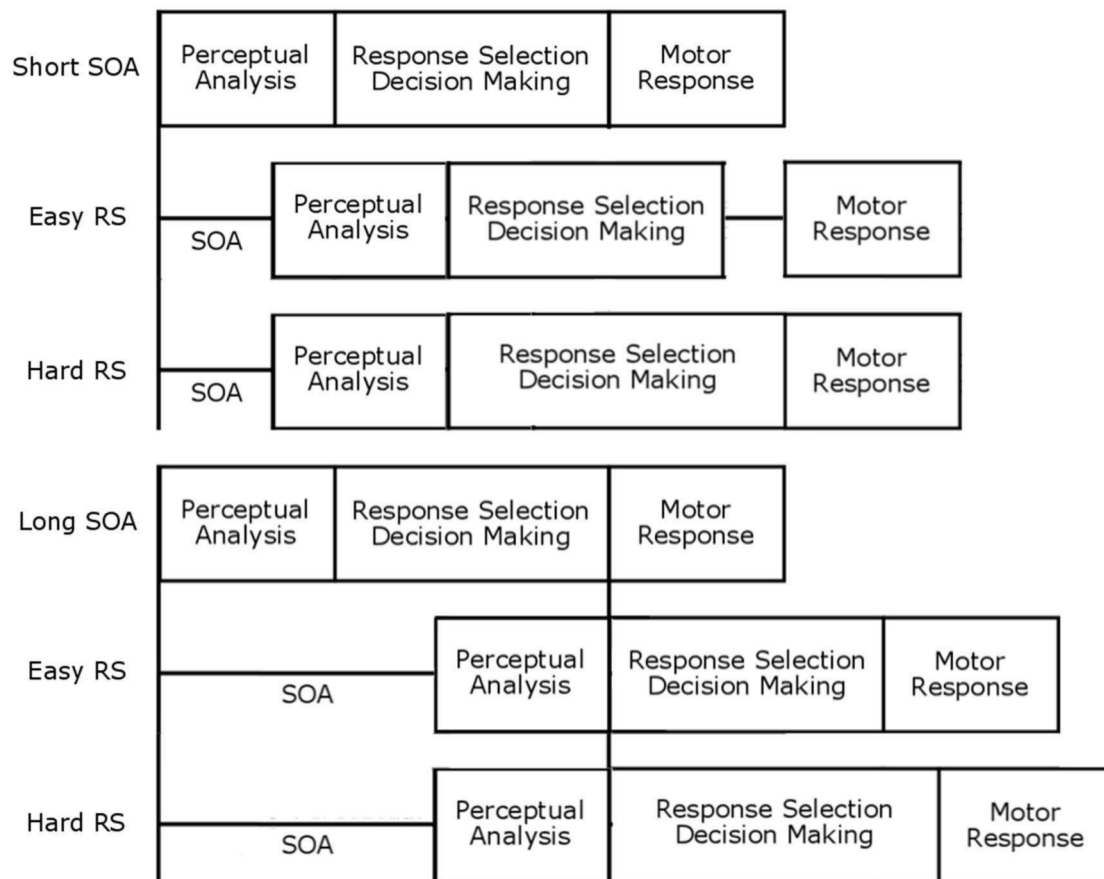


Figure 12: The sub-additive effect of alternative bottlenecks. The response selection stages in Task 1 and Task 2 proceed in parallel and the bottleneck is located after the response selection stages (i.e., at the motor stages). An interruption emerges in the Task 2 chain after the response selection and before the motor stage. An increase of the processing time in Task 2 in the hard compared to the easy condition will be absorbed by the cognitive slack (the interruption) at short SOA. At long SOA there is no cognitive slack and, therefore, the additional processing time in the hard compared to the easy response selection condition will add to the processing time at long SOA. The resulting pattern represents a so-called sub-additive interaction of the difficulty and the SOA effects on the reaction times in Task 2. Adapted from Schubert et al.¹⁹⁰

These findings have led to the idea that the bottleneck may not be the result of a structural limitation, but rather a strategic one.¹⁹² In a strategic bottleneck, the cost of the DT does not come from exceeding the processing capacity of a single channel, but from the ability to separate attention between two similar tasks.^{193,194} Therefore, limited resources would be shared between tasks in different proportions (e.g., 80% for T1 and 20% for T2) and be managed by attentional control, depending on the instructions, priorities between tasks and value of the result,^{194,195} allowing parallelism.^{186,196,197} Thus, the greater the amount of shared resources, the greater the parallel processing.

Some authors have tried to explain why individuals try to perform several tasks simultaneously, despite the risk of interference between tasks and the performance decrement, and the main reason might be that this poor strategy may require less mental effort than that needed to implement strictly serial processing. Yet, serialization tends to be preferred, despite the excess effort needed to maintain a serial organization, whenever performance must be prioritized.^{115,198} In fact, several studies support the view that parallelism is an illusion^{199,200} and that “multi-taskers” in fact alternate rapidly between tasks.¹⁹⁴

How does practice facilitates multi-tasking, then? Studies on single tasking have shown that regular practice leads to reduced processing time in RS stages.²⁰¹ Additionally, neuroimaging findings suggest that this decrease is mirrored by practice-related cortical reorganization, allowing the implementation of faster and more direct neural connections between perceptual and motor regions.²⁰² This decrease in RS time would in theory reduce the DT cost,^{203,204} shortening RS1 and RS2, both being scheduled in such a way that they avoid temporal overlap without achieving complete automatization (*see Fig. 13*).^{203,205}

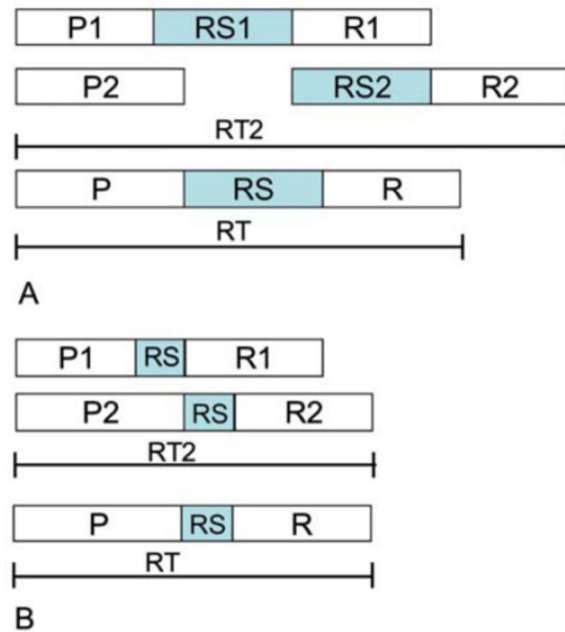


Figure 13: Possible alternatives to reduce the bottleneck. Panel A: Hypothetical processing durations in Task 1, Task 2 and the single task at the beginning of practice. Panel B: hypothetical processing durations in Task 1, Task 2 and the single task at the end of practice. Illustrated is the situation of a latent bottleneck: An unequal practice-related reduction of the duration of the processing stages in Task 1 and Task 2 has caused that the bottleneck stages (RS) in Task 1 and Task 2 do not temporally overlap anymore. In that case, dual-task costs vanish after practice as can be inferred by the comparison of RT2 and RT in panel B. Taken from Schubert et al.¹⁹⁰

Standard models of the RSB assume that central processing follows a predefined sequence of entry and processing: T1 goes through the bottleneck before T2, following a "first-come, first-served" principle.^{3,17,188} In contrast, a more recent model extending the idea of serial processing has proposed an active task management system,^{156,190,195} in which the executive network can adjust the order in which tasks are performed depending on the current goal, context, convenience or experiences, and reduce the DT cost.²⁰⁶ The latest experimental results supports a mixed model, in which the shift between tasks is observed in long SOA situations, when time is available for strategic planning, while "first-come, first-served" is more prevalent when the SOA is short.²⁰⁷

One limitation of the ability to multi-task might also relate to WM, and the ability to maintain an active memory trace of the different templates associated with each task.^{208,209} However, much research needs to be done at this stage, to determine, for instance how many templates can remain in WM in a passive state. Recent studies suggest that only one passive template can be maintained at each

time,^{116,210,211} which must be continuously refreshed to avoid forgetting,²¹² but other studies suggest that it is possible to maintain several active templates at the same time.^{213,214}

One point of debate is whether the memory trace of the template, at the neural level, must be continuous, in which case two templates could not be maintained simultaneously by the same neural population.²¹² Recent DT studies suggest that during the evocation or maintenance of memories, templates maintenance is associated with non-continuous, intermittent activation states. Yet, most of the results available come from studies that average neural activity over time and trials, or across neurons in different sessions^{215,216}: procedures that masks the precise neural dynamics,²¹⁷ and fail to solve the issue. Some studies have bypassed that technical limitation to show that template-related neural activity is typically sparse and compatible with the separated maintenance of different templates.^{218,219} The fact that neurons are not continuously active²²⁰ allows for the sequential rehearsal of multiple templates,^{221–224} and multiplexing.^{212,225}

What is more established is that during DT paradigms, templates alternate between an active state and a latent or passive state, when the task must go to a stand-by mode.^{101,104} This latent state, which is different from complete inactivation, allows the templates to be reused without going through an actual reconfiguration.

The reconfiguration may include changes in the criteria defining task-relevant stimuli (what must be attended), the overall goal of the task itself and the stimulus-response contingency (how to react to the stimuli). This is possible via a series of activations and inhibitions, to activate new task components and suppress components of the previous task.^{110,226}

The shift between tasks comes therefore with a cost, stronger when the two tasks share few components and the reconfiguration is massive.^{175,227} Some authors, like Altmann and Gray²²⁸ believe that the cost can be suppressed when participants are given enough time to reconfigure between tasks, while other, like Meiran²²⁹ claim that the cost cannot be fully suppressed despite the efficiency of the endogenous preparation.

One central factor affecting the efficiency of the reconfiguration is the similarity between the tasks in the DT paradigm, as different tasks can rely on very similar templates,¹¹⁰ for example if a subject were asked to provide names of flying animals first and the name of running animals. Although the two tasks differ, the difference is minor and the type of responses and cognitive processes that must be engaged is similar, making it possible to use the same template for different tasks and shift swiftly between tasks.

DT performance is complicated by the fact during a DT paradigm, higher cognitive areas involved in RS do not distinguish the type of information being processed.^{3,101} This means that tasks with different sensory or motor modalities may experience interference at higher cognitive levels,^{3,230,231} despite the fact that stimuli are auditory in one task and visual in the other, for instance.²³² This is supported by observations in which tasks that use different sensory and motor modalities end up interfering with each other.²³³

One example of highly abstract and amodal region involved in RS is the LPFC.^{205,234,235} A recent functional Magnetic Resonance Imaging (fMRI) and multivariate analysis pattern study mapped different cortical and subcortical areas during experiments of modality manipulation, finding that bilateral AIC and dlPFC contain significantly less information about sensory and/or motor modalities than other regions of interest.²³²

Higher sensory and lower cognitive areas are more modality specific,²³² which means that information from distinct modalities can theoretically be processed in parallel at this level,^{236,237} at least until it reaches amodal areas, mostly in the prefrontal cortex.²³⁸ Purely amodal areas, mostly located in the most rostral part of the prefrontal cortex, are shared by most tasks that require greater executive control and constitute a RSB even when two tasks rely on different modalities.^{3,170,236}

According to Logan and Gordon,¹¹⁵ this intrinsic limitation caused by higher cognitive areas, supporting attentional control and WM, can be minimized by pre-organizing the order in which tasks are executed and use self-regulated serial processing between tasks.^{237,239} According to Pashler,¹⁷⁰ excessive interference should lead individuals to shift naturally from unsuccessful parallelism to serialization. Following that strategy, the executive system can pre-establish a DT order by scheduling attention in a serial way,^{192,240} facilitating the transition from one task to the other while monitoring task performance. In that framework, executive control applies mostly to organize tasks in time, solve the interference,²⁴¹ and improve performance.^{237,239} This is consistent with statements by Brass and Von Cramon,²⁴² who stated that those subjects who invest more cognitive resources in strategic task scheduling have better performance.

Most studies associate the scheduling process with the LPFC.^{236,243–246} In a recent fMRI study, Szameitat and colleagues²⁴⁷ showed a stronger activity during multi-tasking in the LPFC bilaterally, specifically in the left MFG, IFS and Precentral Sulcus, and right anterior Superior Frontal Gyrus (SFG) and posterior IFS/MFG, revealing as well as other studies a more intense and extended activity towards the left hemisphere.^{247–249} Yet, the bottleneck should not be thought as so localized : other areas were activated in relation to DT, including the posterior SFG, AIC, Premotor Cortices, pre-SMA,

SMA, Precentral Gyri, ACC, Inferior Pulvinar extending to IPS and the medial Precuneus, ITG, posterior Occipital areas, Lingual and Fusiform gyri.^{247–249}

Therefore, DT performance decrement cannot be attributed to a single focal portion of the LPFC, but rather to a network whose activity is greater when two tasks are performed in a DT condition, than when the tasks are performed separately.²⁴⁷ The LPFC is only one major node, actively involved to solve interferences between two tasks, as shown by Szameitat and colleagues²⁴⁷ who found a significant negative correlation between activity related to the cost of DT and performance in two areas of the LPFC: the left and right IFS/MFG.

Besides the LPFC, other areas present a stronger activity during DT paradigms. Bush and colleagues²⁵⁰ found that gray matter volumes in the ACC positively correlate with average performance during MT paradigms, probably playing a key role in cognitive, emotional²⁵⁰ and MT processes.²⁵¹

By studying the modular organization of brain networks and their relationship to DT cost, Avalash and colleagues²⁵² found that greater network overlap between simple tasks and less modular flexibility during DT leads to a significant increase in interference. In addition, they found that greater flexibility in the areas of cingular and frontal control, along with less flexibility in right-sided nodes that include the mid-occipital and superior temporal gyri, support enhanced DT performance. Finally, they determined that the topological reconfiguration of each single somatosensorial network in adaptation to the DT condition is associated with less interference during DT.²⁵³

These results suggest that the stability, flexibility and dynamic behavior of brain networks are important in determining the DT cost.^{190,248,253,254} Thus, these networks adapt over time to task conditions,^{255,256} with patterns that can change and become potentially relevant to cognitive and behavioral fluctuations.²⁵⁷ These characteristics appear only when two different and relevant tasks are performed in parallel in a DT, and not when each task is executed individually. Therefore, the DT not only carries an inherent effort in its execution, but also adds an effort in the use of higher cognitive functions. These functions optimize the passage of information through the RSB, consequently improving the performance of the DT.

Although most of the research done on DT has focused on amodal RSB, there are other types of bottlenecks that relate to specific peripheral brain mechanisms for each modality, such as sensory perception (i.e., S1 and S2) and motor response (i.e., R1 and R2) phases.

One particular problem when stimuli of two tasks share the same sensory modality^{3,187,188} is that attention must be divided between them,^{33,34} for example, if someone drives a car while trying to look at a map, the competition between the two tasks is obvious at the sensory level. Therefore, and as we

have discussed previously, two tasks might interfere at the simple level of allocation of sensory attention. Strategic multiplexing is necessary to choose the most important information in a scene at any given time.

The same problem can obviously be found at the response level, since the execution of two motor responses in parallel is not always possible (looking to the right and to the left at the same time). There is an obvious limitation of the motor system to execute two responses at the same time using the same effectors, or even to prepare two movements with the same muscles.²⁴⁷ According to some studies, the execution of R1 delays the execution of R2 by several hundred milliseconds, which impairs DT in many cases.^{189,247,258}

DT is facilitated when the two tasks use different sensory and motor modalities, but specific combinations seem to be easier than others are. For example, a task with visual perception and manual execution combined with another task with auditory perception and vocal execution causes a lower performance drop than the reverse combination (i.e., visual-vocal and auditory-manual). This suggests that certain combinations produce less crosstalk between tasks, since there are "more natural" associations between certain types of processing.^{259,260} This is an interesting avenue of research for ergonomics and design.

” *The moon, by her comparative proximity, and the constantly varying appearances produced by her several phases, has always occupied a considerable share of the attention of the inhabitants of the earth.*

– Jules Verne

The ability to remain focused on an exogenous stimulus or endogenous goal while ignoring irrelevant surrounding elements is crucial for goal-directed behavior. Nevertheless, in certain cases mechanisms already discussed within the orientation network compare highly salient but irrelevant ascending information with template-defining descending signals, with the former bypassing early filters and capturing attention involuntarily.

Such processes, characteristic of distraction, have been promoted by evolution because of their value for survival. According to Lang, being able to reorient attention away from the requirements of the current behavioral mental goal is the result of natural selection, especially when reoriented towards those that threaten the life of the organism.²⁶¹ Yet the distraction process also occurs for irrelevant elements that do not represent a threat, which can then be as distracting as real physical threats.²⁶² We get distracted when the attention-grabbing effect of such stimuli is so strong that we cannot ignore them.²⁶³

Stimuli can capture attention because of their particular physical salience: stimuli that are especially large, bright or noisy, or possess a special significance, such as a person's first name or the face of a relative, capture attention more easily. The capture of attention has positive effects as it ensures that potentially important external events do not go unnoticed, and allows when necessary a renewal of internal goals and an adjustment of behavior to the environment. However, this phenomenon also involves a decrease in performance for the task that was previously being performed.²⁶⁴

Regarding the distraction process, while it is commonly accepted that attentional reorientation towards the distractor forces processing at the level of primary sensory areas,^{265,266} the main debate

questions whether the capture solely proceeds in a bottom-up fashion following a “stimulus-driven” tendency, or whether it is regulated and maybe enhanced by top-down effects following a “goal-driven” tendency.²⁶⁷

Advocates of a purely bottom-up mechanism propose that the allocation of cognitive resources depends exclusively on transient bottom-up processes that mediate the attraction of attention, with no contribution from the prefrontal cortex. According to their view, attention would always reorient towards the most salient physical distractor (i.e., the one with the highest contrast relative to the background), independent of any constraint relative to the current behavioral goal (for instance, what item must be found within a search array).^{268–270} In a visual search experiment, the sudden presentation of a salient singleton would attract attention independently of its resemblance with the target of the search, and increase reaction time (RT) and/or error rate (ER).^{11,271}

Other researchers have proposed that the capture by distracting stimuli is affected by the current task goal.^{272–274} In a classic example of visual search, a cue is presented before each trial. This cue can be a spatially predictive or non-predictive singleton for the target position in the next trial. In the case of a predictive situation, the cue draws attention to the specific position within the visual field, facilitating the perception of the target, causing a spatial cueing effect and decreasing the RT of the task. This effect is only present when the cue matches the target and the actual goal, but the same does not occur with non-predictive cues, indicating that the capture of attention is affected by the current task.^{272–274}

Folk²⁷² concluded that this post-distraction attentional reorientation is not an inevitable consequence of saliency, but occurs because the salient stimuli partially matches current task-relevant attributes (what needs to be attended). In that view, attention would be drawn to those elements that match at least partially what is being searched. This debate has led to diametrically opposed interpretations regarding the phenomena of attention capture.

Current models try to reconcile conflicting views and assume that during the distraction by an external stimulus, attention capture results from the joint influence of factors driven by stimuli and ongoing goals.²⁹ Priority, as in priority maps, would be calculate from these respective influences. Therefore, the more salient a stimulus is, the higher its priority “value”,²⁷¹ regardless of whether it is relevant or not for the task, but its resemblance to the attentional template would also increase that value.^{275,276}

In a study investigating the relationship between bottom-up and top-down processes, subjects were asked to recognize stimuli with different levels of saliency, while keeping different goals in mind that may or may not match the external stimulus just presented. It was found that when the bottom-up

information and the top-down signal do not converge on the same target, regions of the VAN, specifically the IFJ and IPS, activate bilaterally, forcing the reorientation towards the most salient external target. In contrast, it was shown that when bottom-up information and the top-down signal converge on the same target regardless of its saliency, the same regions of the VAN activate together with other areas such as the AIC and the post-central and supramarginal gyri bilaterally.²⁷⁷

According to this, the IFJ would act as an interface between VAN and DAN, mediating the control processes back and forth to the IPS, either acting as a circuit breaker for ongoing top-down processes, or representing the effort of the cognitive system to nullify salient but unimportant information, matching early theories about regulation between networks.^{11,277} This communication between VAN and DAN supports the idea of a circular attention system.

At the same time, the neural activity of the DAN tends to increase and be maintained in the face of distractors of different saliency as well as without them.²⁷⁸ This occurs especially in the FEF and in the SPL near the IPS, including also areas of the executive network such as the dlPFC and the ACC, supporting the idea that their activity is independent of the saliency of the distractor.^{278,279} In addition, studies argue that signal-induced cognitive activity lasts longer than that induced by distraction, so that even in cases where distraction captures attention, the former eventually exhausts itself and attention is reoriented to the mental goal.^{269,271,280}

These findings serve to clarify that top-down control can access and affect attentional orientation away from a salient distractor.^{279,281} According to Gaspelin and colleagues, top-down control can actively inhibit or suppress distractors if higher cognitive resources are used before reorienting attention.⁴ Therefore, the attentional system protects itself from distraction via the executive network, cutting the inflow of information before priority and feature-specific priority maps,²⁸² as demonstrated in Event-related Potentials,^{281,283} behavior and functional oculomotor studies.^{282,284}

The suppression of distracting stimuli has been largely studied in the visual modality. A first model states that the visual system inhibits only specific elements that must be known in advance.²⁸⁵ Another model states that the system does not require any a priori information about the specific features of the element to be suppressed, and simply identifies distractors based on the fact that suppression is simply applied to elements with a high weight in the priority map, so that only the processing of elements matching the current goal is allowed.⁴ Yet, several studies have shown that a distractor can be processed attentively even after such an active suppression.^{286,287}

One interpretation of that phenomenon involves WM: several studies claim that its capacity differs substantially across individuals,^{106,288} and that lower WM would be associated with lower attentional

control and a greater tendency to distraction.^{289–291} Thus, low-capacity subjects may have greater difficulty in avoiding storage of irrelevant items in contrast to high-capacity subjects.²⁹² Additional studies have extended these results, showing that high-capacity individuals are able to resist the capture of attention by irrelevant elements, while low-capacity individuals are less likely to resist it.²⁹³

However, Theeuwes and colleagues²⁹⁴ proposed a variation of that explanation, claiming that all subjects have equal susceptibility to attentional reorientation, but that they vary in the time needed for them to recover. One argument in favor of their interpretation is that high and low WM capacity subjects experience similar effects of attentional reorientation, but that low-capacity subjects take longer to recover from distraction than high-capacity subjects. These results suggest a slow attentional detachment from a distractor may be due to poor attentional control associated with low WM capacity.²⁸⁰

Part II

METHODOLOGY

” *The human brain has 100 billion neurons, each neuron connected to 10 thousand other neurons. Sitting on your shoulders is the most complicated object in the known universe.*

– *Michio Kaku*

My experimental work relied on intracranial electroencephalography (iEEG) to measure brain activity. EEG measures the voltage fluctuations resulting from the flow of ions within brain neurons, known as brain waves or neural oscillations. The main advantage of EEG is its high temporal resolution, at the millisecond level, and it used in many pathologies, such as epilepsy, sleep disorders, depth of anesthesia, coma, encephalopathies as well as to investigate the neural dynamics of normal cognition.²⁹⁵

EEG can be recorded non-invasively at the scalp level, with surface electrodes (surface EEG), and intracranial (iEEG), as in the present thesis. The obvious advantage of scalp EEG is that it is non-invasive,²⁹⁵ however, the skull, meninges and skin distort and blur the signal, which limits its spatial resolution to a few centimeters and prevent the recording of neural activity with frequencies higher than 30-50 Hz,²⁹⁶ in particular the “high-gamma range” [50-150 Hz], which will be discussed extensively.

In contrast, iEEG has a much higher resolution (mm) than scalp EEG,²⁹⁶ and can record from precise cortical regions at the gyrus/sulcus level.²⁹⁷ It has been estimated that each recording site provides an average measure of the electrophysiological activity of about 200,000 to half a million brain cells.²⁹⁸

Further, iEEG has a higher signal-to-noise ratio than EEG (about 100 times higher),²⁹⁹ with less electromagnetic noise from the recording room, and little contamination by physiological noise of the heart signal, muscle contractions or skin potentials (e.g., skin cells on the scalp or ionic potential of sweat glands).³⁰⁰

iEEG also provides a precise and unbiased measure of neural activity in a wide frequency range,²⁹⁶ typically up to 300 Hz, that is only limited by the sampling frequency of the recording device (1024 Hz typically, in Lyon and Grenoble for instance). This allows the extraction of a larger frequency range than that obtainable with scalp EEG, ranging from low frequency activity such as delta (1-3 Hz), theta (4-7 Hz), alpha (8-13 Hz), beta (14-30 Hz), to low gamma (30-50 Hz) and high gamma (50-150 Hz), or High-Frequency Activity (HFA). Other high frequencies such as ripples (150-250 Hz) and fast ripples (250-500 Hz), initially associated with memory consolidation during sleep, are beginning to be analyzed today in different cognitive studies with awake subjects.^{300,301}

The main limitation of iEEG is that it is used specifically for the presurgical exploration of drug-resistant epileptic patients;³⁰² as it is the only diagnostic method capable of delivering sufficient resolution to delineate epileptic zones and map functional areas, which must be spared by the resection.²⁹⁶ Yet, iEEG responses to tasks, which are reproducible across patients with different kinds of epilepsy and different onset zones, are considered as valid for generalization to normal human brains.²⁹⁷

iEEG can be measured using two different types of electrodes: subdural grids/strip (*see Fig. 14: b, c, d*) and depth electrodes (*see Fig. 14: a, e, f*). Both present important differences in data collection and diagnosis of epilepsy.

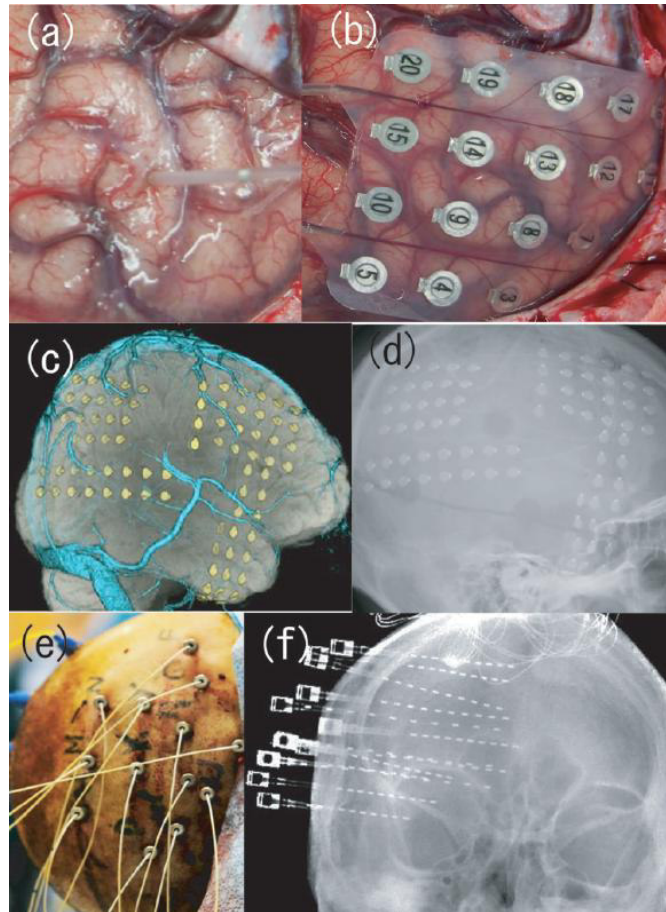


Figure 14: Intracranial electroencephalography (iEEG). a), e) and f) are examples of depth electrodes (SEEG); b), c) and d) are examples of subdural electrodes (ECoG). Taken from Enatsu and Mikuni.²⁹⁶

Subdural electrodes are placed directly onto the exposed surface of the brain. They are useful to localize the onset of seizures and their spatial extent on the cortical surface and delineate the limit between epileptogenic zones and the functional cortex. However, subdural electrodes cannot capture epileptic foci of deeper origin such as the insula or the amygdalo-hippocampal complex.³⁰³

On the other hand, depth electrodes are placed on the parenchymal brain or directly on brain injuries, being usually indicated when depth recordings are necessary for an accurate diagnosis. They provide sufficient resolution to localize epileptic activity at the gyral level, with an accuracy as good as that achieved by fMRI, in many cases surpassing it.²⁹⁷ However, their main limitation is the limited spatial sampling and the difficulties in performing precise anatomical delineation between healthy and epileptic areas.^{304,305} The insertion of these electrodes can be performed bilaterally, but their implantation must be done by a neurosurgeon with previous knowledge in neuronavigation.³⁰⁶

European epilepsy centers mainly use stereotactically implanted depth electrodes for diagnosis (stereo-electroencephalography, or SEEG). The process of implantation is as follows.

1. The planning of the implantation requires a specific hypothesis about the epileptic lesions based on non-invasive evaluation tests, such as seizure semiology, neuroimaging and nuclear imaging.^{307,308}
2. After formulating a location hypothesis, the epileptic target is selected and reached with depth electrodes of different lengths and number of leads, depending on the specific region of the brain to be explored (usually 5 up to 15 depth electrodes, with 5 up to 18 leads per electrode).³⁰⁰ Each electrode has a diameter of 0.8 mm, with leads measuring 2 mm wide and a distance between them of 1.5 mm. They are placed inside hollow plastic tubes that can be inserted into the brain tissue with a stiletto that provides the necessary rigidity.³⁰⁶ Electrodes are usually made of stainless steel or platinum, with the latter material being more appealing as they are non-ferromagnetic and therefore compatible with MRI. They are implanted using conventional stereotactic techniques according to the MNI coordinate system or each patient's own pre-implantation images through drill holes,³⁰⁹ and are usually left implanted for a period of 5 to 14 days (*see Fig. 15*).³¹⁰
3. The local accuracy of each lead is usually higher when each registration site is referred to its nearest neighbor (bipolar montage) than when a remote site is used as a reference for all sites (common reference).²⁹⁷
4. Then follows a prolonged post-surgery examination with video recording and EEG information without anticonvulsant drugs, with the intention of recording epileptic seizures. During this phase, the cortex can be stimulated with electrical pulses that further assist with triangulation.³⁰⁶ It is usual to record intracerebral activity with up to 128 deep electrode leads (up to 1024 Hz sampling rate and a 0.1-200 Hz bandpass filter). Clinical studies in epilepsy usually target frequency activity with a bandwidth between 0.5 and 70 Hz as the gold standard,³¹¹ but this does not mean that epileptic activity cannot be found at much higher frequencies.
5. Next, imaging is used to complement the results obtained. As an example, synchronized oscillatory activity correlates especially well with the hemodynamic activity of post-implantation fMRI, thus the increase in signal power at a particular recording site reflects the local involvement of cortical tissue around the electrode.³¹²
6. Compiled data can then be used to differentiate normal from abnormal neural oscillations, triangulate the anatomical areas that produce these abnormal readings and subsequently resect epileptic foci within established surgical margins.³⁰⁶

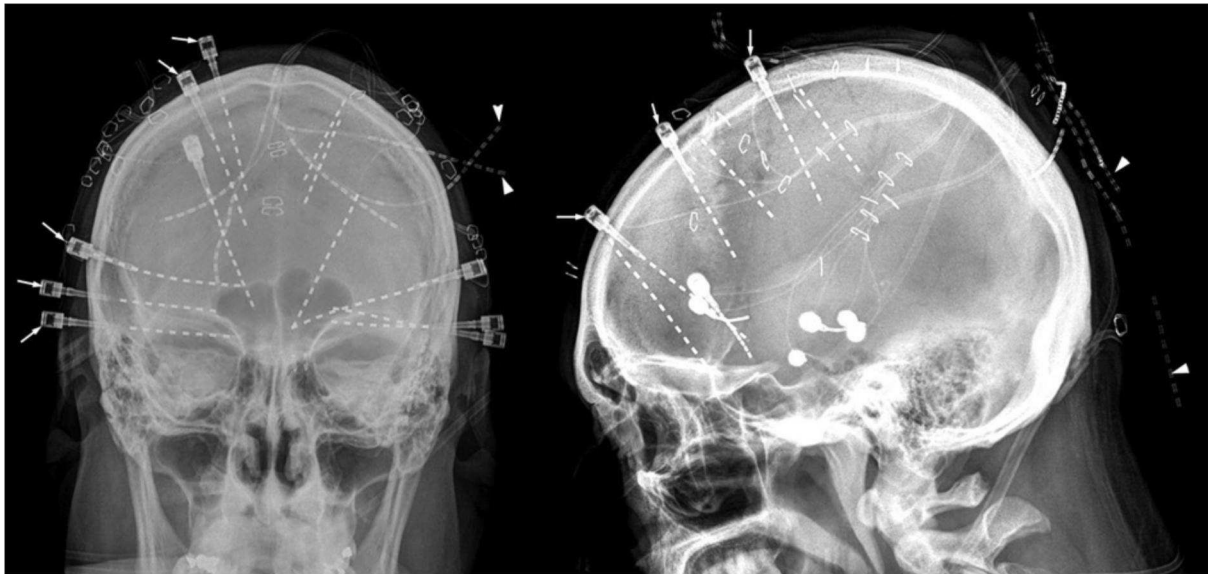


Figure 15: A post-implant skull X-ray showing multiple depth electrodes placed strategically under neuronavigation guidance. The targets are predetermined on the basis of presurgical evaluation. In this individual, the electrodes were placed in bilateral hippocampal formations, orbitofrontal gyri and cingulate gyri. Some of the depth electrodes were secured with an anchor to minimize post-implantation movements (arrows). The fainter electrodes ends represent the tails of the depth electrodes that connects to amplifier and are located over the scalp (arrowheads). Taken from Shah et al.³¹³

As stated above, HFA can be used as a powerful biomarker for most cognitive functions. Sustained HFA has for instance been associated with keeping representations in WM,³¹⁴⁻³¹⁶ maintaining attentional templates with sustained and persistent activity of recurrent connected neurons in short-term memory.²¹² Such persistent activity would facilitate synaptic encoding in long-term memory, thanks to increases in frequency amplitude and subsequent synaptic plasticity.³¹⁷ This phenomenon has been observed in early sensory zones as well as in the extra-striatal visual cortex, and even in non-visual areas, are involved in the maintenance of visual memory traces.^{315,318} This suggests a mechanism of transmission or transformation between synchronous neuronal assemblies, ranging from sensory cortices to high-order cortical regions that may start even during stimuli presentation.³¹⁵

Therefore, HFA can trace neural processing related to perception, attentional orientation and maintenance of working and long-term memories, reflected in increases of amplitude, which are all highly relevant for attention.^{319,320} Nevertheless, whether or not HFA represent a phenomenon that is intrinsic to cognition is still debatable.

5.1 Limitations of Intracranial EEG

While iEEG has its advantages, it also comes with limitations. One of them is that data are collected in patients suffering from epilepsy. Obvious guidelines must be followed, to exclude from the analysis, for instance, iEEG sites in the immediate vicinity of brain lesions or malformations and signals contaminated by epileptiform activity. Any sign of strong performance decrement due to the diseases must also lead to the exclusion of the patient.³⁰² Yet, if such issues are handled with sufficient care, iEEG remains a venue of choice to study the fine neural dynamics supporting human cognition, and it is now at the core of a very active research field in human neuroscience.^{297,315,316,321,322}

A second and somewhat underestimated limitation comes from the limited coverage of the brain surface. This makes the collection of data across different subjects difficult, as the structures chosen for the placement of invasive electrodes are determined for each subject individually and independently of the research objectives.³⁰³ Because traditional group statistics are not possible, our laboratory has created a different approach based on three steps: 1) first we perform a statistical comparison between experimental conditions at each subject level, at each recorded site, to identify regions of interest with task-related neuronal responses. This would include multiple comparison corrections either by direct comparisons between two conditions or comparisons between a condition and a pre-stimulus resting baseline. 2) We then identify the brain regions of interest that show similar effects across several subjects. 3) Finally, we display the individual information for each region of interest, exposing the task-related effects on each patient's anatomy (*see Fig. 16*).^{303,315,322}

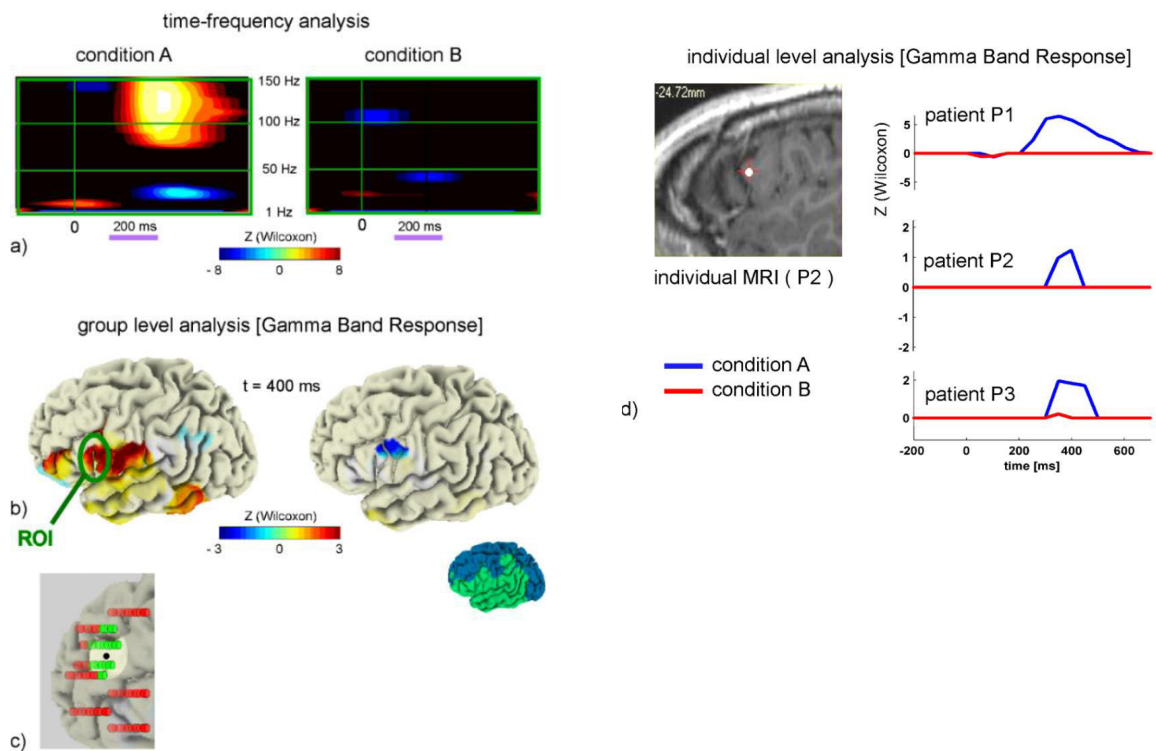


Figure 16: Data collection using SEEG across patients. a) Shows the reaction of an electrode in a particular patient under different experimental conditions; b) and c) show triangulation of anatomical areas in different group levels, according to amplitude in a certain frequency; d) organize functional areas per region. Taken from Jerbi et al.³⁰³

” *Part of what made the Macintosh great was that the people working on it were musicians, poets, and artists, and zoologists, and historians. They also happened to be the best computer scientists in the world. But if it hadn't been computer science, these people would have been doing amazing things in other fields.*

– Steve Jobs

HFA can also be monitored online thanks to the very high signal to noise ratio of iEEG, and our laboratory has created an online monitoring system of intracranial oscillatory activity called BrainTV, which extracts and displays in real-time the variations of several frequency bands – including HFA – , at each recording site in each particular subject. This allows visualizing the immediate effect of the behavior or tasks imposed on brain activity, with a high temporal and spatial resolution.³²³

In addition, our laboratory has also created an off-line monitoring system which mirrors the BrainTV system – but allows the joint visualization of HFA and the video of the patient in his hospital room, while filmed for instance during an experiment (*see Fig. 17*). This software called BrainTV Replay is an off-line monitoring system that allows to extract real-time neural activity and transform it into a HFA envelope for every electrode. This information can be visualized jointly with behavioral responses, recorded videos of each patient during the respective session and a MNI representation of the patient's brain. Besides allowing visualization, it allows to flag events, as well as to check possible correlations between electrodes, making it very convenient to analyze naturalistic experimental paradigms, in which iEEG signals must be interpreted in the context of the interaction of the patient with his environment.

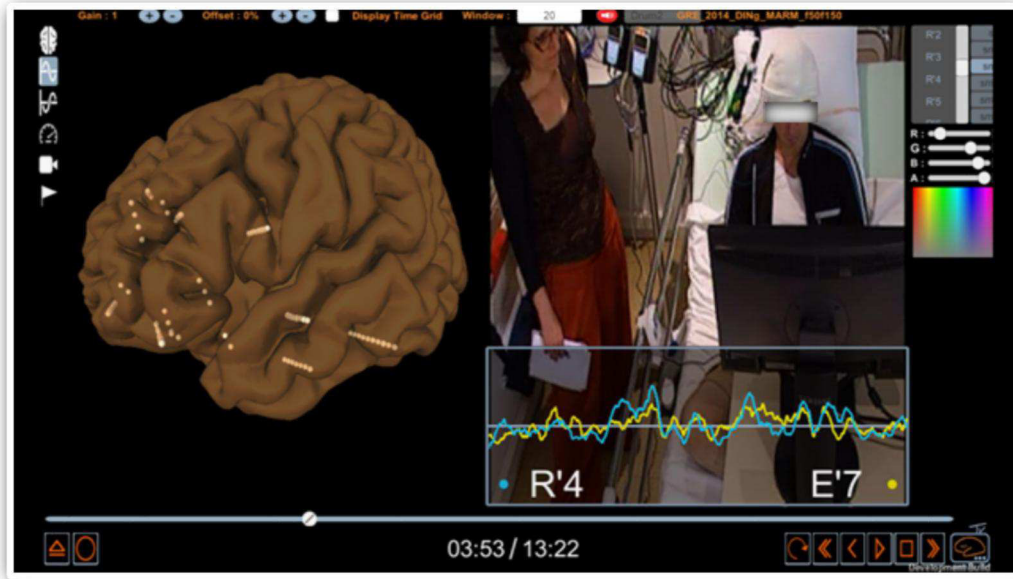


Figure 17: BrainTV Replay

Additionally, data extracted from BrainTV Replay can be fed along into a software called Human Intracranial Brain Observations Player or HiBoP (see Fig. 18). HiBoP allows to unify the anatomical and functional information of a great number of electrodes, allowing its visualization offline, by creating a structural build of a 3D model or mesh for each patient, from MRI pre and post implantation information and electrode depth coordinates and plots iEEG signals on top of it, in a four-dimensional brain visualization. This software also allows to visualize the activity of several depth electrodes for several subjects simultaneously on a common mesh.

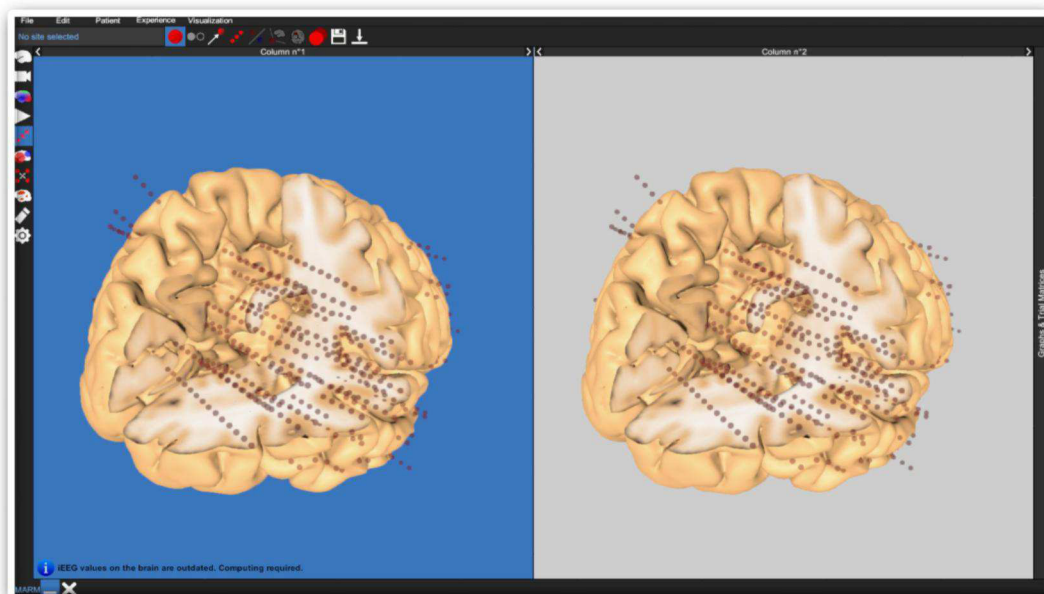


Figure 18: HiBoP. Picture of the Human Intracranial Brain Observation Player.

” *Human Nature is the only science of man; and yet has been hitherto the most neglected universe.*

– *David Hume*

Most conventional paradigms use simple stimuli experiments during which the interaction of the participant with the external world is entirely computerized (for stimulus delivery and response monitoring). Whether the results of such experiments can be generalized to actual, real life situations is a subject of debate. An emerging research field is using stimuli with a greater richness and contextual weight, together with a technological development for a more open interaction, between the participant and his environment.³²⁴

This naturalistic approach focuses on human cognition in ecological or naturalistic situations,³²⁵ closer to everyday conditions than those simulated within four walls.³²⁶ In addition, new evidence and theoretical considerations suggest that the brain may be strongly "tuned" to receive naturalistic stimuli over artificial ones,³²⁷ making it very useful to investigate attention with a practical approach.

Naturalistic designs can be highly valuable to study questions related for instance to multi-tasking and distractions. In particular, the complexity, diversity and unpredictability of the distractions one might encounter in a natural environment, such as a room or an office, are much wider than what can be recreated using a computer. In addition, one might argue that the interaction with a real human being is more complex and taxing than a simulated situation.

In anticipation of the description of the tasks used in this thesis, we can propose that naturalistic distraction (i.e. distraction mimicking what is observed in our daily lives)³²⁸ and its effect on attention could be studied by comparing the pattern of neural activity recorded in a participant performing an attention demanding task a) alone, in a quiet place, and b) with an experimenter sitting next to it, trying to create distraction. Even though the amount of distraction would be less controlled than if monitored by a computer, it would likely be much stronger because of the social interaction involved.

This experimenter-participant interaction is interesting because it provides a new venue to study the neural underpinnings of multi-tasking and distraction, and its effect on attention; for instance by considering two conditions while the participant is already involved in a demanding attention task: 1) one in which the researcher actively asks questions to assess subjects and forces the participant into a secondary verbal fluency test to induce dual-tasking; 2) and another in which the researcher actively attempts to distract subjects by using human or artificially induced movements and/or sounds (e.g., an incoming cell phone call, paper sheet movements). The advantage of such situations is that it is reminiscent of real-life situations encountered by most of us.

One advantage of such designs is to put forward an essential component of modern life: social interaction, which strongly interacts with attention during most of our activities.³²⁹ And social interactions are not easily reproduced by computerized designs, as shown by several studies regarding the neural networks that subserve the perception of communicative cues, such as direct gazes or indirect social gestures, which are more pronounced when delivered in vivo than, for example, through recorded video.³³⁰

In most attention-related research, a software usually controls the delivery of relevant or irrelevant information.^{211,236,247,331} Although the effect achieved may be much cleaner and more stable compared to that of a human being, its effect in influencing a subject's response is, at best, incomplete. This is because by excluding the human factor, we are leaving aside certain attributes that are impossible to achieve with a machine. However, probably the most important ignored characteristic of all is the attribution of a mental state to a second person.³²⁴

When coming into contact with a human being, a large amount of cognitive resources are used to infer his/her mental state, creating representations of intentions and beliefs based on observable behavior, while trying to keep personal and second-person representations in mind simultaneously.³²⁴ Human beings probably attribute a mental state to something that they believe possesses sufficient autonomy to surprise them beyond expectation. Therefore, they are not able to define exactly how someone might react to a particular situation, unlike a computer that has a certain amount of specific responses that do not vary.

Although the specific brain regions that are activated differ across the different paradigms, areas such as ventromedial Prefrontal Cortex (vmPFC), dorsomedial Prefrontal Cortex (dmPFC) and TPJ are consistently activated in the face of task-independent social interaction.^{330,332-334} Similarly, different studies have found responses with greater amplitude changes at occipital locations during social interaction than when interacting with pictures.³³⁵

These considerations motivate a naturalistic approach to address questions about attention with high relevance in our daily lives, because the responses we expect from a neuroscientific inquiry should be applicable to daily life situations, which would not be the case with crude approximations of that reality in the experimental designs. In fact, this approach has been explored several times in neuroimaging, with the experimenter sitting next to the patient in fMRI studies for instance, making eye contact through the borehole of the machinery,³³⁶ holding his hand,³³⁷ or playing collaborative games.³³⁸

Another factor that is often neglected in attention-related research is the inherent richness of a "complex stimulus" versus a "refined stimulus". To perceive complex stimuli requires at least attention, active understanding and integration across multiple time scales.³²⁸ According to Sonkusare and colleagues,³²⁸ sensory systems may be better tuned to receive complex rather than refined stimuli, evidenced by a better perception of natural images over abstract forms, or by the perception of human language over isolated sounds.

Apparently, complex stimuli have a weak dynamic stability,³³⁹ matching that of the sensory systems, which are highly correlated with each other.³⁴⁰ For example, a small part of a dynamic natural event, such as moving a door handle, can lead to a sudden change in a scene, such as a person entering through a door. These dynamic scene changes can lead to dynamic and unstable activities in areas of the nervous system as early as those on the periphery or in primary sensory areas.³⁴¹

Nevertheless, a drawback of using naturalistic paradigms is the lack of means to probe or measure the level of engagement that may vary across participants according to cultural background or personal preferences. Although it is possible to alleviate this by using eye tracking, concurrent physiological recordings and post hoc questionnaires, the nature of the real-time engagement in the absence of action remains unclear.³²⁸

Part III

BACKGROUND AND OBJECTIVES

Overview of our Research

” *Science is more than a body of knowledge. It is a way of thinking; a way of skeptically interrogating the universe with a fine understanding of human fallibility. If we are not able to ask skeptical questions, to interrogate those who tell us that something is true, to be skeptical of those in authority, then, we are up for grabs for the next charlatan (political or religious) who comes rambling along.*

– Carl Sagan

Attention is a dynamic process that involves the activity of different structures that adapt both to our needs and to the world around us. Its process begins at the perceptual level, allowing us to detect elements of the environment by activating sensory areas that send signals to more complex brain regions. At the same time, higher cognitive areas select a mental goal based on memories, experiences and preferences of what to do in certain situations, and send a descending signal that is contrasted with the incoming information. This comparison process consumes a large part of the available cognitive resources, activating and suppressing sets of cortical areas, creating an activation sequence that ensures an adequate motor response. This response in turn allows for feedback on perception and modulation of future behavior.

However, this sustained pattern of attention can be diverted to stimuli that are irrelevant to the task-at-hand, temporarily reducing the amount of cognitive resources available for processing and execution. Among these irrelevant stimuli, the processing and execution of two tasks simultaneously may lower the ability to deliver fast and accurate responses to both activities, while environmental distractions may inadvertently redirect the focus of attention away from the task-at-hand. Therefore,

the main objective of this thesis was to study how a primary task that requires continuous attention can be affected by an additional task or distractions, both at the behavioral and neural levels.

Hence, in the case of the dual task, our main objective was to understand how the execution of two simultaneous tasks decreases its performance, using cognitive resources from common brain areas, causing a bottleneck and forcing serialization. In the case of distraction, our main objective was to understand how an externally induced naturalistic stimulus affects sustained attention, consuming part of the resources allocated on a specific task and disturbs its underlying neural architecture.

To do this, we studied drug-resistant epileptic patients with intracranial electrodes (iEEG) who performed a baseline task called BLAST (Bron/Lyon Attention Stability Test; more details below). Then, the same patients performed BLAST under two new conditions: one in which they had to perform an additional but equally important task; and another in which someone tried to distract them using visual or auditory stimuli. Despite the existence of an extensive literature related to attention control in multitasking situations and distraction, these usually privilege work with non-invasive methods, such as scalp EEG, magnetoencephalography (MEG) or fMRI, but none of these methods is capable of providing anatomical and temporal information as precise as the iEEG. On the other hand, work with epileptic subjects is not without its problems, but our team has the necessary experience to collect and process this information in the best possible way, supported by protocols and results published in high impact journals on numerous occasions.

Furthermore, current trends in neuroscience advocate experimental settings with greater ecological validity, since the human brain seems to be tuned to respond better to complex and enriched scenarios than to simplified ones. This is why we have decided to conduct our experiments using iEEG, specifically SEEG, respecting as much as possible the ecological value in data collection.

Part IV

EXPERIMENTAL RESULTS

Identification of specific neural populations forming a bottleneck that prevents multi-tasking and two possible solutions to reduce interference between attention-demanding tasks

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Under review at Neuroimage

9.1 Abstract

The execution of a continuous attention-demanding task limits the ability to perform a secondary task concurrently, due to resource limitations at the response selection stage, in what is commonly referred to as a “central bottleneck”. The current understanding is that such resources correspond to processing time of specific neural populations necessary for the two tasks. Yet, our understanding of why and how interference occurs is still very limited, mainly because of a virtual lack of data in humans, measuring the dynamics of shared neural ensembles in a dual-task condition. For instance, only direct recordings of well-identified neural populations can reveal a situation in which the time courses of neural recruitment by two tasks are mutually exclusive, what could be called a dynamical incompatibility preventing multiplexing. Such recordings can be obtained in drug-resistant epilepsy patients, implanted with intracerebral electrodes (iEEG). We recorded 12 patients while they performed a sustained attention-task (repeated visual search tasks) and a verbal fluency task in a dual-task paradigm. We found that the two tasks interfered in seven cortical regions involved in imagery and language-related processes and cognitive control. Although the neural activity induced by the attention task was not strictly continuous, gaps were not sufficient for neurons to engage concurrently in the fluency task (dynamical incompatibility). Interference was reduced by strategy changes, and most importantly, through a reduction of cognitive control with no performance decrement. Our results suggest that multi-tasking abilities are partially impaired by a tendency to exert more control than strictly necessary.

9.2 Introduction

Some tasks do not go well together. For example, you might find it difficult to remember your passenger's spouse name while driving in hazardous conditions; because processing external stimuli interferes with the retrieval of information from long-term memory. The interference between attention-demanding tasks²²⁸ has been extensively studied using the dual-task paradigm,³ in which participants must respond to two separate sets of stimuli according to two distinct sets of rules. The main observation is that performance is lower when the tasks are performed together than when they are performed separately, in a single-task condition,^{170,184} even when the stimuli and responses of the two tasks involve distinct sensory and motor systems.^{238,342,343} The performance decrement from the single- to the dual-task (DT) condition has been called the DT cost.¹⁶⁹

The current interpretation of the DT cost is that tasks compete for resources at a stage intermediate between perception and response production, devoted to response selection¹⁹⁶ according to the task-rules.¹⁴ This competition has been theorized in the Response Selection Bottleneck (RSB) model,^{3,170,186} in which any task that is not fully automatized requires the participation of a common set of brain regions: the RSB. The RSB could not process two tasks at the same time and would therefore impose their sequential — rather than parallel — execution.^{188,344}

A direct prediction of the RSB model is that any continuous task should prevent the concurrent performance of a secondary task, if none of the two is fully automatized.³⁴⁵ In practice however, such complete exclusion is rarely observed because very few tasks require the response selection process to be truly continuous. For instance, under normal driving conditions, eye-tracking studies have shown that attentive sampling of environmental stimuli and response selection can occur only once every second, with a minimal impact on performance.³⁴⁶ It leaves some time for a secondary task, such as recovering specific information from long-term memory,³⁴⁷ at least when driving is easy.

It follows that despite the constraint imposed by the RSB, the ability to perform a secondary task T2 during a "continuous" primary task T1 might depend primarily on the existence and duration of recurrent "gaps" during T1, defined as time-intervals with no requirement for the RSB. In other words, the two tasks might be performed "simultaneously" provided that they used the RSB alternatively, in which case they could be said to be "dynamically compatible", because the dynamics of RSB recruitment by the two tasks would be compatible.

The primary goal of the present study was to find neural evidence for dynamic compatibility (or incompatibility) between two tasks and turn that theoretical concept into an observable phenomenon. It required: a) a DT paradigm combining a primary "continuous" task T1 with a

secondary task T2; and b) the identification of neural populations involved in both T1 and T2 (the RSB) as well as c) a time-resolved measure of their activation by T1 to identify possible “gaps” and their duration in relation to T2.

Time-resolved recordings of specific neural populations can be performed in epilepsy patients implanted with intracranial EEG electrodes (iEEG).^{300,305} We recorded twelve patients in a DT paradigm reminiscent of our introductory example: participants were asked to perform a verbal fluency test (T2)^{348,349} while processing and responding quasi-continuously to external visual stimuli (T1: a rapid succession of short visual search tasks).¹⁶⁷ We identified a set of cortical regions involved in perception, language and control processes during T1 and T2 — the bottlenecks — which dynamics of activation was incompatible between the two tasks. However, our data also revealed the neural implementation of clear strategy changes to avoid bottlenecks, including the diminution of an excessive cognitive control. Altogether, our study provides novel insights regarding the impossibility (and possibility) of multi-tasking based on the large-scale dynamics of cortical activations and deactivations.

9.3 Materials and Methods

9.3.1 Participants

Intracranial EEG recordings (iEEG) were collected in twelve patients candidates for epilepsy surgery at the Epilepsy Departments of the Grenoble and Lyon Neurological Hospitals. Eleven to fifteen semi-rigid, multi-lead electrodes were stereotactically implanted in each patient (stereotactic EEG — SEEG, a special type of iEEG).³⁵⁰ Each electrode had a diameter of 0.8 mm and, depending on the target structure, consisted of 10 to 15 contact leads 2 mm wide and 1.5 mm apart (i.e. 3.5 mm center-to-center, DIXI Medical Instruments). Selection of sites to implant was entirely based on clinical purposes, with no reference to the present experimental protocol. All electrodes showing traces of epileptiform activity were excluded from the present study (visual inspection by the clinical team). All participants were native French speakers with normal or corrected-to-normal vision, and had given their written informed consent; all experimental procedures were approved by the Institutional Review Board and by the National French Science Ethical Committee.

9.3.2 Stimuli and Tasks

BLAST (T1) – see annex N°1

The continuous attention task was adapted from the BLAST paradigm published by our group¹⁶⁷ to detect transient failures of executive attention. In short, BLAST repeatedly asks participants to find a target letter (the Target) in a subsequent two-by-two square array of four letters (the Array), with new letters every trial (Target and Array) (*see Fig. 19*). Each trial starts with the central presentation of the Target for 200 ms, followed by a mask (# sign) for 500 ms, until the presentation of the Array which remains on screen until the manual response, or for a maximal duration of 3000 ms. The next trial starts after a 800 ms pause, with no visual or auditory feedback of any kind.

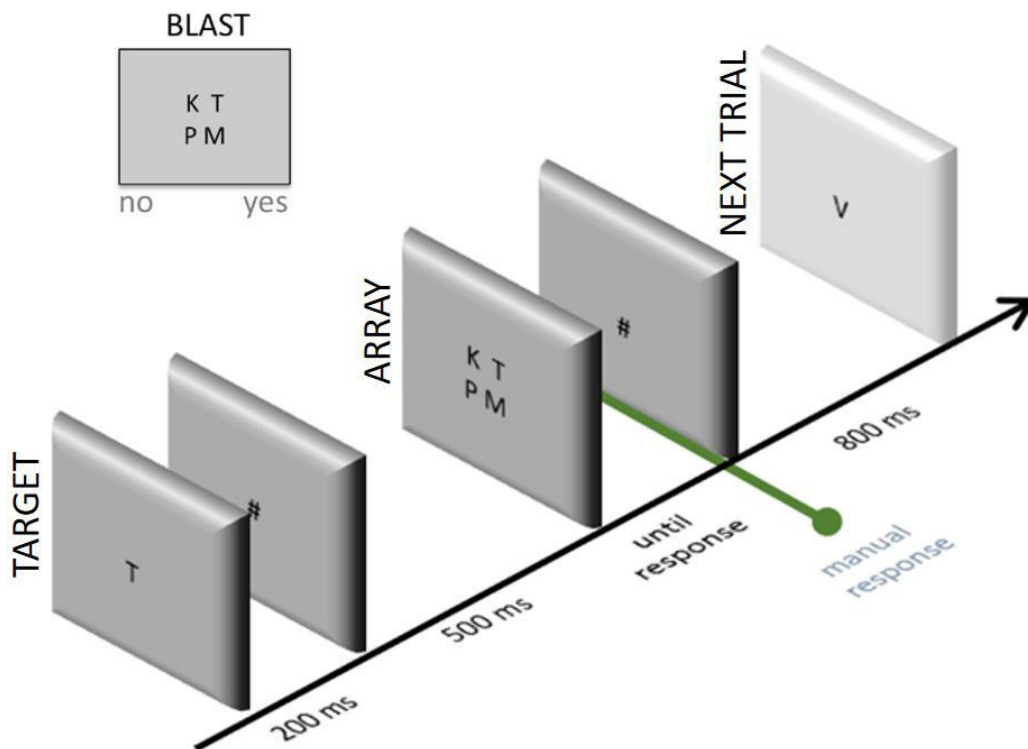


Figure 19: Schematic depiction of BLAST (T1). Each trial starts with the presentation of a Target, followed by a mask (#). Thus, this 700 ms window is known as encoding phase. The mask is then replaced by the Array, which remains on screen until the manual response. Thus, this window of variable length is known as visual search phase. Adapted from Petton et al.¹⁶⁷

Stimuli were delivered on a PC using the Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA), synchronized with the EEG acquisition system. The letters were presented foveally in black on a light gray background. Participants pressed a button on a gamepad with their preferred (resp. non-preferred) index finger to indicate if the Target was absent (resp. present) in the Array. The trials sequence was pseudorandomized, with an equal number of target-present and target-absent trials. Performance was measured over a total of 250 trials, for a total duration around ten minutes (depending on reaction times).

The global instruction was to avoid errors and to keep a steady and reasonably fast pace, with an explicit analogy to car-drivers who avoid accidents at all costs, but nevertheless move forward at a decent speed. BLAST was first performed by participants in a single-task (ST) condition, with no exogenous distractions, and then in a dual-task (DT) condition, simultaneously with a Verbal Fluency Test (see below).³⁴⁸

Verbal Fluency Test (T2)

The Verbal Fluency Test (VFT) is primarily used in clinical settings as a diagnostic tool,³⁵¹ or to assess cognitive functions in patients suffering from Alzheimer Disease or schizophrenia.^{349,352,353} It provides a good evaluation of the ability to retrieve lexical knowledge^{354,355} and more generally, of executive control.^{356,357} In its most typical versions, participants are asked to provide as many words of a given semantic category (semantic VFT) or starting with a given letter (letter or phonemic VFT), as possible in a given time.³⁵⁷ VFT performance relies heavily on language and executive processes³⁵⁸ and at the neural level, on the left Inferior Frontal Gyrus (IFG, including Broca's area), the dorsolateral Prefrontal Cortex (PFC), the premotor cortex, and the right cerebellum.³⁵⁹

To maximize the demand on the central executive system, we combined the two VFT variants into one task: a letter was chosen at the beginning of the experiment and participants had to provide names of a given category (animals, names of people, towns, tools ...) starting with that letter. Category names were given by an experimenter sitting in the same room as the participant, in its remote peripheral field (*see Fig. 20*). The timing of the VFT was not computerized so that the switch to a new category occurred as soon as the participant showed obvious signs s/he was running out of answers — which was better appreciated by an experimenter than by a software. Apart from providing new category names, the experimenter remained still and silent throughout the experiment. VFT performance was analyzed offline from a video recording of the session. To mimic naturalistic conditions, participants received no instruction to prioritize BLAST or the VFT.

In addition, this study makes use of several datasets recorded in separate sessions while participants performed short functional localizers designed to identify iEEG sites involved in visual perception, auditory perception, semantic and phonological processing, verbal and visuo-spatial working memory as well as visual attention respectively.^{279,360} Although those data cannot be fully described in this manuscript (*see Annexes N°2*), we will refer to them each time they provide important insights regarding the function supported by the cortical sites of interest for our study.

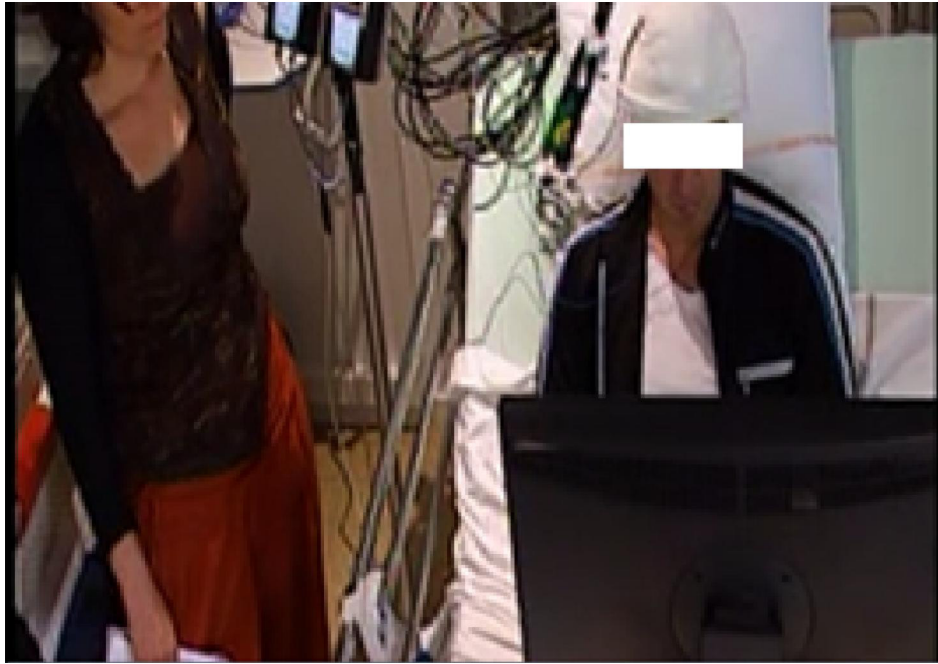


Figure 20: Dual-Task set-up: the experimenter is standing or sitting at the bedside, in the peripheral visual field of the participant while the participant is performing BLAST (T1) - the verbal interaction is limited to a strict minimum, necessary for the VFT (T2).

9.3.3 Behavioral Analysis

Our DT design came with two advantages: a) the experimental situation resembled naturalistic conditions (when asked a question that requires an access to long-term memory, people must rarely give their answer within a precise, computerized time-limit, besides TV shows and video games),³²⁵ and b) it let participants choose the optimal time-windows to carry out the secondary VFT task T2. The downside was that it was difficult to assess precisely when participants engaged in T2. The only periods when participants were surely performing T2 was just before they provided an answer. They might have engaged in T2 at other times covertly, but we chose to study the impact of T2 on BLAST performance and T2-related neural processes in the windows preceding overt verbal responses.

One remaining issue is to estimate the duration of such windows: since the cognitive processes leading to the verbal responses are covert, there is no way to assess their duration and to specify a window during which participants are surely engaged in response selection for the VFT. Yet, a reasonable estimate could be derived from single-unit recordings performed during free-recall. Gelbard-Sagiv and collaborators³⁶¹ observed that the activity of individual neurons in the human hippocampus increased about 1500 ms before the onset of the verbal report, when they recalled video clips they had seen recently and when a neuron with a strong response to that clip was being recorded. Since activity of

individual neurons are thought to reflect the access to long-term memory in situations of recall, we considered specifically the 2000 ms period preceding immediately each verbal response as a wise choice to study T2-related processes (in the following, such windows will be called “T2-windows”).

Once T2 windows were defined, it became possible to evaluate if T2 interfered with T1 at the behavioral level, not only: a) by comparing of course the global performance (i.e. reaction time and accuracy) between the ST and DT conditions (this analysis is referred to as “ST behavioral analysis” in the results section) (see Fig. 21), but more importantly and precisely, within the DT condition, b) by comparing performance during T2-windows and during windows with no verbal response (referred to as, “DT behavioral analysis”). Both behavioral analyses were performed in every participant, extracting the information individually, averaging and comparing by using a T-test with a p-value <0.05.

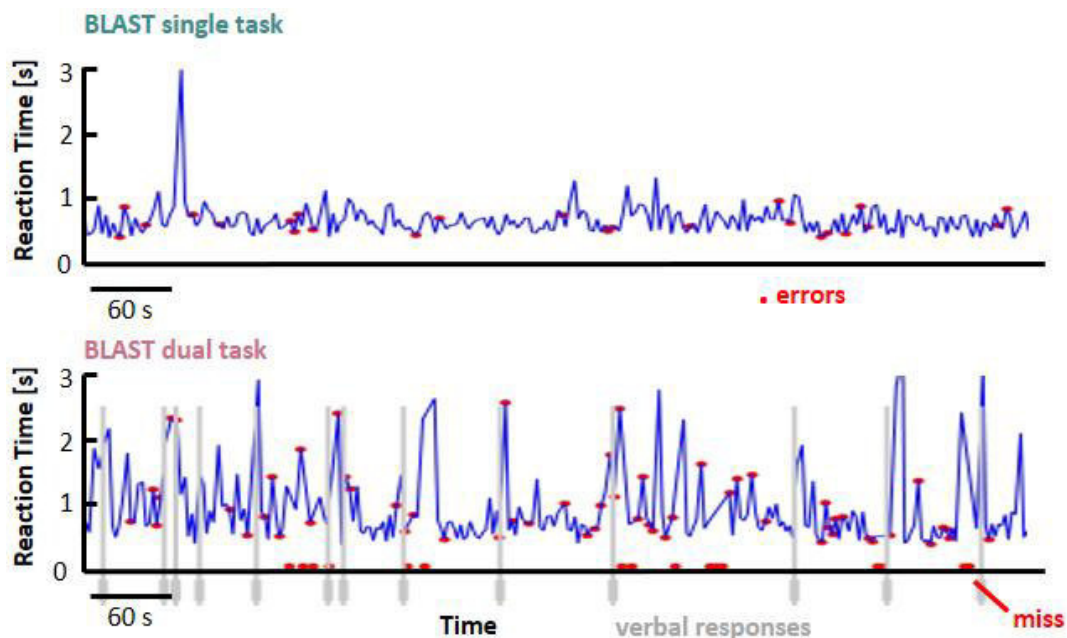


Figure 21: Reaction time on the ST behavioral analysis. it is possible to see the performance of a patient answering T1 within the ST condition (on top) and during the DT conditions (on the bottom), by following the fluctuations of the blue reaction time line, marking mistakes as red dots and grey columns as T2 responses.

The "DT behavioral analysis" was performed as follows: in addition to the T2-windows (one window for every verbal response), all continuous time-segments free of any T2 responses and longer than 2s were divided into consecutive non-overlapping 2s windows called “T2-free windows”. Any difference in performance between T2 and T2-free windows was considered as a strong indication that T2

interfered with T1 at the behavioral level. Of course, participants might have engaged covertly in T2 during “T2-free windows”, but it is our best possible detection of T2-free periods and any misidentification would simply make our analysis too conservative. A straightforward randomization procedure was then designed to statistically estimate the impact of T2 on performance: a) first, the average reaction time (RT+) and accuracy (i.e. % or correct BLAST responses, AC+) were calculated across all T2-windows (N windows for N VFT verbal responses); b) the same procedure was performed on a random selection of N T2-free windows (excluding any window within 2s of a response) to compute a mean reaction time and accuracy value (RT- and AC-) for that selection; c) that last procedure was repeated 10,000 times to generate a distribution of 10,000 surrogate RT- and AC- values, to which RT+ and AC+ were compared, indicating of whether T2 had a significant negative impact on T1’s reaction time and accuracy.

9.3.4 Electrophysiological Analysis

High-Frequency Activity between 50 Hz and 150 Hz (HFA_[50-150] hereinafter, also termed 'high-gamma' by some authors) was extracted from iEEG time-series following our usual procedure. That procedure converts raw signals into time-series of neural activity which approximates neural spiking activity at the population level³⁰³ and correlates tightly with behavior, even in real-time³⁶² and at the single-trials level.²⁷⁹

Bipolar HFA Extraction

The data were recorded with a standard 128-channels acquisition system (Micromed, Treviso, Italy), bandpass filtered online from 0.1 to 200 Hz and sampled at 512 Hz in all patients. At the time of acquisition, the data were recorded using a reference electrode located in white matter, and the signal in each recording site was subsequently re-referenced to an adjacent channel on the same electrode (bipolar montage). A bipolar montage reduces signal artifacts common to adjacent electrode contacts (line-noise and distant physiological artifacts) and improves the spatial resolution of the recording to a few millimeters^{297,303} — slightly from different from subdural grid electrocorticography³⁰³ — by cancelling out effects of distant sources that spread equally to both adjacent sites through volume conduction. It might complicate functional connectivity analysis based on phase estimation,³⁶³ but no such analysis was performed here.

The frequency band of interest [50–150 Hz] was defined from preliminary time–frequency (TF) analyses of the iEEG data using wavelets,³⁶⁴ performed with an in-house software package for electrophysiological signal analyses (ELAN) developed at INSERM U1028, Lyon, France,³⁶⁵ and from previous studies by our group.³⁰³ Raw data was extracted by using a homemade Matlab scripts (the Mathworks, Inc.) and transformed into HFA trial-matrixes with the following procedure.^{279,366}

Continuous iEEG signals were first bandpass-filtered in multiple successive 10 Hz wide frequency bands (e.g. 10 bands from [50–60 Hz] to [140–150 Hz]) using a zero phase shift no causal finite impulse filter with 0.5 Hz roll-off. The envelope of each bandpass-filtered signal was then computed with a standard Hilbert transform (*see Fig. 22*),³⁶⁷ then down-sampled 64 Hz and divided by its means across the entire recording session and multiplied by 100, to express each value as a percentage (%) of that mean (normalization).

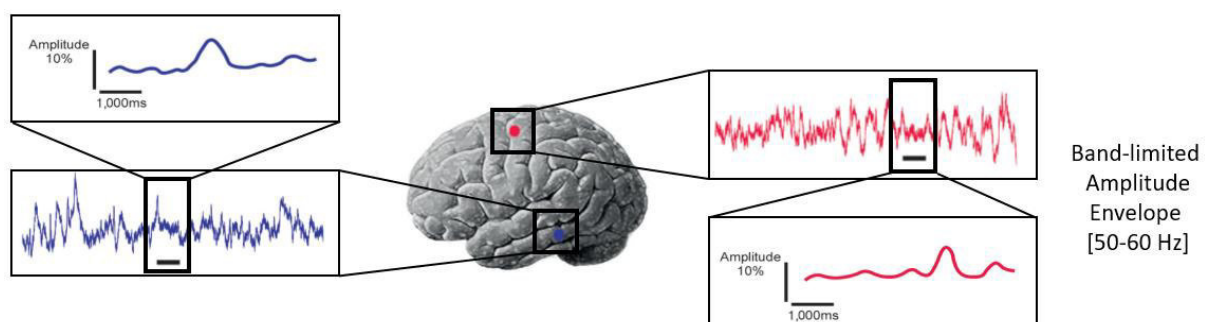


Figure 22: Signal processing. Because the extraction of a wide frequency band causes the spectral power to decrease at higher frequencies, the use of a Hilbert transform compensates for this decrease by creating ten successive envelopes of 10 Hz each, and averaging them all into a single High Frequency Activity (HFA) envelope over the entire session for each electrode, to then create HFA trial-matrixes. Taken from Vidal et al.³⁶⁰

Finally, the normalized envelope signals for each of the ten frequency band were averaged together to provide a single HFA trial-matrix (*see Fig. 23*). By construction, the mean value of that HFA trial-matrix across the entire recording session is equal to 100. The whole procedure is also designed to reduce the 1/f drop-off in amplitude of the raw iEEG signals. To detect task-related HFA increase or decrease induced by BLAST, the HFA trial-matrix was epoched into data segments centered around BLAST target stimuli.

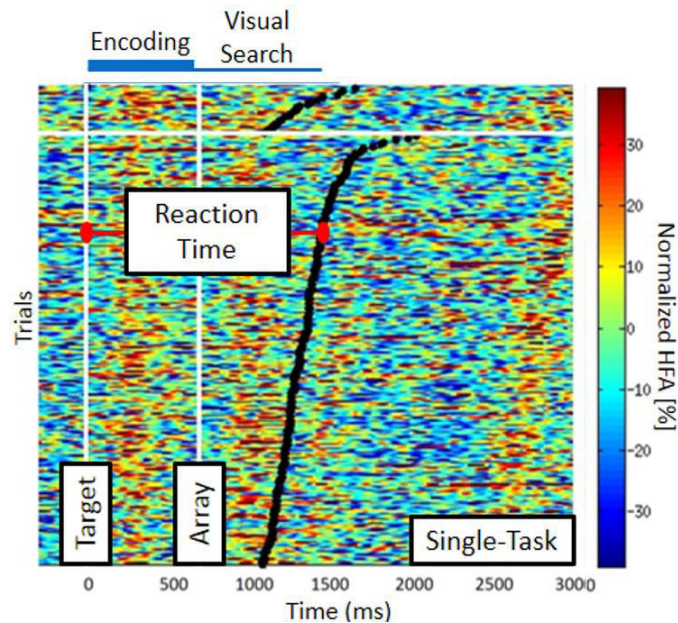


Figure 23: HFA trial matrix. The creation of a HFA trial-matrix was centered on each BLAST stimulus and then were averaged together. Thus, all 250 coloured horizontal lines that forms the trial-matrix correspond to a single trial with normalized amplitude fluctuations according to the bar at the right, with each black dot marking a button press, sorting responses by reaction time. Additionally, the first vertical white line marks the Target presentation, while the second white line marks the Array presentation. In those trial matrixes that included additional conditions to BLAST, we marked with solitary black dots those answers associated to the additional task, or to the onset of a distraction.

HFA Binarization

An additional analysis of HFA trial-matrix was specifically developed to discriminate between “silent” vs “active” time-windows for any given recording site and to identify possible gaps left by T1 during which neurons could engage into T2. While a single-neuron can be said to be silent when it fires no action potential, the concept is difficult to transpose at the population level. In the specific context of this study, the best approximation for such “quiescent” state was during the baseline period of T1 (immediately before the onset of the Target). However, since T2 could potentially generate some intrinsic neural activity — this is our working hypothesis — we had to select episodes of relatively “pure” T1 activity.

For this reason, and considering the impact of T2 on behavioral performance — anticipating the results of the behavioral analysis provided in the results section — the baseline was chosen from the best 50% trials of T1 (the 50% fastest correct trials). Our best estimate of the “neutral” or “quiescent” state of a

given neural population recorded with iEEG, was therefore the activity recorded in the best 50% T1 trials during a period (200 ms) immediately preceding the Target onset (shown in the white frame of Figure 24). The median of all HFA values measured during those windows — called V_{med} — was computed for every iEEG site, and used to binarize the HFA signal: assigning a state ‘on’ or ‘off’ to every time-sample of the experiment. Figure 24 and 25 illustrate that simple procedure, which was performed independently for each iEEG site. The end-result is a binary raster-plot, which reveals the impact of T1 and T2 on the local neural activity in the ST and DT conditions (*see Fig. 25 and 26*). Several statistical procedures were then applied to identify periods with enhanced activity due to T1 or to T2, and to study the interaction between the two.

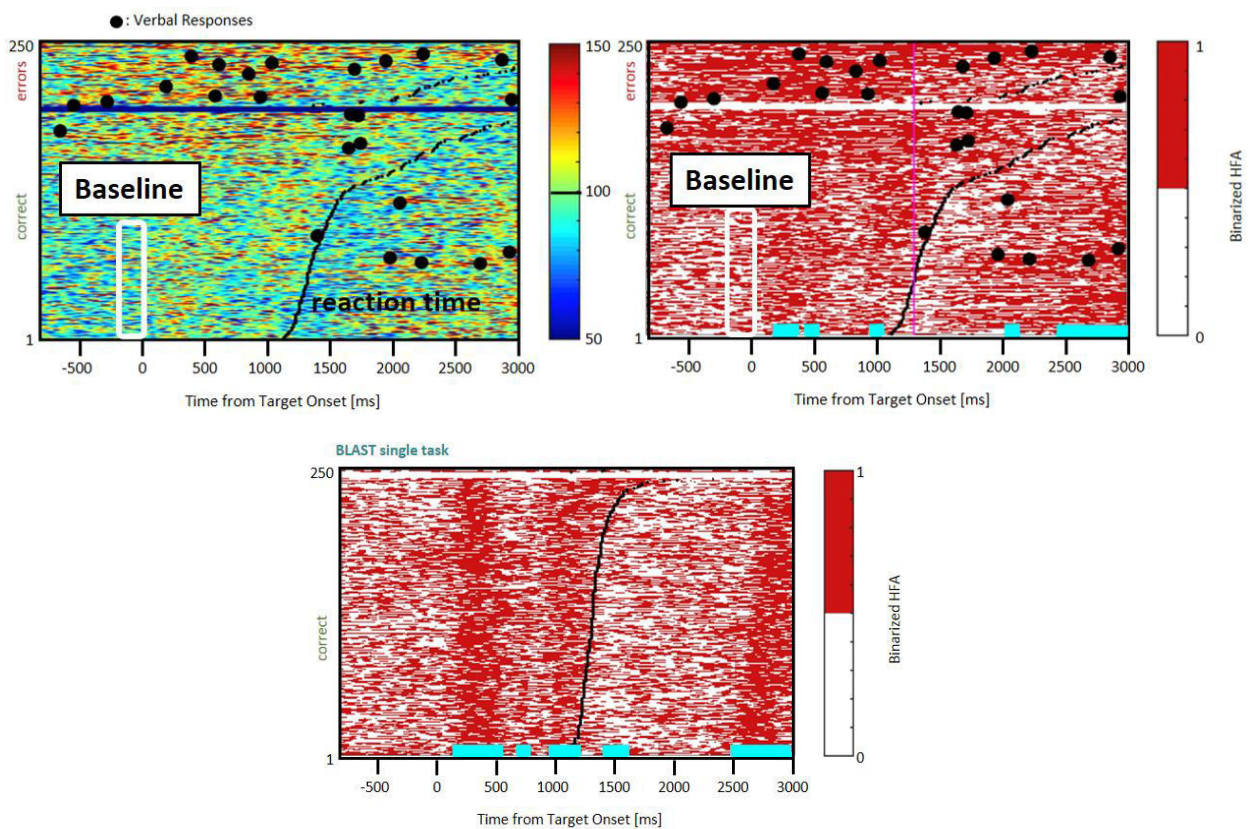


Figure 24 (top left): An example of neural response recorded in the left Precentral Gyrus during T1 in the DT condition, across all trials. Every row of the matrix corresponds to one trial, and HFA is color-coded as a function of time (x-axis). Trials are sorted by reaction time (black line) for correct and incorrect responses (in the lower and upper part of the matrix, respectively). HFA is expressed as a percentage of the average HFA value for that particular iEEG site, across the entire recording. Large black dots indicate verbal responses to T2. The white frame indicates HFA values used to estimate a quiescent baseline state (the prestimulus baseline during the 50 fastest correct trials of T1). The median of all HFA values within that white frame, V_{med} , was used to create the binarized version of the matrix shown in Figure 25.

Figure 25 (top right): Binarized version of the same matrix (DT condition). By definition, 'off' samples in white (resp. 'on' samples, in red) have an HFA value below (resp. above) V_{med} . During the baseline, the signal goes through a noisy succession of 'on' and 'off' states in equal number (at least, and by definition, for the best 50% trials); at other latencies, horizontal cyan lines indicate latencies with an abnormally high (or low) proportion of 'on' samples across the 50% fastest correct trials (see methods for details). By construction, cyan lines indicate time-windows during which the neural population is not available for T2.

Figure 26 (bottom): Binarized trial matrix for the same iEEG site as in Figure 25 but in the ST condition. The comparison between Figure 25 and 26 is illustrative of a strong interference between T1 and T2.

Statistical Analysis

Identification of T1-related neural responses

T1-related activity was detected from the binary raster-plots shown in Figure 25 and 26. When considering the 50% fastest correct trials for a given time sample in T1, (i.e. a vertical slice of the matrix, for instance the M values measured at the Target onset, at 200 ms, across the M fastest correct trials) an effect of the T1 task on neural activity in a given site should result in an abnormal number of 'on' samples relative to the pre-stimulus baseline. Such abnormalities were detected using a Wilcoxon test comparing that distribution of 0's and 1's with the distribution obtained for the [-200 ms : 0 ms] baseline (in all figures, time-segments with a significant deviation from the baseline are indicated by a horizontal cyan lines below the plots; with a statistical threshold of $p < 0.05$ and a False-Discovery Rate correction for multiple comparisons).

Identification of T2-related neural responses

Binarized HFA signals were also used to identify iEEG sites in which T2 had an effect on the local neural activity. Using the same logic as for the behavioral analysis, a T2-window of 2s was defined for each of the N verbal response of the participants. Then, the percentage of 'on' samples was calculated across N T2-windows (PCT+), and for N randomly chosen T2-free windows (PCT-), repeating the surrogate procedure 10,000 times to create a distribution of 10,000 surrogate PCT- values, to which PCT+ was compared to obtain a p-value (and apply a statistical threshold of $p < 0.05$, Bonferroni-corrected for multiple comparisons, as FDR correction could not be applied here; see Fig. 27). In the Results section, iEEG sites identified with that procedure are said to have an "abnormally dense activity" during T2.

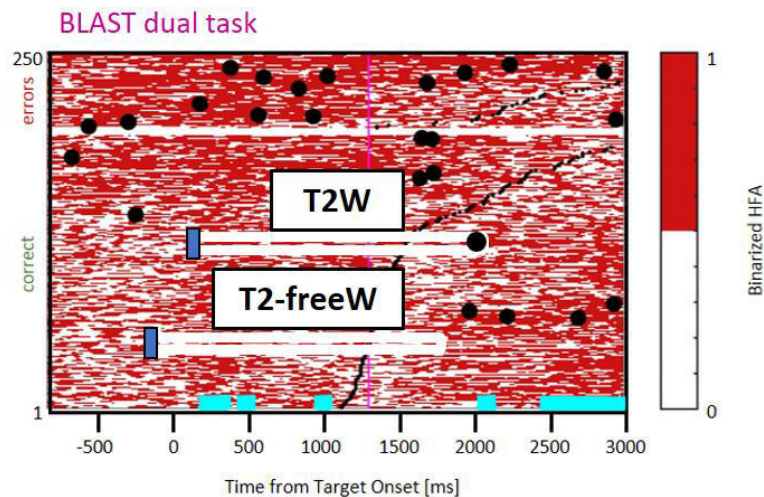


Figure 27: Identification of interference during no-T2 windows. Identification of 'on' samples between 'N' T2W [-2000 : 0 ms] and 10.000 random surrogates not related to T2 (i.e. T2-freeW), and statistical comparison ($p < 0.05$) with a Bonferroni correction.

Detection of sites of interference between T2 and T1

To identify iEEG sites in which T2 interfered with T1, the analysis was based on the observation that T1 trials repeat roughly every 2 seconds: 800 ms of fixation followed by 200 ms of Target presentation, a 500 ms mask and roughly 500 ms before the earliest button presses (see Fig. 19). Given that convenient value, similar to the duration of T2-windows, an estimate of the typical density of 'on' states during optimal T1 performance could be estimated from the fastest correct trials, by calculating the proportion of 'on' sites in a [-800 ms : 1200 ms] surrounding the Target onset (see Fig. 28). Any evidence that the density of 'on' state during T2-windows was greater than during "high performance" T1 windows was indicative of a possible interference between the two tasks at the neural level, with an excess of neural activity due to T2. The actual comparison used a Wilcoxon sign-rank test to compare between the density of 'on' states measured in the N T2-windows (N density values ranging between 0 and 1, i.e. one density value for each T2-window) and the density of 'on' states measured in the N T1 windows corresponding to the N fastest correct trials. The result was an "Interference detection test" which identified all iEEG sites with a higher density of 'on' states during T2-windows ($p < 0.05$, Bonferroni correction).

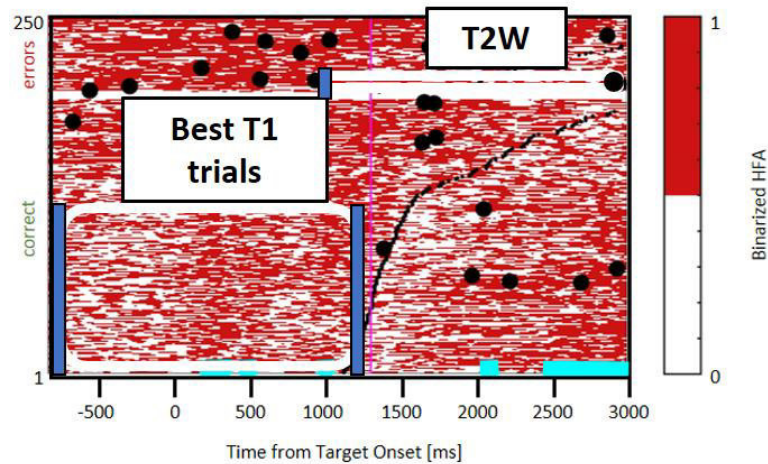


Figure 28: Identification of interference during T1. Identification of ‘on’ samples between ‘N’ T2W [-2000 : 0 ms] and 50% “best” T1 trials [-800 : 1200 ms], and statistical comparison by using a Wilcoxon signed-rank test ($p < 0.05$) with a Bonferroni correction.

Comparison of T1-related activity between the ST and DT conditions.

The direct comparison of HFA signals recorded in separate sessions can be biased by line-noise variations, even if a bipolar montage reduces such contamination. By comparing the binarized HFA trial-matrixes recorded in the ST and DT sessions, we reduced that bias: our analysis compared the proportion of ‘on’ values in the M best trials of the ST and DT conditions for every sample within a [-1000 : 3000 ms] interval surrounding target onset ($T = 0$ ms), where M was set to half the number of correct trials in the DT session (i.e. considering the 50% fastest correct trials of BLAST to minimize the effect of T2). A Wilcoxon test was used to compare for each sample the distributions of M activity values (0’s or 1’s) for the ST and DT conditions ($p < 0.05$, with a False-Discovery Rate correction for multiple-comparisons).

Finally, a similar procedure was used to test whether the activity of specific regions involved in executive control varied between the beginning and the end of the ST session of BLAST. The motivation was to test for a possible automatization of BLAST throughout that initial session (see results). The analysis was as previously described, except that the comparison was performed between the first and last 20% trials (50 trials for each group).

9.3.5 Correlation Analysis

For every pair of iEEG sites, and for every VFT verbal response, we considered a 10s window centered on the response [-6000 : 4000 ms; response = 0 ms] and calculated the correlation coefficient (R+) between the two HFA trial-matrixes for that window. R+ was compared to a population of 10,000 surrogate correlation coefficients created by repeating the following procedure 10,000 times: a) consider two random iEEG sites separated by more than 30 mm and for each of them, a 10s window around a verbal response (with no temporal overlap between the two windows), then b) compute the correlation coefficient R- between the corresponding HFA signal, c) repeat for $i = 1$ to 10,000. The initial R+ coefficient was considered to be significant if greater than all surrogate R- values ($p < 0.0001$, corresponding to a conservative Bonferroni correction). This procedure was used to identify VFT responses with a significant correlation between two iEEG sites.

9.3.6 Anatomical Display

The precise anatomical location of the electrodes (and their MNI coordinates) were obtained by aligning each patient's pre and post-implantation MRIs using the NUTMEG toolbox³⁶⁸ and IntrAnat,³⁶⁹ a specific toolbox interfacing with the BrainVisa software (IntrAnat Electrodes, GIN INSERM U1216, Grenoble, available at <https://f-tract.eu/index.php/software/>). Participants' behavior was recorded and inspected using an in-house software — BrainTV Replay — while anatomical representations were made using HiBoP, also developed by our group and available here (<https://github.com/hbp-HiBoP/HiBoP/releases/tag/2.2.3a>).

BrainTV Replay is an updated version of our original BrainTV software.^{360,370,371} It is designed to visualize a "replay" of the entire experimental session for any participant, with a simultaneous display of the video, the behavioral responses and HFA activity measured for all iEEG sites (*see Fig. 17*) both as time-series and onto a 3D representation of the patient's brain. BrainTV Replay also allows the rapid visual identification of highly correlated HFA fluctuations between iEEG sites. HiBoP was designed to visualize iEEG signals onto 3D anatomy at both group and single-patient level (*see Fig. 18 and 29*). It allows to label iEEG sites using cortical parcellations such as Brodmann's or Marsatlas³⁷² and the Freesurfer/BrainVisa pipeline (available at <http://surfer.nmr.mgh.harvard.edu>).³⁷³ (*see Table I in Annex N°3*)

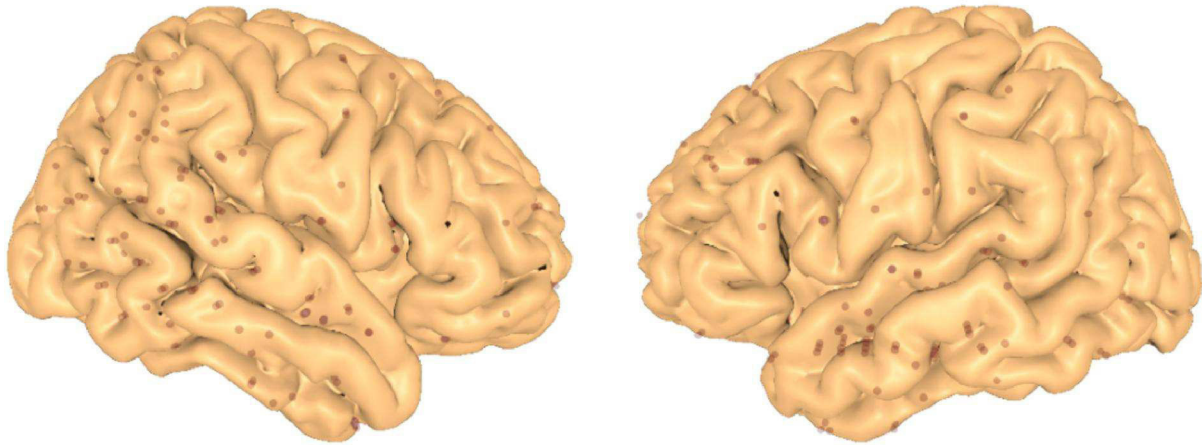


Figure 29: Entry point of iEEG depth-electrodes across all participants. Projected onto the MNI-single participant brain template.

9.4 Results

9.4.1 Behavioral Analysis

Our main assumption was that high performance in T1 (i.e. fast reaction times, few errors) requires a specific dynamic pattern of cortical activations and that T2 might interfere with that pattern in the DT condition to decrease performance. Accordingly, the T1 response selection process should be delayed (slower reaction time) or cancelled (the participant would either not respond or take a bet with a 50% chance of failure) when performing T2 concurrently.

The results of the "ST behavioral analysis" (see Fig. 30) largely confirmed that prediction at the global performance level: overall, reaction times were slower and accuracy lower in the DT than in the ST condition (with a significant increase in reaction time in 11 of the 12 participants). The more detailed "DT behavioral analysis" also revealed that T1 performance in the DT condition was impaired when participants actively searched for T2 answers (all patients had either a significantly slower reaction time or a lower accuracy in periods immediately preceding verbal responses, as exemplified in Figure 31). Overall, the behavioral data obtained in the ST and DT conditions largely confirmed the difficulty for patients to perform both tasks at the same time, which motivated the subsequent search for interferences between the two tasks at the neural level.

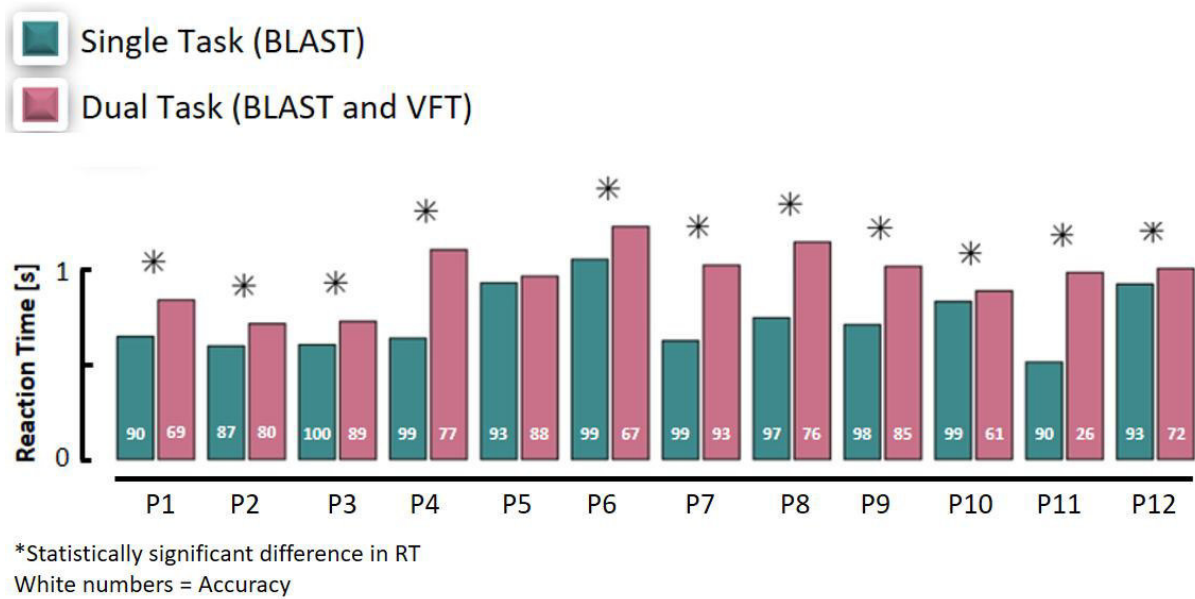


Figure 30: Mean reaction time during T1 for all participants. In the ST (teal) and DT (magenta) conditions (a star sign indicates a significant difference between the two conditions, two-sample t-test; $p < 0,05$). Accuracy is indicated in white (percentage of correct responses).

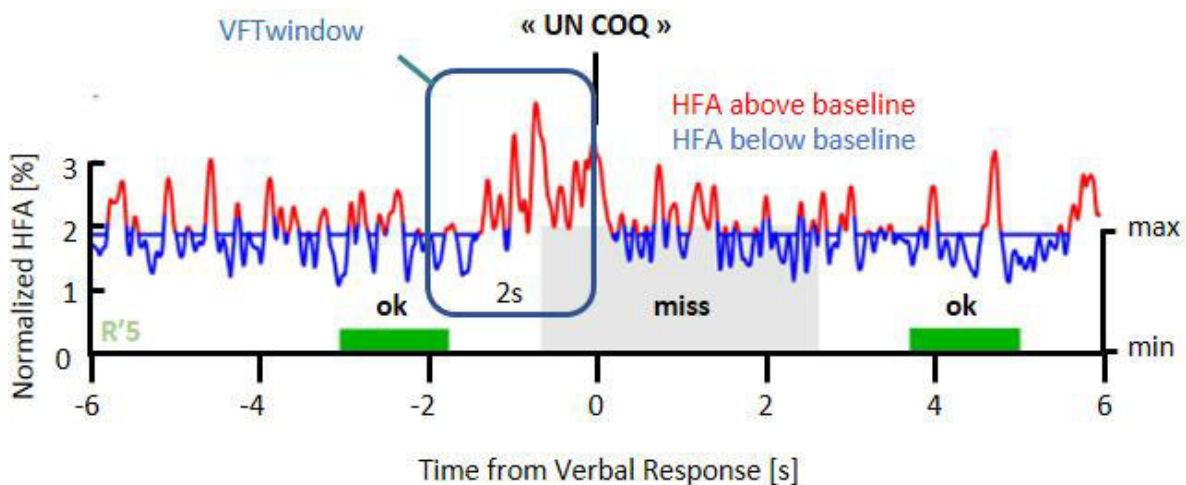


Figure 31: Example of HFA signal measured during a verbal response ("un coq" or "a rooster"). Values above V_{med} ('on' samples) are shown in red, 'off' samples are shown in blue. Several of our analyses measured the proportion of 'on' samples with T2-windows, in the 2 seconds before the response (vertical frame, in blue). T1 performance is color-coded for three consecutive trials (two hits in green, one miss in gray), and the height of the colored rectangles is proportional to reaction time ('min' = minimum reaction time across the entire experiment, same for 'max').

9.4.2 Electrophysiological Analysis

Marked differences were observed between T1 activation patterns in the ST and DT conditions. As an illustrative example and an introduction to our analysis strategy, Figure 32 shows the response in the left Precentral Gyrus to all T1 trials in the two conditions, sorted by reaction time and accuracy. Besides the higher error rate in the DT situation, the most visible difference is the presence of sustained blocks of activation in DT, which are largely absent in ST and incompatible with the fine temporal structure of the neural activation pattern supporting T2 (as visible for the fastest correct trials).

To identify cortical sites with a similar effect, we ran the interference detection procedure described earlier to detect iEEG sites with increased HFA before T2 verbal responses (“T2-windows”), as compared to other time periods of the DT session, including the best T1 trials. We found that the optimal T1 electrophysiological response was disrupted in DT in six major cortical areas: the left Dorsolateral Prefrontal Cortex (DLPFC); the Lateral Temporal Cortex (LTC); the Anterior Insula bilaterally (AI), the junction of the Anterior Cingulate Cortex and the Pre-Supplementary Motor Area (ACC/preSMA), the Precentral Gyrus/Sulcus (Precentral cluster), and the Basal Temporal Cortex (BTC). We now discuss each cluster separately.

Precentral Cluster

In the Precentral cluster, we found effects in the Precentral Gyrus (1 LH, 1 RH, 2 patients) and in the Precentral Sulcus (2LH, 1 RH, 3 patients) with similar neural responses in all sites. The optimal T1 response — for the fastest correct trials in the ST condition — was characterized by two separate phases of activation, in response to the Target and throughout the visual search process, until the manual response (*see Fig. 32*). In the DT condition, a strong and sustained activation was mostly present during the bad trials (i.e. slowest reaction time and/or higher error rate). Recordings from the same sites during additional tasks (the functional localizers) revealed a strong activation during a rhyming task emphasizing phonological processing, and during a verbal working memory task (data not shown).³⁶⁰

These are strong indications that our electrodes sampled a region specialized in covert speech and verbal rehearsal. That might explain the local interference between T1 and T2, because the participants seem to have used a verbal strategy to encode the T1 Target, while the search for specific words in the latter also requires a covert linguistic production. The observed disturbance could most likely be interpreted as direct evidence of a specialized bottleneck, involving a specific cognitive component shared by the two tasks. Yet, we also found clear evidence for a strategy change during T1 for some patients, who seem to have used a non-verbal strategy during the best trials, with a strong attenuation of the double activation peak (see Fig. 32, again).

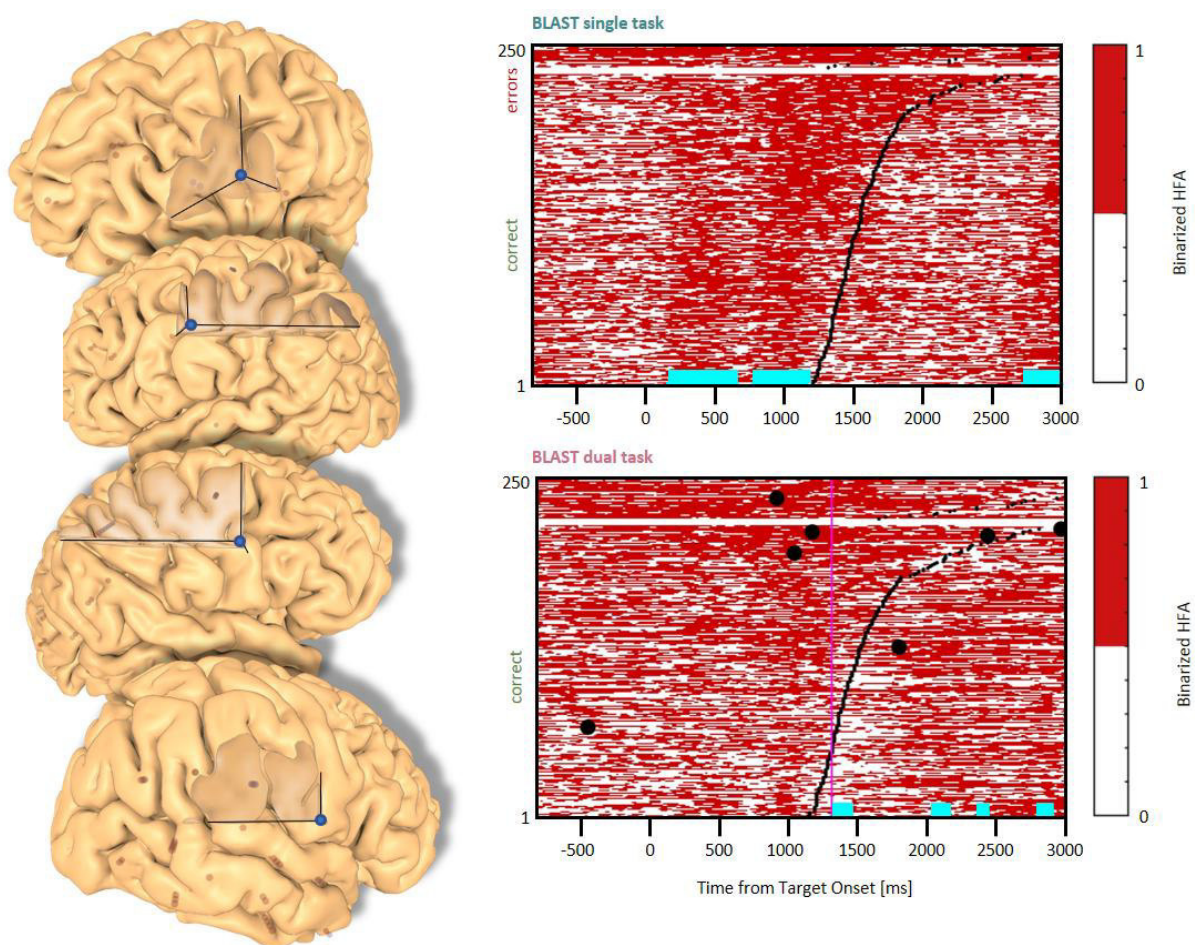


Figure 32: Interference in the Precentral Cluster. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: R'9 [P4]; S'9 [P5] (matrix displayed); M9 [P2]; R9 [P1].

dIPFC Cluster

Two types of effects could be distinguished in the lateral prefrontal cortex. In the Inferior Frontal Sulcus immediately adjacent to Broca's pars triangularis, a double activation peak was observed in three sites (LH, 3 patients) while participants encoded the Target and searched the Array (see Fig. 33), very much as it was observed in the Precentral cluster. In all three sites, the interference in the DT condition produced a response attenuation for the fastest correct trials, and a contamination by T2 during the slower and/or incorrect trials, characterized by a sustained activation. In separate verbal localizers, that sub-cluster was particularly active during semantic and phonological processing, as well as during the retrieval of items stored in verbal working memory. This is consistent with a role in manipulating verbal working memory, information as required by T2 and T1 when the strategy is verbal. The response attenuation in the best trials of the DT condition would again indicate to a shift towards a different strategy, in which the Target would be encoded as a visual template — possibly — rather than in a verbal, phonological form.¹¹¹

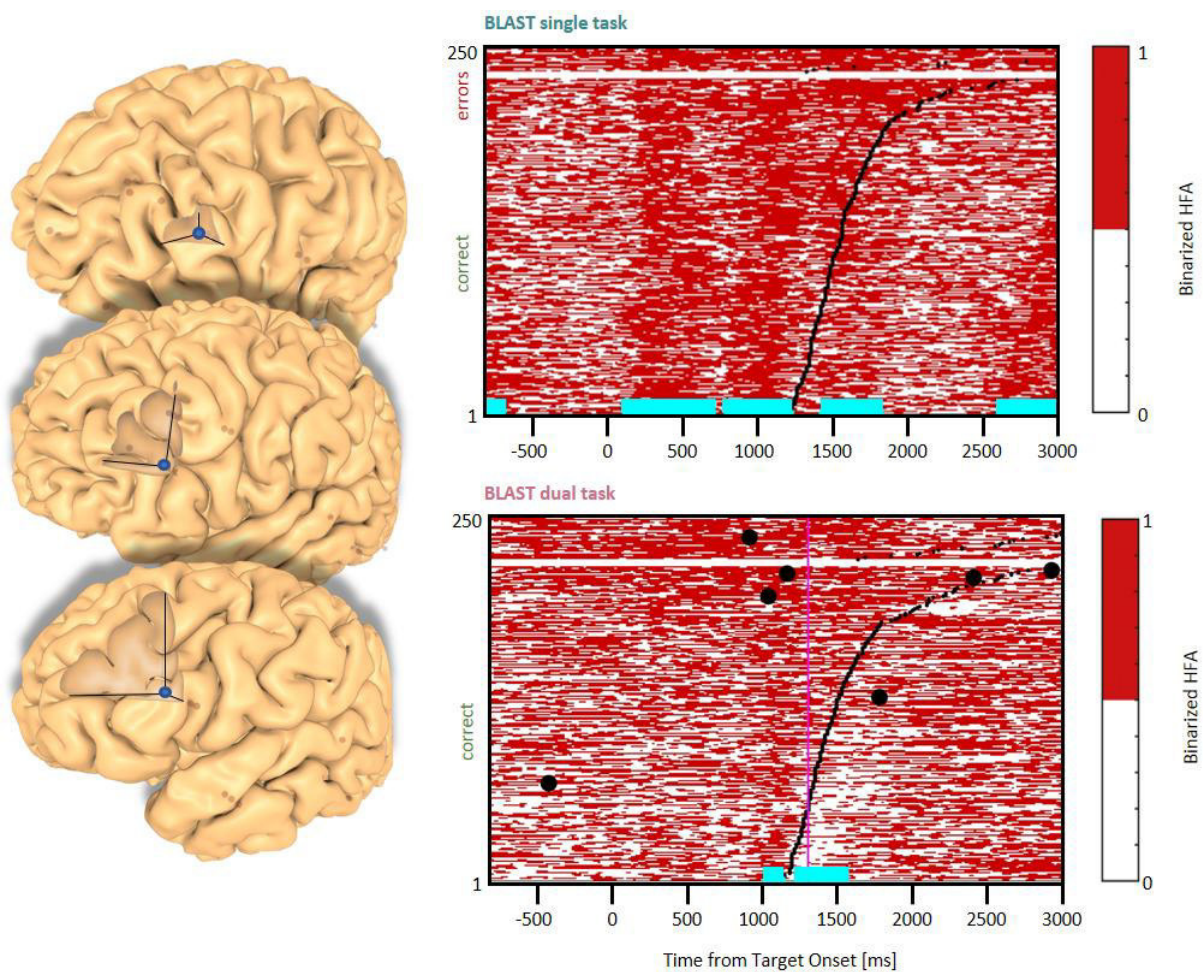


Figure 33: Interference in the Inferior Frontal Gyrus/Sulcus. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's

brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: G'13 [P4]; K'10 [P5] (matrix displayed); Q'2 [P11].

An interference pattern was also observed at three other sites more anterior in the DLPFC, specifically in the Middle Frontal Gyrus above the anterior pars triangularis (LH, 3 patients, see Fig. 34). There, T1-related activity was different from the previous pattern, with no response during the Target presentation and an activation by the end of the Array presentation extending to the short inter-trial pause. The role of that sub-region in both tasks is less easy to understand, but the corresponding sites were selectively activated by language and verbal working memory localizers.

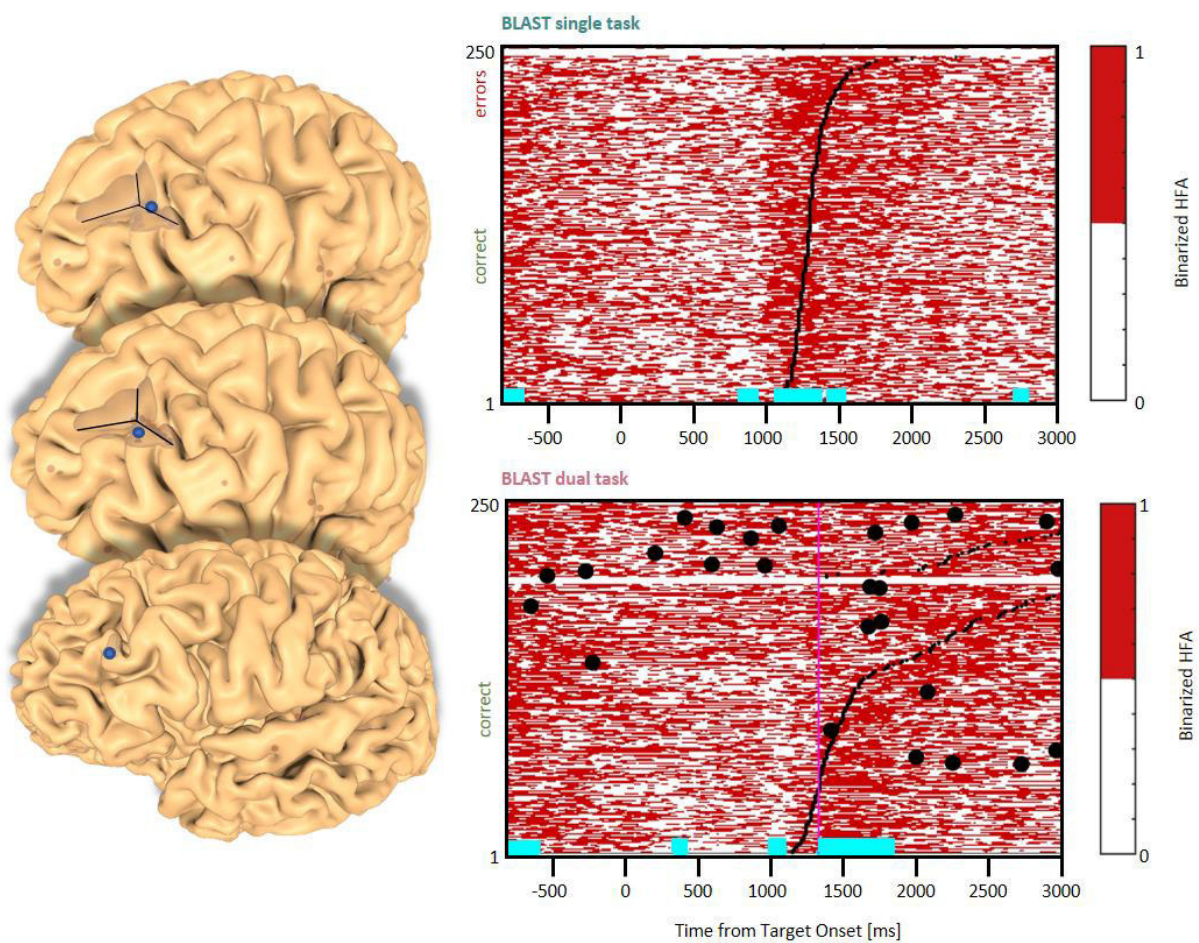


Figure 34: Interference in the Dorsolateral Prefrontal Cortex. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: F'9 [P4] (matrix displayed); Y'13 [P4]; G'12 [P9].

AIC and ACC/preSMA Cluster

In the Anterior Insula, we found six sites (2 in the LH, 2 patients, and 4 in the RH, 4 patients) with a deviation from the optimal T1 dynamics in the DT condition (see Fig. 35). The T1 response pattern was reproducible across sites, with a sustained activation during the display of the Array, time-locked to the response. T2 also produced sustained activations, clearly incompatible with the T1 activation pattern. Both left and right hemisphere sites were activated by a verbal working memory task and by tasks emphasizing semantic and phonological processing.

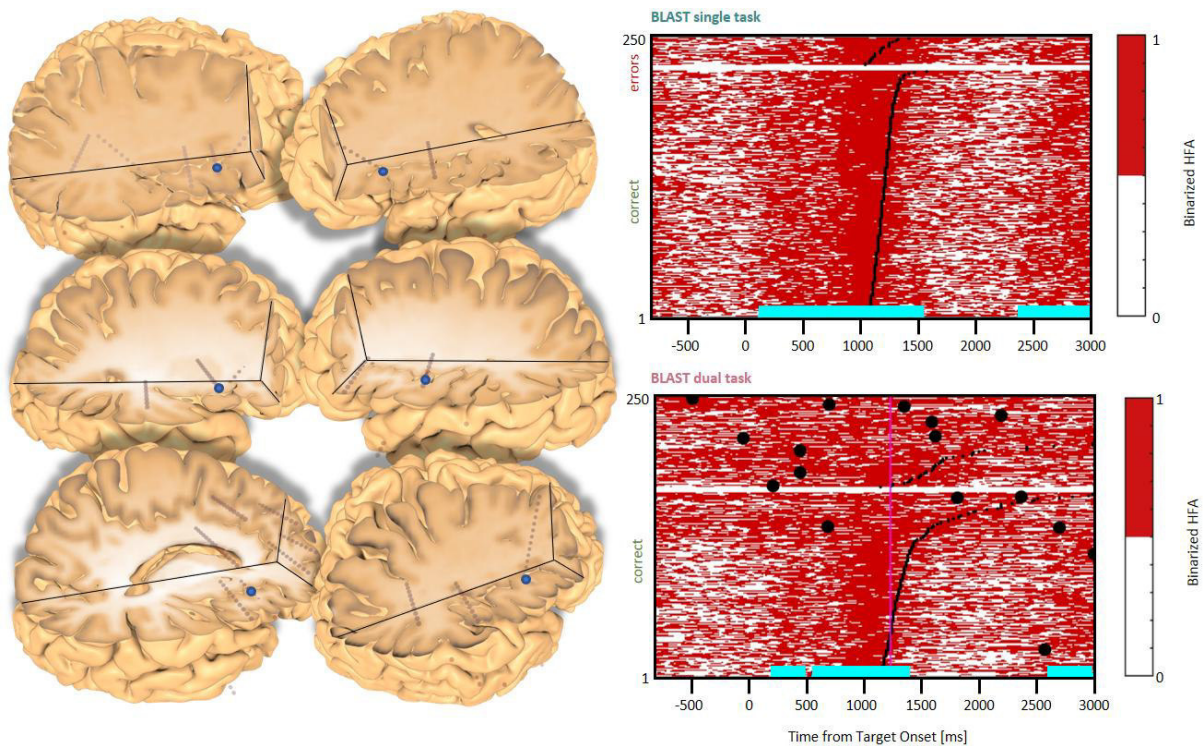


Figure 35: Interference in the Anterior Insula. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: X7 [P3]; X'9 [P3]; X5 [P11]; X'9 [P11] (matrix displayed); E4 [P7]; X7 [P12].

These observations were mirrored by responses in the Paracingulate Sulcus (one site in each hemisphere, 2 patients, *see Fig. 36*) although the activity rose more progressively throughout T1 trials. Data from the functional localizers revealed a similar increase in all tasks, emphasizing executive control (visual search, working memory). As often seen before, the neural activation during the best T1 trials (i.e. 50% fastest correct trials) was weaker or even absent in the DT conditions, compared to the ST condition. That specific result should catch our attention and will be discussed further, considering that this specific anatomical cluster is believed to support general executive control, rather than specific cognitive processes: it suggests the possibility of a general change of approach to cope with the DT situation, much more global than a simple strategy change from a verbal to a visual encoding of the Target, for instance.

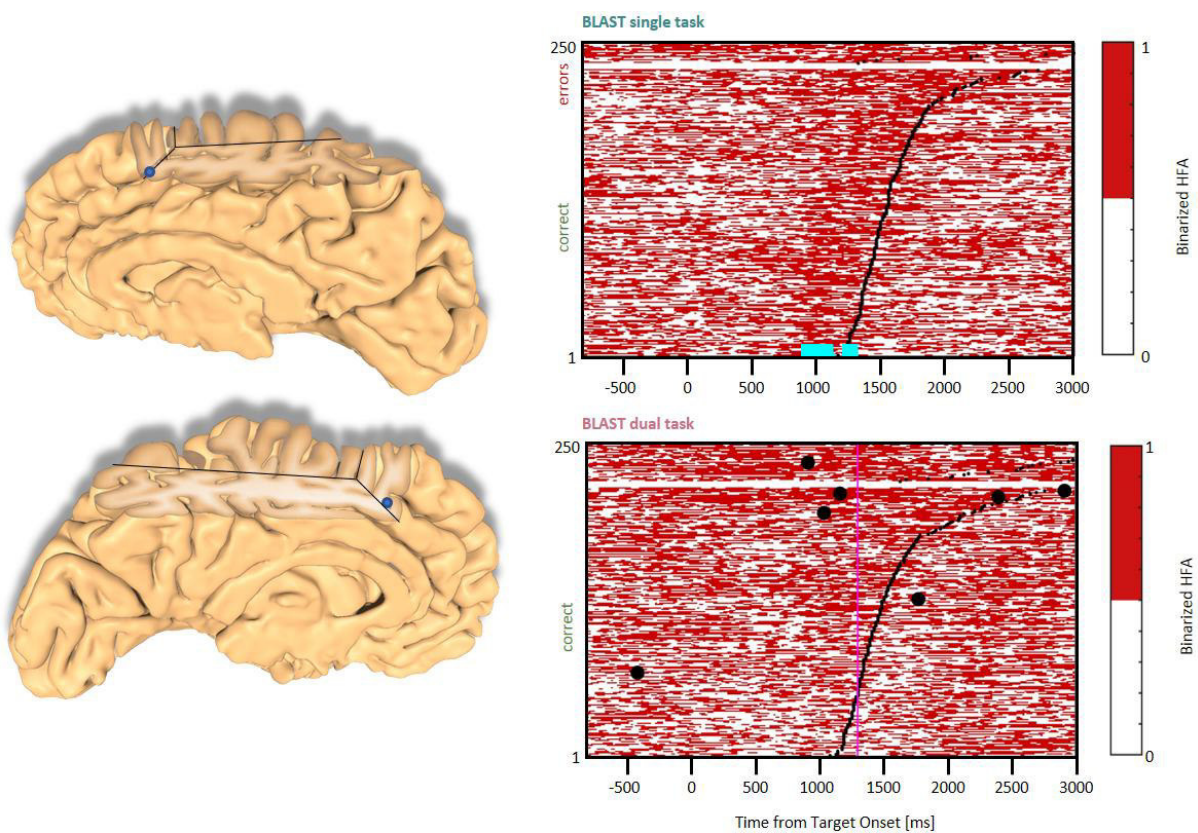


Figure 36: Interference in the Anterior Cingulate Cortex and the Pre-Supplementary Motor Area. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: S2 [P7]; Z'2 [P5] (matrix displayed).

Lateral Temporal Cluster

Three sites activated by T1 in the Middle Temporal Gyrus were also reactive to T2 (see Fig. 37, two sites in the left hemisphere and one in the right hemisphere in two patients). The activation patterns were reminiscent of the Precentral cluster, both for T1 and for the functional localizers, with strong and selective responses to conditions emphasizing verbal processing. We suggest that this cluster might support verbal processes shared by T2 and T1 under a specific verbal strategy. The sharp reduction in activity in the best T1 trials of the DT condition could again be explained by a shift to a non-verbal strategy to reduce interference. Once again, the amount of interference between T1 and T2 seems to depend more on the strategy used rather than on the tasks themselves.

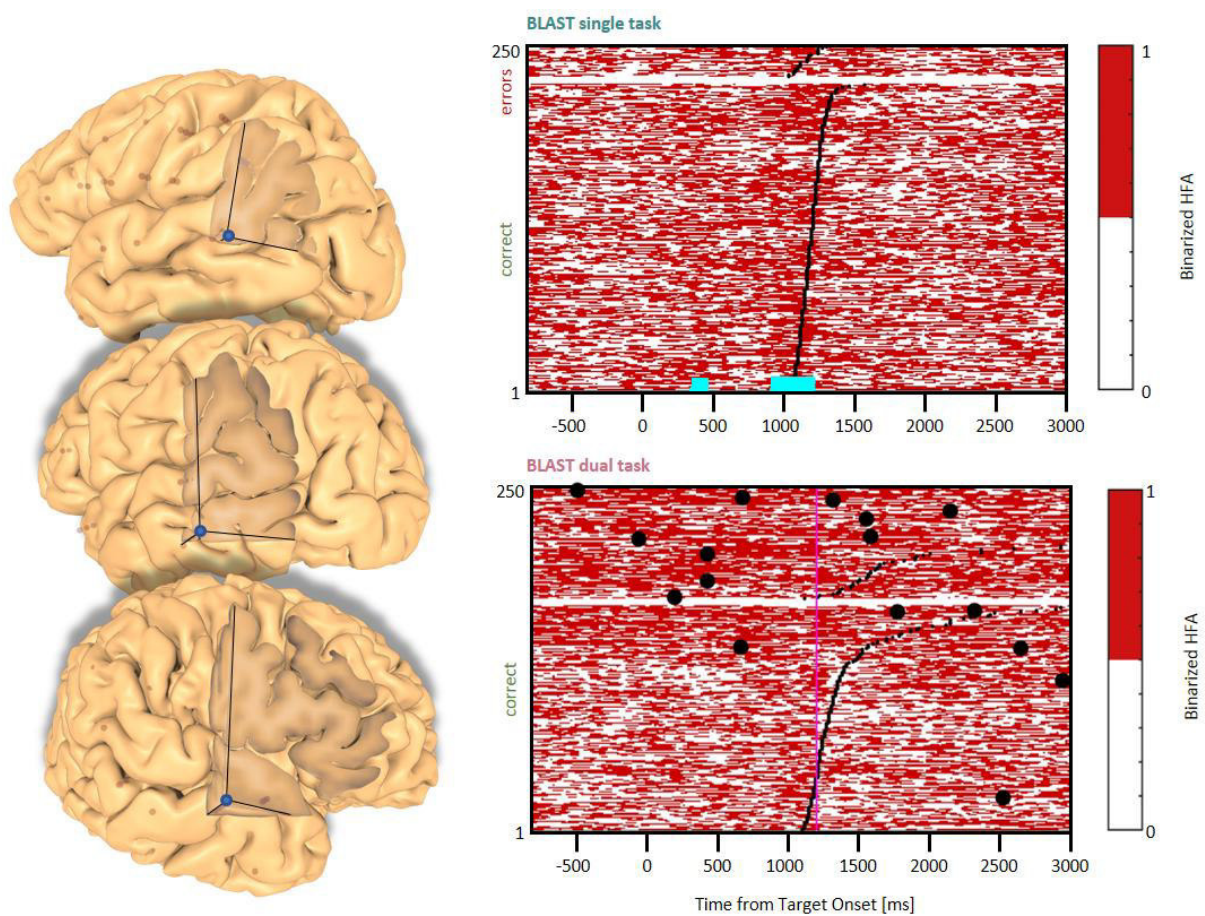


Figure 37: Interference in the Lateral Temporal Cortex. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: D'7 [P6]; C'12 [P11] (matrix displayed); A9 [P12].

Basal Temporal Cluster

Finally, an interference pattern was also observed in three sites around the Fusiform Gyrus (2 in the LH, 1 in the RH) (see Fig. 38). Interestingly, all three sites were located in subregions of the visual cortex specific to precise object categories, as revealed by responses to a functional localizer showing several categories of pictures. Both sites in the left hemisphere were located in the Visual Word Form Area (selective to letter strings), while the right hemisphere site was most efficiently activated by face stimuli (but still responsive to letter strings). The activation of these sites during T2 was not unexpected, since participants could rely on mental imagery to remember specific faces, find names starting with the given letter, or visualize spelling. Still, it is quite remarkable that such activity could be detected online, revealing in real-time the strategy used by the participant. Incidentally, T2-related activities turned out to be stronger in the right hemisphere when the participant was searching for people's names vs. other categories, such as fruits.

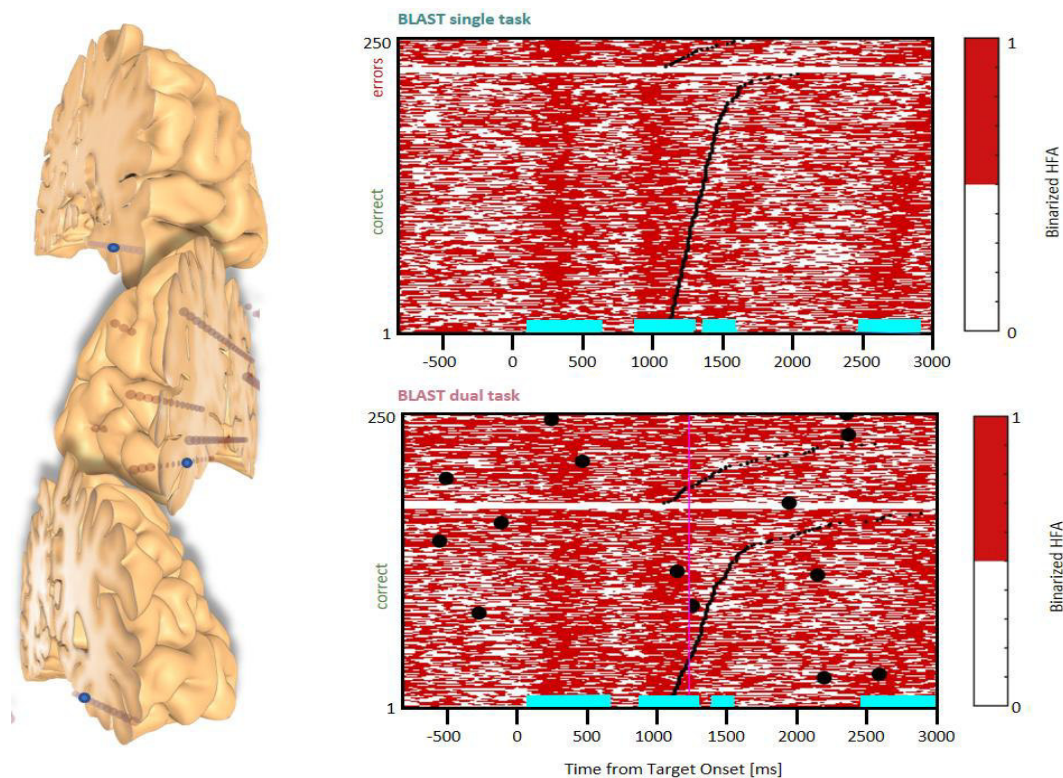


Figure 38: Interference in the Basal Temporal Cortex. Sites with an interference between T1 and T2 are displayed at their precise anatomical location onto a 3D representation of the participant's brain. The matrix representation reproduces the display of Figures 24, 25 and 26, for the single-task and dual-task conditions for one of the sites. Patients id [Px] and iEEG site names, from left to right and top to bottom: E'7 [P4]; F6 [P1] (matrix displayed); L'3 [P5].

9.4.3 Network Analysis (and the possibility of indirect interference)

Our visualization software, BrainTV Replay, allows for the joint review of HFA trial-matrixes of two sites, as superimposed curves synchronized with video recordings, which is extremely convenient to detect high-correlation episodes visually (see Fig. 39). During the preliminary visual review of the data, we were immediately struck by extremely high correlations between HFA time fluctuations of specific sites distant from each other. This motivated a quantitative search for significant functional coupling between the sites reported above, when several clusters could be recorded in the same patient. The analysis revealed patterns of very high and significant correlation episodes for specific verbal responses and cortical areas (as illustrated between the left Precentral cortex and the left BTC in Figure 39a); however, few of them were systematic enough to be reported. The most reproducible correlation was observed in two patients (P3 and P11), between the left and right Anterior Insula, where we found significant correlations between both hemispheres for more than half of T2's verbal responses (13 out of 16 for P3, and 17 out of 31 for P11) (see Fig. 39b for an example). Although limited, our results showed that “the” central bottleneck should rather be thought as a network of bottlenecks, where tasks interact dynamically with each other. This also raises the possibility that a secondary task like T2 could also interfere indirectly with T1, by recruiting cortical regions that do not belong to the T1 network, but that are coupled to some of its components and interact with T1 through that interaction.

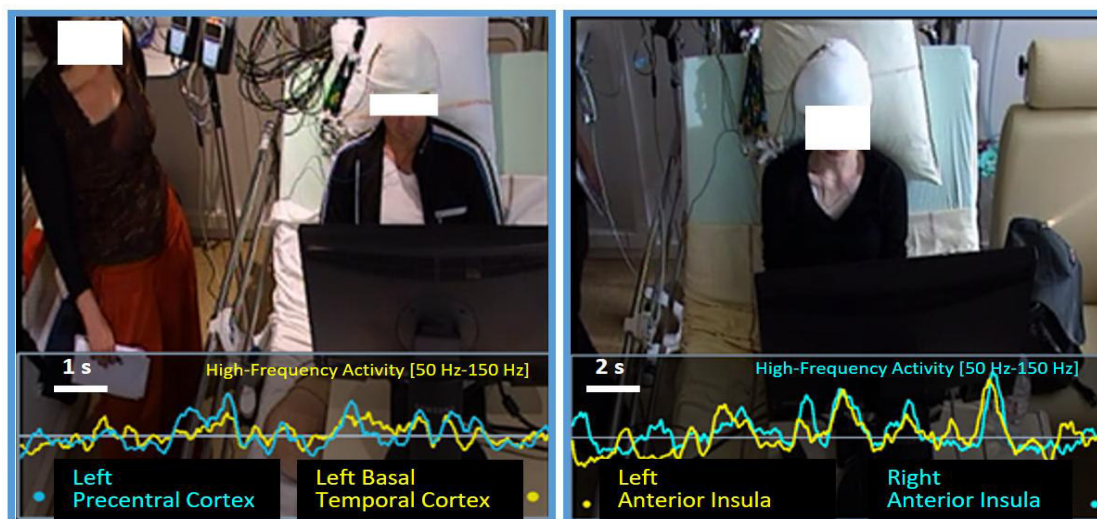


Figure 39: Correlation between bottlenecks. A) BrainTV display showing an episode of very high and sustained correlation between two bottlenecks, one in the Precentral Cluster and the other in the Basal Temporal Cluster. Curves correspond to HFA activity measured in the last 10 or 20 seconds before a verbal VFT response, as indicated in the figure. B) Same representation showing a robust correlation between two sites in the left and right Anterior Insulae

9.4.4 Fine Tuning of Executive Control

To conclude, we specifically investigated the differential involvement of the executive control network in the ST and DT conditions. As reported above, some sites in the DLPFC, the AI and the ACC/preSMA were less active during the best trials of BLAST in the DT than in the ST condition, as recapitulated in Figure 40. The figure reveals a significant difference between the density of 'on' states in the two conditions, when considering the same number of trials with the fastest correct responses (see methods). In some sites situated in essential nodes of a network supporting cognitive control, an attention-demanding task such as BLAST evoked almost no response in the DT condition, which comes as a surprise. We reasoned that participants might have automatized BLAST through the ST session, which always came before the DT session; in which case an attenuation of the response to BLAST should already be visible within the ST session. To test that hypothesis, we tested whether activity in the executive network was lower at the end than at the beginning of the ST session. For all sites discussed in this section, we measured the density of 'on' states for each trial, in a critical [900 : 1200 ms] window relative to the Target onset, and compared the values obtained for the first 20% of the trials (50 trials at the beginning of the ST session) and the last 20%. We found no significant difference except for one site in the ACC where activity was greater by the end of the experiment. It is therefore unlikely that the reduced response of the executive control network in the DT condition was caused by the automatization of BLAST. It is most likely due to an effective reduction of control with no performance decrement, which suggests that participants exerted more control in the ST condition than strictly necessary.

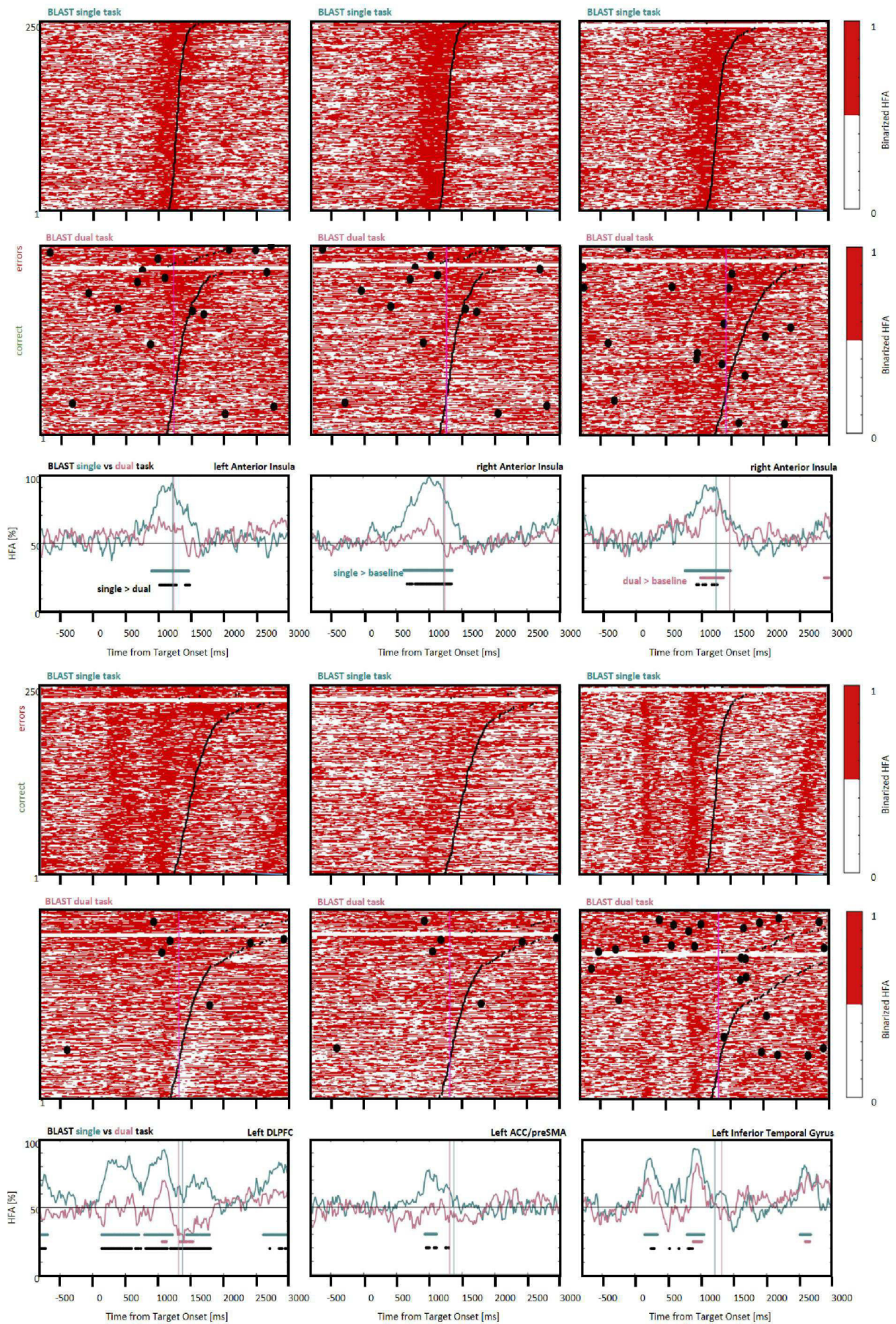


Figure 40: Interference control in the executive network and the visual network. Comparison of BLAST-related activity in the ST and DT conditions for six sites (five of them supporting executive control in the anterior insula, DLPFC and ACC/preSMA, the last one supporting visual processes in the inferior temporal gyrus). For each site, BLAST-related neural activity is represented as a binarized matrix for the ST (top) and DT (middle) conditions. The curves at the bottom correspond to the average of those matrix for the M fastest correct trials, where M equals half the number of correct trials in the DT condition. Horizontal lines indicate samples with a significant difference between the DT and ST curves (black), or a significant increase relative to the [-200:0 ms] pre-Target baseline, for the ST and DT conditions respectively (in teal and magenta) (Kruskal-Wallis test, with a False-Discovery Rate correction for multiple comparisons). From left to right and top to bottom, iEEG sites and [Patients id] are : X'9 [P3]; X7 [P3]; E4 [P7]; K'10 [P5]; Z'2 [P5]; E'7 [P4]

9.5 Discussion

Our main objective was to observe and understand the interference between two attention-demanding tasks at the neural level. To the best of our knowledge, that had never been done with direct electrophysiological recordings that can reveal the recruitment of a focal neural group by a cognitive task at a subsecond temporal scale. Inspired by the Response-Selection Bottleneck theoretical framework,³ we searched for specific neural populations that the two tasks would have to activate at the exact same time, that is, a situation of dynamic incompatibility that would exclude dual-tasking de facto. Although several fMRI studies have already identified potential bottlenecks,^{232,235,236,263,374} their temporal resolution was not sufficient to demonstrate that two tasks are strictly mutually exclusive, with no possibility for a fast-multiplexing process giving the false impression that they are performed simultaneously.³⁷⁵ Also, fMRI suffers from the fact that the BOLD signal is an indirect measure of neural activity: for instance, the observation that two tasks cause an increase of the BOLD signal in the same voxel does not fully explain why the tasks interfere, because that effect could reflect the activation of two different neighbor neuronal populations that do not compete with each other (see Fig. 41).^{375,376} A true bottleneck is a specific neuronal population that is required by the two tasks at the exact same time, and it can only be identified with focal recordings of that population with a very high temporal precision. iEEG is the only measure of human brain activity with the desired spatio-temporal precision.³⁰⁰

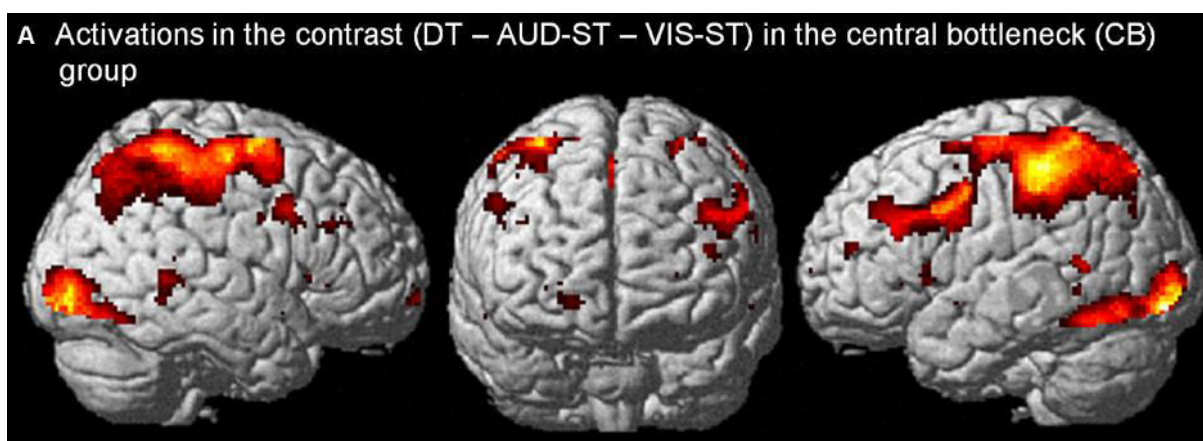


Figure 41: BOLD signal limitations. There is a large number of studies based on fMRI in which it is very difficult to define if during a dual task condition, the increment of activity in a common voxel occurs for both tasks at the same time, or activates for each task separately in time. This is because the BOLD signal only show an indirect measure of the neural activity, with a limited temporal definition that does not allow for a distinction in the range of milliseconds. Taken from Szameitat et al.³⁷⁴

We hypothesized that the simultaneous performance of two attention-demanding tasks T1 and T2 might rely on temporal gaps in the dynamic pattern of neural activations induced by those tasks, e.g. transient time-windows within T1, during which neural activity returns to baseline level and can be used for T2. We reasoned that if such gaps were long enough, it might be possible for neural populations to participate in T2, thanks to a time-sharing mechanism that would enable dual-tasking.¹⁹⁴ We identified gaps in several cortical sites active during T1 but they were usually relatively short — around one second — and not long enough to allow the recall process required by T2, as it had been evaluated by direct neural recordings during a free-recall task similar to the VFT.³⁶¹ In principle, that observation formally excludes any form of parallelism between the two tasks we present, which are quite representative of naturalistic tasks involving a simultaneous attention towards external stimuli and internal representations. Although some authors have proposed that parallelism might be possible in some instances,^{169,377} several arguments go against that hypothesis.^{203,378,379} In short, we propose that our two tasks are "dynamically incompatible": one must be stopped for the other to unfold. Indeed, the participants were mostly confused and frustrated in the DT condition, and reported after the experiment that they found it very difficult to perform the two tasks simultaneously.

We specifically found that the two tasks co-activated iEEG sites in virtually all the regions of the Multiple Demand System (MDS)¹⁵⁹: in the DLPFC (in the Inferior Frontal Sulcus and the Middle Frontal Gyrus), the Anterior Insula, the Precentral Gyrus, and the ACC/preSMA; the remaining component, the Intraparietal Sulcus, is rarely sampled by stereotactic EEG electrodes.¹⁶² The MDS is a broad domain-general and process-general network involved in a large variety of demanding cognitive tasks,^{162,246,380} such as BLAST and VFT. Therefore, it is not surprising that it constitutes a strong bottleneck preventing efficient dual performance. What we show is that quasi-continuous tasks such as BLAST create a situation of dynamical incompatibility in the MDS with tasks that require an access to long-term memory.

We also found clear evidence that cortical regions of the MDS shared by the two tasks do not work in isolation from each other: activity was strongly coupled across large distances, from instance in the Anterior Insula bilaterally. It follows that the central bottleneck should always be considered as a distributed network: interference between tasks is due to a network of bottlenecks, which strongly interact with each other.

Besides the MDS, we also found process-specific bottlenecks in the language network and in high-level visual areas such as the Visual Word Form Area or the Fusiform Face Area. Interestingly, those bottlenecks do not fall into one of the usual categories of the DT literature at central^{14,159} or peripheral levels.^{43,57} Peripheral bottlenecks usually refer to sensory or motor systems which interfere when two

tasks involve sensory stimuli of the same modality (e.g. simultaneous sounds) or overt responses of the same type (e.g. left index movements). Yet, BLAST and the VFT create a competition that is mainly between overt and covert representations: perceiving letters on a screen vs. mentally imagining how a word is spelled. Therefore, our study provides clear evidence that any combination of tasks that involves a competition between sensory perception and imagery should be incompatible, because they rely on common high-level sensory areas (intermediate between peripheral and central bottlenecks).²³⁵

9.5.1 Bypassing the Bottleneck(s)?

Our data revealed two possible mechanisms to reduce interference in a dual-task condition and although they were found for a specific combination of tasks, we believe our findings might extend to more general situations. First, we found evidence for clear strategy changes for the BLAST task between the ST and DT conditions. During BLAST, the target can be encoded, and to some degree searched for, using either verbal or visuo-spatial working memory (rehearsing the letter with covert speech or taking a visual ‘snapshot’). In some participants, their strategy could be deduced from the activity of regions supporting phonological processes, such as the lower Precentral Gyrus, when they were sampled by iEEG electrodes. Our data revealed striking instances where those regions withdrew from the BLAST task for the most successful trials in the DT session. Considering the fact that the VFT task heavily relies on verbal processes,³⁵⁸ it seems like an efficient way of coping with that specific combination of tasks. Interestingly, that effect was not observed for the least successful trials, suggesting that the participants might have found it difficult to stabilize such an alternate and possibly less natural strategy.

We observed similar effects in the MDS, which is much more surprising. The Anterior Insula, the Anterior Cingulate Cortex, the Pre-Supplementary Motor Area and the Inferior Frontal Gyrus are part of a network which activity is not believed to depend on the type of strategy used. A recent article summarizing a number of findings on executive processes concluded that they form the core of the executive Multi-Demand Network (core eMDN), in charge of "executive processing and cognitive control by initiating and maintaining cognitive sets, coordination behavioral responses and guiding behavior in general".¹⁶⁵ Beyond differences in terminology and delineation — core eMDN, MDS or saliency network — these regions are believed to support general cognitive control rather than a particular strategy. BLAST is a demanding task designed to prevent automatization¹⁶⁷ which activates the core eMDN consistently, at least in the ST condition. Therefore, we did not expect that BLAST could

be performed efficiently by some participants with virtually no activation of the core eMDN, especially during the best trials in DT.

One might argue that the core eMDN might primarily activate in the DT condition when participants try to perform both tasks at the same time, because that situation requires more executive control^{141,144,147} — but the core eMDN is also active when BLAST is performed in isolation. Alternatively, one might remind that the AI and ACC have also been associated with error-monitoring^{146,381–383} which could explain their strong activation during the worst trials of BLAST in the DT condition. However, that suggestion is incompatible with the fact that those regions are systematically active in the ST condition, even for successful trials. One remaining explanation is that participants might have automatized BLAST during the ST session, and therefore exert less executive control during the DT session. Yet, BLAST is so repetitive and long — with 250 trials — that signs of automatization should already be visible in the ST condition when comparing the beginning and the end of the experiment. This is not the case.

We believe that our data rather support the following scenario: in the DT condition and consciously or not, participants sometimes shift cognitive control away from BLAST and towards the VFT, with no impact on BLAST performance, quite surprisingly. It follows that BLAST can be performed fast and accurately with less control (i.e. less activation of the eMDN), which provides an unexpected way out of the central bottleneck: performing one of the two tasks “as if” it was fully automatized.

Since cognitive control has been associated with mental fatigue, one might then wonder why participants do not use that strategy also in the ST condition. One possible explanation is that the need for control is so deep that they must be forced to do so by a secondary task: forced to “let go” simply because they are unable to control everything. The implication of that finding is rather profound, as it suggests that we might be exerting too much cognitive control, and therefore too much mental effort, on tasks that could be done almost effortlessly. This conclusion is reminiscent of a study that used the attentional blink phenomenon to show that control participants, compared to meditation experts, over-process task-relevant stimuli³⁸⁴ — too much effort, again. More generally, it should remind us that focused attention should be dissociated from mental effort, as clearly demonstrated by multiple insightful contributions in a seminal book on that topic.³⁸⁵

How environmental distractions interfere with behavioral performance during attention-demanding tasks

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In preparation

10.1 Abstract

As more and more working environments lack spatial separations between co-workers ('open-space'), distraction by environmental sounds and events has become a major concern for productivity-seeking professionals, who fear a negative impact on attention and performance. The objective of the present study was to understand how environmental distractions affect neural activity during attention-demanding tasks. Participants were asked to perform a novel continuous attention task specially designed to detect transient loss of focus due to external conditions (BLAST, a series of short visual search tasks, repeated every 2 seconds). Because distraction is primarily social in working environment, participants were distracted by an experimenter sitting next to them throughout the task, following a predefined series of naturalistic events (sneezing, dropping a pen...) carefully spaced in time. Distractions were identified offline on a video of the experiment to analyze their effect on the large-scale dynamics of the BLAST network, measured with milimetric and millisecond resolution with intracranial EEG (iEEG). IEEG measured in seven participants revealed that external distractions counteract and prevent the suppression of activation in the medial parietal lobe, which is normally inhibited during optimal BLAST performance.

10.2 Introduction

When performing a behavioral task, executive control ensures the optimal performance during attention-demanding tasks - as characterized by stable, fast and accurate behavioral responses.^{246,274} This allows the brain to engage specifically in the perceptual, cognitive and motor processes relevant to the task at the exclusion of any other that might sidetrack limited cognitive resources.²⁹

Distraction occurs when executive control fails to filter out task-irrelevant processes,^{262,263} which might imply excessive processing of external events (external distraction),³³¹ or task-unrelated spontaneous cognition (internal distraction).^{386,387} Although detrimental to performance,²⁶⁴ the capture of attention by stimuli irrelevant to the task at hand has obvious evolutionary advantages: without a defense mechanism to quickly reorient attention towards potentially dangerous stimuli, such as the approach of a predator, our species would most likely have gone extinct.²⁶¹ Nowadays, the same mechanism allows the driver to notice an approaching ambulance even when focused on the cars just in front. Focus and distraction should therefore be thought as two complementary mechanisms, which compensate the excess and pitfalls of each other.²⁶¹

The neural implementation of the distraction by external stimuli has been extensively studied^{263,277,281} and there is now general agreement that the reorientation of attention towards unexpected stimuli outside of the context of the current task is mediated by the VAN, comprising part of the Orienting Network.^{14,16} This VAN would act as a circuit breaker²⁷⁷ while a DAN comprising primarily the FEF and the IPS would ensure that attention stays on task-relevant information.⁴ Recently, our team published a study showing that a region at the interplay between the two networks, in the IFS, might quickly analyze incoming sensory events in relation to ongoing task goals and decide whether they should be processed attentively or discarded.¹²

The current study examines the effect of external distraction on performance. While it is expected that the reorientation of attention away from critical information should impair performance, the exact impact of external distraction on the large-scale networks subserving task performance has yet to be documented. In particular, it remains to be determined how irrelevant external events cause a deviation of such networks from their optimal dynamics, and cause performance decrement.

The main reason for this lack of understanding might be simply be technical: because attention must quickly reorient towards distractors, the effect of such events occurs at the subsecond scale to disrupt the cortical dynamics, and non-invasive neuroimaging techniques lack the temporal resolution to reveal such events.³⁷⁵ In contrast, iEEG has become increasingly popular to study the fine dynamics of

the large-scale networks subtending human cognition, with a very high precision both in time (ms) and in space (mm).³⁷¹

We used iEEG to study the effect of naturalistic external distractions on the dynamic neural architecture of an attention-demanding task, called BLAST (Bron/Lyon Attention Stability Test). BLAST requires that participants perform a paradigmatic working memory/visual search task updated every two seconds, so that the level of attention allocated to the task can be monitored continuously. Seven patients implanted with intracranial electrodes accessing the main attention networks performed BLAST in a distracting environment, with an experimenter sitting next to them to generate frequent naturalistic distractions (sneezing, moving, dropping objects ...) as could occur in a real working environment.

We found that distractions caused an interference with the optimal neural dynamics of the BLAST network in three major regions: in the medial parietal lobe, the anterior insula and the extrastriate cortex. Our results suggest that distraction primarily acts by preventing the narrowing of attention onto the task physical domain - the region of space that should be prioritized for optimal information extraction and by disrupting executive control.

10.3 Materials and Methods

10.3.1 Participants

Intracranial EEG recordings were obtained from seven neurosurgical patients with intractable epilepsy at the Epilepsy Department of Grenoble Neurological Hospital (Grenoble, France) and Epilepsy Department of Lyon Neurological Hospital (Lyon, France). Eleven to fifteen semi-rigid, multi-lead electrodes were stereotactically implanted in each patient (stereotactic EEG – SEEG). The SEEG electrodes had a diameter of 0.8 mm and, depending on the target structure, consisted of 10 to 15 contact leads 2 mm wide and 1.5 mm apart (i.e. 3.5 mm center-to-center, DIXI Medical Instruments). Selection of sites to implant was entirely based on clinical purposes, with no reference to the present experimental protocol. All electrodes showing traces of epileptiform activity were excluded from the present study (visual inspection by the clinical team). All participants were native French speakers with normal vision, and gave written informed consent; all experimental procedures were approved by the Institutional Review Board and by the National French Science Ethical Committee.

10.3.2 Stimuli and Task

BLAST (T1) – see annex N°1

The attention-demanding task was adapted from the BLAST paradigm published by our group.¹⁶⁷ It repeatedly ask participants to find a target letter (the Target) in a subsequent two-by-two square array of four letters (the Array), with new letters every trial (Target and Array) (see Fig. 19). Each trial starts with the presentation of the Target for 200 ms, followed by a mask (#) for 500 ms (also known as the encoding phase), then being replaced by the Array, which remains on screen until the manual response (also known as the visual search phase). The next trial starts after a pause of 800 ms, with no feedback on performance and no auditory stimulus.

During iEEG recordings, BLAST was performed on a PC using Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA) and synchronized with the EEG acquisition system. The letters were presented foveally in black on a light gray background, and participants pressed a button on a gamepad with their preferred/non-preferred index finger to indicate if the Target was absent/present in the Array, respectively. The trials sequence was pseudorandomized, with the same number of trials for « Target present » and « Target absent », and performance was measured on a total of 250 trials, for a total duration around eight minutes (depending on each participant's reaction times).

The global instruction was based on establishing a constant and reasonably fast pace, avoiding errors (with an explicit analogy to car-drivers who avoid accidents at all costs, but nevertheless move forward at a decent speed). BLAST was first performed by participants in an isolated room without exogenous distractions as a single task (ST) condition, and then with exogenous distractions delivered randomly (ST-DIST, see below).

Distraction (DIST)

To determine the effect of distractions on BLAST, both were combined as follows: while each participant performed BLAST, an experimenter sat within its peripheral visual field (see Fig. 20) distracting it with movements and/or sounds caused directly (e.g., an arm stretch or a question aimed at finding out if the task is too difficult) or indirectly (e.g., by moving the pages of a notebook or ringing a cell phone). Because an experimenter provided distractions, it was possible to tailor their frequency to periods of silence with enough distance to avoid keeping participants constantly distracted, by choosing the type of distraction at random. Thus, there were periods within ST-DIST in which the participant was not being distracted (DIST-freeW, see below) and others where it was actively being distracted (DIST-W, see below). BLAST performance was analyzed offline from a video recording of the session. Participants were not given any instruction regarding distractions.

10.3.3 Behavioral Analysis

Our design came with two main advantages: A) the experimental set-up simulated naturalistic conditions (DIST are delivered without prior cues, with a combination of modality and intensity capable of unintentionally surprising the participants), and B) it allowed us to study what happens to the participants who are effectively distracted.

In general, it was simple to specify at what point participants started being susceptible to DIST (i.e., immediately after delivery). However, even now we are not aware of any research with iEEG that explicitly indicates how long its effect lasts at the brain level on a task that requires constant attention. Although there are studies that speak of the activation of the DMN with iEEG (a network usually related to distraction), the majority focused on distractions of endogenous²⁷⁹ but not of exogenous origin. According to the Gatekeeper theory,¹² a distracting stimulus that captures attention involuntarily must first be perceived pre-attentionally and then disturb the task-set imposed by a previously executed task, leading to a decline in its performance. For this, the cortical activity must be

maintained at least over 250 milliseconds to speak of a distractor capable of overcoming this second "attentional filter". Additionally, we granted enough time to participants to experience the distractor and delay their response or make a mistake, finally opting for a 2 seconds post-distraction window (i.e. DIST-W), thus considering the total development of a distraction.

Therefore, it was possible to study the effect of distraction on T1 performance in the following ways: A) comparing the overall performance (i.e., RT Reaction Time and ER Error Rate) between ST and ST-DIST ("ST Behavioral Analysis") conditions; B) in the ST-DIST condition, comparing behavioral performance between an "N" number of DIST-W ("N" being variable among participants) and "other" windows in which the participant was not being distracted, delivering responses to T1 ("DIST Behavioral Analysis"). Both analyses were performed on each participant individually.

For the DIST Behavioral Analysis, all continuous time-segments free of any distraction and longer than 2s were divided into consecutive non-overlapping 2s windows called DIST-freeW (surrogate data), excluding any window within 2s of a distraction. Then for the "N" DIST-W, the average RT and ER were calculated across all T1 responses within the DIST-W and compared to a distribution of 10,000 RT' and ER' values, where RT' and ER' are repeatedly calculated from a randomly selected set of 2-seconds DIST-freeW. We used a T-value with a threshold of $p=0.05$ to assess whether distractions had a punctual effect on RT or ER.

10.3.4 Electrophysiological Analysis

Bipolar HFA Extraction

We followed exactly the same procedure of data collection described in our previous study by extracting raw data using bipolar derivation, taking a frequency band of interest [50 : 150 Hz], dividing the signal in segments of 10 Hz each, converting them into envelopes using the Hilbert transform, and averaging them using the standard method of our team.

HFA Binarization

HFA were binarized for each channel, following our previous approach with the intention to maintain consistency between studies. The procedure was the following one: a neutral baseline was approximated (with little or no influence of T1 or DIST related processes) from the HFA measured during the pre-stimulus (a 200 ms immediately preceding T1's Target onset) for the "best" trials; that

is, correct T1 trials with the fastest reaction time (in that case, the 50% fastest correct trials). The median value was calculated over all samples within the baseline of those trials ($P \times B$ samples, where P is the number of samples within the $[-200 : 0 \text{ ms}]$ window and B the number of "best" trials), serving as a threshold T_{med} to define "on" vs "off" states: a sample was considered "on" if HFA is above that threshold. This procedure converted the original HFA trial-matrix for the entire experiment into a binary signal, allowing computing the density of "on" samples for any time-window.

Statistical Analysis

Identification of iEEG Sites Responsive to T1

To select sites "directly" responsive or "indirectly" coupled to DIST, we initially considered only those sites whose HFA was also modulated by T1. These were identified based on their 50% "best" T1 trials with a simple Wilcoxon sign-ranked test, comparing the distribution of "on" and "off" samples (0s and 1s) at a given latency after the Target presentation with the distributions of "on" and "off" samples at the baseline of the same trials, between $[-200 : 0 \text{ ms}]$. T1-responsive sites were characterized either by a significant increase or by decrease of "on" states at certain latencies induced by T1.

Identification of iEEG Sites Responsive to DIST

The procedure to identify sites responsive to DIST was based on the comparison between the density of "on" samples in the 2s windows following the distractions (DIST-W), and the density of "on" samples in 2s windows centered on the 50% best T1 trials (T1-BEST-W). More precisely, "N" DIST events were identified in the video, and for each of them, a proportion of "on" samples was computed within a $[0 : 2000 \text{ ms}]$ window (with 0 ms indicating the onset of the distraction), and compared with the proportion of "on" samples computed within a $[-800 \text{ ms} : 1200 \text{ ms}]$ window surrounding T1 trials (with 0 ms indicates the onset of the Target) using a Kruskal-Wallis comparison. Any significant difference between the two density distributions was considered an indicative that distractions cause an excess of "on samples" in DIST-W relative to T1-BEST-W, and a sign that DIST possibly interferes over T1.

Identification of iEEG Sites Coupled to DIST

This procedure was motivated by the visual inspection of the data that revealed that in some participants there was a striking correlation between the HFA in the auditory cortex triggered by

auditory DIST and other specific sites. Given that most DIST were associated with sounds, we considered such sites as responsive to DIST, and investigated whether some of them supported T1-related processes, in which case external sounds would affect T1-related processes indirectly through, or in relation with, the auditory cortex.

We considered for each participant one site particularly responsive to DIST sounds, from the correlation of its HFA with the envelope of the sound track of the video. Each site was used as a seed to calculate the correlation coefficient “R” between its smoothed HFA trial-matrix and all other iEEG sites (smoothing was performed by convolution with a 2500 ms square window). Each R correlation coefficient was compared with a distribution of 10,000 correlation coefficients R_i ($i = 1$ to 10,000) calculated between random pairs of iEEG sites, making sure that one of the two signals was flipped in time. The comparison with the surrogate provided a p-value and we considered as significant any R-value higher than 0.05 divided by the number of iEEG sites (Bonferroni correction). Both detection procedures complemented each other: the first may not have detected sites that respond strongly to visual DIST (e.g., motion), while the second may not have detected sites that respond primarily to auditory DIST.

HFA and Performance

We hypothesized that if the activation of some sites by DIST interferes with T1, the activity should be significantly different between the best and the worse T1 trials. To detect such effects, the 20% best T1 trials (50 fastest correct trials) and the 20% worst T1 trials (including 50 misses, errors, and slowest correct trials) were defined and compared by their HFA measured in a critical [0-1200 ms] window using a Kruskal-Wallis comparison.

10.4 Results

10.4.1 Behavioral Analysis

Overall, the global performance was not affected by DIST, indicating that the effect of distractions on ST-DIST was transient (*see Fig. 42*). Additionally, the analysis comparing the detailed performance between DIST-W and DIST-freeW revealed in some participants a significant slowing down of RT (one participant) or ER (three participants) after DIST.

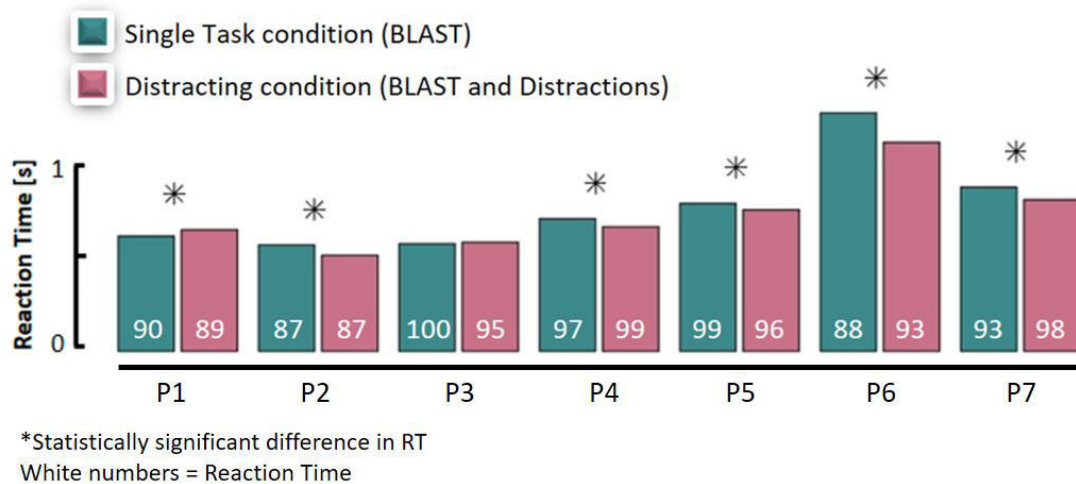


Figure 42: Mean reaction time during T1 for all participants. In the ST (teal) and ST-DIST (magenta) conditions (a star sign indicates a significant difference between the two conditions, two-sample t-test; $p < 0,05$). Error rate is indicated in white.

10.4.2 Electrophysiological Analysis

The aim of our analysis was to detect sites that were both responsive to DIST and to T1 (and therefore, are part of the T1 network). All such sites are possible locations where DIST could interfere with optimal T1 performance. Overall, only three cortical clusters displayed a reproducible response to DIST in more than one participant, apart from the auditory cortex (we do not include it because it does not support T1-related process and cannot be a site of interference). These clusters included the Posterior Cingulate Cortex (PCC) and Precuneus (both in the posterior medial wall), the Anterior Insular Cortex (AIC) and the Extrastriate Visual Cortex (EVC). Additionally, two T1-related regions showed particularly clear effects for DIST, but since they were found each in a single participant, they are presented as anecdotic results by the end of this section. We now discuss each cluster separately.

Anterior Insular Cortex (AIC)

Two participants had electrodes passing through the right AIC. One of the two sites increased its activity during DIST-W (see Fig.43, top half), while the other was detected via a positive correlation with the auditory cortex (see Fig.43, bottom half). In line with our previous description of the T1 network, both sites were activated during the visual search phase (between the Array presentation and the manual response), and after errors. This activity is usually interpreted as a neural correlate of

goal-oriented behavior,^{151,388} and its response to distracting events as the necessity for increased control when attention is drawn away from T1 by DIST. An alternate interpretation recognizes the AIC is a key component of the salience network,³⁸⁹ reacting to potentially important incoming stimuli. However, the lack of response to T1 Targets does not fit with this interpretation, given that Targets are highly relevant stimuli in the present context. One might argue that the AIC reacts only to unpredicted stimuli, but again, this is hard to reconcile with the activity observed during T1's visual search phase.

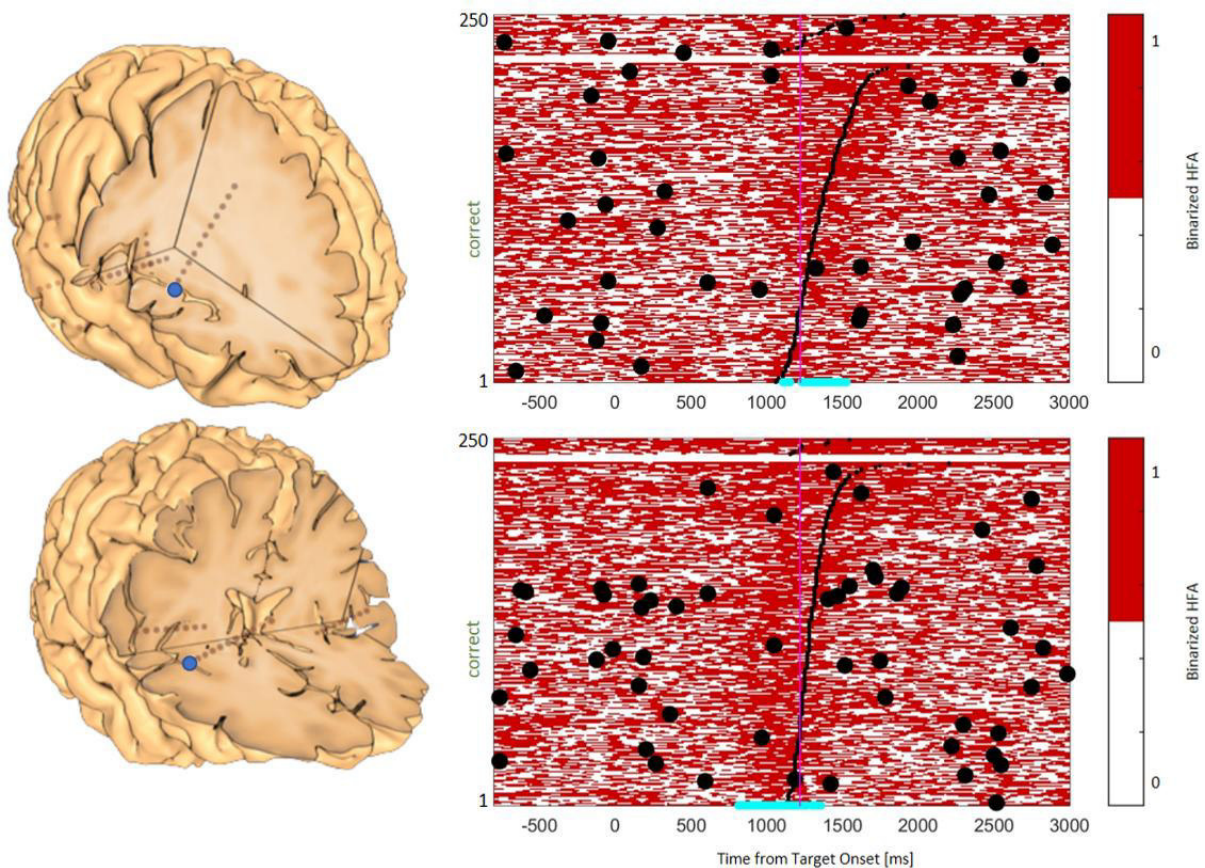


Figure 43: Binarized electrodes in the right AIC during the ST + DIST condition. Left half: precise location of each sites on each patient's individual anatomy. Right half: each spectrogram corresponds to its respective brain at the side. Their construction is the same as the one explained in Figure 24 before binarizing. Each one shows HFA amplitude changes between electrophysiological responses to BLAST. Top right: the dark blue rectangle on the top marks encoding phase (between Target and Array presentation), and the light blue line marks visual search phase (between Array and Button-press). The white horizontal line divides between right (trial on the bottom) and wrong trials (trials on top).

PCC/Precuneus

Two participants showed a very similar response pattern in the medial region within the lower parietal cortex: one in the left hemisphere (see Fig. 44, top half) and the other in the right hemisphere (see Fig. 44, bottom half). Activity during T1 was characterized in both sites by a neural suppression relative to the pre-stimulus baseline level (suppression of HFA). Interestingly, the comparison between the best and worst trials of T1 (see Material and Methods – HFA and Performance) revealed that the suppression was reduced or absent in the worst trials, which should be considered in relation to the fact that both sites were positively correlated with the auditory cortex. Consequently, DIST sounds driving activity in the auditory cortex might increase neural activity in the PCC/Precuneus, which must be suppressed for optimal T1 performance. This might cause a performance decrement when an attention-demanding task is performed in a noisy environment.

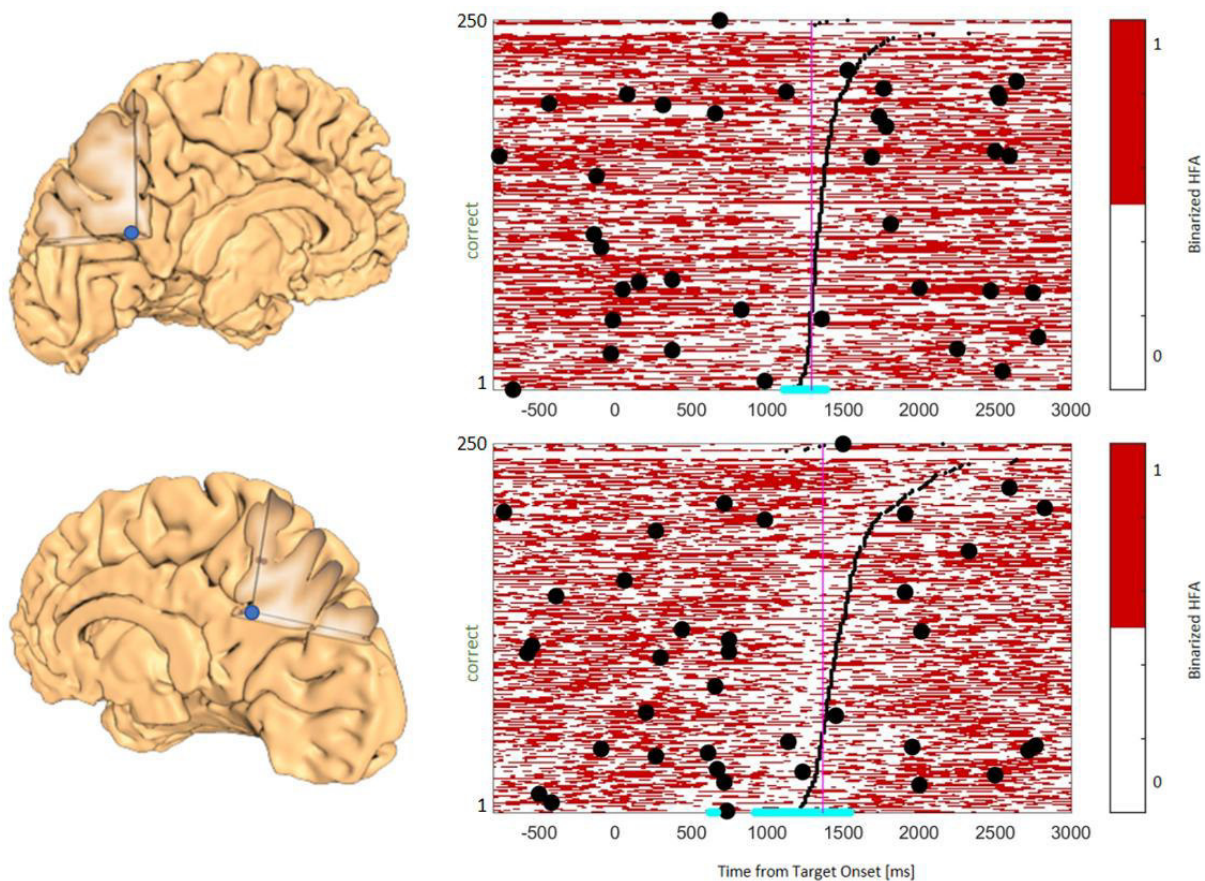


Figure 44: Binarized electrodes in the bilateral Posterior Cingulate Cortex/Precuneus during the ST + DIST condition.

Extrastriate Visual Cortex (EVC)

Two participants displayed a response to distractions in the visual cortex, specifically in the calcarine sulcus (see Fig. 45). Quite expectedly, both electrodes showed a strong activity during T1's visual search phase but not to the appearance of the Target, which might indicate a peripheral receptive field. Careful inspection of the video revealed clear responses to movements of the experimenter, consistent with a processing of peripheral visual events. Processing of lateral visual stimuli might disrupt normal neural processing during the visual search phase and slow it down.

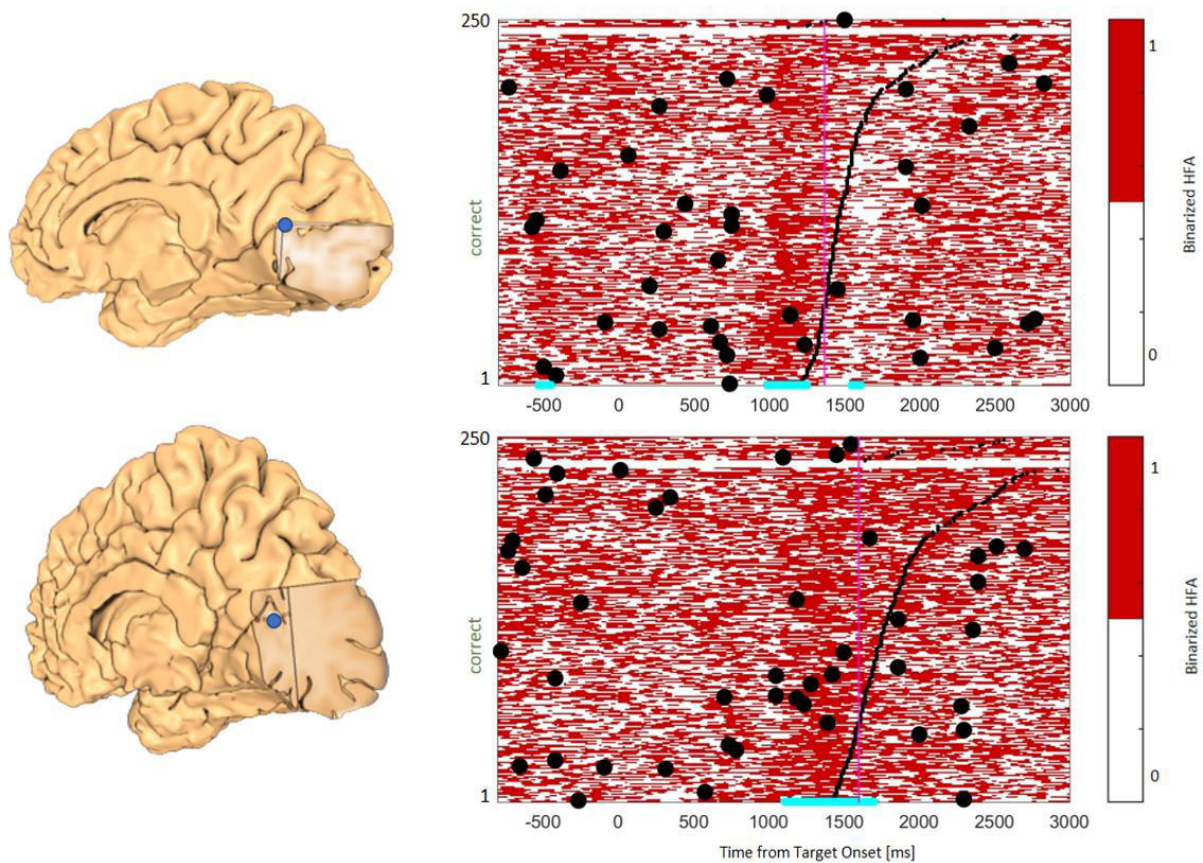


Figure 45: Binarized electrodes in the right Extrastriate Visual Cortex during the ST + DIST condition.

Single-Case Observations

Two notable observations caught our attention, despite the fact that they were found in isolated participants. In the case of Figure 46, its activity in the right IFG was positively correlated with the

activity in the auditory cortex driven by DIST sounds (mostly speech, matching with its anatomical localization as part of the language network). The site was active during T1’s visual search phase – and to a less extent, during T1’s encoding phase – and might participate in a verbal strategy (“rehearing” the letter which must be found until it is detected in the array) considering the role of the IFG in verbal working memory. Activation by DIST sounds might correspond to a similar verbal process triggered by speech, in which case one would expect interference with T1. It is very unlikely that this response is specific to that particular participant, since it matches the function described in the literature for the IFG, thereby clarifying that it would be desirable to have a larger pool of participants.

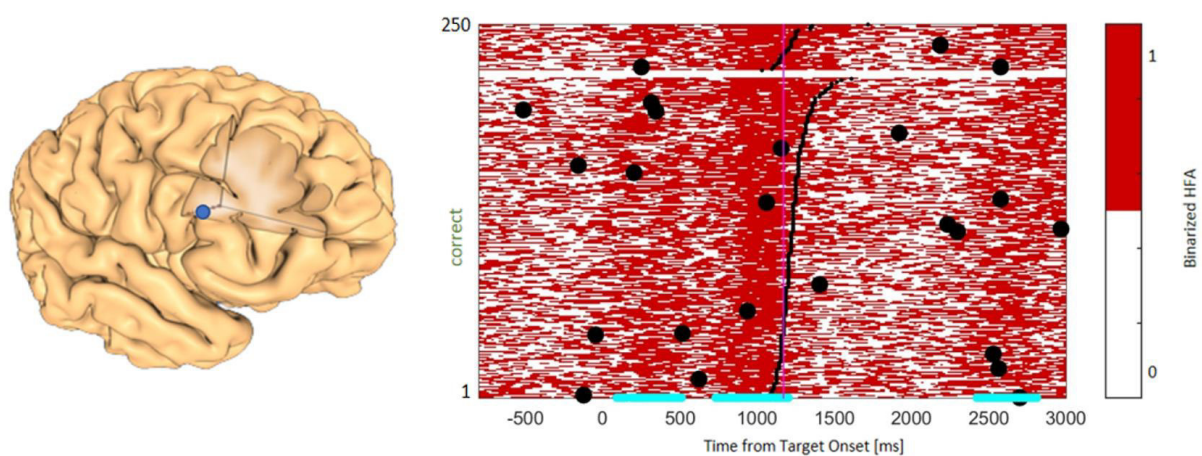


Figure 46: Binarized electrode in the right Inferior Frontal Gyrus during the ST + DIST condition.

In the *Figure 47*, its activity in the basal temporal cortex (BTC) was positively correlated with the auditory cortex. The interesting aspect of that area is that its activity was suppressed throughout T1 to rebound after the button-press. Given the anatomical location of that area, deep within early visual cortices, that modulation is characteristic of a narrowing of the visual attention field during the active processing of central stimuli (characteristic of T1), and effect studies by our team during the use of mobile devices (*see Annex N°4*).³⁹⁰ It follows that DIST may cause a widening of the visual attention field which contradicts the narrowing effect induced by T1, proposing another source of interference.

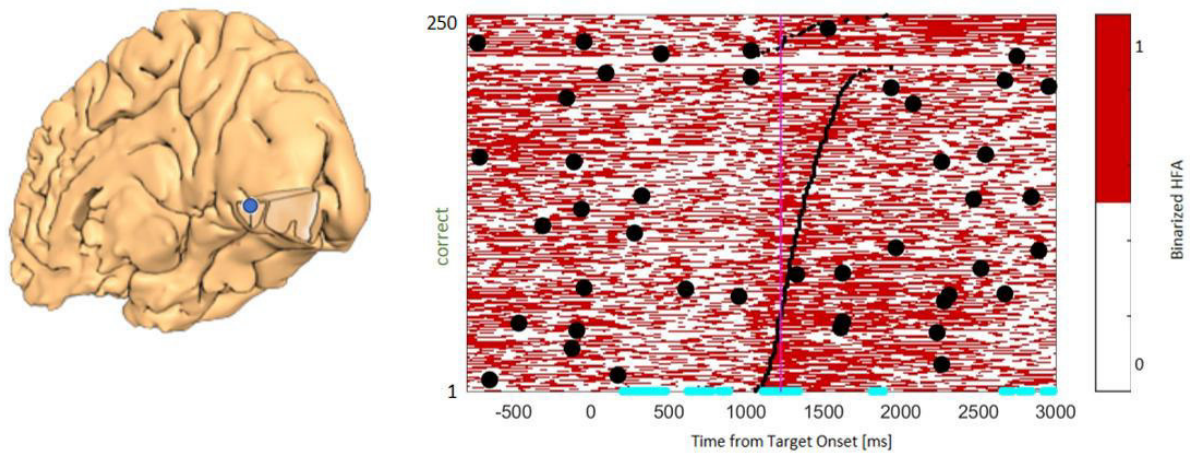


Figure 47: Binarized electrode in the right Basal Temporal Cortex during the ST + DIST condition.

10.5 Discussion

Our main objective was to demonstrate how a salient exogenous distraction affects the execution of a task that demands constant attention, and how it can disrupt its functioning by consuming available cognitive resources. For this, we tried to find specific neuronal populations recruited during distraction that could hinder the execution of the primary task. Based on current models of attention in which target selection depends on the combined influence of exogenous stimulus-driven factors and endogenous goal-driven objectives, we attempted to deliver distractors salient enough to redirect attention by surpassing the cognitive control delivered by the executive network. We addressed these issues by using a naturalistic strategy and recording with iEEG, in order to provide a direct way to measure neural activity with high temporal and spatial accuracy.³⁰⁰ We reasoned that a stimulus that is distracting enough to attract attention unintentionally should activate cortical areas used by the main task that interrupt its proper processing.

We identified those electrodes that presented a longer or denser high-gamma band activity during distraction than during the best BLAST trials, labelling them in different cortical regions. Subsequently, we relied on responsive auditory electrodes to identify by coupling other cortical areas related to over-activation during auditory distractions. Through both methods, we were able to create a widely distributed interference network in the cerebral cortex. Below, we will discuss each area where these electrodes are found and their function.

10.5.1 Anterior Insular Cortex

Thanks to our analysis, we were able to find two electrodes positioned on the right AIC. The AIC, along with other frontal and prefrontal areas, is consistently activated through a variety of non-automated cognitive tasks that demand control. As already mentioned, it participates in maintaining top-down control, guiding goal-oriented behavior^{151,388} and increasing its activation during mental effort, thus justifying the increase of HFA during incorrect responses, especially on the right side.^{391–393} The AIC is part of a saliency network within the Cingulo-Opercular Network,^{14,15,389,394,395} setting the presence of new and salient events in a transitory way³⁹⁶ or relevant to behavior in a continuous way. Within the possibilities of our electrodes, we found no evidence of transient activity during BLAST Target presentation or the encoding phase, but we did find evidence of sustained activity during the memory recall and visual search phase.

According to Cai,³⁹⁷ the AIC detects increased sensory demands for cognitive control by mediating the salience of a target with the executive network, and then triggers and maintains the necessary actions for goal-directed behavior. According to our results, distraction would not hinder BLAST's encoding phase, but instead affect its evocation from memory and subsequent visual search, forcing a sustained response in the most difficult and wrong tests. In addition, the AIC tends to activate continuously during the appearance of salient elements, but focusing on maintaining cognitive control over exogenous stimuli,³⁹⁴ participating also in the detection of mistakes³⁸² and activating itself with greater intensity against those perceived consciously.³⁸¹

10.5.2 PCC/Precuneus

We were able to find two electrodes on the boundary between the PCC and the Precuneus. Both areas are part of the DMN, with the PCC experiencing increments of HFA during momentary lapses of attention³⁹⁸ and task independent thoughts,³⁹⁹ and suppressions during cognitively demanding tasks,^{400,401} being able to predict its performance according to the degree of suppression.^{402,403} This turns the DMN with the PCC into an essential network for interactions with the outside world, coinciding with our bilateral findings, characterized by high gamma band suppression in the visual search phase in most trials.

Although the PCC is typically associated with the evocation of autobiographical memories, forward planning and unrestricted rest, it also seems to take a direct role in controlling the balance between an internal and external focus of attention.⁴⁰⁴ Thus, the PCC would participate in social cognitive processing, especially when it comes to attributing value to a socially relevant everyday situation.⁴⁰⁵

Furthermore, there is evidence that an external auditory distraction may affect the execution of a visual task of high cognitive load, with the PCC experiencing an increase in HFA around or above the baseline.⁴⁰⁶ These situations partially explain the decrease or absence of suppression experienced by our electrodes in the worst trials, which additionally correlates with an increase in HFA in the primary auditory cortex. This means that distracting sounds could increase the neural activity in the PCC and Precuneus, affecting the performance of BLAST.

10.5.3 Visual Cortices

Those electrodes located in visual areas (two in the right Extrastriate Visual Cortex and one in the right Basal Temporal Cortex) belong to different parts of the visual system and the Dual Visual Stream.⁴⁷ The first two locate specifically in the calcarine sulcus and form part of the Dorsal Visual Stream, which extends from V1 to the intraparietal sulcus, sensing motion information, optic flow and self-motion of the perceived elements.^{407,408} Its most elementary information is collected in V1 foveally, and sent subsequently to secondary visual areas that expand the surrounding visual field, possibly creating rudimentary directional maps⁴⁰⁹ that are sent towards the middle temporal gyrus, where the size of the receptive field is increased.⁴¹⁰ This matches with our findings as there is no activation during the appearance of the BLAST Target, but there is during the expansion of the visual field to search for the Array. An alternative (or complementary) explanation comes from more updated theories about the Dual Visual Stream that divide it into a lateral part, related to the recognition of object movement and self-motion, and a medial part, related to the continuous monitoring of the location of objects in space, reaching-grasping and vision-for-action processes.⁴¹¹ This also matches well with our findings, as our extrastriatal electrodes are placed in medial areas, being activated before the button is pressed, and when facing distracting movements of the experimenter in the peripheral visual field.

Moreover, our electrode in the Basal Temporal Cortex is part of the Ventral Visual Stream, specifically located in the lingual gyrus forming part of V1 and possibly V2. According to its location, it should contribute in the sense of major form-processing changes, such as fixing primordial contour-based object representation, and minor color-processing changes.⁴¹² Its HFA pattern remains inactive in most of BLAST but increases around the button-press. Since this electrode possibly forms part of the periphery of the retinotopic map, it could experience a lack of activation during almost all trials due to a visual narrowing, caused by the attention deposited on a foveal element while trying to ignore all surrounding elements.⁴¹³ Additionally, the increase in HFA after the button-press could be due to a visual field reset, which attempts to encompass a bird's eye view image of the scene including peripheral visual elements, becoming more noticeable when the participant makes mistakes.

10.5.4 Frontal Cortex

Finally, our inferior front gyrus electrode experiences an increase in HFA during the BLAST visual search phase, as well as during speech-related distractions. This is probably due to its participation in the auditory processing network⁴¹⁴ as well as in the overlaying reading network related to language production, word phonological recording,⁴¹⁵ and verbal working memory, activating the phonological loop and forcing a constant rehearsal of the exposed letter.¹⁰⁴

To summarize, high saliency distractions can interrupt the processing of tasks that require constant attention, both directly by consuming cognitive resources necessary for the task, as well as indirectly by disturbing the functioning of areas do not take part of the task, but affect other associated functions. Thus, distractions not only affect areas that are currently in use, but extend beyond them, causing an overall effect that can take someone completely out of focus. This expanded perturbation fits with a vision of cooperative work, with an orchestrated participation between the different brain systems, leading to a harmonic result that can be unbalanced by a foreign event.

Although the extraction of information from epileptic patients presents a risk for data contamination,³⁰⁰ our team has been able to create a set of strict rules that minimize these effects.³⁷¹ Additionally, and despite the low number of electrodes with significant activity, the use of iEEG with a very high signal-to-noise ratio allows us to obtain statistically significant results with high test-retest reliability between trials, allowing us to draw conclusions even from two electrodes positioned in the same cortical zone.³⁷¹

The use of naturalistic conditions makes the data ecologically valid and more consistent with what can usually be found in nature, but at the same time adds uncontrolled variables that could lead to results that are more difficult to reproduce. Despite that they may complicate the control of the experimental protocol, evidence suggests that they cause a greater reaction in participants than those delivered by a computer.³²⁵ That might be because humans often assign mental states to second persons during social interactions due to the uncertainty of their behavior.³²⁴ This makes sense, considering that movement or speech perception triggers several of our electrodes. Furthermore, human brains may be better calibrated to receive ecologically loaded stimuli than artificial ones³²⁷ that are more complex than refined or simplified ones.³²⁸ Despite this, the use of ecologically loaded distractors makes them difficult to standardize because of how noticeable they can be and because of their inherent social burden.³²⁹ For this reason, we believe that in the future it would be interesting to complement our results with physiological and eye activity recordings.

Part V

GENERAL DISCUSSION

Attention allows cognitive resources to be focused on a particular behavioral goal. Those resources can be diverted away by external or endogenous distractions, imposing a greater load on cognitive control mechanisms to minimize performance decrease. The central objective of this thesis was to study how a primary attention-demanding task can be affected by additional tasks or distractions, at both behavioral and neural levels. That task had been created by our team - the Bron/Lyon Attention Stability Test, or BLAST¹⁶⁷ – to track transient fluctuations of attention and to measure the ability to stay on task.

BLAST was performed by participants in three separate conditions: first in a quiet environment, with no external stimuli (the Single-Task, or ST condition); then while asked to perform a Verbal Fluency Test (VFT) of equal importance during BLAST (Dual-Tasking, or DT); and finally, in a distracting environment, with an experimenter sitting nearby (ST + DIST). These last two conditions were intended to increase the attentional load (ST), affecting performance (i.e., BLAST speed and accuracy) and BLAST-related neural activity. Deviation from the optimal BLAST cortical dynamics could be observed by comparing the DT and the ST + DIST conditions with the ST conditions, using intracranial electroencephalography (iEEG).

In the DT condition, we searched for cortical sites which activity was modulated by BLAST and by the VFT to identify sources of interference between the two tasks. We then organized those sites into functional Regions of Interest. In the ST + DIST condition, we identified iEEG recording sites responsive to external distractions among those activated or suppressed by BLAST. The identification procedure relied on a) a simple statistical detection of neural activity increases after distracting events (visual and auditory), and b) a correlation analysis with sites in the auditory cortex activated by distracting sounds, to reveal cortical regions driven by auditory inputs. Both methods led to the identification of the cortical regions involved in BLAST that were affected by the distractions or the additional task.

11.1 Dual-Tasking

At the behavioral level, performing two tasks at the same time (BLAST and VFT) led to a performance decrease globally, in line with the general consensus on multi-tasking that any attempt to perform two tasks simultaneously – with no specific training – leads to a drop in performance, compared to the execution of each task in isolation.³ Additionally, in DT condition, all participants had a lower performance (accuracy and/or speed) in BLAST while searching for answers for the other task (VFT). Our hypothesis, that we could validate, was that the two tasks used common cognitive resources in specific cortical areas that worked as bottlenecks.^{170,393}

The executive system partially solves the bottleneck issue by forcing a serial – rather than parallel – execution of the tasks.¹⁹⁸ Once the decision to engage in one of the two tasks has been made, the executive system exerts a top-down influence on regions that must be prioritized for the task, configuring what is called the task-set.¹¹¹ Yet, this alternation is possible only if each one of the two tasks can be put on hold sufficiently long to perform the other one, what we called “dynamic compatibility” between two tasks: it implies that none of the two tasks requires truly continuous attention. To test whether BLAST and VFT were dynamically compatible, we identified neural populations (i.e. iEEG sites) activated by the two tasks and checked the duration of their activation. We organized those populations into functional clusters or Regions of Interest: the Precentral Gyrus/Sulcus; the dlPFC; the Lateral Temporal Cortex (LTC); a cluster combining the AIC, the ACC and the Pre-Supplementary Motor Area; and the Basal Temporal Cortex. Dynamical incompatibility was established for any of those neural populations when the VFT triggered a sustained increase in neural activity longer than the longest silent (i.e. inactive) period during BLAST trials.

Additionally, we searched for neural populations causing indirect interference between the two tasks. Those were characterized by a) a strong reactivity to BLAST (i.e. a participation in the BLAST network) and b) a significant correlation with neural populations activated by VFT. In other words, such populations are not directly active during the VFT, but the correlation suggests that they can be driven by a coherent activity in the VFT network, which might create an interference with BLAST, given that those populations are reactive to BLAST. We found one such candidate in the ACC/preSMA, correlated with the AIC (two patients), indicating that indirect interference might happen, in addition to more direct bottlenecks. This is because the activation of a task-set involves the participation of multiple neural networks, including some not directly involved in the attentional network, such as the DMN or WM, which could be activated by another task and interrupt the processing of BLAST.

The comparison of the neural responses in the ST and DT conditions brought more insight on how the two tasks might interact. In the Precentral cluster, we found that the response to BLAST differed

between the ST condition, and the best and the worst trials of the DT condition. The ST response was characterized by a double peak, while the best trials of DT showed in contrast a suppression of activity, and an increase selective to the visual search phase in the worst trials. Additional data collected in other tasks in the same participants (functional localizers) showed that this region participates in verbal/phonological tasks, in line with the classic functional interpretation of that area.^{279,416} Participants would then use a verbal strategy to perform BLAST, at least in the ST condition, interacting with VFT that has a strong verbal component. However, the lack of activation in the best trials of DT suggest that participants change their strategy to avoid that interference and to minimize the impact on BLAST, at least when they can. In contrast, the failure to shift to a “less verbal” strategy during the worse trials of DT would lead to a drop of BLAST performance. A strategy change seems like a natural way out of the bottleneck problem.

In the dIPFC cluster, half of the electrodes showed exactly the same response as the Precentral Cluster, in a region that has been also associated with language processes, including verbal working memory.^{416,417} The remaining sites were located in the Middle Frontal Gyrus with an increased activity during the visual search phase, both in the ST and DT conditions. Recordings during the functional localizers revealed a sensitivity to semantic and phonological processing, as well as verbal working memory,¹⁰⁴ and their activity during BLAST (and VFT) might be interpreted as signs of a verbal strategy. Again, the interference between BLAST and VFT should be thought as occurring not between tasks, but between strategies.

Responses in the Lateral Temporal Cortex confirm this interpretation: we found that in both hemispheres, neural activity was increased in the Middle Temporal Gyrus during the visual search phase of BLAST, in both the ST and DT conditions. Again, functional localizers revealed that this region reacts well to tasks involving verbal working memory and language BLAST and VFT.^{418,419}

The Cluster formed by AIC, ACC and preSMA point to a somewhat richer understanding of multi-tasking. Sites in the AIC showed a sustained activity increase during the visual search, for all trials in the ST condition, while that increase was much weaker in the DT condition for the fastest trials, and stronger in the slowest, more difficult trials. This difference between ST and DT could be due to the role of the AIC within the salience network,³⁸⁹ but more likely in relation to cognitive control,^{151,383,391,397,420} when errors become aware.^{381,382} The implication is that the AIC might act as a central bottleneck,³⁹³ preventing simultaneous processing of VFT and BLAST.²³⁵ Nevertheless, the lack of activation in the best trials of the DT condition, during BLAST, is intriguing, as it suggests that, again, the bottleneck might be avoided via a change of strategy: a strategy that would reduce executive

control to a minimum, during BLAST, would still be compatible with high performance while allowing VFT.

The same pattern was observed in the ACC/preSMA, and the implications are similar. Such similarity makes sense, considering that the ACC/preSMA and the AIC belong to the same functional networks for executive control (the cingulo-opercular network) and for salience detection.³⁸⁹ The ACC receives direct inputs from the AIC,^{393,397} to update the internal task-set models in response to stimuli considered as potentially relevant.^{383,396} However, we could observe a slight difference of the response patterns of the AIC and ACC, with a sustained activity after the button-press in the AIC only. One interpretation is that the ACC is not a conflict detector like the AIC,⁴²¹⁻⁴²³ but participates in reward-based decision making, receiving feedback from the AIC to decide how much cognitive control to use to control task execution,¹⁴⁶ in turn justifying the increase in cognitive activity in more difficult trials.

The cluster in the Basal Temporal Cortex was sampled by three iEEG sites, two of them in the Visual Word Form Area (in the left hemisphere), and one in the Fusiform Face Area (right hemisphere). There, activity increased during both the encoding and visual search phase, both in the ST and DT conditions. Functional localizers revealed, expectedly, that the VWFA processed character strings,⁴²⁴ and it worth noticing that they were also active when participants searched for names starting with a given letter (VFT), which suggests that the VWFA is active as soon as writing is involved, either exogenously or endogenously: the VWFA would therefore constitute a local, peripheral bottleneck specific of the BLAST-VFT interaction, that would lay intermediate between a pure 'sensory' bottleneck and a central, amodal, bottleneck. This conclusion was reinforced by our observations in the FFA, which was particularly active while searching for names of people, argues for the existence of several level bottlenecks ranging from purely sensory or purely motor to central, rather than the classic dichotomy emphasizing only those extremes.

Altogether, our results confirm that the interference between two tasks performed simultaneously is largely due to the difficulty of sharing common cognitive resources. However, we went far beyond that interpretation by identifying the neural substrates of such resources. We proved that they correspond to the activation of a set of cortical regions supporting higher cognitive functions (as cognitive control in the cingulo-opercular network) as well as 'low-level' functions at the perceptual level (visual processing and visual imagery of letters, for instance, in the VWFA). We found that two tasks can be said to be truly incompatible because they relied on specific dynamics of activation that exclude each other, but that the interference should be thought of as occurring between strategies rather than between tasks. Surprisingly, even central bottlenecks considered as indispensable components of tasks requiring executive control, in the ACC and the AIC, can be avoided by strategies

reducing the amount of control of one of the two tasks, this might be the most important result of this thesis: we might apply too much control over what we are doing, while high performance could be obtained with less. This echoes frequent observations by elite athletes and coaches that excessive control over routine actions might be detrimental to performance.

11.2 BLAST and Distractions

At the behavioral level, external distractions (DIST) did not significantly impair the global performance of the participants; yet reaction times and/or error rates were transiently impaired by distracting events. The emerging picture is that the executive system overactivates in response to distractions to decrease globally their impact and keep the performance intact.^{29,281}

At the cortical level, we identified three main regions of interest responsive to external distractions: the right AIC (rAIC), the bilateral Posterior Cingulate Cortex/Precuneus (PCC/Precuneus), and the right Extrastriatal Visual Cortex (rEVC). All three ROIs showed reproducible responses across patients. They were completed by two other regions, in which a strong reaction to exogenous distractions was observed, although in one patient only, but these are worth mentioning: the right Temporal Basal Cortex (rBTC), and the other in the right Inferior Frontal Gyrus (rIFG).

During BLAST, the AIC was especially active during the visual search phase (between the display of the Array and the button-press). This is somewhat consistent with the literature, which predicts that the AIC should be transiently activated when attention redirects towards novel, salient stimuli,³⁹⁶ and longer during attentive processing of stimuli that are behaviorally relevant.^{151,383} We therefore expected that sustained increase of activity of the AIC during the visual search phase that was even greater as the task became more difficult due to distractions and the need to exert a stronger cognitive control.³⁹¹ We also expected the strong activity of the AIC after erroneous responses, because this region is known to be involved in conscious error detection^{381,382} and coordinates sensory inputs to domain-specific control processes.^{392,425} Altogether, our observations fit with the general idea that the AIC, together with the ACC, the Amygdala and the IFG,³⁹⁵ form a saliency network,^{389,394} in which the AIC performs a type of analysis/interpretation of the stimulus, and the ACC updates the task-set models in response to stimuli that are considered relevant.³⁸³ It is worth mentioning that the increase of activity in the right AIC reaches a plateau faster than the left AIC,^{391,393} because that saturation has been proposed to be one of the main "limiting" factors of amodal central processing.

The PCC/Precuneus is a major node of the Default Mode Network (DMN). We found a gradual increase of neural activity during the visual search of BLAST, starting with a marked suppression in the easier

trials, shifting to a positive increase in the harder trials (longer reaction times). Major theories regarding the role of the PCC predict that its activity should be transiently suppressed by salient stimuli⁴⁰² and during attentive processing of external stimuli.⁴⁰³ The main cognitive processes associated with that region are the recovery of autobiographical memories, planning for the future,^{386,426} as well as the regulation of the focus of attention,^{427,428} and the control of the balance between internally and externally directed thought.^{404,429} This matches our findings, as the PCC should have its activity suppressed during the best trials, and increased during poor performance, since distractions alter the execution of tasks that require constant attention. In addition, the activity of PCC electrodes was correlated to that of primary auditory areas (i.e., reaction to auditory distractions), matching the findings of a study by Smucny and colleagues,⁴⁰⁶ in which PCC activity increased after auditory distractions during a visual task. In addition, the fact that most of these auditory distractions had a social origin is consistent with the fact that the PCC has been associated with social cognition,⁴⁰⁵ especially when it comes to attributing value to a socially relevant daily auditory situation.⁴³⁰

Sites in EVC increased their activity exclusively during the visual search phase, which suggests that they do not encode foveal information, but rather more peripheral visual information. Their anatomical location suggest that they belong to the Dorsal Visual Stream, with a preference for motion-related information^{407,408} and peripheral visual activity,^{409,410} in line with our observations that those iEEG sites were particularly reactive to visual – not auditory – distractions. If we try to be even more precise, our sites would lie in the medial portion of the Dorsal Visual Stream and support most specifically the identification of object movement in three-dimensional spaces, gripping range, and vision-for-action.⁴¹¹

In addition to the previous regions of interest, we found isolated effects of distractions in the Basal Temporal Cortex and in the Inferior Frontal Gyrus, both in the right hemisphere. The BTC site showed no activity during the target encoding and the visual search, possibly participating in peripheral visual perception only. Its activity was correlated to fluctuations in the primary auditory cortex caused by distracting sounds, possibly marking a multi-sensory expansion of the visual attention field. This would be consistent with the results of another study by our group (*see Annex N°4*)³⁹⁰ showing that peripheral parts of the visual cortex are inhibited during the attentive processing of central visual stimuli (the effect we report in this thesis would be the symmetric of that narrowing effect). The IFG showed a slight response during the encoding of the target followed by large increase during the visual search phase. Due to its anatomical situation, this pattern was expected in relation to verbal working memory and the phonological loop.^{104,418,419} That recruitment of the IFG would depend upon the strategy used by the participants: performing BLAST using verbal working memory would lead to interference when the language network is activated by social distractions.

Altogether, we believe we have fulfilled our initial objective: we have identified several key regions where external distractions interfere at the neural level with our attention-demanding task, and provided a plausible reason for the transient decrement of performance they generate. Among those regions, the AIC, which integrates the salience network³⁸⁹ and the cingulo-opercular network,¹⁴ together with the PCC/Precuneus, a key node of the DMN,⁴⁰³ might harbor limited cognitive resources susceptible to be used by distractors, possibly in interaction with each other.^{396,431} Other regions like the EVC, that react to distractors, could also generate interference, but most likely under the control of higher cognitive areas in charge of executive control.

11.3 Weaknesses in our Study

Of course, our studies come with some limitations that should be acknowledged. Firstly, the relatively small number of participants prevented a large and exhaustive sampling of our main Regions of Interest. It is possible that we identified only some of the regions involved in the distraction phenomenon, yet, the areas we could identify, even if some were sampled in a single patient, matched the main regions associated with multi-tasking and exogenous distraction. One might also complain that our conclusions were drawn from patients suffering from a several neurological condition, but iEEG cognitive research has now gone for almost three decades, and multiple guidelines have been provided to maximize the generalizability of intracranial observations (among which, the consistency of the results across patients, or the adequacy established principles of the brain functional architecture).³⁷¹ Nevertheless, a larger population of patients and a denser cortical sampling across individuals would certainly have led to more robust conclusions. Another potential source of concern is that the naturalistic conditions used in our paradigms could not provide a perfect control over the experimental conditions, with some obvious variability in the timing and nature of the endogenous or exogenous events, obviously. Yet, we believe that our observations are sufficiently robust and facilitated by the high signal-to-noise ration of iEEG signals, which allows visible effects to be identified at the single-trial level, without the need to average across a large number of strictly identical stimuli.

11.4 Future Improvements

Arguably, I recommend that new data be collected from a larger group of patients, for a denser mapping of the cortical mantle and a higher number of reproducible observations. I would also recommend a finer-level analysis of the impact of the type of search in the VFT paradigm (searching for names of tools vs animals, for instance), or the distractions, to dissociate for instance the effect of visual vs. auditory distractions in the DIST experiment. Since strategy seems to be a key – yet uncontrolled – factor affecting the ability to multi-task, future studies should probably suggest some possible strategies to the patients and contrast their impact on performance, or at least use verbal reports techniques to collect data about those strategies. Other possible improvements include: a) providing a feedback after each response in BLAST (to identify areas processing feedback information) and b) include additional measures to complement results, such as IQ tests;³⁹³ and c) use of eye-tracker for a more careful monitoring of the executive network supporting cognitive control.³⁹¹

In conclusion, we believe that attention control is necessary to efficiently direct our limited cognitive resources to specific tasks in a selective way. Although there are control mechanisms to preserve these resources, certain circumstances, such as additional tasks or distractions side-track these resources and impair the execution of the primary task, either directly by disrupting the activity of key functional regions involved in that task, or indirectly by activating associated regions interacting closely with those key regions. In short, we believe that attention is essential for the efficient interaction with the environment, and for adapted and timely behavioral decisions based on our internal objectives, experiences and personal preferences.

Part VI

REFERENCES

1. Raymond, J. E., Shapiro, K. L. & Arnell, K. M. Temporary Suppression of Visual Processing in an RSVP Task: An Attentional Blink? *J. Exp. Psychol. Hum. Percept. Perform.* (1992). doi:10.1037/0096-1523.18.3.849
2. Tsotsos, J. K. *et al.* Modeling visual attention via selective tuning. *Artif. Intell.* (1995). doi:10.1016/0004-3702(95)00025-9
3. Pashler, H. Dual-task interference in simple tasks: Data and theory. *Psychol. Bull.* **116**, 220–244 (1994).
4. Gaspelin, N. & Luck, S. J. The Role of Inhibition in Avoiding Distraction by Salient Stimuli. *Trends in Cognitive Sciences* (2018). doi:10.1016/j.tics.2017.11.001
5. Corbetta, M., Miezin, F., Dobmeyer, S., Shulman, G. & Petersen, S. Selective and divided attention during visual discriminations of shape, color, and speed: functional anatomy by positron emission tomography. *J. Neurosci.* (2018). doi:10.1523/jneurosci.11-08-02383.1991
6. Kandel, E. & Wurtz, R. Constructing the Visual Image. in *Principles of Neural Science* (eds. Kandel, E., Schwartz, J. & Jessell, T.) 420–435 (McGraw-Hill, 2000).
7. Wurtz, R. & Kandel, E. Central Visual Pathway. in *Principles of Neural Science* (eds. Kandel, E., Schwartz, J. & Jessell, T.) 448–468 (McGraw-Hill, 2000).
8. Wurtz, R. & Kandel, E. Perception of Motion, Depth, and Form. in *Principles of Neural Science* (eds. Kandel, E., Schwartz, J. & Jessell, T.) 469–488 (McGraw-Hill, 2000).
9. Verhagen, J. V. & Engelen, L. The neurocognitive bases of human multimodal food perception: Sensory integration. *Neuroscience and Biobehavioral Reviews* (2006). doi:10.1016/j.neubiorev.2005.11.003
10. Verhagen, J. V. The neurocognitive bases of human multimodal food perception: Consciousness. *Brain Research Reviews* (2007). doi:10.1016/j.brainresrev.2006.09.002
11. Corbetta, M. & Shulman, G. L. Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* **3**, 201–215 (2002).
12. Perrone-Bertolotti, M. *et al.* A real-time marker of object-based attention in the Human Brain. A possible component of a “Gate-Keeping Mechanism” performing late attentional selection in the Ventro-Lateral Prefrontal Cortex. *Neuroimage* (2020).
13. Corbetta, M., Kincade, J. M., Ollinger, J. M., McAvoy, M. P. & Shulman, G. L. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nat. Neurosci.* (2000). doi:10.1038/73009
14. Petersen, S. E. & Posner, M. I. The Attention System of the Human Brain: 20 Years After. *Annu. Rev. Neurosci.* **35**, 73–89 (2012).
15. Posner, M. The Attention System Of The Human Brain. *Annu. Rev. Neurosci.* (1990). doi:10.1146/annurev.neuro.13.1.25
16. Corbetta, M., Patel, G. & Shulman, G. L. The Reorienting System of the Human Brain: From

- Environment to Theory of Mind. *Neuron* (2008). doi:10.1016/j.neuron.2008.04.017
17. Broadbent, D. E. Perception and communication. *Educ. + Train.* (1958). doi:10.1108/eb015727
 18. Deutsch, J. A. & Deutsch, D. Attention: Some theoretical considerations. *Psychol. Rev.* (1963). doi:10.1037/h0042712
 19. Treisman, A. Monitoring and storage of irrelevant messages in selective attention. *J. Verbal Learning Verbal Behav.* (1964). doi:10.1016/S0022-5371(64)80015-3
 20. Wickens, C. D. Multiple resources and performance prediction. *Theor. Issues Ergon. Sci.* (2002). doi:10.1080/14639220210123806
 21. Wickens, C. D. Multiple Resources and Mental Workload. *Hum. Factors J. Hum. Factors Ergon. Soc.* (2008). doi:10.1518/001872008x288394
 22. Young, M. S. & Stanton, N. A. Malleable attentional resources theory: A new explanation for the effects of mental underload on performance. *Human Factors* (2002). doi:10.1518/0018720024497709
 23. Treisman, A. *The perception of features and objects. Attention: Selection, awareness, and control: A tribute to Donald Broadbent* (Vancouver studies in cognitive science, Vol. 8. Visual attention (p. 26–54). Oxford University Press, 1993).
 24. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu Rev Neurosci* **18**, 193–222 (1995).
 25. Craighero, L., Fadiga, L., Rizzolatti, G. & Umiltà, C. Action for perception: A motor-visual attentional effect. *J. Exp. Psychol. Hum. Percept. Perform.* (1999). doi:10.1037/0096-1523.25.6.1673
 26. Craighero, L., Bello, A., Fadiga, L. & Rizzolatti, G. Hand action preparation influences the responses to hand pictures. *Neuropsychologia* (2002). doi:10.1016/S0028-3932(01)00134-8
 27. Woodman, G. F. & Luck, S. J. Do the Contents of Visual Working Memory Automatically Influence Attentional Selection During Visual Search? *J. Exp. Psychol. Hum. Percept. Perform.* (2007). doi:10.1037/0096-1523.33.2.363
 28. Han, S. W. & Kim, M. S. Do the Contents of Working Memory Capture Attention? Yes, But Cognitive Control Matters. *J. Exp. Psychol. Hum. Percept. Perform.* (2009). doi:10.1037/a0016452
 29. Wolfe, J. M. Guided Search 4.0: Current Progress with a Model of Visual Search. in *Integrated Models of Cognitive Systems* (2012). doi:10.1093/acprof:oso/9780195189193.003.0008
 30. Treisman, A. M. & Gelade, G. A feature-integration theory of attention. *Cogn. Psychol.* (1980). doi:10.1016/0010-0285(80)90005-5
 31. Treisman, A. & Gormican, S. Feature Analysis in Early Vision: Evidence From Search Asymmetries. *Psychol. Rev.* (1988). doi:10.1037/0033-295X.95.1.15
 32. Treisman, A. Search, Similarity, and Integration of Features Between and Within Dimensions. *J. Exp. Psychol. Hum. Percept. Perform.* (1991). doi:10.1037/0096-1523.17.3.652
 33. Marois, R., Yi, D. J. & Chun, M. M. The Neural Fate of Consciously Perceived and Missed Events in the Attentional Blink. *Neuron* (2004). doi:10.1016/S0896-6273(04)00012-1
 34. Kranczioch, C., Debener, S., Schwarzbach, J., Goebel, R. & Engel, A. K. Neural correlates of

- conscious perception in the attentional blink. *Neuroimage* (2005). doi:10.1016/j.neuroimage.2004.09.024
35. Dehaene, S. *et al.* Cerebral mechanisms of word masking and unconscious repetition priming. *Nat. Neurosci.* (2001). doi:10.1038/89551
 36. Beck, D. M., Rees, G., Frith, C. D. & Lavie, N. Neural correlates of change detection and change blindness. *Nat. Neurosci.* (2001). doi:10.1038/88477
 37. Koch, C. & Ullman, S. Shifts in Selective Visual Attention: Towards the Underlying Neural Circuitry. in *Matters of Intelligence* (1987). doi:10.1007/978-94-009-3833-5_5
 38. Treisman, A. The binding problem. *Curr Opin Neurobiol* **6**, 171–178 (1996).
 39. Egeth, H. E. Parallel versus serial processes in multidimensional stimulus discrimination. *Percept. Psychophys.* (1966). doi:10.3758/BF03207389
 40. Itti, L., Koch, C. & Niebur, E. A model of saliency-based visual attention for rapid scene analysis. *Trans. Pattern Anal. Mach. Intell.* **20**, (1998).
 41. Zelinsky, G. J. & Bisley, J. W. The what, where, and why of priority maps and their interactions with visual working memory. *Ann. N. Y. Acad. Sci.* **1339**, 154–164 (2015).
 42. Fecteau, J. H. & Munoz, D. P. Saliency, relevance, and firing: a priority map for target selection. *Trends in Cognitive Sciences* (2006). doi:10.1016/j.tics.2006.06.011
 43. Veale, R., Hafed, Z. M. & Yoshida, M. How is visual saliency computed in the brain? Insights from behaviour, neurobiology and modeling. *Philos. Trans. R. Soc. B Biol. Sci.* **372**, (2017).
 44. Kulke, L. V. *et al.* Neural differences between covert and overt attention studied using EEG with simultaneous remote eye tracking. *Front. Hum. Neurosci.* (2016). doi:10.3389/fnhum.2016.00592
 45. Felleman, D. J. & Van Essen, D. C. Distributed hierarchical processing in the primate cerebral cortex. *Cereb. Cortex* (1991). doi:10.1093/cercor/1.1.1
 46. Bogler, C., Bode, S. & Haynes, J. D. Decoding successive computational stages of saliency processing. *Curr. Biol.* (2011). doi:10.1016/j.cub.2011.08.039
 47. Goodale, M. A. & Milner, A. D. Separate visual pathways for perception and action. *Trends in Neurosciences* (1992). doi:10.1016/0166-2236(92)90344-8
 48. Stein, B. E. The development of a dialogue between cortex and midbrain to integrate multisensory information. in *Experimental Brain Research* (2005). doi:10.1007/s00221-005-2372-0
 49. Hikosaka, O. & Wurtz, R. H. Visual and oculomotor functions of monkey substantia nigra pars reticulata. IV. Relation of substantia nigra to superior colliculus. *J. Neurophysiol.* (2017). doi:10.1152/jn.1983.49.5.1285
 50. Cowey, A. & Perry, V. H. The projection of the fovea to the superior colliculus in rhesus monkeys. *Neuroscience* (1980). doi:10.1016/0306-4522(80)90070-6
 51. Fries, W. Cortical projections to the superior colliculus in the macaque monkey: A retrograde study using horseradish peroxidase. *J. Comp. Neurol.* (1984). doi:10.1002/cne.902300106
 52. Schiller, P. H., Stryker, M., Cynader, M. & Berman, N. Response characteristics of single cells in the monkey superior colliculus following ablation or cooling of visual cortex. *J. Neurophysiol.* (2017). doi:10.1152/jn.1974.37.1.181

53. Gattass, R., Galkin, T. W., Desimone, R. & Ungerleider, L. G. Subcortical connections of area V4 in the macaque. *J. Comp. Neurol.* (2014). doi:10.1002/cne.23513
54. Webster, M. J., Bachevalier, J. & Ungerleider, L. G. Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. *Cereb. Cortex* (1994). doi:10.1093/cercor/4.5.470
55. Ungerleider, L. G., Desimone, R., Galkin, T. W. & Mishkin, M. Subcortical projections of area MT in the macaque. *J. Comp. Neurol.* (1984). doi:10.1002/cne.902230304
56. Cowey, A., Stoerig, P. & Bannister, M. Retinal ganglion cells labelled from the pulvinar nucleus in macaque monkeys. *Neuroscience* (1994). doi:10.1016/0306-4522(94)90445-6
57. Diederich, N. J., Stebbins, G., Schiltz, C. & Goetz, C. G. Are patients with Parkinson's disease blind to blindsight? *Brain* (2014). doi:10.1093/brain/awu094
58. Gegenfurtner, K. R. Cortical mechanisms of colour vision. *Nat. Rev. Neurosci.* (2003). doi:10.1038/nrn1138
59. Livingstone, M. & Hubel, D. Segregation of form, color, movement, and depth: Anatomy, physiology, and perception. *Science* (80-.). (1988). doi:10.1126/science.3283936
60. Betz, T., Wilming, N., Bogler, C., Haynes, J.-D. & Konig, P. Dissociation between saliency signals and activity in early visual cortex. *J. Vis.* (2013). doi:10.1167/13.14.6
61. Yoshida, M. *et al.* Residual attention guidance in blindsight monkeys watching complex natural scenes. *Curr. Biol.* (2012). doi:10.1016/j.cub.2012.05.046
62. Wurtz, R. H. & Mohler, C. W. Organization of monkey superior colliculus: enhanced visual response of superficial layer cells. *J. Neurophysiol.* (2017). doi:10.1152/jn.1976.39.4.745
63. Davidson, R. M. & Bender, D. B. Selectivity for relative motion in the monkey superior colliculus. *J. Neurophysiol.* (2017). doi:10.1152/jn.1991.65.5.1115
64. White, B. J., Boehnke, S. E., Marino, R. A., Itti, L. & Munoz, D. P. Color-Related Signals in the Primate Superior Colliculus. *J. Neurosci.* (2009). doi:10.1523/jneurosci.1986-09.2009
65. Berman, R. A. & Wurtz, R. H. Functional Identification of a Pulvinar Path from Superior Colliculus to Cortical Area MT. *J. Neurosci.* (2010). doi:10.1523/jneurosci.6176-09.2010
66. Berman, R. A. & Wurtz, R. H. Signals Conveyed in the Pulvinar Pathway from Superior Colliculus to Cortical Area MT. *J. Neurosci.* (2011). doi:10.1523/jneurosci.4738-10.2011
67. Bogler, C., Bode, S. & Haynes, J. D. Orientation pop-out processing in human visual cortex. *Neuroimage* (2013). doi:10.1016/j.neuroimage.2013.05.040
68. Mazer, J. A. & Gallant, J. L. Goal-related activity in V4 during free viewing visual search: Evidence for a ventral stream visual salience map. *Neuron* (2003). doi:10.1016/S0896-6273(03)00764-5
69. Moore, T. & Armstrong, K. M. Selective gating of visual signals by microstimulation of frontal cortex. *Nature* (2003). doi:10.1038/nature01341
70. Ogawa, T. & Komatsu, H. Neuronal dynamics of bottom-up and top-down processes in area V4 of macaque monkeys performing a visual search. *Exp. Brain Res.* (2006). doi:10.1007/s00221-006-0362-5
71. Buschman, T. J. & Miller, E. K. Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science* (80-.). (2007).

- doi:10.1126/science.1138071
72. Ibos, G., Duhamel, J.-R. & Ben Hamed, S. A Functional Hierarchy within the Parietofrontal Network in Stimulus Selection and Attention Control. *J. Neurosci.* (2013). doi:10.1523/jneurosci.4058-12.2013
 73. Fernandes, H. L., Stevenson, I. H., Phillips, A. N., Segraves, M. A. & Kording, K. P. Saliency and saccade encoding in the frontal eye field during natural scene search. *Cereb. Cortex* (2014). doi:10.1093/cercor/bht179
 74. Thompson, K. G. & Bichot, N. P. A visual salience map in the primate frontal eye field. *Progress in Brain Research* (2004). doi:10.1016/S0079-6123(04)47019-8
 75. Kaya, E. M. & Elhilali, M. Investigating bottom-up auditory attention. *Front Hum Neurosci* (2014). doi:10.3389/fnhum.2014.00327
 76. Pulvermüller, F. & Shtyrov, Y. Language outside the focus of attention: The mismatch negativity as a tool for studying higher cognitive processes. *Progress in Neurobiology* (2006). doi:10.1016/j.pneurobio.2006.04.004
 77. Mesgarani, N. & Chang, E. F. Selective cortical representation of attended speaker in multi-talker speech perception. *Nature* (2012). doi:10.1038/nature11020
 78. Atiani, S. *et al.* Emergent selectivity for task-relevant stimuli in higher-order auditory cortex. *Neuron* (2014). doi:10.1016/j.neuron.2014.02.029
 79. Ahveninen, J. *et al.* Task-modulated 'what' and 'where' pathways in human auditory cortex. *Proc. Natl. Acad. Sci. U. S. A.* **103**, (2006).
 80. Kayser, C., Petkov, C. I., Lippert, M. & Logothetis, N. K. Mechanisms for allocating auditory attention: An auditory saliency map. *Curr. Biol.* (2005). doi:10.1016/j.cub.2005.09.040
 81. Kalinli, O. & Narayanan, S. A saliency-based auditory attention model with applications to unsupervised prominent syllable detection in speech. in *International Speech Communication Association - 8th Annual Conference of the International Speech Communication Association, Interspeech 2007* (2007).
 82. Tsuchida, T. & Cottrell, G. W. Auditory saliency using natural statistics. in *Proc. Annual Meeting of the Cognitive Science* (2012).
 83. Bregman, A. S. *Auditory scene analysis: the perceptual organization of sound.* (The MIT Press, 1990).
 84. Kondo, H. M., van Loon, A. M., Kawahara, J.-I. & Moore, B. C. J. Auditory and visual scene analysis: an overview. *Philos. Trans. R. Soc. B Biol. Sci.* **372**, 20160099 (2017).
 85. Alain, C., Arnott, S. R. & Picton, T. W. Bottom-up and top-down influences on auditory scene analysis: Evidence from event-related brain potentials. *J. Exp. Psychol. Hum. Percept. Perform.* (2001). doi:10.1037/0096-1523.27.5.1072
 86. Winkler, I., Takegata, R. & Sussman, E. Event-related brain potentials reveal multiple stages in the perceptual organization of sound. *Cogn. Brain Res.* (2005). doi:10.1016/j.cogbrainres.2005.06.005
 87. Sussman, E. S., Horváth, J., Winkler, I. & Mark, O. The role of attention in the formation of auditory streams. *Percept. Psychophys.* (2007). doi:10.3758/BF03194460
 88. Cusack, R., Deeks, J., Aikman, G. & Carlyon, R. P. Effects of location, frequency region, and

- time course of selective attention on auditory scene analysis. *J. Exp. Psychol. Hum. Percept. Perform.* (2004). doi:10.1037/0096-1523.30.4.643
89. Snyder, J. S., Alain, C. & Picton, T. W. Effects of attention on neuroelectric correlates of auditory stream segregation. *J. Cogn. Neurosci.* (2006). doi:10.1162/089892906775250021
 90. Pressnitzer, D., Sayles, M., Micheyl, C. & Winter, I. M. Perceptual Organization of Sound Begins in the Auditory Periphery. *Curr. Biol.* (2008). doi:10.1016/j.cub.2008.06.053
 91. Bidet-Caulet, A. & Bertrand, O. Neurophysiological mechanisms involved in auditory perceptual organization. *Frontiers in Neuroscience* (2009). doi:10.3389/neuro.01.025.2009
 92. Kaya, E. M. & Elhilali, M. Modelling auditory attention. *Philos. Trans. R. Soc. B Biol. Sci.* **372**, (2017).
 93. Rauschecker, J. P. & Tian, B. Mechanisms and streams for processing of 'what' and 'where' in auditory cortex. *Proc. Natl. Acad. Sci.* (2000). doi:10.1073/pnas.97.22.11800
 94. Kashino, M. & Kondo, H. M. Functional brain networks underlying perceptual switching: Auditory streaming and verbal transformations. *Philos. Trans. R. Soc. B Biol. Sci.* **367**, 977–987 (2012).
 95. Thaut, M. H., Demartin, M. & Sanes, J. N. Brain networks for integrative rhythm formation. *PLoS One* (2008). doi:10.1371/journal.pone.0002312
 96. Teki, S., Grube, M., Kumar, S. & Griffiths, T. D. Distinct neural substrates of duration-based and beat-based auditory timing. *J. Neurosci.* (2011). doi:10.1523/JNEUROSCI.5561-10.2011
 97. Nadel, L., Hupbach, A., Gomez, R. & Newman-Smith, K. Memory formation, consolidation and transformation. *Neuroscience and Biobehavioral Reviews* (2012). doi:10.1016/j.neubiorev.2012.03.001
 98. Miller, E. K., Lundqvist, M. & Bastos, A. M. Working Memory 2.0. *Neuron* (2018). doi:10.1016/j.neuron.2018.09.023
 99. Atkinson, R. C. & Shiffrin, R. M. Human memory: A proposed system and its control processes BT - Human memory: A proposed system and its control processes. *Hum. Mem. A Propos. Syst. its Control Process.* (1968).
 100. Craik, F. I. M. & Lockhart, R. S. Levels of processing: A framework for memory research. *J. Verbal Learning Verbal Behav.* (1972). doi:10.1016/S0022-5371(72)80001-X
 101. Baddeley, A. Working memory: Looking back and looking forward. *Nat. Rev. Neurosci.* (2003). doi:10.1038/nrn1201
 102. Tulving, E. Episodic Memory: From Mind to Brain. *Annu. Rev. Psychol.* (2002). doi:10.1146/annurev.psych.53.100901.135114
 103. Eustache, F. & Desgranges, B. MNESIS: Towards the integration of current multisystem models of memory. *Neuropsychology Review* (2008). doi:10.1007/s11065-008-9052-3
 104. Baddeley, A. Working memory: Theories, models, and controversies. in *Exploring Working Memory: Selected works of Alan Baddeley* (2017). doi:10.4324/9781315111261
 105. Alvarez, G. A. & Cavanagh, P. The Capacity of Visual Short-Term Memory Is Set Both by Visual Information Load and by Number of Objects. *Psychol. Sci.* (2004). doi:10.1111/j.0963-7214.2004.01502006.x
 106. Awh, E., Barton, B. & Vogel, E. K. Visual working memory represents a fixed number of items

- regardless of complexity. *Psychol. Sci.* (2007). doi:10.1111/j.1467-9280.2007.01949.x
107. Lewis-Peacock, J. A. & Postle, B. R. Temporary activation of long-term memory supports working memory. *J. Neurosci.* (2008). doi:10.1523/JNEUROSCI.1953-08.2008
 108. Fukuda, K. & Woodman, G. F. Visual working memory buffers information retrieved from visual long-term memory. *Proc. Natl. Acad. Sci. U. S. A.* (2017). doi:10.1073/pnas.1617874114
 109. Luck, S. J. & Vogel, E. K. Visual working memory capacity: From psychophysics and neurobiology to individual differences. *Trends in Cognitive Sciences* (2013). doi:10.1016/j.tics.2013.06.006
 110. Monsell, S. Task switching. *Trends Cogn Sci* (2003).
 111. Rogers, R. D. & Monsell, S. Costs of a Predictable Switch Between Simple Cognitive Tasks. *J. Exp. Psychol. Gen.* (1995). doi:10.1037/0096-3445.124.2.207
 112. Meiran, N. Reconfiguration of processing mode prior to task performance. *J. Exp. Psychol. Learn. Mem. Cogn.* (1996). doi:10.1037/0278-7393.22.6.1423
 113. Steinhauser, M. & Hübner, R. Automatic activation of task-related representations in task shifting. *Mem. Cogn.* (2007). doi:10.3758/BF03195950
 114. Sakai, K. Task Set and Prefrontal Cortex. *Annu. Rev. Neurosci.* (2008). doi:10.1146/annurev.neuro.31.060407.125642
 115. Logan, G. D. & Gordon, R. D. Executive control of visual attention in dual-task situations. *Psychol. Rev.* (2001). doi:10.1037/0033-295X.108.2.393
 116. Olivers, C. N. L., Peters, J., Houtkamp, R. & Roelfsema, P. R. Different states in visual working memory: When it guides attention and when it does not. *Trends in Cognitive Sciences* (2011). doi:10.1016/j.tics.2011.05.004
 117. Manohar, S. G., Zokaei, N., Fallon, S. J., Vogels, T. P. & Husain, M. Neural mechanisms of attending to items in working memory. *Neuroscience and Biobehavioral Reviews* (2019). doi:10.1016/j.neubiorev.2019.03.017
 118. Emrich, S. M., Lockhart, H. A. & Al-Aidroos, N. Attention mediates the flexible allocation of visual working memory resources. *J. Exp. Psychol. Hum. Percept. Perform.* (2017). doi:10.1037/xhp0000398
 119. Dube, B., Emrich, S. M. & Al-Aidroos, N. More than a filter: Feature-based attention regulates the distribution of visual working memory resources. *J. Exp. Psychol. Hum. Percept. Perform.* (2017). doi:10.1037/xhp0000428
 120. Carlisle, N. B. Flexibility in attentional control: Multiple sources and suppression. *Yale Journal of Biology and Medicine* (2019).
 121. Meyers, E. M., Freedman, D. J., Kreiman, G., Miller, E. K. & Poggio, T. Dynamic population coding of category information in inferior temporal and prefrontal cortex. *J. Neurophysiol.* (2008). doi:10.1152/jn.90248.2008
 122. Stokes, M. G. *et al.* Dynamic coding for cognitive control in prefrontal cortex. *Neuron* (2013). doi:10.1016/j.neuron.2013.01.039
 123. Fuster, J. M. & Alexander, G. E. Neuron activity related to short-term memory. *Science* (80-). (1971). doi:10.1126/science.173.3997.652
 124. Funahashi, S. Prefrontal cortex and working memory processes. *Neuroscience* (2006).

- doi:10.1016/j.neuroscience.2005.07.003
125. Diamond, A. Bootstrapping conceptual deduction using physical connection: rethinking frontal cortex. *Trends Cogn. Sci.* (2006). doi:10.1016/j.tics.2006.03.003
 126. Thompson-Schill, S. L. *et al.* Effects of frontal lobe damage on interference effects in working memory. *Cogn. Affect. Behav. Neurosci.* (2002). doi:10.3758/CABN.2.2.109
 127. Todd, J. J., Han, S. W., Harrison, S. & Marois, R. The neural correlates of visual working memory encoding: A time-resolved fMRI study. *Neuropsychologia* (2011). doi:10.1016/j.neuropsychologia.2011.01.040
 128. Harrison, S. A. & Tong, F. Decoding reveals the contents of visual working memory in early visual areas. *Nature* (2009). doi:10.1038/nature07832
 129. D’Esposito, M. & Postle, B. R. The cognitive neuroscience of working memory. *Annu Rev Psychol* **66**, 115–142 (2015).
 130. Lee, S.-H. & Baker, C. I. Multi-Voxel Decoding and the Topography of Maintained Information During Visual Working Memory. *Front. Syst. Neurosci.* (2016). doi:10.3389/fnsys.2016.00002
 131. Kumar, S. *et al.* A Brain System for Auditory Working Memory. *J. Neurosci.* (2016). doi:10.1523/jneurosci.4341-14.2016
 132. Cole, M. W., Bagic, A., Kass, R. & Schneider, W. Prefrontal Dynamics Underlying Rapid Instructed Task Learning Reverse with Practice. *J. Neurosci.* (2010). doi:10.1523/jneurosci.1662-10.2010
 133. Cole, M. W., Etzel, J. A., Zacks, J. M., Schneider, W. & Braver, T. S. Rapid Transfer of Abstract Rules to Novel Contexts in Human Lateral Prefrontal Cortex. *Front. Hum. Neurosci.* (2011). doi:10.3389/fnhum.2011.00142
 134. Cole, M. W., Ito, T. & Braver, T. S. The Behavioral Relevance of Task Information in Human Prefrontal Cortex. *Cereb. Cortex* (2016). doi:10.1093/cercor/bhv072
 135. Christophel, T. B., Klink, P. C., Spitzer, B., Roelfsema, P. R. & Haynes, J. D. The Distributed Nature of Working Memory. *Trends in Cognitive Sciences* (2017). doi:10.1016/j.tics.2016.12.007
 136. Koch, I., Poljac, E., Muller, H. & Kiesel, A. Cognitive Structure, Flexibility, and Plasticity in Human Multitasking – An Integrative Review of Dual-Task and Task-Switching Research. *Psychol. Bull.* 1–97 (2018).
 137. Cole, M. W., Laurent, P. & Stocco, A. Rapid instructed task learning: A new window into the human brain’s unique capacity for flexible cognitive control. *Cognitive, Affective and Behavioral Neuroscience* (2013). doi:10.3758/s13415-012-0125-7
 138. McGuire, J. T. & Botvinick, M. M. Prefrontal cortex, cognitive control, and the registration of decision costs. *Proc. Natl. Acad. Sci.* (2010). doi:10.1073/pnas.0910662107
 139. Westbrook, A. & Braver, T. S. Cognitive effort: A neuroeconomic approach. *Cogn. Affect. Behav. Neurosci.* **15**, 395–415 (2015).
 140. Asplund, C. L., Todd, J. J., Snyder, A. P. & Marois, R. A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. *Nat. Neurosci.* (2010). doi:10.1038/nn.2509
 141. Dosenbach, N. U. F., Fair, D. A., Cohen, A. L., Schlaggar, B. L. & Petersen, S. E. A dual-networks

- architecture of top-down control. *Trends Cogn. Sci.* **12**, 99–105 (2008).
142. Dehaene, S. & Changeux, J. P. Experimental and Theoretical Approaches to Conscious Processing. *Neuron* **70**, 200–227 (2011).
 143. Shenhav, A., Botvinick, M. M. & Cohen, J. D. The expected value of control: An integrative theory of anterior cingulate cortex function. *Neuron* (2013). doi:10.1016/j.neuron.2013.07.007
 144. Rushworth, M. F. S., Kolling, N., Sallet, J. & Mars, R. B. Valuation and decision-making in frontal cortex: One or many serial or parallel systems? *Current Opinion in Neurobiology* (2012). doi:10.1016/j.conb.2012.04.011
 145. Kolling, N., Behrens, T. E. J., Mars, R. B. & Rushworth, M. F. S. Neural mechanisms of foraging. *Science (80-.)*. (2012). doi:10.1126/science.1216930
 146. Shenhav, A., Cohen, J. D. & Botvinick, M. M. Dorsal anterior cingulate cortex and the value of control. *Nature Neuroscience* (2016). doi:10.1038/nn.4384
 147. Dosenbach, N. U. F. *et al.* Distinct brain networks for adaptive and stable task control in humans. *Proc. Natl. Acad. Sci.* **104**, 11073–11078 (2007).
 148. Allman, J. M., Watson, K. K., Tetreault, N. A. & Hakeem, A. Y. Intuition and autism: A possible role for Von Economo neurons. *Trends Cogn. Sci.* (2005). doi:10.1016/j.tics.2005.06.008
 149. Botvinick, M. M., Carter, C. S., Braver, T. S., Barch, D. M. & Cohen, J. D. Conflict monitoring and cognitive control. *Psychol. Rev.* (2001). doi:10.1037/0033-295X.108.3.624
 150. Botvinick, M. M., Cohen, J. D. & Carter, C. S. Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences* (2004). doi:10.1016/j.tics.2004.10.003
 151. Dosenbach, N. U. F. *et al.* A Core System for the Implementation of Task Sets. *Neuron* (2006). doi:10.1016/j.neuron.2006.04.031
 152. Miller, B. T. & D’Esposito, M. Searching for ‘the top’ in top-down control. *Neuron* (2005). doi:10.1016/j.neuron.2005.11.002
 153. Vogelsang, D. A. & D’Esposito, M. Is there evidence for a rostral-caudal gradient in fronto-striatal loops and what role does dopamine play? *Frontiers in Neuroscience* (2018). doi:10.3389/fnins.2018.00242
 154. Badre, D. Cognitive control, hierarchy, and the rostro-caudal organization of the frontal lobes. *Trends in Cognitive Sciences* (2008). doi:10.1016/j.tics.2008.02.004
 155. Badre, D. & D’Esposito, M. Is the rostro-caudal axis of the frontal lobe hierarchical? *Nature Reviews Neuroscience* (2009). doi:10.1038/nrn2667
 156. Koechlin, E., Ody, C. & Kouneiher, F. The Architecture of Cognitive Control in the Human Prefrontal Cortex. *Science (80-.)*. (2003). doi:10.1126/science.1088545
 157. Koechlin, E. & Summerfield, C. An information theoretical approach to prefrontal executive function. *Trends Cogn. Sci.* (2007). doi:10.1016/j.tics.2007.04.005
 158. Botvinick, M. M. Hierarchical models of behavior and prefrontal function. *Trends in Cognitive Sciences* (2008). doi:10.1016/j.tics.2008.02.009
 159. Duncan, J. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends in Cognitive Sciences* (2010). doi:10.1016/j.tics.2010.01.004

160. Crittenden, B. M. & Duncan, J. Task difficulty manipulation reveals multiple demand activity but no frontal lobe hierarchy. *Cereb. Cortex* (2014). doi:10.1093/cercor/bhs333
161. Lu, J. *et al.* The multiple-demand system in the novelty of musical improvisation: Evidence from an MRI study on composers. *Front. Neurosci.* (2017). doi:10.3389/fnins.2017.00695
162. Fedorenko, E., Duncan, J. & Kanwisher, N. Broad domain generality in focal regions of frontal and parietal cortex. *Proc. Natl. Acad. Sci. U. S. A.* (2013). doi:10.1073/pnas.1315235110
163. Cole, M. W. & Schneider, W. The cognitive control network: Integrated cortical regions with dissociable functions. *Neuroimage* (2007). doi:10.1016/j.neuroimage.2007.03.071
164. Vincent, J. L., Kahn, I., Snyder, A. Z., Raichle, M. E. & Buckner, R. L. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J. Neurophysiol.* (2008). doi:10.1152/jn.90355.2008
165. Camilleri, J. A. *et al.* Definition and characterization of an extended multiple-demand network. *Neuroimage* **165**, 138–147 (2018).
166. Shashidhara, S., Mitchell, D. J., Erez, Y. & Duncan, J. Progressive Recruitment of the Frontoparietal Multiple-demand System with Increased Task Complexity, Time Pressure, and Reward. *J. Cogn. Neurosci.* (2019). doi:10.1162/jocn_a_01440
167. Petton, M. *et al.* BLAST: A short computerized test to measure the ability to stay on task. Normative behavioral data and detailed cortical dynamics. *Neuropsychologia* (2019). doi:10.1016/j.neuropsychologia.2019.107151
168. Neisser, U. & Becklen, R. Selective looking: Attending to visually specified events. *Cogn. Psychol.* (1975). doi:10.1016/0010-0285(75)90019-5
169. Spelke, E., Hirst, W. & Neisser, U. Skills of divided attention. *Cognition* (1976). doi:10.1016/0010-0277(76)90018-4
170. Pashler, H. E. *The Psychology of Attention.* (1998).
171. Posner, M. I. & Snyder, C. R. Attention and cognitive control. *Inf. Process. Cogn. Loyola Symp.* (1975).
172. Navon, D. & Gopher, D. On the economy of the human-processing system. *Psychol. Rev.* (1979). doi:10.1037/0033-295X.86.3.214
173. Feng, S. F., Schwemmer, M., Gershman, S. J. & Cohen, J. D. Multitasking versus multiplexing: Toward a normative account of limitations in the simultaneous execution of control-demanding behaviors. *Cogn. Affect. Behav. Neurosci.* (2014). doi:10.3758/s13415-013-0236-9
174. Strobach, T., Wendt, M. & Janczyk, M. Editorial: Multitasking: Executive functioning in dual-task and task switching situations. *Front. Psychol.* **9**, 1–5 (2018).
175. Grange, J. A. & Houghton, G. Task Switching and Cognitive Control: An Introduction. in *Task Switching and Cognitive Control* 1–27 (Oxford University Press, 2014).
176. Rubin, O. & Meiran, N. On the origins of the task mixing cost in the cuing task-switching paradigm. *J. Exp. Psychol. Learn. Mem. Cogn.* (2005). doi:10.1037/0278-7393.31.6.1477
177. Mari-Beffa, P. & Kirkham, A. The Mixing Cost as a Measure of Cognitive Control. in *Task Switching and Cognitive Control* 74–100 (Oxford University Press, 2014).
178. Waszak, F., Hommel, B. & Allport, A. Task-switching and long-term priming: Role of episodic stimulus-task bindings in task-shift costs. *Cogn. Psychol.* (2003). doi:10.1016/S0010-

0285(02)00520-0

179. Koch, I. Sequential task predictability in task switching. *Psychon. Bull. Rev.* (2005). doi:10.3758/BF03196354
180. Kiesel, A. *et al.* Control and interference in task switching-a review. *Psychol. Bull.* (2010). doi:10.1037/a0019842
181. Arrington, C. M. The effect of stimulus availability on task choice in voluntary task switching. *Mem. Cogn.* (2008). doi:10.3758/MC.36.5.991
182. Ort, E., Fahrenfort, J. J. & Olivers, C. N. L. Lack of Free Choice Reveals the Cost of Having to Search for More Than One Object. *Psychol. Sci.* (2017). doi:10.1177/0956797617705667
183. Telford, C. W. The refractory phase of voluntary and associative responses. *J. Exp. Psychol.* (1931). doi:10.1037/h0073262
184. Huestegge, L., Pieczykolan, A. & Koch, I. Talking while looking: On the encapsulation of output system representations. *Cogn. Psychol.* (2014). doi:10.1016/j.cogpsych.2014.06.001
185. Smith, M. C. Theories of the Psychological Refractory Period. *Psychol. Bull.* (1967). doi:10.1037/h0020419
186. Tombu, M. & Jolicoeur, P. A Central Capacity Sharing Model of Dual-Task Performance. *J. Exp. Psychol. Hum. Percept. Perform.* (2003). doi:10.1037/0096-1523.29.1.3
187. Sternberg, S. The discovery of processing stages: extensions of Donders' method. in *Acta Psychologica* **30**, 276–315 (Attention and Performance, 1969).
188. Welford, A. T. The “psychological refractory period” and the timing of high-speed performance. *Br. J. Psychol* **43**, 2–19 (1952).
189. Schubert, T. Processing differences between simple and choice reactions affect bottleneck localization in overlapping tasks. *J. Exp. Psychol. Hum. Percept. Perform.* (1999). doi:10.1037/0096-1523.25.2.408
190. Schubert, T. The central attentional limitation and executive control. *Front. Biosci.* (2008). doi:10.2741/2950
191. Schumacher, E. H. *et al.* Concurrent response-selection processes in dual-task performance: Evidence for adaptive executive control of task scheduling. *J. Exp. Psychol. Hum. Percept. Perform.* (1999). doi:10.1037/0096-1523.25.3.791
192. Meyer, D. E. & Kieras, D. E. A Computational Theory of Executive Cognitive Processes and Multiple-Task Performance: Part 1. Basic Mechanisms. *Psychol. Rev.* (1997). doi:10.1037/0033-295X.104.1.3
193. Allport, D. A., Antonis, B. & Reynolds, P. On the division of attention: a disproof of the single channel hypothesis. *Q. J. Exp. Psychol.* (1972). doi:10.1080/00335557243000102
194. Fischer, R. & Plessow, F. Efficient multitasking: Parallel versus serial processing of multiple tasks. *Front. Psychol.* **6**, (2015).
195. Sigman, M. & Dehaene, S. Dynamics of the central bottleneck: Dual-task and task uncertainty. *PLoS Biol.* **4**, 1227–1238 (2006).
196. Navon, D. & Miller, J. Queuing or sharing? A critical evaluation of the single-bottleneck notion. *Cogn. Psychol.* (2002). doi:10.1006/cogp.2001.0767

197. Egeth, H. & Kahneman, D. Attention and Effort. *Am. J. Psychol.* (1975). doi:10.2307/1421603
198. Miller, J., Ulrich, R. & Rolke, B. On the optimality of serial and parallel processing in the psychological refractory period paradigm: Effects of the distribution of stimulus onset asynchronies. *Cogn. Psychol.* **58**, 273–310 (2009).
199. Ruthruff, E., Pashler, H. E. & Klaassen, A. Processing bottlenecks in dual-task performance: Structural limitation or strategic postponement? *Psychon. Bull. Rev.* (2001). doi:10.3758/BF03196141
200. Levy, J. & Pashler, H. Is Dual-Task Slowing Instruction Dependent? *J. Exp. Psychol. Hum. Percept. Perform.* (2001). doi:10.1037/0096-1523.27.4.862
201. Pashler, H. & Baylis, G. Procedural Learning: 1. Locus of Practice Effects in Speeded Choice Tasks. *J. Exp. Psychol. Learn. Mem. Cogn.* (1991). doi:10.1037/0278-7393.17.1.20
202. Pollmann, S. & Maertens, M. Shift of activity from attention to motor-related brain areas during visual learning. *Nat. Neurosci.* (2005). doi:10.1038/nn1552
203. Ruthruff, E., Johnston, J. C., Van Selst, M., Whitsell, S. & Remington, R. Vanishing Dual-Task Interference after Practice: Has the Bottleneck been Eliminated or is it Merely Latent? *J. Exp. Psychol. Hum. Percept. Perform.* (2003). doi:10.1037/0096-1523.29.2.280
204. Ruthruff, E., Van Selst, M., Johnston, J. C. & Remington, R. How does practice reduce dual-task interference: Integration, automatization, or just stage-shortening? *Psychol. Res.* (2006). doi:10.1007/s00426-004-0192-7
205. Dux, P. E. *et al.* Training Improves Multitasking Performance by Increasing the Speed of Information Processing in Human Prefrontal Cortex. *Neuron* **63**, 127–138 (2009).
206. Vandierendonck, A., Liefvooghe, B. & Verbruggen, F. Task Switching: Interplay of Reconfiguration and Interference Control. *Psychol. Bull.* (2010). doi:10.1037/a0019791
207. Strobach, T., Hendrich, E., Kübler, S., Müller, H. & Schubert, T. Processing order in dual-task situations: The “first-come, first-served” principle and the impact of task order instructions. *Attention, Perception, Psychophys.* (2018). doi:10.3758/s13414-018-1541-8
208. Anderson, D. E., Vogel, E. K. & Awh, E. Selection and storage of perceptual groups is constrained by a discrete resource in working memory. *J. Exp. Psychol. Hum. Percept. Perform.* (2013). doi:10.1037/a0030094
209. Johnson, J. S., Hollingworth, A. & Luck, S. J. The Role of Attention in the Maintenance of Feature Bindings in Visual Short-Term Memory. *J. Exp. Psychol. Hum. Percept. Perform.* (2008). doi:10.1037/0096-1523.34.1.41
210. Peters, J. C., Goebel, R. & Roelfsema, P. R. Remembered but unused: The accessory items in working memory that do not guide attention. *J. Cogn. Neurosci.* (2009). doi:10.1162/jocn.2009.21083
211. van Moorselaar, D., Battistoni, E., Theeuwes, J. & Olivers, C. N. L. Rapid influences of cued visual memories on attentional guidance. *Ann. N. Y. Acad. Sci.* (2015). doi:10.1111/nyas.12574
212. van Vugt, M. K., Chakravarthi, R. & Lachaux, J. P. For whom the bell tolls: Periodic reactivation of sensory cortex in the gamma band as a substrate of visual working memory maintenance. *Front. Hum. Neurosci.* (2014). doi:10.3389/fnhum.2014.00696
213. Beck, V. M., Hollingworth, A. & Luck, S. J. Simultaneous Control of Attention by Multiple

- Working Memory Representations. *Psychol. Sci.* (2012). doi:10.1177/0956797612439068
214. Beck, V. M. & Hollingworth, A. Competition in saccade target selection reveals attentional guidance by simultaneously active working memory representations. *J. Exp. Psychol. Hum. Percept. Perform.* (2017). doi:10.1037/xhp0000306
 215. Miller, E. K., Erickson, C. A. & Desimone, R. Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *J. Neurosci.* (1996).
 216. Pasternak, T. & Greenlee, M. W. Working memory in primate sensory systems. *Nature Reviews Neuroscience* (2005). doi:10.1038/nrn1603
 217. Stokes, M. & Spaak, E. The Importance of Single-Trial Analyses in Cognitive Neuroscience. *Trends in Cognitive Sciences* (2016). doi:10.1016/j.tics.2016.05.008
 218. Kucewicz, M. T. *et al.* Dissecting gamma frequency activity during human memory processing. *Brain* (2017). doi:10.1093/brain/awx043
 219. Lundqvist, M., Herman, P., Warden, M. R., Brincat, S. L. & Miller, E. K. Gamma and beta bursts during working memory readout suggest roles in its volitional control. *Nat. Commun.* (2018). doi:10.1038/s41467-017-02791-8
 220. Naud, R. & Sprekeler, H. Sparse bursts optimize information transmission in a multiplexed neural code. *Proc. Natl. Acad. Sci. U. S. A.* (2018). doi:10.1073/pnas.1720995115
 221. Buschman, T. J. & Miller, E. K. Shifting the spotlight of attention: Evidence for discrete computations in cognition. *Frontiers in Human Neuroscience* (2010). doi:10.3389/fnhum.2010.00194
 222. VanRullen, R. Perceptual Cycles. *Trends in Cognitive Sciences* (2016). doi:10.1016/j.tics.2016.07.006
 223. Fiebelkorn, I. C., Pinsk, M. A. & Kastner, S. A Dynamic Interplay within the Frontoparietal Network Underlies Rhythmic Spatial Attention. *Neuron* (2018). doi:10.1016/j.neuron.2018.07.038
 224. Helfrich, R. F. *et al.* Neural Mechanisms of Sustained Attention Are Rhythmic. *Neuron* (2018). doi:10.1016/j.neuron.2018.07.032
 225. Bahramisharif, A., Jensen, O., Jacobs, J. & Lisman, J. Serial representation of items during working memory maintenance at letter-selective cortical sites. *PLoS Biol.* (2018). doi:10.1371/journal.pbio.2003805
 226. Oberauer, K., Souza, A. S., Druery, M. D. & Gade, M. Analogous mechanisms of selection and updating in declarative and procedural working memory: Experiments and a computational model. *Cogn. Psychol.* (2013). doi:10.1016/j.cogpsych.2012.11.001
 227. Schneider, D. W. & Logan, G. D. Tasks, Task Sets, and the Mapping Between Them. in *Task Switching and Cognitive Control* 27–44 (Oxford University Press, 2014).
 228. Altmann, E. M. & Gray, W. D. An Integrated Model of Cognitive Control in Task Switching. *Psychol. Rev.* (2008). doi:10.1037/0033-295X.115.3.602
 229. Meiran, N., Hommel, B., Bibi, U. & Lev, I. Consciousness and control in task switching. *Conscious. Cogn.* (2002). doi:10.1006/ccog.2001.0521
 230. Zylberberg, A., Slezak, D. F., Roelfsema, P. R., Dehaene, S. & Sigman, M. The brain's router: A cortical network model of serial processing in the primate brain. *PLoS Comput. Biol.* (2010).

doi:10.1371/journal.pcbi.1000765

231. Liu, T. & Becker, M. W. Serial Consolidation of Orientation Information Into Visual Short-Term Memory. *Psychol. Sci.* (2013). doi:10.1177/0956797612464381
232. Tamber-Rosenau, B. J., Dux, P. E., Tombu, M. N., Asplund, C. L. & Marois, R. Amodal Processing in Human Prefrontal Cortex. *J. Neurosci.* (2013). doi:10.1523/jneurosci.4601-12.2013
233. Kamienkowski, J. E., Pashler, H., Dehaene, S. & Sigman, M. Effects of practice on task architecture: Combined evidence from interference experiments and random-walk models of decision making. *Cognition* (2011). doi:10.1016/j.cognition.2010.12.010
234. Marois, R., Larson, J. M., Chun, M. M. & Shima, D. Response-specific sources of dual-task interference in human pre-motor cortex. *Psychol. Res.* (2006). doi:10.1007/s00426-005-0022-6
235. Tombu, M. N. *et al.* A Unified attentional bottleneck in the human brain. *Proc. Natl. Acad. Sci.* **108**, 13426–13431 (2011).
236. Sigman, M. & Dehaene, S. Brain Mechanisms of Serial and Parallel Processing during Dual-Task Performance. *J. Neurosci.* (2008). doi:10.1523/jneurosci.0948-08.2008
237. Ruiz Fernández, S., Leonhard, T., Rolke, B. & Ulrich, R. Processing two tasks with varying task order: Central stage duration influences central processing order. *Acta Psychol. (Amst.)* (2011). doi:10.1016/j.actpsy.2011.01.016
238. Tamber-Rosenau, B. & Marois, R. Central attention is serial but mid-level and peripheral attention are parallel—a hypothesis. *Attention, Percept. Psychophys.* **78**, 1874–1888 (2016).
239. Szameitat, A. J., Lepsien, J., Von Cramon, D. Y., Sterr, A. & Schubert, T. Task-order coordination in dual-task performance and the lateral prefrontal cortex: An event-related fMRI study. *Psychol. Res.* (2006). doi:10.1007/s00426-005-0015-5
240. Jong, R. De. The Role of Preparation in Overlapping-task Performance. *Q. J. Exp. Psychol. Sect. A* (1995). doi:10.1080/14640749508401372
241. Kiesel, A. & Dignath, D. Effort in multitasking: Local and global assessment of effort. *Front. Psychol.* **8**, 1–13 (2017).
242. Brass, M. & Von Cramon, D. Y. The role of the frontal cortex in task preparation. *Cereb. Cortex* **12**, 908–914 (2002).
243. Heekeren, H. R., Marrett, S., Ruff, D. A., Bandettini, P. A. & Ungerleider, L. G. Involvement of human left dorsolateral prefrontal cortex in perceptual decision making is independent of response modality. *Proc. Natl. Acad. Sci.* (2006). doi:10.1073/pnas.0603949103
244. Jiang, Y. & Kanwisher, N. Common Neural Mechanisms for Response Selection and Perceptual Processing. *J. Cogn. Neurosci.* (2003). doi:10.1162/089892903322598076
245. Rushworth, M. F. S. Attentional Selection and Action Selection in the Ventral and Orbital Prefrontal Cortex. *J. Neurosci.* (2005). doi:10.1523/jneurosci.2765-05.2005
246. Miller, E. K. & Cohen, J. D. An Integrative Theory of Prefrontal Cortex Function. *Annu. Rev. Neurosci.* (2001). doi:10.1146/annurev.neuro.24.1.167
247. Szameitat, A. J., Vanloo, A. & Müller, H. J. Central as well as Peripheral Attentional Bottlenecks in Dual-Task Performance Activate Lateral Prefrontal Cortices. *Front. Hum.*

- Neurosci.* **10**, 1–14 (2016).
248. Szameitat, A. J., Schubert, T., Müller, K. & Von Yves Cramon, D. Localization of executive functions in dual-task performance with fMRI. *J. Cogn. Neurosci.* (2002). doi:10.1162/089892902760807195
 249. Stelzel, C., Brandt, S. A. & Schubert, T. Neural mechanisms of concurrent stimulus processing in dual tasks. *Neuroimage* **48**, 237–248 (2009).
 250. Bush, G., Luu, P. & Posner, M. I. Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences* (2000). doi:10.1016/S1364-6613(00)01483-2
 251. Zhang, R. T. *et al.* Structural neural correlates of multitasking: A voxel-based morphometry study. *PsyCh J.* **5**, 219–227 (2016).
 252. Alavash, M., Hilgetag, C. C., Thiel, C. M. & Gießing, C. Persistency and flexibility of complex brain networks underlie dual-task interference. *Hum. Brain Mapp.* **36**, 3542–3562 (2015).
 253. Alavash, M., Thiel, C. M. & Gießing, C. Dynamic coupling of complex brain networks and dual-task behavior. *Neuroimage* (2016). doi:10.1016/j.neuroimage.2016.01.028
 254. Marois, R. & Ivanoff, J. Capacity limits of information processing in the brain. *Trends Cogn. Sci.* **9**, 296–305 (2005).
 255. Wang, Z. *et al.* Changes in the brain intrinsic organization in both on-task state and post-task resting state. *Neuroimage* (2012). doi:10.1016/j.neuroimage.2012.04.051
 256. Bola, M. & Sabel, B. A. Dynamic reorganization of brain functional networks during cognition. *Neuroimage* (2015). doi:10.1016/j.neuroimage.2015.03.057
 257. Zalesky, A., Fornito, A., Cocchi, L., Gollo, L. L. & Breakspear, M. Time-resolved resting-state brain networks. *Proc. Natl. Acad. Sci.* (2014). doi:10.1073/pnas.1400181111
 258. Ulrich, R. *et al.* Motor limitation in dual-task processing under ballistic movement conditions. *Psychol. Sci.* (2006). doi:10.1111/j.1467-9280.2006.01783.x
 259. Hazeltine, E., Ruthruff, E. & Remington, R. W. The role of input and output modality pairings in dual-task performance: Evidence for content-dependent central interference. *Cogn. Psychol.* (2006). doi:10.1016/j.cogpsych.2005.11.001
 260. Göthe, K., Oberauer, K. & Kliegl, R. Eliminating dual-task costs by minimizing crosstalk between tasks: The role of modality and feature pairings. *Cognition* **150**, 92–108 (2016).
 261. Lang, P. J., Bradley, M. M. & Cuthbert, B. N. Motivated attention: Affect, activation, and action. in *Attention and Orienting: Sensory and Motivational Processes* (1997).
 262. Li, F. F., VanRullen, R., Koch, C. & Perona, P. Rapid natural scene categorization in the near absence of attention. *Proc. Natl. Acad. Sci. U. S. A.* (2002). doi:10.1073/pnas.092277599
 263. Salo, E., Salmela, V., Salmi, J., Numminen, J. & Alho, K. Brain activity associated with selective attention, divided attention and distraction. *Brain Res.* **1664**, 25–36 (2017).
 264. Frank, D. W. & Sabatinelli, D. Primate visual perception: Motivated attention in naturalistic scenes. *Frontiers in Psychology* (2017). doi:10.3389/fpsyg.2017.00226
 265. Salmi, J., Rinne, T., Koistinen, S., Salonen, O. & Alho, K. Brain networks of bottom-up triggered and top-down controlled shifting of auditory attention. *Brain Res.* (2009). doi:10.1016/j.brainres.2009.06.083

266. Alho, K., Salmi, J., Koistinen, S., Salonen, O. & Rinne, T. Top-down controlled and bottom-up triggered orienting of auditory attention to pitch activate overlapping brain networks. *Brain Res.* (2015). doi:10.1016/j.brainres.2014.12.050
267. Posner, M. I. Orienting of attention. *Q. J. Exp. Psychol.* (1980). doi:10.1080/00335558008248231
268. Theeuwes, J. Perceptual selectivity for color and form. *Percept. Psychophys.* (1992). doi:10.3758/BF03211656
269. Theeuwes, J. Top-down and bottom-up control of visual selection. *Acta Psychol. (Amst)*. (2010). doi:10.1016/j.actpsy.2010.02.006
270. Yantis, S. & Jonides, J. Abrupt visual onsets and selective attention: evidence from visual search. *J. Exp. Psychol. Hum. Percept. Perform.* (1984). doi:10.1037//0096-1523.10.5.601
271. Lamy, D. & Zoraris, L. Task-irrelevant stimulus salience affects visual search. *Vision Res.* **49**, 1472–1480 (2009).
272. Folk, C. L., Remington, R. W. & Johnston, J. C. Involuntary Covert Orienting Is Contingent on Attentional Control Settings. *J. Exp. Psychol. Hum. Percept. Perform.* (1992). doi:10.1037/0096-1523.18.4.1030
273. Folk, C. L. & Remington, R. Selectivity in Distraction by Irrelevant Featural Singletons: Evidence for Two Forms of Attentional Capture. *J. Exp. Psychol. Hum. Percept. Perform.* (1998). doi:10.1037/0096-1523.24.3.847
274. Bacon, W. F. & Egeth, H. E. Overriding stimulus-driven attentional capture. *Percept. Psychophys.* (1994). doi:10.3758/BF03205306
275. Theeuwes, J. Cross-dimensional perceptual selectivity. *Percept. Psychophys.* (1991). doi:10.3758/BF03212219
276. Yantis, S. & Jonides, J. Abrupt Visual Onsets and Selective Attention: Voluntary Versus Automatic Allocation. *J. Exp. Psychol. Hum. Percept. Perform.* (1990). doi:10.1037/0096-1523.16.1.121
277. Corradi-Dell'Acqua, C., Fink, G. R. & Weidner, R. Selecting category specific visual information: Top-down and bottom-up control of object based attention. *Conscious. Cogn.* **35**, 330–341 (2015).
278. Tang, H. *et al.* Cascade of neural processing orchestrates cognitive control in human frontal cortex. *Elife* **5**, 1–18 (2016).
279. Ossandón, T. *et al.* Efficient 'Pop-Out' Visual Search Elicits Sustained Broadband Gamma Activity in the Dorsal Attention Network. *J. Neurosci.* **32**, 3414–3421 (2012).
280. Fukuda, K. & Vogel, E. K. Individual differences in recovery time from attentional capture. *Psychol. Sci.* (2011). doi:10.1177/0956797611398493
281. Kiss, M., Grubert, A., Petersen, A. & Eimer, M. Attentional capture by salient distractors during visual search is determined by temporal task demands. *J. Cogn. Neurosci.* (2012). doi:10.1162/jocn_a_00127
282. Gaspelin, N. & Luck, S. J. Distinguishing among potential mechanisms of singleton suppression. *J. Exp. Psychol. Hum. Percept. Perform.* (2018). doi:10.1037/xhp0000484
283. Burra, N. & Kerzel, D. The distractor positivity (Pd) signals lowering of attentional priority:

- Evidence from event-related potentials and individual differences. *Psychophysiology* (2014). doi:10.1111/psyp.12215
284. Gaspelin, N., Leonard, C. J. & Luck, S. J. Suppression of overt attentional capture by salient-but-irrelevant color singletons. *Attention, Perception, Psychophys.* (2017). doi:10.3758/s13414-016-1209-1
 285. Vatterott, D. B. & Vecera, S. P. Experience-dependent attentional tuning of distractor rejection. *Psychon. Bull. Rev.* (2012). doi:10.3758/s13423-012-0280-4
 286. Folk, C. L., Leber, A. B. & Egeth, H. E. Made you blink! Contingent attentional capture produces a spatial blink. *Percept. Psychophys.* (2002). doi:10.3758/BF03194741
 287. Lamy, D., Leber, A. & Egeth, H. E. Effects of task relevance and stimulus-driven salience in feature-search mode. *J. Exp. Psychol. Hum. Percept. Perform.* (2004). doi:10.1037/0096-1523.30.6.1019
 288. Rouder, J. N. *et al.* An assessment of fixed-capacity models of visual working memory. *Proc. Natl. Acad. Sci.* (2008). doi:10.1073/pnas.0711295105
 289. Engle, R. W., Laughlin, J. E., Tuholski, S. W. & Conway, A. R. A. Working memory, short-term memory, and general fluid intelligence: A latent-variable approach. *J. Exp. Psychol. Gen.* (1999). doi:10.1037/0096-3445.128.3.309
 290. Shipstead, Z., Harrison, T. L. & Engle, R. W. Working Memory Capacity and Fluid Intelligence: Maintenance and Disengagement. *Perspect. Psychol. Sci.* (2016). doi:10.1177/1745691616650647
 291. Schwarb, H., Nail, J. & Schumacher, E. H. Working memory training improves visual short-term memory capacity. *Psychol. Res.* (2016). doi:10.1007/s00426-015-0648-y
 292. Vogel, E. K., McCollough, A. W. & Machizawa, M. G. Neural measures reveal individual differences in controlling access to working memory. *Nature* (2005). doi:10.1038/nature04171
 293. Fukuda, K. & Vogel, E. K. Human Variation in Overriding Attentional Capture. *J. Neurosci.* (2009). doi:10.1523/jneurosci.2145-09.2009
 294. Theeuwes, J., Atchley, P. & Kramer, A. F. On the time course of top-down and bottom-up control of visual attention. *Atten. Perform.* (2000).
 295. Tatum, W., Husain, A. M., Benbadis, S. & Kaplan, P. *Handbook of EEG Interpretation.* (Demos Medical, 2014).
 296. Enatsu, R. & Mikuni, N. Invasive evaluations for epilepsy surgery: A review of the literature. *Neurologia Medico-Chirurgica* (2016). doi:10.2176/nmc.ra.2015-0319
 297. Lachaux, J. P., Rudrauf, D. & Kahane, P. Intracranial EEG and human brain mapping. in *Journal of Physiology Paris* (2003). doi:10.1016/j.jphysparis.2004.01.018
 298. Miller, K. J., Sorensen, L. B., Ojemann, J. G. & Den Nijs, M. Power-law scaling in the brain surface electric potential. *PLoS Comput. Biol.* (2009). doi:10.1371/journal.pcbi.1000609
 299. Ball, T., Kern, M., Mutschler, I., Aertsen, A. & Schulze-Bonhage, A. Signal quality of simultaneously recorded invasive and non-invasive EEG. *Neuroimage* (2009). doi:10.1016/j.neuroimage.2009.02.028
 300. Parvizi, J. & Kastner, S. Promises and limitations of human intracranial

- electroencephalography. *Nature Neuroscience* (2018). doi:10.1038/s41593-018-0108-2
301. Kucewicz, M. T. *et al.* High frequency oscillations are associated with cognitive processing in human recognition memory. *Brain* (2014). doi:10.1093/brain/awu149
302. Crone, N. E., Sinai, A. & Korzeniewska, A. High-frequency gamma oscillations and human brain mapping with electrocorticography. *Prog. Brain Res.* **159**, 275–295 (2006).
303. Jerbi, K. *et al.* Task-related gamma-band dynamics from an intracerebral perspective: Review and implications for surface EEG and MEG. *Hum. Brain Mapp.* **30**, 1758–1771 (2009).
304. Zumsteg, D. & Wieser, H. G. Presurgical Evaluation: Current Role of Invasive EEG. *Epilepsia* (2000). doi:10.1111/j.1528-1157.2000.tb01535.x
305. Enatsu, R. *et al.* Combining stereo-electroencephalography and subdural electrodes in the diagnosis and treatment of medically intractable epilepsy. *J. Clin. Neurosci.* (2014). doi:10.1016/j.jocn.2013.12.014
306. Shah, A. & Mittal, S. Invasive electroencephalography monitoring: Indications and presurgical planning. *Ann. Indian Acad. Neurol.* **17**, 89 (2014).
307. Gonzalez-Martinez, J. *et al.* Stereoelectroencephalography in children and adolescents with difficult-to-localize refractory focal epilepsy. *Neurosurgery* (2014). doi:10.1227/NEU.0000000000000453
308. Rosenow, F. & Lüders, H. Presurgical evaluation of epilepsy. *Brain* **124**, 1683–1700 (2001).
309. Bancaud, J. *et al.* Functional stereotaxic exploration (SEEG) of epilepsy. in *Electroencephalography and clinical neurophysiology* (1970).
310. Nair, D. R., Burgess, R., McIntyre, C. C. & Lüders, H. Chronic subdural electrodes in the management of epilepsy. *Clinical Neurophysiology* (2008). doi:10.1016/j.clinph.2007.09.117
311. Jin, B., So, N. K. & Wang, S. Advances of Intracranial Electroencephalography in Localizing the Epileptogenic Zone. *Neuroscience Bulletin* (2016). doi:10.1007/s12264-016-0035-8
312. Nir, Y. *et al.* Coupling between Neuronal Firing Rate, Gamma LFP, and BOLD fMRI Is Related to Interneuronal Correlations. *Curr. Biol.* (2007). doi:10.1016/j.cub.2007.06.066
313. Shah, A. K. & Mittal, S. Invasive electroencephalography monitoring: Indications and presurgical planning. *Ann. Indian Acad. Neurol.* (2014). doi:10.4103/0972-2327.128668
314. Howard, M. W. *et al.* Gamma Oscillations Correlate with Working Memory Load in Humans. *Cereb. Cortex* (2003). doi:10.1093/cercor/bhg084
315. Mainy, N. *et al.* Neural correlates of consolidation in working memory. *Hum. Brain Mapp.* (2007). doi:10.1002/hbm.20264
316. Axmacher, N., Schmitz, D. P., Wagner, T., Elger, C. E. & Fell, J. Interactions between medial temporal lobe, prefrontal cortex, and inferior temporal regions during visual working memory: A combined intracranial EEG and functional magnetic resonance imaging study. *J. Neurosci.* (2008). doi:10.1523/JNEUROSCI.1778-08.2008
317. Jensen, O. & Lisman, J. E. Hippocampal sequence-encoding driven by a cortical multi-item working memory buffer. *Trends Neurosci.* (2005). doi:10.1016/j.tins.2004.12.001
318. Tallon-Baudry, C., Bertrand, O., Hénaff, M. A., Isnard, J. & Fischer, C. Attention modulates gamma-band oscillations differently in the human lateral occipital cortex and fusiform gyrus. *Cereb. Cortex* (2005). doi:10.1093/cercor/bhh167

319. Daitch, A. L. *et al.* Mapping human temporal and parietal neuronal population activity and functional coupling during mathematical cognition. *Proc. Natl. Acad. Sci. U. S. A.* (2016). doi:10.1073/pnas.1608434113
320. Tang, H. *et al.* Spatiotemporal Dynamics Underlying Object Completion in Human Ventral Visual Cortex. *Neuron* (2014). doi:10.1016/j.neuron.2014.06.017
321. Lachaux, J. P., Hoffmann, D., Minotti, L., Berthoz, A. & Kahane, P. Intracerebral dynamics of saccade generation in the human frontal eye field and supplementary eye field. *Neuroimage* (2006). doi:10.1016/j.neuroimage.2005.11.023
322. Jung, J. *et al.* The neural bases of attentive reading. *Hum. Brain Mapp.* (2008). doi:10.1002/hbm.20454
323. Lachaux, J. P. *et al.* A Blueprint for Real-Time Functional Mapping via Human Intracranial Recordings. *PLoS One* (2007). doi:10.1371/journal.pone.0001094
324. Zaki, J. & Ochsner, K. The need for a cognitive neuroscience of naturalistic social cognition. in *Annals of the New York Academy of Sciences* (2009). doi:10.1111/j.1749-6632.2009.04601.x
325. Tikka, P. & Kaipainen, M. Y. From naturalistic neuroscience to modeling radical embodiment with narrative enactive systems. *Front. Hum. Neurosci.* (2014). doi:10.3389/fnhum.2014.00794
326. Schmuckler, M. A. What is Ecological Validity? A Dimensional Analysis. *Infancy* (2001). doi:10.1207/S15327078IN0204_02
327. Schultz, J. & Pilz, K. S. Natural facial motion enhances cortical responses to faces. *Exp. Brain Res.* (2009). doi:10.1007/s00221-009-1721-9
328. Sonkusare, S., Breakspear, M. & Guo, C. Naturalistic Stimuli in Neuroscience: Critically Acclaimed. *Trends in Cognitive Sciences* (2019). doi:10.1016/j.tics.2019.05.004
329. Schilbach, L. *et al.* Toward a second-person neuroscience. *Behav. Brain Sci.* (2013). doi:10.1017/S0140525X12000660
330. Redcay, E. & Schilbach, L. Using second-person neuroscience to elucidate the mechanisms of social interaction. *Nat. Rev. Neurosci.* (2019). doi:10.1038/s41583-019-0179-4
331. van Moorselaar, D., Theeuwes, J. & Olivers, C. N. L. In competition for the attentional template: Can multiple items within visual working memory guide attention? *J. Exp. Psychol. Hum. Percept. Perform.* (2014). doi:10.1037/a0036229
332. Rice, K. & Redcay, E. Interaction matters: A perceived social partner alters the neural processing of human speech. *Neuroimage* (2016). doi:10.1016/j.neuroimage.2015.11.041
333. Kuhlen, A. K., Bogler, C., Brennan, S. E. & Haynes, J. D. Brains in dialogue: Decoding neural preparation of speaking to a conversational partner. *Soc. Cogn. Affect. Neurosci.* (2017). doi:10.1093/scan/nsx018
334. Redcay, E. *et al.* Live face-to-face interaction during fMRI: A new tool for social cognitive neuroscience. *Neuroimage* (2010). doi:10.1016/j.neuroimage.2010.01.052
335. Wykowska, A., Wiese, E., Prosser, A. & Müller, H. J. Beliefs about the minds of others influence how we process sensory information. *PLoS One* (2014). doi:10.1371/journal.pone.0094339
336. Cavallo, A. *et al.* When gaze opens the channel for communication: Integrative role of IFG and

- MPFC. *Neuroimage* (2015). doi:10.1016/j.neuroimage.2015.06.025
337. Coan, J. A., Schaefer, H. S. & Davidson, R. J. Lending a hand: Social regulation of the neural response to threat. *Psychol. Sci.* (2006). doi:10.1111/j.1467-9280.2006.01832.x
338. Kokal, I., Gazzola, V. & Keysers, C. Acting together in and beyond the mirror neuron system. *Neuroimage* (2009). doi:10.1016/j.neuroimage.2009.06.010
339. Munn, B. & Gong, P. Critical Dynamics of Natural Time-Varying Images. *Phys. Rev. Lett.* (2018). doi:10.1103/PhysRevLett.121.058101
340. Friston, K., Breakspear, M. & Deco, G. Perception and self-organized instability. *Front. Comput. Neurosci.* (2012). doi:10.3389/fncom.2012.00044
341. Tkačik, G. *et al.* Thermodynamics and signatures of criticality in a network of neurons. *Proc. Natl. Acad. Sci. U. S. A.* (2015). doi:10.1073/pnas.1514188112
342. Pashler, H. & Johnston, J. C. Chronometric Evidence for Central Postponement in Temporally Overlapping Tasks. *Q. J. Exp. Psychol. Sect. A* (1989). doi:10.1080/14640748908402351
343. Sigman, M. & Dehaene, S. Parsing a cognitive task: A characterization of the mind's bottleneck. *PLoS Biol.* **3**, 0334–0349 (2005).
344. Han, S. W. & Marois, R. The source of dual-task limitations: Serial or parallel processing of multiple response selections? *Attention, Perception, Psychophys.* **75**, 1395–1405 (2013).
345. Levy, J., Pashler, H. & Boer, E. Central interference in driving: Is there any stopping the psychological refractory period? *Psychol. Sci.* (2006). doi:10.1111/j.1467-9280.2006.01690.x
346. Lachaux, J.-P. SMS, TÉLÉPHONE, GPS: Fatales Distractions... *Cerveau & Psycho* 64–66 (2018).
347. Land, M. & Tatler, B. *Looking and Acting: Vision and Eye Movements in Natural Behaviour.* (2012). doi:10.1093/acprof:oso/9780198570943.001.0001
348. Borkowski, J. G., Benton, A. L. & Spreen, O. Word fluency and brain damage. *Neuropsychologia* (1967). doi:10.1016/0028-3932(67)90015-2
349. Woods, D. L., Wyma, J. M., Herron, T. J. & Yund, E. W. Computerized analysis of verbal fluency: Normative data and the effects of repeated testing, simulated malingering, and traumatic brain injury. *PLoS One* **11**, 1–37 (2016).
350. Kahane, P., Minotti, L., Hoffmann, D., Lachaux, J. P. & Ryvlin, P. Invasive EEG in the definition of the seizure onset zone: depth electrodes. *Handbook of Clinical Neurophysiology* (2003). doi:10.1016/S1567-4231(03)03009-0
351. Andreou, G. & Trott, K. Verbal fluency in adults diagnosed with attention-deficit hyperactivity disorder (ADHD) in childhood. *ADHD Atten. Deficit Hyperact. Disord.* (2013). doi:10.1007/s12402-013-0112-z
352. Sumiyoshi, C. *et al.* Semantic structure in schizophrenia as assessed by the category fluency test: Effect of verbal intelligence and age of onset. *Psychiatry Res.* (2001). doi:10.1016/S0165-1781(01)00345-6
353. Duff-Canning, S. J. D., Leach, L., Stuss, D., Ngo, L. & Black, S. E. Diagnostic utility of abbreviated fluency measures in Alzheimer disease and vascular dementia. *Neurology* (2004). doi:10.1212/WNL.62.4.556
354. Federmeier, K. D., McLennan, D. B., de Ochoa, E. & Kutas, M. The impact of semantic memory organization and sentence context information on spoken language processing by younger

- and older adults: An ERP study. *Psychophysiology* (2002). doi:10.1017/S0048577202001373
355. Federmeier, K. D., Kutas, M. & Schul, R. Age-related and individual differences in the use of prediction during language comprehension. *Brain Lang.* (2010). doi:10.1016/j.bandl.2010.07.006
 356. Fitzpatrick, S., Gilbert, S. & Serpell, L. Systematic review: Are overweight and obese individuals impaired on behavioural tasks of executive functioning? *Neuropsychology Review* (2013). doi:10.1007/s11065-013-9224-7
 357. Shao, Z., Janse, E., Visser, K. & Meyer, A. S. What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Front. Psychol.* **5**, 1–10 (2014).
 358. Weiss, E. M. *et al.* Brain activation pattern during a verbal fluency test in healthy male and female volunteers: A functional magnetic resonance imaging study. *Neurosci. Lett.* (2003). doi:10.1016/j.neulet.2003.08.071
 359. McGraw, P., Mathews, V. P., Wang, Y. & Phillips, M. D. Approach to functional magnetic resonance imaging of language based on models of language organization. *Neuroimaging Clinics of North America* (2001).
 360. Vidal, J. R. *et al.* Localizing cognitive functions in epilepsy with intracranial gamma-band dynamic responses. in *Neuropsychology in the Care of People with Epilepsy* (eds. Helmstaedter, C., Lassonde, M., Hermann, B., Kahane, P. & Arzimanoglou, A.) 323–334 (John Libbey Eurotext, 2011).
 361. Gelbard-Sagiv, H., Mukamel, R., Harel, M., Malach, R. & Fried, I. Internally generated reactivation of single neurons in human hippocampus during free recall. *Science* (80-.). (2008). doi:10.1126/science.1164685
 362. Hamamé, C. M. *et al.* Reading the mind's eye: Online detection of visuo-spatial working memory and visual imagery in the inferior temporal lobe. *Neuroimage* (2012). doi:10.1016/j.neuroimage.2011.07.087
 363. Arnulfo, G., Hirvonen, J., Nobili, L., Palva, S. & Palva, J. M. Phase and amplitude correlations in resting-state activity in human stereotactical EEG recordings. *Neuroimage* (2015). doi:10.1016/j.neuroimage.2015.02.031
 364. Tallon-Baudry, C., Bertrand, O., Delpuech, C. & Pernier, J. Oscillatory γ -band (30-70 Hz) activity induced by a visual search task in humans. *J. Neurosci.* (1997). doi:10.1523/jneurosci.17-02-00722.1997
 365. Aguera, P. E., Jerbi, K., Caclin, A. & Bertrand, O. ELAN: A software package for analysis and visualization of MEG, EEG, and LFP signals. *Comput. Intell. Neurosci.* (2011). doi:https://doi.org/10.1155/2011/158970
 366. Perrone-Bertolotti, M. *et al.* How silent is silent reading? Intracerebral evidence for top-down activation of temporal voice areas during reading. *J. Neurosci.* (2012). doi:10.1523/JNEUROSCI.2982-12.2012
 367. Le Van Quyen, M. *et al.* Comparison of Hilbert transform and wavelet methods for the analysis of neuronal synchrony. *J. Neurosci. Methods* (2001). doi:10.1016/S0165-0270(01)00372-7
 368. Dalal, S. S. *et al.* NUTMEG: A neuromagnetic source reconstruction toolbox. *Neurol. Clin. Neurophysiol.* **52**, (2004).
 369. Deman, P. *et al.* IntraAnat Electrodes: A Free Database and Visualization Software for

- Intracranial Electroencephalographic Data Processed for Case and Group Studies. *Front. Neuroinform.* (2018). doi:10.3389/fninf.2018.00040
370. Lachaux, J. P. *et al.* BrainTV: A novel approach for online mapping of human brain functions. in *Biological Research* (2007). doi:10.4067/S0716-97602007000500004
371. Lachaux, J. P., Axmacher, N., Mormann, F., Halgren, E. & Crone, N. E. High-frequency neural activity and human cognition: Past, present and possible future of intracranial EEG research. *Progress in Neurobiology* (2012). doi:10.1016/j.pneurobio.2012.06.008
372. Auzias, G., Coulon, O. & Brovelli, A. MarsAtlas: A cortical parcellation atlas for functional mapping. *Hum. Brain Mapp.* (2016). doi:10.1002/hbm.23121
373. Fischl, B. FreeSurfer. *NeuroImage* (2012). doi:10.1016/j.neuroimage.2012.01.021
374. Szameitat, A. J., Vanloo, A. & Müller, H. J. Central as well as Peripheral Attentional Bottlenecks in Dual-Task Performance Activate Lateral Prefrontal Cortices. *Front. Hum. Neurosci.* (2016). doi:10.3389/fnhum.2016.00119
375. Lee, A. T., Glover, G. H. & Meyer, C. H. Discrimination of Large Venous Vessels in Time-Course Spiral Blood-Oxygen-Level-Dependent Magnetic-Resonance Functional Neuroimaging. *Magn. Reson. Med.* (1995). doi:10.1002/mrm.1910330602
376. Yacoub, E. & Wald, L. L. Pushing the spatio-temporal limits of MRI and fMRI. *NeuroImage* (2018). doi:10.1016/j.neuroimage.2017.11.034
377. Lehle, C., Steinhauser, M. & Hübner, R. Serial or parallel processing in dual tasks: What is more effortful? *Psychophysiology* (2009). doi:10.1111/j.1469-8986.2009.00806.x
378. Ruthruff, E., Johnston, J. C. & Remington, R. W. How Strategic Is the Central Bottleneck: Can It Be Overcome by Trying Harder? *J. Exp. Psychol. Hum. Percept. Perform.* **35**, 1368–1384 (2009).
379. Dux, P. E. *et al.* Training Improves Multitasking Performance by Increasing the Speed of Information Processing in Human Prefrontal Cortex. *Neuron* (2009). doi:10.1016/j.neuron.2009.06.005
380. Duncan, J. An adaptive coding model of neural function in prefrontal cortex. *Nature Reviews Neuroscience* (2001). doi:10.1038/35097575
381. Klein, T. A. *et al.* Neural correlates of error awareness. *NeuroImage* (2007). doi:10.1016/j.neuroimage.2006.11.014
382. Klein, T. A., Ullsperger, M. & Danielmeier, C. Error awareness and the insula: links to neurological and psychiatric diseases. *Front. Hum. Neurosci.* **7**, 1–14 (2013).
383. Han, S. W., Eaton, H. P. & Marois, R. Functional Fractionation of the Cingulo-opercular Network: Alerting Insula and Updating Cingulate. *Cereb. Cortex* (2019). doi:10.1093/cercor/bhy130
384. Slagter, H. A. *et al.* Mental training affects distribution of limited brain resources. *PLoS Biol.* (2007). doi:10.1371/journal.pbio.0050138
385. Bruya, B. *Effortless attention: A new perspective in the cognitive science of attention and action.* (Bradford, 2010). doi:https://doi.org/10.7551/mitpress/9780262013840.001.0001
386. Mason, M. F. *et al.* Wandering minds: The default network and stimulus-independent thought. *Science* (80-.). (2007). doi:10.1126/science.1131295

387. Christoff, K., Gordon, A. M., Smallwood, J., Smith, R. & Schooler, J. W. Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proc. Natl. Acad. Sci. U. S. A.* (2009). doi:10.1073/pnas.0900234106
388. Veroude, K. *et al.* Anterior cingulate activation during cognitive control relates to academic performance in medical students. *Trends Neurosci. Educ.* (2013). doi:10.1016/j.tine.2013.10.001
389. Seeley, W. W. *et al.* Dissociable intrinsic connectivity networks for salience processing and executive control. *J. Neurosci.* (2007). doi:10.1523/JNEUROSCI.5587-06.2007
390. Chatard, B. *et al.* V2 suppression in an attentive reading task: Why SMS and street crossing don't go well together. *Cortex (submitted)* (2019).
391. Engström, M., Karlsson, T., Landtblom, A. M. & Bud Craig, A. D. Evidence of conjoint activation of the anterior insular and cingulate cortices during effortful tasks. *Front. Hum. Neurosci.* (2015). doi:10.3389/fnhum.2014.01071
392. Cai, W., Chen, T., Ide, J. S., Li, C. S. R. & Menon, V. Dissociable fronto-operculum-insula control signals for anticipation and detection of inhibitory sensory cues. *Cereb. Cortex* (2017). doi:10.1093/cercor/bhw219
393. Wu, T. *et al.* Anterior insular cortex is a bottleneck of cognitive control. *Neuroimage* (2019). doi:10.1016/j.neuroimage.2019.02.042
394. Sridharan, D., Levitin, D. J. & Menon, V. A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proc. Natl. Acad. Sci. U. S. A.* (2008). doi:10.1073/pnas.0800005105
395. Seth, A. K., Suzuki, K. & Critchley, H. D. An interoceptive predictive coding model of conscious presence. *Front. Psychol.* (2012). doi:10.3389/fpsyg.2011.00395
396. Menon, V. & Uddin, L. Q. Saliency, switching, attention and control: a network model of insula function. *Brain structure & function* (2010). doi:10.1007/s00429-010-0262-0
397. Cai, W. *et al.* Causal Interactions Within a Frontal-Cingulate-Parietal Network During Cognitive Control: Convergent Evidence from a Multisite-Multitask Investigation. *Cereb. Cortex* **26**, 2140–2153 (2016).
398. Weissman, D. H., Roberts, K. C., Visscher, K. M. & Woldorff, M. G. The neural bases of momentary lapses in attention. *Nat. Neurosci.* **9**, 971–978 (2006).
399. Buckner, R. L., Andrews-Hanna, J. R. & Schacter, D. L. The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences* (2008). doi:10.1196/annals.1440.011
400. Raichle, M. E. *et al.* A default mode of brain function. *Proc. Natl. Acad. Sci. U. S. A.* (2001). doi:10.1073/pnas.98.2.676
401. Greicius, M. D., Krasnow, B., Reiss, A. L. & Menon, V. Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proc. Natl. Acad. Sci. U. S. A.* (2003). doi:10.1073/pnas.0135058100
402. Hayden, B. Y., Smith, D. V. & Platt, M. L. Electrophysiological correlates of default-mode processing in macaque posterior cingulate cortex. *Proc. Natl. Acad. Sci. U. S. A.* (2009). doi:10.1073/pnas.0812035106
403. Ossandón, T. *et al.* Transient Suppression of Broadband Gamma Power in the Default-Mode

- Network Is Correlated with Task Complexity and Subject Performance. *J. Neurosci.* **31**, 14521–14530 (2011).
404. Leech, R. & Sharp, D. J. The role of the posterior cingulate cortex in cognition and disease. *Brain* **137**, 12–32 (2014).
 405. Brewer, J. A., Garrison, K. A. & Whitfield-Gabrieli, S. What about the ‘self’ is processed in the posterior cingulate cortex? *Front. Hum. Neurosci.* (2013). doi:10.3389/fnhum.2013.00647
 406. Smucny, J., Rojas, D. C., Eichman, L. C. & Tregellas, J. R. Neuronal effects of auditory distraction on visual attention. *Brain Cogn.* (2013). doi:10.1016/j.bandc.2012.11.008
 407. Duffy, C. & Wurtz, R. Response of monkey MST neurons to optic flow stimuli with shifted centers of motion. *J. Neurosci.* (1995). doi:10.1523/jneurosci.15-07-05192.1995
 408. Raffi, M., Persiani, M., Piras, A. & Squatrito, S. Optic flow neurons in area P_{EC} integrate eye and head position signals. *Neurosci. Lett.* (2014). doi:10.1016/j.neulet.2014.03.042
 409. Lu, H. D., Chen, G., Tanigawa, H. & Roe, A. W. A Motion Direction Map in Macaque V2. *Neuron* (2010). doi:10.1016/j.neuron.2010.11.020
 410. Brooks, K. R., Morris, T. & Thompson, P. Contrast and stimulus complexity moderate the relationship between spatial frequency and perceived speed: Implications for MT models of speed perception. *J. Vis.* (2011). doi:10.1167/11.14.19
 411. Galletti, C. & Fattori, P. The dorsal visual stream revisited: Stable circuits or dynamic pathways? *Cortex* **98**, 203–2017 (2018).
 412. Perry, C. J. & Fallah, M. Feature integration and object representations along the dorsal stream visual hierarchy. *Front. Comput. Neurosci.* (2014). doi:10.3389/fncom.2014.00084
 413. Lachaux, J. P. *et al.* The many faces of the gamma band response to complex visual stimuli. *Neuroimage* (2005). doi:10.1016/j.neuroimage.2004.11.052
 414. Rauschecker, J. P. & Scott, S. K. Maps and streams in the auditory cortex: Nonhuman primates illuminate human speech processing. *Nature Neuroscience* (2009). doi:10.1038/nn.2331
 415. Sandak, R., Mencl, W. E., Frost, S. J. & Pugh, K. R. The neurobiological basis of skilled and impaired reading: Recent findings and new directions. *Sci. Stud. Read.* (2004). doi:10.1207/s1532799xssr0803_6
 416. Sinai, A. *et al.* Electrocorticographic high gamma activity versus electrical cortical stimulation mapping of naming. *Brain* (2005). doi:10.1093/brain/awh491
 417. Vidal, J. R. *et al.* Long-distance amplitude correlations in the high gamma band reveal segregation and integration within the reading network. *J. Neurosci.* (2012). doi:10.1523/JNEUROSCI.4363-11.2012
 418. Mashal, N., Faust, M., Hendler, T. & Jung-Beeman, M. An fMRI study of processing novel metaphoric sentences. *Laterality* (2009). doi:10.1080/13576500802049433
 419. Price, C. J. The anatomy of language: A review of 100 fMRI studies published in 2009. *Annals of the New York Academy of Sciences* (2010). doi:10.1111/j.1749-6632.2010.05444.x
 420. Craig, A. D. How do you feel - now? The anterior insula and human awareness. *Nature Reviews Neuroscience* (2009). doi:10.1038/nrn2555
 421. Botvinick, M. M. Conflict monitoring and decision making: Reconciling two perspectives on

- anterior cingulate function. *Cognitive, Affective and Behavioral Neuroscience* (2007). doi:10.3758/CABN.7.4.356
422. Mansouri, F. A., Buckley, M. J. & Tanaka, K. Mnemonic function of the dorsolateral prefrontal cortex in conflict-induced behavioral adjustment. *Science* (80-.). (2007). doi:10.1126/science.1146384
423. Boschini, E. A., Brkic, M. M., Simons, J. S. & Buckley, M. J. Distinct Roles for the Anterior Cingulate and Dorsolateral Prefrontal Cortices During Conflict Between Abstract Rules. *Cereb. Cortex* **27**, 34–45 (2017).
424. Dehaene, S. & Cohen, L. The unique role of the visual word form area in reading. *Trends in Cognitive Sciences* (2011). doi:10.1016/j.tics.2011.04.003
425. Cai, W., Ryali, S., Chen, T., Li, C. S. R. & Menon, V. Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: Evidence from intrinsic and task-related functional parcellation, Connectivity, And response profile analyses across multiple datasets. *J. Neurosci.* (2014). doi:10.1523/JNEUROSCI.3048-14.2014
426. Gusnard, D. A., Akbudak, E., Shulman, G. L. & Raichle, M. E. Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proc. Natl. Acad. Sci. U. S. A.* (2001). doi:10.1073/pnas.071043098
427. Gusnard, D. A. & Raichle, M. E. Searching for a baseline: functional imaging and the resting human brain. *Nat. Rev. Neurosci.* **2**, 685–694 (2001).
428. Hahn, B., Ross, T. J. & Stein, E. A. Cingulate activation increases dynamically with response speed under stimulus unpredictability. *Cereb. Cortex* (2007). doi:10.1093/cercor/bhl075
429. Leech, R., Kamourieh, S., Beckmann, C. F. & Sharp, D. J. Fractionating the default mode network: Distinct contributions of the ventral and dorsal posterior cingulate cortex to cognitive control. *J. Neurosci.* (2011). doi:10.1523/JNEUROSCI.5626-10.2011
430. Arsenault, J. T., Nelissen, K., Jarraya, B. & Vanduffel, W. Dopaminergic Reward Signals Selectively Decrease fMRI Activity in Primate Visual Cortex. *Neuron* (2013). doi:10.1016/j.neuron.2013.01.008
431. Craig, A. D. The sentient self. *Brain structure & function* (2010). doi:10.1007/s00429-010-0248-y

Part VII

ANNEXES

Annex N°1 – BLAST: A short computerized test to measure the ability to stay on task

14

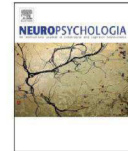
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BLAST: A short computerized test to measure the ability to stay on task. Normative behavioral data and detailed cortical dynamics.



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ABSTRACT

This article provides an exhaustive description of a new short computerized test to assess on a second-to-second basis the ability of individuals to « stay on task », that is, to apply selectively and repeatedly task-relevant cognitive processes. The task (Bron/Lyon Attention Stability Test, or BLAST) lasts around 1 min, and measures repeatedly the time to find a target letter in a two-by-two letter array, with an update of all letters every new trial across thirty trials. Several innovative psychometric measures of attention stability are proposed based on the instantaneous fluctuations of reaction times throughout the task, and normative data stratified over a wide range of age are provided by a large (> 6000) dataset of participants aged 8 to 70. We also detail the large-scale brain dynamics supporting the task from an in-depth study of 32 participants with direct electrophysiological cortical recordings (intracranial EEG) to prove that BLAST involves critically large-scale executive attention networks, with a marked activation of the dorsal attention network and a deactivation of the default-mode network. Accordingly, we show that BLAST performance correlates with scores established by ADHD-questionnaires.

1. Introduction

The ability to maintain focused attention on a task until its full completion is crucial in many aspects of life, and has become a major topic of interest in several fields including education and professional sport (Kolb et al., 2011; Mangine et al., 2014; Caron, 2015; Diamond and Ling, 2016; Romeas et al., 2016). In most practical situations, however, performance is impaired by Momentary Lapses of Attention or MLA (Weissman et al., 2006), which can last a few seconds or less (Peiris et al., 2006) during which cognitive resources are side-tracked towards processes unrelated to the instructed task (Smallwood and Schooler, 2006). MLA are pervasive in our daily life (Robertson et al., 1997; Killingsworth and Gilbert, 2010) and can have mildly negative to catastrophic effects from missing a crucial word in a complex explanation to hitting a bike rider while driving. MLA can be conceptually interpreted as a disruption of executive attention, as defined by Posner (“the volitional and controlled aspect of the attentional system”) (Rosario Rueda et al., 2005). It implies a goal-driven constraint on both

the sensory input selection and the response selection process, following rules stored in the task-set (Sakai, 2008).

The behavioral characteristics and neuronal substrates of MLA remain to be established. More research has been done regarding a related phenomenon - Mind-Wandering (MW) - with clear evidence that the Default-Mode Network (Raichle et al., 2001) is critically involved (Mason et al., 2007; Christoff et al., 2009; Stawarczyk et al., 2011; Esterman et al., 2013; Poerio et al., 2017). MLA can be arbitrarily short, be caused by external events and mostly reveal themselves through behavior via isolated errors and/or a transient slowing down of reaction time (Weissman et al., 2006). In contrast, MW is still often defined as a more sustained and internally-triggered phenomenon, during which participants are “zoning out”, transiently forget the task and engage into sustained mental simulations (task-unrelated thoughts that they can report on when asked by thought-probes). However, it should be acknowledged that the difference between MLA and MW is becoming increasingly subtle, as some authors propose that any deviation from the task at hand (during which attention “wanders”) could be called

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“Mind-Wandering” (McVay and Kane, 2010). Yet, most tasks used to study sustained MW episodes are not well-suited to study MLA: in popular designs such as the continuous performance test (CPT) or the Sustained Attention to Response Task (SART) (Bender et al., 2015; Phillips et al., 2015), participants are driven to automatize a specific behavioral response to frequent stimuli, while infrequent stimuli require a different response and failure to withhold the automated behavior in response to rare stimuli are indicative of MW. Such designs are well-adapted to study long and slow drifts away from the task - and their fMRI signature - but short MLA that would occur during frequent stimuli would remain unnoticed, since processing of such stimuli relies on systematic stimulus-response contingency that is largely automated and less vulnerable to executive failure.

We propose a new task specifically designed to detect MLA, and assess the ability to resist them and « stay on task », on a second-to-second basis: BLAST (Bron Lyon Attention Stability Task) measures the ability to activate selectively the right set of cognitive processes to continuously perform a short task with optimal performance, during one or 2 min, that is the duration of many task-units which require continuous and undivided attention (listening to a complex explanation, reading one or two pages of a book or playing a point in tennis). Such task-units are ubiquitous in daily life, and most longer tasks can be broken down into consecutive units of such duration, with little breaks in between. BLAST reveals fluctuations of attention within such units, with a temporal resolution on the order of 1 s; in that sense, it markedly differs from classic neuropsychology pen-and-pencil papers assessing attention only globally over the whole test. This is especially important as the variability of reaction times is increasingly used as a measure of attention instability for the diagnosis of attention deficit hyperactivity disorder (ADHD) (Tamm et al., 2012; Gmehl et al., 2016).

The paper combines three studies in one: a) an in-depth analysis of behavioral data in a large population of children and teenagers (> 800) which reveals the main factors impacting attention stability (age, sex, ADHD-scores), b) normative behavioral data stratified by age from a larger (> 6000) population aged 8 to 70 and c) a detailed analysis of the large-scale and highly dynamic cortical network supporting BLAST, from the most precise neural recordings available in humans (intracranial EEG).

2. Participants and materials

2.1. Behavioral study

Behavioral data were collected in schools (SCHOOL database) from 859 participants (446 females, 103 left-handers), aged 8 to 18, all free of psychiatric/neurological disorders and with an appropriate behavior during the test (silent, showing no obvious lack of motivation). Participants performed the task on iPads wearing headphones and facing a wall with no view of each other, in groups of one to four, in a large classroom. Sessions lasted 1 h to include BLAST, plus several variants of the main task (see tasks description). The study was approved by a national ethical committee (IRB00003888 - FWA00005831).

In addition, a larger normative sample was collected within a science exhibit (« expo cerveau » - cité des sciences de la Villette, Paris) where BLAST was proposed as an interactive test to evaluate the visitors' ability to resist endogenous distractions. The test comprised a series of 30 trials, after a learning stage of 15 trials. Immediately after task completion, visitors indicated their age, gender and whether they had been distracted by external events. The MUSEUM database consists of 6954 participants under 70 (4049 females) reporting no external distractions (74% of 9446 visitors).

2.2. Electrophysiological study

Intracranial EEG recordings (iEEG) were obtained from 32 patients

(19 women, mean age: 28.7, Std: 8.6) candidate for epilepsy surgery. Two patients were not able to perform the task and were excluded from the analysis. Participants were stereotactically implanted with multi-lead EEG depth electrodes following the classic clinical procedures of the neurological hospitals in Grenoble and Lyon. They had previously written informed consent to participate in the study and experiment have been approved by the local ethical Committee of Grenoble Sud-Est V (Study 0907 - ISD et SEEG, CPP 09-CHUG-12).

Five to seventeen semi-rigid electrodes were stereotactically implanted in each participant. Each electrode was a linear array with a diameter of 0.8 mm, and included between 5 and 18 contact leads along its shaft (2 mm wide, with a 3.5 mm center-to-center spacing between consecutive leads) (DIXI Medical, Besançon, France). The precise anatomical location of each lead was measured from patient's individual pre-implant MRI, co-registered with post-implant MRI using an in-house BrainVisa plugin (IntrAnat), that enables the trajectory reconstruction of precise models of the SEEG electrodes onto post-implant MRI (see BrainVisa, brainvisa.info).

Intracranial EEG (iEEG) was recorded with standard 128-channels and 256-channels iEEG acquisition system (Micromed, Treviso, Italy), with a reference in the white matter. Data were bandpass-filtered online [0.1–200 Hz] and sampled at a minimal frequency of 512 Hz, then re-referenced offline by subtracting for each site the signal recorded 3.5 mm away on the same linear electrode (the nearest neighbor: bipolar montage).

Signals were visually inspected with an in-house, freely downloadable software package for electrophysiological analysis (ELAN-pack) (Aguera et al., 2011) to reject leads and trials with epileptiform activity, including all sites considered by clinicians to be in the epileptogenic zone (leading to the rejection of an average of 10% of the recording sites in individual patients). High-Frequency Activity [50–150 Hz], or “high-gamma activity”, was extracted with in-house scripts in Matlab (the Mathworks, inc) following our usual procedure (Ossandón et al., 2012). That procedure can be summarized as follows: bipolar iEEG signals are first bandpass-filtered in ten consecutive 10-Hz-wide frequency bands (50–60 Hz, 60–70 Hz, ..., 140–150 Hz). Each of those ten bandpass-filtered signal is then transformed into its envelope using a standard Hilbert transform and each envelope is then expressed in % of its mean value (as calculated across the entire experiment). In other words, each envelope time series is simply divided by its mean across the entire recording session and multiplied by 100. In the last step, the ten normalized envelope signals (in %) are averaged together (across the ten frequency bands) to provide one single time-series: the High-Frequency Activity [50–150 Hz], or HFA. Significant stimulus-induced HFA variations are detected statistically by comparing HFA for each time sample [between 0 and 3000 ms relative to the first stimulus of a trial] with the mean HFA during a [-200 ms: 0 ms] prestimulus baseline (Wilcoxon signed rank test followed by a False-Discovery Rate correction across all time bins and electrodes with $p = 0.05$, following our classic procedure, Genovesi et al., 2002). HFA measured in specific windows following the initial stimulus (e.g. [100 ms: 200 ms post stimulus onset]) is compared across experimental conditions using nonparametric Kruskal-Wallis tests (FDR correction with $p = 0.05$).

Dynamic, group-level visualizations of task-induced HFA variations onto the standard Montreal Neurological Institute (MNI) single-subject brain were performed with HiBoP (Human Intracranial Brain Observations Player), a new iEEG visualization software developed in our laboratory within the Human Brain Project, which will be released freely in the coming year.

2.3. Tasks description

2.3.1. BLAST

BLAST repeatedly asks participants to find a target letter (the Target) in a subsequent two-by-two array of four letters (the Array),

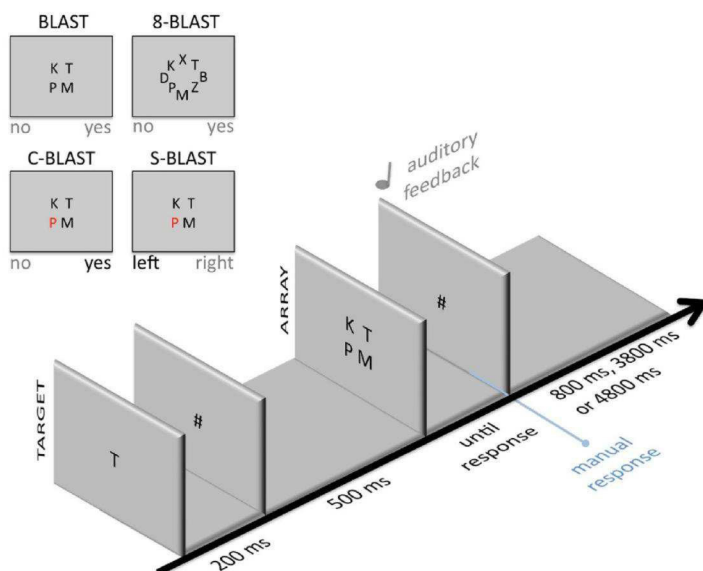


Fig. 1. General design of BLAST and its variants. The lower panel shows the general structure of a trial with the sequential display of the Target and the Array, and new letters every trial. The duration of the inter-trial mask depends on the participant's response (800 ms when the response was correct, 4800 ms if it was incorrect, and 3800 ms when the participant did not respond). The upper panel shows the specificities of the three main variants of BLAST in the case of a left-handed participant: the only difference with BLAST is the Array screen, with eight letters in 8-BLAST instead of four, four letters in C-BLAST with a salient color for the target when it is present, and four letters in S-BLAST with a red letter every time, indicating which side of the screen must be touched (the same as the red letter). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

with new letters every trial (Target and Array) (Fig. 1). Each trial starts with the presentation of the Target for 200 ms, followed by a mask (#) replaced after 500 ms by the Array (which stays on screen until the manual response). The next trial starts after a pause of 800 ms if the previous response was correct (with a central fixation symbol #), 4800 ms if it was incorrect (which corresponds to a time penalty of 4000 ms) and 3800 ms if the participant did not respond. The penalty system encourages participants to respond only if they are sure of their choice. Experiments were run on a tactile tablet for the SCHOOL and MUSEUM populations: participants were instructed to hold both hands slightly above the screen, on each side of the letter display, and give a gentle touch with their dominant hand (resp. non-dominant hand) when the target was absent (resp. present). During iEEG recordings, patients performed BLAST on a PC synchronized with the EEG acquisition system (The experiment was performed using Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA); they pressed gamepad buttons with their left or right index finger (using the same “dominant/non-dominant hand”- “no/yes” mapping as participants of the SCHOOL and MUSEUM populations). Letters were presented foveally in black on a light gray background. Motor responses were immediately followed by a 50 ms auditory beep signal indicating success or failure (one sound for each outcome), at comfortable hearing level. The sequence of « target present » and « target absent » trials was pseudorandom, with the same number of trials for both types. Performance was measured on a total of 30 trials, for a total duration around 1-min (depending on reaction times).

The global instruction was to settle in a steady and reasonably fast pace while avoiding errors (with an explicit analogy to car drivers who avoid accidents at all costs, but nevertheless move forward at a decent speed). The time penalty was precisely to discourage risky strategies, and to minimize the distraction caused by errors and negative feedbacks on subsequent trials: participants were given time to refocus.

2.3.2. Variations of BLAST: adding and removing cognitive components

Participants of the MUSEUM database performed BLAST after a separate training phase of 10 trials. Participants of the SCHOOL database were tested during a 1-h session which included BLAST, plus several additional tasks (C-BLAST, S-BLAST and 8-BLAST, Table .1)

Table 1

Versions of BLAST used for each subpopulation.

Population	Versions of BLAST
SCHOOL	BLAST, C-BLAST, S-BLAST, 8-BLAST
MUSEUM	BLAST
SEEG	BLAST, C-BLAST, S-BLAST

defined as follows (Fig. 1 and Table 1): C-BLAST (“Color-BLAST”) was a simplified version of BLAST, with no memory or visual search component: the Target letter was displayed in red in the Array to pop out when it was present (other letters were black). The instruction was simply to indicate manually if one of the letters in the Array was red (« no » with the dominant hand, and « yes » with the other hand, as in BLAST). S-BLAST (“Side-BLAST”) pushed the simplification one step further, with a direct stimulus-response contingency: a singleton red Target was present in all Arrays and participants simply had to touch the screen on the same side as the Target (simple reaction task). In addition, 8-BLAST was designed to be a more difficult version of BLAST with a circular eight-letters Array instead of the square four-letters Array (longer visual search). Trials in all tasks had similar timing parameters (as described earlier).

C-BLAST, S-BLAST and 8-BLAST were used to evaluate the cost and benefit (in reaction time) of adding or removing critical cognitive components to BLAST. More importantly, the C-BLAST and S-BLAST variants were designed to facilitate the association of subcomponents of the neural response occurring at specific latencies with each stage of the BLAST task: encoding, maintenance, visual search and motor response. Such association is based on the timing of each subcomponent and its variation across tasks. For instance, any neural activity that is absent, or weaker, in S-BLAST is not related to the motor response, because S-BLAST involves a response. Also, neural activity associated with the motor response should be time-locked to motor execution. Neural activity related to encoding should occur in the interval between the target and the array, and should be absent or reduced in S-BLAST and C-BLAST which can be performed without encoding (even if we cannot exclude that some level of automatic encoding occurs in those

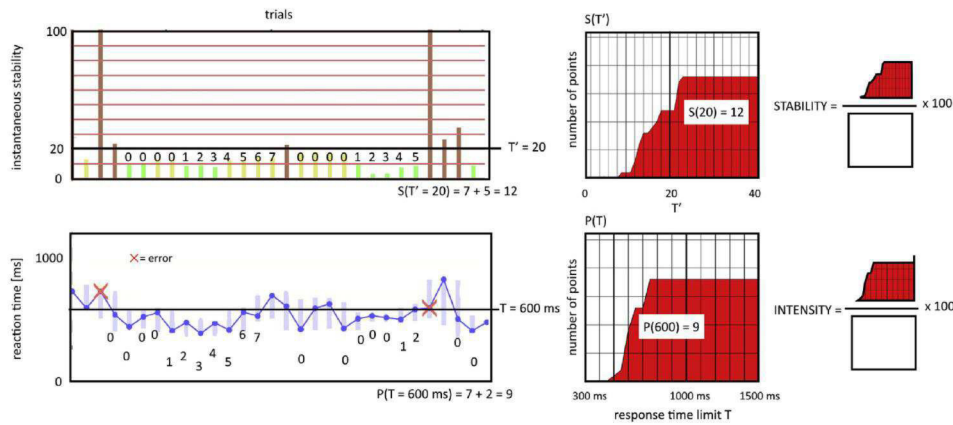


Fig. 2. Scoring systems for INTENSITY and STABILITY. INTENSITY and STABILITY are computed from graphs P(T) and S(T') respectively (bottom and top right panels, respectively), from the ratio of the area under the curve (red) divided by the total area of the square englobing that curve (white). The bottom left graph illustrates the calculation of P(T) from the reaction times for an example value of the response time limit T (600 ms: 9 points) (« instantaneous » standard deviations of reaction times - computed over three consecutive trials, are shown as gray vertical bars). The procedure is repeated for all T values between 300 ms and 1500 ms to generate the red plot P(T). The top left graph illustrates the calculation of S(T') from the « instantaneous » standard deviation $s(\text{trial})$ of the normalized reaction times $r(\text{trial})$, see methods) for an example value of T' (20 : 12 points). The normalized reaction times $r(\text{trial})$ are simply reaction times expressed as % of the median reaction time. S is depicted in the top left graph as vertical bars (green = s less than 10; yellow = s otherwise, note that s is set to 40 for every error) and red vertical bars in the upper left graph). The procedure is repeated for all T' between 0 and 40 to generate red plot S(T') on the right. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

conditions). Finally, activity starting at the array onset and sustained until the response should be interpreted as participating to visual search, and not to memory maintenance (because maintenance should not be triggered by the array, but by the target) (see [supplementary Table 1](#) for a schematic dynamic and functional dissociation between BLAST variants).

All variants were performed during a specific session following an adaptive design (see next paragraph). The description of that design, and the presentation of the corresponding results can be found in the next section (“Adaptive version of BLAST”).

2.3.3. Adaptive versions of BLAST

In schools and during iEEG sessions, C-BLAST, S-BLAST, 8-BLAST (and BLAST, in addition to the standard design described above) were performed in an adaptive, staircase, design, in which participants were asked to achieve a series of five consecutive successful trials, under increasing time pressure. Trials of each task were designed as in BLAST, with the presentation of the Target (200 ms), followed by the mask (700 ms) and the Array until the participant's motor response (i.e. the same timing as BLAST). The overall task design differed from BLAST, however, in order to evaluate how fast a participant could respond under such an accuracy constraint. In the adaptive design, the explicit objective was to achieve series of five consecutive correct trials, faster than an adaptive response time limit which decreased with each successful series, until the participant could no longer succeed. We measured TIME_LIMIT, the best response time limit s/he could reach and the median of all correct reaction times MEDIAN_RT_CORRECT. The response time limit was initialized to 10 s, then updated after each successful series to the slowest reaction time of that series, minus a 20 ms decrement (to converge as fast as possible to the participant's response time limit): the participant was challenged to achieve a slightly faster series. Series were immediately interrupted after any response incorrect or too slow (relative to the ongoing time limit), and the new time limit was simply increased by a 20 ms step for a new, easier, challenge. The objective (five trials) is obviously arbitrary: it is a compromise between a goal that is too hard (and would discourage

participants) and one that is too easy (and can easily be achieved by chance).

2.4. Post-test questionnaires

Participants of the SCHOOL population filled up a questionnaire immediately after the experiment to rate several subjective factors including i) their motivation during the task (MOTIV, on a 1 to 10 scale from ‘not motivated at all’ to ‘extremely motivated’); ii) if they had to focus during the task (FOCUS, on a 1 to 10 scale); iii) how stressed they felt (STRESS, on a 1 to 10 scale); iv) if they felt they had been mind-wandering during the task (MW on a 1 to 4 scale, from “not at all” to “a lot”), and v) if they had been distracted by external noise (NOISE, on a 1 to 4 scale, from « never » to « very often »).

Another questionnaire, filled at home by parents, asked about various aspects of the participants' life outside of school, focusing on TV and video-game usage (number of hours) and hobbies (sport and artistic activities). Finally, parents also filled an ADHD rating scale IV home version (DuPaul et al., 1998) based on the global behavior of their son or daughter the past 6 months. This questionnaire includes 18 questions addressing separately two dimensions (inattention and hyperactivity/impulsivity); it assesses symptoms of attention deficit/hyperactivity disorder (ADHD) according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV).

2.5. Behavioral indices

During BLAST, reaction time (between the onset of the Array and the response) and accuracy were measured for 30 consecutive trials. Attention stability indices were computed from those measures. Our primary intention was to reveal the propensity to undergo momentary lapses of attention (MLA, or conversely, momentary “peaks of attention”). It led us to depart from standard measures such as the variance of the entire reaction times series, which fails to capture the moment-to-moment dynamics of attention (since the variance might be the same for a participant alternating between highly focused and highly

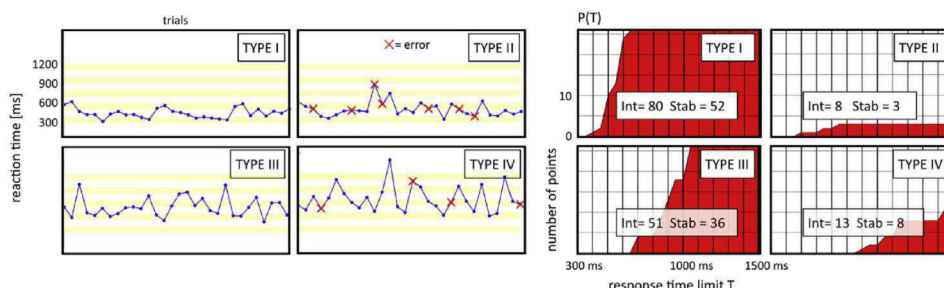


Fig. 3. Examples of response profiles for BLAST. The left panel displays reaction times and errors for four participants (same age-group: 16-17 year-old), which correspond to four different response-types (right panel). Type I is fast, steady and accurate and exemplifies what we called FAST AND FOCUSED individuals. P(T) (right panel) is high for short reaction times and quickly reaches maximal values: most of the square is red. Type II is as fast as Type I, but has many errors (IMPULSIVE type): consequently, P(T) mostly colors the bottom end of the square, from fast to slow reaction times. Type III corresponds to the METICULOUS type, with very few errors but slow reaction times. P(T) mostly colors the right end of the square. Finally, Type IV corresponds to the SLOW INATTENTIVE type, with many errors and slow reaction times. Neuropsychologists might derive a parallel typology from STABILITY graphs. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

distracted episodes, and another participant mildly focused throughout the task). Clearly, new indices had to be designed to integrate the number, the duration and the local stability of attentive episodes. It is not uncommon to propose several scores for the same test to measure slightly different cognitive components (Christidi et al., 2015). In the following, we describe and motivate the indices we derived from BLAST for neuropsychological assessment. All indices can be adapted to any task with constant difficulty which measures reaction times repeatedly and steadily.

2.5.1. INTENSITY

The first behavioral measure, INTENSITY (Fig. 2), derives from the natural assumption that highly focused individuals tend to respond fast and with few errors. In other words, a performance graph showing reaction times (y-axis) for all the trials (x-axis) should display long series of hits below a given response time limit T (horizontal line), even when T is low (see Fig. 3, bottom panel on the left). If we cumulate the length of all successful series below T (i.e. with a reaction time consistently faster than response time limit T), we reach a measure P(T) which should be high for “highly-focused” individuals even when T is small (i.e., 500 ms). To penalize errors and to be consistent with the adaptive designs which required participants to generate successful series of five trials (in reference to the description of “adaptive version of BLAST” above), we computed a measure P(T), which included only series longer than five consecutive wins, cumulating N-5 « points » for every such series (where N is the length of that series). P(T) is the number of points for response time limit T; it is computed for every value of T between 300 ms and 1500 ms (no one could generate series of hits faster than 300 ms). That scoring system penalized errors, as any error interrupted the ongoing series and the participant had to succeed at least five new times before her score increased again. Graph P(T), which increases with longer T, immediately distinguishes visually between several types of participants/strategies (Fig. 3): fast reaction times with many errors (‘globally impulsive participants’), slow reaction times with few errors (‘globally meticulous’), slow reaction times with many errors (‘slow inattentive’ type) and fast reaction times with few errors (‘fast and focused’). Fast and focused participants are characterized by a large area under the curve P(T): for that reason, we defined a behavioral indice of attention, $INTENSITY = 100 \times AUC(P) / \max(AUC)$, where AUC is the area under the curve P(T) and $\max(AUC)$ its maximal theoretical value. INTENSITY refers to, and is high for, the “fast and focused» type. One might object that lower values of INTENSITY might not disambiguate the ‘impulsive’ and the ‘meticulous’ types, but those two profiles can be differentiated by considering also

the median of their reaction times (and graph P(T)).

2.5.2. STABILITY

One limitation of INTENSITY is that it is mathematically lower for participants with slower reaction times (typically, elderly people). Yet, it is clear that someone with slow but close to constant reaction times, and no errors, is fully «on-task ». Therefore, INTENSITY should be complemented with another measure which emphasizes stability more than speed: this is STABILITY (Fig. 2). STABILITY was derived from the assumption that task-irrelevant cognitive processes add “noise” to reaction times (Gmehlin et al., 2016): it was thus computed from the “instantaneous” stability of reaction times $r(\text{trial } i)$. And since our intention was to minimize the effect of the overall speed, we considered the stability of “normalized reaction times”; i.e. reaction times expressed in % of the median reaction time for the entire task: $r(\text{trial } i) = 100 \times r(\text{trial } i) / \text{median}(r(\text{all trials}))$. We defined the instantaneous stability of attention for trial i as $\text{instab}(\text{trial } i) = \text{std}(r(\text{trial } i-1); r(\text{trial } i+1))$, it is computed over sliding windows of three consecutive trials for maximal temporal precision. STABILITY was computed from $\text{instab}(\text{trial } i)$ following a procedure similar to the computation of INTENSITY from $r(\text{trial } i)$. To penalize errors as in INTENSITY, instab was set to a maximal value (40) for unsuccessful trials. As with INTENSITY, we devised a scoring system $S(T)$ which accumulates N-5 points for each series of $N > 4$ winning trials for which instab stays below T (a procedure repeated for T values between 0 and a maximum of 40). Graphically, instab measures the width of the « tube » in which the reaction time plot seems to be confined locally (i.e. for three consecutive trials) (Fig. 2), and $S(T)$ integrates the length of such series, excluding series shorter than 5 for the same reason as in INTENSITY. In short, STABILITY evaluates the ability to generate long and narrow « tubes » of reaction times: $STABILITY = 100 \times AUC(S) / \max(AUC)$, where AUC is the area under the curve $S(T)$ and $\max(AUC)$ its maximal theoretical value.

2.5.3. Other behavioral indices

In addition to INTENSITY and STABILITY, we considered more standard indices such as the overall duration of the task (including time penalties and divided by the number of trials: MEAN_DURATION), the percentage of incorrect trials (PCT_ERRORS), the median and the standard deviation of the entire series of reaction time (excluding time penalties: MEDIAN_RT and STD_RT). Finally, upon the repeated request of teachers helping with data collection, we designed a measure of the duration participants actually spend “on-task” during BLAST (expressed in % of the task duration). Assuming again that episodes spent “on-task”

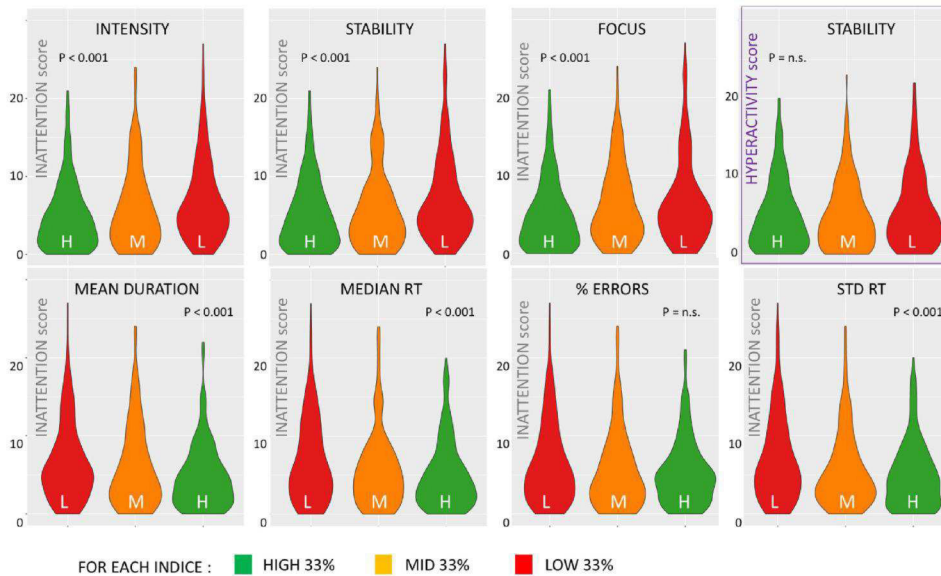


Fig. 4. Distribution of Inattention scores (ADHD rating scale) for low (L, red), medium (M, orange) and high (H, green) performers according to each of the seven indices considered in this study (following the H,M,L grouping procedure defined in paragraph 4.1.2); (geom_violin graph, ggplot2 library, R). P-values correspond to the Kruskal-Wallis comparisons across groups (H,M,L) as in Table 2. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

are characterized by stable and accurate responses, we proposed a measure based on instab(trial i): FOCUS. FOCUS is the percentage of trials for which instab(trial i) is less than 20 (remember that instab is set to 40 for unsuccessful trials). We are fully aware that the cut-off value of 20 is arbitrary: it was chosen after numerous attempts to relate instab with self-reports of how participants felt. A special version of BLAST was designed to interrupt the task at any moment and ask participants about their attention. They felt reasonably on task with the feeling of being focused when instab was less than 20. Although debatable, a choice had to be made and alternative cut-off values (i.e., 10) resulted in measures highly correlated with FOCUS.

2.6. Statistical analysis

Unless specified otherwise, the effect of a given factor (e.g. AGE) was tested using a non-parametric Kruskal-Wallis test (abbreviated KW) with a significance threshold set to 0.01, as Kolmogorov-Smirnov (KS) test revealed general non-normality of our indices. For some analysis, carefully identified in the result section, indices were first normalized within each age group (Z-score normalization: subtract the mean value for that particular age group and divide by the standard deviation), to study the effect of a factor independently of age (e.g. GENDER). This normalization is explicitly mentioned in the text each time it is used.

3. Results

3.1. Behavioral results

We tested several major predictions: i) that the ability to stay-on-task would increase from children to teenagers and adults, with a plateau in the early twenties at the end of the maturation of the prefrontal cortex and the executive system (Gogtay et al., 2004; Toga et al., 2006); ii) that children and teenagers with high inattention scores (according to the ADHD questionnaire) would perform worse than participants

matched in age with lower inattention scores, and iii) that attention might be affected negatively or positively by extra-curricular activities (TV and video-games, art, sport) and by socio-demographic factors (e.g., education level of the parents) (but we found no significant effect, see suppl. Materials). The SCHOOL database was designed to test those predictions, as it combined BLAST behavioral measures with questionnaires filled by parents. In addition, short questionnaires filled by participants at the end of the test allowed us to evaluate whether they had performed the test in good conditions (motivated, with no external distractions) and considered actually BLAST as attention-demanding.

3.1.1. Analysis of post-test questionnaires (self-reports)

BLAST was designed to be attention-demanding and yet pleasant, although not to the degree reached by video-games carefully designed to capture and hold the player's attention. Participants confirmed we reached our goal: a large majority enjoyed BLAST and said they had to focus (MOTIV, "did you enjoy the test?": 92% above 5, 64% above 7.5 on a 0 to 10 scale; FOCUS, "how focused were you?": 92% above 5, 69% above 7.5 on a 0 to 10 scale). They also reported little or no distraction by external noises (NOISE: "were you disturbed by external noise?": 95% below 2 on a 1 to 4 scale, i.e. « never » or « rarely »), which means that our experiment was well-suited to study *endogenous* distraction, as intended.

3.1.2. BLAST scores and ADHD rating scale

A standard ADHD-questionnaire was collected from 692 participants (SCHOOL database), with nine questions related to inattention specifically and nine questions related to hyperactivity (DuPaul et al., 1998). Parents were asked to rate each statement between 0 and 3 (from 0 - « almost never » - to 3 - « very often »), leading to a global inattention score (for nine questions, from 0 to 27), a global hyperactivity score (0-27) and a global ADHD score (the sum of the two). We tested for relationships between each global score and each individual question, and all behavioral indices (see Supplementary Fig. 1 for a display

Table 2
Statistical values for all tests reported in paragraph 4.1.2 (BLAST scores and ADHD rating scale). KW = Kruskal-Wallis Chi-squared values.

	INATT (df = 2)		HYPER (df = 2)		TOTAL (df = 2)	
	KW	p-value	KW	p-value	KW	p-value
INTENSITY	18.96	7e-05	2.81	0.2	10.44	0.005
STABILITY	16.03	0.0003	2.29	0.3	10.73	0.004
FOCUS	15.70	0.0004	4.64	0.1	11.44	0.003
MEAN_DURATION	16.65	0.0002	2.55	0.3	11.98	0.002
STD_RT	14.42	0.0007	0.75	0.7	7.43	0.02
MEDIAN_RT	13.78	0.001	3.80	0.1	5.93	0.05
% ERRORS	4.41	0.1	1.83	0.4	4.59	0.1

of ADHD, Inattention and hyperactivity scores as a function of age and sex).

To test for possible relationships between global scores and BLAST indices (e.g., INTENSITY, ...), BLAST indices of each participant were transformed into a group letter (H, M or L), indicating whether that participant was in the higher, middle or lower 33% of her age group for that particular index (performance-wise). We tested the Ho-hypothesis that global scores did not differ across groups (H,M,L) and rejected that hypothesis for the global INATTENTION score (KW, $p < 0.005$) for all indices except the error percentage (STABILITY, INTENSITY, FOCUS, MEAN_DURATION, MEDIAN_RT and STD_RT): participants had a higher inattention score in groups (i.e., letters) with the poorest performance. In contrast, no significant difference between groups were found when considering the global Hyperactivity score. The global ADHD score, which adds the global inattention and hyperactivity scores, differed across groups when considering indices INTENSITY, STABILITY, FOCUS and MEAN_DURATION (KW, $p < 0.01$) (see Fig. 4 and Table 2 for complete statistics).

Overall, our analysis indicates that BLAST is almost uniquely sensitive to the Inattention component of the ADHD rating scale (a more detailed question-by-question analysis revealed a finer relationship with our indices. More precisely with the observed inability to stay-on-task; see suppl. materials).

3.1.3. Normative data and age and sex effects

Normative data were computed from the MUSEUM database and displayed graphically for all behavioral indices in Fig. 5 in a form that reveals a clear effect of age. All performance indices were affected by age, including all measures of attention (Kruskal-Wallis, $p < 10^{-22}$ for all), with a systematic increase of performance with age for participants younger than 25. Participants also reported their gender, and we found significant differences between the two genders on two behavioral indices (Kruskal-Wallis, $p < 0.01$ for PCT_ERRORS and MEDIAN_RT), even when considering normalized scores (relative to same-age participants, see methods). Females were slower than males but made fewer errors (see Supplementary Fig. 2 and Table 3 for complete statistics).

The pervasive influence of age led us to compute and display nine quantiles (10–90%, by step of 10%) as a function of age, with a one-year stratification between 8 and 18. A neuropsychologist using the graphs to interpret BLAST scores, should identify the age of the participant on the y-axis and her score on the x-axis, then use the color-code to evaluate immediately the proportion of participants of the same age with a higher score (90, 80, 70% ...). Supplementary Fig. 3 also show polynomial functions modelling the age effect, where the dependence of quantile values on age was nicely fitted by third-order polynomial functions $q(\text{age}) = a.y^3 + by^2 + cy + d$, where $y = \log(\text{age})$ (polynomial fitting in MATLAB interface, the Mathworks, inc.).

It is worth noticing that none of the distributions is bimodal, for any age group. The distributions of all behavioral indices have only one peak, and any attempt to define a cutoff score to identify impairment ("high" vs "low" attention scores) would be arbitrary and debatable.

3.1.4. Test-retest

Test-retest reliability was evaluated from data of 122 participants who performed BLAST twice, using two measures: the Pearson's correlation coefficient (Rho) and the intraclass correlation coefficient - (icc; irr package of R with parameters: 'oneway' and 'consistency'). Data are shown in Table 4; unsurprisingly, the most reliable measure is the median reaction time (Pearson Rho = 0.93, icc = 0.90), while most measures reach 0.6 or higher with both methods, with a maximum reliability for INTENSITY (Rho = 0.8, icc = 0.81) and a minimum reliability for MEAN_DURATION (Rho = 0.49, icc = 0.49). These values are in line with test-retest reliability measures of standard tests of executive functions (Lowe and Rabbitt, 1998).

3.1.5. Comparison of BLAST and CODE

Thirty-seven participants of the same age group (16–17) performed both BLAST and a standard pencil-and-paper test of sustained attention (CODE), a subtest of processing speed index from the Wechsler Intelligence Scale for children and the Wechsler Adult Intelligence Scale respectively WISC-IV and WAIS-IV (Wechsler, 2003; 2008). CODE consists in matching symbols to numbers as quickly as possible during 2 min, according to written instructions. We found significant correlations between CODE (number of correct responses) and most behavioral indices of BLAST: INTENSITY (Spearman Rho Correlation Coefficient = 0.57, $p = 0.0002$); STABILITY (Rho = 0.48, $p = 0.002$); MEAN_DURATION (Rho = -0.59, $p < 1e-5$; participants better at CODE were faster at BLAST); FOCUS (Rho = 0.61, $p < 1e-5$); MEDIAN_RT (Rho = -0.55, $p = 0.0004$); PCT_ERRORS (Rho = -0.39, $p < 0.05$ - less errors at BLAST for higher scores at CODE).

3.1.6. One minute or 10 min?

Considering that BLAST lasts only about 1 min - in its thirty-trials version - one might question its validity to assess the ability to stay on task for longer durations, over segments of 10 min for instance. One might argue that individuals who can remain sharply focused for 1 min are not necessarily the same who can perform steadily for 10 min. We addressed this question with a database of 121 participants aged 10–12 (65 males) performing a 200 trials version of BLAST (separate from the SCHOOL and MUSEUM datasets and participants). We computed our main indices over the first 30 trials and correlated their values with the same indices measured over the entire session (200 trials), Table 5 contains the result, as well as the same correlation analysis when considering the first 40, 50 and 60 trials. We found that for several indices (INTENSITY, MEAN_DURATION and MEDIAN_RT), the correlation (Pearson's correlation coefficient) was already high for 30 trials (0.75, 0.75 and 0.87 respectively), meaning that the ability of an individual to be fast and focused during 10 min could be fairly well estimated in 1 min only. The full analysis suggests that the STABILITY and FOCUS indices over 10 min should rather be estimated with a 50 trials version of BLAST ($R = 0.78$ and 0.67 respectively). The conclusion that long-term (10 min) attention stability can be estimated in around 1 min has important bearings for neuropsychologists who must often perform testing sessions under strong time-constraints (Fig. 6).

3.2. Electrophysiological study

This section describes the large-scale cortical dynamics during individual trials of BLAST and its variants, from the onset of the target letter to the motor response, with a millisecond and millimetric precision. Our strategy was to identify all major brain regions supporting BLAST from iEEG HFA_[50-150 Hz] data and examine the specific dynamic of activation of each of those Regions of Interest (ROI) from iEEG of individual patients. The main objective was to associate precise cortical regions with each of the three main cognitive components of BLAST: i) encoding and maintenance of the Target letter, ii) visual search of the Array, iii) motor response, which can be done by comparing HFA induced by BLAST and variants of BLAST lacking one or several of those

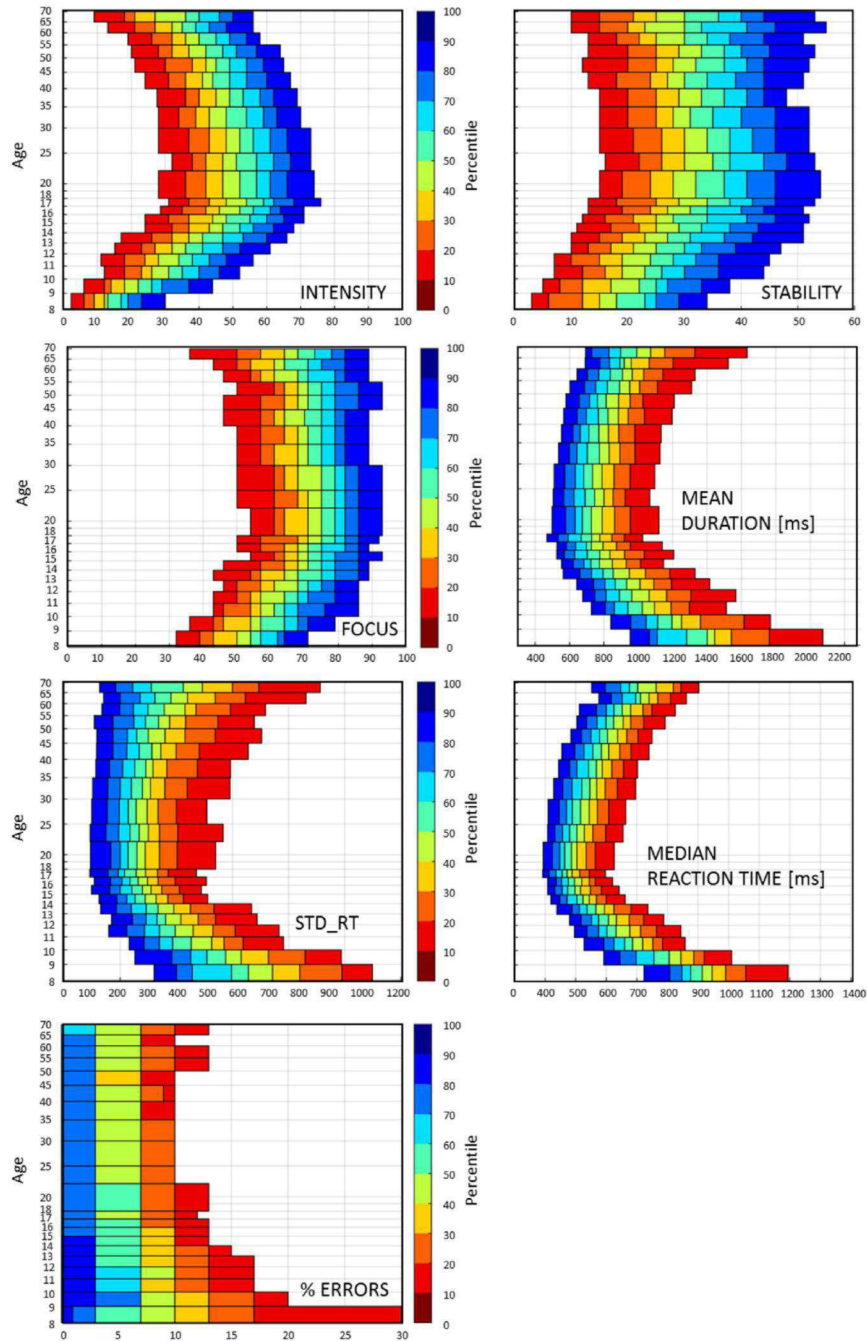


Fig. 5. Age-stratified normative data for the main behavioral indices quantifying the ability to stay on task in BLAST. A neuropsychologist using the graphs to interpret BLAST scores, should identify the age of the participant on the y-axis and his/her score on the x-axis, then use the color-code to evaluate immediately the proportion of participants of the same age with a lower score (90, 80, 70% ...). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 3

Statistical values for the effect of sex and age on BLAST indices. KW = Kruskal-Wallis Chi-squared values.

	AGE (df = 1)		SEX (df = 1)	
	KW	p-value	KW	p-value
INTENSITY	1075	1e-174	1.55	0.2
STABILITY	416	2e-47	5.76	0.02
FOCUS	447	7e-53	0.69	0.4
MEAN_DURATION	1001	8e-160	0.18	0.7
MEDIAN_RT	2040	0	15.5	8e-5
% ERRORS	265	5e-22	16.3	5e-5

Table 4

Test-retest reliability for the main behavioral indices of BLAST performance.

	icc (all)	R pearson (all)
INTENSITY	0.80	0.81
STABILITY	0.65	0.65
FOCUS	0.52	0.55
MEAN_DURATION	0.49	0.49
STD-RT	0.60	0.61
MEDIAN_RT	0.90	0.93

Table 5

Correlation between behavioral indices measured over 200 trials, and the first 30, 40, 50, 60 trials of BLAST respectively (Pearson's correlation coefficients).

	30 trials	40 trials	50 trials	60 trials	200 trials
INTENSITY	0.75	0.81	0.86	0.88	1
STABILITY	0.58	0.68	0.78	0.81	1
FOCUS	0.53	0.62	0.67	0.71	
MEAN_DURATION	0.75	0.81	0.84	0.86	
MEDIAN_RT	0.87	0.87	0.90	0.92	

Table 6

Exact location of all cortical regions activated and deactivated during BLAST. **Nb Sites/Patients:** number of sites with significant activation or deactivation, with the following code: "7[3]/8-9" means that 7 sites were found significant without FDR correction, 3 after FDR correction, in 8 different patients, out of 9 sites in that anatomical landmark. **Box Mni:** area containing all sites of the Region of Interest in the MNI space. **Anatomical landmark:** precise anatomical location where effects were observed. Abbreviations: ITG = Inferior Temporal Gyrus; IPS = IntraParietal Sulcus; PreC = PreCentral Gyrus/Sulcus; ACC = Anterior Cingulate Cortex; preSMA = preSupplementary Motor Area; DLPFC = Dorso-Lateral Prefrontal Cortex; VPMC = Ventral Premotor Cortex; F Oper = Frontal Operculum; OFC = OrbitoFrontal Cortex; VMPFC = Ventral Medial Prefrontal Cortex; PCC = Posterior Cingulate Cortex; MTC = Middle Temporal Cortex; TPJ = TemporoParietal Junction; L/R = Left/Right.

	Sites/Patients	Mni Box	Anatomical Landmark
ACTIVATIONS			
L ITG	3[3]/3 - 3	[-54; -67] _x [-50; -47] _y [-16; -18] _z	Inferior Temporal gyrus
L IPS	3[3]/3 - 3	[-29; -38] _x [-46; -35] _y [34; 43] _z	Intra-Parietal sulcus
R IPS	3[3]/3 - 3	[25; 30] _x [-60; -57] _y [44; 49] _z	idem
L PreC	3[3]/3 - 3	[-37; -54] _x [-12; -3] _y [43; 51] _z	Upper precentral gyrus/sulcus
R PreC	3[3]/3 - 3	[52; 54] _x [2; 3] _y [31; 34] _z	idem
L ACC/preSMA	2[2]/2 - 4	[-11; -12] _x [6; 16] _y [48; 52] _z	Region between the cingulate/paracingulate sulci
R ACC/preSMA	6[5]/4 - 6	[7; 10] _x [0; 15] _y [30; 52] _z	idem
L DLPFC	2[2]/2 - 2	[-41; -50] _x [21; 26] _y [19; 24] _z	Inferior Frontal Sulcus
R DLPFC	3[3]/3 - 3	[37; 44] _x [23; 33] _y [6; 16] _z	idem
L VPMC	6[6]/6 - 6	[-46; -54] _x [-1; 5] _y [14; 23] _z	Lower precentral sulcus, posterior to Broca area
R F Oper	2[2]/2 - 2	[37; 50] _x [14; 23] _y [4; 12] _z	Frontal Operculum
DEACTIVATIONS			
L OFC	3[2]/4 - 3	[-33; -37] _x [37; 43] _y [-17; -15] _z	Orbital sulcus
R OFC	5[4]/4 - 5	[36; 49] _x [28; 46] _y [-12; -10] _z	idem
L VMPFC	5[2]/4 - 5	[-7; -17] _x [39; 55] _y [-16; -4] _z	Paracingulate and anterior rostral sulcus
R VMPFC	7[7]/6 - 7	[3; 13] _x [26; 57] _y [-27; -3] _z	idem
L PCC	7[5]/9 - 7	[-6; -16] _x [-59; -37] _y [25; 38] _z	Posterior Cingulate sulcus
R PCC	7[3]/7 - 9	[7; 12] _x [-49; -36] _y [29; 42] _z	idem
L MTC	16[10]/9 - 16	[-51; -65] _x [-47; -13] _y [-29; -3] _z	Inferior and Superior Temporal sulci
R MTC	10[4]/9 - 11	[53; 65] _x [-39; -3] _y [-19; -3] _z	idem
L TPJ	1[1]/4 - 4	[-44; -64] _x [51; -45] _y [36; 57] _z	Ascending branch of Superior Temporal Sulcus
R TPJ	6[1]/5 - 6	[52; 63] _x [-46; -36] _y [29; 50] _z	idem

components (C-BLAST and S-BLAST) (see §3.3.2 for details). We report only ROIs where similar activation patterns were observed in at least two different patients, following our standard procedure for iEEG analysis (Lachaux et al., 2012). Note that we don't report cortical regions with unspecific visual responses (so as to avoid including the entire visual cortex). Also, our analysis does not include subcortical responses, which might play an important role in BLAST but were not recorded. Finally, all sites with pathological activity and/or within the seizure onset zone were carefully excluded from the analysis.

We found only seven ROIs with increased HFA during BLAST relative to baseline (see Table 6 for a complete overview with both uncorrected - Wilcoxon, $p < 0.01$ - and FDR-corrected results, with exact anatomical locations relative to landmarks identified on individual MRIs and based on the nomenclature of (Donkelaar Ten et al., 2018)): the left Inferior Temporal Gyrus (ITG), the left ventral PreMotor Cortex (vPMC), the right and left dorsolateral Prefrontal Cortex (DLPFC), symmetric portions of precentral gyrus/sulcus left and right (PreC), a region extending bilaterally over the Supplementary Motor Area and the anterior Cingulate Cortex (ACC/preSMA), the IntraParietal Sulcus (IPS) on both sides and the right Frontal Operculum (F Oper). In addition, five ROIs showed a reverse pattern of HFA decrease during BLAST: the middle Temporal Gyrus in the Lateral Middle Temporal Cortex (MTC), the OrbitoFrontal Cortex (OFC), the ventromedial Prefrontal Cortex (VMPFC), the Temporal Parietal Junction (TPJ) and the Posterior Cingulate Cortex (PCC), all bilaterally. Fig. 7 summarizes the location of those Regions of Interest and the timing of their activation/deactivation.

The portion of the left ITG active during BLAST matched the location and functional specificity of the word-form area, WFA, a region of the left inferior temporal gyrus supporting visual processing of letters and letter-strings (Sup. Fig. 5). The dynamics of activation during BLAST revealed two phases: during the presentation of the Target and during the display of the Array, as expected in response to letters. However, the statistical comparison of BLAST and its variants C-BLAST and S-BLAST revealed that the response to the letter was strong and

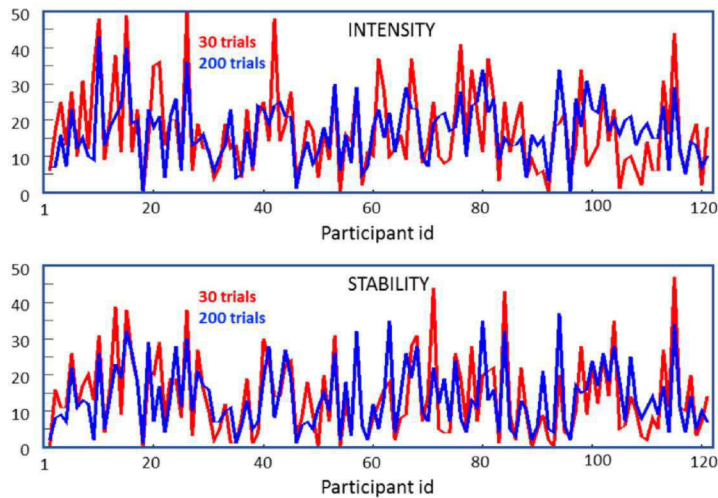


Fig. 6. Comparison of INTENSITY and STABILITY computed over 30 vs. 200 trials. The graphs show values computed over 30 trials (red) versus 200 trials (blue) for INTENSITY and STABILITY for each participant. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

sustained only when the Target must be encoded into working memory (BLAST) (Sup Fig. 5). It was also stronger when the Array was searched attentively (i.e. in BLAST). Therefore, the WFA participated actively to both the encoding phase and the search phase of BLAST.

Reactive sites in the DLPFC (i.e. sites with a significant HFA deviation relative to baseline) were located in the Inferior Frontal Sulcus and were especially active during the Array presentation with a stronger activity when the participant took longer to respond, compatible with a role in the target detection process (Sup Figs. 6 and 7). The left vPMC (sites in the lower part of the precentral Sulcus immediately posterior to Broca) and the right frontal Operculum reacted to both the Target and the Array, particularly in the BLAST condition (Sup Figs. 6 and 7). Note that the letter stimulus has the same physical characteristics in BLAST, C-BLAST and S-BLAST, but carries task-relevant information only in BLAST, in which it must be encoded and maintained in short-term memory to serve as a template for the visual search. Single trial representation (matrix representation in Sup Figs. 6 and 7) shows that activity was sustained continuously until task completion in the Frontal Operculum, but extended beyond the reaction time in the vPMC, suggesting a participation to motor programming and execution for that region in addition to the more cognitive aspects of BLAST. Fig. 8 displays the comparative timing of activation of ROIs recorded in the same patient (for two patients): the data largely confirm for instance that areas involved in the visual search process have different functions, as we just described. For example, the DLPFC and Frontal Operculum peaks occur much earlier than in the vPMC. In fact, a careful examination of Sup Figs. 6 and 7 reveals that activity of the former return towards baseline level before the motor response, while the vPMC response extends hundreds of millisecond later. Additional subtler differences in timing between regions are harder to interpret but indicate a sequence of processing across cortical areas rather than a fully integrated network acting as one functionally unified block.

All other ROIs stopped their activity upon task completion. The activation of the IntraParietal Sulcus (IPS) occurred mostly during the Array with a stronger response in the two BLAST variants with a red singleton in that Array (Sup Fig. 7), compatible with a role of that region in spatial attention shifts and attentional capture by salient stimuli. It might also participate in a large-scale top-down process to sustain activation in letter-specific areas of the inferior Temporal Lobe, as part of a larger Dorsal Attention Network (Corbetta and Shulman, 2002), which also includes the Frontal Eye Field, or FEF. Accordingly, the large

Precentral region of interest (PreC) included sites compatible with the location of the Frontal Eye Field (see Precentral, Sup Fig. 7), with a response specific to Targets which must be encoded into working memory (BLAST), and must therefore be attended.

Similar patterns of activation were observed in the ACC/preSMA (Sup Fig. 7), between the cingulate and paracingulate sulci. This region, with the DLPFC, is a hallmark of the frontal executive system which mediates cognitive control and goal-directed behavior in general, and the ability to stay-on-task in particular. Unsurprisingly, both ROIs were active during the encoding and during the search phase, with a steady activity increase in the latter until task completion.

In the five ROIs deactivated by BLAST, HFA suppressions observed in individual patients revealed a stronger deactivation in the most difficult task (BLAST) in most instances (Sup Fig. 8). They had a slow dynamics with a negative peak while participants processed the Array. Single trial matrixes suggest that the five ROIs might have different temporal characteristics; but HFA decreases, although significant, were not sufficiently strong to elaborate further on their dynamics, in contrast with the massive HFA increases seen in other ROIs. All ROIs deactivated during BLAST are part of the Default-Mode Network (Raichle et al., 2001), in line with recurrent observations that activity is suppressed in the DMN when processing external stimuli attentively.

4. Discussion

Our objective was to propose a test that measures « the ability to stay on-task », with a well-identified cortical network and age-stratified normative data. We focused on the ability to apply consistently and selectively the set of cognitive processes necessary and sufficient to perform the task at hand, with no interference from irrelevant processes. BLAST (Bron/Lyon Attention Stability Test) is to our knowledge the first test meeting all such requirements, with a performance that is related selectively to inattention, not hyperactivity. In addition, intracranial EEG data provide clear evidence that BLAST involves primarily the frontal executive and dorsal attention network, including all major components of the executive attention system in the prefrontal cortex, together with a reduction of activity in the Default-Mode Network.

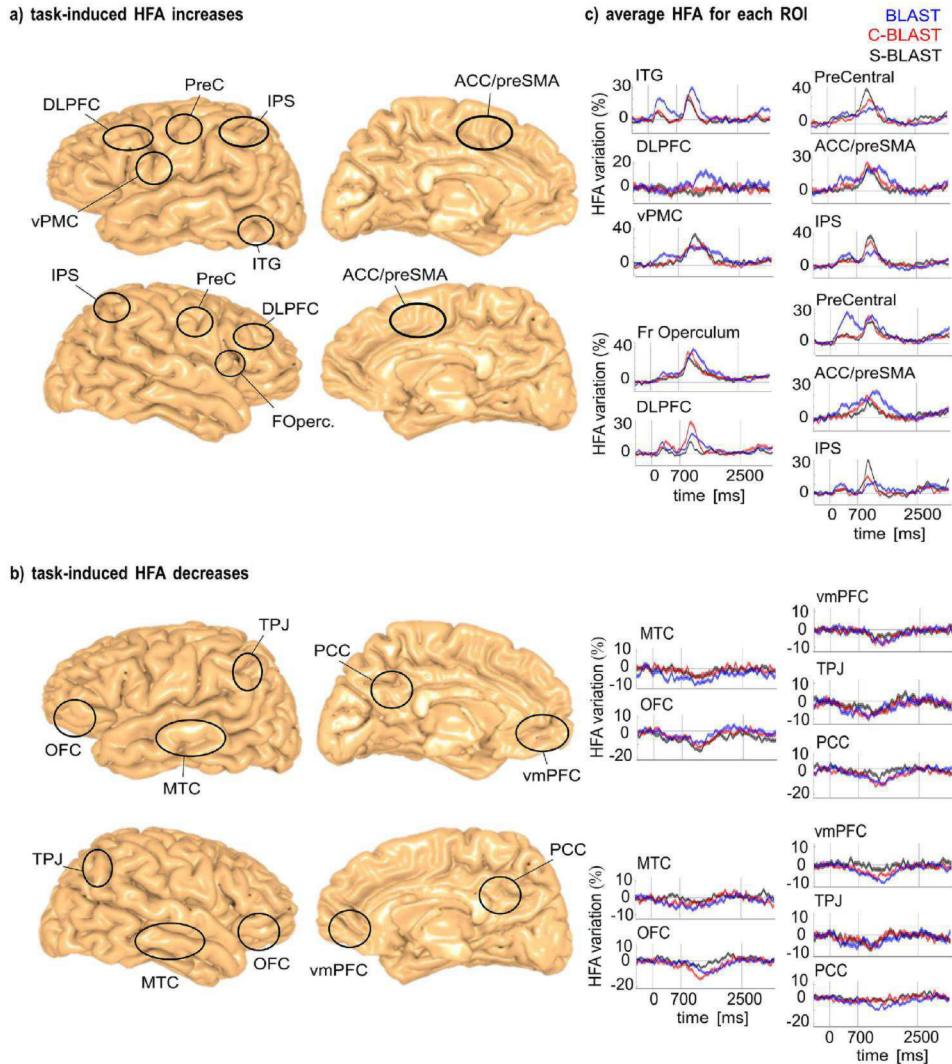


Fig. 7. Cortical regions activated and deactivated during BLAST. a) anatomical location of the major regions with task-related HFA increases during BLAST (see the table in the main text for precise anatomical information); b) anatomical location of task-related HFA decreases. c) average dynamics of responsive sites in each ROI, expressed in % of the mean HFA value across the entire experiment. Vertical lines indicate target and array onsets at 0 ms and 700 ms. Experimental conditions are color-coded: blue for BLAST, red for C-BLAST, black for S-BLAST. Activated ROIs are the left inferior temporal cortex (ITG), the left ventral premotor cortex (vPMC), the Dorsal-Lateral Prefrontal Cortex on both sides (DLPFC), the right Frontal Operculum (F Operc.), a region encompassing the PreCentral gyrus and sulcus (PreC), a region encompassing the Anterior Cingulate Cortex and the pre-Supplementary Motor Area (ACC/preSMA) and the IntraParietal Sulcus (IPS) on both sides. Deactivated ROIs are the middle temporal cortex (MTC), the orbitofrontal cortex (OFC), the ventromedial prefrontal cortex (vmPFC), the Temporo-Parietal Junction (TPJ) and the posterior cingulate cortex (PCC). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

4.1. Task design

We argue here that there are very few possible alternatives to BLAST, in terms of task-design, to measure attentional stability with a close-to-second temporal resolution. BLAST provides a reaction time

every 2 s on average, which defines the temporal precision at which fluctuations of attention can be detected. It matches the time-scale of short MLA which can make us «miss» an important word in an explanation, for instance. It is hard to imagine a task with a better temporal precision, considering the minimal duration of cognitive stimulus-

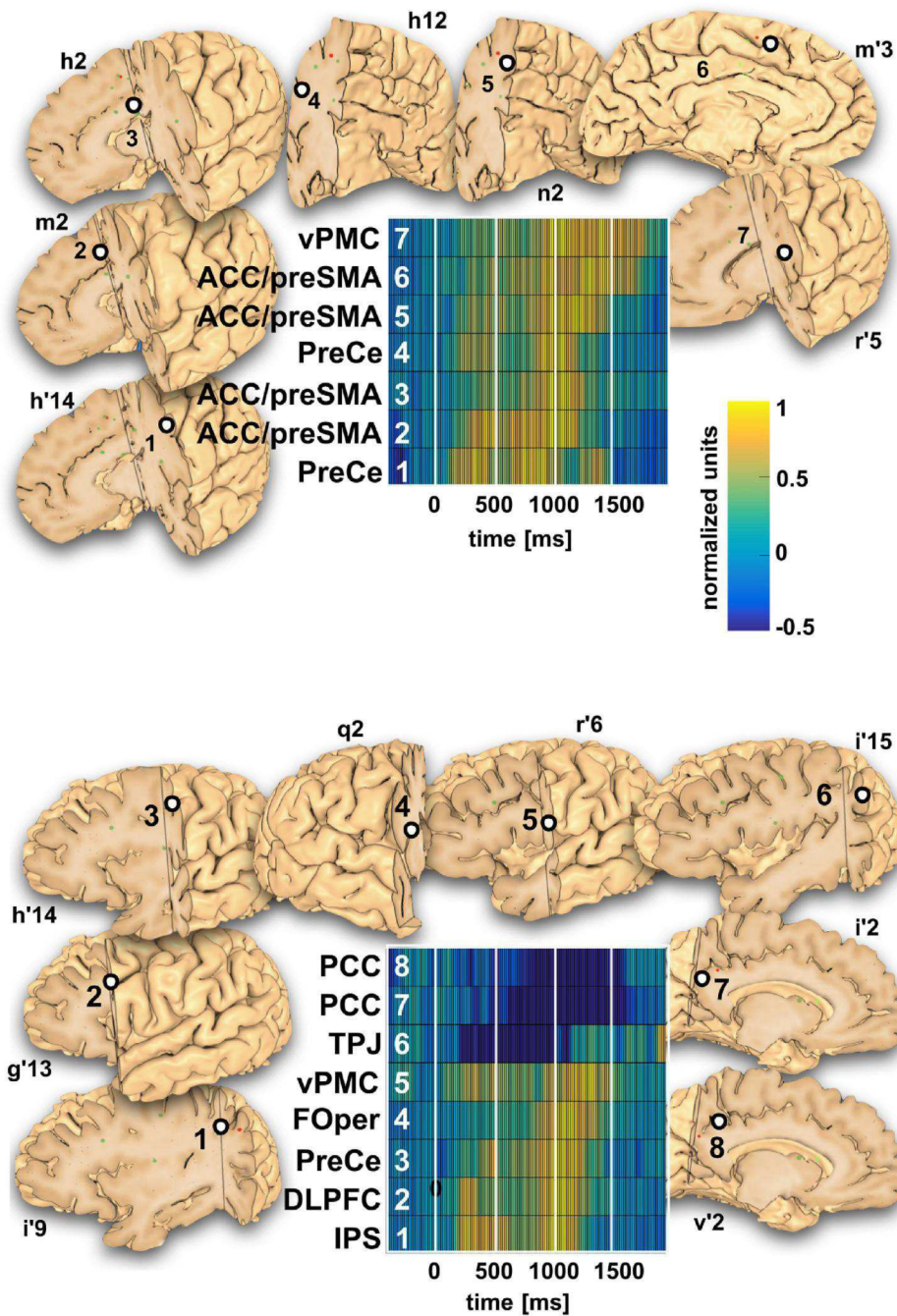


Fig. 8. Comparative timing of neural activation and deactivation during BLAST. The upper and lower panels display the neural responses in different cortical sites for two representative patients (HFA, [50–150 Hz], normalized for each site to the response peak). Sites are sorted vertically according to their response peak latency. Abbreviations: vPMC = ventral PreMotor Cortex; ACC = Anterior Cingulate Cortex; preSMA = preSupplementary Motor Area; PreCe = PreCentral Gyrus/Sulcus; PCC = Posterior Cingulate Cortex; TPJ = Temporo-Parietal Junction; FOper = Frontal Operculum; DLPFC = Dorso-Lateral PreFrontal Cortex; IPS = Intra-Parietal Sulcus.

to-response cycles (Madl et al., 2011) and the constraint to avoid muscular fatigue. In theory, a finer time resolution could be achieved if participants had to react continuously to a changing stimulus (with a continuous behavioral response, as when tracking a moving dot with a joystick); however, to the best of our knowledge, no such task keeps difficulty constant over time (for instance, in tracking tasks, parts of the trajectory with high, changing curvatures are harder to track than smoother parts), and therefore, performance over time does not depend solely upon the participant's attention. Tasks in which behavioral measures are discrete in time, like BLAST, involve repeated presentations of a sensory stimulus followed by a participant's overt response, at a pace which determines the temporal resolution of the performance measurement. Such discrete tasks must themselves obey several constraints to ensure that performance depends solely (or as much as possible) upon the attention allocated by the participant to the task: i) the inter-stimulus interval should be constant (to keep task difficulty constant) and on the order of one or 2 s to avoid muscular fatigue and allow reasonable time to process the stimulus. Such constraints already allow to define tasks which can successfully be used to detect off-task episodes, such as the Metronome task (Seli et al., 2013). However, to minimize the possibility of automatization (which would reduce the behavioral impact of lapses of attention), we add the additional constraint that ii) the rule defining stimulus-response association should vary from trial to trial: this implies that participants should be informed of that association-rule before each trial by a cue, shown before stimulus presentation so that cue- and stimulus-processing do not compete for attention resources; and yet iii) the overall task-set (the principle of stimulus-response association) should remain the same throughout the task, as it is known that task-set changes within tasks induce switch costs which affect behavior negatively independently of attention. This set of constraints sums up to allow only designs in which in each trial, a cue instructs participants - with a metronomic timing - to process the upcoming stimulus in a unique, but yet stereotyped way, to choose one of several motor responses. In BLAST, the cue is a target letter which instructs participants to decide whether that letter is among the four letters shown 700 ms after that stimulus. The stimulus-response association rule is not rigid (the same stimulus is not always associated with the same motor response), and yet, the task set remains the same throughout the task. Alternatives to BLAST are of course possible to track attention on a second-to-second basis, but we claim that all of them would follow the same organizing principle.

There are of course computerized tests to evaluate the ability to sustain attention over time and help diagnose ADHD, such as the Conners' Continuous Performance Test (Homack and Riccio, 2006). But none of them was designed to capture brief lapses of attention as only a minority of the trials really require attentive processing. Interestingly, a task-design very similar to BLAST has been used to study the neural mechanisms of visual attention in non-human primates: the task used an array of four tilted bars instead of letters (Buschman and Miller, 2007). But the trials did not repeat as in BLAST and the authors did not study the variability of reaction times.

4.2. Neural correlates of BLAST

Our electrophysiological study suggests the following scenario during successful trials of BLAST: after an initial and transient response of early visual areas, activation triggered by the Target letter would reach a region of the basal temporal lobe specialized for letter-forms: the Word Form Area or WFA. The WFA would then hold the search template until and throughout the search process (the display of the Array). If the participant strategy implies subvocal rehearsal, the left Ventral PreMotor Cortex adjacent to Broca, possibly in synergy with the Precentral Cluster, would support an additional, phonological, maintenance process using the phonological loop (in agreement with the classic model of verbal working memory (Baddeley, 2000). The Dorsal Attention Network, or DAN (Corbetta and Shulman, 2002), including

the dorsolateral Prefrontal Cortex, the Frontal Eye Field and the Intraparietal sulcus would a) facilitate visual memory maintenance in the WFA (as the DAN has been shown to sustain and bias activity in visual areas via top-down influences, Noudoost et al., 2010; Seidl et al., 2012), and b) guide visual attention within the Array in line with its primary functional role (Corbetta and Shulman, 2002). The DLPFC might orchestrate the encode-then-search process, given its known ability to maintain task-instructions (the "task sets", Sakai, 2008): it would hold the « program » to encode the search template (the Target) in the WFA, then compare sequentially or in parallel each letter of the Array with that template and support the decision process to press with the right or left index finger. Finally, a region at the interface between the pre-SMA and the dorsal Anterior Cingulate Gyrus would ensure that attention is « on-task », in line with its known implication in cognitive control. The final motor response would obviously be produced by the premotor and motor cortex. In that scenario, a sudden increase in reaction times might be due to a less efficient encoding and maintenance of the search template in the WFA (insufficient top-down influences from the DAN), or a discontinuous search process (again, inefficient or insufficient activation of the DAN or the pre-SMA). In terms of timing, the model implies that the WFA should respond immediately to the target, followed by an activation of the DAN that would last until the response, including the IPS, in parallel with an activation of the DLPFC. The ACC/preSMA should increase its activity throughout the task until its completion and the motor cortex activity should be time-locked to the response. In case of subvocal rehearsal, the vPMC should be active shortly after the ITG activity, and throughout the search process. Data from two patients in which seven and eight sites (respectively) were responsive to BLAST are consistent with that model (Fig. 8).

This global and highly organized activation pattern does not occur in isolation, but together with a somewhat smoother deactivation process of an entire network called DMN (the Default-Mode Network or task negative network: the Temporal Parietal Junction, the posterior Cingulate Cortex, the medial Prefrontal Cortex, the ventral lateral Prefrontal Cortex and the lateral Temporal Cortex) (Raichle et al., 2001). Activity in the DMN is classically associated with spontaneous, task-unrelated cognition, which might interfere with active visual processing of external stimuli, and its deactivation during BLAST was predicted by the literature (Weissman et al., 2006; Li et al., 2007; Esposito et al., 2009; Anticevic et al., 2010; Mayer et al., 2010; Anticevic, 2013). However, the precision of iEEG reveals a surprisingly dynamic behavior (Sup Fig. 8) with a brief reactivation in the ultra-short interval (800 ms) between two consecutive trials, which can be seen as a brief reactivation of DMN functions whenever possible (Lachaux et al., 2008; Ossandon et al., 2012).

To summarize, BLAST exemplifies the interplay between the DAN and the DMN which is typical of sustained and demanding visual attention tasks (Langner and Eickhoff, 2013; Christoff et al., 2016). It is therefore ideal to study the ability to stay on-task, and follow the dynamic competition between the DAN and the DMN on a trial-by-trial basis, with second-by-second precision.

4.3. Possible limitations of BLAST

A first possible objection to the present study is that the cortical network supporting BLAST was identified in patients suffering from epilepsy. Although it is true that their brain can only be considered as a proxy of a healthy brain, that criticism has been addressed repeatedly over the years and detailed responses including precise guidelines have been published (see for instance, Lachaux et al., 2012). In short: researchers analyzing iEEG carefully check that recordings are made outside epileptogenic networks and are free of epileptiform activity; and that similar observations can be made in the same cortical structure in patients with different types of epilepsy and medications. Thanks to such sanity checks, iEEG has become in twenty years a premium methodology to study the neural dynamics of human cognition

(Lachaux et al., 2012; Ritaccio et al., 2014), which results are now widely incorporated in our global understanding of human brain functions.

Regarding the task design, one might criticize that BLAST difficulty is not strictly constant across trials, because some letters might be easier to spot than others, because the location of the target within the array (when present) is likely to have an impact, and because it might take longer to figure out that the target is not in the array. We acknowledge such effects fully, but argue - and checked visually - that the variations in reaction times induced by such factors were minimal compared to the effect of momentary lapses of attention. A third possible criticism changes of strategy might cause fluctuations of reaction times independently of attention (for instance, in a change in the speed/accuracy trade-off), but that particular criticism applies to any design using reaction times to assess attention. Our assumption is that changes of strategy should not cause instability of reaction times on a trial-to-trial basis, but rather a slower change with stable periods lasting several trials; therefore, it is likely that short-scale fluctuations in reaction times that we take as a measure of inattention are indeed due to inattention. Finally, we are fully aware that behavioral performance can only provide an indirect estimate of the level of attention allocated to the task; however, one might argue that in real-life situations, it is also performance, not attention in itself, which ultimately matters.

4.4. Conclusion

In summary, BLAST provides one of the few possible task designs to measure fluctuations of executive attention behaviorally on a second-to-second basis, and because performance is measured so often, it can provide a first indication of an individual's ability to stay on task in less than a minute, with numerous possible applications (testing the effects of a pharmacological treatment, evaluating the cognitive impact of short pathophysiological events such as epileptic spikes, measuring the benefits of cognitive rehabilitation or attention training programs, ...). In addition, the comparison of performance between BLAST and its simplified versions can potentially reveal a deficit in a specific cognitive process, such as encoding/maintenance or visual search, which can then be related with specific brain regions thanks to our detailed knowledge of the BLAST cortical network. For basic research purposes, BLAST is also currently used to understand the neural basis of endogenous attention fluctuations and MLA, and the neural correlates of transient performance decrement observed after external distractions or during multi-tasking.

CRediT authorship contribution statement

Mathilde Petton: Data curation, Formal analysis, Investigation, Visualization, Writing - original draft. **Marcela Perrone-Bertolotti:** Data curation, Formal analysis, Investigation, Visualization, Writing - original draft. **Diego Mac-Auliffe:** Data curation, Investigation, Visualization, Writing - original draft. **Olivier Bertrand:** Funding acquisition, Project administration, Resources. **Pierre-Emmanuel Aguera:** Software. **Florian Sipp:** Software. **Manik Batthacharjee:** Software. **Jean Isnard:** Data curation, Writing - original draft. **Lorella Minotti:** Data curation, Writing - original draft. **Sylvain Rheims:** Data curation, Writing - original draft. **Philippe Kahane:** Data curation, Writing - original draft. **Vania Herbillon:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing - original draft. **Jean-Philippe Lachaux:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neuropsychologia.2019.107151>.

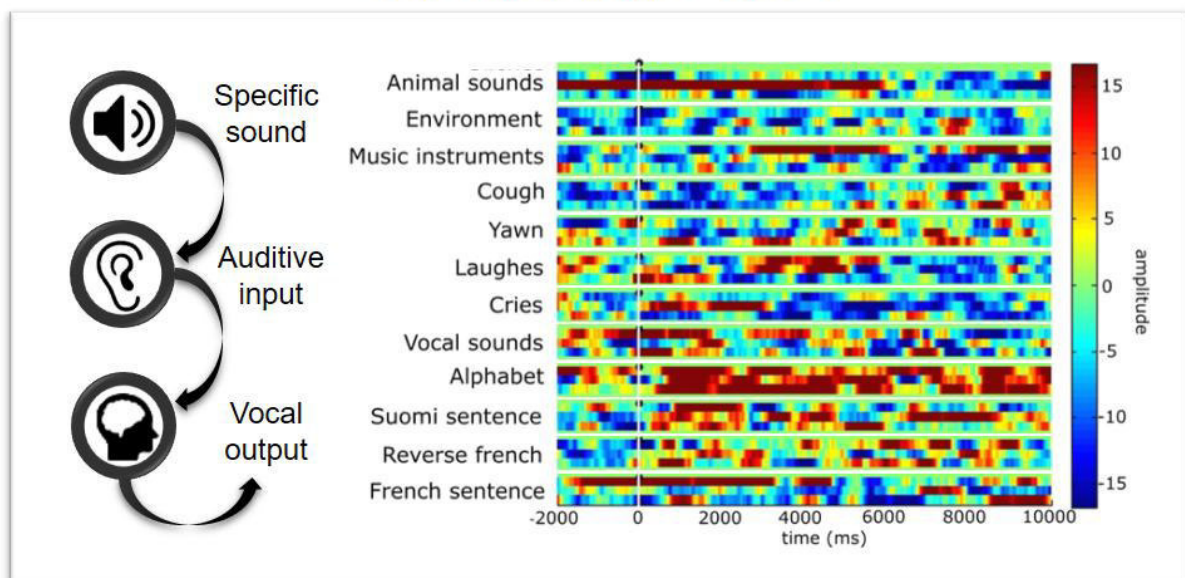
References

- Aguera, P.E., Jerbi, K., Caclin, A., Bertrand, O., 2011. ELAN: a software package for analysis and visualization of MEG, EEG, and LFP signals. *Comput. Intell. Neurosci.* 2011.
- Anticicic, 2013. The Role of Default Network Deactivation in Cognition and Disease, vol. 16, pp. 584–592.
- Anticicic, A.I., Repovs, G., Shulman, G.L.B.D., 2010. NIH public access. *Neuroimage* 49, 2638–2648.
- Baddeley, A., 2000. The episodic buffer—a new component of working memory? [Internet]. *Trends Cogn. Sci.* 4, 417–423. Available from: <http://eprints.whiterose.ac.uk/66016/>.
- Bender, S., Banaschewski, T., Roessner, V., Klein, C., Rietschel, M., Feige, B., et al., 2015. Variability of single trial brain activation predicts fluctuations in reaction time [Internet]. *Biol. Psychol.* 106, 50–60. Available from: <https://doi.org/10.1016/j.biopsycho.2015.01.013>.
- Buschman, T.J., Miller, E.K., 2007. Top down versus bottom up control of attention in the prefrontal and posterior parietal cortices [Internet]. *Science* 315 (80), 1860–1862. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17395832>.
- Caron, A., 2015. Aider son enfant à gérer l'impulsivité et l'attention - Attentif à la maison. Christidi, F., Kararizou, E., Triantafyllou, N., Anagnostouli, M., Zalonis, I., 2015. Derived Trail Making Test indices: demographics and cognitive background variables across the adult life span. *Aging Neuropsychol. Cognit.* 22, 667–678.
- Christoff, K., Gordon, A.M., Smallwood, J., Smith, R., Schooler, J.W., 2009. Experience sampling during fMRI reveals default network and executive system contributions to mind wandering [Internet]. *Proc. Natl. Acad. Sci.* 106, 8719–8724. Available from: <http://www.pnas.org/cgi/doi/10.1073/pnas.0900234106>.
- Christoff, K., Irving, Z.C., Fox, K.C.R., Spreng, R.N., Andrews-Hanna, J.R., 2016. Mind-wandering as spontaneous thought: a dynamic framework [Internet]. *Nat. Rev. Neurosci.* 17, 718–731. Available from: <http://www.nature.com/doi/10.1038/nrn.2016.113>.
- Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain [Internet]. *Nat. Rev. Neurosci.* 3, 215–229. Available from: <http://www.nature.com/doi/10.1038/nrn755>.
- Diamond, A., Ling, D.S., 2016. Interventions, programs, and approaches that appear promising for improving executive functions and those that, despite much hype, do not [Internet]. *Dev. Cogn. Neurosci.* 18, 34–48. Available from: <https://doi.org/10.1016/j.dcn.2015.11.005>.
- Donkelaar Ten, H.J., Tzourio-Mazoyer, N., Mai, J.K., 2018. Toward a common terminology for the gyri and sulci of the human cerebral cortex. *Front. Neuroanat.* 12, 93.
- DuPaul, G.J., Power, T.J., Anastopoulos, A.D., Reid, R., 1998. ADHD Rating Scale-IV. Checklists, Norms and Clinical Interpretation. 1998.
- Esposito, F., Aragri, A., Latorre, V., Popolizio, T., Scarabino, T., Cirillo, S., et al., 2009. Does the default-mode functional connectivity of the brain correlate with working-memory performances? *Arch. Ital. Biol.* 147, 11–20.
- Esterman, M., Noonan, S.K., Rosenberg, M., Degutis, J., 2013. In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. *Cerebr. Cortex* 23, 2712–2723.
- Genovese, C.R., Lazar, N.A., Nichols, T., 2002. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage* 15, 870–878.
- Gmelin, D., Fuermaier, A.B.M., Walther, S., Tucha, L., Koerts, J., Lange, K.W., et al., 2016. Attentional lapses of adults with attention deficit hyperactivity disorder in tasks of sustained attention. *Arch. Clin. Neuropsychol.* 31, 343–357.
- Gogtay, N., Giedd, J.N., Lusk, L., Hayashi, K.M., Greenstein, D., Vaituzis, A.C., et al., 2004. Dynamic mapping of human cortical development during childhood through early adulthood. *Proc. Natl. Acad. Sci. U.S.A.* 101, 8174–8179.
- Homack, S., Riccio, C.A., 2006. Conners' continuous performance test (2nd ed.; CCPT-II) task demands and descriptive information [Internet]. *J. Atten. Disord.* 9, 556–558. Available from: <http://journals.sagepub.com/doi/pdf/10.1177/1087054705283578>.
- Killingsworth, M.A., Gilbert, D.T., 2010. A wandering mind is an unhappy mind [Internet]. 80-. *Science* 330 932–932. Available from: <http://www.sciencemag.org/cgi/doi/10.1126/science.1192439>.

- Kolb, J., Beauchamp, P., Faubert, J., 2011. Visual perception training: cutting edge psychophysics and 3D technology applied to sport science. *Circuit* 1–14.
- Kuzovkin, I., Vicente, R., Petton, M., Lachaux, J.P., Bacia, M., Kahane, P., Rheims, S., J., Vidal, A., 2018. Activations of deep convolutional neural networks are aligned with gamma band activity of human visual cortex. *Commun. Biol.* 1 (1), 107.
- Lachaux, J.-P., Axmacher, N., Mormann, F., Halgren, E., Crone, N.E., 2012. High-frequency neural activity and human cognition: past, present and possible future of intracranial EEG research [Internet]. *Prog. Neurobiol.* 98, 279–301. Available from: <https://doi.org/10.1016/j.pneurobio.2012.06.008>.
- Lachaux, J.P., Jung, J., Mainy, N., Dreher, J.C., Bertrand, O., Bacia, M., et al., 2008. Silence is golden: transient neural deactivation in the prefrontal cortex during attentive reading. *Cerebr. Cortex* 18, 443–450.
- Langner, R., Eickhoff, S.B., 2013. Sustaining attention to simple tasks: a meta-analytic review of the neural mechanisms of vigilant attention. [Internet]. *Psychol. Bull.* 139, 870–900. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3627747&tool=pmcentrez&rendertype=abstract>.
- Li, C.S.R., Yan, P., Bergquist, K.L., Sinha, R., 2007. Greater activation of the 'default' brain regions predicts stop signal errors. *Neuroimage* 38, 640–648.
- Lowe, C., Rabbitt, P., 1998. Test/re-test reliability of the CANTAB and ISPOCD neuropsychological batteries: theoretical and practical issues. *Neuropsychologia* 36, 915–923.
- McVay, J.C., Kane, M.J., 2010. Does mind wandering reflect executive function or executive failure? Comment on Smallwood and Schooler (2006) and Watkins (2008). *Psychol. Bull.* (2), 188–197 Mar;136.
- Mad, T., Baars, B.J., Franklin, S., 2011. The timing of the cognitive cycle. *PLoS One* 6, Mangine, G.T., Hoffman, J.R., Wells, A.J., Gonzalez, A.M., Rogowski, J.P., Townsend, J.R., et al., 2014. Visual tracking speed is related to basketball-specific measures of performance in NBA players. *J. Strength Cond. Res.* 28, 2406–2414.
- Mason, et al., 2007. Wandering minds: the default network and stimulus-independent thought. *Science* 315, 399–395.
- Mayer, J.S., Roebroek, A., Maurer, K., Linden, D.E.J., 2010. Specialization in the default mode: task-induced brain deactivations dissociate between visual working memory and attention. *Hum. Brain Mapp.* 31, 126–139.
- Noudoost, B., Chang, M.H., Steinmetz, N.A., Moore, T., 2010. Top-down control of visual attention [Internet]. *Curr. Opin. Neurobiol.* 20, 183–190. Available from: <https://doi.org/10.1016/j.conb.2010.02.003>.
- Ossandon, T., Vidal, J.R., Ciomas, C., Jerbi, K., Hamame, C.M., Dalal, S.S., et al., 2012. Efficient 'Pop-Out' visual search elicits sustained broadband gamma activity in the dorsal attention network [Internet]. *J. Neurosci.* 32, 3414–3421. Available from: <http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.6048-11.2012>.
- Petris, M.T.R., Jones, R.D., Davidson, P.R., Carroll, G.J., Bones, P.J., 2006. Frequent lapses of responsiveness during an extended visuomotor tracking task in non-sleep-deprived subjects. *J. Sleep Res.* 15, 291–300.
- Phillips, R.C., Salo, T., Carter, C.S., 2015. Distinct neural correlates for attention lapses in patients with schizophrenia and healthy participants. [Internet]. *Front. Hum. Neurosci.* 9, 502. Available from: <http://journal.frontiersin.org/article/10.3389/fnhum.2015.00502/abstract>.
- Poerio, G.L., Sormaz, M., Wang, H.T., Margulies, D., Jefferies, E., Smallwood, J., 2017. The role of the default mode network in component processes underlying the wandering mind. *Soc. Cogn. Affect. Neurosci.* 12, 1047–1062.
- Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. [Internet]. *Proc. Natl. Acad. Sci. U.S.A.* 98, 676–682. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=14647&tool=pmcentrez&rendertype=abstract>.
- Ritaccio, A., Brunner, P., Gunduz, A., Hermes, D., Hirsch, L.J., Jacobs, J., et al., 2014. Proceedings of the Fifth International Workshop on Advances in Electroencephalography [Internet], vol. 41. *Epilepsy Behav.* pp. 183–192. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1525505014004466>.
- Robertson, I.H., Manly, T., Andrade, J., Baddeley, B.T., Yiend, J., 1997. Oops! performance correlates of everyday attention failures in traumatic brain injured and normal subjects. *Neuropsychologia* 35, 747–758.
- Romeas, T., Guldner, A., Faubert, J., 2016. 3D-Multiple Object Tracking training task improves passing decision-making accuracy in soccer players. *Psychol. Sport Exerc.* 22, 1–9.
- Rosario Rueda, M., Posner, M.I., Rothbart, M.K., 2005. The development of executive attention: contributions to the emergence of self-regulation. *Dev. Psychol.* 28 (2), 573–594.
- Sakai, K., 2008. Task set and prefrontal cortex [Internet]. *Annu. Rev. Neurosci.* 31, 219–245. Available from: <http://www.annualreviews.org/doi/10.1146/annurev.neuro.31.060407.125642>.
- Seidl, K.N., Peelen, M.V., Kastner, S., 2012. Neural evidence for distracter suppression during visual search in real-world scenes [Internet]. *J. Neurosci.* 32, 11812–11819. Available from: <http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.1693-12.2012>.
- Seli, P., Cheyne, J.A., Smilek, D., 2013. Wandering minds and wavering rhythms: linking mind wandering and behavioral variability. *J. Exp. Psychol. Hum. Percept. Perform.* 39 (1), 1–5.
- Smallwood, J., Schooler, J.W., 2006. The restless mind. [Internet]. *Psychol. Conscious. Theory Res. Pract.* 1, 130–149. <https://doi.org/10.1037/0033-2909.132.6.946>. Available from: <http://doi.apa.org/getdoi.cfm?>
- Stawarczyk, D., Majerus, S., Maquet, P., D'Argembeau, A., 2011. Neural correlates of ongoing conscious experience: both task-unrelatedness and stimulus-independence are related to default network activity. *PLoS One* 6.
- Tamm, L., Narad, M.E., Antonini, T.N., O'Brien, K.M., Hawk, L.W., Epstein, J.N., 2012. Reaction time variability in ADHD: a review. *Neurotherapeutics* 9, 500–508.
- Toga, A.W., Thompson, P.M., Sowell, E.R., 2006. Mapping brain maturation. *Trends Neurosci.* 29, 148–159.
- Wechsler, D., 2003. Wechsler intelligence scale for children-Fourth Edition (WISC-IV) [Internet]. San Antonio, TX: Psychological Corp. Available from: <https://www.pearsonassessments.com/HAIWEB/Cultures/en-us/ProductDetail.htm?Pid=015-8979-044&Mode=resource%5Chttp://www.pearsonclinical.com/psychology/products/100000310/wechsler-intelligence-scale-for-children-fourth-edition-wisciv.html?Pid=015-8979-044&Mo>.
- Wechsler, D., 2008. Wechsler adult intelligence scale-Fourth Edition (WAIS-IV) [Internet]. San Antonio, TX: NCS Pearson. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Wechsler+Adult+Intelligence+Scale+_+3rd+edition#3%0A <http://www.statisticssolutions.com/academic-solutions/resources/directory-of-survey-instruments/wechsler-adult-intelligence-scale-fourth-edition>.
- Weissman, D.H., Roberts, K.C., Visscher, K.M., Woldorff, M.G., 2006. The neural bases of momentary lapses in attention. [Internet]. *Nat. Neurosci.* 9, 971–978. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16767087>.

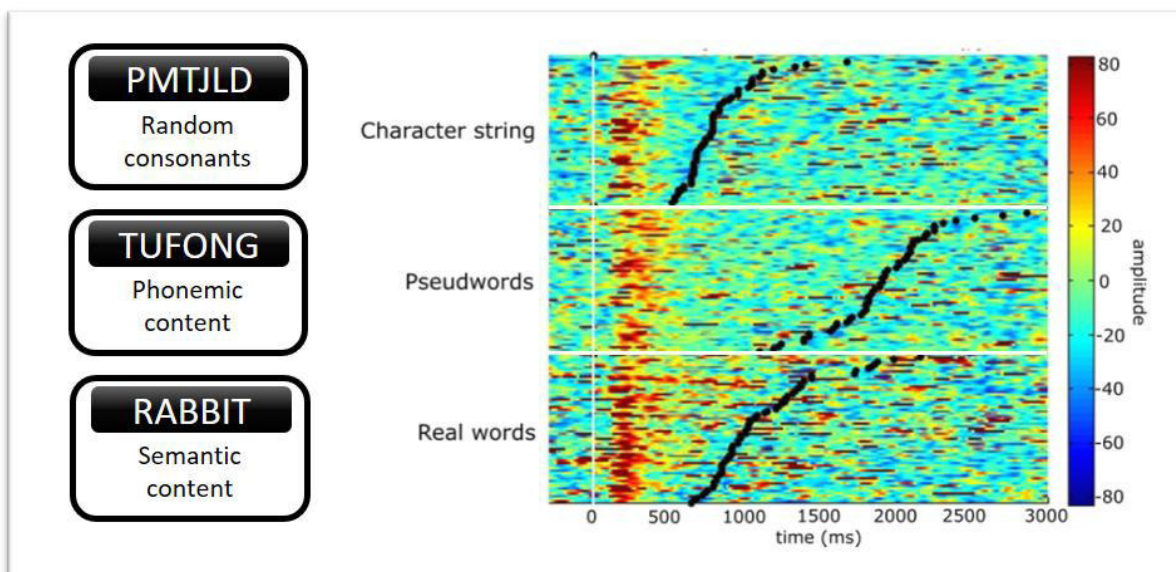
Explanation of each localizer used during the thesis. Each localizer allow the analysis of HFA variations under different experimental conditions to elicit different fundamental sensory, cognitive and motor processes. We used seven types of localizers.

AUDI: left vIPMC - Broca



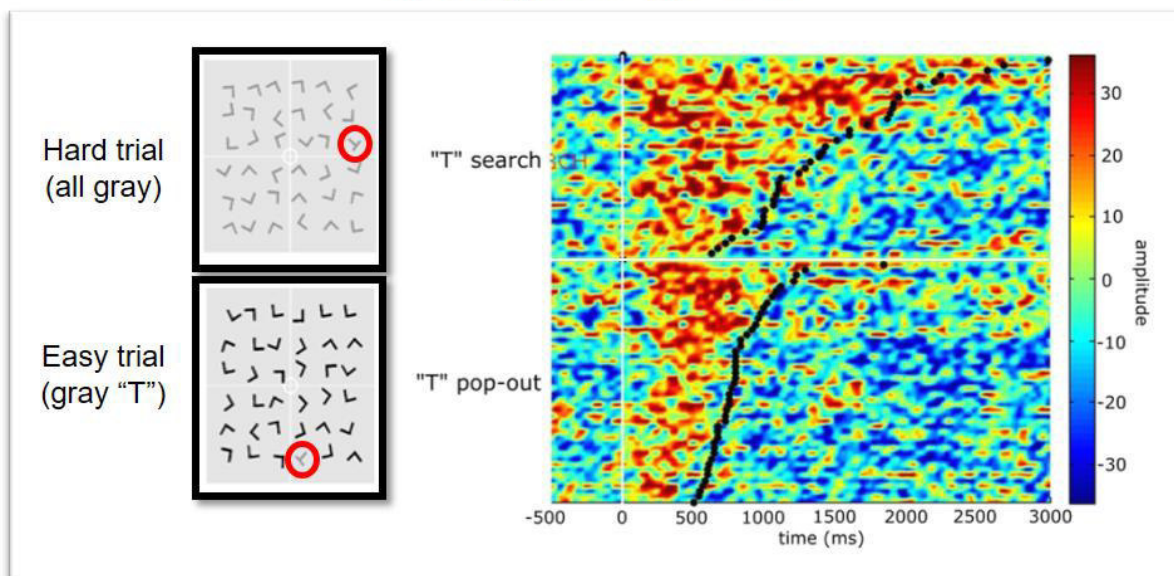
AUDI: each patient must recognize the specific sound within each sound possibility in the Y-axis, and respond aloud.

LEC: left MTG - VWFA



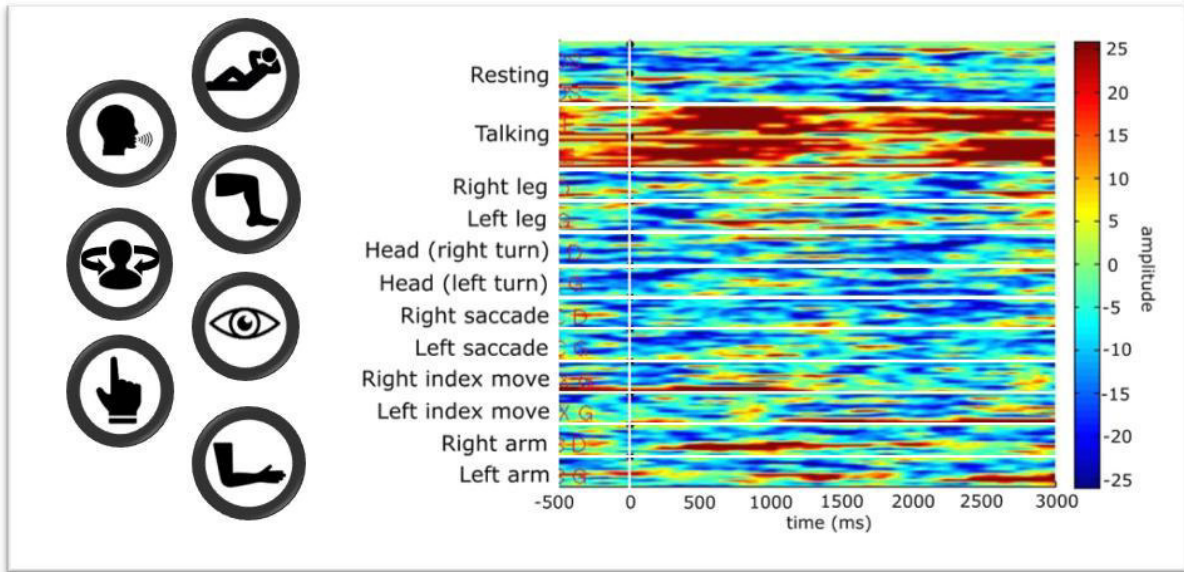
LEC: each patient must recognize if a series of five letters form a string of words with semantic content, a pseudoword with phonemic content, or a random consonant string, and press a button in a gamepad.

ATT: right dIPMC - FEF



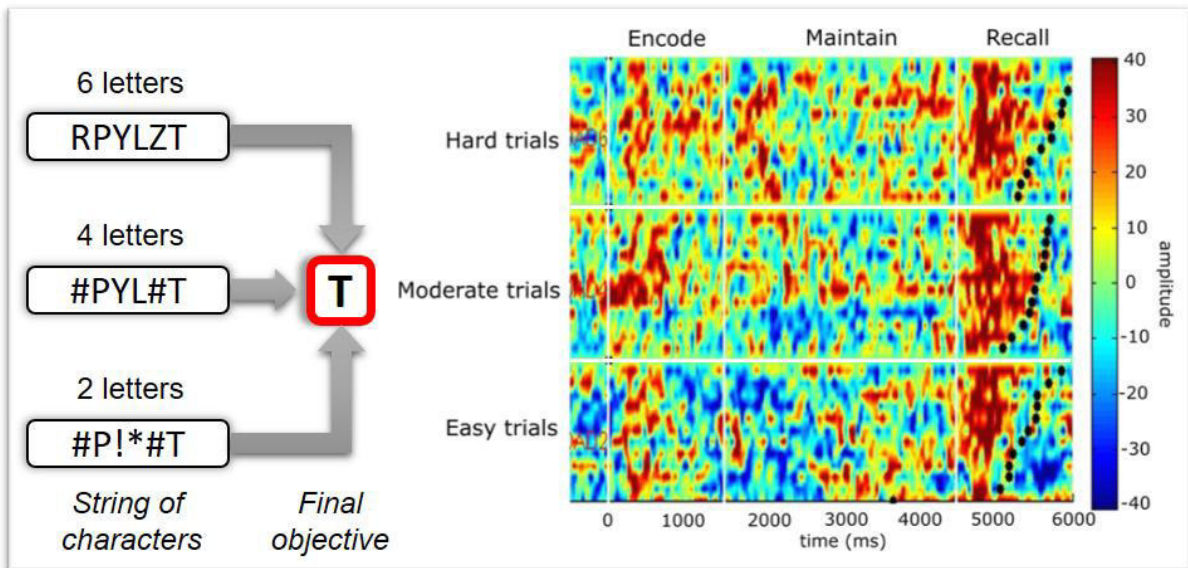
ATT: each patient must recognize if a gray "T" appears at random in the upper or lower half of a 12x12 array. In the easy version, the letter "T" is surrounded by black letters "L" ("T" pop-out), while in the difficult version, the letter "T" is surrounded by grey letters "L" ("T" search), and press a button in a gamepad.

MOTO: left motor cortex – head homunculus



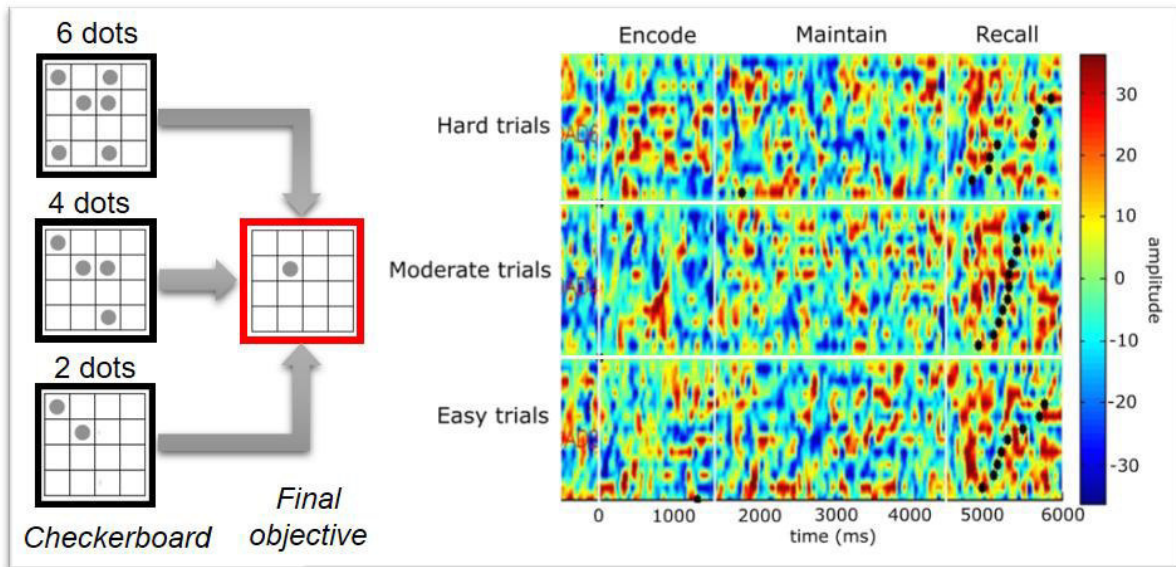
MOTO: each patient must execute different movements under command within each possibility in the Y-axis.

VEBM: left dIPMC



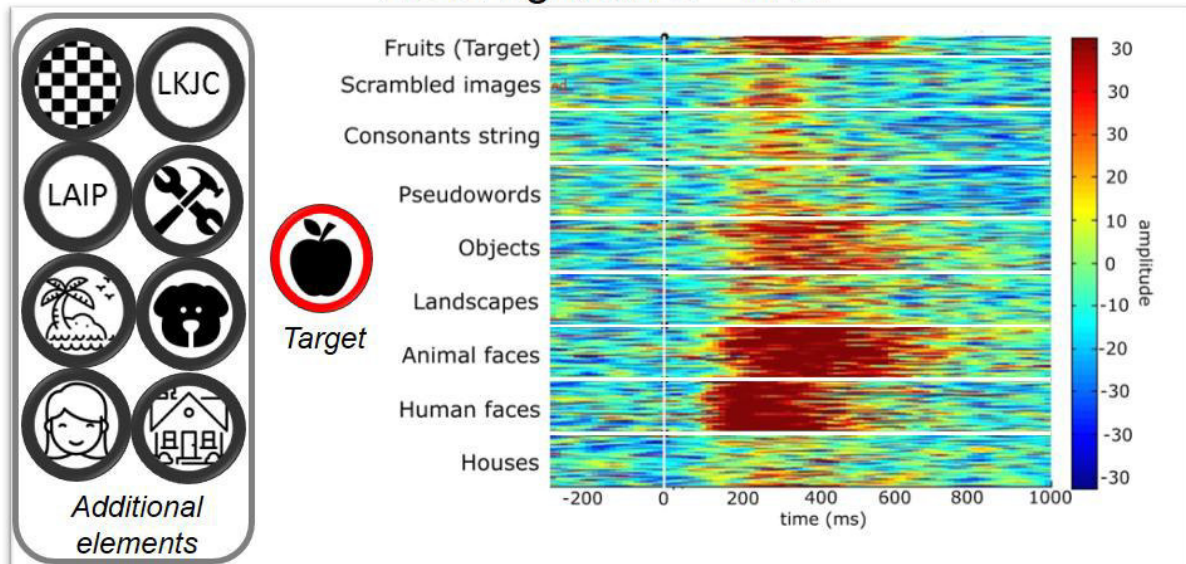
VEBM: each patient must identify whether a particular letter is within a string of six characters. Each string string has six slots, of which 2, 4 or 6 slots can be alphabet letters (easy, moderate or hard trials respectively). The string is shown (encode), to be replaced by a momentary fix and then by a single letter, which must be confirmed or not by the patient as part of the string (recall).

VISM: left anterior vlPFC



VISM: each patient must identify if a particular dot is part of a 4x4 checkboard dotted with 2, 4 or 6 random black dots (easy, moderate or hard trial respectively). The dotted checkboard is shown (encode), to be replaced by a momentary fix and then by a checkboard with a single dot, which must be confirmed or not by the patient as part of the dotted checkboard (recall).

VISU: right dITG - FFA



VISU: each patient must observe images with different topics within each possibility delivered in the Y-axis, and identify the fruits by pressing a button on a gamepad.

Annex N°3 – Table I: MNI-coordinates

For each site displayed in the figures with the anatomical labelization provided by the Freesurfer software (corrected when obviously inaccurate) (<https://surfer.nmr.mgh.harvard.edu>)

Patient id	iEEG site	x	y	z	Freesurfer labelization
P1	R9	67	0	10	Subcentral gyrus
P1	F6	41	-50	-13	Lateral Occipito-Temporal Sulcus
P2	M9	38	8	33	Inferior Frontal Sulcus
P3	X7	34	25	2	Anterior Insula
P3	X'9	-30	23	5	Anterior Insula
P4	R'9	-61	7	16	Precentral Gyrus
P4	G'13	-45	33	21	Inferior Frontal Sulcus
P4	F'9	-28	44	30	Middle Frontal Sulcus
P4	Y'13	-31	50	27	Middle Frontal Gyrus
P4	E'7	-50	-37	-21	Inferior Temporal Gyrus
P5	S'9	-41	0	40	Precentral Sulcus
P5	K'10	-42	35	12	Inferior Frontal Sulcus
P5	Z'2	-11	19	46	Anterior Cingulate Gyrus/Sulcus
P5	L'3	-36	-52	-11	Lateral Occipito-Temporal Sulcus
P6	D'7	-55	-42	8	Superior Temporal Sulcus
P7	E4	41	17	4	Anterior Insula
P7	S2	11	16	52	Anterior Cingulate Gyrus/Sulcus

P9	G'12	-45	41	14	Middle Frontal Gyrus
P11	Q'2	-40	25	14	Inferior Frontal Sulcus
P11	X5	30	20	-6	Anterior Insula
P11	X'9	-30	23	5	Anterior Insula
P11	C'12	-60	-37	-12	Middle Temporal Gyrus
P12	X7	33	17	10	Anterior Insula
P12	A9	52	-3	-20	Middle Temporal Gyrus

V2 suppression in an attentive reading task : Why SMS and street crossing don't go well together

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Keywords: Induced gamma response, Event-related potential, Attention, Intracranial EEG

1. Letter

1.1. Experiment

Tasks such as reading sms, which require focused attention on the central visual field are now routinely performed in situations that require constant peripheral monitoring of potential life-threatening events. This has led to such an increase in street accidents that some countries have launched national prevention campaigns warning against the use of smartphones during street crossing (cf Commercial done by the Lausanne police for road safety (multimédia)). In principle, though, such accidents should be prevented by the ventral attentional network (VAN) which main function is to act as a circuit-breaker and reorient visual attention towards salient peripheral events (Corbetta & Shulman, 2002). Yet, accidents suggest that the VAN is either inhibited during attentive reading, or that the processing of peripheral visual information is blocked at an earlier stage. Indeed, intracranial EEG studies in Humans have shown that flashed foveal visual stimuli induce a transient suppression of activity in the Peripheral Primary Visual Cortex (in V2) (Lachaux et al., 2005). In this study, we present results from a simple reading task showing that this effect is accentuated by attention : the suppression is longer when the central stimulus is processed attentively and requires high-level processing, as sms do. We recorded intracranial EEG in four participants implanted with stereo-EEG electrodes in the parietal, occipital and temporal cortex, including area V2. The participants were asked to read a story shown word by word at a rapid pace (700 ms Inter-Stimulus Interval) interspaced with frequent distractors (words to be ignored, cf fig1 for details). We analyzed the variation of High-Frequency Activity (HFA , between 50 Hz and 150 Hz) as a proxy of population-level spiking activity (Buzsáki et al., 2012) induced by word stimuli and compared pre- vs. post-stimulus activity to detect positive or negative responses (Wilcoxon test $p < 0.01$, fig1). We found that words flashed in the foveal field

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elicit a neural activity suppression in representations of the peripheral field in V2 (i.e. sites that elicited peripheral phosphenes when stimulated electrically at 50 Hz during the usual clinical stimulation procedure). This suppression was predicted by earlier reports of similar suppressions in response to faces (Lachaux et al., 2005). We reveal here that this suppression is modulated by the task-relevance of the stimulus : attended words induced a longer significant suppression than unattended words.

1.2. Discussion

Given that natural sentence reading is paced by quasi-periodic fixations every 300-400 ms on average (Vidal et al., 2012), our results predict a close-to-continuous activity suppression in V2 while reading sms attentively, for neurons with peripheral receptive fields, and that could explain why salient peripheral events can fail to attract attention under such conditions. In principle, the VAN should act as a circuit-breaker to interrupt reading, but anatomical studies have shown that the VAN receives its visual inputs from primary visual areas and might therefore not react if their activity is suppressed. Although we could only show suppression in V2, similar V1 suppression has been found in non-humans primates in a study combining electrophysiological recording and fMRI (Shmuel et al., 2006). One might object to our proposal that it is based on an additive model of V2 responses, in which peripheral stimuli would fail to elicit a normal V2 response because that response would be cancelled by the sharp activity suppression caused by attending a foveal stimulus just before. Indeed, we acknowledge that future experiments should demonstrate reduced V2 responses to peripheral stimuli shown shortly after a central target. At the behavioral level, it is already well documented that participants fail to notice central targets flashed in the vicinity of an immediately preceding stimulus (a phenomenon known as forward masking), and the V2 suppression described here might contribute to the masking effect. Note that masking is maximal until the second stimulus is presented around 200 ms after the masking stimulus, that is, when the neural response to that second stimulus occurs during the peak of the suppression caused by the first stimulus (Habak et al., 2006). It remains to be determined why visual words trigger a longer V2 suppression in the attention condition : it mirrors the longer activation triggered by the same stimuli in other parts of the visual system (Wilcoxon test $p < 0.01$, supp fig1). The latter has been described as combining two components : a) an initial bottom-up stimulus-driven response superimposed with b) a second, later component due to top-down attentional processes (Pooremaeili & Roelfsema, 2014). One interesting possibility is that the neural suppression in V2 is also composed of an initial "reflexive" negative response followed by a late suppression driven by top-down attentional processes, which role might be to protect active processing in other parts of the visual system from interference by potential distractors. It remains to be understood however, why the suppression would last until 400 ms while the central stimulus stays only on screen for 200 ms.

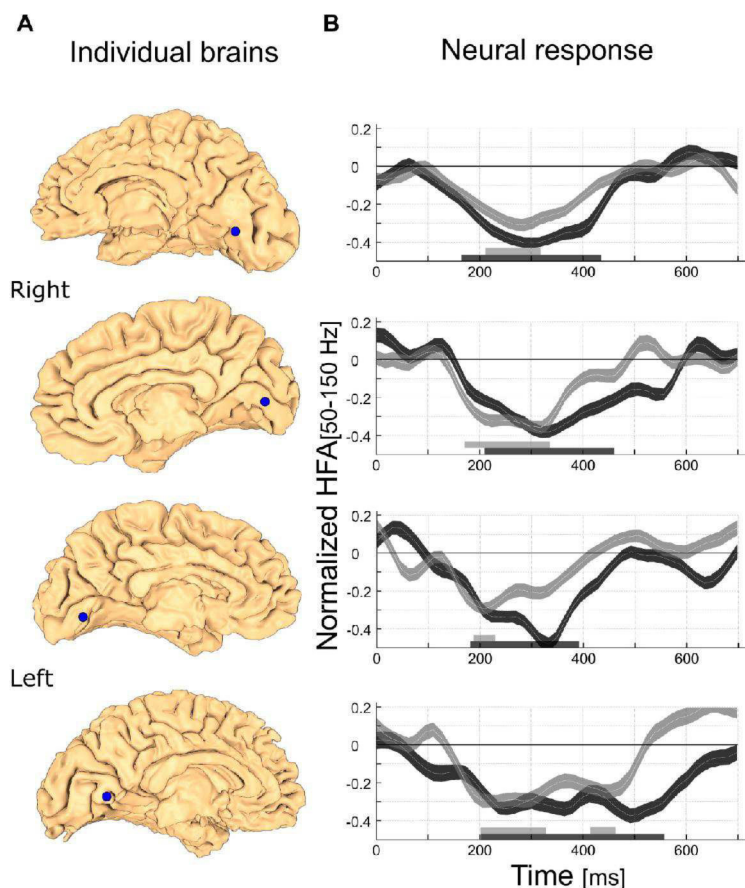


Figure 1: Central visual stimuli elicit a suppression of neural activity in V2, enhanced by attention. (A) Precise location of the recording sites for each patient (2 males, 2 females, 16 to 33 y.o.). In all sites, standard clinical electrical stimulations at 50 Hz elicited peripheral visual phosphenes. (B) Participants were presented with white and grey words flashed for 200 ms at the center of a computer screen : white words had to be ignored (IGN, grey plots) while grey words had to be read (ATT, in black) and formed a story that the participant had to report at the end. Right graphs show normalized HFA for each recording site between 0 and 700 ms following stimulus onset averaged across 200 words (+/- s.e.m). Bars above the time axis indicated time windows with significant deactivation relative to prestimulus baseline (-200:0 ms; Wilcoxon test, $p < 0.01$).

References

- Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents — EEG, ECoG, LFP and spikes. *Nature reviews. Neuroscience*, *13*, 407–420.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, *3*, 201.
- Habak, C., Wilkinson, F., & Wilson, H. R. (2006). Dynamics of shape interaction in human vision. *Vision Research*, *46*, 4305–4320.
- Lachaux, J.-P., George, N., Tallon-Baudry, C., Martinerie, J., Hugueville, L., Minotti, L., Kahane, P., & Renault, B. (2005). The many faces of the gamma band response to complex visual stimuli. *NeuroImage*, *25*, 491–501.
- multimédia, D. d. I. V. e. c.-W. . (). Anastase: le tour de magie, plus de 5 millions de vues !
- Pooresmaeili, A., & Roelfsema, P. R. (2014). A Growth-Cone Model for the Spread of Object-Based Attention during Contour Grouping. *Current Biology*, *24*, 2869–2877.
- Shmuel, A., Augath, M., Oeltermann, A., & Logothetis, N. K. (2006). Negative functional MRI response correlates with decreases in neuronal activity in monkey visual area V1. *Nature Neuroscience*, *9*, 569–577.
- Vidal, J. R., Freyermuth, S., Jerbi, K., Hamamé, C. M., Ossandon, T., Bertrand, O., Minotti, L., Kahane, P., Berthoz, A., & Lachaux, J.-P. (2012). Long-Distance Amplitude Correlations in the High Gamma Band Reveal Segregation and Integration within the Reading Network. *Journal of Neuroscience*, *32*, 6421–6434.

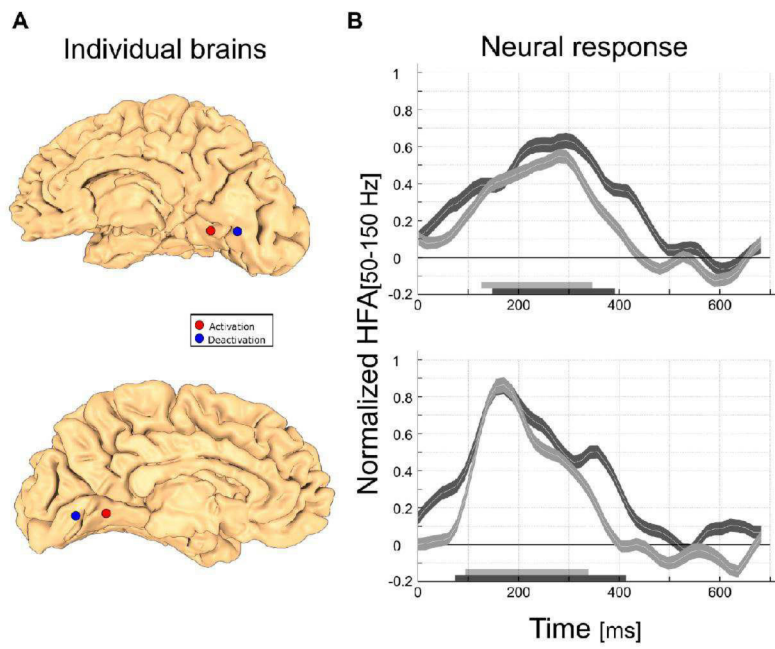


Figure 2: Supplementary. Timing of neural activation induced by visual stimuli (A) individual anatomy showing sites in which central visual stimuli trigger an increase (red) vs. a decrease (blue) of neural activity. (B) Normalized HFA[50-150 Hz] for each recording site in the 700 ms following stimulus onset (onset at 0 ms) (median \pm s.e.m, $n = 200$ trials). Horizontal bars indicate time windows with significant HFA increase relative to pre-stimulus baseline level (-200:0 ms; Wilcoxon test, $p < 0,01$).