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Content and frequency of dream reports : psychological and neurophysiological correlates

Raphaël Vallat

To cite this version:

Raphaël Vallat. Content and frequency of dream reports : psychological and neurophysiological correlates. Neuroscience. Université de Lyon, 2017. English. NNT : 2017LYSE1335 . tel-01737934

HAL Id: tel-01737934

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THÈSE DE DOCTORAT DE L'UNIVERSITÉ DE LYON

Opérée au sein de

l'Université Claude Bernard Lyon 1

École doctorale

Neurosciences et Cognition (ED476)

Spécialité de doctorat

Neurosciences

Soutenue publiquement le 8 décembre 2017 par

Raphael Vallat

FRÉQUENCE ET CONTENU DU RAPPORT DE RÊVE: Approches Comportementales et Neurophysiologiques

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DOCTORAL THESIS OF LYON UNIVERSITY

Delivered by

Lyon 1 University

Doctoral School

Neurosciences and Cognition (ED476)

Publicly defended on the December 8th, 2017, by

Raphael Vallat

CONTENT AND FREQUENCY OF DREAM REPORTS

Psychological and Neurophysiological Correlates

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— **Jean-Jacques Grandville**
Second rêve: une promenade dans le ciel. 1847

Abstract

Humans have been intrigued by their dreams since the dawn of time. Yet, despite millennia of exploration, several questions regarding dreaming are still unresolved. The goal of the present thesis was to improve our understanding of this phenomenon through several studies, involving different methodologies and each addressing a particular aspect of dreaming. First, we investigated the mechanism of dream recall by comparing the cognitive, psychological and brain functioning of high and low dream recallers (HR and LR, respectively) during sleep and wakefulness (Studies 1 to 4). Second, we investigated the content and function of dreaming through an extensive behavioral analysis of the relationship between waking-life and dream content (Study 5). Finally, we leveraged our expertise in sleep science to develop an open-source and comprehensive software dedicated to sleep analysis (Study 6).

With regards to dream recall, our results revealed that the ability to recall dream is positively associated with a specific neurophysiological profile, characterized notably by an increased activity in the default mode network during both sleep and wakefulness. For instance, we observed that, as compared to LR, HR exhibit a greater functional connectivity in regions critical to memory encoding just after awakening from sleep. HR also showed longer intra-sleep awakenings and higher scores of creative-thinking than LR. These findings led us to propose an integrative and comprehensive model of the dream recall process. Furthermore, the results of Study 5 enhanced and refined our comprehension of the continuity between waking-life and dream content, and provided support for the hypothesis of an active role of dreaming in emotional regulation. In conclusion, the experimental, theoretical and methodological contributions of the present work could serve as a basis for future research, in the hope that someday, we will be able to apprehend dreaming in all its richness and diversity.

Keywords: Dream, sleep, awakening, memory, magnetic resonance imaging, electroencephalography, brain networks, software development

Résumé

Objet de nombreuses spéculations religieuses, philosophiques et scientifiques, le rêve reste encore l'une des grandes *terra incognita* de la cognition humaine. Le présent travail de thèse s'est attaché à améliorer notre compréhension de ce phénomène, en abordant ses multiples facettes à l'aide de méthodes comportementales et neuroscientifiques. Dans un premier temps, nous avons étudié les mécanismes du rappel du rêve en comparant le fonctionnement cognitif et cérébral de personnes se souvenant de leurs rêves très fréquemment (*Rêveurs*) ou très rarement (*Non-rêveurs*). Dans un deuxième temps, nous avons abordé la question de la fonction du rêve, en caractérisant notamment l'influence de la vie éveillée sur le contenu onirique. En parallèle de ces travaux, nous avons joué un rôle fondateur dans le développement d'un logiciel libre permettant la visualisation et l'analyse de tracés polysomnographiques de sommeil.

Nos résultats ont montré que la capacité à se souvenir de ses rêves est associée à un profil neurophysiologique et cognitif spécifique, caractérisé entre autre par une plus forte activité dans le réseau par défaut au cours de l'éveil, du sommeil, et dans les premières minutes suivant le réveil, période critique pour l'encodage du rêve en mémoire. Combinant ces résultats et la littérature existante, nous avons proposé un modèle intégratif du processus de mémorisation du rêve. Par ailleurs, nos observations comportementales ont permis d'améliorer notre compréhension de la continuité entre le contenu du rêve et la vie éveillée, et ont remarquablement suggéré que le rêve pourrait avoir un rôle actif dans des processus de régulation émotionnelle. En conclusion, de par ces apports expérimentaux, théoriques et méthodologiques, la présente thèse pourra servir, nous l'espérons, de support pour les futurs travaux visant à appréhender ce phénomène dans toute sa richesse et sa diversité.

Mots-clés: Rêve, sommeil, éveil, mémoire, imagerie par résonance magnétique, électroencéphalographie, réseaux cérébraux, développement logiciel

Acknowledgements

Je tiens avant toute chose à remercier ma directrice de thèse, Perrine Ruby, dont la confiance et le soutien ont rendu possible ce travail. Elle sait, je l'espère, toute la considération et l'amitié que j'ai pour elle, et je ne la remercierai jamais assez de m'avoir toujours poussé vers l'avant, en me donnant les moyens par exemple de participer à de nombreux colloques internationaux. Sa rigueur et son honnêteté scientifique, ainsi que son engagement indéfectible pour ses étudiants, sont autant de qualités que je souhaiterai avoir s'il m'est donné un jour d'encadrer à mon tour des étudiants.

Ma pensée se tourne ensuite vers tous les membres du laboratoire DYCOG avec qui j'ai vécu et partagé des moments inoubliables tout au long de ces quatre dernières années. Sans pouvoir citer, par soucis écologique, toutes les personnes avec qui j'ai échangé, je tiens tout de même à évoquer mes collègues et amis du bureau d'en haut, Laurie-Anne, Kony, Etienne, Enrico, Stefano, dont la présence au Vinatier ne relève sans doute pas d'un hasard total ; les copains du café de 7 h et du saucisson de 19 h, Florian, Benoit, Thibault ; l'équipe des méditants Croix-roussien, Kristien, Antoine, Jelle, Oussama, pour ces moments de rire au milieu des fameux bouchons Lyonnais ; et bien sûr tous les autres doctorants, étudiants, ingénieurs, chercheurs, et personnels administratifs, qui de par leur bonne humeur et leur expertise ont rendu cette thèse si agréable.

Toute ma gratitude se porte également aux participants de nos expériences, d'imagerie ou de comportement, qui sont de fait la composante essentielle de ce travail. Ils nous ont prêté leurs rêves et leurs cerveaux, tout en gardant une motivation sans faille et un sourire constant.

Je pense ensuite à mes amis de longue date, Ylane, Caroline, Olivier, Géraud, Alex, Matthieu, Bertrand, qui ont su égayer ma vie durant toutes ces années, à coup de rires, de délires et de musique.

Le meilleur pour la fin dit-on - je remercie du fond du cœur mes parents, Isabelle et Alain ainsi que ma sœur Amélie et sa petite famille grandissante, sans qui tout cela n'aurait jamais été possible. Ma pensée finale se tournera vers Alisé, qui en plus d'être un sujet idéal pour étudier le sommeil au quotidien, est la personne avec qui je souhaite construire mes rêves.

List of acronyms

AEP: Auditory evoked potential

BOLD: Blood-oxygen-level dependent

DAN: Dorsal attention network

DLPFC: Dorsolateral prefrontal cortex

DMN: Default mode network

DRF: Dream recall frequency

DST: Descending subtraction task

EEG: Electroencephalography

EMG: Electromyography

EOG: Electrooculography

ERP: Event-related potential

fMRI: Functional magnetic resonance imaging

HR: High-(dream)-recaller

ICA: Independent component analysis

KC: K-complex

LR: Low-(dream)-recaller

MPFC: Medial prefrontal cortex

MT: Muscle twitch

NREM: Non-rapid eye movement (sleep)

PET: Positron emission tomography

PSG: Polysomnography

REM: Rapid eye movement (sleep)

ROI: Region of interest

RS: Resting-state

SM: Sensori-motor (network)

TPJ: Temporo-parietal junction

WLE: Waking-life experiences

NB: These acronyms are always first defined in the text before being used as abbreviations.

Curriculum vitæ

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2014–17: Teaching fellow in Neurosciences (200h), Lyon 1 University

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2012: Two-year merit scholarship, from the French Ministry of Education

2014: Three-year PhD fellowship, from the French Ministry of Higher Education and Research

Teaching activities

Neurobiology & Neuroanatomy courses, 1st and 2nd year of Bachelor Degree

Social science courses, 1st year of Medicine

Neuro-imaging courses, Master degree in Neuroscience

Supervision of two students (Graduate and under-graduate in cognitive sciences)

Elected representative of the non-permanent members of the CRNL

List of publications

Peer-reviewed publications

Vallat R., Lajnef T., Eichenlaub J.-B., Berthomier C., Jerbi K., Morlet D., and Ruby P. (2017). Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall. Frontiers in Human Neuroscience, 11.

Vallat R.*, Combrisson E.*, Eichenlaub J-B., O'Reilly C., Lajnef T., Guillot A., Jerbi K. and Ruby P. (2017). Sleep: an open-source python software for visualization, analysis and staging of sleep data. Frontiers in Neuroinformatics, 11. - * *Co-first authors*

Vallat R., Chatard B., Blagrove M. and Ruby P. (2017) Characteristics of the memory sources of dreams: a new version of the content-matching paradigm to take mundane and remote memories into account. Plos One, 12.

Under review

Vallat R., Meunier D., Nicolas A. and Ruby P. Reduced default mode network connectivity and anti-correlation in the minutes following awakening from N2 and N3 sleep: an EEG-fMRI study.

Vallat R., Eskinazi M., Nicolas A. and Ruby P. Sleep habits and dream recall frequency in a representative sample of French students.

In preparation

Vallat R., Nicolas A. and Ruby P. Brain functional connectivity upon awakening from sleep predicts between-subject differences in dream recall frequency.

Vallat R., Nicolas A. and Ruby P. High dream recall frequency is associated with increased creativity and functional connectivity in the default mode network.

Combrisson E., Vallat R., O'Reilly C., Pascarella A., Saive A-L., Thiery T., Meunier D., Althukov D., Lajnef T., Ruby P., Guillot A. and Jerbi K. Visbrain: A multi-purpose GPU-accelerated open-source suite for brain data visualization.

Eskinazi M., Bouet R., Vallat R., Peter-Derex L. and Ruby P. Activity in the hippocampus during arousing reaction from sleep: an intracranial EEG study.

Ruby P., Chatard B., Vallat R., Hoyer R. and Bidet-Caulet A. Top-down and bottom-up attentional processes in high and low dream recallers: an EEG study.

Plailly J., Villalba M., Vallat R., Nicolas A. and Ruby P. Recalling a dream related to a recent experience: does it help episodic memory consolidation?

Oral presentations

Vallat R., Nicolas A. and Ruby P. Brain functional connectivity upon awakening from sleep predicts between-subject differences in dream recall frequency. *Oral presentation for **IASD 2017** conference (USA)*

Vallat R., Meunier D., Nicolas A. and Ruby P. Reduced default mode network connectivity and anti-correlation in the minutes following awakening from N2 and N3 sleep: an EEG-fMRI study. *Oral presentation for **IASD 2016** conference (The Netherlands)*

Vallat R., Lajnef T., Eichenlaub J.-B., Berthomier C., Jerbi K., Morlet D., and Ruby P. (2017). Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall. *Oral presentation for **IASD 2015 and 2014** conferences (USA) and **NPSA 2015** conference (The Netherlands)*

Conference posters

Vallat R., Meunier D., Nicolas A. and Ruby P. Reduced default mode network connectivity and anti-correlation in the minutes following awakening from N2 and N3 sleep: an EEG-fMRI study. *Poster/abstract for **WSC 2017** conference (Czech Republic), **ESRS** 2016 conference (Italia) and **FENS** 2016 conference (Denmark)*

Eskinazi M., Bouet R., Vallat R., Peter-Derex L. and Ruby P. Activity in the hippocampus during arousing reaction from sleep: an intracranial EEG study. *Poster/abstract for **WSC 2017** conference (Czech Republic)*

Vallat R.*, Combrisson E.*, Eichenlaub J-B., O'Reilly C., Lajnef T., Guillot A., Jerbi K. and Ruby P. (2017). Sleep: an open-source python software for visualization, analysis and staging of sleep data. *Poster/abstract for **WSC 2017** conference (Czech Republic)*

Vallat R., Lajnef T., Eichenlaub J.-B., Berthomier C., Jerbi K., Morlet D., and Ruby P. (2017). Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall. *Poster/abstract for **ASSC 2015** conference (France)*

Vallat R., Chatard B., Blagrove M. and Ruby P. (2017) Characteristics of the memory sources of dreams: a new version of the content-matching paradigm to take mundane and remote memories into account. *Poster/abstract for **ASSC 2015** conference (France)*

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“

Dreams are but interludes which Fancy makes;
When monarch Reason sleeps, this mimic wakes:
Compounds a medley of disjointed things,
A mob of cobblers, and a court of kings:
Light fumes are merry, grosser fumes are sad;
Both are the reasonable soul run mad;
And many monstrous forms in sleep we see,
That neither were, nor are, nor e’er can be.
Sometimes forgotten things long cast behind
Rush forward in the brain, and come to mind.
The nurse’s legends are for truths received,
And the man dreams but what the boy believed.
Sometimes we but rehearse a former play,
The night restores our actions done by day;
As hounds in sleep will open for their prey.
In short, the farce of dreams is of a piece,
Chimeras all; and more absurd, or less.

”

— **John Dryden**
Fables, Ancient and Modern. 1700

Part I

GENERAL INTRODUCTION

1 Methods and problems in dream research

> *La science du rêve occupe, sous ces rapports, une situation intermédiaire entre l'histoire et la biologie. Elle est une science d'observation en ce que l'observation y joue le rôle essentiel, mais elle est une science historique en ce sens que le rêve écoulé ne peut jamais être reproduit et qu'il est étudié, non directement, mais par l'intermédiaire du souvenir.*[1]
>
> — **Yves Delage**
> Le rêve. Etude psychologique, philosophique et littéraire. 1920

1.1 Dreams

1.1.1 Definition

Dreaming has fascinated and intrigued mankind since the earliest times. For thousand of years, humans have tried to decipher their dreams and have speculated on their nature and function. Surprisingly however, there is still no consensual and clear-cut definition for the word *dreaming* (Pagel et al., 2001). Rather, the definition has evolved over the centuries along with the ever-growing understanding of this phenomenon. To cite a few examples, dreams were believed to be messages from deities in ancient times (section 4.1.1), thoughts produced upon awakening in the nineteenth century (section 1.3.1), or an epiphenomenom of a specific brain state during sleep in the second half of the last century (section 4.2.1).

The present thesis uses the working definition and model proposed by Guénolé (2009), who stated that *"dreaming is a mental experience during sleep, which can be remembered and reported at wake"*. Accordingly, he proposed that dreaming can be decomposed into three successive and intertwined steps, namely the dream experience, the dream recall, and the dream report (Fig 1.1). These three steps are detailed as follow. First, the primordial state of dreaming is a mental experience that happens during sleep, although we still do not know precisely when (see section 1.3). Very little is known of the dream experience *per se* because it is unobservable to the waking consciousness, be it that of an external observer, or that of the dreamer him- or herself. In order to become observable to the waking consciousness, dreams have to be remembered upon awakening, via the introspective recall of the dreamer (or *"retrospection"*, Schwartz et al., 2005). As any memory trace,

[1] Free English translations of French quotes can be found at the end of the thesis in the *Translations* section.

the dream recall is therefore likely to differ from the original dream experience due to possible forgetting, reconstruction and censorships mechanisms (Schwartz and Maquet, 2002; Schwartz et al., 2005). Finally, the last step is the dream report, which refers to the transcript of the dream memory using either words or pictures. This process leads once more to a potential loss of information because of description difficulties, censorships, shortening and modifications of the dream content. Still, most of the scientific research on dreaming has focused on dream reports since it is the only step that is eligible to empirical and objective investigation.

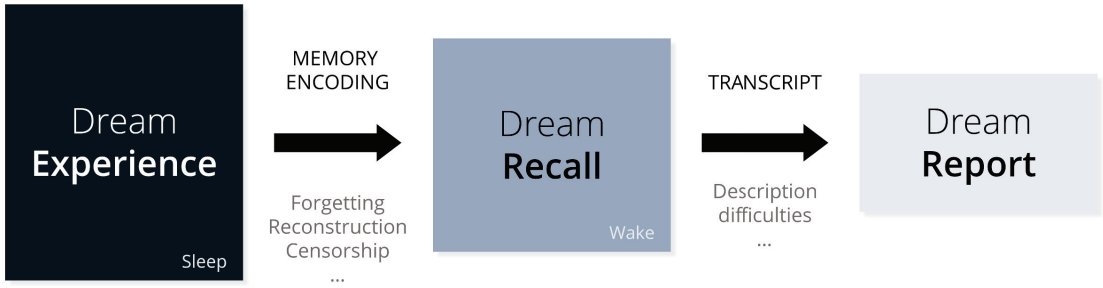


Fig. 1.1 The three successive and intertwined steps of dreaming according to Guenolé's framework. Adapted from Guénolé (2009)

The fact that dreaming can only be observed, at least with objective measures, *"during its absence"* (Paul Valery, Analecta, 1926; see also the epigraph of this chapter) represents one of the greatest impediment to the understanding of its nature and function. For that reason, dreaming remains one of the last *terra incognita* of the human cognition, and many questions regarding its nature, correlates and function are still unresolved. Do we dream during the whole night? If not, when and for how long? Why do we sometimes recall our dreams and sometimes not? To which extent do dream reports obtained after awakening accurately depict the mental experiences during sleep? What is, or what are, the function(s) of dreaming? What are the neurophysiological correlates of dream content and dream recall frequency? The aim of the present thesis is to offer a contribution to the ongoing effort to solve these questions.

1.2 Sleep

Although some authors have postulated that dreaming was not produced during sleep but at the moment of awakening (see section 1.3.1), this hypothesis has been since refuted and the scientific community generally agrees with Schopenhauer's saying that *"the characteristic of dreaming is the condition of sleep peculiar to it"*. Sleep can be defined as a reversible physiological and periodic state which is typically characterized by vigilance suspension, reduced interactions with surroundings, behavioral quiescence and closed eyes. According to the current dominant theory on sleep regulation, namely the *two-process model* (Borbély, 1982), sleep is under the influence of both circadian rhythms (humans are physiologically programmed to sleep at night) and homeostatic drive (the longer an individual remains awake, the sleepier he or she becomes). Furthermore, since prolonged sleep deprivation in animals reliably produces severe pathology and death

(Rechtschaffen et al., 1983; Rechtschaffen et al., 1989), it is now well admitted that *"sleep is the price we pay for being alive"* (Tononi and Cirelli, 2014). Although the full extent of its function is unknown, sleep seems to be critically involved in the restoration of the immune system (Bryant et al., 2004), thermo-regulation (Krueger and Takahashi, 1997), emotional regulation (Goldstein and Walker, 2014) and memory consolidation (Diekelmann and Born, 2010). Long regarded as an idle state, it is becoming increasingly evident that sleep is *"first and foremost a brain process"* (Hirshkowitz, 2004) in which the brain is *"hard at work and helps makes something of the world"*, to borrow the words of Heraclitus (for an exhaustive review of the cognitive processes occurring during sleep, see Andrillon, 2016).

1.2.1 Sleep stages

The invention of electro-encephalography (EEG) by Hans Berger in 1928 has paved the way for the scientific study of sleep. It was indeed soon after that discovery that Alfred Loomis first described a global slowing down of the brain rhythm during sleep, associated with the apparition of several grapho-elements such as K-complexes. Since then, sleep researchers have used EEG to monitor brain waves, electrooculography (EOG) to monitor eye movements and electromyography (EMG) to measure skeletal muscle activity. The simultaneous collection of these measurements is called polysomnography (PSG) and provides sufficient information to identify sleep stages according to standard international established guidelines. PSG is the gold standard in modern sleep science and is used in both clinical and research settings.

A first set of rules were published by Rechtschaffen and Kales (R&K) in 1968 and proposed to divide sleep into 5 stages with distinct electrophysiological properties, named rapid-eye movement (REM) and non-REM (NREM) stages 1, 2, 3, 4. This nomenclature was updated in 2007 by the American Academy of Sleep Medicine (Iber, 2007). Sleep stages 3 and 4 were merged into a single stage, and the four remaining sleep stages were renamed as follow: REM, N1, N2, N3. Below are summarized EEG-EOG-EMG characteristics for wakefulness and the different sleep stages in healthy individuals (Hirshkowitz, 2004; Iber, 2007; see also Fig 1.2).

Wakefulness Eyes-closed quiet wakefulness is accompanied by an EEG rhythm predominantly in the alpha range (8 - 12 Hz). Opening the eyes or engaging in a significant mental task (for example mental calculation) reduces or blocks the alpha activity. Fairly high muscle activity can be present and slow or rapid eye movements may occur.

N1 sleep Stage N1 corresponds to the transitional period between wakefulness and sleep. The brain rhythm progressively decreases from alpha to theta (5 – 7 Hz), and the EOG is characterized by slow waves corresponding to rolling eye movements. N1 sleep represents approximatively 5% of a normal night of sleep.

N2 sleep Each night, we spend more than half of the night's sleep in N2 sleep. The EEG activity during this stage is characterized by a predominance of theta waves, recurrently interrupted by two grapho-elements, the spindles and K-complexes, which are the landmarks of this sleep stage. K-complexes are defined as sharp negative waves followed by a positive component, prominent over frontal scalp electrodes and lasting more than 0.5 seconds. Spindles refer to burst of 11 to 16 Hz waves predominant over central scalp electrodes and lasting between 0.5 and 2 seconds. Beyond that, N2 sleep is characterized by an absence of eye movements as well as decreased muscle tone and brain metabolism.

N3 sleep N3 sleep, also referred to as deep sleep or slow-wave sleep, is characterized by a predominance (> 20% of the 30-sec time window) of high amplitude (> 75 μV) delta waves (0.5 – 4 Hz). Eye motility, muscle tone and brain metabolism are even more decreased than in N2 sleep. N3 sleep represents approximatively 20% of a normal night of sleep.

REM sleep As its name suggests, rapid eye movements (REM) sleep is characterized by rapid eye movements easily observable on the EOG channels. They consist of conjugate, irregular and sharply peaked eye movements, similar to some extent to those exhibited during wakefulness. Another fundamental aspect of REM sleep is the muscle atonia, revealed by a low EMG activity, which was discovered by Michel Jouvet in Lyon in 1959 (see section 1.3.2). However, some transient muscle activity or muscle twitching (MTs) can also be observed. These short irregular bursts of EMG activity are superimposed on the background of low EMG activity. Brain metabolism is similar to that of wakefulness, and the EEG is marked by mixed low-amplitude waves predominantly in the theta band (saw-tooth waves), as well as a complete absence of delta rhythms. REM sleep is also accompanied by clitoris and penile erections (Fisher et al., 1965; Abel et al., 1979). This sleep stage constitutes approximatively 20% of a normal night of sleep.

1.2.2 Sleep architecture

A normal night of sleep consists of a repetition of four or five 90 to 110 minutes long cycles in which sleep stages follow each other in a specific order. The identification of sleep stages (a process called sleep scoring or sleep staging) is generally done visually by inspecting consecutive polysomnographic segments of 30 seconds. It results in a hypnogram which represents the succession of sleep stages across time (Fig 1.3). In his overview of the human sleep, Hirshkowitz (2004) described five generalizations about normal sleep architecture:

1. Sleep is entered through non-REM sleep
2. Non-REM and REM sleep alternate approximately every 90 to 120 minutes
3. N3 sleep predominates in the first third of the night
4. REM sleep predominates in the last half of the night
5. REM sleep occurs in four to six discrete episodes each night with episodes generally lengthening as sleep period progresses

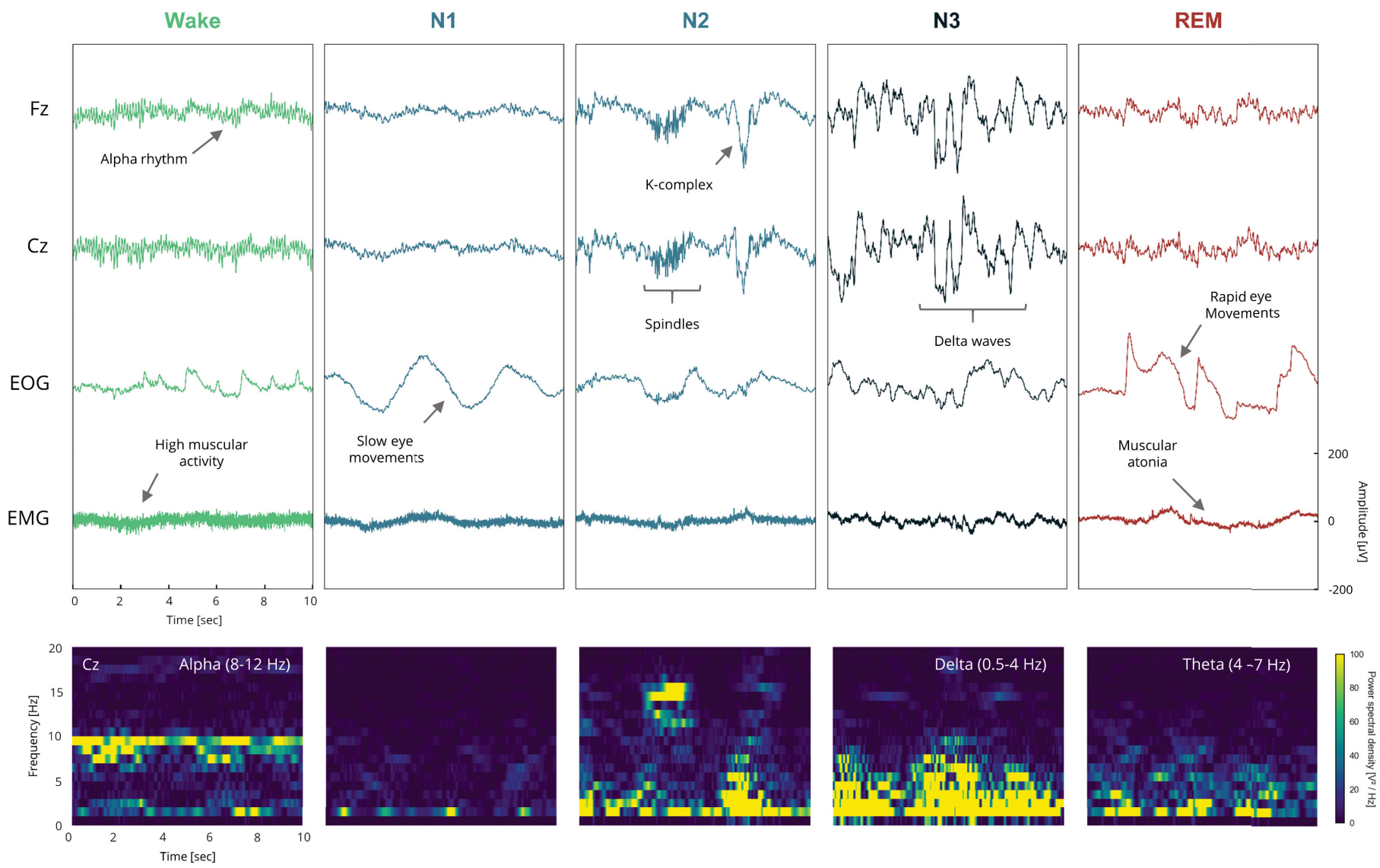


Fig. 1.2 **Polysomnographic recordings across sleep and wakefulness**. Top: Scalp EEG (Fz and Cz electrodes), EOG and EMG recorded in one healthy young adult during wakefulness, N1, N2, N3 and REM sleep. The main features of each vigilance state are described. Bottom: Spectral properties of each stage obtained by computing the spectrogram of the Cz EEG signal atop.

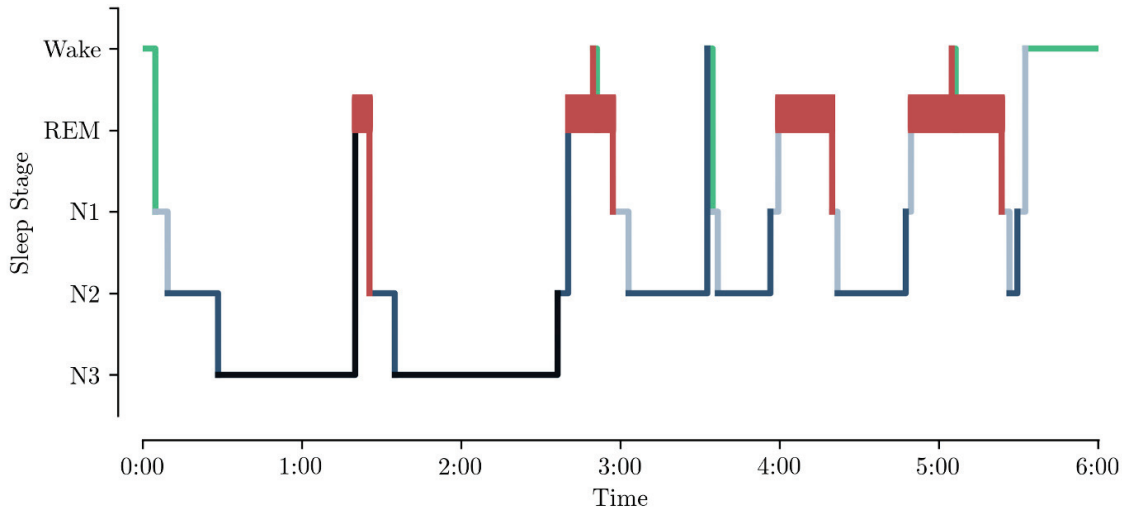


Fig. 1.3 **Hypnogram of a healthy adult**. It represents the stages of sleep as a function of time. One can easily recognize the succession of sleep cycles and especially the alternation of NREM (blue gradient) and REM sleep (red).

1.2.3 Awakenings and arousals during sleep

Periods of intra-sleep wakefulness are a common and physiological component of normal sleep, which frequently occur at the end of the sleep cycle. Wakefulness is considered as a sleep stage by the standard scoring rules, meaning that any segment of polysomnographic recording containing at least 50% (i.e. 15 seconds) of wakefulness activity must be scored as wakefulness. Intra-sleep wakefulness should not be confused with *arousals*, which are a distinct component of normal sleep, scored independently of the standard sleep stages (i.e. an arousal can be scored in NREM or REM sleep alike). Arousals correspond to *"abrupt and short shifts toward high EEG frequencies indicating a transient intrusion of wakefulness into sleep, or at least a sudden brief elevation of the level of vigilance"* (Peter-Derex et al., 2015). According to the American Sleep Disorders Association (ASDA) criteria, arousals are defined as abrupt EEG frequency shifts occurring after at least 10 seconds of stable sleep and lasting 3 to 15 seconds (American Sleep Disorders Association, 1992; Bonnet et al., 2007). Arousals are far more frequent than intra-sleep awakenings in a normal night of sleep. The number of arousals per hour is typically around 10 in healthy young subjects, and tends to increase with age and decrease after sleep deprivation (De Gennaro et al., 2001; Bonnet and Arand, 2007). With regards to dreaming, several studies indicate that the frequency of intra-sleep wakefulness is positively associated with the frequency of dream recall (see section 2.3.3). By contrast, the relationship between arousals and dream recall has never been investigated, and will be addressed in one of the study of the present thesis (see section 5.2).

1.2.4 Sleep inertia

Another aspect of sleep that is particularly relevant with regards to dreaming is the transition from sleep to wakefulness. This transitional period between sleep and wake

is often referred to as *sleep inertia*, and is marked by impaired cognitive and physical performance, reduced vigilance, and a desire to return to sleep. Although the duration of sleep inertia is not consensual and varies depending on the outcome measure used, it is generally admitted that most of the behavioral effects dissipate progressively in the first 30 minutes after awakening. Severity of sleep inertia has been positively associated to several factors such as prior sleep deprivation, awakening near the circadian trough of body temperature and awakening in N3 sleep (see Tassi and Muzet, 2000; Trotti, 2016). Surprisingly, although the behavioral aspects of sleep inertia are well documented, very few studies have investigated its neural correlates. Furthermore, some evidences suggest that sleep inertia could be a critical factor mediating the forgetting or recall of dreams upon awakening (see section 2.4.6), an hypothesis that has however never been experimentally tested. As we will detail later (section 5.3), one of the main goal of the present thesis was to investigate the neural substrate of sleep inertia and its relationship to dream recall.

1.3 Link between dreaming and sleep stages

1.3.1 Goblot's hypothesis

> *The dream, some said, is the thought of sleep. Has someone ever questioned the accuracy of this formula? I think it should be amended and rather say: the dream that one remembers is the thought of awakening.*[2]
>
> — **Edmond Goblot**
> Le souvenir des rêves. 1896

It is with these words that Goblot (1896) introduces the hypothesis that dreaming does not occur during sleep but only at the moment of awakening. To support his arguments, Goblot notably used the famous Guillotine dream, in which Alfred Maury described how the abrupt awakening induced by the fall of the head-board on his neck inspired a long dream, which ended with a guillotine blade falling at the exact same point where the head-board of the bed had actually struck his cervical vertebrae (Maury, 1865). According to Goblot, the fall of the head-board (i.e. external stimulus) created the dream story, thus meaning that the dream content was contained, as a whole, in an ephemeral *"thought of awakening"*.

While this claim has enthralled several philosophers and neurobiologists in the twentieth century, numerous and robust experimental data in sleep psychophysiology clearly demonstrated that dreaming does take place during sleep and not at the moment of awakening (reviewed in Guénolé and Nicolas, 2010). Perhaps one of the most significant evidence against this claim is the scientifically-verified existence of lucid dreaming during REM sleep (i.e. the ability to become self aware of dreaming during a dream, see section 1.4.2; LaBerge and Rheingold, 1991; Dresler et al., 2012), which clearly shows that dreaming (albeit a somewhat modified form of it) does occur during sleep. Other proofs against

this hypothesis come from the study of parasomnias, such as sleep-talking or REM sleep behavior disorder, during which the dream content is (sometimes) correlated to the sleep behavior (Ellman and Antrobus, 1991; Schenck and Mahowald, 2002; Leclair-Visonneau et al., 2010; Valli et al., 2012). Further evidence can be found by looking at the incorporation of non-awakening stimulations in subsequent dream reports. Using such a paradigm, Dement and Wolpert (1958) found that tactile (water) stimulation was incorporated 42% of the time, and reported that the subjective time interval between the incorporation of the stimulus and the awakening was comparable within the dream and in waking-life.

1.3.2 The REM sleep hypothesis of dreaming

In the early fifties, Nathaniel Kleitman and his doctoral student Eugene Aserinsky, discovered in humans the existence of periods of sleep with an EEG similar to wakefulness (low voltage and fast frequencies), rapid eye movements and neurovegetative responses (Aserinsky and Kleitman, 1953). This discovery had a strong and persistent impact on dream and sleep research. The authors have indeed proposed that the rapid eye movements corresponded to the scanning of dream images. They reached this conclusion by comparing the proportion of dream reports obtained upon awakening in periods of eye motility and outside these periods, respectively 75% and 11% in their 1953's study, and 80% and 7% in their 1957's study (Dement and Kleitman, 1957). They concluded that their newly-discovered REM sleep stage was the neurophysiological basis of dreaming. A few years later, the French neurophysiologist Michel Jouvet, who had started working on sleep in cats, found that REM sleep was associated with muscular atonia (Jouvet et al., 1959), a finding that was soon after replicated in humans (Berger, 1961). Pursuing his research on REM sleep, or *"paradoxical sleep"* as he named it, Jouvet had the idea to suppress the muscular atonia in cats by injuring the brain region responsible for it (i.e. brain stem). To his astonishment, he found that the injured cats were performing, during REM sleep, complex motor sequences, that he named *"oneiric behavior"* (Sastre and Jouvet, 1979). For him and the scientific community at the time, it was clear that these motors sequences were directly related to the cat's dreams, and this experiment provided a significant evidence in favor of the REM sleep hypothesis of dreaming.

However, even though equating dreaming with REM sleep provided a useful way to scientifically explore dreaming, it soon became apparent that dreaming was in fact not a specificity of REM sleep but was also present during all the other sleep stages. Few years after the initial discovery of REM sleep, several researchers reported a much higher proportion of dream report in non-REM sleep than what was expected based on the findings of the Kleitman's team. Goodenough et al. (1959) found that, when awakened during NREM sleep, 17% and 53% of awakenings were associated with a dream report in individuals who never, or frequently, remembered their dreams, respectively. The recall rate went up to 54% in Foulkes (1962)'s study which comprised 200 awakenings. Since then, numerous studies have replicated the finding of mentation outside of REM sleep (reviewed in Nielsen, 2000), even in the periods of non-REM sleep located before the first nocturnal episode of REM sleep (Noreika et al., 2009). In addition, it has become apparent that a significant proportion of REM sleep awakenings were not followed by a dream report.

Taken together, these results demonstrate that REM sleep is not the neurophysiological substrate of dreaming. It is noteworthy that this hypothesis is still predominant in the public mind, and to some extent in the scientific community. As Schwartz and colleagues aptly pointed out, *"REM sleep is not a necessary, but a facilitating condition for dreaming to occur. Conversely, there is little doubt that dreaming was a necessary condition for REM sleep to become famous"* (Schwartz et al., 2005).

1.3.3 The fore-brain hypothesis of dreaming

Fervent supporter of the REM sleep hypothesis of dreaming, Allan Hobson argued that dreaming was generated by random neural signals originating within the brainstem during REM sleep (see section 4.2.1, Hobson et al., 1998). His theory was the dominant view for several decades until Mark Solms refuted it using neuropsychological evidences. He examined 361 neurological patients and asked them in detail about their dream memories (Solms, 1997). He found that out of 26 case reports of REM sleep loss or alteration following a lesion in the brainstem (Pons area), 25 were not associated with subsequent alterations in dream reporting. By contrast, he reported that in most cases global cessation of dream reporting (a condition referred to as the Charcot-Wilbrand syndrome) followed lesions in or near the temporo-parietal junction (TPJ) and the medial prefrontal cortex (MPFC; see Fig 1.4). Importantly, damage in these two regions were rarely associated with REM sleep disturbances. This double dissociation provides a clear argument that not only dreaming can occur outside of REM sleep, but also that dreaming and REM sleep are subserved by different brain mechanisms. This led Solms to put forward the fore-brain dream-on hypothesis of dreaming, according to which dreaming is initiated, and controlled by dopaminergic forebrain mechanisms involving at least the TPJ and the MPFC (Solms, 2000).

1.3.4 A continuum of mentation during sleep

Based on Solms's findings, some authors have postulated that instead of relying on REM sleep mechanisms, dreaming might be best described along a continuum of mentation during sleep, ranging from the hypnagogic reveries typical of sleep onset to florid and vivid experiences often reported after awakening from REM sleep (Schwartz et al., 2005). A brief description of the different type of mental activities during sleep is reported in Table 1.1.

1.4 Attempts to study the cerebral correlates of dreaming

Thanks to the continuous advances in neuroimaging techniques, we have the means to measure, with unprecedented spatial and temporal accuracy, a part of what is happening in the brain at a specific moment in time (see Methods section). Yet, since it is now

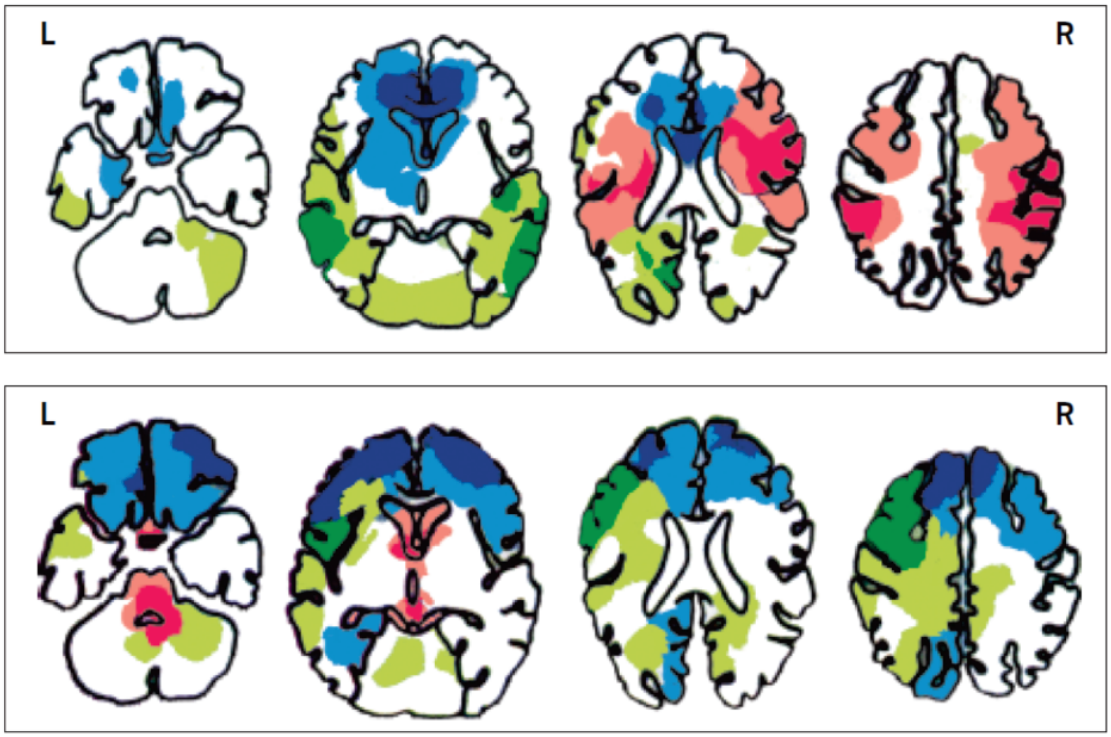


Fig. 1.4 **Lesion maps associated with cessation (top) vs preservation (bottom) of dream reporting.** Top: Global cessation of dream reporting was found following parietal lobe lesions (6 cases, inferior lobule and supramarginal gyrus; red), medial frontal lesions (9 cases; blue), and posterior lesions (8 cases; green). Bottom: Preserved dream reporting was found following left hemispheric and frontal convexity lesions (15 cases; green), bifrontal lesions (14 cases; blue), and brainstem lesions (17 cases; red). Reproduced from Schwartz et al. (2005)

well-accepted that dreaming can occur in all sleep stages, and because dream content is only accessible after awakening, it is therefore impossible to be sure that dreaming is happening at a specific time point during sleep. This conceptual issue has not prevented sleep and dream researchers to attempt to identify the cerebral correlates of dreaming. The main methods and findings are summarized in the following paragraphs.

1.4.1 Brain activity during REM sleep

On the basis of the REM sleep hypothesis of dreaming, which was predominant during the nineties, researchers used functional neuroimaging techniques such as positron emission tomography (PET) to investigate the brain activity during REM sleep. They reported that, despite similarities between the wake and REM sleep electrophysiological scalp signals, the brain metabolism in these two vigilance states was different (Maquet et al., 1996; Braun et al., 1997). Among the most notable findings, the regional cerebral blood flow (rCBF) was decreased in several brain regions including the dorsolateral prefrontal cortex (DLPFC), and was increased in other regions (occipital, temporal, and superior parietal cortices, hippocampal formation, anterior cingulate and the pons).

Table 1.1 **A brief description of sleep mentation in their typical order of placement during the sleep cycle**. Modified from De Koninck (2012)

Name	Description	Sleep stage
Hypnagogic reverie	Simple images	Sleep onset mentation (N1 or early N2 sleep)
Reflections	Thoughts with no hallucinatory content	N2 sleep
Vivid dreams	Vivid imagery and sequences, presence of characters, interactions and emotions	REM and NREM sleep
Lucid dreams	The dreamer is conscious of dreaming and can sometimes controls the dream scenario	REM sleep
Nightmares, bad dreams	Unpleasant and highly anxiogenic dream. The content of nightmare actually awakens the dreamer	REM and NREM sleep
Hypnopompic reverie	Characterized by elaborate imagery	Sleep offset mentation (REM or NREM sleep)

Following these works, researchers postulated that these changes in the brain functional organization could explain the phenomenological characteristics of dream reports (Hobson et al., 2000; Schwartz and Maquet, 2002; Maquet et al., 2005; Nir and Tononi, 2010; Ruby, 2011). For instance, increased occipital cortex activity during REM sleep could explain the clear predominance of visual modality in dream reports, a phenomenon that Vincent van Gogh had already noticed when he wrote: *"I often think that the night is more alive and more richly colored than the day"* (Vincent van Gogh, 1888). Second, the increased activity during REM sleep in the hippocampal formation, a region well-known for its role in memory encoding and retrieval, could account for the presence of known places and characters in dreams. Finally, the decreased activity in the dorsolateral prefrontal cortex, a region involved in executive function, cognitive control and working memory, could account for the lack of consistency, voluntary control and logical reasoning over the dream story. This is consistent with studies on lucid dreaming showing a partial reactivation of this area in lucid dreams compared to non-lucid dreams (see section below). While these findings seem appealing, it should be noted, however, that the main argument against those is the simple observation that dreaming is not specific to REM sleep and can also occur during other sleep stages. If the phenomenological characteristics of dream reports are related to the REM sleep brain functional organization, and given that NREM and REM sleep are very different at the neurophysiological level, how, then, do we explain that a non-negligible proportion of NREM dream reports are *"indistinguishable by any criterion from those obtained from post-REM awakenings"* (Hobson, 1988)?

1.4.2 Brain activity during lucid dreaming

Long considered as a fantasy, lucid dreaming - the ability to become self-aware of dreaming during a dream, and in some cases, to control the dream scenario – has recently gained considerable interest among researchers and the public. The scientific study of lucid dreaming started in the nineteenth century when Hervey de Saint Denys, a learned oneirologist, published in 1867 his landmark book *"Dreams and the Ways to Direct Them: Practical Observations"*, in which he described his own lucid dream experiences. More than a century later, more objective methods such as EEG and functional magnetic resonance imaging (fMRI) have become the technique of choice for investigating the cerebral correlates lucid dreams.

Applying the method of pre-determined ocular signaling, developed by the pioneering lucid dreaming researcher Stephen Laberge (see LaBerge and Rheingold, 1991), to fMRI, Dresler et al. (2012) was remarkably able to measure, the brain activity during lucid REM sleep and non-lucid REM sleep (though only one subject out of four had lucid dreams of sufficient length). Lucid REM sleep was associated with a reactivation of areas that are normally deactivated during REM sleep, such as bilateral precuneus, parietal lobules and prefrontal and occipito-temporal cortices. Phenomenologically, these regions are either involved in self-awareness and executive functions, and their reactivation during lucid dreaming could account for the resurgence of a certain level of self-awareness and voluntary control. Even more recently, Voss et al. (2014) was able to induce an increased level of self-reflective awareness during dreaming using fronto-temporal transcranial alternating current stimulation. Consistent with their previous EEG results (Voss et al., 2009), the authors reported that increased lucidity was most prominent during stimulation in the lower gamma band. However, the lucidity was not assessed directly by the dreamer but assumed a posteriori if the subjects reported elevated ratings on a lucidity scale. In conclusion, while lucid dreaming seems to provide an appealing and elegant way to study the dreaming brain, one should keep in mind that the inherent problem with this method lies precisely in the fact that lucid dreams are, by nature, different from non-lucid dreams. As exciting as the results are, it would be however difficult to generalize them to the research on non-lucid dreams (in addition with the fact that lucid dreams are difficult to obtain under laboratory conditions).

1.4.3 Brain activity in the minutes preceding a dream report

Another line of research consists in comparing the pre-awakening sleep EEG spectral power associated with the presence or absence of a dream report. This paradigm has been used in several studies over the years, the findings of which are summarized in Table 1.2. Esposito et al. (2004) reported that in both REM and N2 sleep, dream recall was associated with a lower alpha and delta power in the 3 minutes preceding awakening. According to the authors, the alpha effect may reflect increased cognitive elaboration and visual imagery as well as increased attention and memory processes. Marzano et al. (2011) found that dream recall after morning awakening from REM sleep was associated with a higher frontal 5–7 Hz (theta) activity in the 5 minutes preceding awakening. In N2 sleep,

dream recall was associated with a decrease in alpha power, an observation consistent with Esposito's results. The same year, another study reported a lower delta power for the dream recall condition following awakening from N2 sleep, and a higher alpha and beta power in occipital derivations for REM sleep (Chellappa et al., 2011). Finally, a recent study reported that in both N2 and REM sleep, dream recall was associated with local decreases in delta power in posterior cortical regions in the 2 minutes preceding awakening (Siclari et al., 2017). The authors were able to predict whether an individual reported dreaming or the absence of dream experiences after awakening from N2 sleep by monitoring this posterior 'hot zone' in real time. However, it should be noted that the authors did not cite the numerous previous studies using the same methodology, and did not as a consequence discuss their findings in comparison to previous ones. This is regrettable given the great heterogeneity, and even contradiction, in the results of all these studies. Furthermore, there are two major issues with this methodology. First, we can never be sure whether the dream actually took place in the minutes just before awakening or several tens of minutes before. Second, as we already pointed out, it is impossible to know for sure whether the failure to recall a dream actually means that the sleeper was not dreaming, or rather that the sleeper was dreaming but did not remember it. In this view, one can assume that rather than looking at the cerebral correlates of dreaming, these studies in fact investigated the cerebral correlates of dream recall.

1.4.4 Dreaming as a subsystem of the default mode network

The past few years have witnessed the emergence of a new conceptual framework of dreaming, centered on the idea that dreaming is a form of mind-wandering, whose cerebral correlates are a subsystem of the default mode network (DMN; see Methods section; Maquet et al., 2005; Domhoff, 2011; Domhoff and Fox, 2015; Christoff et al., 2016). Based on the fact that dreaming and waking spontaneous thought share many features (i.e. predominance of the audiovisual modalities, centered on one's current goals and concerns, draw heavily on semantic and episodic memory in constructing simulations and future plans, presence of a wide range of affect), some authors have postulated that dreaming is a *"type of spontaneous thought that is highly unconstrained, hyper-associative and highly immersive"* (Christoff et al., 2016). Using the results of lesion and REM sleep neuroimaging studies, they argued that dreaming should be accompanied, at the neural level, by a strong recruitment of the default mode network medial temporal lobe (MTL)-centered subsystem and strong deactivations in frontoparietal control network regions (such as the DLPFC). Activation of the former areas could be related to the generation of spontaneous thoughts, during both wake and sleep, while the deactivation of the latter areas could explain the high volatility and variability of dream content over time. However, this theoretical framework remains to be experimentally tested and validated.

1.4.5 Limitations

Several methodologies and frameworks have been proposed over the years to decipher the neurophysiological correlates of dreaming. However, while the findings of these

Table 1.2 **Review of the studies that investigated the pre-awakening sleep EEG spectral power associated with the presence or absence of a dream report.** ↗ The EEG spectral power is increased in this frequency band when subjects recalled a dream compared to when they did not recall one. ↘ The EEG spectral power is decreased in this frequency band when subjects recalled a dream compared to when they did not recall one. = No EEG spectral power difference in this frequency band were found, or measured, between the two conditions. * Higher occipital alpha, decreased frontal alpha. N = number of participants.

Study	N	δ (0.5-4Hz)	θ (4-7Hz)	α (8-12Hz)	β (>13Hz)
REM sleep					
Moffitt, 1982	8	=	=	=	=
Lehmann et al., 1981	-	↘	↘	↘	=
Wollman and Antrobus, 1987	30	=	=	=	=
Rochlen et al., 1998	17	=	=	=	↗
Germain et al., 1999	41	=	=	↗	↗
Takeuchi et al., 2003	8	=	=	↘	=
Esposito et al., 2004	11	↘	=	↘	=
Marzano et al., 2011	30	=	↗	=	=
Chellappa et al., 2011	17	=	=	↗↘*	↗
Scarpelli et al., 2015	6	=	↗	=	=
Siclari et al., 2017	46	↘	=	=	=
Non-REM sleep					
Moffitt, 1982	8	↘	=	=	=
Williamson et al., 1986	6	=	=	=	=
Morel et al., 1991	40	=	=	=	=
Takeuchi et al., 2003	8	=	=	↗	=
Wittmann et al., 2004	6	=	=	=	=
Esposito et al., 2004	8	↘	=	↘	=
Marzano et al., 2011	35	=	=	↘	=
Chellappa et al., 2011	17	↘	=	=	↘
Scarpelli et al., 2017	14	↘	=	=	=
Siclari et al., 2017	46	↘	=	=	=

studies may shed light on specific aspects of the dreaming phenomenon (e.g. REM sleep dreaming, lucid dreaming, dream recall), they usually do not encompass and explain the wide spectrum of dreaming-related mental activities during sleep. One way around this problem is to investigate the neural correlates of dreaming indirectly, for example through the study of the correlates of the frequency of dream recall. This proposal will be the subject of the next chapter.

Dream recall frequency

2

> *We must also inquire what the dream is, and from what cause sleepers sometimes dream, and sometimes do not; or whether the truth is that sleepers always dream but do not always remember (their dream); and if this occurs, what its explanation is.*
>
> — **Aristotle**
> On Sleep and Sleeplessness. 350 B.C.

2.1 Measuring dream recall frequency

As Aristotle had rightly pointed out, we do not always remember our dreams. More than two thousand years after, modern research has confirmed that the dream recall frequency (DRF) – i.e. the number of dream reports over a given period of time - is indeed highly variable both within individuals over the life course, but also between individuals (Schredl et al., 2003b; Ruby, 2011). There is no gold standard for measuring DRF, and each method has its pros and cons. In research settings, three methods are commonly applied: questionnaire scales, dream diaries, and laboratory awakenings (Schredl, 1999). The former consists in asking the participants to estimate their dream recall frequency over the last few weeks or months. This method has the advantage of being fast, inexpensive, and unaffected by the measurement, however, the DRF could be over- or under-estimated due to erroneous or incomplete recollection. Regarding dream diaries, the participants are asked to report each morning whether they have recalled a dream or not. This method minimizes the bias of retrospective estimation, but has the disadvantages of potentially increasing drastically the dream recall frequency, especially in persons who usually almost never recall their dreams (Schredl, 2002). Finally, laboratory awakenings consist in awakening the participants in the sleep lab and asking them whether they recall a dream or not. While this method has the clear advantage that the experimenters can measure physiological parameters (EEG, EOG, ECG, respiration and heart rate) prior, during and after the awakening, it is also time-consuming and expensive. Moreover, as for dream diaries, laboratory awakenings are associated with a dramatic increase in DRF, especially for low dream recallers.

2.2 DRF in the general population

2.2.1 Average DRF

Measured by questionnaire, the average weekly DRF was 2.58 ± 2.03 in 444 German students (Schredl et al., 2003b) and 0.83 ± 1.57 in a representative German sample of 931 participants (Schredl, 2008). Using dream diaries, the average weekly DRF was 3.1 ± 1.5 in 70 Finnish children (Valli et al., 2005) and 3.9 ± 2.5 in a sample of 196 German student (Schredl and Fulda, 2005). In lights of these results, we can conclude that the average weekly DRF in the general population lies between 1 and 3 dream reports per week.

2.2.2 Intra-individuals variability

Daily experience suggest that our ability to recall dream fluctuates over time. Investigating this issue using the diary technique in 169 participants, Schredl and Fulda (2005) reported that the stability of DRF was very high over a period of one month. Similarly, he reported high DRF stability coefficients in a sample of older adults who had been interviewed weekly about their dream life over a period of 26 weeks (Schredl et al., 2001). However, to our knowledge, there are no studies evaluating the stability of DRF in the same individuals over an extended period of time.

2.2.3 Inter-individuals variability

DRF varies drastically between individuals: some persons almost never recall a dream, whereas others can recall one or several dreams every morning. In an Austrian sample of 1000 persons, Stepansky et al. (1998) found that 31% of the participants reported 10 dreams or more per month, 37% reported between one and nine dreams per month, and 32% reported less than one dream per month. In a sample of 285 German students, Schredl (2002) found that 44% reported dreams four or more times per weeks, 44% reported a dream one time per week and 12% reported a dream less than one time per month. This variability allows to differentiate behavioral profiles of DRF: high dream recallers (HR), who can recall a dream almost every morning (e.g. more than 5 mornings a week, Schredl and Fulda, 2005) and low dream recallers (LR), who almost never recall a dream (e.g. less than one dream per month, Goodenough et al., 1959). Importantly, the frequency of HR is higher in the general population, and even more in young and/or student sample (Schredl and Fulda, 2005).

2.3 Parameters correlated with DRF

2.3.1 Physiological and psychological factors

First, increased professional or personal stress is positively associated with DRF (Schredl, 1999). Similarly, an interest in dreams, or a positive attitude towards dreams is positively associated with DRF, as is frequent day-dreaming and rich fantasy life (Schredl et al.,

2003b). DRF decreases with age and is slightly higher in women, who are also typically more interested in dreams (Schredl, 2008; Schredl and Reinhard, 2008). Regarding personality dimensions, studies have found positive correlations between DRF and thin boundaries, anxiety, and openness to experience (Hartmann, 1989; Schredl et al., 2003b; Schredl et al., 2003a). However, most of the correlations between DRF and personality traits are low and explain only a small percentage of the total variance.

2.3.2 Cognitive factors

Regarding cognitive abilities, a simple explanation of why individuals differ in their ability to remember dreams could be because they differ in some more general memory abilities (verbal, visual, short and long term). However, the literature yielded contradictory results, with some support for a positive association between DRF and visual memory, but also evidence against it for verbal and visual material and short-or long-term story narrative recall (Ruby, 2011; Blagrove and Pace-Schott, 2010). On another note, several studies have consistently reported that DRF is positively correlated with creativity (Fitch and Armitage, 1989; Schredl, 1995; Schredl et al., 2003b) and intelligence scales (multiple-choice vocabulary test, Schonbar, 1959, Shipley-Hartford intelligence scale, Connor and Boblitt, 1970).

2.3.3 Sleep parameters

First, DRF varies according to the sleep stage preceding awakening (see Nielsen, 2000 for a review). More dream reports are obtained after an awakening during REM sleep than after an awakening during NREM sleep. These results inspired the REM sleep hypothesis of dreaming discussed earlier in section 1.3.2. However, when a dream is not reported on awakening, there is no method of establishing whether it did not happen or was forgotten. This idea was rightly pointed out by Conduit et al. (2004): *"An ongoing assumption made by sleep scientists is that since dreams are more often recalled on awakening from REM sleep, dreams must occur more often during this sleep stage. An alternative hypothesis is that cognition occurs throughout sleep, but the recall of mentation differs on awakenings"*.

This idea that DRF variability is not a matter of dream production during sleep, but of dream recall during awakening, is the core of several models of dream recall (detailed later in section 2.4), among which the arousal-retrieval model is one of the most significant. In its simplest form, it claims that a period of wakefulness must occur just after dreaming so that the dream content can be transferred from short term to long term memory (Koulack and Goodenough, 1976) Several studies support this model. First, using retrospective evaluation, Schredl et al. (2003b) found a positive correlation between the number of nocturnal awakenings and DRF. Second, De Gennaro et al. (2010) reported that recovery sleep following a full night of sleep deprivation was characterized by an almost complete abolition of dream recall, paralleled with a lower number of nocturnal awakenings, which could, according to them, have *"reduced the contents available in memory as possible cues for retrieval of dream experiences at morning"*. Finally, these results were recently reinforced

by a full-night PSG study in 36 subjects (18 HR and 18 LR; Eichenlaub et al., 2014a; Fig 2.1). HR showed in average longer intra-sleep wakefulness than LR (30 min vs 15 on average). The number of awakenings (the number of phases composed of consecutive pages of awakening) was not significantly different between the 2 groups, but the mean duration of the awakenings was (HR, 1.90 ± 0.91 min; LR, 0.95 ± 0.40 min).

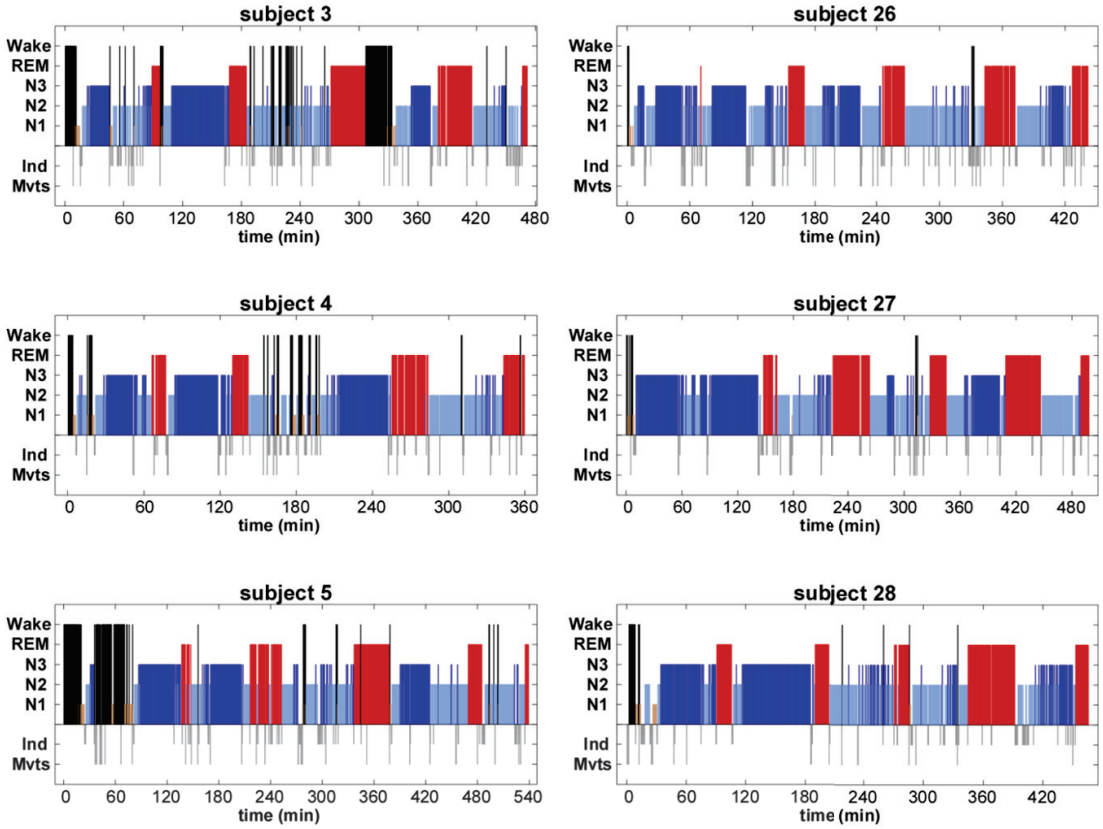


Fig. 2.1 **Hypnograms of three representative HR (left) and three representative LR (right).** Full night PSG recordings were acquired in the sleep lab in 18 HRs and 18 LRs. Wake: wakefulness (black); N1, N2, and N3: sleep stages N1 (very light gray), N2 (light gray), and N3 (dark gray), respectively; REM: REM sleep (medium gray); Ind: pages for which the dominant sleep stage could not be determined; Mvts: movements. From these 6 examples, it can be observed that the wakefulness periods during the sleep period time are longer in HR than in LR. Adapted from Eichenlaub et al. (2014a)

2.3.4 Neurophysiological parameters

The neurophysiological parameters that covary with DRF had scarcely been investigated until the doctoral work of Jean-Baptiste Eichenlaub, conducted with Perrine Ruby a few years ago. They compared the brain activity of HR and LR during both sleep and wakefulness and using several neuroimaging techniques such as auditory evoked potentials (AEP) and positron emission tomography (PET). The main findings from Eichenlaub's doctoral thesis are summarized below and in Fig 2.3.

First, they conducted a sleep lab study in which they compared the brain reactivity (AEP) of 18 HRs (DRF = 4.4 ± 1.0 dream reports per week) and 18 LRs (0.25 ± 0.1) during sleep

and wakefulness (Ruby et al., 2013; Eichenlaub et al., 2014a). During data acquisition, the subjects were presented with sounds to be ignored (first names randomly presented among pure tones) while they were watching a silent movie or sleeping (Fig 2.2). They found that brain responses to first names dramatically differed between the 2 groups during both sleep and wakefulness (Fig 2.3A). During wakefulness, the attention-orienting brain response (P3a) and a late parietal response were larger in HR than in LR. During sleep, there were between-group differences at the latency of the P3a during N2 sleep and at later latencies during all sleep stages. Second, they used PET to compare the resting state cerebral blood flow of 21 HRs (DRF = 5.2 ± 1.4 dream reports per week) and 20 LRs (DRF = 0.5 ± 0.3 dream reports per week) during sleep and wakefulness (Eichenlaub et al., 2014b). Compared with LRs, HRs showed higher rCBF in the TPJ during REM sleep, N3, and wakefulness, and in the MPFC during REM sleep and wakefulness (Fig 2.3B).

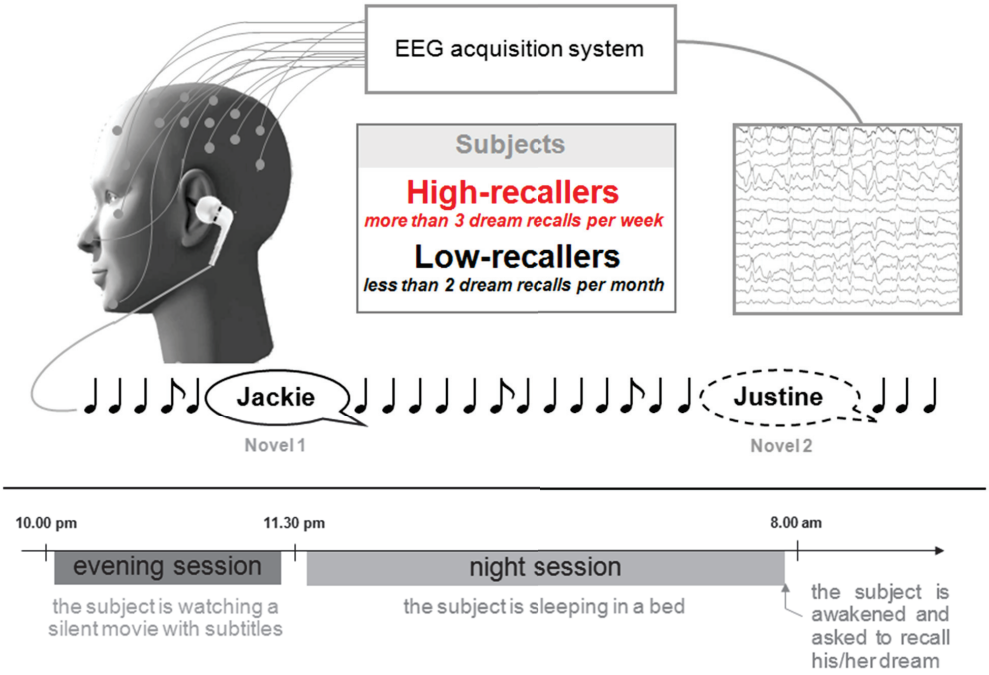
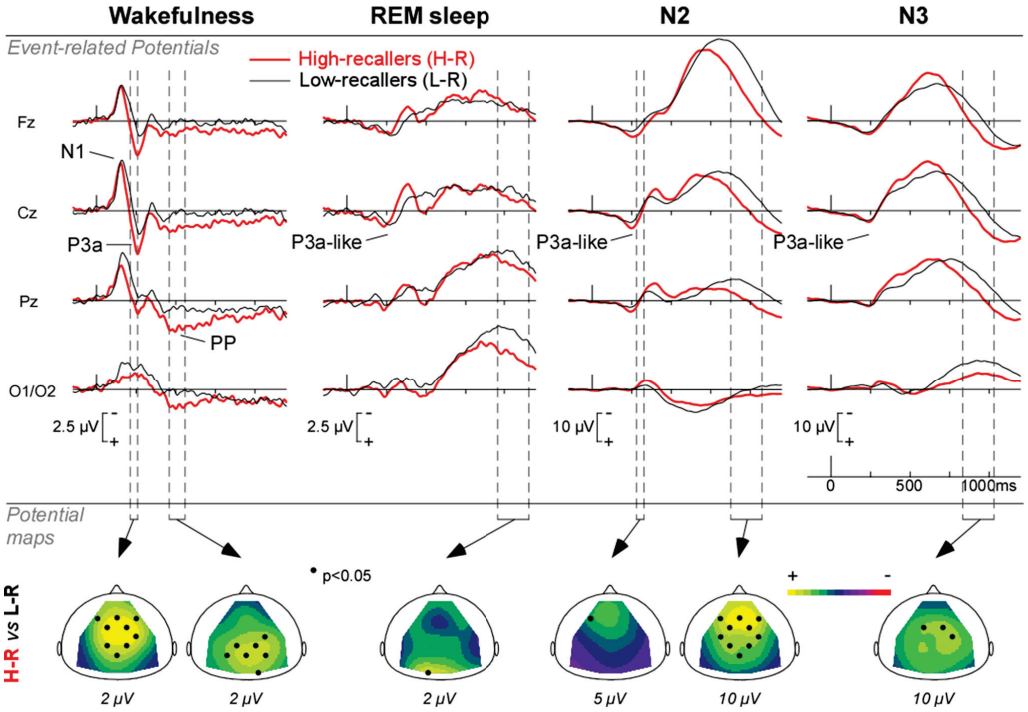


Fig. 2.2 **Experimental design of Eichenlaub et al. (2014a) EEG study**. Polysomnographic data were acquired from 18 HR and 18 LR presented with auditory stimuli (oddball novelty paradigm) while watching a silent movie with subtitles (evening session) or while sleeping (night session). Stimuli: standard tones, deviant tones and 2 spoken first names (novel stimuli), the subject's first name (novel 1, P=0.02) and an unfamiliar first name (novel 2, P=0.02). The stimuli were presented binaurally at 50 dB above the subject's hearing level. Reproduced from Eichenlaub et al. (2014a)

Altogether, these findings show that HR and LR have different neurophysiological traits: spontaneous and evoked brain activity of HR and LR differ during wakefulness and sleep. They argued that HR's neurophysiological profile could promote mental imagery during sleep and the encoding or retrieval of the dream memory during wakefulness. Notably, increased attention-orienting responses during sleep in HR could promote intra-sleep awakenings, which in turn would facilitate the encoding of dreams according to the arousal-retrieval model, and finally result in a higher likelihood of dream recall in the morning after awakening.

A) Eichenlaub et al., *Cerebral Cortex*, 2014



B) Eichenlaub et al., *Neuropsychopharmacology*, 2014

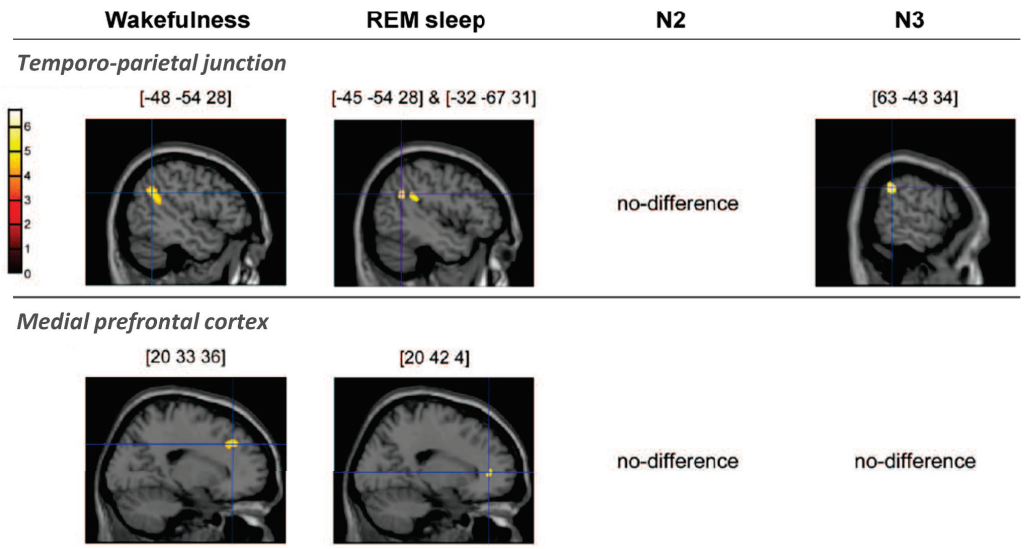


Fig. 2.3 **Summary of the results obtained in Eichenlaub's PhD thesis.** *Top*. EEG study. Compared to LR, HR showed larger brain responses to auditory stimuli (first names) during wakefulness, REM sleep, N2 sleep and N3 sleep. *Bottom*. PET study. Compared to LR, HR showed increased spontaneous rCBF in the TPJ during wakefulness, REM sleep and N3 sleep, and in the MPFC during wakefulness and REM sleep. Altogether, these findings show spontaneous and evoked brain activity of HR and LR differ during both wakefulness and sleep, thus suggesting that DRF is associated with a specific brain functional organization.

2.3.5 Link between neurophysiological and psychological traits

In conclusion, we have seen that many parameters covary with DRF. The ability to recall dreams seems to be associated with psychological and personality factors on one hand, and neurophysiological trait factors on the other hand. These results should be regarded as complementary. For instance, the fact that HRs demonstrate higher rCBF during sleep and wakefulness in the TPJ and MPFC, two regions of the DMN, is consistent with the DMN hypothesis of dreaming, and is well in line with the finding that HRs are more often absorbed in their inner worlds (i.e. day-dreaming, fantasy) and more anxious. Indeed, studies have reported a positive correlation between the activity of the MPFC during wakefulness and scores of openness to experience (Sutin et al., 2009) and neuroticism (Zald et al., 2002).

2.4 Theories on dream recall

This section summarizes the main theories to explain variability in DRF (see also Schredl and Montasser, 1996).

2.4.1 Freud's repression hypothesis

Freud believed that the function of dreams is to preserve sleep by representing as fulfilled wishes that would otherwise awaken the dreamer. According to him, *"the forgetting of the dream is in a large measure the work of the resistance"* (Freud, 1900), which means that dreams that are not sufficiently disguised to pass the censor will be entirely repressed and therefore forgotten. However, as highlighted by Schredl (1999), it is currently impossible to test this hypothesis because we cannot access the non-recalled dreams in order to compare them to the recalled ones.

2.4.2 Life-style hypothesis

Schonbar was one of the first to investigate the psychological correlates of differential DRF. She proposed that DRF can be better explained as part of a general life-style and personality traits (Schonbar, 1965). According to her work, high dream recallers are characterized by an 'inner-acceptant' life-style, which involves higher creativity, introspection, fantasy proneness and openness to experience. This hypothesis has been corroborated by several experimental studies that reported a positive association between DRF on one hand and openness to experience, absorption and creativity on the other hand (see section 2.3.5).

2.4.3 Salience hypothesis

Based on the idea that the principles of waking memory apply to dream recall, Cohen developed in the seventies the interference hypothesis (Cohen and Wolfe, 1973) followed

by the salience hypothesis (Cohen and MacNeilage, 1974). The interference hypothesis postulates that the dream memory trace remains so long as there is no distraction or interference. Otherwise, dreams are forgotten in order to maximize the memory capacity for the day ahead. This echoes French philosopher Roger Caillois's idea on dream forgetting: *"Dreams are quickly forgotten because they have no consequences on waking life and there is only benefits in forgetting them*[3]*"* (Caillois, 1956). In more practical terms, the central idea of this theory is that the dreamer must voluntary pay attention to the dream immediately after awakening. In this respect, it overlaps the life-style hypothesis since high dream recallers are expected to be more interested in their dreams and therefore put more attention on them upon awakening.

Cohen further extended his model in the salience hypothesis, which states that the more salient a dream (e.g. a vivid, bizarre, and highly emotional dream content), and the less interferences there are during the recall process, the more likely the dream is to be recalled. Several findings are in favor of this hypothesis. For example, it has been shown that bizarreness (Cipolli et al., 1993) and emotionality (Schredl and Doll, 1998) enhance recall of dream content (an observation that was however not replicated when taking the effect of dream length into account; Schredl, 2000b). More recently, Parke and Horton (2009) have studied the combined effect of interference and salience processes on dream recall. The findings suggest that a link is present, as the more interference experienced has tended to reduce the length of the dream recall in turn reducing the reported salience.

2.4.4 Arousal-retrieval model

Koulack and Goodenough (1976) proposed in their so-called arousal-retrieval model that a short period of wakefulness (arousal) must occur immediately after dreaming in order to transfer the dream content from short-term memory to long term memory. Furthermore, they drew on Cohen's work to propose that the salience of dream content and lack of interferences during the recall process were critical for a successful recall of the stored dream (retrieval). The arousal-retrieval model is one of the most comprehensive model of dream recall and has received great support from the literature, reviewed earlier in section 2.3.3.

2.4.5 State-shift hypothesis

Extending these arousal-based ideas, Koukkou and Lehmann (1983) proposed the state-shift hypothesis which emphasizes the state dependent effects of dream recall rather than short-term memory effects. According to them, *"forgetting of dreams is a function of the magnitude of the difference between states during encoding and recall"* (Koukkou and Lehmann, 1983). Consequently, the closer two functional states are, the better is the transference of information. Thus, according to them, dreams are better recalled when the awake functional state is similar to the sleeping functional state. It was argued that such compatibility occurs between wakefulness and REM sleep, enabling better recall of REM dreams. By contrast, the slow EEG frequencies of NREM sleep (and especially N3 sleep)

are functionally very different from wakefulness, and this could account for the poorer NREM dream recall.

2.4.6 Sleep inertia

Conduit et al. (2004) demonstrated that the cognitive performance during or shortly after awakening is of importance for the process of dream recall. The design of their study is as follows. Participants were instructed to produce an eye movement signal whenever they heard a tone, presented at increasing volume during N2 and REM sleep until an eye movement signal verification was observed. Ninety seconds after signal verification, participants were awakened and asked if they remembered hearing the tone or responding with the EM signal. Such recollection of signal verified tone presentations was significantly less after Stage 2 sleep (65%) compared to REM sleep (100%) presentations. Furthermore, signal verified tone recall was significantly correlated with reported dream recall frequency. They concluded that *"quite possibly, brain functioning underlying the reporting and non-reporting of dreams does not exist within the pre-sleeping period at all, but within the period just after awakening, when cognitive resources are in demand to recall and/or consolidate events which have just occurred within the previous sleeping period"* (Conduit et al., 2004). Echoing these findings, Schredl et al. (2003b) noted that cognitive functioning in the period just after awakening is often severely impaired (an effect referred to as sleep inertia; Tassi and Muzet, 2000; Trotti, 2016), and that it would be in consequence *"promising to correlate inter-individual differences regarding the sleep inertia with DRF"*. This issue will form a large part of the doctoral work hereby presented and we will return to this in section 5.3.

2.4.7 Towards a unifying theory of dream recall

This brief overview leads to the observation that there is a broad spectrum of dream recall theories, ranging from relating to the content of the dream (Freud's repression and Cohen's salience hypotheses) to accounting for the psychological (life-style hypothesis), cognitive and physiological processes (arousal-retrieval, state-shift hypothesis, sleep inertia; see Fig 2.4). The empirical data seems hitherto to fit best into the arousal-retrieval model (which integrates elements of both the Salience and Interference hypotheses) and the life-style hypothesis. A comprehensive, unified theory of dream recall should combine these two models, for example using the arousal-retrieval model to account for day-to-day variability in DRF (state factors), and the life-style hypothesis to account for the large inter-individual DRF variability (traits factors). Moreover, there is a currently a lack of evidence for the state-shift hypothesis (due to the difficulty of deriving valid quantitative measures for the closeness of functional states; Schredl, 1999) and the sleep inertia theory, which both insist on brain functioning within the period just after awakening.

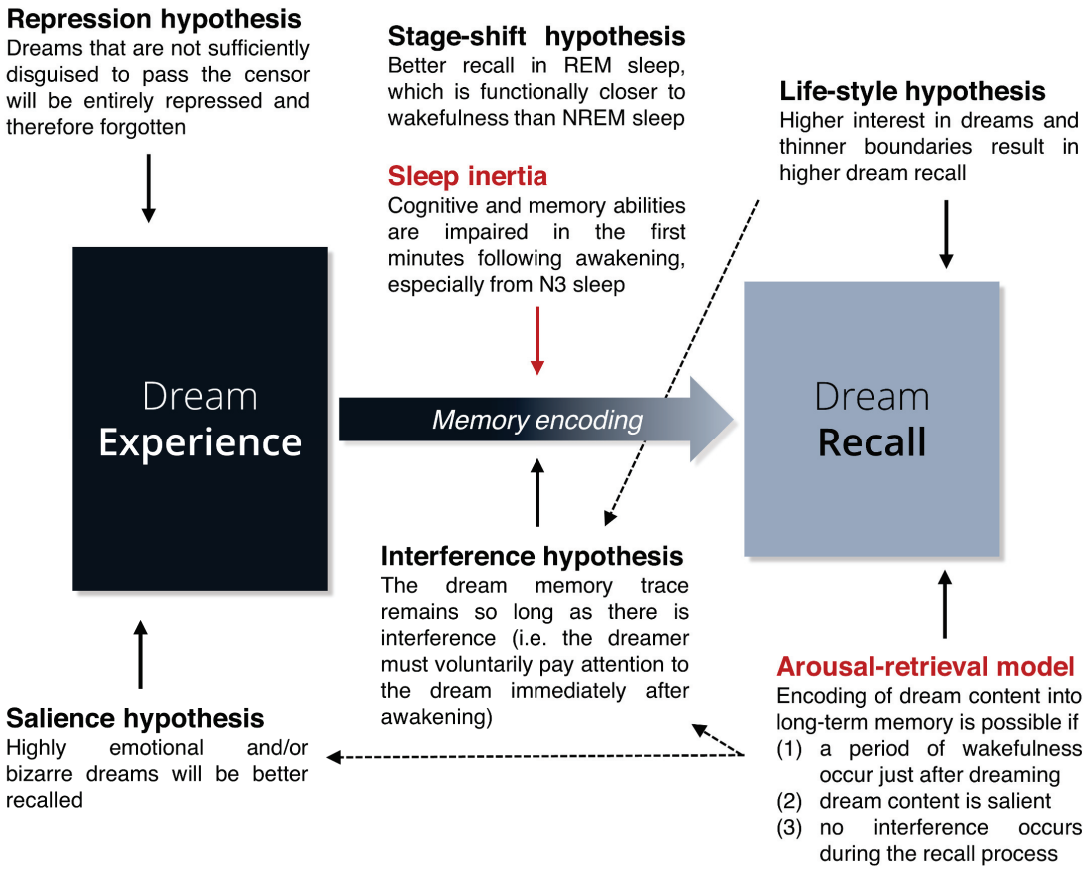


Fig. 2.4 **Dream recall theories.** The arousal-retrieval model provides so far the most comprehensive theory on dream recall and is firmly grounded in empirical evidence. At its simplest, it states that a short period of wakefulness must occur just after dreaming (arousal) in order to transfer the dream content from short to long term memory, which is otherwise impossible during sleep. In addition, it postulates that the dream content must be salient (Salience hypothesis, e.g. highly emotional, vivid and/or bizarre) and that the dreamer must voluntarily pay attention to the dream content (Interference hypothesis). Notably, it is very probable that the individuals with the greatest interest in dreams (Life-style hypothesis) are also the ones which focus the more on their dreams immediately after awakening, thus reducing encoding interferences. This would provide a link between the Life-style hypothesis and the arousal-retrieval model. Finally, sleep inertia could be a important explanatory factor with regards to DRF. It is possible that low dream recallers experience more acute sleep inertia upon awakening, whatever the sleep stage before awakening. More impaired memory and cognitive abilities upon awakening would in turn prevent the encoding of dreams to long term-memory. However, this hypothesis remains to be tested empirically.

Dream content

3

> *Prétendre donner les rêves comme de simples jeux de la pensée, de simples images de l'imagination, c'est témoigner d'un manque de réflexion ou de loyauté ; car de toute évidence ils en diffèrent spécifiquement. Les images de l'imagination sont faibles, languissantes, incomplètes, partielles et si fugitives qu'on peut à peine fixer dans sa mémoire pendant quelques secondes les traits d'un absent, et que même le jeu le plus vif de l'imagination ne peut nullement entrer en comparaison avec la réalité palpable que le rêve met sous nos yeux.*[4]
>
> — **Schopenhauer**
> Parerga und Paralipomena. 1851

3.1 Measuring dream content

Empirical investigation of dreams started in the nineteenth century when scholars started to quantify aspects of their dream content. One notable example is the pioneering paper of Mary Calkins (1893), entitled *"Statistics of dreams"*, in which she reported, inter alia, statistics concerning dream length and vividness, dream characters and dream-waking-life associations. Since then, a considerable numbers of scales and rating systems for reducing and analyzing dream content have been developed, all based on the assumption that *"particular aspects of the verbal material ... have to be quantified in order to carry out statistical analyses"* (Schredl, 2010b). Perhaps one of the most famous is the Hall & Van de Castle coding system (1966), whose basic idea is to divide dream content into several empirical categories (e.g. settings, objects, characters, interactions, emotions, misfortunes) that can be then used to find patterns and identify prevalent themes among groups of dreamers. The Hall & Van de Castle coding system remains today the major reference since it has proven stable over at least one generation (Hall et al., 1982). More recently, Schwartz (1999) proposed an automatic analysis of the lexical content of dream reports, without any a priori coding of their content, a method which has the advantage of minimizing the experimenter bias and being easily replicable by others.

As pointed out by Schredl (2010b), dream content analysis has several flaws. First, these scales, by reducing dream content to specific dimensions, voluntarily omit a certain amount of the information comprised within the dream report. Second, the results of these scales can drastically differ depending on whether the dream content is self-rated by the dreamer or rated by an external judge. As an example, Sikka et al. (2014) recently demonstrated that self-ratings resulted in greater estimates of emotional dreams, and especially positively

valenced dreams, that are often found to be a minority when dreams are rated by external judges.

3.2 Phenomenology of dreams

The empirical analyze of dream content using various scales has allowed to describe several generalizations about the phenomenology of dreams (reviewed in Hall and Van de Castle, 1966; Schwartz, 1999; Schredl, 2010a; Ruby, 2011; Domhoff, 2013; Windt, 2015). These are detailed as follows:

- Dreams tend to be negatively valenced
- Aggressions are more frequent in dreams than friendly interactions
- The visual modality is the predominant sensory modalities in dreams
- The dream drama is mostly lived by the dreamer from a first-person perspective
- Some elements of real-life events previously experienced by the dreamer often contribute to dream content
- Most of the time, the dream sequence is not within the dreamer's voluntary control
- With the exception of lucid dreaming, the dreamer is convinced that the dream's sequence is really happening.
- Dream content often contains temporal and spatial inconsistencies
- Dream content is often full of people interacting with each other (e.g., discussions, fights, pursuit, sexuality)
- Emotions are frequently present during dreams

3.3 Factors influencing dream content

De Koninck (2012) has reviewed in his book entitled *"Sleep, dreams and dreaming"* the factors enabling dream construction, as well as their relative contribution to the dream content. He proposed that the different sources of dreams are best represented in a pyramidal manner, from low levels, predominant in shaping the dream content, to higher levels that carry much less influence to the dream content (Fig 3.1). A non-exhaustive list of the experimental findings related to each of these *"layers"* of the dream construction is reported in the following paragraphs (see Blagrove and Pace-Schott, 2010; Schredl, 2010a; Ruby, 2011; De Koninck, 2012)

Cognitive organization, maturity and intellectual ability De Koninck's model situates the cognitive organization and capacity as the more crucial determinant in the elaboration of dream content. In line with this, several studies indicated that the cognitive organization of dreams follows the cognitive development of children (Foulkes, 1982; Foulkes et al., 1990), and that, similarly, even in adults and elderly, the organization and content of dreams

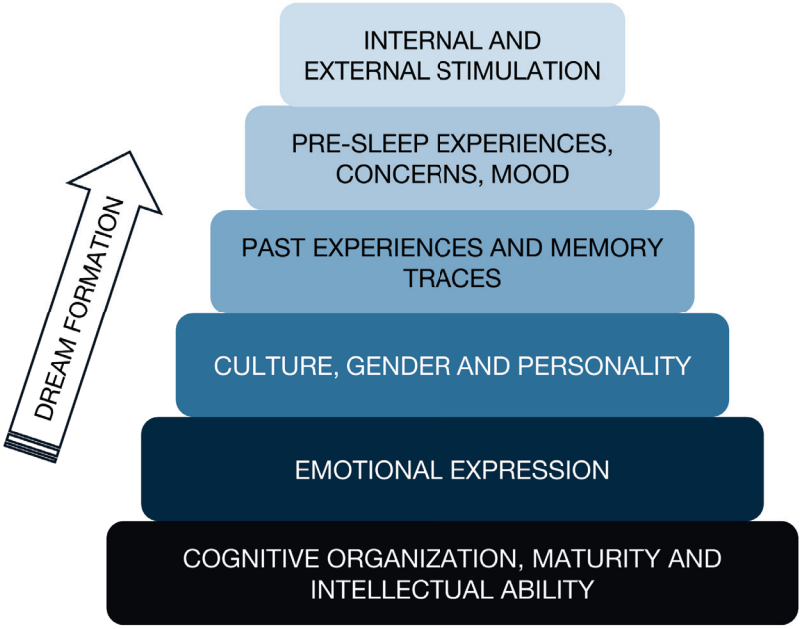


Fig. 3.1 **Factors involved in the construction of dreams.** The various factors in the elaboration of dreaming are illustrated as a pyramid suggesting their order and importance. Adapted from De Koninck (2012).

parallels the waking cognitive ability of the dreamer (see Cavallero and Foulkes, 1993). Based on these findings, Domhoff (2001) has postulated that *"dreaming is a cognitive achievement"* that depends upon the maturation of forebrain areas.

Emotional expression It is now well admitted that waking emotionality is an important contributor to dream formation. Notably, negative emotion seems to prevail in dreams, and can culminate in nightmares or bad dreams (Zadra and Donderi, 2000; Zadra et al., 2006). This observation led Hartmann to propose that emotions are the primary generator of dream (Hartmann, 2007; Hartmann, 2008). According to him, emotions could *"guide the creation of connections to existing memory systems that in turn lead to new associations that have an adaptive value"* (De Koninck, 2012).

Culture, gender and personality Experimental findings suggest that there are both similarities and differences in dream content across culture and societies (Domhoff and Schneider, 2008a). Apparent similarities include dream content seems to be universally more negative than positive (i.e. with a predominance of aggression, misfortune, failure). At the same time, culture-specific differences were observed, for example, in the percentages of animals characters and in the rate of aggressive interactions per character. Gender differences in dream content have been consistently reported, with men reporting more often physical aggression and sex than women (Nielsen et al., 2003; Schredl et al., 2004). Personality seems also to influence dream content, and especially moderate the magnitude of continuity between waking and dreaming (Schredl et al., 1996; Schredl, 2010a).

Past experiences and memory traces There is ample evidence that waking experience finds its way into dreams. Many aspects of the subject's daily life influence dream content, including news event, musical practice, current concerns and religious beliefs, chronic pain, mood or living in a violent environment (see Ruby, 2011). This observation has led to the so-called *"continuity hypothesis of dreaming"* which simply states that dreams reflect waking life experiences (Schredl and Hofmann, 2003). However, the characteristics and time course of the waking memory sources integrated into dreams are still unclear. Furthermore, there is a rising consensus that dream content very rarely replays an episodic memory exactly as it was originally experienced (Fosse et al., 2003; Nielsen and Stenstrom, 2005). Rather, one hypothesis is that episodic memories are replayed fragmentarily because *"only that which is novel or salient need be consolidated and incorporated into longer-term memory schema"* (Malinowski and Horton, 2014b, see also Schwartz, 2003)

Several factors have been positively associated with the likelihood of a waking life experience to be incorporated into dreams (reviewed in Schredl, 2010a). First, there seems to be a linear decrease in temporal references identified in dreams (i.e. recent experiences are more incorporated into dreams than older ones Botman and Crovitz, 1990; Strauch and Meier, 2004; Grenier et al., 2005), an observation supporting the notion of continuity between waking and dreaming memory processes. However, and contrarily to what would be expected according to this memory decay with time, some studies reported an overrepresentation in dreams of waking experiences that happened approximately one week before the dream (Nielsen and Powell, 1992; Marquardt et al., 1996; Blagrove et al., 2011a). This so-called *"dream-lag effect"* was however not consistently found and seems to be specific to REM dreams (Blagrove et al., 2011b; van Rijn et al., 2015). Second, all waking life activities are not represented in the same proportion in dreams (Hartmann, 1996; Schredl, 2000a). Focused thinking activity (e.g. using a computer or reading) occurs less frequently than unfocused activities such as talking with friends. Third, several studies reported a preferential incorporation of emotional waking-life experiences into dreams (Malinowski and Horton, 2014a; Schredl, 2006). Interestingly, these authors reported that emotional intensity, but not emotional tone, seems to affect the incorporation into subsequent dreams.

Pre-sleep experiences, concerns, mood Several studies (Botman and Crovitz, 1990; Nielsen and Powell, 1992; Marquardt et al., 1996) have confirmed that a significant proportion of dreams contain elements that refer to experiences of the preceding day, a phenomenon known as day-residues and mentioned by Freud who considered them as *"a necessary ingredient in dream formation"* (Freud, 1900). Interestingly, the incorporation of pre-sleep experiences seems to be influenced by chronobiological factors, such as sleep cycles and time of the night (Malinowski and Horton, 2014c). As an example, Roffwarg et al. (1978) found that dream reports from the first part of the night comprise more day-residues while dream reports from the second part of the night contain more elements from the distant past. Current concerns and pre-sleep mood also influence dream content. Studying dream content and concerns over a period of 5 months in depressed and controls subjects who were all going through a divorce, Cartwright et al. (2006) remarkably found that the degree of waking concern about the ex-spouse was significantly correlated with the number of dreams in which the former partner appeared as a dream character.

Furthermore, she reported that not only dream content is related to the ongoing emotional concerns of the dreamer, it seems *per se* to play an active role in the down-regulation of disturbed mood (see section 4.2.4, Cartwright, 1991; Cartwright et al., 1998a; Cartwright et al., 1998a; Cartwright et al., 2006).

External and internal stimulation *"From this it is manifest that the stimulatory movements based upon sensory impressions, whether the latter are derived from external objects or from causes within the body, present themselves not only when persons are awake, but also then, when this affection which is called sleep has come upon them, with even greater impressiveness"* (Aristotle, On Dreams, 350 B.C.E). More than two thousand years ago after Aristotle's famous essay, experimental studies have confirmed that external stimulation can be incorporated into dream content. For instance, as we mentioned earlier in section 1.3.1, Dement and Wolpert (1958) have reported an incorporation of non-awakening water stimulations in 42% of the subsequent dream reports. Such incorporation of external stimuli into dreams also inspired the famous Dali painting *Dream Caused by the Flight of a Bee Around a Pomegranate a Second Before Awakening*.

Dream function

4

> *J'ai rêvé tant et plus, mais je n'y entends note.*[5]
>
> — **François Rabelais**
> Pantagruel, 1532

4.1 Historical perspective

4.1.1 Ancient and classical history

Since the dawn of times, humans have tried to assign meaning to their dreams. In many ancient civilizations, dreams were considered as omens or messages from deities, and needed therefore to be correctly interpreted. Numerous examples of dreams sent by Gods can be found in Mesopotamian, Egyptian and Greek mythological narratives, as well as in the sacred books of the three main monotheistic religions (see De Koninck, 2012). Greek philosophers, however were the first to consider dreaming as a natural phenomenon. They provided different explanations of the nature and meaning of dreams, some of which are well in tune with modern dream research. For example, anticipating the notion of continuity between waking and dreaming, Cicero and Herodotus believed that dreams are produced by thoughts, concerns and conversations a dreamer had during the preceding days. Plato on the contrary viewed dreams as the expression of hidden desires and intolerable behaviors, an idea consistent with Freud's repression hypothesis. Finally, Aristotle thought that dreams were caused by external and internal bodily sensations, an idea consistent with Hobson's stochastic theory of dream generation.

4.1.2 The royal road to the unconscious

The father of psychanalysis viewed dreams as the *"royal road to the unconscious"* (Freud, 1900). He defined the unconscious as a part of our mind made up of thoughts, desires, emotions, and knowledge that we are unaware of, but that nevertheless profoundly influence and guide our behaviors. Freud believed that the ego's defenses are lowered during dreaming, which allows the unconscious mind and the repressed material (i.e. material made unavailable to consciousness because morally unacceptable) to come through awareness, albeit in a distorted form to avoid sleep disturbances, hence his famous aphorism that *"dreams are the guardians of sleep"*. For him, the dream is formed of the manifest content (i.e. the dream as the dreamer recalls it), which is often based on mundane and insignificant day-residues, and the latent content (i.e. symbolic meaning

of the dream). The latent content of the dream can be extract from the manifest content using free-association in order to unravel the unconscious thoughts expressed in the dream. Therefore, in Freud's model, the dream need to be explicitly remembered and interpreted to possess an adaptive value (thought the sleep protection mechanism might be adaptive *per se*). It is noteworthy that his hypothesis *"has rarely been considered by neuroscientists who often consider Freud's work and theory unscientific"* (Ruby, 2011). Yet, this issue of whether Freud's theory is scientifically valid, i.e. with experimentally testable predictions and the possibility to falsify it (Popper, 2014), has been recently addressed by Guénolé et al. (2013) who concluded that *"Freud's theory of the basic function of dreaming is empirically testable ... and can be considered as a valuable contribution to the scientific knowledge"*.

4.1.3 Psychological individualism

Michel Jouvet, one of the pioneers of sleep research, co-discoverer of REM sleep, was also greatly interested in dreams. He kept a dream diary for years, which he used to describe several quantitative measures of dream content. For instance, he was one of the first to report the dream-lag effect (Jouvet, 1979). With regards to the function of dreaming, which he equated at the time to the function of REM sleep, he first proposed at the beginning of his career that it allowed the maintenance of typical behaviors of species, an idea that stems from his own findings on the complex motor sequences exhibited by cats during REM sleep after suppressing muscular atonia (see section 1.3.2). Later on, he modified this theory and proposed that dreaming is in fact a kind of iterative neurological programming system whose aim is to preserve the expression of the genetic program that codes for psychological characteristics. According to him, this process would ensure the stability of personality traits across time (Jouvet, 1991).

4.2 Modern theories

4.2.1 An epiphenomenom of REM sleep

Based on the neurophysiological properties of REM sleep, which he equated with dreaming, Alan Hobson proposed that dreaming is an epiphenomenon of REM sleep (Hobson et al., 1998). According to him, the dream imagery is the result of cortical centers trying to create meaning from brainstem-driven signals generated during REM sleep (the so-called activation-synthesis model). In this theory, the dream content is therefore stochastic and is very unlikely to represent an adaptive advantage. It should be noted, however, as noticed by Windt (2015), that *"Hobson does not deny that dreams can have meaning and can reflect the personality and concerns of the dreamer. He just thinks that their meaning is transparent and immediately obvious to the dreamer, rather than requiring an elaborate process of interpretation"*.

4.2.2 Threat / Social simulation theory

Revonsuo (2000) proposed that dreaming is a virtual reality in which the dreamer can simulate threatening events and therefore be better prepared to face upcoming dangers in waking life (the so-called threat simulation theory, TST). According to him, *"dream consciousness is essentially an ancient biological defense mechanism, evolutionarily selected for its capacity to repeatedly simulate threatening events"* (Valli et al., 2005). As such, dream content is more consistent with the original evolutionary environment of the human species (e.g. high level of violence and intergroup aggression between males) rather than the present one, and this could for example explain that the most frequent type of social interaction found in dreams, especially in males, is aggression (Hall and Van de Castle, 1966). Valli et al. (2005) further tested this hypothesis by analyzing the content of dream reports from severely traumatized and non-traumatized children. As predicted by the theory, the reported dreams of severely traumatized children included a higher number of threatening events than those of non-traumatized children. These threats were also more severe in nature than the threats of non-traumatized children.

The same team has recently proposed that, more than a simulation of threats, dreaming is a global simulation platform, with a strong focus on social perception and interactions (the so-called social simulation theory, SST; Revonsuo et al., 2015), which are, from an evolutionary standpoint, as relevant as threats (it is now well accepted that the social environment has afflicted strong selection pressures on human cognition). As this theory is very new, its main predictions remain to be experimentally confirmed or refuted.

4.2.3 Memory consolidation

There is converging evidences from both animal and human research that sleep optimizes and consolidates the memory of newly acquired information (Rasch et al., 2007; Diekelmann and Born, 2010). Based on this, a current hypothesis in dream research is that dreaming in itself is related to sleep-dependent memory consolidation (review in Schredl, 2017). This proposal was tested in Wamsley and Stickgold (2010) in a study where 50 subjects were trained on a virtual navigation task before taking a 45 min nap. Remarkably, subjects who dreamed about the task had better post-nap performances than subjects who did not dream. However, as only 4 out of 50 subjects actually dreamed about the task (among which two reports just included hearing the music presented during the training session), the statistical power of this study is very low and it would seem premature to draw conclusions from this single finding. The same year, Schredl and Erlacher (2010) investigated whether dream characteristics are related to the over-night improvement of a mirror tracing task (i.e. the participants must trace different figures they only saw in a mirror). They were unable to find an effect of direct incorporations of the mirror tracing task into the dream on over-night improvement. It should be noted however that, again, the rate of direct incorporation of the task was very low, which consequently results in a low statistical power. Another methodological bias is that these studies focused only, and for obvious reason, on recalled dreams and thus omit a large fraction of non-recalled dreams. The role of the different sleep stages in the putative role of dreaming in memory

consolidation needs to be further investigated. To sum up, these results are hitherto inconclusive on the role of dreaming in memory consolidation.

4.2.4 Emotional regulation

Cartwright proposed that dreaming is involved in emotional regulation (Cartwright et al., 1998a; Cartwright et al., 1998b). She reached this conclusion after observing that, in healthy subjects, the depression level before sleep was significantly correlated with affect in the first REM report. In the same study, she also observed that low scorers on the depression scale displayed a flat distribution of positive and negative affect in dreams, whereas those with a depressed mood before sleep showed a pattern of decreasing negative and increasing positive affect in dreams reported from successive REM periods. Secondly, she observed that among individuals who were depressed following a divorce, those who reported more negative dreams early in the night and fewer at late-night were more likely to be in remission one year later, compared to subjects in which this pattern was inverted. From these two works, she proposed that dreaming may actively moderate mood overnight in healthy individuals, with the decreasing rate of negative dreams across the night reflecting a within-sleep emotional regulation process.

Linking emotional regulation and memory consolidation processes, Perogamvros and Schwartz (2012) recently proposed the Reward Activation Model according to which emotionally relevant experiences (including threat-related information) have a higher probability of being activated during sleep and have a preferential access to sleep-related memory consolidation processes. According to them, one of the main functions of dreaming is *"to expose the sleeper to rewarding or aversive stimuli, in order to maintain and improve offline memory consolidation processes and performance in real life situations, while also contributing to emotion regulation processes"* (Perogamvros and Schwartz, 2013).

4.2.5 Summary

Despite several decades of scientific research on dream content, there is still no consensus on whether dreaming serves a function or not. As Blagrove (2011) stated in the summary of his chapter on dream function, *"There is to my knowledge no evidence that dreaming has a functional effect, or is associated with any brain process that is having a functional effect, as the literature on the supposed consequences of particular dream imagery is composed of correlational studies"*. Further research is therefore needed to move forward on this issue, notably by experimentally testing the main predictions of these theories in order to confirm or refute them.

Hypothesis and objectives

5

> *Le fait de rêver est sans doute une des données, plus nombreuses qu'on ne le pense, qui, mieux encore que le soleil ou la pluie, placent les hommes de tout climat, de toute époque et de toute condition devant des problèmes identiques.*[6]
>
> — **Roger Caillois**
> L'incertitude qui vient des rêves. 1956

5.1 Unresolved issues

From this review of the scientific literature on dreaming, it appears that many questions on the nature, function, and neurophysiological correlates of dreaming remain open, some of which are reported below.

Phenomenology of dreaming

- Do we dream during the whole night? If not, when do we dream during the night and for how long?
- Which factors influence the (dis-)continuity between waking and dreaming?
- What are the neurophysiological correlates of dream content? And can we explain the phenomenological content of dream content based on these correlates ?
- To what extent lucid dreaming resemble or differ from non-lucid dreaming?
- To what extent dreaming resemble or differ from other forms of spontaneous thoughts such as mind-wandering and daydreaming?

Dream recall

- Why are there such intra- and inter-individual differences in dream recall frequency?
- What are the neurophysiological correlates of dream recall?
- Why more dream reports follow awakening from REM sleep than from NREM sleep? Does that mean that the actual *production* of dreams is higher during REM sleep than NREM sleep, or rather than the *recall* of dreams is better following REM sleep?
- More broadly, does failure to recall dream upon awakening mean that the sleeper was not dreaming before awakening? Or does this reflect a failure to encode dream content into memory, for example caused by sleep inertia or interference mechanisms?

Function of dreaming

- Does dreaming serve an adaptive function *per se*? If so, do dreams need to reach consciousness and be remembered in order to be functional? Or do they need to be worked, or interpreted as believed by many?

The present thesis aims at contributing to the ongoing effort to solve these questions, by addressing, in parallel and with different paradigms, several aspects of dreaming. First, we investigated the mechanisms of dream recall by comparing the cerebral and behavioral functioning of high and low dream recallers (HR and LR, respectively). In Study 1 (section 5.2), we used EEG recordings to compare the sleep macro- and micro-structure of HR and LR, as well as their brain responses to stimuli during sleep. In Study 2 (section 5.3), we compared the cognitive performances and brain functional connectivity of HR and LR during sleep inertia using an EEG-fMRI paradigm. In addition with studying the brain and cognitive alterations during sleep inertia (part 1), our study is the first to experimentally test the hypothesis of a differential sleep inertia between HR and LR (part 2). In Study 3 (section 5.4), we further analyzed the data of this EEG-fMRI study to specifically compare the global default mode network functional connectivity in HR and LR, regardless of the effect of sleep inertia. At the same time, we measured, and compared between HR and LR, several cognitive and personality variables. In Study 4 (section 5.5), we took advantage of the considerable number of responses obtained in the online recruitment survey of this EEG-fMRI study to collect epidemiological data on dream and sleep habits of a large sample of French college students. In Study 5 (section 5.6), we used dream questionnaires to improve our understanding of the filter that dreaming applies to the waking life memories, and at the same time try to decipher the possible functions of dreaming. Finally, in Study 6 (section 5.7), we leveraged our expertise in sleep analysis to develop a free and open-source software dedicated to the reading, scoring and analysis of sleep data.

5.2 Study 1. DRF and intra-sleep awakening: brain mechanisms and functional properties

We have seen in section 2.3 that HR tend to have longer awakenings than LR during sleep (2 vs 1 min on average), and consequently a longer duration of intra-sleep wakefulness (30 vs 15 min on average in a full night of polysomnographic-recorded sleep), without any other differences in the duration and proportion of sleep stages (Eichenlaub et al., 2014a). These findings support the arousal-retrieval model which states that nocturnal awakenings are necessary to encode dreams into long-term memory. However, if awakenings are crucial for dream recall as these findings seems to suggest, one may ask if there is a minimum duration of awakenings to allow for the successful encoding of dreams into long-term memory, and if so, if this duration varies depending on the pre-awakening sleep stage. This issue was not directly addressed by Koulack and Goodenough (1976), who merely stated that arousal have to be of *"sufficient duration to permit consolidation of the dream experience in a form that is accessible in the waking state"*.

Consequently, we decided to experimentally test this issue by re-analyzing the data of Eichenlaub et al. (2014a) (see section 2.3.4) in order to score arousals. Arousals correspond to brief and phasic EEG frequency shifts lasting typically between 3 and 15 seconds, and scored independently of the sleep stages (see section 1.2.3). To our knowledge, the relationship between DRF and arousals has never been been investigated. In addition with the scoring of arousals, we performed a close comparison of sleep microstructure of HR and LR, in order to extent our knowledge of the influence of sleep parameters on DRF. This analysis included spindles, K-complexes, rapid eye movements and muscle twitches, which were scored either visually or automatically using dedicated algorithms. We also re-examined the data to see whether the longer awakening duration found in HR was limited to a specific sleep stages (e.g. longer nocturnal awakenings following periods of REM sleep), or was present in all sleep stages.

Second, we took the opportunity of the arousals scoring to address another issue, which is related to the finding of differential brain reactivity to auditory stimuli in high and low dream recallers (see section 2.3.4). As a reminder, Eichenlaub et al. (2014a) found that the amplitude of the attention-orienting brain response (P3a) to first names was higher in HR than in LR during both sleep and wakefulness (Fig 2.3A). These findings, along with the longer intra-sleep wakefulness in high recallers, suggest that there might be a causal link between neurophysiological responses to auditory stimuli and intra-sleep wakefulness during sleep. For instance, the amplitude of brain responses to auditory stimuli could be predictive of subsequent awakening or arousal reactions. Consequently, HR, who have larger brain responses to auditory stimuli, would have in turn more or longer awakenings during sleep and therefore more opportunities to encode their dreams into long term memory. One way to test this hypothesis would be to show that the amplitude of brain responses to auditory stimuli inducing an awakening or an arousal reaction is significantly higher than the amplitude of brain responses to stimuli that do not induce such reactions. Remarkably, this effect has already been reported for painful stimuli by Bastuji et al. (2008), who found that *"a late positive component (450–650 ms) was recorded in both stage 2 and paradoxical sleep, the amplitude of which was significantly enhanced in trials that were followed by an arousal"*. According to the authors, this brain response, which appeared functionally related to the P3 wave, might be associated to conscious perception and memory encoding. At the time of the original study, Eichenlaub et al. (2014a) were however not able to test this hypothesis given that they did not have the arousals scoring and that only too few auditory stimuli induced awakening reactions. The scoring of arousals, which are physiologically far more numerous than awakenings, made it possible to compare the auditory evoked potentials to arousing and non arousing stimuli.

Our predictions were the following ones. First, we expected no differences in the sleep microstructure of HR and LR, including the number and density of arousals, rapid-eye movements, spindles and K-complexes. Our hypothesis was that intra-sleep awakening, and not sleep microstructure, is the critical factor to explain variability in DRF. In line with this, we predicted that the duration of intra-sleep awakenings should be higher, in HR as compared to LR, whatever the sleep stages prior to awakening is. Third, consistent with previously reported with painful stimuli, we expected that the amplitude of brain

responses to arousing auditory stimuli will be significantly higher than the one of non-arousing stimuli, i.e. that larger brain responses predict subsequent awakening or arousal reactions. If this is the case, this result would provide a strong argument in favor of a causal link between brain responses during sleep, nocturnal awakenings, and dream recall frequency.

5.3 Study 2. The awakening brain: sleep inertia and its link with DRF

5.3.1 Part 1: Brain networks dynamics during sleep inertia

In addition with comparing the differential brain functional organization of high and low dream recallers during sleep inertia (see next section), this study offers the possibility to investigate thoroughly - by pooling the two groups - the brain networks dynamics across the first minutes after awakening. Indeed, while the behavioral aspects of sleep inertia are well documented, only a limited amount of studies investigated its cerebral correlates until now. In order to fill this gap, we designed a combined EEG-fMRI study to investigate sleep inertia in high and low dream recallers in the minutes following awakening from a 45 minutes mid-afternoon nap (see Fig 5.1). Resting-state scans were acquired before the nap, 5 min and 25 min after awakening to investigate the brain functional connectivity during sleep inertia, and each scan was associated with a mental calculation task to measure the cognitive impairments associated with sleep inertia. Our paradigm therefore provides an unique opportunity to study the brain and cognitive alterations during sleep inertia. For instance, one can observe the alterations in functional connectivity that are specific to sleep inertia by contrasting the 5 min post-awakening fMRI scan (RS2, see Fig 5.1) to the pre-sleep fMRI scan (RS1). Similarly, the evolution of the cerebral alterations of sleep inertia can be evaluated by contrasting the 25 min post-awakening fMRI scan (RS3) to the 5 min post-awakening scan (RS2). Furthermore, it should be noted that participants were partially sleep deprived on the night before, and awakened from a 45 minutes mid-afternoon nap, if possible in N3 sleep. Both sleep deprivation and awakening in N3 sleep have been associated with increased sleep inertia (Tassi and Muzet, 2000). Therefore, in addition with being ecological (short nights compensated by a daytime nap being common in young adults (Faraut et al., 2016), this paradigm will allow us to study sleep inertia in its most intensified form.

5.3.2 Part 2: Sleep inertia in high and low dream recallers

The second objective of this study was to test the hypothesis of a differential cognitive and brain functioning during the transition from sleep to wake between HR and LR. Indeed, as we have seen earlier (section 2.4.6)), several studies indicate that sleep inertia could be a critical factor mediating the forgetting or recall of dreams upon awakening (Schredl et al., 2003b; Conduit et al., 2004), an hypothesis that has however never been experimentally tested. In order to fill this gap, we designed the previously described EEG-

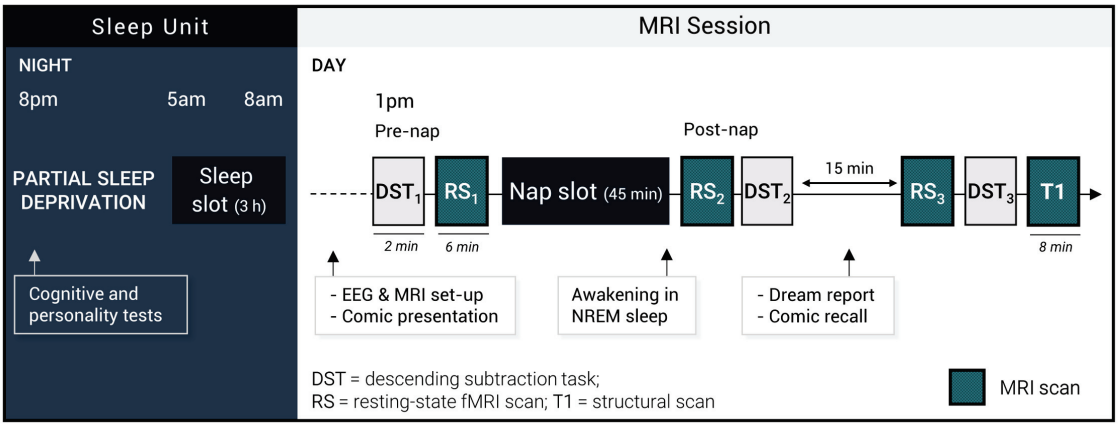


Fig. 5.1 **Experimental design of the sleep inertia fMRI study.**
Participants. Participants were selected if they reported and subsequently confirmed during a phone interview having a high or low DRF (DRF superior to 5 dream recalls per week and inferior to 2 dream recalls per month respectively) and having no sleep disturbances.
Evening and night. Participants arrived in the sleep unit of the hospital Le Vinatier (Lyon, France) at 8 pm on the evening prior to the experimental day. From 8 pm to 10 pm, they underwent several personality and cognitive tests administered by R.V. They were then instructed to stay awake until 5 am, at which point they were allowed to sleep for 3 hours until 8 am in a bed in the sleep unit.
Day. After lunch, participants were conducted to the neuroimaging center (CERMEP). During the first half hour, experimenters installed on the participant's head a MRI compatible EEG cap. Participants were then installed in the MRI scanner. They read a 5 min comic during the calibration of the eye-tracking camera, and then performed a mental calculation task (descending subtraction task, DST) for 2 minutes. The first resting-state scan was then acquired, with the instructions to remain awake and look at a central fixation cross on the screen. At the end of the scan, participants were informed that they could sleep during the next 45 min. During the nap, the experimenter used the EEG recordings to visually monitor, in real-time, the sleep stages. At the end of the nap slot, participants were awakened, if they were sleeping, by calling their first name and the 2nd resting state scan was acquired. At the end of the scan, the 2nd DST was performed. During the following 10 minutes, subjects were asked about their dream(s) and the comic they had read earlier. Then the 3rd resting state scan and DST were performed (about 25 min after awakening). Finally, an 8-min T1 anatomical scan was acquired. EEG data was acquired during the whole session. MRI data were only acquired during the functional (RS1-3) and anatomical (T1) scans.

fMRI study to study the cognitive and brain functioning upon awakening from sleep, and specifically included in our study participants that were either HR or LR. Our hypothesis was that LR would suffer from more acute sleep inertia upon awakening and that stronger impairment of cognitive functioning would prevent the short term memory of dreams from surviving the sleep-wake transition. Accordingly, we predicted that HR would show (1) more frequent dream recall upon awakening (2) a higher functional connectivity within the default mode network (see section 1.4.4 and 2.3.4) (3) less cognitive performance impairments, suggesting a faster recovery from sleep of regions involved in executive and memory processes. In other words, we hypothesized that the brain functional organization during sleep inertia would differ between high and low dream recallers and would reflect between group differences in dream recall.

5.4 Study 3. DRF, cognitive abilities, and default mode network

As we have seen earlier, there is ample evidence that DRF is positively correlated with psychological factors such as creativity or some personality traits (e.g. openness to experience, see section 2.3.1 and 2.3.1). On the other hand, recent findings indicate that DRF is also positively associated with distinct neurophysiological traits during both sleep and wakefulness, such as a higher regional cerebral blood flow within core regions of the default mode network. These two observations are remarkably consistent with the emerging view that dreaming and creative-thinking pertain to the same family of spontaneous mental processes, which could be underpinned by a strong recruitment of the default mode network (DMN, Christoff et al., 2016, see section 1.4.4) To better delineate the relationship between DRF and the DMN, we re-analyzed the fMRI data of Study 2 to compare, between HR and LR, the functional connectivity of the default mode network, independently of sleep inertia. To this aim, we concatenated the three resting-state scans acquired for each subject, and subsequently compared the global DMN functional connectivity of HR and LR.

Furthermore, we analyzed in this study the numerous cognitive and personality tests that were administered between 8pm and 10pm, on the evening prior to the partial sleep deprivation. Examples of these include the Guildford's Alternate Uses Task (Guildford et al., 1978), which measures creativity, the Wechsler Memory Scale (Wechsler, 2001) to measure memory abilities, and the Big Five Inventory (John and Srivastava, 1999) which measures an individual on the big five personality dimensions. Regarding the results, we expected that HR would exhibit a higher DMN functional connectivity, specifically between the TPJ and MPFC (see section 2.3.4), as well as higher scores of creativity and higher scores on certain personality dimensions such as openness to experience. In view of the literature, we did not expect HR to show higher memory abilities than LR.

5.5 Study 4. Sleep and dream habits in a sample of French students

Epidemiological investigations in healthy subjects combining questions on both sleep and dreaming are relatively rare. Such measures are yet necessary to establish and keep up to date sleep and dream norms in the general population. Of particular interest is the college population, which is more at risk of suffering from sleep difficulties than the general population (Buboltz et al., 2001; Curcio et al., 2006; Forquer et al., 2008; Lund et al., 2010).

In order to recruit participants for our above-mentioned fMRI sleep study (section 5.3), we have sent an announcement to several mailing lists of students from Lyon University. The announcement comprised a link to an online questionnaire about sleep and dream habits that participants had to fill out. The analysis of the responses provided up-to-date data on sleep and dream habits of a large sample of French college students, pertaining to different academic fields (i.e. humanities, science, medicine). Because our survey included relatively rare questions (e.g. frequency of recurrent and lucid dreams, sleepwalking, sleep-talking, sleep agitation), and thanks to a large sample of students including much more males than in previous studies (i.e. more than one third), we believe that this study will make a significant contribution to the limited number of previous epidemiological studies. Among our main points of interests were (1) to evaluate the sleep patterns of French college students (2) to find whether we could replicate previously reported gender differences in sleep and dream patterns (3) to find whether we could observe some inter academic fields differences.

5.6 Study 5. The relationship between waking life and dream content

As we mentioned earlier, there are numerous results showing that waking-life experience (WLE) finds its way into dreams (which led to the so-called continuity hypothesis, Schredl and Hofmann, 2003). However, the selection rule and time course of the WLE integration into dreams are still unclear. For instance, few studies have so far investigated the incorporation of WLE from the distant past as well as the incorporation of trivial, mundane, WLE. This is partly due to the classic method used in experimental studies so far, i.e. the content matching paradigm. It requires the participants to rate a posteriori (i.e. at the end of several days of experiment), similarities between a day diary and a dream diary completed for 14 days (e.g. Schredl, 2006; Malinowski and Horton, 2014a). Such a method has the advantage of controlling for retrospective availability of memories for elements when participants relate dream content to WLEs, but it may have the drawback of missing numerous mundane WLE that are not recorded in the day diary (typically insignificant day-residues), and at the same time overestimating the proportion of emotionally intense WLE. As a consequence, previous studies could not fully assess whether mundane WLEs and/or WLEs from the distant past were incorporated into dreams.

To address this problem, we designed a study which aimed at investigating in further details the characteristics of the WLEs incorporated into dreams, notably by assessing their remoteness on a life-time scale and by taking mundane WLEs into account. To do so, instead of asking dreamers to keep a day diary, we asked participants to report and characterize the WLEs related to their dreams immediately upon awakening. This strategy presents several advantages regarding previous methods. Firstly, any remembered WLE at any timescale can be considered. This method offers then the possibility of investigating the incorporation of WLEs across the whole life span, which has been rarely attempted until now (Grenier et al., 2005; Marquardt et al., 1996). Secondly, as the reported memory sources of a dream are dependent on the delay between the dream and the task to report memory sources, the sooner the task after the dream, the more chances we have to identify the true memory sources of the dream (Cavallero, 1987). Thirdly, as the connections between elements of waking life and dream content are assessed when the memories of the preceding days are still fresh, this method enables the recall of trivial WLEs from at least the few days before the dream. Using this new approach, we were able to test whether emotional WLEs are still preferentially incorporated into dream reports when trivial WLEs are taken into account and to investigate the emotionality and significance of WLEs incorporated into dreams as a function of their remoteness.

We predicted that this methodology would enable us to observe that a large proportion of the WLEs incorporated into dreams are mundane. Regarding the temporal remoteness of the WLEs incorporated into dreams, we expected to find not only a large contribution of the day before the dream (Marquardt et al., 1996) but also a significant contribution of remote WLEs (Verdone, 1965; Grenier et al., 2005; Llewellyn, 2013). Finally, given previous results showing a tendency for dreams to incorporate preferentially emotional WLEs (Schredl, 2006; Malinowski and Horton, 2014a), and the claim that day residues are predominantly mundane (Freud, 1900), we predicted an interaction between remoteness and emotionality for WLEs incorporated into dreams. Specifically, we expected that day residues would be scored as less important and less emotionally intense than would be more remote WLEs incorporated into dreams.

5.7 Study 6. An open-source software for sleep reading and analysis

During my PhD thesis, I have been working extensively on polysomnographic sleep recordings, notably to score sleep microstructural events (e.g. arousals, rapid eye movements; see section 5.2) and sleep stages (see section 5.3). While the detection of sleep microstructural events is usually done with automatic algorithms, the identification of sleep stages is traditionally done visually by an expert. For both visual sleep staging and automatic microstructural analysis, sleep researchers use either commercial or in-house softwares. In many cases, these softwares come with their own data and hypnogram file formats, and this heterogeneity can represent a substantial obstacle for sharing of algorithms and sleep data across laboratories.

In view of this, I developed, during my PhD thesis, a free and open-source software capable of reading numerous file formats, and integrating several signal processing tools and automatic detection of sleep microstructure. At first intended for my personal use, it soon extended into a fully developed and comprehensive software, thanks to a collaboration with my fellow PhD student Etienne Combrisson[1]. This software was integrated into a broader neuroscientific suite named Visbrain[2], and the specific sleep module was named *SLEEP*. The primary aim of *SLEEP* is to provide a fast and intuitive graphical user interface (GUI) to visualize and score polysomnographic sleep recordings. In order to be widely disseminated, the software must support a large range of data file formats, both proprietary (e.g. BrainVision) and public (e.g. European Data Format). It should also be able to handle the great heterogeneity in hypnogram formats (e.g. sampling rate of the hypnogram, values assigned to each sleep stage). Finally, to provide a significant scoring aid, the software should include several automatic detection algorithms (e.g. spindles, K-complexes, slow-waves) and several signal processing tools (e.g. filtering, referencing). Altogether, we believe that this software could represent a major methodological development in the field of sleep research.

5.8 Summary

[1]https://etiennecmb.github.io/
[2]http://visbrain.org/

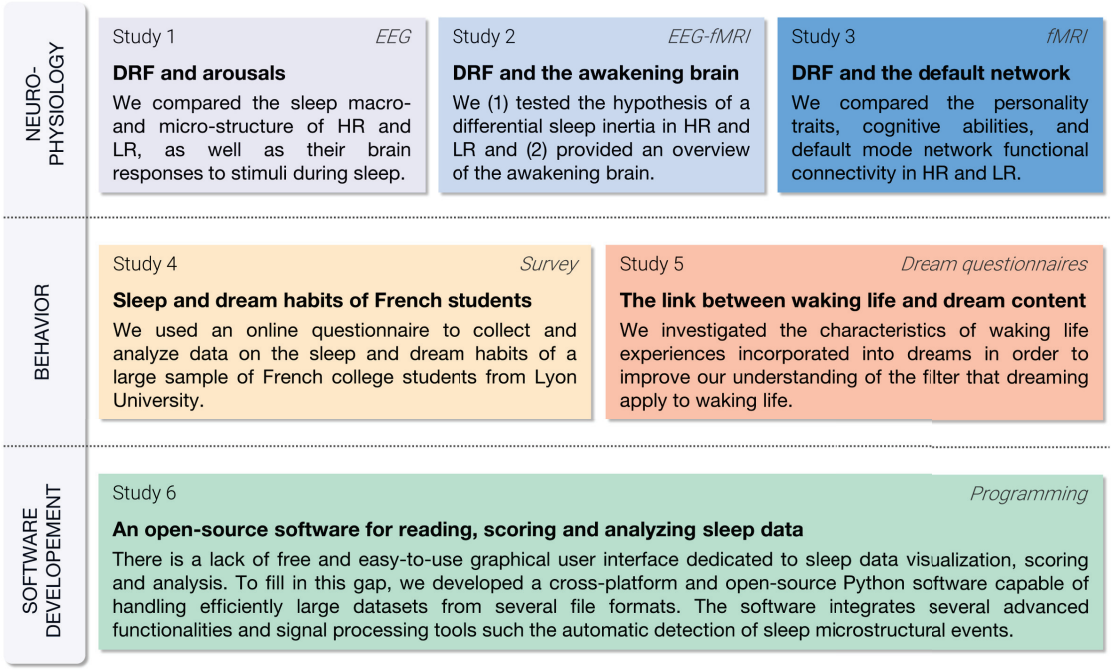


Fig. 5.2 **Summary of the studies conducted during my PhD thesis.** In Studies 1, 2 and 3, we investigated the neurophysiological correlates of dream recall frequency (DRF), by comparing the sleep parameters, cognitive abilities and brain functional connectivity of high and low dream recallers (HR and LR respectively). Second, we used behavioral methods to collect data on the sleep and dream habits of college students (Study 4), as well as the relationship between waking life and dream content (Study 5). Finally, Study 6 relates to the ongoing development of an open-source software dedicated to sleep data.

Part II

METHODS

EEG and event-related potentials

6

6.1 Electro-encephalography (EEG)

The first recording of the electric field of the human brain was made by the German psychiatrist Hans Berger in 1924. He named this recording electroencephalogram (EEG; Berger, 1929). Since then, EEG and event-related potentials (ERP; see next section) have become one of the most prominent technique in research (e.g. neuroscience, psychology) and medical settings (e.g. epilepsy, sleep disorders). EEG records voltage fluctuations resulting from ionic current within large assemblies of neurons in the brain. The brain electrical activity is measured with electrodes that are placed either along the scalp or, in rarer circumstances, directly on the exposed surface of the brain (electro-corticography or intra-cranial EEG). Through the current thesis, we will focus solely on the former and non-invasive, scalp EEG method, which is also one of the three essential electrophysiological measurements of polysomnography, along with EOG and EMG (see section 1.2.1).

6.1.1 International 10-20 system

EEG is generally recorded from multiple electrodes distributed across the scalp. To allow reproducibility both within and between individuals, the placement of these electrodes is defined in the internationally standardized 10-20 system, which relies on the relationship between the location of an electrode and the underlying area of cerebral cortex (Fig 6.1). Electrode location are determined using two standard anatomical landmarks, the nasion and inion, respectively located between the eyes and at the back of the skull. From these points, the skull perimeters are measured in the transverse and median planes and electrode locations are determined by dividing these perimeters into 10% and 20% distance intervals. Electrodes names refer to their locations on the cerebral cortex. Thus, the first letter refers to the brain lobe on which they are located (F = frontal, C = central, P = parietal, O = occipital), while the number corresponds to the hemispheres (3 = left, 4 = right). For example, F3 is located on the left hemisphere of the frontal lobe, while P4 lies on the right hemisphere of the parietal lobe.

6.1.2 Amplification, filtering and montage

The brain electrical activity is quite small (usually under 100 μV). For that reason, the EEG signal recorded on the scalp must be first amplified by several thousand times. In modern, digital EEG, the signal from each channel is then turned into a series of discrete digital values, with a sampling frequency generally comprised between 200 to 5000 Hz.

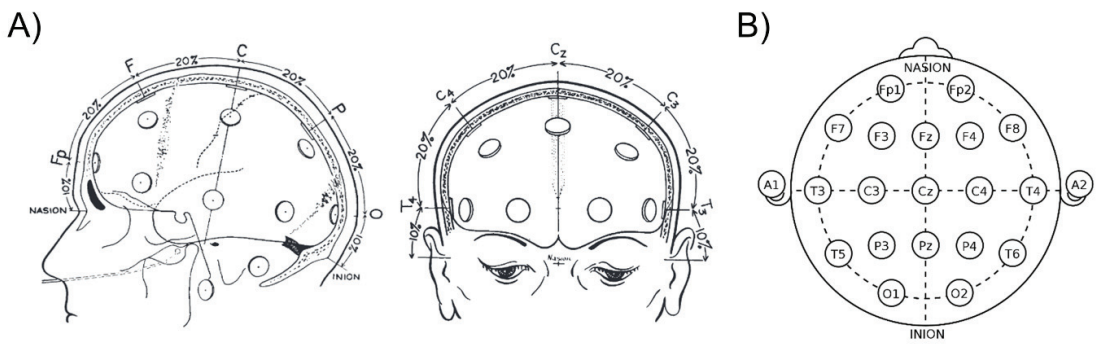


Fig. 6.1 **Electrode locations of International 10-20 system for EEG recording**. (A) Lateral and frontal views of the skull showing the methods of measurement for electrode placement (adapted from Klem et al., 1999). (B) Single plane projection of the head showing all standard positions and names of electrodes according to the 10-20 system.

The signal is then filtered and displayed on a computer screen using dedicated softwares such as Elan (Aguera et al., 2011) or EEGLAB (Delorme and Makeig, 2004). Typical filters include high-pass (<0.1 Hz), low-pass (35-70 Hz), and notch (50 or 60 Hz) to remove very slow artefacts, high-frequency artefacts (such as electromyographic activity) and electrical noise, respectively. Since the EEG is measured as the voltage (i.e. potential for electrical charges to move between two locations) between two electrodes, the display of EEG may be set up in several ways, referred to as montage. In the standard, referential montage, a single reference electrode, located at a site thought to be electrically neutral, such as the earlobe or the mastoid, is typically used for all the active scalp electrodes. By contrast, in the average reference montage, the averaged signal across all electrodes is used as the common reference for each channel.

6.1.3 Neural oscillations

The spontaneous brain electrical activity is characterized by rhythmic oscillations, which are sometimes referred to as neural oscillations or, more popularly, as *brain waves*. These oscillations are generated by the summation of synchronous activity of thousands or millions or neurons (mainly cortical pyramidal neurons). They have characteristic frequency ranges, spatial distributions and are associated with different states of brain functioning (e.g. waking and the various sleep stages; see Fig 6.2).

6.2 Event-related potentials (ERP)

6.2.1 Definition and methods

Event-related potentials (ERPs) are *"electrical potentials generated by the brain that are related to specific internal or external events such as stimuli, responses or decisions"* (Luck, 2014). A single ERP, usually recorded by means of scalp EEG, has an amplitude ranging

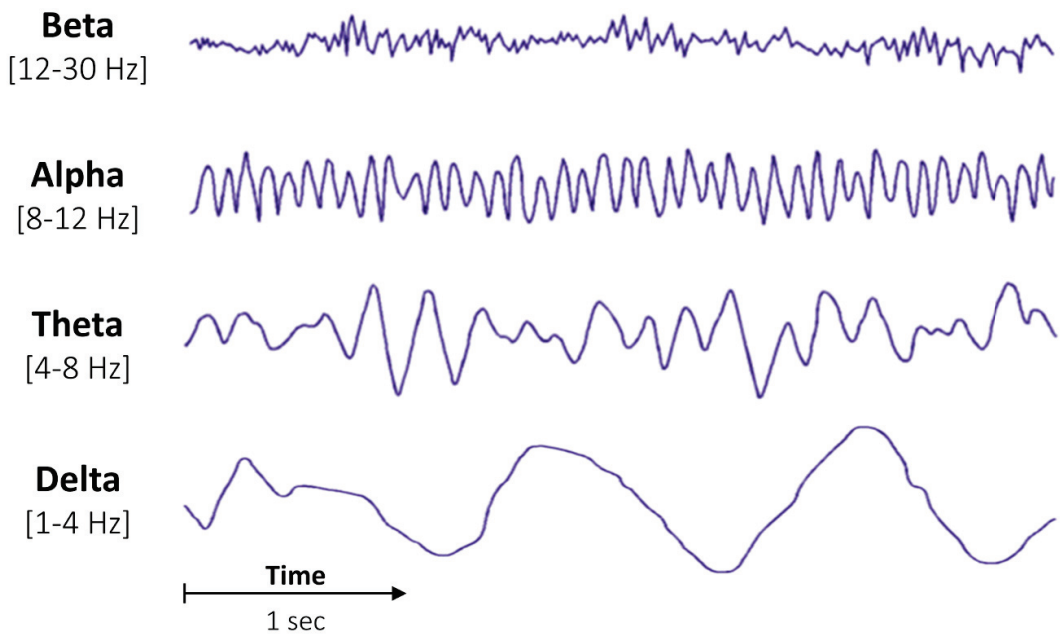


Fig. 6.2 **Brain rhythms**. Beta waves are prominent over occipital and parietal areas during normal waking wakefulness. Alpha waves are prominent in occipital regions during eyes-closed wakefulness. Theta waves are detectable during N2 sleep and REM sleep. Delta waves are visible during N3 sleep (also called slow-wave sleep or deep sleep) and have a large amplitude (>75 μV) due to a high level of neural synchronization.

from 0.5 to 15 μV, and is therefore much lower than the spontaneous background EEG (100 μV). As a consequence, a single ERP is not visible to the naked eye in the EEG signal. In order to disentangle and reveal the specific relevant ERP from the irrelevant background EEG, ERP technique relies on the mathematical principle of summation. It consists of averaging hundreds of time-locked repetitions of the same experimental condition in order to attenuate activities that are unrelated to the specific internal or external event. The resulting waveform contains a series of positive and negative peaks (components) that are thought to reflect activity (i.e. postsynaptic potentials) in underlying generators within the brain. These components are usually referred to with acronyms (e.g. contingent negative variation, CNV) or by a letter indicating polarity (N = negative, P = positive), followed by a number indicating the latency in milliseconds from stimulus onset (e.g. N100 is a negative peak arising approximatively 100 ms after stimulus). Early components, which arise approximatively less than 80 ms after the stimulus, are thought to reflect sensory processes and are therefore intrinsically linked to the physical characteristics of the stimulus. By contrast, late components (>100ms) are thought to reflect more cognitive processes such as attention, memory and response preparation. They differ from the former in the sense that they are not systematically elicited but rather require the participant to be involved in some stimulus-related task (e.g. a detection task). While some potentials are easily obtain by repetition of stimuli (e.g. the N100 potential, elicited by perception of auditory stimuli), others potentials are elicited by more complex paradigm. One of the most famous is probably the oddball-paradigm, in which low-probability target (or *deviant*) items are mixed with high-probability non-target (or *standard*) items. Target items elicit a

late positive component, the P300, though to reflect brain processes involved in stimulus evaluation or categorization.

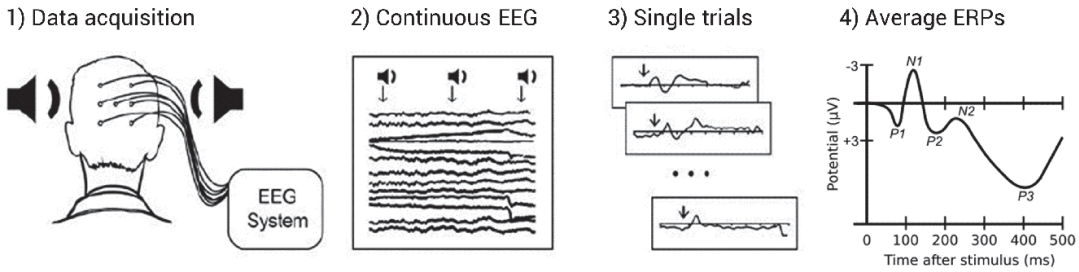


Fig. 6.3 **Schematic representation of ERP acquisition**. (1) Scalp electrodes record electrical brain activity while auditory stimuli are presented repeatedly through headphones or speakers. (2) Stimulus onset/offset markers are recorded along with the continuous EEG signal. (3) Individual segments locked to stimulus onset are extracted from the continuous EEG and include a brief pre-stimulus baseline in addition to post-stimulus period of interest. (4) Averaged ERP waveform showing several components (including the N100 and P300) reflecting time- and phase-locked neural activity associated with stimulus processing. Note that the ERP is plotted with negative voltages upward, a common, but not universal, practice in ERP research. Adapted from Key (2016)

6.2.2 The use of ERP in sleep research

ERP is a method of choice for the investigation of the normal and pathological human sleep (Bastuji and García-Larrea, 1999; Colrain and Campbell, 2007). One reason for this is that it allows to study objectively information processing during sleep, limited otherwise by the lack of the ability of subjects to make verbal or motor responses to stimuli. It provides a powerful, objective and non-invasive means to study for example the extent of sensory integration during sleep, or the neurological abnormalities related to sleep disorders, or sleep inertia upon waking (Bastuji et al., 2003). ERP studies greatly improved our understanding of sleep, from the classical view that sleep is a *little death* (illustrated by the fraternal link between Hypnos, God of Sleep, and Thanatos, God of Death, in the Greek mythology; see Mazza et al., 2014), to the emerging idea that sleep is a dynamic process in which complex cognitive processing occur (see Andrillon, 2016). For example, a P300 component has been observed during REM sleep in response to target stimuli presented within an oddball paradigm (Bastuji et al., 1995). Similarly, there is a persistence of the brain's ability to detect semantic incongruity during REM sleep (N400; Perrin et al., 2002). It should however be noted that considerable differences exist between waking, NREM and REM sleep ERP components (Bastuji and García-Larrea, 1999; Colrain and Campbell, 2007). Specifically, while early sensory components (i.e. peripheral and brainstem responses) remain unaffected by the sleep cycle, early cortical responses are drastically modified, in part because the thalamus stops relaying sensory information to the brain. Finally, late cortical responses displays profound changes during NREM sleep, which revert in REM sleep.

7 fMRI and functional connectivity

7.1 Structural and functional magnetic resonance imaging

7.1.1 Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) is probably the *"most important imaging advance since the introduction of X-rays by Conrad Röntgen in 1895"* (Logothetis, 2008). It is undoubtedly true that the emergence of MRI has indeed marked the beginning of a new era in diagnostic medicine and basic research. MRI is based upon nuclear magnetic resonance, the physical phenomenon by which nuclei placed in an external magnetic field absorb and re-emit radio-frequency energy. MRI is the technique of choice for imaging brain structure, in part because magnetic properties of hydrogen nuclei vary with the biological tissue in which they are. Consequently, the rate of spin relaxation (i.e. how quickly spins *forget* the direction in which they are oriented) is not the same between gray and white matter, which thus makes it possible to construct detailed images of the brain at any location and orientation with sub-millimeter resolution.

7.1.2 Functional MRI (fMRI)

Functional MRI (fMRI), built on the earlier concept of MRI, is a technique for measuring hemodynamic changes (i.e. blood flow dynamic) in the brain due to changing neural activity. Compared to structural MRI, the brain is scanned at lower spatial resolution (2-3 mm) but at a higher temporal resolution (typically a few seconds). Specifically, fMRI relies on the fact that hemoglobin in blood slightly distorts the magnetic resonance properties of hydrogen nuclei in its vicinity, and the amount of magnetic distortion changes depending on whether the hemoglobin has oxygen bound to it. For example, when neurons of a specific brain area become active, local blood flow to this region increase, and oxygen-rich (oxygenated) blood displaces oxygen-depleted (deoxygenated) blood around 2 seconds later (a phenomenon known as the hemodynamic response). These changes in the concentration of oxygen and blood flow lead to localized blood oxygenation level-dependent (BOLD) changes in the magnetic resonance signal. It is generally accepted that, in most brain regions, the fMRI signal is coupled to the level of excitatory and inhibitory synaptic transmission and therefore reflect the level of information processing (Logothetis, 2008).

7.1.3 Task-based and resting-state paradigms

Traditionally, fMRI has been used to produce maps of task-dependent brain function using block or event-related designs, which are based on the subtraction paradigm. In such designs, one infers the level of activation of certain brain areas by looking at the relative changes from baseline (resting or control condition) in the BOLD signal during the performance of a task or in response to a stimulus. During these designs, participants are instructed to perform specific tasks, which are generally designed to target a single brain function such as vision, attention, memory, emotion recognition and so on. These paradigms have allowed brain science to take giant strides, in particular on the issue of linking brain areas with specific functions (which was in the past only possible by studying cerebral lesions).

More recently, there has been a growing interest in the application of resting-state fMRI (RS-fMRI). Indeed, soon after the development of fMRI, some researchers observed that the resting brain was not silent but contained information about its functional organization (Biswal et al., 1995). Specifically, they reported that, during rest, time courses of low frequency fluctuations (<0.1 Hz) in somatomotor brain areas, showed a high degree of temporal correlation. They argued that this correlation, which may arise from fluctuations in blood oxygenation or flow, is a manifestation of functional connectivity of the brain. Although at the time Biswal's seminal observation was mostly disregarded, it laid the basis for the now widely-used resting-state fMRI paradigm, which measures how different regions of the brain communicate while participants are not performing any active task. Although both resting-state and task-related designs measures BOLD signal, there are several major differences between the two, which are reported in Table 7.1.

7.2 Functional connectivity

7.2.1 Overview

Functional connectivity can be defined as *"the temporal dependence of neuronal activity patterns of anatomically separated brain regions"* (van den Heuvel and Hulshoff Pol, 2010). It can be measured as long-range synchronization of the EEG, magneto-encephalography (MEG), or other dynamic brain signals. Applied to fMRI, functional connectivity reflects the temporal correlation of low frequency (<1 Hz) BOLD spontaneous fluctuations in spatially distinct brain regions (Fig 7.1). Although the true neuronal basis of these slow BOLD fluctuations is not yet fully understood, there is converging evidence that they result from co-activation in the underlying spontaneous neuronal activation patterns. As a consequence, they are thought to reflect functional communication between brain areas. There are also several evidences that spontaneous BOLD fluctuations are partly constrained by anatomic connectivity (Van Dijk et al., 2010).

In more practical terms, these intrinsic BOLD fluctuations are nearly always measured at rest in order to minimize task-evoked effect. Resting-state fMRI has also the advantage

Table 7.1 **Key differences between task-based fMRI and resting-state fMRI according to Smitha et al. (2017)**

	Task-based fMRI	Resting-state fMRI
Design	Analyses of the relative changes from baseline in the BOLD signal during a task or in response to a stimulus	Analyses of the spontaneous BOLD signal in the absence of any explicit task or input
Energy consumption	Task-specific increase in neuronal metabolism are less than 5%	60–80% of brain's energy is consumed during resting state
Brain areas	The focus is only on a very small fraction of the brain's overall activity	The focus is on large-scale brain networks
Signal-to-noise ratio	Low since 80% of the BOLD modulation is discarded as noise	Good since it takes the overall spontaneous low frequency fluctuations
Patient cooperation	Patient cooperation is essential	Pediatric, psychiatric and comatose patients can do it
Duration	Requires a large number of repetitions	Usually 6 to 10 minutes

of being quite simple to implement. For that reason, functional connectivity resting-state MRI has become the technique of choice to study the intrinsic functional organization of the brain in healthy individuals across a variety of vigilance states (such as sleep) but also in patients (e.g. comatose and psychiatric patients).

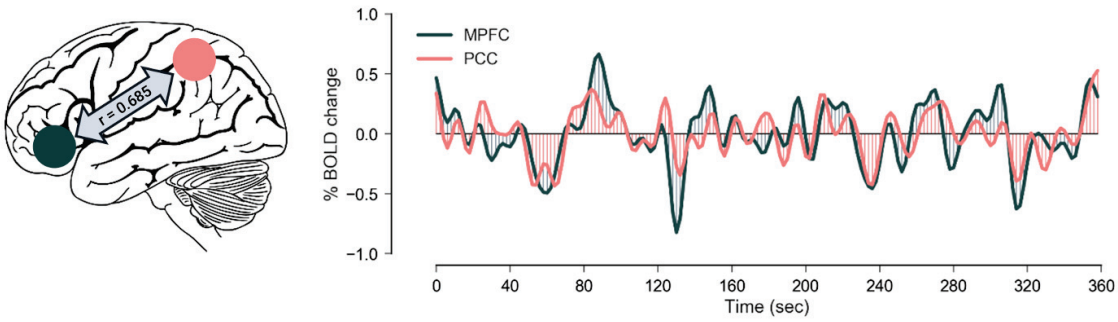


Fig. 7.1 **The basic strategy of functional connectivity MRI.** The basis of functional connectivity is that spontaneous BOLD fluctuations measured at rest are correlated between spatially distinct brain regions. In this example, spontaneous BOLD fluctuations in the medial prefrontal cortex (MPFC) and posterior cingulate cortex (PCC) are correlated (Pearson r = 0.685). These data come from a 6-min resting state scan acquired in a single individual on a 3-tesla MRI scanner.

7.2.2 Large-scale brain networks

A decade of resting-state fMRI research has revealed that the human brain is organized into several large-scale functionally-correlated brain networks, which are consistently found

in healthy subjects, different stages of consciousness and across species (Fox and Raichle, 2007; Yeo et al., 2011). Because they are preferentially identified during resting-state fMRI, these networks are often referred to as resting-state networks. They are comprised of different brain regions that each have their own task and function, but which are continuously exchanging information with each other. Remarkably, they closely match the topographies of functional responses obtained by task-related fMRI using typical sensory, motor, and cognitive paradigms. The main functional networks of the human brain are depicted in Fig 7.2. The visual and somatomotor networks include regions of the primary and secondary visual and sensory-motor cortex respectively. These two sensory networks are characterized by a clear coupling between anatomic and functional connectivity (Van Dijk et al., 2010). Next, come the so-called task-positive networks, namely the frontoparietal (FP; sometimes referred to as executive, or control) network, the dorsal attention network (DAN), and the salience network. They are all involved in attentional processes. For instance, the DAN is thought to support selective attention to sensory features of the environment, while the salience network is involved in monitoring the salience of external inputs and internal brain events. There is emerging evidence that the FP network, originally thought to be involved in the selection of sensory contents by attention, may also orchestrate the interactions between other networks (Christoff et al., 2016).

Finally, the last and perhaps most investigated brain network is the default mode network (DMN, sometimes referred to as task-negative network), which was originally identified as a set of brain areas consistently deactivated across a range of externally oriented tasks (Raichle et al., 2001). It has been linked to internal mental processes, such as introspection, mind-wandering but also episodic memory retrieval and autobiographical future thinking. The DMN includes several subsystems which are supposedly involved in different functional roles (Fig 7.3; Andrews-Hanna et al., 2010). The DMN is probably one of the more robust brain network, and it has been identified across several vigilance states, including NREM and REM sleep (Horovitz et al., 2009; Larson-Prior et al., 2009; Larson-Prior et al., 2011; Wu et al., 2012). Recently, some authors have postulated that the DMN might be involved in the production and/or encoding of dreams (see section 1.4.4).

7.2.3 Anti-correlations between networks

Fox et al. (2005) reported that the DMN is negatively coupled (anti-correlated) to brain networks involved in focused external visual attention (i.e. mainly the DAN). In other words, when the spontaneous BOLD fluctuations increase in the DMN, they decrease in the DAN. This dynamic interplay between two large, spatially distributed networks representing a priori opposing components of our mental lives (the DMN is involved in internal mental processes, while the DAN is involved in external attention) may *"mark a fundamental feature of brain organization that had not been appreciated by earlier techniques"* (Buckner et al., 2013). Remarkably, a decrease anti-correlation between the DMN and the DAN has been consistently reported in a variety of altered vigilance states such as during NREM sleep (review in Picchioni et al., 2013) and after total sleep deprivation (De Havas

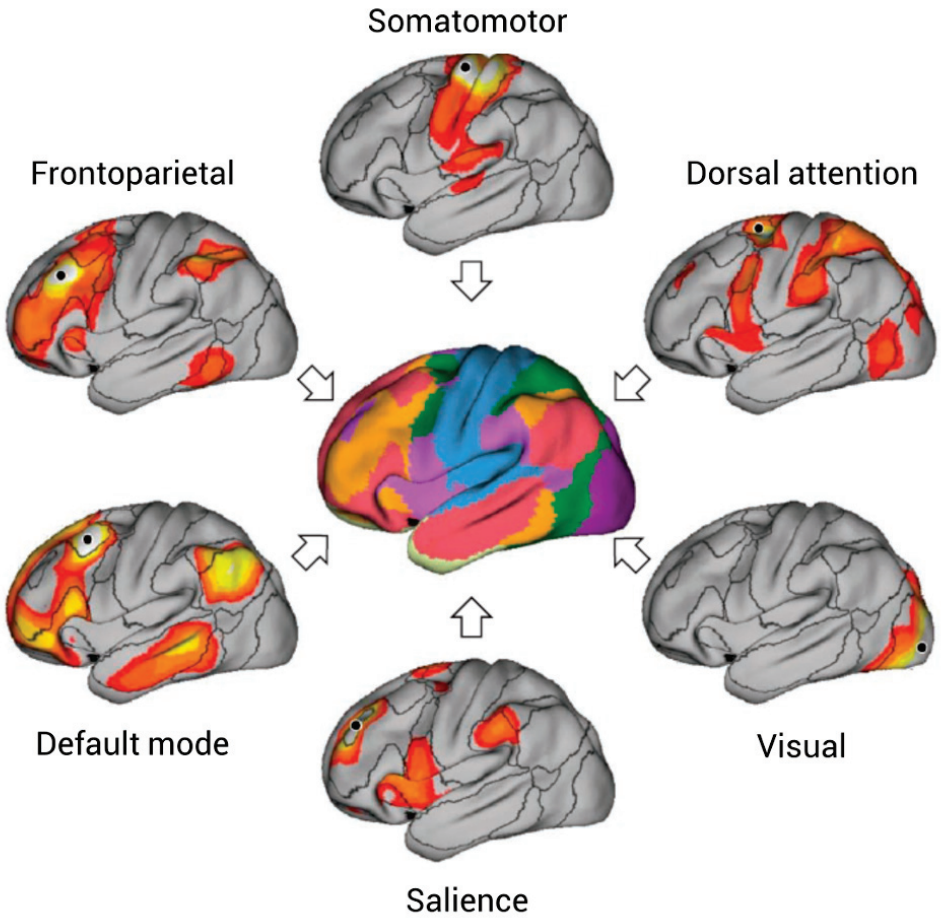


Fig. 7.2 **Large-scale brain networks identified with resting-state functional connectivity fMRI**. Outer maps show the functional connectivity maps for a single seed region (black circle) placed in a different cortical region, obtained using resting-state fMRI data in 1000 subjects. Center map shows a composite estimate of the networks using an analytical approach to parcellate cortical regions into their most dominant network. Originally published in Buckner et al. (2013)

et al., 2012). This suggests that anti-correlation between these networks is an essential part of the brain normal functional organization.

7.3 Resting-state fMRI data analysis

The aim of this section is to provide a brief overview of the numerous processing steps that must be performed to go from the raw structural and functional MRI images to the group-level statistical analysis. These steps are summarized in Fig 7.4.

7.3.1 Preprocessing

Steps in the spatial preprocessing of task-related and resting state fMRI data are similar. The first step is usually slice-timing correction, which aims at correcting temporal offset

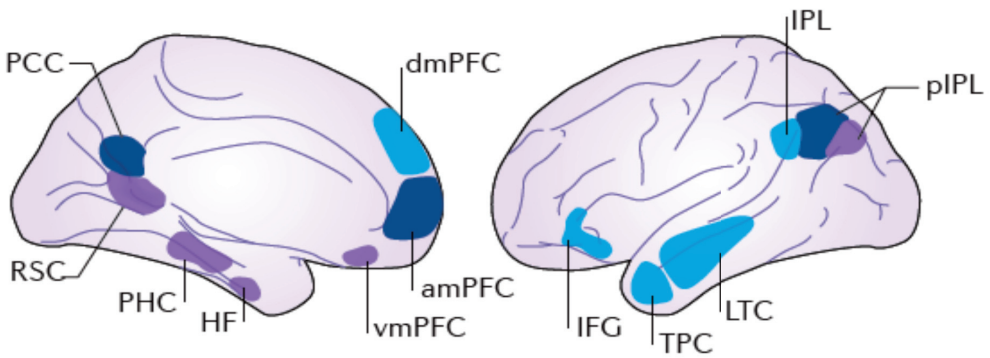


Fig. 7.3 **The default mode network and its subcomponents.** The DMN is centered on the medial prefrontal cortex (MPFC), the medial parietal cortex and the lateral parietal cortex, and extends into the temporal lobe and lateral prefrontal cortex. Three subcomponents within the DMN have been identified. The first, the core DMN subsystem (deep blue) includes the MPFC, posterior cingulate cortex (PCC) and posterior inferior parietal lobule (pIPL). It is characterized by its hub-like properties and its contributions to internally oriented cognition. The second subcomponent (purple), which is known for its roles in memory and mental simulation, is centered on the medial temporal lobe (MTL), and includes as well the hippocampal formation (HF) and parahippocampal cortex (PHC). The third subcomponent (cyan) extends more dorsally and includes the dorsomedial prefrontal cortex (dmPFC), the lateral temporal cortex (LTC), the temporopolar cortex (TPC) and parts of the inferior frontal gyrus (IFG). It seems to be linked to a wide range of functions, including mentalizing, conceptual processing and emotional processing. Originally published in Christoff et al. (2016).

between slices within a repetition time by applying a temporal data interpolation to each voxel of the brain. Indeed, an fMRI scanner typically requires 2 seconds (i.e. repetition time or TR) to construct a full 3D brain volume by slicing the brain into multiple 2D layers (acquired either in ascending or interleaved order). Consequently, the BOLD signal (hemodynamic response) acquired in the last slice (late in the TR) peaks earlier than those in the slices acquired early in TR, even though the underlying activity is identical. Slice-timing correction applies a temporal data interpolation to each voxel of the brain in order to reconstruct a signal as if all the slices within a TR were acquired at the same exact time point. The second main step is the coregistration which refers to the alignment of functional and structural images from the same subject to map functional information into anatomical space. In layman's term, this step ensures that the brain images acquired from a single individual are always in the same position and space. This step is particularly important in resting-state fMRI due to the global effect of head movements on spontaneous BOLD fluctuations. Next comes normalization, which refers to the spatial transformation of individual brains into a common space (typically Montreal Neurological Institute (MNI) space), a step crucial in order to make brain volumes acquired in different subject with different brain morphologies comparable to each other. A temporal filtering is sometimes applied to remove or attenuate frequencies within the raw signal that are not of interest. For instance, as functional connectivity fMRI studies the spontaneous low-frequency BOLD fluctuations, a bandpass filter on frequencies between 0.01 Hz - 0.1 Hz is usually applied. Finally, the last preprocessing step is generally the spatial smoothing, which aims at further increasing the signal-to-noise ratio by filtering out high frequency regions. Smoothing is a prerequisite to parametric statistical analysis (such as the Gaussian random fields) which assume that data are well-modeled by a normal distribution, however, there is a

controversy as to the role of smoothing in resting-state fMRI (and notably graph analysis) in which increased spatial dependency introduced by smoothing might confound local connectivity strength (Hayasaka and Laurienti, 2010).

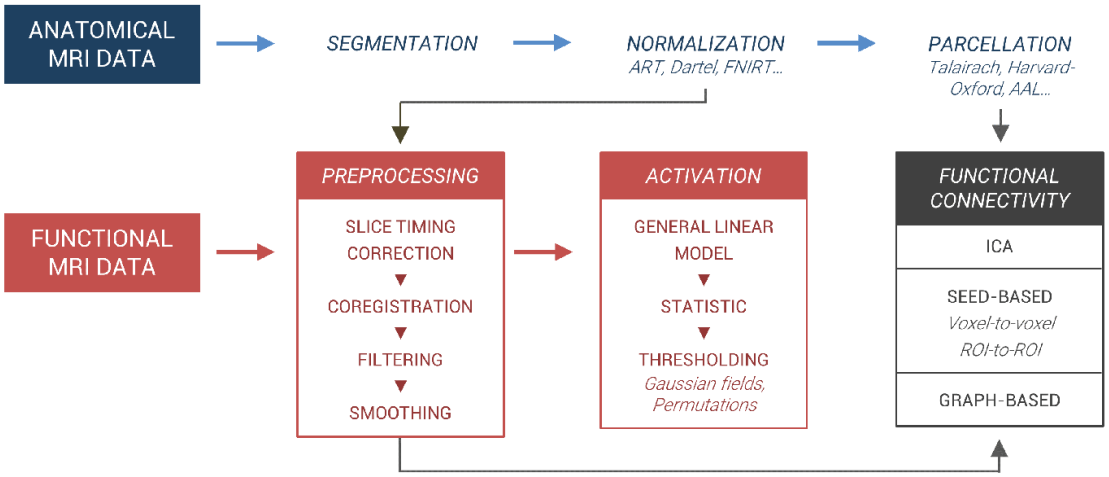


Fig. 7.4 **Overview of the fMRI processing pipeline.** ICA = independent component analysis, ROI = regions of interests. Adapted from an original idea of Oussama Abdoun.

7.3.2 Functional connectivity analysis

There are three prominent methods to analyze preprocessed resting-state fMRI data (Fig 7.5). The first one is independent component analysis (ICA), which is a statistical method for separating a multivariate signal into additive subcomponents. Applied to brain functional connectivity data, it allows for example to separate distinct brain networks, without making any kind of initial assumptions (Beckmann et al., 2005). Because it requires no a priori defined regions of interests (ROIs), it can be quite easily implemented to identify brain networks or to remove noisy components of the signal (e.g. physiological noise, scanner drift). The second approach is based on a priori defined cluster of voxels (referred to as seeds, or ROIs). In this case, the signal from a specific seed is correlated either with all the other voxels of the brain (voxel-to-voxel approach) or others ROI (ROI-to-ROI approach). The ROI-to-ROI method is particularly well-suited to analyze within and between networks interactions, provided that the ROIs are defined a priori (for example using an ICA or a brain atlas). Finally, an emerging method in resting-state fMRI analysis is graph theory, which studies the spatio-temporal properties of brain networks using mathematical tools (Bullmore and Sporns, 2009).

7.3.3 Combined EEG-fMRI recordings

Simultaneous recording of EEG and MRI allow researchers to benefit from the excellent temporal resolution of EEG combined with the high spatial accuracy of fMRI. Applied to sleep, it allows for example to perform correlation between sleep features (detected using classic EEG-based criteria), and BOLD-fMRI signal (Duyn, 2012). The EEG can also be used to detect online the different sleep stages, thus allowing the experimenter

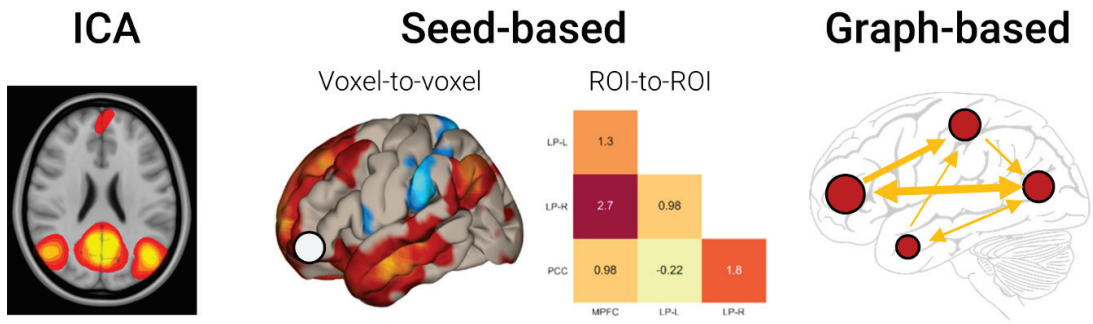


Fig. 7.5 **The three main methods of resting-state fMRI data analysis**. (1) ICA is a highly data-driven method which is typically used to identify brain networks (in this example, the core regions of the DMN) or remove noisy components. (2) Seed-based connectivity requires one or several regions of interests (ROIs) to be a priori defined in order to compute the correlations between the seed regions and all the others voxels in the brain (voxel-to-voxel) or between specific ROIs (ROI-to-ROI). In this example, a symmetric correlation matrix was obtained by computing all the pairwise correlations within the DMN. (3) Graph-based connectivity studies the topological features of brain networks, which are defined in this context as a set of nodes (ROIs) linked by connections (edges). Using mathematical tools, several parameters can be computed such as the global efficiency and the level of modularity / clustering.

to decide when to launch an fMRI scan. Simultaneous EEG-fMRI is therefore a valuable tool for investigating brain function across the spectrum of vigilance states. However, there are a number of technical challenges that need to be overcome in order to improve EEG-fMRI data acquisition. Most importantly, EEG signals acquired during simultaneous fMRI are affected by several artefacts, namely the gradient artefact (caused by the changing magnetic fields gradients required for fMRI) and the cardio-ballistic artefact (linked to cardiac pulsations). Fortunately, these artefacts can be almost entirely removed, a posteriori but also in real-time, using dedicated softwares or algorithms.

Part III

EXPERIMENTAL RESULTS

8

Study 1. DRF and intra-sleep awakening: brain mechanisms and functional properties

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 21 March 2017
doi: 10.3389/fnhum.2017.00132

Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall

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High dream recallers (HR) show a larger brain reactivity to auditory stimuli during wakefulness and sleep as compared to low dream recallers (LR) and also more intra-sleep wakefulness (ISW), but no other modification of the sleep macrostructure. To further understand the possible causal link between brain responses, ISW and dream recall, we investigated the sleep microstructure of HR and LR, and tested whether the amplitude of auditory evoked potentials (AEPs) was predictive of arousing reactions during sleep. Participants (18 HR, 18 LR) were presented with sounds during a whole night of sleep in the lab and polysomnographic data were recorded. Sleep microstructure (arousals, rapid eye movements (REMs), muscle twitches (MTs), spindles, KCs) was assessed using visual, semi-automatic and automatic validated methods. AEPs to arousing (awakenings or arousals) and non-arousing stimuli were subsequently computed. No between-group difference in the microstructure of sleep was found. In N2 sleep, auditory arousing stimuli elicited a larger parieto-occipital positivity and an increased late frontal negativity as compared to non-arousing stimuli. As compared to LR, HR showed more arousing stimuli and more long awakenings, regardless of the sleep stage but did not show more numerous or longer arousals. These results suggest that the amplitude of the brain response to stimuli during sleep determine subsequent awakening and that awakening duration (and not arousal) is the critical parameter for dream recall. Notably, our results led us to propose that the minimum necessary duration of an awakening during sleep for a successful encoding of dreams into long-term memory is approximately 2 min.

Keywords: EEG, dreaming, awakenings, arousals, sleep, oddball paradigm

OPEN ACCESS

Edited by:
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Reviewed by:
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Received: *07 February 2017*
Accepted: *07 March 2017*
Published: *21 March 2017*

Citation:
Vallat R, Lajnef T, Eichenlaub J-B, Berthomier C, Jerbi K, Morlet D and Ruby PM (2017) Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall. Front. Hum. Neurosci. 11:132. doi: 10.3389/fnhum.2017.00132

Abbreviations: AEP, Auditory evoked potential; AI, Arousal Index; BSW, Before sleep wakefulness; EEG, Electroencephalogram; EMG, Electromyogram; EOG, Electro-oculogram; ERP, Event related potential; HR, High dream recallers; Inds, Indeterminate; ISW, Intra sleep wakefulness; KCs, K-complexes; LR, Low dream recallers; MTs, Muscle twitches; Mvts, Movements; REMs, Rapid eyes movements; TST, Total Sleep Time.

INTRODUCTION

Nearly everyone has awakened once with a dream in mind. The dream recall frequency however can vary substantially between individuals and even within one person from time to time. For more than a century, researchers have investigated whether some psychological parameters could explain dream recall frequency variability (for a review see Ruby, 2011), but it's only recently that physiological parameters have been considered. Using Electroencephalogram (EEG) and PET we found neurophysiological differences between high dream-recallers (HR) and low dream-recallers (LR) during both sleep and wakefulness (Ruby et al., 2013b; Eichenlaub et al., 2014a,b). Notably, during wakefulness, in response to auditory novel stimuli, the attention-orienting brain response (P3a) and a late parietal component were found to be larger in HR than in LR. During sleep, between-group differences were also observed for auditory evoked potentials (AEPs) to the same stimuli, at the latency of the P3a in N2 and at later latencies during all sleep stages. Finally, at the behavioral level HR showed more intra-sleep wakefulness (ISW) than LR (∼15 min more on average, see Eichenlaub et al., 2014a).

Taken together, these results suggest a causal link between neurophysiological responses to auditory stimuli and ISW. We proposed that this link could be subserved by the amplitude of the brain response to external stimuli (Eichenlaub et al., 2014a), and hypothesized that large neurophysiological responses to sounds during sleep are responsible for subsequent awakenings. Indeed, Bastuji et al. (2008) demonstrated that during sleep (N2 and rapid eye movements (REMs)), the amplitude of a late parietal positive component (450–650 ms) in response to painful stimulation was significantly enhanced in trials that were followed by an arousing reaction (be it a short arousal of 3–15 s or an awakening lasting more than 15 s). The authors concluded that laser-evoked response to nociceptive stimuli during sleep predicted subsequent arousing reactions. However, such results remain to be demonstrated for auditory stimuli. This hypothesis was not tested in our previous study because of a too small number of sounds followed by an awakening which prevented us from computing reliable AEPs (Eichenlaub et al., 2014a). Awakenings (lasting at least 15 s by definition) are indeed far less frequent for auditory stimuli than for painful stimuli (Bastuji et al., 2008). Nonetheless, considering that arousals (short awakenings lasting less than 15 s) are also far more frequent than full awakenings (twice more numerous in Bastuji et al.'s (2008) study), we hoped that considering arousals in addition to awakenings would allow us to investigate event-related potentials (ERPs) to auditory arousing stimuli (which are far more frequent than painful stimuli during sleep in everyday life).

Mechanisms responsible for arousing reactions are important to consider regarding dream recall since the arousal-retrieval model postulates that ISW is the enabling factor for dreams to be encoded in long term memory (Koulack and Goodenough, 1976). Previous results from our group and other teams (Schredl et al., 2003; De Gennaro et al., 2010) argue in favor of this hypothesis but several parameters remain to be investigated to clarify and strengthen our understanding of the link between ISW and dream recall. Notably, sleep macro and microstructure need to be exhaustively investigated to identify or exclude the involvement of other sleep parameters in dream recall, and to specify the characteristics of awakenings associated with a higher dream recall frequency (e.g., distribution in the sleep cycle, duration and alpha frequency).

The goals of the present study were to further investigate the hypothesis of a causal link between AEPs and subsequent arousing reactions (Eichenlaub et al., 2014a) and the hypothesis of a causal link between ISW and dream recall (Koulack and Goodenough, 1976; Eichenlaub et al., 2014a). To this purpose, we first scored arousals in data previously acquired and reported in Eichenlaub et al. (2014a), to have a full assessment of the arousing reactions in the subjects' sleep. Thanks to this scoring, AEPs to arousing stimuli (i.e., stimuli followed by an arousal or a full awakening in the first 15 s post stimulus) and to non-arousing stimuli were then computed. Second, several parameters of the sleep macrostructure were computed such as the distribution of awakenings and the number of stage shifts across the sleep cycle, spectral power of the delta rhythm during the first sleep cycle, frequency and spectral power of the alpha rhythm during intra-sleep and before-sleep wakefulness (BSW). Finally, as many previous results justified to investigate sleep microstructural components regarding dream recall, a thorough analysis of the sleep microstructure of HR and LR was conducted. Sleep spindles and the alpha frequency during wakefulness have been related to memory abilities (Klimesch, 1997; Ulrich, 2016), the REMs of REM sleep to dream content (Dement and Kleitman, 1957; Roffwarg et al., 1962; Molinari and Foulkes, 1969), K-complexes (KCs) to sleep stability (Bastien et al., 2000; Colrain, 2005; Halász, 2005) and muscles twitches may be considered as the physiological expression of oneiric behaviors thought to be an acting out of dreams (Wolpert, 1960; Sastre and Jouvet, 1979). Each of these parameters was computed using either visual (arousals), semi-automatic (REMs, muscle twitches (MTs), KCs) and automatic validated methods (alpha, spindles). Such a systematic analysis of macrostructural and microstructural sleep parameters have scarcely been reported in healthy subjects, especially using automatic methods, and never among HR and LR.

MATERIALS AND METHODS

We re-analyzed data presented in previous articles (Eichenlaub et al., 2012, 2014a; Ruby et al., 2013a,b).

Subjects

Eighteen HR (age = 22.7 ± 0.6 years old; dream recall = 4.4 ± 0.25 mornings per week) and 18 LR (age = 22.4 ± 0.9 years old; dream recall = 0.25 ± 0.02 morning per week) were selected out of 1000 participants who completed an online questionnaire on their sleep and dream habits (importantly, they were unaware that dream recall frequency was an inclusion criterion). Participants were subsequently contacted by telephone and selected as HR or LR upon confirming dream recall on >3 mornings per week or <2 mornings per month

respectively. Gender, age, habitual sleep duration, habitual sleep time, education level and the size of the place of residence of the subjects were controlled and did not differ between the two groups. The local ethics committee (Centre Leon Bérard, Lyon) approved this study, and subjects provided written, informed consent in accordance with the Declaration of Helsinki. The subjects were paid for their participation. For more details concerning inclusion criteria refer to Eichenlaub et al. (2014a).

Stimuli

During both sleep and pre-sleep wakefulness subjects were presented with two different first names included as novels in an oddball novelty paradigm. The first names consisted of the first name of the subject (novel 1) and an unfamiliar first name (novel 2). They were normalized for duration and amplitude and presented with a probability of occurrence of 0.02 each. Responses to frequent standard tones ($p = 0.82$) and rare deviant tones ($p = 0.14$) were not considered in this study. Stimulus onset asynchrony was set at 650 ms, except for the standard following a novel, which appeared 1260 ms after the novel onset, whatever the duration of the novel. Stimuli were presented in a pseudo-randomized order (Eichenlaub et al., 2012), binaurally and at 50 dB above the hearing threshold of the subject.

Electrophysiological Recordings

EEG data were recorded from 21-Ag/AgCl electrodes placed according to the extended International 10–20 System. The electro-oculogram (EOG) was recorded from two electrodes placed on the supraorbital ridge of the left eye and on the infraorbital ridge of the right eye. Muscle activity electromyogram (EMG) was recorded from two electrodes attached to the chin. Polysomnographic data (EEG, EMG, EOG) were continuously recorded using a BrainAmp system (Brain Products GmbH, Germany) with an amplification gain of 12,500, a high-pass filter of 0.1 Hz, and a sampling rate of 1000 Hz.

Procedure

Subjects slept at night in a bed in the lab while polysomnographic data were acquired. Stimuli were presented through earphones during the whole night, thus ensuring constancy of stimulus input throughout the night despite head movements (Cote et al., 1999). When possible, subjects were awakened in the morning by the experimenters after 5–10 min of REM sleep and were subsequently asked to report any dreams or sleep mentation. For more details see Eichenlaub et al. (2014a).

Data Analysis

Sleep Macrostructure

Polysomnographic data have been scored according to the standard guidelines (Iber et al., 2007; Silber et al., 2007) using 30-s epochs to identify the sleep macrostructure of the subjects. Scoring was done both by an automatic software (ASEEGA version 3.30.14, Physip, France, Berthomier et al., 2007) and by an expert scorer (JBE; for more details see Eichenlaub et al., 2014a). The epoch-by-epoch comparison between JBE and ASEEGA shown 83.6% of agreement with a Cohen's kappa coefficient of 0.77. All further analyses in the present study are based solely on the visually-scored hypnograms. For each group, the following sleep parameters were measured.

Awakenings

Total number of awakenings over the sleep period time; Awakening index, defined as the number of awakenings per hour of sleep, computed for the total sleep time (TST), N1, N2, N3 and REM sleep; Awakening duration, defined as the average duration of awakenings; Awakening type, defined as the percentage of long and short awakenings (0–1 min, 1–5 min and 5–30 min, as in Goldenberg et al., 1981).

Stage shifts

Total number of stage shifts over the sleep period time (includes transitions from and to W, N1, N2, N3 and REM).

Sleep Microstructure

Arousals

Arousals were visually scored according to the ASDA 92 criteria (American Sleep Disorders Association, 1992). They were defined as any shift in the EEG frequency to alpha or theta for at least 3 s irrespective of changes in submental EMG during NREM sleep but accompanied by a at least 3 s increase in EMG amplitude during REM sleep. Typically, arousals last between 3 s and 15 s (see Supplementary Figure S1 for an example of arousal). However, since arousal scoring is independent from the scoring of sleep macrostructure, arousals may last more than 15 s (but not more than 30 s without being considered as awakenings according to the standard guidelines (if they start on one page and continue on the next one). Moreover, the ASDA rules also state that an arousal has to be preceded by at least 10 s of continuous sleep which means that a minimum of 10 s of intervening sleep is necessary between two arousals. Arousal were scored by RV and PR. RV scored arousal first, PR reviewed the scoring realized by RV and proposed modifications, then RV checked the propositions and in case of disagreement a consensus was reached after discussion. The parameters that were considered in the present study are: (1) the total number of arousals over the sleep period time; (2) the arousal index (AI), defined as the number of arousals per hour of sleep, computed for TST, N1, N2, N3, REM as well as for epochs scored as indeterminate (Inds) and movements (Mvts); and (3) the arousal duration, defined as the average duration of arousals.

Rapid eye movements

REMs are a core feature of REM sleep (Iber et al., 2007; Silber et al., 2007). In order to assess if there is any difference in the amount of REMs during REM sleep between HR and LR, we developed a semi-automatic detection of saccades in the EOG (see Supplementary Figure S2). We used independent component analysis to extract EOG-components free from artifacts from the original polysomnographic data. Then for each subject, two components showing eye movements were visually selected and subsequently analyzed with the following method. The signal was smoothed using a moving average with a window

of 100 ms. The first derivative of the signal was computed and converted into absolute value. A 40 ms step was chosen for the derivative since most of naturally occurring human saccades have magnitudes of 15° or less and last thus no more than 30–40 ms (the maximum velocity of a saccade is above 500°/s, see Bahill et al., 1975). We then applied an arbitrary threshold (mean + 4 standard deviations (SD)) to allow for an optimal detection of REMs. Finally, the quality of the detection was visually checked on a subpart of the data of several subjects. The total number of REMs was defined as the sum of non-concomitant REMs detected in the two components during REM sleep.

Muscle twitches

REM sleep is characterized by a flat muscle tone (atonia) and MTs which can be identified using electromyographic recordings with electrodes on the chin (Iber et al., 2007; Silber et al., 2007). To compare MTs between HR and LR, a semi-automatic analysis of the EMG was developed (see Supplementary Figure S3). First, a notch filter at 50 Hz was applied on the EMG signal. Second, the envelope of the signal was computed using standard Hilbert transform (frequency band: 60–450 Hz; Vidal et al., 2012). The obtained envelope was normalized and smoothed using a moving average with a 500-ms window. As for REMs, a threshold (3.25 SD) was empirically chosen to obtain an optimal detection of MTs. Each supra-threshold clusters with a duration superior to 100 ms were scored as MTs. Finally, the quality of the detection was visually checked on a subpart of the data of several subjects. Three subjects were excluded from the analysis because of a too noisy EMG signal. We assessed the total number of REMs and MTs in REM sleep and the density of REMs/MTs, defined as the average number of REMs/MTs per minute for the total REM sleep duration.

Sleep spindles

A sleep spindle is a train of distinct 11–16 Hz waves, predominant over central EEG derivations and lasting more than 0.5 s (Iber et al., 2007; Silber et al., 2007). An automatic data-driven method was used to detect sleep spindles (ASEEGA). This iterative approach uses recording-specific automatic thresholds, based on EEG power ratios in frequency bands. The detection was performed on CzPz channel, both raw EEG data and sigma-filtered EEG were used in the analysis (for more details refer to Dang-Vu et al., 2015).

K-complexes

K-complexes (KCs) are defined by the AASM (Iber et al., 2007; Silber et al., 2007) as *"a well delineated negative sharp wave immediately followed by a positive component with a total duration ≥0.5 s, typically maximal at frontal electrodes"*. KCs were semi-automatically detected using an open-access validated method (Lajnef et al., 2015, 2017) which is based on a combination of the tunable Q-factor wavelet transform and a morphological component analysis. This approach requires an initial calibration step where a small subset of the data is visually scored for KCs and then used to derive an optimal threshold. Once the training is achieved, the algorithm runs on the entire dataset to automatically detect KCs. For both KCs and spindles, the outcome measures were the total number of KCs/spindles detected and the density which is the number per min of N2 sleep.

Spectral and Frequency Analysis

Delta power

EEG delta spectral power in the first sleep cycle is a marker of homeostatic sleep pressure (Achermann et al., 1993; Huber et al., 2004). Calculation of the normalized spectral power of CzPz in the delta band (0.1–4 Hz) was performed using a fast Fourier transform with Hanning window for consecutive 30-s epochs after automatic artifact rejection (ASEEGA).

Alpha power and predominant frequency

A specific analysis of the alpha band (8–12 Hz) was performed after automatic artifact rejection. For each 30 s epoch of the EEG CzPz signal, the alpha normalized power and the mean of the instantaneous frequency weighted by the alpha power (Berthomier, 1983) were computed (ASEEGA). We assessed the predominant frequency and normalized power of alpha band for intra-sleep wakefulness (ISW) and BSW epochs and the normalized power of delta band in the first sleep cycle.

For both delta and alpha power, values are reported in percent after band-wise normalization in five frequency bands (delta = 0.1–4 Hz, theta = 4–8 Hz, alpha = 8–12 Hz, beta = 12–16 Hz, sigma = 16–50 Hz) in order to avoid low frequency artifact and powerline artifacts. Hence, for each 30-s epoch, the sum of normalized values in the five bands is equal to 100.

Event-Related Potentials Analysis

AEPs were analyzed using Elan pack software (Aguera et al., 2011) and Matlab (Mathworks). AEPs elicited by first names were averaged over an epoch of 1100 ms, including a prestimulus period of 100 ms. Prior to averaging, trials were automatically excluded if the overall electrophysiological signal amplitude exceeded 400 μV during N2. Epoch were baseline corrected according to the pre-stimulus period and a 30-Hz low-pass butterworth (order 3) digital filter was applied to averaged responses. Arousing reactions were considered as stimulus-related if occurring within 15 s after stimulus onset (American Sleep Disorders Association, 1992).

Statistical Analysis

Between-group comparisons of the sleep characteristics were achieved using Student *t*-tests (two-tailed, level of significance, $p < 0.05$). In addition, a nested two-way ANOVA tested the sleep stage (four levels: N1, N2, N3, REM sleep) and the group (two levels: HR, LR) effects on the parameters of the macrostructure (number and duration of awakenings) and microstructure of sleep (number and duration of arousals). *Post hoc* analyses (*t*-tests) were used in case of significance.

The analysis of the AEPs was performed using non-parametric tests at each sampling point and at each *a priori* chosen electrode (Fp1, Fp2, F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, O2) for grand averaged responses. We used Wilcoxon matched rank sign tests to compare AEPs between

conditions (arousing vs. non-arousing; two-tailed, $p < 0.05$). To take into account the issue of multiple comparisons, we chose to apply both spatial limitations based on previous results (according to the results of Bastuji et al. (2008) and Eichenlaub et al. (2014a), we expected condition effects for the contrast arousing stimuli vs. non-arousing stimuli on AEPs at frontal and parieto-occipital electrodes), i.e., to consider only a limited amount of electrodes, and temporal and spatial constraints to decrease the chances of false positive, i.e., considering a difference significant only if more than 15 consecutive samples (15 ms) were significantly different for at least two adjacent electrodes (Guthrie and Buchwald, 1991). This method has the advantage of taking spatial and temporal priors into account and is classically used in electrophysiology to correct for multiple comparisons (e.g., Caclin et al., 2008; Bidet-Caulet et al., 2012; Eichenlaub et al., 2014a).

RESULTS

Sleep Parameters

Table 1 shows the main sleep parameters of the experimental night in the lab for the two groups reported in Eichenlaub et al.'s (2014a) study (reproduced with permission). HR showed more ISW (wake after sleep onset, WASO) in average than LR and consequently a shorter TST. Except for these parameters, no other between groups difference was observed in the sleep architecture (notably in the proportion and latency of each sleep stage).

Table 2 presents the new parameters of the macrostructure (notably the distribution of awakenings across the sleep cycle and the proportion of long and short awakenings) and several parameters of the microstructure of sleep that have been investigated thanks to the re-analysis of the data.

TABLE 1 | Mean ± SEM of the main sleep parameters obtained in the original study.

Sleep parameters	High-recallers	Low-recallers	Standard
TIB (min)	449 ± 10	479 ± 15	*390–510*
SPT (min)	428 ± 11	449 ± 11	
WASO (min)	30 ± 4*	14 ± 5	*20–30*
TST (min)	398 ± 11*	435 ± 12	
Sleep efficiency (%)	89 ± 1.4	91 ± 1.8	*80–90*
Sleep stage, % of TST			
N1 (%)	4 ± 0.6	2 ± 0.6	*5–10*
N2 (%)	39 ± 1.7	41 ± 2.1	*40–55*
N3 (%)	36 ± 1.5	36 ± 2.3	*25–30*
REM sleep (%)	21 ± 1.2	21 ± 1.1	*20–25*
N2 latency from lights out (min)	19 ± 2.6	29 ± 6.2	*20–30*
N3 latency from lights out (min)	21 ± 3.3	32 ± 6.3	
REM latency from lights out (min)	120 ± 13.2	133 ± 16.4	
N3 latency from N2 (min)	5 ± 1.8	5 ± 1.5	
REM latency from N2 (min)	104 ± 11.9	106 ± 12.9	*60–120*
WASO (%)	7 ± 0.9*	3 ± 1.1	*5*
Movements (%)	4 ± 0.5	4 ± 0.5	
Indeterminate (%)	10 ± 1.4	10 ± 0.9	

*Table 1 is reproduced and modified from Eichenlaub et al. (2014a) with permission of the authors. Only values obtained with visual scoring (JBE) are reported. TIB refers to time in bed; SPT, sleep period time; WASO, wakefulness after sleep onset; TST, total sleep time; REM, rapid eye movement sleep; min, minutes. In comparison with the standard values presented in the last column (Hirshkowitz, 2004), the quality of sleep was generally preserved for the 36 subjects. *$p < 0.05$.*

Awakenings

A two-way ANOVA yielded a significant sleep stage effect on the awakening index ($F_{(1,3)} = 47.0$, $p < 0.000$), no significant group effect and no group × sleep stage interaction (**Figure 1A**). *Post hoc* tests revealed that the awakening index in N1 was significantly higher than in all other sleep stages ($p < 0.000$ for all the comparisons between N1 and another sleep stage) and that it was also higher in N2 than in N3 ($p = 0.003$). Regarding the duration of awakenings, a two-way ANOVA showed a group effect ($F_{(1,3)} = 13.6$, $p < 0.001$) but no sleep stage effect or interaction group × sleep stage (**Figure 1D**). After classifying awakenings into three categories according to their duration i.e., 0–1 min, 1–5 min and 5–30 min (Goldenberg et al., 1981), we observed a significant interaction group × duration ($F_{(1,2)} = 14.75$, $p < 0.001$; **Figure 1C**). *Post hoc* comparisons revealed that HR showed less short awakenings lasting less than 1 min (66.1 ± 3% in HR vs. 82.9 ± 3% in LR, $p < 0.001$) but more long awakenings lasting more than 1 min than LR (1–5 min, 24.6 ± 2% in HR vs. 16.1 ± 3% in LR, $p = 0.03$; 5–30 min, 9.4 ± 2.5% in HR vs. 1 ± 0.6% in LR, $p = 0.003$).

Arousals

The total number of arousals was not significantly different between the two groups ($p = 0.19$). A two-way ANOVA on the AI showed a significant sleep stage effect ($F_{(1,5)} = 88$, $p < 0.001$), no group effect (a tendency towards a larger AI in HR than in LR was observed regardless of the sleep stages, $p = 0.07$) and no group × sleep stage interaction (**Table 2**). The distribution of arousals across sleep stages is in accordance with previous studies (De Gennaro et al., 2001) even if AI was slightly lower than expected in all sleep stages (**Figure 1B**). In De Gennaro et al.'s (2001) study, the categories indeterminate (Inds) and movements (Mvts) were not considered in the sleep scoring whereas in the present study the majority of arousals were found in epochs scored as Inds or Mvts. This could explain the lower AI in each sleep stage (N1, N2, N3 and REM sleep) found in our study. The AI did not correlate significantly with any other sleep parameters, including the awakening index (Pearson's $r = 0.24$, $N = 36$, $p = 0.15$, two-tailed). A two-way ANOVA on arousals duration showed a significant sleep stage effect ($F_{(1,5)} = 35$, $p < 0.000$), but no group effect nor interaction group × sleep stage. Arousals were significantly longer in epochs scored as Mvts than all other epochs (N1, 9.7 ± 0.6 s, N2, 8.5 ± 0.4, N3, 9.5 ± 0.7, REM, 9.3 ± 0.5, Inds, 9.1 ± 0.3, Mvts, 16.4 ± 2.0, $p < 0.000$ for all pairwise comparisons between Mvts and the other stages).

Arousing Stimuli

In average ($N = 36$), 2.2 ± 0.2% of auditory stimuli (first names) that occurred during either N2, N3 or REM sleep were associated with an arousing reaction (be it an arousal or an awakening) in the following 15 s (see Supplementary Figure S1 for examples of arousing and non arousing stimuli). A two-way ANOVA showed a sleep stage effect ($F_{(1,2)} = 13.2$, $p < 0.001$),

TABLE 2 | Mean ± SEM of supplementary macrostructural and microstructural sleep parameters calculated in this study.

Sleep parameters	High-recallers	Low-recallers	Standard
Sleep macrostructure			
Awakenings, no.	17.5 ± 2.1	12.1 ± 2.9	9.6 (Hirshkowitz, 2004)
Awakenings, duration (min)	1.9 ± 0.2**	0.95 ± 0.1	1.4 (Benoit et al., 1981)
Awakenings index, no. per hour	3.2 ± 0.4	2.2 ± 0.6	4.2 (Wamsley et al., 2012)
N1	27.3 ± 4.8	34.6 ± 7	
N2	3.3 ± 0.7	1.8 ± 0.7	
N3	0.9 ± 0.2	1.1 ± 0.3	
REM	3.6 ± 1.5	1.0 ± 0.3	
Awakenings duration (%)			
0–1 min	66.1 ± 3.2**	82.9 ± 3.3	87 (Goldenberg et al., 1981)
1–5 min	24.6 ± 2.1*	16.1 ± 3.3	11 (Goldenberg et al., 1981)
5–30 min	9.4 ± 2.5**	1.0 ± 0.6	3 (Goldenberg et al., 1981)
Number of stage shifts	63.6 ± 4.2	71.6 ± 7.2	47 (Hirshkowitz, 2004)
Alpha power (%), in B.S.W	32 ± 4.6	30.5 ± 3.9	
Alpha power (%), in I.S.W	21 ± 3.1	24.4 ± 2.5	
Alpha frequency (Hz), in B.S.W	9.88 ± 0.1	9.86 ± 0.1	
Alpha frequency (Hz), in I.S.W	9.64 ± 0.1	9.65 ± 0.1	
Delta power (%), in first sleep cycle	79.7 ± 1.7	80.8 ± 1.6	
Arousing stimuli (%)	2.9 ± 0.3**	1.6 ± 0.2	
Arousing, latency after stim. onset	5.3 ± 0.2	5.8 ± 0.3	
Sleep microstructure			
Arousals, no.	76.3 ± 8.5	61.2 ± 7.2	83 (Bonnet and Arand, 2007)
Arousals, duration (sec)	10.2 ± 0.3	11.2 ± 0.4	
Arousal index	11.1 ± 1	8.3 ± 1	10.8 (Bonnet and Arand, 2007)
Spindles, no. per min. of N2	3.5 ± 0.3	3.5 ± 0.4	2.1 (Wamsley et al., 2012)
K-complex density, no. per min. of N2	2.0 ± 0.2	2.5 ± 0.2	1–3 (Halász, 2005)
REMs, no. per min of REM sleep	10.9 ± 0.3	10.3 ± 0.3	3.7 (Andrillon et al., 2015)
MTs, no. per min of REM sleep	0.8 ± 0.1	0.8 ± 0.1	

*REMs refers to rapid eye movements; ISW, intra-sleep wakefulness; BSW, before-sleep wakefulness; TST, total sleep time; Normalized spectral power (alpha and delta) is relative to the power in the other frequency bands; MT, muscle twitches; min, minute; no, number. Sleep onset was considered as the first epoch of N2 for the calculation of intra-sleep awakenings. Sleep onset was considered as the first epoch of N1 for arousals. Supplementary Table S1 reports awakening parameters using the first epoch of N1 as sleep onset. Last column represents standard values. One-way and two-way ANOVA for independent samples (High-recallers vs. Low-recallers) are presented: *$p < 0.05$, **$p < 0.01$.*

a group effect ($F_{(1,2)}$ = 13.1, p = 0.001) and no interaction effect on the rate of arousing stimuli. *Post hoc* comparisons revealed that there was a higher rate of arousing stimuli in N2 and REM as compared to N3 sleep (N2, 3.1 ± 0.4%; REM, 2.4 ± 0.3%; N3, 1.4 ± 0.2%; $p < 0.000$ for the two comparisons), but no differences between N2 and REM. HR showed a higher proportion of arousing reactions than LR (HR, 2.9 ± 0.3%, LR, 1.6 ± 0.2%, p = 0.001), whatever the sleep stage (no significant interaction was observed). The latency between the stimulus onset and the beginning of the arousing reaction was 5.6 ± 0.2 s in average. A two-way analysis of variance revealed a significant sleep stage effect on this delay ($F_{(1,2)}$ = 3.7, p = 0.03), no group effect or interaction group × sleep stage. *Post hoc* tests showed that arousing reactions were more delayed in REM sleep (6.5 ± 0.4 s) than in N2 (5.0 ± 0.2 s) and N3 (5.2 ± 0.3 s) ($p < 0.01$ and $p < 0.05$ respectively). Most arousing stimuli were associated with short arousing reactions (75.6 ± 2.5% of the arousing stimuli were followed by an arousal, the remaining 24.4% were followed by an awakening). A two-way ANOVA yielded a significant sleep stage effect on the type of arousing reaction ($F_{(1,2)}$ = 23.7, $p < 0.000$) but no group effect or interaction group × sleep stage. Arousing reaction in N3 were less often short arousals (50.8 ± 6.1%) than in N2 (89.1 ± 2.7%) or REM sleep (87.8 ± 3.1%; $p < 0.000$ for the two tests).

Other Microstructural Parameters

Number of stage shifts, sleep spindles density, KCs density, REMs density and MTs density were not significantly different between the two groups (p = 0.35, p = 0.98, p = 0.16, p = 0.25 and p = 0.74 respectively; see **Table 2** for details).

Spectral Power and Predominant Frequency

Two-way ANOVAs yielded that the alpha predominant frequency and spectral power were significantly decreased during ISW as compared to BSW (*Frequency*, $F_{(1,1)}$ = 32.1, $p < 0.000$. *Power*, $F_{(1,1)}$ = 22.2, $p < 0.000$). For both parameters there were no group effect or interaction between group and time of the night. Moreover, delta power in the first sleep cycle was not significantly different between the two groups.

Auditory Evoked Potentials

Arousing Stimuli after Artifact Rejection

N2—3.0 ± 0.4% of auditory stimuli were associated with an arousing reaction within 15 s (13.6 ± 1.8 stimuli in average per subject). Arousals prevailed (89.5%) over awakenings (10.5%). The mean latency between stimulus onset and arousing reactions was 4.5 s in N2.

REM sleep —2.2 ± 0.3% of auditory stimuli were associated with an arousing reaction within 15 s (4.2 ± 0.5 stimuli in average per subject). Arousals prevailed (87.7%) over awakenings (12.3%)

The mean latency between stimulus onset and arousing reactions was 6.2 s in REM sleep.

As expected for auditory stimuli (Bastuji et al., 2008; Bastuji and Lavigne, 2016), a small percentage of stimuli led to an arousing reaction. For the evoked potential analysis, to avoid a poor signal-to-noise ratio, we retained for further analysis subjects with at least 10 arousing stimuli in the same sleep stage. These constraints restricted the analysis to the most represented sleep stage i.e., N2, for which 19 subjects (12 HR and 7 LR) showed more than 10 arousing stimuli after artifact rejection.

AEPs to Arousing vs. Non-Arousing Stimuli in N2

Grand averaged responses to arousing and non-arousing stimuli in N2 are displayed in **Figure 2**. A sample of non-arousing stimuli was randomly selected so that the number of averaged stimuli was equivalent for the arousing and non-arousing conditions. Significant differences between the two conditions in N2 were found at frontal and occipital topographies. The amplitudes of a late positive and a late negative (peaking at 800–1000 ms) components were significantly enhanced for arousing stimuli at occipital electrodes (O1 and O2) and frontal electrodes respectively (FP1, FP2, Fz, F3).

AEPs to Arousing vs. Non-Arousing Stimuli in N2 as a Function of the Delay Between Stimuli and Arousing Reactions

According to the hypothesis that the amplitude of the AEPs to stimuli presented during sleep is related to the subsequent reaction of the sleeper, one would expect that the shorter the delay between the stimulus and the arousing reaction, the larger the amplitude of the evoked response to the stimulus. To test this hypothesis, we compared AEPs to stimuli quickly followed by an arousing reaction (arousing reaction in the 5 s after stimulus onset) and to stimuli followed by a late arousing reaction (5–15 s after stimulus onset). For this analysis paired statistics were not possible because of an insufficient number of subjects having more than 10 events in both conditions. Instead, we used the Kruskal-Wallis test to compare nine subjects with more than 10 events within 0–5 s post-stimuli (18.5 ± 2.1 events in average) and 10 subjects with more than 10 events within 5–15 s post-stimuli (16.7 ± 1.7 events in average). Grand averaged responses are displayed in **Figure 3**. At occipital electrodes, the amplitude of a late parietal positivity was significantly enhanced when the arousing reaction occurred within the first 5 s as compared to the last 10 s. A comparable effect was observed at frontal electrodes for the amplitude of a large negative wave peaking between 800 ms and 1000 ms.

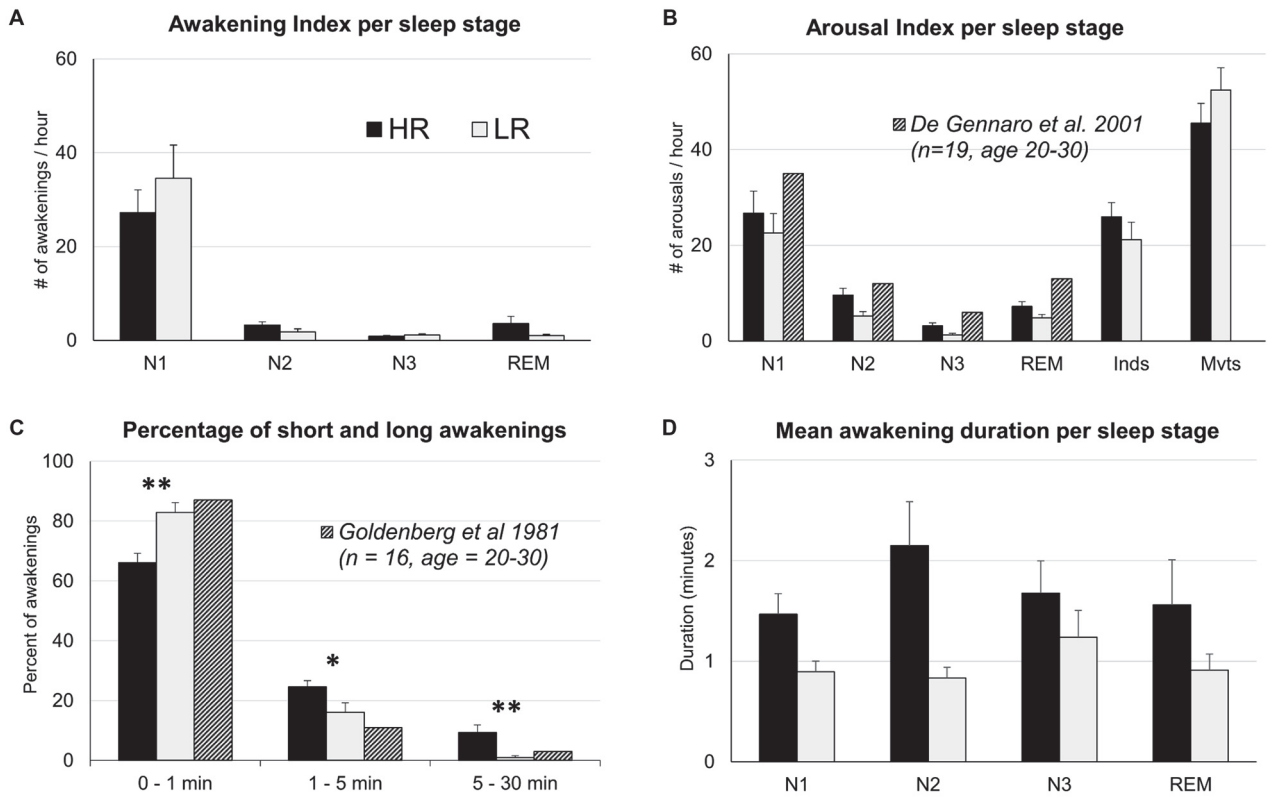

FIGURE 1 | Means and SEM of sleep parameters for High and Low dream recallers (HR and LR). (A) Awakening index per sleep stage (number of awakenings per hour in each sleep stage). **(B)** Arousal index (AI) per sleep stage (number of arousals per hour in each sleep stage). **(C)** Percentage of short and long awakenings. **(D)** Mean duration of awakenings per sleep stages. Hatched columns represent standards values. $^{*}p < 0.05$, $^{**}p < 0.01$.

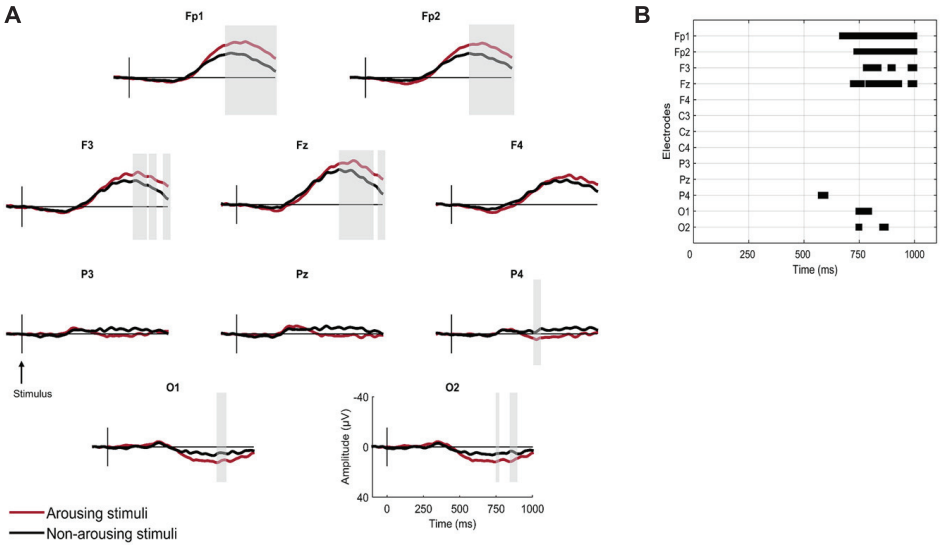

FIGURE 2 | Brain responses to first names according to the presence or absence of an arousing reaction following the stimulus in N2 sleep. (A) Grand averaged responses. Gray vertical bars highlight significant differences (sample-by-sample Wilcoxon test, $p < 0.05$ for more than 15 ms). **(B)** Statistical significance of sample-by-sample Wilcoxon test ($p < 0.05$ for more than 15 ms) performed at 10 electrodes in the post-stimulus period.

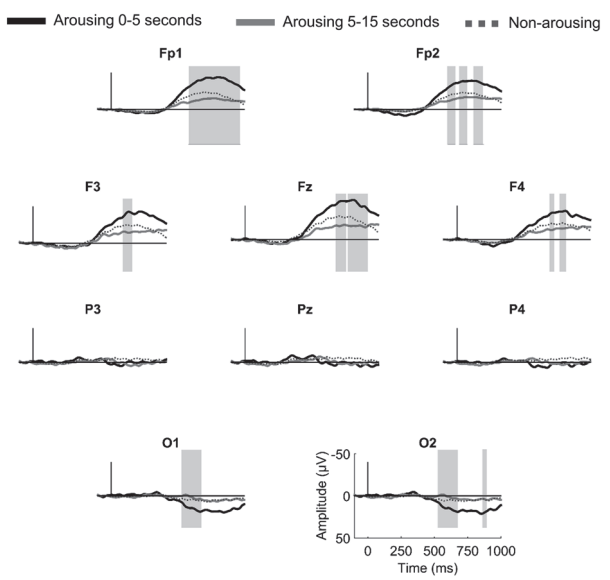

FIGURE 3 | Brain responses to first names leading to a rapid arousing reaction (in the 5 s post stimulus, black thick line), to a delayed arousing reaction (between 5 s and 15 s post-stimulus, gray thick line) and to no arousing reactions (dotted line) in N2 sleep. Gray vertical bars highlight significant differences between rapid and delayed arousing reactions (sample-by-sample Kruskal-Wallis test, $p < 0.05$ for more than 15 ms).

DISCUSSION

In this study, we further investigated the hypothesis of a causal link between ERPs to auditory stimuli and subsequent arousing reactions (Eichenlaub et al., 2014a), and the hypothesis of a causal link between ISW and dream recall (Koulack and Goodenough, 1976; Eichenlaub et al., 2014a). The reanalysis of EEG data (Eichenlaub et al., 2012, 2014a; Ruby et al., 2013a,b) enabled us to characterize more precisely the sleep macro and microstructure of HR and LR thanks to visual, semi-automatic and validated automatic methods. For intra-sleep awakenings no interaction between group and sleep stages was found (be it for the awakening index or for awakenings duration) showing that awakenings were longer in HR than in LR whatever the sleep stage. We also observed significantly more long awakenings (longer than 1 min) and less short ones in HR than in LR. Regarding the alpha predominant frequency and alpha power during ISW and BSW, no between-group differences were found, but the overall frequency and power of the alpha rhythm was slightly lower in ISW than in BSW. There were no between-group differences in the delta power during the first sleep cycle or in the number of stage shifts during SPT. Moreover, no between-group difference was found for the parameters of the sleep microstructure considered, namely arousals (density, duration and distribution), sleep spindles (density in N2), KCs (total number and density in N2), REMs (total number and density in REM sleep), MTs (total number and density in REM sleep). Finally, thanks to the scoring of arousals, we could compute AEPs to arousing and non-arousing stimuli and reproduce the results obtained for painful stimuli showing that the amplitude of the AEPs was predictive of the subsequent arousing reaction.

AEPs to Arousing and Non-Arousing Stimuli

The scoring of arousals in Eichenlaub et al.'s (2014a) data resulted in a great increase of the stimuli categorized as

arousing. Still, auditory stimuli presented at an average intensity (50 dB above the hearing level of the subject) induced far less arousing reaction (2.2%) than did laser nociceptive stimuli (30.6% in Bastuji et al., 2008). Among all the arousing reactions, arousals largely prevailed over awakenings (three-to-one ratio). Considering both arousals and awakening improved our ability to test whether AEPs amplitude to stimuli presented during sleep was related to subsequent arousing reactions, but only in N2, the most represented sleep stage. Results revealed that auditory first names followed within 15 s by an arousing reaction elicited a larger occipital positivity and also a larger frontal negative wave than non-arousing stimuli. Similarly Bastuji et al. (2008) found that arousing laser nociceptive stimuli induced a larger late parietal positive component than non-arousing stimuli in N2 and REM sleep. We further found that the shorter (less than 5 s vs. more than 5 s) the delay between the stimulus onset and the subsequent arousing reaction, the larger the amplitude of the AEPs. These results tie convincingly the AEPs' amplitude to subsequent arousing reaction and question the fact that arousing reaction arising between 5 s and 15 s after the stimulus onset are truly stimulus related. Our results show that arousing auditory stimuli induce arousing reaction through a cerebral mechanism similar to the one described for nociceptive stimuli i.e., an increased amplitude of the evoked response. Interestingly the topographies of the responses for the two sensory modalities are different. No frontal difference was found between ERPs to arousing and non-arousing stimuli in Bastuji et al.'s (2008) study whereas we found a large one in our study. The large amplitude of this frontal wave might have masked the parietal component that was reported in Bastuji et al.'s (2008) study on parietal electrodes. It may explain that the arousing effect appeared only on occipital electrodes in our study since they are less influenced by frontal components.

The late parieto-occipital components have traditionally been associated with complex cognitive processes, such as semantic or memory processes (Curran, 2004; Eichenlaub et al., 2012). This could reflect a high level cognitive processing of the stimuli possibly triggering a subsequent arousing reaction. The frontal component, larger for arousing auditory stimuli, is thought to reflect evoked KCs or N550 (Cote et al., 1999; Bastien et al., 2002; Bastuji et al., 2008). According to previous work, KCs have been traditionally viewed as indicative of an arousal process (for a review see Colrain, 2005). Halász (2005) also suggested that they could reflect an arousal response to exogenous stimuli, since they are often followed by arousing reactions. This view fits well with the fact that this frontal response is enhanced for auditory arousing stimuli as compared to non-arousing stimuli, but it does not fit with the fact that this component is more prominent for the auditory stimuli than for painful stimuli which are more arousing. This frontal response may rather be explained by an opposite functional role proposed for KCs. Some studies have shown that there is an increased proportion of KCs in situation of increased sleep drive and thus decreased arousability (Bastien et al., 2000, 2002; Nicholas et al., 2002; Peszka and Harsh, 2002; Colrain, 2005). These latter results are more in favor of an endogenous nature of KCs which could help maintaining sleep (Jahnke et al., 2012). This interpretation of KCs may explain that auditory stimuli are less arousing than painful ones due to their elicitation of a sleep-protective component (the frontal component) in addition to an arousing component (the parieto-occipital one).

These findings suggest that the amplitude of ERPs to stimuli presented during sleep is predictive, whatever the sensory modality, of a subsequent arousing reaction. Such a link was previously shown for somatosensory painful stimulation—i.e., potentially dangerous stimuli—but not for sounds which are much more frequent in our daily life and far less often dangerous than painful ones.

Intra-Sleep Awakenings and Dream Recall

The increased amount of ISW in HR reported in our previous work raised several questions. If ISW is increased in HR as compared to LR, is it also true for arousals? What is the minimum duration of an awakening to allow for the encoding of some information into long term memory? What about the other components of the sleep microstructure?

Many previous results justified to investigate sleep microstructural components regarding dream recall. Sleep spindles and the alpha frequency during wakefulness have been related to memory abilities (Klimesch, 1997; Ulrich, 2016), the REMs of REM sleep to dream content (Dement and Kleitman, 1957; Roffwarg et al., 1962; Molinari and Foulkes, 1969), KCs to sleep stability (Bastien et al., 2000; Colrain, 2005; Halász, 2005) and muscles twitches may be considered as the physiological expression of oneiric behaviors thought to be an acting out of dreams (Wolpert, 1960; Sastre and Jouvet, 1979). Interestingly, our in-depth analysis of the sleep structure revealed no differences in the sleep microstructure of HR and LR for any of the parameters considered (i.e., arousals, sleep spindles, KCs, REMs and MTs). Since the number of stage shifts and the delta power in the first sleep cycle were also not significantly different between groups, these results leave awakenings as the only sleep parameter differentiating HR and LR sleep architectures. Our further analysis of these awakenings, notably their distribution in the sleep cycle, revealed that the higher dream recall frequency of HR could not be explained by the REM sleep hypothesis of dreaming (Dement and Kleitman, 1957; Ruby, 2011) since awakenings were not found to be more numerous or longer in REM sleep in HR as compared to LR (**Figures 1A,D**). Interestingly, we found that the frequency of the alpha predominant rhythm was slightly lower (of ∼0.2 Hz) during ISW as compared to BSW. This is consistent with previous results that showed an increased power in the lower alpha range in the first minutes following an awakening as compared to the corresponding pre-sleep period (Ferrara et al., 2006). According to Klimesch (1997) which showed that the alpha frequency of good memory performers is about 1 Hz higher than those of bad performers, the decrease of alpha frequency in ISW could explain the difficulties in memory recall at awakening (recall of dreams or of awakenings during sleep). However alpha frequency was not different in HR and LR and can thus not explain their differences in dream recall.

What seems to be the best predictor of dream recall is the intra-sleep awakenings duration. During a night of sleep in the lab with sound presentation, in average, the awakenings of HR were twice longer than those of LR. The reanalysis of the data further showed that if the distribution of short (<1 min) and long awakenings (>1 min) is as expected in young healthy subjects (Goldenberg et al., 1981) i.e., with a great majority of short awakenings—the proportion of each category of awakenings was significantly different between the two groups. HR experienced a significantly higher proportion of long awakenings than LR, while LR experienced more short awakenings than HR. This result is interesting to discuss regarding those of a study which investigated the relationship between the duration of polysomnographic-defined awakenings and awakenings' awareness (Campbell and Webb, 1981). The subjects' task was to press a push-button whenever they gained awareness of being awake during sleep while polysomnographic data were acquired. They found that 84% of the unreported arousals/awakenings were shorter than 2 min (1.88 min). This result in addition to ours (awakenings but no arousals difference between HR and LR, average awakenings duration of 2 min vs. 1 min in HR vs. LR, more awakenings longer than 1 min in HR than in LR) suggest that awareness and/or memory of intra-sleep awakenings and dreams is dependent on the duration of intra-sleep awakenings and that the minimum duration for an awakening to allow for memory encoding is approximately 2 min. Given that according to available data the brain is not able to encode new information into explicit memory during sleep (Aarons, 1976), and that the brain is in a very different state during sleep and wakefulness, it seems not unrealistic that some time is needed to restore the encoding-in-memory ability of the brain at awakening.

Our results support but also extend and precise the arousal-retrieval model proposed by Koulack and Goodenough (1976). We found that intra-sleep awakenings duration is the only candidate among the numerous tested parameters assessing sleep macro and microstructure to explain dream recall, that the duration of awakenings rather than the frequency was the critical factor and that the required duration for an awakening to allow for memory encoding was approximately 2 min.

A limitation of this study is the smaller number of stimulus-related arousing reactions as compared to Bastuji et al. (2008) study with painful stimuli. For this reason we could not investigate AEPs in all the sleep stages. Second, automatic vs. visual detection of microstructural sleep parameters is a debated issue in the sleep community (e.g., Wallant et al., 2016). As a consequence even if no between groups difference have been observed, the figures (number of K complexes, spindles, MTs and REMs during REM sleep) have to be considered cautiously since they may have been different if the detection had been made visually. Thirdly, it should be kept in mind that our sleep measures does not reflect natural sleep since sounds were presented to participants during the whole night. That said, most of the computed sleep parameters were close or within the range of standard values, and it is therefore reasonable to assume that sleep quality was generally preserved despite the experimental setup and auditory stimuli. Finally, regarding the interpretation of the AEPs to arousing stimuli it should be kept in mind that the functional role of KCs regarding sleep depth is still unclear and debated, since it has been found that: (1) KCs do not change in the recovery night after sleep deprivation (Curcio et al., 2003); (2) KCs show a linear decline across the adult lifespan (Colrain et al., 2010); (3) they drop in patients with Alzheimer disease (Crowley et al., 2005); and (4) sensory stimulation increases their probability in the ascending slopes of the sleep cycles to a higher degree than in the descending ones (Colrain, 2005).

CONCLUSION

We have shown that brain responses to auditory stimuli in N2 are larger when followed by a subsequent arousing reaction in the 5 s. Coherently with our previous results suggesting a greater brain reactivity in HR, HR demonstrated more arousing stimuli than LR during sleep. Finally, the reanalysis of our previous data (Eichenlaub et al., 2014a) highlighted that HR do not show any other sleep differences with LR apart from longer intra-sleep awakenings and, more precisely, more long and less short intra-sleep awakenings than LR. The results of our team lead us to propose the following mechanism leading to a better recall of dreams in HR than in LR. An increased activity in the temporo-parietal junction at rest in HR as compared to LR (Eichenlaub et al., 2014b) would lead to a greater brain reactivity to external stimuli (Eichenlaub et al., 2014a), i.e., larger brain responses to stimuli, which in turn would trigger more and longer arousing reactions during sleep. These intra-sleep awakenings would finally give more opportunities to the brain to restore his memory-encoding abilities and therefore to encode the dream in long term memory.

AUTHOR CONTRIBUTIONS

PMR, DM, J-BE designed the experiment and acquired data. RV, TL, J-BE, CB, KJ, DM and PMR participated in the data analysis. RV and PMR wrote the initial draft.

FUNDING

This research was financially supported by a grant from the French National research Agency (Agence Nationale de la Recherche, ANR-07-JCJC-0095). This work was partly performed within the framework of the LABEX CORTEX (ANR-11-LABX-0042) of Université de Lyon, within the program ANR-11-IDEX-0007.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fnhum.2017.00132/full#supplementary-material

REFERENCES

Aarons, L. (1976). Sleep-assisted instruction. *Psychol. Bull.* 83, 1–40. doi: 10.1037/0033-2909.83.1.1

Achermann, P., Dijk, D.-J., Brunner, D. P., and Borbély, A. A. (1993). A model of human sleep homeostasis based on EEG slow-wave activity: quantitative comparison of data and simulations. *Brain Res. Bull.* 31, 97–113. doi: 10.1016/0361-9230(93)90016-5

Aguera, P.-E., Jerbi, K., Caclin, A., and Bertrand, O. (2011). ELAN: a software package for analysis and visualization of MEG, EEG, and LFP signals. *Comput. Intell. Neurosci.* 2011:158970. doi: 10.1155/2011/158970

American Sleep Disorders Association (1992). EEG arousals: scoring rules and examples. *Sleep* 15:173. doi: 10.1093/sleep/15.2.173

Andrillon, T., Nir, Y., Cirelli, C., Tononi, G., and Fried, I. (2015). Single-neuron activity and eye movements during human REM sleep and awake vision. *Nat. Commun.* 6:7884. doi: 10.1038/ncomms8884

Bahill, A. T., Clark, M. R., and Stark, L. (1975). Glissades—eye movements generated by mismatched components of the saccadic motoneuronal control signal. *Math. Biosci.* 26, 303–318. doi: 10.1016/0025-5564(75)90018-8

Bastien, C. H., Crowley, K. E., and Colrain, I. M. (2002). Evoked potential components unique to non-REM sleep: relationship to evoked KCs and vertex sharp waves. *Int. J. Psychophysiol.* 46, 257–274. doi: 10.1016/s0167-8760(02)00117-4

Bastien, C. H., Ladouceur, C., and Campbell, K. B. (2000). EEG characteristics prior to and following the evoked K-Complex. *Can. J. Exp. Psychol. Can. Psychol.* 54, 255–265. doi: 10.1037/h0087345

Bastuji, H., and Lavigne, G. (2016). "Pain perception during sleep," in *Pain and the Conscious Brain*, eds L. Garcia-Larrea and P. L. Jackson (Philadelphia, PA: Wolters Kluwer Health), 61–74.

Bastuji, H., Perchet, C., Legrain, V., Montes, C., and Garcia-Larrea, L. (2008). Laser evoked responses to painful stimulation persist during sleep and predict subsequent arousals. *Pain* 137, 589–599. doi: 10.1016/j.pain.2007.10.027

Benoit, O., Lacombe, J., Bouard, G., Foret, J., and Marc, M.-E. (1981). Durée habituelle de sommeil, modifications du rythme veille-sommeil et éveils nocturnes. *Rev. Electroencephalogr. Neurophysiol. Clin.* 11, 89–95. doi: 10.1016/s0370-4475(81)80038-x

Berthomier, C. (1983). Instantaneous frequency and energy distribution of a signal. *Signal Process.* 5, 31–45. doi: 10.1016/0165-1684(83)90033-6

Berthomier, C., Drouot, X., Herman-Stoïca, M., Berthomier, P., Prado, J., Bokar-Thire, D., et al. (2007). Automatic analysis of single-channel sleep EEG: validation in healthy individuals. *Sleep* 30, 1587–1595. doi: 10.1093/sleep/30.11.1587

Bidet-Caulet, A., Barbe, P.-G., Roux, S., Viswanath, H., Barthélémy, C., Bruneau, N., et al. (2012). Dynamics of anticipatory mechanisms during predictive context processing. *Eur. J. Neurosci.* 36, 2996–3004. doi: 10.1111/j.1460-9568.2012.08223.x

Bonnet, M. H., and Arand, D. L. (2007). EEG arousal norms by age. *J. Clin. Sleep Med.* 3, 271–274.

Caclin, A., McAdams, S., Smith, B. K., and Giard, M.-H. (2008). Interactive processing of timbre dimensions: an exploration with event-related potentials. *J. Cogn. Neurosci.* 20, 49–64. doi: 10.1162/jocn.2008.20.1.49

Campbell, S. S., and Webb, W. B. (1981). The perception of wakefulness within sleep. *Sleep* 4, 177–183. doi: 10.1093/sleep/4.2.177

Colrain, I. M. (2005). The K-complex: a 7-decade history. *Sleep* 28, 255–273. doi: 10.1093/sleep/28.2.255

Colrain, I. M., Crowley, K. E., Nicholas, C. L., Afifi, L., Baker, F. C., Padilla, M., et al. (2010). Sleep evoked delta frequency responses show a linear decline in amplitude across the adult lifespan. *Neurobiol. Aging* 31, 874–883. doi: 10.1016/j.neurobiolaging.2008.06.003

Cote, K. A., de Lugt, D. R., Langley, S. D., and Campbell, K. B. (1999). Scalp topography of the auditory evoked K-complex in stage 2 and slow wave sleep. *J. Sleep Res.* 8, 263–272. doi: 10.1046/j.1365-2869.1999.00164.x

Crowley, K., Sullivan, E. V., Adalsteinsson, E., Pfefferbaum, A., and Colrain, I. M. (2005). Differentiating pathologic delta from healthy physiologic delta in patients with Alzheimer disease. *Sleep* 28, 865–870. doi: 10.1093/sleep/28.7.865

Curcio, G., Ferrara, M., Pellicciari, M. C., Cristiani, R., and De Gennaro, L. (2003). Effect of total sleep deprivation on the landmarks of stage 2 sleep. *Clin. Neurophysiol.* 114, 2279–2285. doi: 10.1016/s1388-2457(03)00276-1

Curran, T. (2004). Effects of attention and confidence on the hypothesized ERP correlates of recollection and familiarity. *Neuropsychologia* 42, 1088–1106. doi: 10.1016/j.neuropsychologia.2003.12.011

Dang-Vu, T. T., Salimi, A., Boucetta, S., Wenzel, K., O'Byrne, J., Brandewinder, M., et al. (2015). Sleep spindles predict stress-related increases in sleep disturbances. *Front. Hum. Neurosci.* 9:68. doi: 10.3389/fnhum.2015.00068

De Gennaro, L., Ferrara, M., and Bertini, M. (2001). EEG arousals in normal sleep: variations induced by total and selective slow-wave sleep deprivation. *Sleep* 24, 673–679. doi: 10.1093/sleep/24.6.673

De Gennaro, L., Marzano, C., Moroni, F., Curcio, G., Ferrara, M., and Cipolli, C. (2010). Recovery sleep after sleep deprivation almost completely abolishes dream recall. *Behav. Brain Res.* 206, 293–298. doi: 10.1016/j.bbr.2009.09.030

Dement, W., and Kleitman, N. (1957). The relation of eye movements during sleep to dream activity: an objective method for the study of dreaming. *J. Exp. Psychol.* 53, 339–346. doi: 10.1037/h0048189

Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Ruby, P. (2014a). Brain reactivity differentiates subjects with high and low dream recall frequencies during both sleep and wakefulness. *Cereb. Cortex* 24, 1206–1215. doi: 10.1093/cercor/bhs388

Eichenlaub, J.-B., Nicolas, A., Daltrozzo, J., Redouté, J., Costes, N., and Ruby, P. (2014b). Resting brain activity varies with dream recall frequency between subjects. *Neuropsychopharmacology* 39, 1594–1602. doi: 10.1038/npp.2014.6

Eichenlaub, J.-B., Ruby, P., and Morlet, D. (2012). What is the specificity of the response to the own first-name when presented as a novel in a passive oddball paradigm? An ERP study. *Brain Res.* 1447, 65–78. doi: 10.1016/j.brainres.2012.01.072

Ferrara, M., Curcio, G., Fratello, F., Moroni, F., Marzano, C., Pellicciari, M., et al. (2006). The electroencephalographic substratum of the awakening. *Behav. Brain Res.* 167, 237–244. doi: 10.1016/j.bbr.2005.09.012

Goldenberg, F., Goldenberg, E., LaComber, J., and Benoit, O. (1981). Eveil intra-sommeil chez de mauvais dormeurs de 20 a 30 ans. Correlation avec le niveau d'anxiete et la personnalite. *Rev. Electroencephalogr. Neurophysiol. Clin.* 11, 102–109. doi: 10.1016/s0370-4475(81)80040-8

Guthrie, D., and Buchwald, J. S. (1991). Significance testing of difference potentials. *Psychophysiology* 28, 240–244. doi: 10.1111/j.1469-8986.1991.tb00417.x

Halász, P. (2005). K-complex, a reactive EEG graphoelement of NREM sleep: an old chap in a new garment. *Sleep Med. Rev.* 9, 391–412. doi: 10.1016/j.smrv.2005.04.003

Hirshkowitz, M. (2004). Normal human sleep: an overview. *Med. Clin. North Am.* 88, 551–565. doi: 10.1016/j.mcna.2004.01.001

Huber, R., Ghilardi, M. F., Massimini, M., and Tononi, G. (2004). Local sleep and learning. *Nature* 430, 78–81. doi: 10.1038/nature02663

Iber, C., Ancoli-Israel, S., Chesson, A. L. Jr., Quan, S. F. (2007). *The AASM Manual for The Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications.* Westchester, IL: American Academy of Sleep Medicine.

Jahnke, K., von Wegner, F., Morzelewski, A., Borisov, S., Maischein, M., Steinmetz, H., et al. (2012). To wake or not to wake? The two-sided nature of the human K-complex. *Neuroimage* 59, 1631–1638. doi: 10.1016/j.neuroimage.2011.09.013

Klimesch, W. (1997). EEG-alpha rhythms and memory processes. *Int. J. Psychophysiol.* 26, 319–340. doi: 10.1016/s0167-8760(97)00773-3

Koulack, D., and Goodenough, D. R. (1976). Dream recall and dream recall failure: an arousal-retrieval model. *Psychol. Bull.* 83, 975–984. doi: 10.1037/0033-2909.83.5.975

Lajnef, T., Chaibi, S., Eichenlaub, J.-B., Ruby, P. M., Aguera, P.-E., Samet, M., et al. (2015). Sleep spindle and K-complex detection using tunable Q-factor wavelet transform and morphological component analysis. *Front. Hum. Neurosci.* 9:414. doi: 10.3389/fnhum.2015.00414

Lajnef, T., O'Reilly, C., Combrisson, E., Chaibi, S., Eichenlaub, J.-B., Ruby, P. M., et al. (2017). Meet spinky: an open-source spindle and K-complex detection toolbox validated on the open-access montreal archive of sleep studies (MASS). *Front. Neuroinform.* 11:15. doi: 10.3389/fninf.2017.00015

Molinari, S., and Foulkes, D. (1969). Tonic and phasic events during sleep: psychological correlates and implications. *Percept. Mot. Skills* 29, 343–368. doi: 10.2466/pms.1969.29.2.343

Nicholas, C. L., Trinder, J., and Colrain, I. M. (2002). Increased production of evoked and spontaneous KCs following a night of fragmented sleep. *Sleep* 25, 882–887. doi: 10.1093/sleep/25.8.42

Peszka, J., and Harsh, J. (2002). Effect of sleep deprivation on NREM sleep ERPs and related activity at sleep onset. *Int. J. Psychophysiol.* 46, 275–286. doi: 10.1016/s0167-8760(02)00115-0

Roffwarg, H. P., Dement, W. C., Muzio, J. N., and Fisher, C. (1962). Dream imagery: relationship to rapid eye movements of sleep. *Arch. Gen. Psychiatry* 7, 235–258. doi: 10.1001/archpsyc.1962.01720040001001

Ruby, P. (2011). Experimental research on dreaming: state of the art and neuropsychoanalytic perspectives. *Front. Psychol.* 2:286. doi: 10.3389/fpsyg.2011.00286

Ruby, P., Blochet, C., Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Bidet-Caulet, A. (2013a). Alpha reactivity to complex sounds differs during REM sleep and wakefulness. *PLoS One* 8:e79989. doi: 10.1371/journal.pone.0079989

Ruby, P., Blochet, C., Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Bidet-Caulet, A. (2013b). Alpha reactivity to first names differs in subjects with high and low dream recall frequency. *Front. Psychol.* 4:419. doi: 10.3389/fpsyg.2013.00419

Sastre, J.-P., and Jouvet, M. (1979). Le comportement onirique du chat. *Physiol. Behav.* 22, 979–989. doi: 10.1016/0031-9384(79)90344-5

Schredl, M., Wittmann, L., Ciric, P., and GÖtz, S. (2003). Factors of home dream recall: a structural equation model. *J. Sleep Res.* 12, 133–141. doi: 10.1046/j.1365-2869.2003.00344.x

Silber, M. H., Ancoli-Israel, S., Bonnet, M. H., Chokroverty, S., Grigg-Damberger, M. M., Hirshkowitz, M., et al. (2007). The visual scoring of sleep in adults. *J. Clin. Sleep Med.* 3, 121–131.

Ulrich, D. (2016). Sleep spindles as facilitators of memory formation and learning. *Neural Plast.* 2016:1796715. doi: 10.1155/2016/1796715

Vidal, J. R., Freyermuth, S., Jerbi, K., Hamamé, C. M., Ossandon, T., Bertrand, O., et al. (2012). Long-distance amplitude correlations in the high gamma band reveal segregation and integration within the reading network. *J. Neurosci.* 32, 6421–6434. doi: 10.1523/JNEUROSCI.4363-11.2012

Wallant, D., Maquet, P., and Phillips, C. (2016). Sleep spindles as an electrographic element: description and automatic detection methods. *Neural Plast.* 2016:6783812. doi: 10.1155/2016/6783812

Wamsley, E. J., Tucker, M. A., Shinn, A. K., Ono, K. E., McKinley, S. K., Ely, A. V., et al. (2012). Reduced sleep spindles and spindle coherence in schizophrenia: mechanisms of impaired memory consolidation? *Biol. Psychiatry* 71, 154–161. doi: 10.1016/j.biopsych.2011.08.008

Wolpert, E. A. (1960). Studies in psychophysiology of dreams: II. An electromyographic study of dreaming. *JAMA. Arch. Gen. Psychiatry* 2, 231–241. doi: 10.1001/archpsyc.1960.03590080107014

Conflict of Interest Statement: CB has ownership and directorship in Physip S.A. Company. The other authors declare no conflict of interest.

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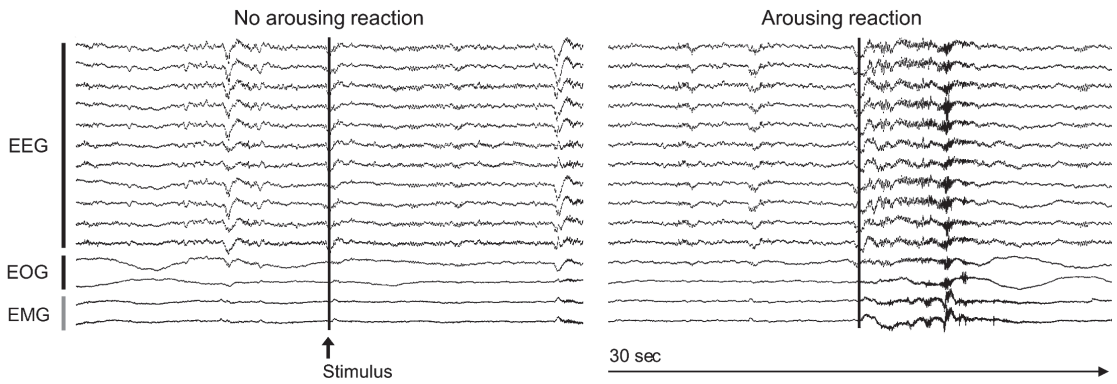
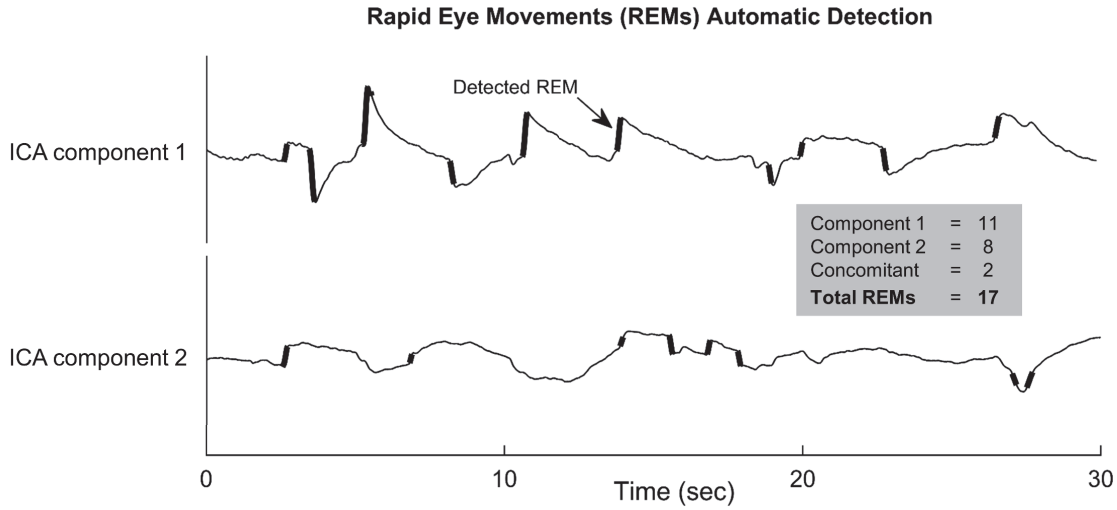
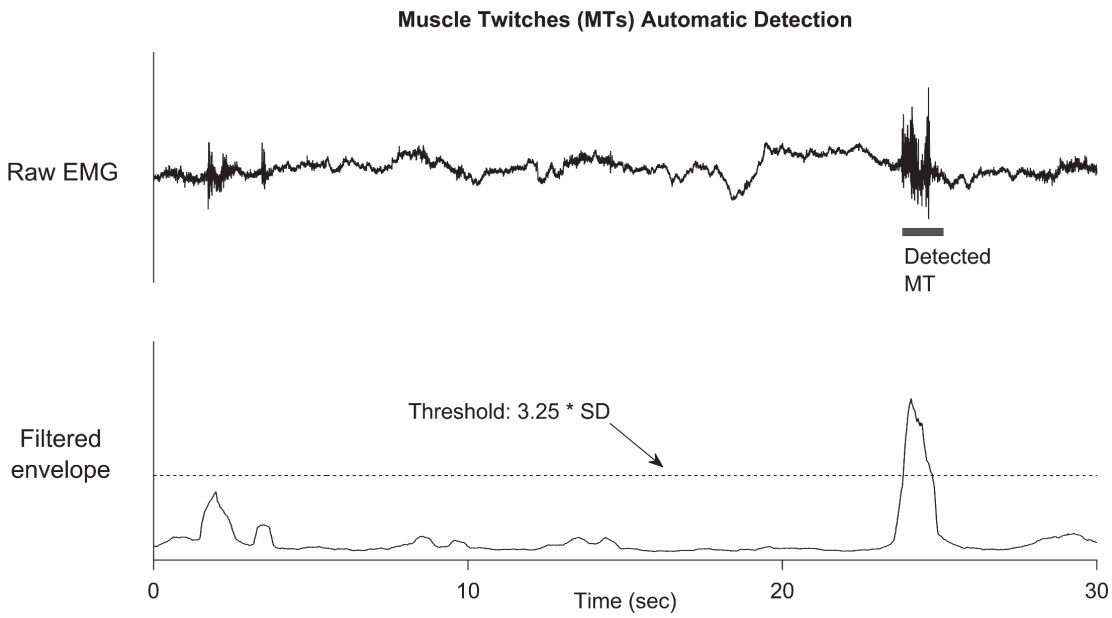
Supplementary materials



S1 Fig. Examples of arousing and non-arousing reactions to auditory stimuli in N2 sleep.



S2 Fig. Example of automatic detection of rapid eye movements (REMs) in REM sleep.



S3 Fig. Example of automatic detection of muscle twitches (MTs). Top: Raw EMG signal. Bottom: Smoothed and filtered Hilbert envelope of raw EMG signal.

S1 Table. Mean ± S.E.M of supplementary macro-structural parameters in High and Low dream recallers, with sleep onset defined as the first page of N1. Last column represents standard values. One-way and two-way ANOVA for independent samples (High-recallers versus Low-recallers) are presented: p<.05*, p<.01**.

Sleep parameters	High-recallers	Low-recallers	Standard
Awakenings, no.	19.7 ± 2.2	16.3 ± 4.1	9.6
Awakenings, duration (min)	1.9 ± 0.2 **	1.1 ± 0.1	1.4
Awakenings Index, no. per hour	3.6 ± 0.5	2.8 ± 0.7	4.2
N1	26.5 ± 3.9	33.6 ± 4.9	
N2	3.4 ± 0.7	1.9 ± 0.8	
N3	1.0 ± 0.2	1.1 ± 0.3	
REM	3.6 ± 1.5	1.0 ± 0.3	
Awakenings duration (%)			
0-1 min	63.3 ± 3.5 **	80.3 ± 3.3	87
1-5 min	28.9 ± 2.5 *	18.1 ± 3.2	11
5-30 min	7.8 ± 2.0 **	1.6 ± 0.7	3

9

Study 2. The awakening brain: sleep inertia and its link with DRF

9.1 Part 1. Brain networks dynamics during sleep inertia

Reduced default mode network connectivity and anti-correlation in the minutes following awakening from N2 and N3 sleep: an EEG-fMRI study

Under review at *Neuroimage*

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Summary

The transition from sleep to wake is characterized by reduced vigilance, sleepiness and impaired performances, a state often referred to as sleep inertia. Even though the behavioral aspects of sleep inertia are well documented, its cerebral correlates remain poorly understood. Using combined EEG-fMRI in 55 participants, we examined the brain functional connectivity during sleep inertia before and after a 45 minutes mid-afternoon nap. Resting-state scans were acquired before the nap, 5 min and 25 min after awakening from N2 sleep (n=14) or N3 sleep (n=20). Results showed that sleep inertia is associated with an intrusion of sleep specific functional connectivity into wakefulness, which severity is dependent of the prior sleep duration and sleep depth. Awakening in N3 sleep induced the most robust changes and was characterized by a loss of brain functional segregation between task-negative and task-positive networks.

Keywords Sleep inertia, awakening, default mode network, combined EEG-fMRI, functional connectivity, dorsal attention network

Introduction

Sleep inertia is defined as a transient period occurring just after awakening from sleep, and characterized by reduced vigilance, sleepiness and impaired cognitive and physical performances (Tassi and Muzet, 2000; Trotti, 2016). As Trotti clearly pointed out in the title of her article *"waking up is the hardest thing I do all day"*, sleep inertia is also usually experienced as unpleasant. Although its duration is not consensual and varies depending on the outcome measure used, it is generally admitted that most of the behavioral effects of sleep inertia dissipate progressively in the first 30 minutes post awakening. Severity of sleep inertia has been positively associated to several factors such as prior sleep deprivation, awakening near the circadian trough of body temperature, awakening in slow-wave sleep (see Tassi and Muzet (2000) for a review) and some sleep disorders. Excessive sleep inertia, sometimes referred to as sleep drunkenness, is indeed a core feature of idiopathic

hypersomnia, and a component of delayed sleep phase disorder and NREM arousal parasomnias (Trotti, 2016). A better understanding of sleep inertia is needed for the development of new strategies to reduce its detrimental effects on cognitive and physical performances, in pathological or physiological context alike. Sleep inertia may indeed have critical consequences in emergency situations when individuals are required to make vital decisions or actions immediately upon awakening (e.g. medical staff, firemen, pilots, military). In the general population, sleep inertia represents the main limiting factor to the numerous beneficial effects of daytime napping (Faraut et al., 2016).

The behavioral aspects of sleep inertia are well documented, but only a limited amount of studies investigated its cerebral correlates until now. Using EEG, some studies have found a persistence of slow wave activity in the minutes following awakening, specifically in posterior areas, a phenomenon which has been suggested to represent the electrophysiological signature of sleep inertia (Ogilvie and Simons, 1992; Ferrara et al., 2006; Marzano et al., 2011; Gorgoni et al., 2015). Using PET, Balkin et al. (2002) reported that the brain areas whose regional cerebral blood flow (rCBF) was increasing between 5 to 20 min post awakening (p-a) were primarily anterior heteromodal areas (e.g. lateral prefrontal cortices, and anterior insula). They also reported shifts in the relative levels of rCBF between pairs of brain regions (orbitofrontal cortex and ventromedial caudate nucleus, dorsolateral prefrontal cortex and mesencephalic reticular formation) between 5 and 20 min post awakening, leading them to propose that recovery from sleep inertia could hinge on a resumption of normal levels of both rCBF and functional connectivity between brain areas. The latter hypothesis has been tested in two recent resting-state functional magnetic resonance imaging (fMRI) studies which investigated the variations in brain connectivity between pre-sleep wakefulness, nocturnal sleep (without previous sleep deprivation) and post-sleep wakefulness (Wu et al., 2012; Tsai et al., 2014). Using paired comparisons between pre- and post-sleep wakefulness, they found a decreased connectivity within the sensory-motor (SM) network at awakening but no alterations in the default mode network (DMN). This altered connectivity within the sensory-motor network is coherent with the poor motor performances observed at awakening but does not explain the impairments observed in other domains (e.g. cognitive tasks such as mental calculation, Tassi and Muzet, 2000; Trotti, 2016).

Some modifications of the DMN connectivity could be expected at awakening since several neuroimaging studies showed consistent alterations of the DMN connectivity during sleep, fatigue and/or falling asleep (see Picchioni et al. (2013) for a review). During N1 and N2 sleep, several teams found a decrease in the anti-correlation between the default mode network on one hand and task-positive networks on the other (i.e. dorsal attention and executive control networks). This decreased anti-correlation has also been observed during wake after total or partial sleep deprivation, in addition with robust alterations across the whole brain functional connectome (Sämann et al., 2010; De Havas et al., 2012; Yeo et al., 2015; Kaufmann et al., 2015; Tüshaus et al., 2017). Finally, during deep sleep (N3 or slow-wave sleep), several studies reported a strong disruption of DMN connectivity and anti-correlation (Horovitz et al., 2009; Larson-Prior et al., 2011; Sämann et al., 2011), as well as an absence of frontoparietal connectivity (Spoormaker et al., 2012)). Altogether, these results argue in favor of a progressive loss of functional segregation of brain networks

from sleep onset to deep sleep, which might explain why the behavioral impairments at awakening are the most acute when individuals are awakened in N3 sleep and lead to the hypothesis that awakening from N3 sleep should be associated with DMN functional connectivity disruption.

In order to improve our understanding of sleep inertia, we designed a study with several novelties compared to previous ones. First, we used a combined EEG-fMRI method to acquire resting state scans before sleep, 5 min after awakening and 25 min after awakening in 55 healthy young participants. This design enabled us to investigate the dynamic of functional connectivity in several brain networks during the first half hour following awakening. Second, participants were partially sleep deprived on the night before and awakened from a 45 min mid-afternoon nap, in the deepest possible sleep stage (N3 sleep). Both sleep deprivation and awakening in N3 sleep have been associated with increased sleep inertia (Tassi and Muzet, 2000). In addition with being ecological (short nights compensated by a daytime nap being common in young adults (Faraut et al., 2016), this paradigm allowed us to study sleep inertia in its most intensified form. Finally, each resting-state scan was paired with a mental calculation task in order to measure the behavioral effects of sleep inertia.

Using such a design we aimed at characterizing the brain functional connectivity just after awakening from deep sleep (N3) and its modulation in the first half hour after awakening. A total of 55 participants were included, of which 20 were awakened in N3 sleep and 14 in N2 sleep, allowing us to describe and compare the functional connectivity during sleep inertia following awakening from these two distinct sleep stages. We expected a decrease in performances 5 min p-a compared to pre-sleep and 25 min p-a. We hypothesized that (1) the functional connectivity 5 min after awakening would share some features with the one of the sleep stage that was ongoing before awakening, i.e. we notably expected to observe a decrease in DMN connectivity and anti-correlation after awakening from N2 or N3 sleep (2) a decreased connectivity within the SM network (3) a positive correlation between the severity of performance impairments and functional connectivity disruption at awakening on the one hand and sleep depth before awakening on the other hand.

Methods

Participants

Fifty-five participants (28 males, mean age = 22.55, standard deviation = 2.41, range = 19–29) were included in the study. The subjects were informed of the study through an announcement sent to several mailing lists of Lyon University. Participants were selected if they reported having a regular sleep-wake schedule, no difficulty to fall asleep, being occasional or frequent nappers and having preferentially already done an MRI brain scan in the past few years. They had no history of neurological and psychiatric disorders, and had no sleep disturbances. They provided written informed consent according to the Declaration of Helsinki and received monetary compensation for their participation. The

study was approved by the local ethics committee (CCPPRB, Centre Leon Berard, Lyon, France).

Experimental design

The experimental design is presented in Fig 1 (see Fig 5.1).

Evening and night. Participants arrived in the sleep unit of the hospital Le Vinatier (Lyon, France) at 8 pm on the evening prior to the experimental day. From 8 pm to 10 pm, they underwent several personality and cognitive tests (results will be presented elsewhere) administered by R.V. They were then instructed to stay awake until 5 am (the possible activities were reading, making puzzles and watching movies), at which point they were allowed to sleep for 3 hours until 8 am in a bed in the sleep unit. Energy drinks or physical activity were prohibited during the partial sleep deprivation, and nurses regularly checked that the subject did not fall asleep. The monitoring of body movements through wrist actigraphy (Actigraph, Pensacola, USA) during the whole night made it possible to check a posteriori that the subject did not fall asleep before 5 am. In the morning, participants were offered breakfast and a shower and then occupied themselves (reading or internet) under the experimenters' supervision until the MRI session.

Day. After lunch at 11.30 am, participants were conducted to the neuroimaging center (CERMEP). During the first half hour, experimenters installed on the participant's head a MRI compatible EEG cap (EASYCAP®). Participants were then installed in the MRI scanner at about 1.20 pm (1.17 pm ± 13 min). They read a 5 min cartoon during the calibration of the eye-tracking camera, and then did the DST for 2 minutes. The first resting-state scan was then acquired, with the instructions to remain awake and look at a central fixation cross on the screen. At the end of the scan, participants were informed that they could sleep (at 1.39 pm ± 14 min in average) during the next 45 min. At the end of the nap slot, participants were awakened, if they were sleeping, by calling their first name and the 2nd resting state scan was acquired in the following minutes. At the end of the scan, the 2nd DST was performed. During the following 10 minutes, questions about sleep in the scanner and about the cartoon were asked to the subjects (results will be reported elsewhere). Then the 3rd resting state scan and DST were performed (about 25 min after awakening). Finally, an 8-min T1 anatomical scan was acquired. When they got out of the MRI, participants completed a questionnaire about their thoughts during the three resting state scans.

Behavioral tasks

To evaluate the time course of the dissipation of sleep inertia we used the descending subtraction task (DST) that has been previously used to evidence performances decrement and normalization in the first 30 min post awakening (Dinges et al., 1985; Evans and Orne, 1975; Stampi et al., 1990). Subjects were presented with a three-digit number. They were

instructed to subtract 9, saying the operation and the result aloud, and then continue by subtracting 8 from the remainder, then 7, and so on until they had to subtract 1. At this point they were to start the cycle of descending subtractions again. They had to do the task for two minutes and were instructed to be as fast and accurate as possible. As this task has a substantial practice effect over the first trials (Dinges et al., 1985), participants were trained the night before the fMRI session (they performed the task six times during the evening in the sleep unit).

The outcome measures from the DST are: (1) the total number of responses, which is an index of the speed of information processing, (2) the percentage of mistakes, which is a marker of accuracy and (3) the percentage of correct responses (relative to pre-nap performances), which is a marker of both speed and accuracy (Dinges et al., 1985). Since several studies reported that speed is generally more impaired than accuracy during sleep inertia (Trotti, 2016), we expected a significant decrement of post-nap performances especially for the total number and percentage of responses.

EEG data collection

Polysomnography data were recorded using a 15 channels MR-compatible cap designed for sleep studies i.e. with a layout designed according to American Academy of Sleep Medicine Guidelines 2007 (EasyCap, Brain Products GmbH, Gilching, Germany). It comprised 9 EEG electrodes placed according to the international standard 10/20 system (O1, O2, C3, C4, F3, F4, M1, M2, Cz, FCz was used as reference and AFz as ground), 2 EOG electrodes, 3 EMG electrodes, and an electrocardiogram electrode placed on the back of the participant. The sampling rate was 5000 Hz and an analog band-pass filter was set to 0.01 – 250 Hz. To score sleep online during the fMRI session, a real-time pulse-artefact correction was applied using the BrainVision Recorder (Version 1.2) and BrainVision RecView (Version 1.4) softwares (Brain Products).

To ensure that participants were not closing their eyes during the resting state scans, eye movements were monitored during the experiment using an EyeLink 1000 fMRI eye tracking system (SR Research Ontario, Canada). Eye position was calibrated at the beginning of the experiment and monitored throughout.

MRI data collection

MRI scans were obtained from a MAGNETOM Prisma 3.0 T scanner (Siemens Healthcare, Erlangen, Germany) at the Primage neuroimaging platform (CERMEP). Structural MRI were acquired with a T1-weighted (0.9-mm isotropic resolution) MPRAGE sequence and functional MRI data with a T2*-weighted 2D gradient echo planar imaging sequence (EPI) with 180 volumes (TR/TE: 2000/ 25 ms; flip angle: 80°; voxel size: 2.68 × 2.68 × 3 mm; slices: 40, duration: 6 minutes). Functional and anatomical scans were performed using a

20-channel head coil. The coil was foam-padded to improve subject comfort and restrict head motion.

EEG analysis

Artifacts related to gradient switching and cardiac pulse (cardio-ballistic artifact) were removed using standard routines available in BrainVision Analyzer version 2.0 software (Brain Products). Polysomnographic data were downsampled to 1000 Hz and band-pass filtered between 0.5 and 25 Hz. Offline sleep stage scoring was performed using EEG epochs of 30 seconds following standard AASM rules (Iber, 2007; Silber et al., 2007) visualized using SLEEP software (Combrisson et al., 2017). S1 Fig shows the hypnogram during the nap slot for one subject who reached N3 sleep.

fMRI analysis

Preprocessing and quality check were performed using standard routine in SPM12 software (Wellcome Department of Imaging Neuroscience). Preprocessing included functional realignment, slice-time correction, coregistration to structural scan, spatial normalization and spatial smoothing using a 6 mm full-width at half-maximum isotropic Gaussian kernel filter. Individual T1 images were segmented into gray matter, white matter and cerebrospinal fluid tissue maps. Functional and structural images were then normalized to MNI152 space (Montreal Neurological Institute). Functional images underwent artifact and motion regression in the Artifact Detection Toolbox (ART[1]) using the following criteria to define outliers: global signal intensity changes greater than 9 standard deviations and movement exceeding 2 mm. SPM motions parameters and outliers were subsequently included as covariates in connectivity analyses.

Resting-state networks and their main regions of interests (ROIs) were defined from a brain parcellation atlas implemented in the CONN Toolbox[2] version 17f (Whitfield-Gabrieli and Nieto-Castanon, 2012). This atlas was obtained using an independent component analysis (ICA) on 467 subjects from the Human Connectome Project. Subcortical ROIs (hippocampus, thalamus, and amygdala) were defined from the Harvard-Oxford maximum likelihood subcortical atlas. Spatial maps of the ROIs used in further connectivity analyses for each network of interest are displayed in S2 Fig.

Connectivity analysis were performed using the CONN toolbox version 17f. First, we performed a denoising step including a regression of the 6 motion correction parameters and their corresponding first-order temporal derivatives, as well as a component-based strategy (aCompCor, Behzadi et al., 2007) to identify and remove physiological confounds that are unlikely to be related to neural activity. The resulting BOLD time series were band-pass filtered (0.008 – 0.09 Hz) to further reduce noise and increase sensitivity

[1]https://www.nitrc.org/projects/artifact_detect/
[2]http://www.nitrc.org/projects/conn

(Weissenbacher et al., 2009). Then, intra- and inter-network connectivity were calculated for each subject by extracting the mean BOLD time series of each ROI of a given network and by correlating them with the average BOLD time series of every other ROI from this network or of the other networks included in the analysis. The mean network connectivity was then computed as the mean of all pair-wise Fischer-transformed correlation coefficient within a network and compared within subjects between conditions and between subjects. In addition with the previously described ROI-to-ROI analysis, we performed seed-to-voxel analysis on the posterior cingulate cortex (PCC), one core region of the DMN which demonstrates notable disruption during NREM sleep (Picchioni et al., 2013; center of mass in MNI coordinates: 1, -61, 38).

Statistics

For the descending subtraction task, between-group comparisons were achieved using a mixed two-way repeated measures ANOVA with a group factor (two levels: N2 sleep and N3 sleep, see results section) and a time factor (within subject factor with three levels: Pre-sleep, 5 min p-a, 25 min p-a). Post hoc analyses (t-tests) were used in case of significance. ROI-to-ROI connectivity analysis were conducted using two-sided t-tests corrected for multiple comparisons using the false discovery rate (FDR, $p<.05$). Seed-based connectivity analysis were performed using a cluster-defining voxel-wise height threshold of $p<.01$ (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of $p<.05$.

Results

Sleep parameters

Despise the sleep deprivation, 20 out of 55 participants did not reach or maintain NREM sleep during the 45-min nap slot in the scanner. This result was not a surprise given the discomfort and stress inherent to the MR environment (Duyn, 2012). One subject out of the 35 remaining was discarded because of a technical failure during data acquisition, leading thus to a total of 34 participants included in the final analysis. We further divided these participants as a function of the sleep stages they were in before awakening. Twenty participants were awakened in N3 sleep (N3 group) and 14 participants were awakened in N2 sleep (N2 group). This allowed us to compare the functional connectivity during sleep inertia after awakening from both N2 and N3 sleep. Between-group comparisons were performed both for the functional connectivity and the behavioral data. Means of the main sleep parameters in the two groups are presented in Table 1. Importantly, there was no group difference in the latency between the awakening and the first and second post-awakening resting-state scan, respectively. Note that as expected, the sleep deprivation did succeed to maximize sleep inertia at awakening. Indeed a few participants experienced very difficult awakenings marked by a short period of panic, claustrophobia

and blast of hot air, often accompanied by strong neurovegetative responses (tachycardia, hyperventilation, sudation).

Table 1. Sleep parameters (Mean ± SD) of the subjects in the N3 (n=20) and N2 (n=14) groups. TST = Total Sleep Time, SE = Sleep Efficiency, Wake (W), N1, N2 and N3 = Total duration of each sleep stage in minutes. LAS1 = latency (min) between the awakening and the start of the first post-awakening resting-state scan. LAS2 = latency (min) between the awakening and the start of the second post-awakening resting-state scan.

Group	TST	SE (%)	W	N1	N2	N3	LAS1	LAS2
N2	38.2 ± 7.1	87.4 ± 9.6	9.1 ± 4.0	14.2 ± 7.6	21.6 ± 6.2	2.9 ± 4.4	3.7 ± 1.9	23.8 ± 3.7
N3	37.3 ± 5.0	87.5 ± 7.4	9.2 ± 4.2	9.0 ± 5.7	17.7 ± 4.9	11.0 ± 4.6	4.8 ± 3.9	24.4 ± 4.2
T-test	.68	.99	.95	.03	.05	<.001	.34	.63

Descending subtraction task

Performance at the DST during the fMRI session are presented in Fig 2. As expected, we observed a significant main effect of time [F(2, 32)=4.0, p=.02] in the total number of responses. The total number of response was lower at 5 min post-awakening as compared to 25 min post-awakening (p=.008 ; Fig 2A). There was a tendency for a reduced total number of responses at 5 min compared to pre-sleep (p=.07). No group effect or interaction were found for the total number of responses. This decrease in calculation speed at 5 min post-awakening was not associated with a significant increase in the percentage of mistakes (Fig 2B). This result is consistent with the generally held view that speed is more impaired than accuracy during sleep inertia (Trotti, 2016). However, there was a significant interaction between time and group factors [F(2,32)=3.60, p=.03]. Post-hoc tests revealed that the N2 group had a higher percentage of mistakes at 5 min post-awakening compared to the N3 group (p<.001). Finally, regarding the percentage of correct responses, which is a marker of both speed and accuracy, we also found a significant main effect of time [F(2, 32)=3.13, p=.05]. The number of correct responses was lower at 5 min post-awakening than at 25 min post-awakening (p=.01), but not significantly different before the nap as compared to 5 min after awakening (p=.17; Fig 2C). As for the total number of responses, no group effect or interaction was found for the percentage of correct responses.

Functional connectivity alterations following awakening from N3 sleep

The brain functional connectivity at 5 min after awakening from N3 sleep showed important alterations. ROI-to-ROI analysis demonstrated a disrupted pattern of connectivity between several brain networks at 5 min p-a compared to pre-nap and 25 min p-a. Fig 3A illustrates the connectivity between several network, notably the DMN, DAN, fronto-parietal executive

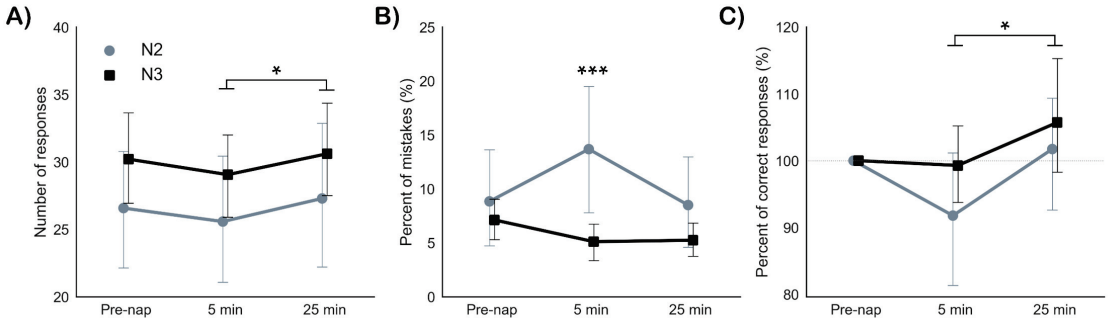


Fig 2. Performances of the Descending Subtraction Task. Blue gray lines, N2 group (n=14), black lines, N3 group (n=20). (A) Total number of responses (index of speed). (B) Percentage of mistakes (marker of accuracy). (C) Percentage of correct responses relative to pre-nap performances (marker of both speed and accuracy). Error bars represent 95% confidence intervals. * $p<.05$, *** $p<.001$

network (FP), sensori-motor (SM), salience and visual networks, in the pre-nap and 25 min p-a conditions as compared to the 5 min p-a condition. Fig 3B shows mean pairwise connectivity within and between networks. One of the most significant result was the large decrease of the anti-correlation (i.e. increased connectivity between networks that are normally anti-correlated) at 5 min p-a between the DMN and several other networks, namely the DAN, the SM, and the salience networks (Fig 3A and 3B, right). Interestingly, we observed alterations in the between-networks functional connectivity, whereas the mean within-network functional connectivity within each of these networks was not reduced at 5 min p-a compared to the two other conditions (Fig 3B, left). Seed-based analysis confirmed the disruption of the anti-correlation between the DMN (seed in the PCC) and SM network at 5 min p-a compared to pre-sleep and 25 min p-a (Fig 3C and S1 Table). In addition, there was a reduced connectivity at 5 min p-a compared to pre-sleep between the PCC and the inferior temporal gyrus, a region considered to be a part of the extended DMN and known for its role in memory and mental simulations (Christoff et al., 2016).

Functional connectivity alterations following awakening from N3 sleep

Awakening from N2 sleep was also associated with some alterations in the brain connectivity. As compared to pre-sleep, the functional connectivity at 5 min p-a was reduced between the SM and two regions of the FP network, the SM and the right hippocampus and between the ventral and dorsal part of the visual network. By contrast, the connectivity at 5 min p-a was increased between two regions of the DMN and the hippocampus and between the salience and SM networks (Fig 4A). As compared to 25 min p-a, the functional connectivity at 5 min p-a was reduced within the DAN, within the ventral and dorsal part of the visual network, and between the SM and FP networks. By contrast, connectivity was increased between the visual and salience networks (Fig 4A). The mean connectivity within and between networks was not significantly altered at 5 min p-a after an awakening in N2 sleep (Fig 4B). In accordance with these results, seed-based analysis showed an increased connectivity at 5 min-pa compared to pre-sleep between the PCC and several regions including the hippocampus and part of the SM network (Fig 4C and S2 Table).

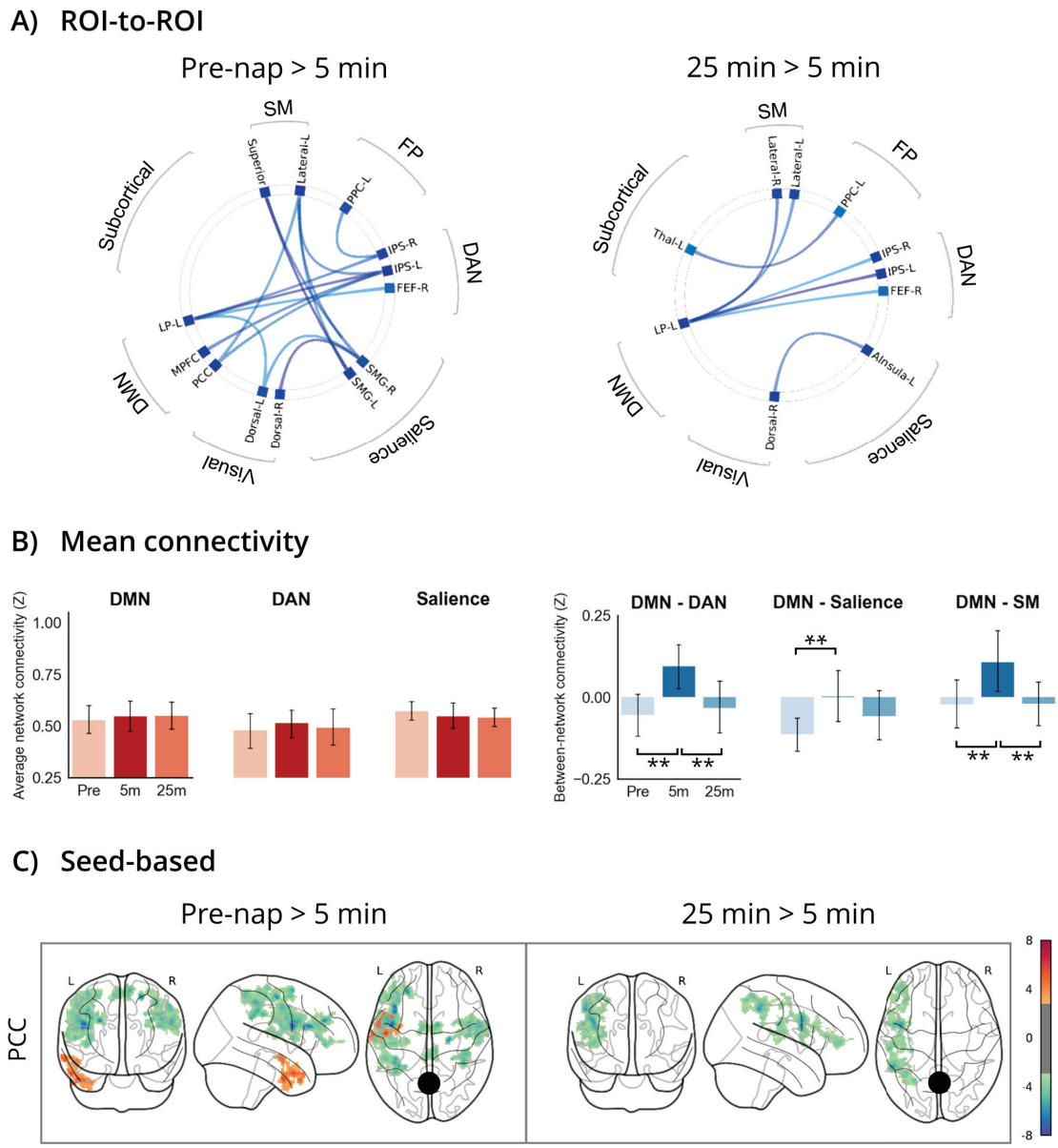


Fig 3. Functional connectivity disruption after awakening from N3 sleep (n=20). (A) ROI-to-ROI results for the two contrasts (left, Pre-nap minus 5 min p-a; right, 25 min p-a minus 5 min p-a). Blue connections indicate regions with significantly increased pairwise connectivity (two-sided paired t-test, p<.05 FDR-corrected) at 5 min p-a compared to the pre-nap condition (left) and compared to the 25 min p-a condition (right). (B) Mean pairwise connectivity within (left, red bars) and between (right, blue bars) networks. Stars denote significant post-hoc comparisons (t-tests, ** p<.01). (C) Seed-based connectivity results for the two contrasts (left, Pre-nap minus 5 min p-a; right, 25 min p-a minus 5 min p-a). Seed region is the posterior cingulate cortex (PCC), one core region of the DMN which demonstrates notable disruption during NREM sleep (center of mass in MNI coordinates: 1, -61, 38). Statistical parametric maps are reported using an uncorrected two-sided cluster-defining voxel-wise height threshold of p<.01 and a whole-brain FWE-corrected extent threshold of p<.05. Yellow-red colors indicate increased connectivity at pre-nap and/or 25 min p-a compared to the 5 min p-a scan. Green-blue colors indicate increased connectivity at 5 min p-a compared to the two other scans.

PCC connectivity was not significantly different at 25 min p-a compared to both pre-sleep and 5 min p-a.

Comparison of the functional connectivity alterations following N2 and N3 sleep awakenings

To further investigate the relationship between functional connectivity alterations and the sleep stage before awakening, we compared the brain connectivity between the N2 and the N3 groups. First, we looked at ROI-to-ROI differences at each resting-state scan (Fig 5A). Interestingly, during the pre-nap scan, the connectivity between the FP network and two regions, the lateral parietal (part of the DMN) and hippocampus, was decreased in the N3 group. At 5 min p-a, participants awakened in N3 sleep had a significantly increased connectivity between the DMN and DAN and between the SM and three networks (DMN, FP, Visual). There was no group difference at 25 min p-a. Next, at 5 min p-a, there was a tendency for a reduced mean DMN connectivity ($p=.07$) and increased DAN connectivity ($p=.08$) in the N3 group (Fig 5B, left). Third, the anti-correlations between the DMN and the attentional network and the DMN and the sensori-motor network were significantly decreased in the N3 group (Fig 5B, right, Fig 5D and S3 Table). Finally, we found a significant negative correlation between the mean DMN connectivity at 5 min p-a and the duration of N2/N3 sleep during the nap (Spearman $r = -.43$, $p = .01$, Fig 5C). This latter results shows that functional alterations within the DMN are associated with the prior sleep duration.

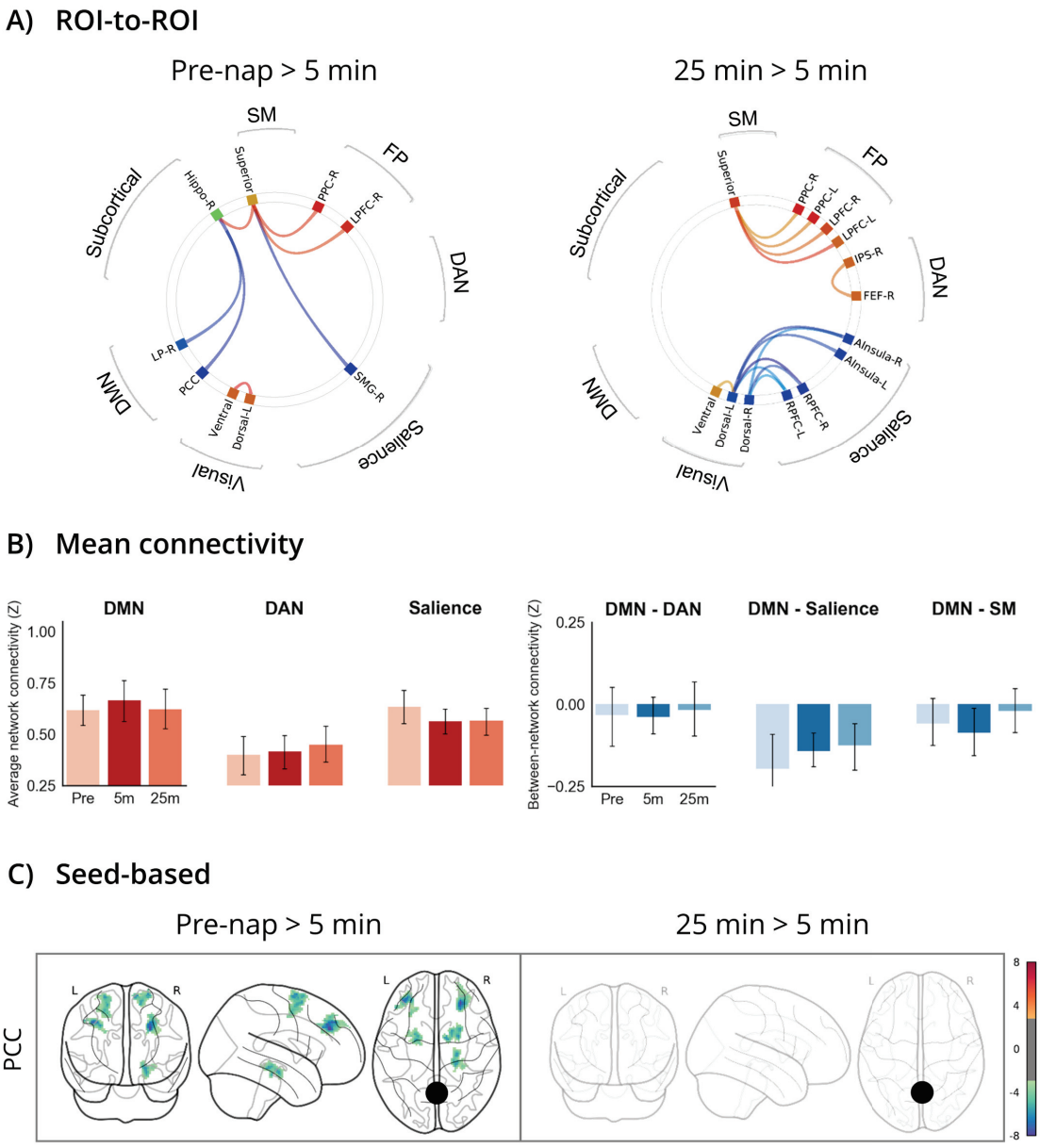


Fig 4. Functional connectivity disruption after awakening from N2 sleep (n=14). (A) ROI-to-ROI results for the two contrasts (left, Pre-nap minus 5 min p-a; right, 25 min p-a minus 5 min p-a). Connections indicate regions with significantly increased (blue lines) or decreased (red lines) pairwise connectivity at 5 min p-a compared to the pre-nap and 25 min p-a scans, respectively (two-sided paired t-test, p<.05 FDR-corrected). (B) Mean pairwise connectivity within (left, red bars) and between (right, blue bars) networks. (C) Seed-based connectivity results for the two contrasts (left, Pre-nap minus 5 min p-a; right, 25 min p-a minus 5 min p-a). Seed region is the posterior cingulate cortex (PCC), one core region of the DMN which demonstrates notable disruption during NREM sleep (center of mass in MNI coordinates: 1, -61, 38). Statistical parametric maps are reported using an uncorrected two-sided cluster-defining voxel-wise height threshold of p<.01 and a whole-brain FWE-corrected extent threshold of p<.05. Yellow-red colors indicate increased connectivity at pre-nap and/or 25 min p-a compared to the 5 min p-a scan. Green-blue colors indicate increased connectivity at 5 min p-a compared to the two other scans.

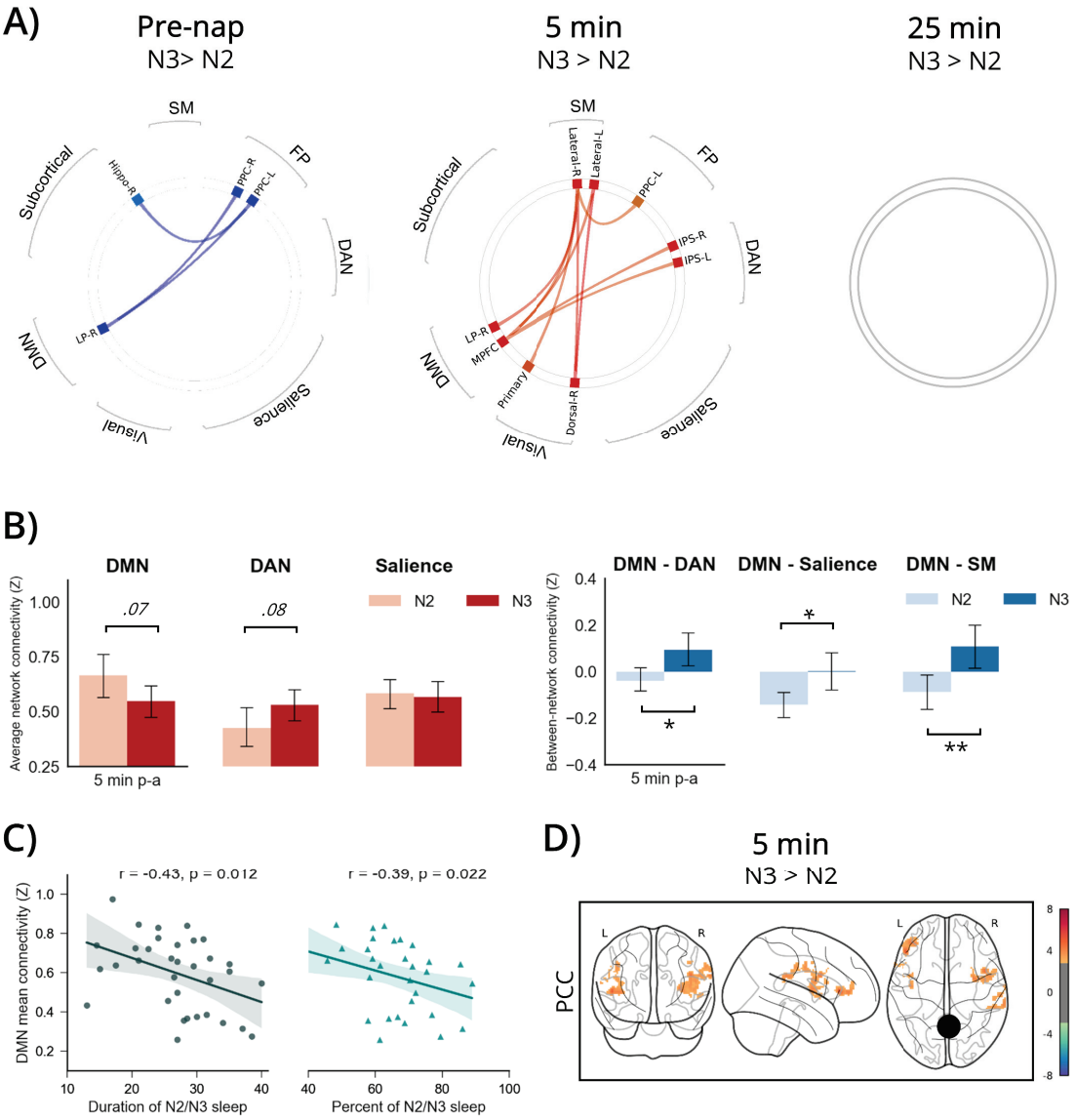


Fig 5. Comparison of the functional connectivity after awakening from N3 sleep (n=20) and N2 sleep (n=14). (A) ROI-to-ROI results at the pre-nap, 5 min and 25 min p-a scans for the contrast N3 minus N2. Blue connections indicate regions with significantly increased (red lines) or decreased (blue lines) connectivity (two-sided t-test, p<.05 FDR-corrected). No difference was found for the 25 min p-a scan. (B) Mean pairwise connectivity within (left, red bars) and between (right, blue bars) networks. Stars denote significant between-group comparisons (t-tests, * p<.05, ** p<.01). (C) Significant negative correlations between the DMN average functional connectivity at 5 min p-a and the duration (left) and percentage (right) of N2 and N3 sleep during the nap. (D) Seed-based connectivity results at 5 min p-a for the contrast N3 minus N2. Seed region is the posterior cingulate cortex (PCC), one core region of the DMN which demonstrates notable disruption during NREM sleep (center of mass in MNI coordinates: 1, -61, 38). Statistical parametric maps are reported using an uncorrected two-sided cluster-defining voxel-wise height threshold of p<.01 and a whole-brain FWE-corrected extent threshold of p<.05. Yellow-red colors indicate increased functional connectivity in the N3 group as compared to the N2 group.

Discussion

In a recent review on sleep inertia, Trotti (2016) proposed as first item on a 5-items research agenda that *"if as suggested by PET imaging, resumption of normal waking cognition on awakening requires reorganization of cognitive networks, can other functional neuro-imaging and/or neurophysiologic studies better delineate these necessary network changes?"*. The present study aimed at addressing this issue using combined EEG-fMRI, by characterizing the changes in brain networks functional connectivity across the first half hour following awakening from NREM N2 and N3 sleep (resting state scans acquired at 3 time points : pre-sleep, 5 and 25 minutes post-awakening). By contrast with previous studies we also measured behavioral performance (DST) and maximized sleep inertia by partially sleep-depriving the subjects on the night before the experiment, and awakening them after a sustained period of N2 and/or N3 sleep when possible.

Performance impairments at awakening

Using the DST we managed to evidence a decrement in performance after awakening even though the measure was made about 9 minutes after awakening (duration of the resting state scan = 6 min + the average delay between awakening and the scan onset = 3 ± 2 min). We indeed chose to favor the estimation of functional connectivity over the estimation of performance at awakening. For this reason behavioral effects were most probably underestimated in our study.

We found no significant decrement in performance at 5 min p-a compared to pre-sleep. This may be due to the delay between awakening and the first DST and/or to the fact that participants were tired before the nap due to their short night sleep. The total number of responses however was reduced, regardless of the awakening sleep stage and without any significant change in the number of mistakes, at 5 minutes p-a compared to 25 minutes p-a. This observation confirms that sleep inertia effects are conspicuous after a short daytime nap, comprising or not N3 sleep, and is consistent with the generally held view that speed is more impaired than accuracy at awakening (Tassi and Muzet, 2000; Trotti, 2016). The relatively smaller decrement in performances observed in the present study compared to previous studies that have used the DST immediately after awakening (Dinges et al., 1985; Evans and Orne, 1975; Stampi et al., 1990) may be accounted for by the delay between the awakening and the task. Our results may therefore suggest that the behavioral aspects of sleep inertia evolve rapidly after awakening and/or are compensated by the beneficial effect of sleep on cognitive performance (Faraut et al., 2016).

Interestingly we found significantly more mistakes in the N2 group than in the N3 group at 5 min p-a. This finding comes against the idea that the deeper the sleep prior awakening, the worse the performance upon awakening. One explanation could be that the beneficial effect of deep sleep may exceed the detrimental effect of sleep inertia, especially after the above-mentioned 9 min delay between awakening and the first post-sleep DST. Second, this effect may be task-specific. Indeed, the functional connectivity disruptions observed

at 5 min p-a from N2 and N3 sleep certainly impact different tasks differently. To our knowledge, no previous studies reported DST performance separately for N2 and N3 sleep. According to our results, the functional connectivity disruptions observed at 5 min p-a from N2 impacts more the performance at the DST than the functional connectivity disruptions observed at 5 min p-a from N3 sleep. The impact on performance may have been reversed if we had used a different task.

Functional connectivity alterations after awakening from N3 sleep

Awakening from N3 sleep was associated with robust and global alterations in the brain connectivity. The most significant finding was the decreased anti-correlation between networks normally anti-correlated during resting wakefulness, such as the task-negative (DMN) on the one hand and the task-positive (DAN, salience) networks on the other hand. This disruption of anti-correlation between task-positive and task-negative networks has been observed in a large palette of states including general anesthesia (Boveroux et al., 2010), sleep deprivation (De Havas et al., 2012; Sämann et al., 2010; Wang et al., 2016) and most importantly during NREM sleep (Larson-Prior et al., 2011; Sämann et al., 2011). This suggests that the functional connectivity during the first minutes following awakening from N3 sleep is marked by an intrusion of sleep specific connectivity into the wakefulness state. Another key finding was that as compared to 5 min p-a, the functional connectivity at 25 min p-a was partially restored between the DMN and DAN and between the thalamus and the frontoparietal network. This change in the dynamic of thalamo-cortical connectivity corroborates previous EEG studies that showed a progressive dissipation of slow wave activity during sleep inertia (Ogilvie and Simons, 1992; Ferrara et al., 2006; Marzano et al., 2011; Gorgoni et al., 2015). Finally, using seed-based analyses, we were able to evidence a decreased connectivity between the PCC and the inferior / middle temporal gyrus at 5 min p-a compared to pre-sleep. The middle temporal gyrus has been recently described as part of a DMN subcomponent involved in memory, constructive mental simulations, and according to the author's postulate, dreaming (Christoff et al., 2016). It is noteworthy that we observed a reduced connectivity of this region after awakening from N3 sleep which is well known to lead to less dream reports than any other sleep stages (Nielsen, 2000; Ruby, 2011).

Functional connectivity alterations after awakening from N2 sleep

Participants awakened in N2 sleep exhibited little alterations regarding the DMN connectivity and anti-correlations using ROI-to-ROI analysis. One notable exception is the increased connectivity between the DMN and hippocampus at 5 min p-a compared to pre-sleep, which has been reported to predicts subjective sleepiness and worsened working-memory performance under conditions of sleep loss (see Krause et al., 2017). This and the relative decrease of connectivity in the FP network observed in both ROI-to-ROI and seed-based analysis, could therefore be good candidates to explain the increased percent of mistakes in the N2 group at 5 min p-a compared to the N3 group. Apart from this, we have found at

5 min p-a compared to both pre-sleep and 25 min p-a a strong decrease in the connectivity between the SM and FP networks as well as an increased connectivity between the visual and salience networks. A suboptimal functional connection between the somato-motor network and the executive network may explain the decreased sensori-motor performances (e.g. grip strength, steadiness and coordination) after awakening from N2 sleep reported in several behavioral studies. Similarly the reduced functional connection between the visual and the salience network may be the reason for the deficits in visuo-perceptual tasks at awakening (see Tassi and Muzet, 2000). Finally, at 5 min p-a compared to pre-sleep, seed-based analysis revealed a large increase in the connectivity between the PCC and the parahippocampal gyrus, a region involved in memory retrieval. Such a functional modification may participate in the well-known variability in dream recall between sleep stages (Nielsen, 2000; Ruby, 2011).

Link between functional alterations and prior sleep depth / duration

Several conclusions may be drawn in the light of the above. Awakenings from N2 and N3 sleep were both associated with alterations in functional connectivity. Some of these alterations overlapped and some did not. Regarding the overlap, in both sleep stages we have found strong alterations in the SM network at 5 min p-a. This disruption of SM connectivity was previously reported in two previous studies (Wu et al., 2012; Tsai et al., 2014) and appears to be the physiological signature of the motor impairments and clumsiness classically reported during sleep inertia. Most importantly, there were also several discrepancies in the alterations following N2 or N3 sleep awakening. N3 sleep was characterized by a more robust loss of functional segregation between several networks. Notably, we found large reductions in the anti-correlation between the DMN and task-positive networks (FP, DAN, SM, Salience) as well as an increased connectivity between sensory networks (visual and FP). One key finding is the negative significant correlation between the average DMN mean connectivity and the duration (and percentage) of N2 and N3 sleep during the nap. This result and the previous ones suggest that alterations in the DMN functional connectivity upon awakening are directly linked to the prior sleep duration and depth at least in the first sleep cycle. From a phenomenological standpoint, the intense disruption of the DMN connectivity after awakening from N3 sleep may account for internally-oriented cognitive impairments such as feeling of disorientation, desire to return to sleep and rapid vanishing of short-term memory content (i.e. dreams) frequently observed after awakening from this sleep stage. By contrast, disrupted anti-correlations between the DMN and attentional networks, in addition with reduced FP connectivity, may explain the hypovigilance and reduced cognitive performances which have been consistently reported during sleep inertia. On a more practical level, our findings provide experimental evidences in favor of the general public health advice to take short naps (< 20-30 min) in order to avoid entering N3 sleep, which may suppress the cognitive advantage of taking a nap.

Limitations

Due to the partial sleep deprivation, the functional connectivity during the pre-sleep scan was probably altered as compared to rested wakefulness after a full night of sleep (Sämann et al., 2010; De Havas et al., 2012; Yeo et al., 2015; Kaufmann et al., 2015; Tüshaus et al., 2017). It follows that our results most probably underestimate the functional connectivity disruption associated with sleep inertia. Finally, it is also possible that the MRI scan noise may have had a positive alerting effect on vigilance and therefore reduced the severity of sleep inertia. However, only one study has so far investigated the effect of a pink noise at 75 dB on sleep inertia. The authors reported inconclusive results on whether noise improved or worsened sleep inertia effects after a nap (Tassi et al., 1992).

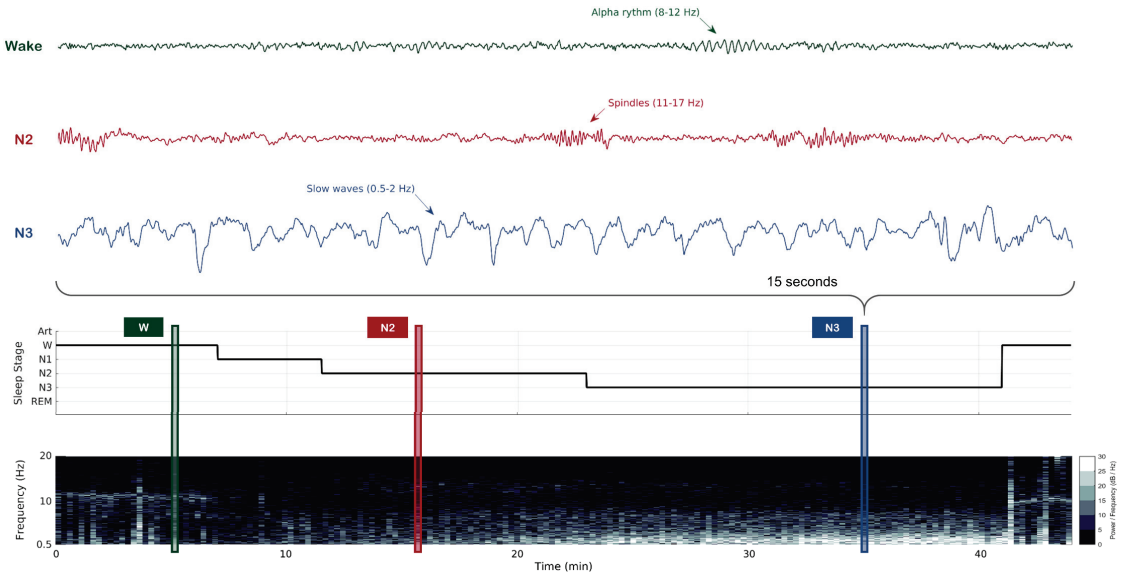
Conclusion

The present combined EEG-fMRI study provides for the first time a measure of both brain functional connectivity and behavioral performance at 5 and 25 minutes post awakening from N2 and N3 NREM sleep. By splitting participants who were awakened in N2 and N3 sleep, and thanks to a large number of participants (n=55), we were able to provide an exhaustive overview of the functional connectivity alterations following awakening from these two sleep stages. Our results support the hypothesis of Balkin et al. (2002) and show that the functional connectivity is altered at awakening from both N2 and N3 sleep, but in a much severe way after an awakening from N3 sleep. Importantly, awakening from N3 sleep induced a severe disruption of the functional connectivity in the default mode network which was not the case for awakening from N2 sleep. In addition, awakenings from N3 sleep were associated with a robust loss of brain functional networks segregation, which severity was correlated with prior sleep duration. Our result provide, as whished by Trotti (2016) in her recent review, the *"which an how"* functional brain networks are altered at awakening and show that sleep inertia is the result of an intrusion of sleep specific features in the functional connectivity of the awake brain.

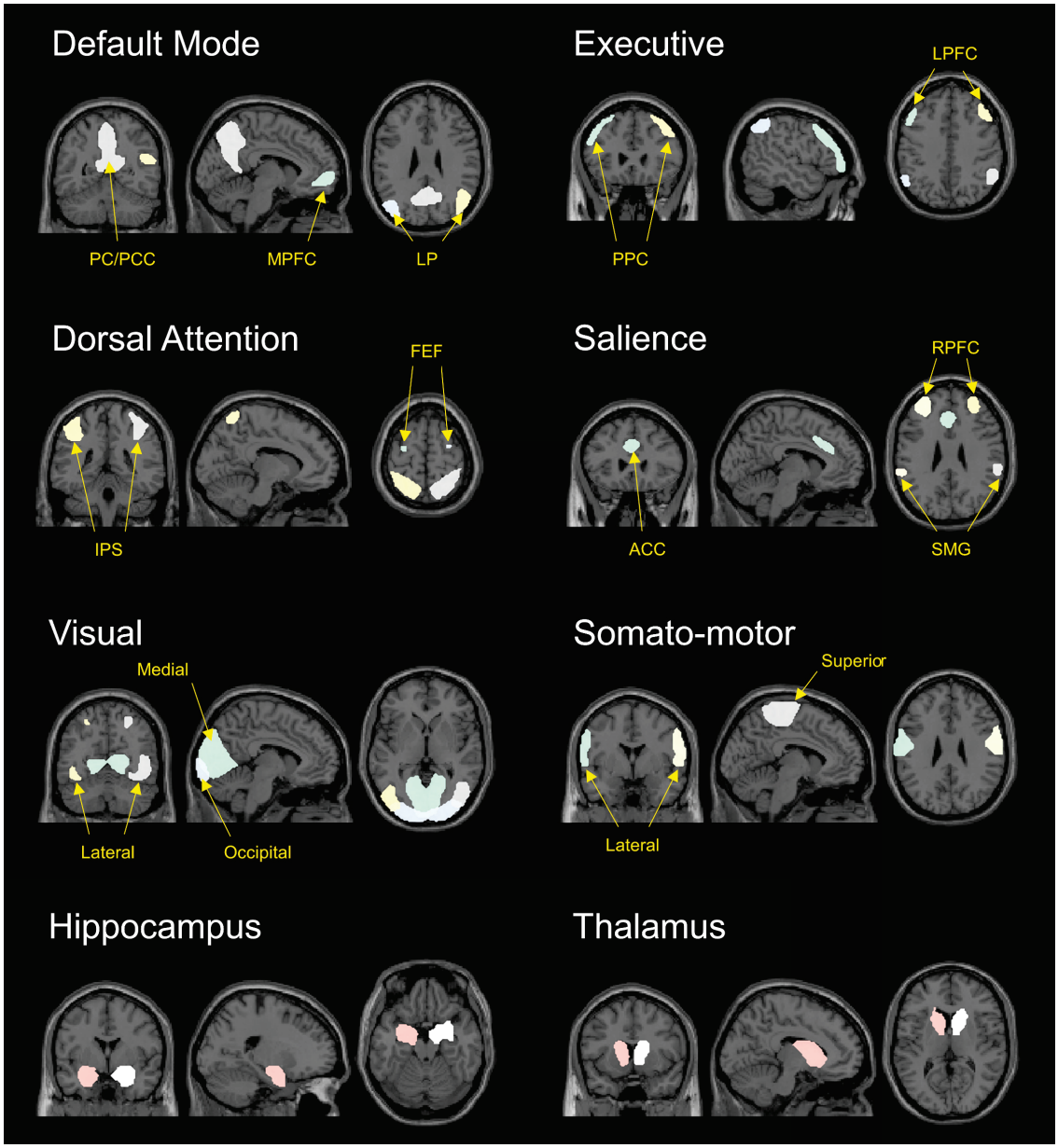
Acknowledgments The authors would like to thank Basak Turker, Morgane Hamon, Franck Lamberton and Danielle Ibarrola for substantial help in data collection and analysis, as well as Jamila Lagha for her help in administrative work.

Author contribution R.V and P.R designed the study, acquired the data and wrote the paper. D.M helped in data analysis. A.N participated to the design and provided access to his sleep unit to conduct the sleep deprivation.

Supplementary materials



S1 Fig. Hypnogram and EEG data (Cz) acquired during the nap slot in one subject. Top. 15-seconds frames of wakefulness, N2 and N3 sleep. Middle. Hypnogram showing vigilance states as function of time during the nap slot. Bottom. Spectrogram showing the normalized power in the 0.5 – 20 Hz range for each 15-seconds frames (lighter colors indicate higher power).



S2 Fig. Networks and regions included in the connectivity analysis. Abbreviations: PCC/PC, Posterior Cingulate Cortex / Precuneus – MPFC, Medial Prefrontal Cortex – LP, Lateral Parietal – FEF, Frontal Eye Fields – IPS, Intraparietal Sulcus – PPC, Posterior Parietal Cortex – LPFC, Lateral Prefrontal Cortex – ACC, Anterior Cingulate Cortex – RPFC, Rostral Prefrontal Cortex – SMG, Supra-Marginal Gyrus. Note that the salience network also includes the anterior insula (not visible).

S1 Table. Seed-based functional connectivity results for the N3 group (n=20). Seed region is the posterior cingulate cortex (PCC, center of mass in MNI coordinates = 1, -61, 38). Statistical analyses were performed using a cluster-defining voxel-wise height threshold of p<.01 (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of p<.05 to show brain areas either positively or negatively correlated with the seed region. PG, precentral gyrus - SMG, supramarginal gyrus – ITG, inferior temporal gyrus – SPL, superior parietal lobule – SFG, superior frontal gyrus – *N.S*, not significant.

			MNI coordinates				
Contrast	Region	Brodmann area	X	Y	Z	T value	Cluster size
Pre-sleep > 5 min	PG L	BA44	-42	4	26	-6.45	2980
	PG R	BA6	22	-14	58	-6.36	1462
	SMG L	BA40	-34	-44	34	-5.05	922
	ITG L	BA20	-48	-6	-36	6.89	742
	SPL R	BA2	40	-38	52	-5.10	390
	PG R	BA4	8	-26	60	-4.14	295
	SFG R	BA6	10	4	66	-5.51	277
Pre-sleep > 25 min	*N.S*	-	-	-	-	-	-
25 min > 5 min	PG L	BA44	-42	4	24	-6.68	1595
	SMG L	BA40	-52	-46	44	-5.56	879

S2 Table. Seed-based functional connectivity results for the N2 group (n=14). Seed region is the posterior cingulate cortex (PCC, center of mass in MNI coordinates = 1, -61, 38). Statistical analyses were performed using a cluster-defining voxel-wise height threshold of p<.01 (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of p<.05. DLPFC, dorsolateral prefrontal cortex – PHG, parahippocampal gyrus – SFG, superior frontal gyrus - N.S, not significant.

Contrast	Region	Brodmann area	MNI coordinates X	Y	Z	T value	Cluster size
Pre-sleep > 5 min	DLPFC R	BA9/46	28	40	32	-5.89	464
	SFG L	BA6	-22	-2	68	-6.10	351
	SFG R	BA6	26	2	72	-6.20	271
	PHG. R	BA34	22	-30	-12	-8.40	258
	DLPFC R	BA9/46	-38	42	40	-7.01	254
Pre-sleep > 25 min	N.S	-	-	-	-	-	-
25 min > 5 min	N.S	-	-	-	-	-	-

S3 Table. Seed-based functional connectivity results for the group comparison (N3 (n=20) minus N2 (n=14)). Seed-based functional connectivity results for the group comparison (N3 (n=20) minus N2 (n=14)). Seed region is the posterior cingulate cortex (PCC, center of mass in MNI coordinates = 1, -61, 38). Statistical analyses were performed using a cluster-defining voxel-wise height threshold of p<.01 (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of p<.05 to show brain areas either positively or negatively correlated with the seed region. PG, precentral gyrus - IFG, inferior frontal gyrus – SMG, supramarginal gyrus - *N.S*, not significant.

Scan	Region	Brodmann area	MNI coordinates X	Y	Z	T value	Cluster size
Pre-sleep	*N.S*	-	-	-	-	-	-
5 min	PG R	BA44	46	8	26	4.63	595
	IFG L	BA45	-48	32	6	5.08	314
	PG L	BA4	-42	-10	36	4.90	264
	SMG R	BA40	68	-32	26	4.46	253
25 min	*N.S*	-	-	-	-	-	-

9.2 Part 2. Sleep inertia in high and low dream recallers

Brain functional connectivity upon awakening from sleep predicts between-subject differences in dream recall frequency

In preparation

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Summary

Dreaming is a fascinating and universal experience that remains still poorly understood. Perhaps one of its most intriguing aspect relates to why some people recall up to several dreams per day while some hardly ever recall one. Previous results suggest that memory performance during wake could not explain such inter-individual differences in dream recall but that the brain transitional state during sleep inertia immediately following awakening could . To test this hypothesis we designed a combined EEG-fMRI study. We aimed at investigating the brain functional connectivity of high dream recallers (HR, n=27) and low dream recallers (LR, n=27) in the minutes following awakening from a 45 min mid-afternoon nap. Resting-state scans were acquired before the nap, 5 min and 25 min after awakening and were each paired with a mental calculation task. Between-group contrasts of the functional connectivity at 5 min post-awakening revealed a pattern of enhanced connectivity in HR within the default mode network and regions involved in memory retrieval (i.e. medial prefrontal cortex, precuneus, left medial temporal lobe, left dorsolateral prefrontal cortex). These findings are discussed regarding the idea of a neurophysiological trait difference between HR and LR .

Keywords Dream recall, sleep inertia, awakening, EEG-fMRI, functional connectivity, default mode network

Introduction

Dreaming is a universal and fascinating experience which happens most probably every night when we plunge into sleep. However, several aspects of dreaming are still poorly understood, among which is the large inter-individuals difference in dream recall frequency (DRF). Previous results demonstrated that intra-sleep wakefulness is one explaining factor of DRF variability (Eichenlaub et al., 2014a; Vallat et al., 2017). However this factor does not explain everything since controlled awakenings in the lab still result in drastically more frequent dream recall in high dream recallers (HR) than in low dream recallers (LR)

whatever the sleep stage (Goodenough et al., 1959; Eichenlaub et al., 2014b; Eichenlaub et al., 2014a).

Sleep inertia, the transient period following awakening and associated with impaired performances (Tassi and Muzet, 2000; Trotti, 2016), could be the missing link. Awakenings would enable the encoding of the dream into long term memory when the transition between sleep and wakefulness spare the short term memory of the dream (Koulack and Goodenough, 1976). The hypothesis is thus that, compared to HR, LR would show more cognitive impairments and functional connectivity disturbances caused by sleep inertia in the first minutes following awakening from sleep. This hypothesis is supported by previous results which have shown functional brain differences between HR and LR using EEG (Eichenlaub et al., 2014a) and PET (Eichenlaub et al., 2014b). As compared to LR, HR notably showed an increased regional cerebral blood flow (rCBF) in the medial prefrontal cortex (MPFC) and temporo-parietal junction (TPJ).

The proper functioning of these regions, known to be involved in dream production and/or recall (i.e. lesions of one or both of these regions induce a cessation of dream reports; Solms, 1997; Solms, 2000) could thus explain the successful retrieval of dream content upon awakening. Specifically, we postulate that the strength of the functional connectivity in the network comprising these two regions, namely the default mode network (DMN), is required to recall dreams at awakening. The DMN is a set of functionally coupled brain areas (Raichle et al., 2001; Legrand and Ruby, 2009; Sestieri et al., 2011) that are highly activated during mental imagery and episodic memory retrieval, and whose functional connectivity is diminished during sleep (Horovitz et al., 2009; Larson-Prior et al., 2011; Sämann et al., 2011). Several authors have postulated that the DMN might be the brain network underlying the dreaming experience (Domhoff, 2011; Christoff et al., 2016).

The present study aims therefore at testing the hypothesis of a differential brain functioning of HR and LR specifically during the period following awakening from sleep. This hypothesis has surprisingly never been experimentally tested before, despite several studies mentioning the brain and cognitive functioning immediately upon awakening as a potential explaining factor of DRF variability (Schredl et al., 2003b; Conduit et al., 2004). The period following awakening from sleep is a distinct and transient state that is measurably different from wakefulness since it is characterized by impaired performance, hypovigilance and sleepiness. We therefore hypothesized that sleep inertia and its cerebral correlates may account for the inter-individual differences in DRF. In other words we expected more impaired cognitive performances and functional connectivity at awakening in LR than in HR.

Several studies are consistent with this hypothesis. First, sleep inertia is higher following sleep deprivation or awakening from N3 sleep, which are both factors associated with a lower rate of dream recall (Nielsen, 2000; De Gennaro et al., 2010). Second, Conduit et al. (2004) found that memory abilities after awakening from N2 sleep were lower than after awakening from REM sleep, and that these impairments were significantly correlated with reported dream recall frequency (i.e. better memory performances and better dream recall after awakening from REM sleep).

To test our hypotheses, we designed a combined EEG-fMRI study. We aimed at investigating the brain functional connectivity in the minutes following awakening from a 45 minutes mid-afternoon nap in HR vs LR. Resting-state scans were acquired before the nap, 5 min and 25 min after awakening to investigate the dynamics of brain functional reorganization during the first half hour following awakening, and each scan was associated with a mental calculation task to measure the cognitive impairments of sleep inertia. We predicted that HR would show (1) more dream recall following awakening from sleep (2) a higher functional connectivity within the DMN and between regions involved in memory retrieval (3) less cognitive performance impairments, suggesting a faster recovery of normal cognitive functioning upon awakening.

Methods

Participants

Behavioral and neurophysiological data were acquired from 55 healthy subjects (28 males, mean age = 22.55, standard deviation = 2.41, range = 19–29). The subjects were informed of the study through an announcement sent to the mailing list of Lyon University, which briefly described the study and included a link to a questionnaire concerning sleep and dream habits. Subjects were selected if they reported and subsequently confirmed during a phone interview: (1) having a high or low DRF (DRF superior to 5 dream recalls per week and inferior to 2 dream recalls per month respectively) (2) having a regular sleep-wake schedule, no difficulty to fall asleep, being occasional or frequent nappers and having preferentially already done an MRI brain scan in the past few years. Importantly, the subjects were unaware that DRF was the main criterion for inclusion in the study. Among the 55 participants, 28 of them were high dream recallers (HR; mean DRF = 6.6 ± 0.7 dream reports per week) and 27 were low dream recallers (LR; mean DRF = 0.2 ± 0.1 dream report per week). Apart from the DRF ($p < .001$), the two groups did not differ in age, habitual sleep duration or education level (see Table 1 of section 10). They had no history of neurological and psychiatric disorders, and had no sleep disturbances. They provided written informed consent according to the Declaration of Helsinki and received monetary compensation for their participation. The study was approved by the local ethics committee (CCPPRB, Centre Leon Berard, Lyon, France).

Behavioral tests

The night before the experiment, the subjects underwent a partial sleep deprivation (they were allowed to sleep between 5 am and 8 am; see Procedure). Between 9 pm and 11 pm, the subjects were presented with various tests to assess the potential between group differences at the cognitive and personality levels, the results of which will be detailed elsewhere.

In addition, participants trained on the descending subtraction task (DST), which was used to evaluate cognitive performances during the MRI session on the following day, in order to avoid a practice effect over the first trials (Dinges et al., 1985). The DST has been previously used to evidence performances decrement and normalization in the first 30 min post awakening (Evans and Orne, 1975; Dinges et al., 1985; Stampi et al., 1990). Subjects were presented with a three-digit number. They were instructed to subtract 9, saying the operation and the result aloud, and then continue by subtracting 8 from the remainder, then 7, and so on until they had to subtract 1. At this point they were to start the cycle of descending subtractions again. They had to do the task for two minutes and were instructed to be as fast and accurate as possible.

Procedure

Evening and night. To facilitate sleep in the MRI environment, participants underwent a 3 h partial sleep deprivation on the night before the experiment. Specifically, they arrived in the sleep unit of the hospital Le Vinatier (Lyon, France) at 8 pm. During two hours they performed the previously described personality and cognitive tests, administered by R.V. They were then instructed to stay awake until 5 am (the possible activities were reading, making puzzles and watching movies), at which point they were allowed to sleep for 3 hours until 8 am in a bed in the sleep unit. Energy drinks or physical activity were prohibited during the partial sleep deprivation, and nurses regularly checked that the subject did not fall asleep. The monitoring of body movements through wrist actigraphy (Actigraph, Pensacola, USA) during the whole night made it possible to check a posteriori that the subject did not fall asleep before 5 am. In the morning, participants were offered breakfast and a shower and then occupied themselves (reading or internet) under the experimenters' supervision until the MRI session.

Day. The MRI procedure is shown in Fig 5.1. After lunch at 11.30 am, participants were conducted to the neuroimaging center (CERMEP). During the first half hour, experimenters installed on the participant's head a MRI compatible EEG cap (EASYCAP®). Participants were then installed in the MRI scanner at about 1.20 pm (1.17 pm ± 13 min). They read a 5 min cartoon during the calibration of the eye-tracking camera, and then performed the descending subtraction task (DST) for 2 minutes. The first resting-state scan was then acquired, with the instructions to remain awake and look at a central fixation cross on the screen. At the end of the scan, participants were informed that they could sleep (at 1.39 pm ± 14 min in average) during the next 45 min. At the end of the nap slot, participants were awakened, if they were sleeping, by calling their first name and the 2nd resting state scan was acquired. At the end of the scan, the 2nd DST was performed. During the following 10 minutes, subjects were asked about their dream(s) and sleep in the scanner and about the cartoon. Then the 3rd resting state scan and DST were performed (about 25 min after awakening). Finally, an 8-min T1 anatomical scan was acquired.

Data collection

EEG and eye movement recordings Polysomnography data was recorded using a 15 channels MR-compatible cap designed for sleep studies i.e. with a layout designed according to American Academy of Sleep Medicine Guidelines 2007 (EasyCap, Brain Products GmbH, Gilching, Germany). It comprised 9 EEG electrodes placed according to the international standard 10/20 system (O1, O2, C3, C4, F3, F4, M1, M2, Cz, FCz was used as reference and AFz as ground), 2 EOG electrodes, 3 EMG electrodes, and an electrocardiogram electrode placed on the back of the participant. The sampling rate was 5000 Hz and an analog band-pass filter was set to 0.01 – 250 Hz. To score sleep online during the fMRI session, a real-time pulse-artefact correction was performed using the BrainVision Recorder (Version 1.2) and BrainVision RecView (Version 1.4) softwares (Brain Products).

To ensure that participants were not closing their eyes during the resting state scans, eye movements were monitored during the experiment using an EyeLink 1000 fMRI eye tracking system (SR Research Ontario, Canada). Eye position was calibrated at the beginning of the experiment and monitored throughout.

MRI acquisition MRI scans were obtained from a MAGNETOM Prisma 3.0 T scanner (Siemens Healthcare, Erlangen, Germany) at the Primage neuroimaging platform (CERMEP). Structural MRI were acquired with a T1-weighted (0.9-mm isotropic resolution) MPRAGE sequence and functional MRI data with a T2*-weighted 2D gradient echo planar imaging sequence (EPI) with 180 volumes (TR/TE: 2000/ 25 ms; flip angle: 80°; voxel size: 2.68 × 2.68 × 3 mm; slices: 40, duration: 6 minutes). Functional and anatomical scans were performed using a 20-channel head coil. The coil was foam-padded to improve subject comfort and restrict head motion.

Data analysis

EEG Artifacts related to gradient switching and cardiac pulse (cardio-ballistic artifact) were removed using standard routines available in BrainVision Analyzer version 2.0 software (Brain Products). Polysomnographic data were downsampled to 1000 Hz and band-pass filtered between 0.5 and 25 Hz. Offline sleep stage scoring was performed using EEG epochs of 30 seconds following standard AASM rules (Iber, 2007) visualized using SLEEP software (Combrisson et al., 2017).

fMRI Preprocessing and quality check were performed using standard routine in SPM12 software (Wellcome Department of Imaging Neuroscience). Preprocessing included functional realignment, slice-time correction, coregistration to structural scan, spatial normalization and spatial smoothing using a 6 mm full-width at half-maximum isotropic Gaussian kernel filter. Individual T1 images were segmented into gray matter, white matter and cerebrospinal fluid tissue maps. Functional and structural images were then normalized to MNI152 space (Montreal Neurological Institute). Functional images underwent artifact

and motion regression in the ART toolbox using the following criteria to define outliers: global signal intensity changes greater than 9 standard deviations and movement exceeding 2 mm. SPM motions parameters and outliers were subsequently included as covariates in connectivity analyses.

Connectivity analysis were performed using the CONN toolbox version 17f. First, we performed a denoising step including a regression of the 6 motion correction parameters and their corresponding first-order temporal derivatives, as well as a component-based strategy (aCompCor, Behzadi et al., 2007) to identify and remove physiological confounds that are unlikely to be related to neural activity. The resulting BOLD time series were band-pass filtered (0.008 – 0.09 Hz) to further reduce noise and increase sensitivity (Weissenbacher et al., 2009). We then performed seed-to-voxel analysis using a seed in the medial prefrontal cortex (MPFC; center of mass in MNI coordinates: 1, 55, -3), one core region of the DMN which is critically involved in dream recall (Solms, 1997; Eichenlaub et al., 2014a).

Statistics For the DST, between-group comparisons were achieved using a mixed two-way repeated measures ANOVA with a group factor (two levels: HR and LR) and a time factor (within subject factor with three levels: Pre-sleep, 5 min p-a, 25 min p-a). Post hoc analyses (t-tests) were used in case of significance. Seed-based connectivity analysis were performed using a cluster-defining voxel-wise height threshold of $p<.01$ (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of $p<.05$.

Results

Sleep parameters

As expected and due to the inherent discomfort of the MRI environment, 11 out of 55 participants were not able to reach N2 sleep during the 45 min nap slot. One subject out of the 44 remaining was discarded because of a technical failure during data acquisition, leading thus to a total of 43 participants included in the final analysis (21 HR, 22 LR). Means of the main sleep parameters in the two groups are presented in Table 1. Importantly, there was no significant group difference for any of the sleep parameters considered or in the latency between the awakening and the two post-awakening resting-state scans.

Behavioral results

DST DST performances are reported in S2 Fig. A two-way ANOVA revealed a significant effect of time in the number of responses ($F(2, 41) = 7.44$, $p = .001$) and percentage of correct responses ($F(2, 41) = 5.03$, $p = .009$) compared to pre-nap performances. Specifically, the total number of responses was reduced at 5 min p-a compared to pre-nap and 25 min p-a ($p = .003$ and $p < .001$, respectively). There was no main effect of time in the percentage of mistakes, a finding in line with the generally held view that speed

Table 1. Mean sleep parameters of the HR (n=21) and LR (n=22) groups. TST = Total Sleep Time, SE = Sleep Efficiency, Wake (W), N1, N2 and N3 = Total duration of each sleep stage in minutes. LAS1 = latency (min) between the awakening and the start of the first post-awakening resting-state scan. LAS2 = latency (min) between the awakening and the start of the second post-awakening resting-state scan. N.S = not significant.

Group	TST	SE (%)	W	N1	N2	N3	LAS1	LAS2
HR	35.6	85.7	9.3	12.9	16.8	6.3	3.4	24.3
SD	8.4	11.9	5.0	7.9	5.6	6.4	1.0	4.2
LR	36.3	83.6	11.2	11.5	18.7	6.4	4.8	23.5
SD	6.3	11.7	5.2	6.9	7.3	6.0	4.0	3.6
T-test	*.78*	*.57*	*.23*	*.54*	*.36*	*.96*	*.12*	*.54*

is more impaired than accuracy during sleep inertia (Trotti, 2016). Most importantly, there was no main effect of group or interaction between group and time for any of the three outcome measures considered. Sleep inertia, as measured by the DST, did not differ between the two groups.

Dream recall After awakening from the partial sleep deprivation in the sleep unit, more HR reported dreams than did LR (64% of HR and 19% of LR reported a full or a white dream, $X^2 = 11.6$, $p < .001$). This was also the case after awakening from the 45 min nap inside the MRI (75% of HR versus 33% of LR, $X^2 = 9.45$, $p = .002$).

Functional connectivity

The results of functional connectivity contrasts between HR and LR in the three resting-state scans are presented in Fig 1 and Table 2. First, and perhaps most importantly, we found that during the resting-state scan conducted 5 min after awakening from NREM sleep, HR demonstrated an increased functional connectivity between the MPFC and other core regions of the DMN, including the precuneus and temporal fusiform cortex, and between the MPFC and dorsolateral prefrontal cortex (DLPFC). Second, at 25 min post-awakening, seed-based analysis revealed an increased functional connectivity in HR between the MPFC and caudate nucleus. No between-group differences were found during the pre-sleep resting-state scan.

Discussion

This study is the first to compare the brain functional connectivity and cognitive performances of high and low dream recallers in the minutes following awakening from sleep, in an effort to understand the basis for these individual differences in dream recall. The main findings are the followings. First, as expected significantly more HR reported a dream upon awakening than LR. Second, compared to LR, the brain functional connectivity of HR at 5 min post-awakening was significantly increased in several regions that all have in

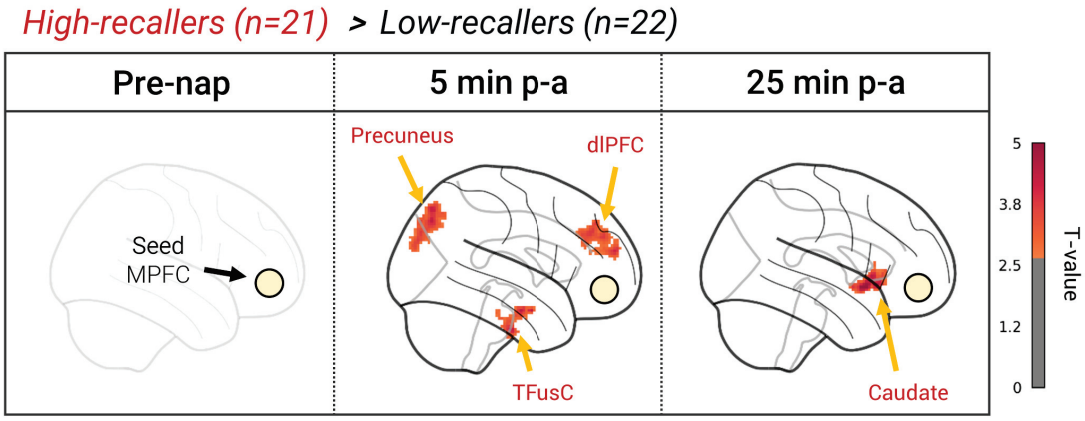


Fig 1. Functional connectivity differences between High-recallers (HR) and Low-recallers (LR) during pre-sleep scan, 5 min post-awakening scan and 25 min post-awakening scan. Seed-based connectivity results showing foci with higher activation in HR than in LR. Seed region (yellow circle) is the medial prefrontal cortex (MPFC, center of mass in MNI coordinates: 1, 55, -3), a region critically involved in dream recall. Statistical parametric maps are superimposed on a glass brain using an uncorrected two-sided cluster-defining voxel-wise height threshold of p<.01 and a whole-brain FWE-corrected extent threshold of p<.05. MPFC = medial prefrontal cortex, dlPFC = dorsolateral prefrontal cortex, TFusC = temporal fusiform cortex. Faded brain denotes an absence of significant differences between the two groups.

Table 2. Seed-based functional connectivity results for the group comparison (HR (n=21) minus LR (n=22)). Seed region (black circle) is the medial prefrontal cortex (MPFC, center of mass in MNI coordinates = 1, 55, -3). Statistical analyses were performed using a cluster-defining voxel-wise height threshold of p<.01 (uncorrected, two-sided) and a whole-brain family-wise error (FWE) corrected extent threshold of p<.05.

		MNI coordinates				
Scan	Brain region	X	Y	Z	T value	Cluster size
Pre-sleep	*N.S*	-	-	-	-	-
5 min p-a	Precuneus L	-6	-76	42	4.97	512
	DLPFC L	-34	60	20	4.86	356
	TFC L	-40	-18	-38	5.49	251
25 min p-a	Caudate R	14	12	-8	6.01	277

common to be involved in memory processes. Third, the arithmetic performances of both HR and LR were significantly impaired at 5 min post-awakening compared to pre-nap and 25 min post awakening, but no between group differences was observed. The significance of these findings is discussed below.

Between-group contrasts of the functional connectivity at 5 min post-awakening revealed a pattern of enhanced connectivity in HR within the DMN (namely the precuneus, medial prefrontal cortex and left medial temporal lobe) and between the DMN and the left DLPFC. Remarkably, all these regions have been associated with memory processes. In a meta-analysis of the brain areas associated with episodic encoding and retrieval, Spaniol et al. (2009) reported that the largest clusters associated with retrieval success were located in the precuneus, the anterior prefrontal cortex, the left DLPFC and, to a lesser extent, the middle temporal gyrus. These are almost exactly the same regions found to be more functionally connected in HR than LR during the first minutes following awakening.

Based on these findings, one may conclude that HR were deliberately involved in memory retrieval during the resting-state scans, hence an increase functional connectivity in these specific regions. This hypothesis is however unlikely given that subjects were asked to remember the content of their dreams only during the interval between the 5 min and 25 min post-awakening scans. Moreover, only 5 subjects (4 HR) reported that they were actively trying to recall the content of their dreams during the 5 min post-awakening scan. Another possible interpretation is that these results reflect neurophysiological trait differences rather than strategy/task differences between HR and LR. This interpretation is supported by previous results showing, in HR, increased brain responses to auditory stimuli during wakefulness and sleep (Eichenlaub et al., 2014a), and increased regional cerebral blood flow in the MPFC and TPJ, also during sleep and wakefulness (Eichenlaub et al., 2014b). Since it is generally admitted that sleep inertia interferes with memory retrieval on awakening rather than memory consolidation (Bonnet, 1983; Dinges, 1990; Tassi and Muzet, 2000; Conduit et al., 2004), the findings of the present study support the hypothesis of a differential brain functional organization upon awakening between HR and LR. Specifically, increased functional connectivity between regions involved in memory retrieval would facilitate dream recall in HR, while decreased connectivity in those same regions would prevent successful dream recall in LR. These results suggest that the difference in DRF between HR and LR is not the result of a differential production of dreams, but rather of a differential recall of dreams upon awakening .

Limitations

First, the present study reported the brain functional connectivity of HR and LR following awakening from sleep stages, namely N2 and N3 sleep. It would be interesting to extend these data to N1 sleep and REM sleep. This latter, which has traditionally been viewed as the neural substrate of dreaming, is however very difficult to observe in an fMRI setting, unless applying a severe and specific REM sleep deprivation in the night(s) before (Duyn, 2012), which is of course not ideal to study functional connectivity given the huge impact

of severe sleep deprivation on the brain functional connectome (De Havas et al., 2012; Yeo et al., 2015; Krause et al., 2017). Given the higher rate of dream recall following REM sleep than any other sleep stages (Nielsen, 2000; Ruby, 2011), one would expect that the functional connectivity between regions involved in memory retrieval would be higher following awakening from REM sleep than NREM sleep. This would in turn explain the better cognitive and memory performances (i.e. lesser sleep inertia) following REM sleep than NREM sleep (Bonnet, 1983; Koukkou and Lehmann, 1983; Conduit et al., 2004).

On another note, we were not able to evidence between-group differences in cognitive performances, measured by the DST, at 5 min post-awakening. There are two possible reasons for this. First, the DST was not performed immediately after awakening but after the 6 min resting-state scans, because we choose to favor the estimation of functional connectivity rather than cognitive performances directly upon awakening. Bonnet (1983) reported that the impairment of cognitive and memory performance upon awakening decreases as a function of time awake. Therefore the delay between awakening and the DST could account for a relatively small decrease in performance compared to pre-nap performances and the absence of group main effect. Second, while the DST has been previously reported to be affected by sleep inertia (Dinges et al., 1985), it is possible that this arithmetic task do not capture well the brain functioning and dream recall differences between HR and LR, as would have for instance a task more-specifically designed to assess memory retrieval.

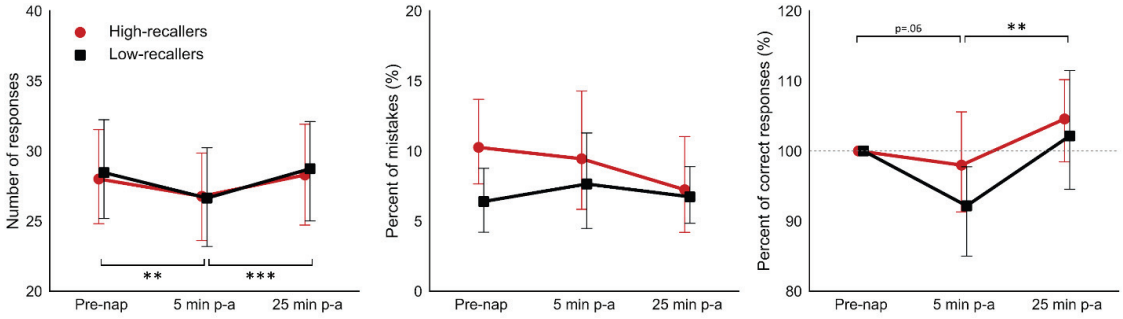
Conclusion

The present study showed that inter-individual differences in dream recall frequency are associated with a differential brain functional connectivity in the minutes following awakening. Specifically, a higher functional connectivity between regions involved in memory retrieval just after awakening could facilitate in HR the retrieval of pre-awakening experiences and thus promote dream recall. More broadly, these results contribute to the growing body of evidence that trait differences in dream recall are supported by trait neurophysiological correlates. Further work is needed to better delineate the interactions between neurophysiological factors, psychological factors and inter-individual differences in dream recall.

Supplementary materials

S1 Fig is a duplicate of Fig 5.1 of the present thesis.

S1 table is a duplicate of Table 1 of Study 3 (see chapter 10).



S2 Fig. Performances of the Descending Subtraction Task. Red lines, High-recallers (n=21), black lines, Low-recallers (n=22). (A) Total number of responses (index of speed). (B) Percentage of mistakes (marker of accuracy). (C) Percentage of correct responses relative to pre-nap performances (marker of both speed and accuracy). Error bars represent 95% confidence intervals. * p<.05, *** p<.001

10

Study 3. DRF, cognitive abilities, and default mode network

High dream recall frequency is associated with increased creativity and functional connectivity in the default mode network

In preparation

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Summary

Several results suggest that the frequency of dream recall is positively correlated with personality traits such as creativity and openness to experience. These findings are coherent with neuroimaging result showing different neurophysiological profiles in high dream recallers (HR) and low dream recallers (LR). As compared to LR, a higher regional cerebral blood flow within core regions of the default mode network has been observed in HR during sleep and wakefulness. These observations are consistent with the emerging view that dreaming and mind wandering pertain to the same family of spontaneous mental processes, subserved by the default mode network. To further test this hypothesis, we assessed in HR (n=28) and LR (n=27) the (1) functional connectivity in the default mode network during resting wakefulness using fMRI as well as (2) creative-thinking, personality traits and cognitive abilities. As expected, HR demonstrated a greater DMN connectivity than LR, higher scores of creativity, and no significant difference in cognitive or memory abilities. These results support the forebrain and the DMN hypotheses of dreaming and suggest that increased activity in the DMN promote creative-thinking during both wakefulness and sleep.

Keywords Dream recall, creativity, resting state, functional connectivity, default mode network

Introduction

Despite recent advances, the cerebral mechanisms favoring the production or memory of dreams are still poorly understood (see Ruby, 2011). While dreaming has long been equated with rapid eye movement (REM), it is now well established that dreaming can also occur in any sleep stages and is therefore not exclusive to a specific functional brain state. Since it is impossible to know for sure when one is actually dreaming while asleep, most empirical investigation of dreaming are therefore based on the study of dream report after awakening the dreamer (Schwartz et al., 2005).

As a consequence, neurophysiological studies on dreaming have either focused on comparing the brain activity in the minutes preceding an awakening associated with the presence or absence of dream recall (Esposito et al., 2004; Wittmann et al., 2004; Chellappa et al., 2011; Marzano et al., 2011; Scarpelli et al., 2015; Siclari et al., 2017), or on investigating the cognitive and brain functioning associated with high or low dream recall frequency (DRF; Eichenlaub et al., 2014a; Eichenlaub et al., 2014b).

With respect to the second line of research, recent works from our team highlighted several neurophysiological differences between high dream recallers (HR) and low dream recallers (LR), not only during sleep but also during wakefulness Eichenlaub et al., 2014a; Eichenlaub et al., 2014b; Vallat et al., 2017. For instance, we compared using PET the spontaneous regional cerebral blood flow (rCBF) of HR and LR during sleep and wakefulness, and showed that HR have a higher spontaneous rCBF than LR in the temporo-parietal junction (TPJ) and in the medial prefrontal cortex (MPFC) during REM sleep, N3 sleep and wakefulness (Eichenlaub et al., 2014b). We argued that these two regions must play a key role in dream production or recall since lesions of these same areas have been found to be consistently correlated with global or partial cessation of dream reporting (without any concurrent sleep disturbance; see Solms, 1997). It is noteworthy that the MPFC and TPJ are part of the default mode network (DMN), a set of functionally-coupled brain regions which are highly activated during internally oriented mental processes and memory retrieval (Gusnard and Raichle, 2001; Raichle et al., 2001). This network is centered on the MPFC, the posterior cingulate cortex (PCC) and the lateral parietal (LP) areas around the TPJ area.

The finding of a higher spontaneous rCBF within core regions of the DMN in HR compared to LR provides strong evidence supporting the hypothesis of a differential cognitive and brain functioning between high and low frequency dream recallers. This idea was first put forward by Schonbar (1965) who postulated that high dream recall is part of a general life style characterized, inter alia, by creativity, divergent thinking and introspection. Several subsequent works confirmed this hypothesis by showing a substantial correlation between DRF and creativity (Fitch and Armitage, 1989; Schredl, 1995; Schredl et al., 2003b), and DRF and personality traits such as openness to experience (Hartmann, 1989; Schredl et al., 1996; Schredl et al., 2003a). These observations fit remarkably well within the emerging view that dreaming and creative-thinking are both members of a broad family of spontaneous-thought phenomena, which also includes mind-wandering and daydreaming (Christoff et al., 2016). Several works indicate that dreaming and creativity could be both underpinned by a strong recruitment of the DMN, and especially the prefrontal areas (Domhoff, 2011; Ellamil et al., 2012; Jung, 2013; Beaty et al., 2014; Mok, 2014; Beaty et al., 2015; Christoff et al., 2016).

The main conclusion to be drawn from these studies is that high dream recall seems to be on one hand related to the spontaneous activity of the DMN, and the other hand related to a general life style involving at least higher creativity. The purpose of the present study is to go a step further by characterizing the intrinsic DMN functional connectivity of HR and LR during resting-state wakefulness, as well as measures of personality, cognitive abilities and creativity. The results highlight a greater DMN connectivity in HR which was

concomitant with higher scores of creativity. These results were not associated with further group differences in cognitive or memory abilities.

Methods

Participants

Behavioral and neurophysiological data were acquired from 55 healthy subjects (28 males, mean age = 22.55, standard deviation = 2.41, range = 19–29). The subjects were informed of the study through an announcement sent to the mailing list of Lyon University, which briefly described the study and included a link to a questionnaire concerning sleep and dream habits. Subjects were selected if they reported and subsequently confirmed during a phone interview: (1) having a high or low DRF (DRF superior to 5 dream recall per week and inferior to 2 dream recall per month respectively) (2) having a regular sleep-wake schedule, no difficulty to fall asleep, being occasional or frequent nappers and having preferentially already done an MRI brain scan in the past few years. Importantly, the subjects were unaware that DRF was the main criterion for inclusion in the study.

Among the 55 participants, 28 of them were high dream recallers (HR; mean DRF = 6.6 ± 0.6 dream reports per week) and 27 were low dream recallers (LR; mean DRF = 0.2 ± 0.1 dream report per week). Apart from the DRF ($p<.0001$), the two groups did not differ in age, habitual sleep duration or education level (Table 1). They had no history of neurological and psychiatric disorders, and had no sleep disturbances. The local ethics committee (Centre Leon Bérard, Lyon) approved this study, and subjects provided written, informed consent in conformity with the Declaration of Helsinki. The subjects were paid for their participation.

Procedure

This study is related to a larger combined EEG-fMRI study investigating the differences between high and low dream recallers during the minutes following awakening from a short daytime nap. On this occasion, we acquired three six minutes resting-state scans, located before, 5 min after awakening and 25 min after awakening, respectively. The procedure is detailed as follows. After lunch at 11.30 am, participants were conducted to the neuroimaging center (CERMEP). During the first half hour, experimenters installed on the participant's head a MRI compatible EEG cap (EASYCAP®). Participants were then installed in the MRI scanner at about 1.20 pm (1.17 pm ± 13 min). The first resting-state scan was then acquired, with the instructions to remain awake and look at a central fixation cross on the screen. At the end of the scan, participants were informed that they could sleep during the next 45 min. At the end of the nap slot, participants were awakened, if they were sleeping, by calling their first name and the 2nd resting state scan was acquired. During the following 10 minutes, subjects were asked about their dream(s) and sleep in the scanner. Then the 3rd resting state scan was performed about 25 min

after awakening. Finally, an 8-min T1 anatomical scan was acquired. To facilitate sleep in the MRI environment, participants were allowed to sleep between 5 am and 8 am the night before the experiment. The partial sleep deprivation took place under the constant supervision of nurses in the sleep unit of Le Vinatier Hospital.

Data collection and analysis

MRI acquisition MRI scans were obtained from a MAGNETOM Prisma 3.0 T scanner (Siemens Healthcare, Erlangen, Germany) at the Primage neuroimaging platform (CERMEP). Structural MRI were acquired with a T1-weighted (0.9-mm isotropic resolution) MPRAGE sequence and functional MRI data with a T2*-weighted 2D gradient echo planar imaging sequence (EPI) with 180 volumes (TR/TE: 2000/ 25 ms; flip angle: 80°; voxel size: 2.68 × 2.68 × 3 mm; slices: 40, duration: 6 minutes). Functional and anatomical scans were performed using a 20-channel head coil. The coil was foam-padded to improve subject comfort and restrict head motion.

Behavioral tests In addition with neurophysiological measures, participants were presented with various tests to assess the potential between group differences at the cognitive and personality levels. These tests were administered by author R.V during the evening prior to the partial sleep deprivation. A detail description follows.

BFI. The Big Five Inventory (BFI) is a self-report inventory designed to measure the Big Five dimensions (John and Srivastava, 1999), which have been typically labelled as O (Openness to experience), C (Conscientiousness), E (Extraversion), A (Agreeableness), N (Neuroticism). We used the validated French version (BFI-Fr; Plaisant et al., 2010), which includes 45 items presenting a collection of statements concerning interpersonal relationships and personality. Each item is scored on a 5-point Likert-type response scale, ranging from 'strongly disagree' (1) to 'strongly agree' (5).

STAI. The State-Trait Anxiety Inventory (STAI) is a self-report inventory consisting of 40 items pertaining to anxiety affect (Spielberger et al., 1970). The STAI purports to measure one's conscious awareness at two extremes of anxiety affect, labeled state anxiety (A-state), and trait anxiety (A-trait), respectively. The A-Trait and A-State scales comprise 20 items each, scored on a 4-point Likert-type response scale. Scores range from 20 to 80, with higher scores suggesting greater levels of anxiety.

PQSI. The Pittsburgh Sleep Quality Index (PQSI) is a self-rated questionnaire which assesses sleep quality and disturbances over a one-month time interval (Buysse et al., 1989). It comprises 19 individual items concerning among others subjective sleep quality, sleep latency, sleep duration and daytime dysfunction. Higher scores at the PQSI indicate poorer sleep quality.

MEM-III. The MEM-III is the validated French version of the Wechsler Memory Scale (WMS-third edition, WMS-III; Wechsler, 2001). We used a subtest to assess immediate and

delayed memory. Participants were read the first story, after which they were instructed to say out loud everything they could remember of this story. The experimenter rated how many items (maximum 25) the participants were able to recall. Twenty five minutes later, the subjects were asked again to recall the stories (delayed memory). Importantly, the subjects were not aware that they would have to recall any of the images at any point after the test. For both immediate and delayed recall, scores were averaged over the two stories and therefore range from 0 to 50, with higher scores reflecting greater memory performances.

Digit span. Individual memory abilities were also assessed using a digit span task, which measures the working memory's number storage capacity. Participants were asked to repeat a heard sequence of numerical digits, the length of which increases at each trial. Digit span was assessed first forwards (maximum score 16) and then backwards (maximum score 14). The digit span index was obtained by averaging the two scores. Higher scores (maximum 30) indicate higher working memory abilities.

Guildford's Alternative Uses Task. The Guildford Uses Task (Guildford et al., 1978) is a creativity test in which participants are asked to list as many possible uses for an everyday object. Participants were shown images of three objects (a pen, a mug, a chair) in a randomized order and subsequently asked to list, during 2 minutes, as many alternative or unusual uses for this object. The fluency index is the total number of responses averaged across the three items. Higher scores indicate higher creativity. Additionally, we computed for each subject and each item the number of rare uses (top 10% rarest uses, i.e. uses found by 5 or less participants). The rare uses index is the total number of rare uses averaged across the three items. Higher scores indicate higher creativity.

fMRI analysis One subject (HR) was excluded from the MRI analysis because of a technical failure during MRI acquisition, leading to a total of 27 HR and 27 LR. As the failure only concerned MRI acquisition, the behavioral and cognitive measures of this participant were still included in the analysis. For the remaining subjects, preprocessing and quality check were performed using standard routine in SPM12 software (Wellcome Department of Imaging Neuroscience). Preprocessing included functional realignment, slice-time correction, coregistration to structural scan, spatial normalization and spatial smoothing using a 6 mm full-width at half-maximum isotropic Gaussian kernel filter. Individual T1 images were segmented into gray matter, white matter and cerebrospinal fluid tissue maps. Functional and structural images were then normalized to MNI152 space (Montreal Neurological Institute). Functional images underwent artifact and motion regression in the Artifact Detection Toolbox using the following criteria to define outliers: global signal intensity changes greater than 9 standard deviations and movement exceeding 2 mm. SPM motions parameters and outliers were subsequently included as covariates in connectivity analyses.

Connectivity analysis were performed on the concatenated resting-state scans (3 scans x 6 minutes = 18 minutes resting-state data) using the CONN toolbox version 17f (Whitfield-Gabrieli and Nieto-Castanon, 2012). As the aim of this study was to compare the DMN connectivity during resting-state between HR and LR, we selected 4 main regions of

interests (ROIs) corresponding to the core nodes of the DMN (see Fig 1A). These include the Posterior Cingulate Cortex (PCC; center of mass in MNI coordinates: 1, -61, 38), the Medial Prefrontal Cortex (MPFC; 1, 55, -3) and bilateral Lateral Parietal cortices (LP; left: -39, -77, 33, right: 47, -67, 29). These regions are implemented within the CONN Toolbox version 17f as part of a parcellation atlas of the main brain networks, obtained by applying an independent component analysis on 467 subjects from the Human Connectome Project.

The connectivity analysis included the following steps: first, we performed a denoising step including a regression of the 6 motion correction parameters and their corresponding first-order temporal derivatives, as well as a component-based strategy (aCompCor, Behzadi et al., 2007) to identify and remove physiological confounds that are unlikely to be related to neural activity. The resulting BOLD time series were band-pass filtered (0.008 – 0.09 Hz) to further reduce noise and increase sensitivity (Weissenbacher et al., 2009). Then, Pearson's correlation coefficients were calculated for each pair-wise connection across the 4 nodes of the DMN, resulting in a single skew-symmetric connectivity matrix with 6 correlation coefficients for each subject. These values were normalized using a Fisher's r-to-Z transformation and then compared between HR and LR (two-sided t-tests corrected for multiple comparisons using the false discovery rate (FDR, $p<.05$)). Finally, the mean DMN connectivity (average of all pair-wise correlations) was calculated and compared between groups.

Statistics As several studies reported a higher creativity in HR than in LR, between group comparisons of the fluency index and rare uses index were achieved using one-tailed T-test ($p<.05$). Similarly, as we expected HR to demonstrate a higher DMN functional connectivity than LR, between group statistical comparisons of the mean DMN functional connectivity was achieved using one-tailed T-test. All the other comparisons were achieved using two-sided T-tests.

Results

Table 1. Subject information. DRF: habitual weekly dream recall frequency (the number of awakenings per week with a dream in mind). Gender: subject's gender (F, female; M, male). Age: subject's age (years). Sleep duration: habitual sleep duration during the week (hours). Education: number of years of education. Age, habitual sleep duration and education level were not significantly different between High-recallers and Low-recallers; however, the DRF was significantly larger in High-recallers than in Low-recallers (t-test, ***P<0.0001).

Group	N°	DRF	Gender	Age	Sleep duration	Education
High recallers	1	6	M	19.3	7	0
	2	7	M	23.9	8	3
	3	7	M	22.6	8	4
	4	7	F	21.0	9	3
	5	7	F	24.1	8.3	5
	6	7	F	19.4	7.5	1
	7	5	F	23.7	8.33	4
	8	7	M	23.8	8	3
	9	6	M	27.2	7.5	8
	10	7	M	23.9	8	5
	11	7	F	18.9	9	1
	12	7	F	24.2	8.5	5
	13	6	M	23.0	6	5
	14	6	F	21.1	8.5	3
	15	7	F	20.6	8.5	3
	16	6	M	28.1	7	9
	17	7	F	19.6	8	1
	18	7	F	23.9	7	5
	19	6	M	22.7	9	4
	20	6	M	21.8	9	3
	21	7	F	20.8	8	4
	22	7	M	26.3	7	4
	23	7	F	19.1	8	1
	24	7	F	21.1	7	4
	25	7	F	22.7	6	4
	26	7	F	23.2	9	5
	27	6	M	22.3	8	10
	28	6	M	21.0	7	3
Low recallers	1	0.5	F	25.3	8	4
	2	0.5	M	23.3	8	4
	3	0	M	21.0	6	2
	4	0	M	23.7	9	5
	5	0.3	M	28.2	7.5	7
	6	0.3	F	21.2	9	3
	7	0.25	M	23.2	6.5	5
	8	0	F	25.0	8	6
	9	0.25	F	22.2	8	2
	10	0.1	F	19.2	9.5	1
	11	0.1	M	21.1	8	4
	12	0.3	F	21.6	7	4
	13	0.25	F	19.1	8	1
	14	0.25	F	18.9	8.5	2
	15	0.25	F	22.9	6.5	5

	16	0.25	M	25.0	8	5
	17	0.25	M	21.2	8	3
	18	0.5	M	23.8	7	6
	19	0.1	M	24.0	7	6
	20	0.3	M	29.1	7	4
	21	0.25	M	22.8	8	4
	22	0.25	F	23.3	7	5
	23	0	F	21.0	6	4
	24	0.25	F	21.1	6	3
	25	0.25	M	20.8	8	3
	26	0	M	21.0	8	4
	27	0.25	M	20.0	8	2
Mean HR		**6.6**		**22.5**	**7.9**	**3.9**
STD HR		0.6		2.4	0.9	2.3
Mean LR		**0.2**		**22.6**	**7.6**	3.9
STD LR		0.1		2.5	0.9	**1.6**
T-test		<.0001		0.89	0.28	0.89

Behavioral tests

Results of the cognitive and personality tests are reported in Table 2. First, we did not find any significant differences in the memory abilities of HR and LR, as measured by the MEM-III scale and digit span task. Second, there was no significant difference in the PQSI score. Third, there was no difference in the state and trait anxiety levels, as measured by the STAI self-report scale. Fourth, the Big Five personality dimensions were not significantly different between the two groups, however there was a tendency (p=.07) for a higher agreeableness score in HR than in LR, a dimension related to the tendency to be compassionate and cooperative rather than suspicious and antagonistic towards others.

Finally, we observed significant between group differences in creativity scores (Fig 2). HR were found to have a higher fluency index at the Guildford's alternate uses task. The effect was significant for the pen object (HR = 8.4 ± 2.6, LR = 6.6 ± 2.1, T(53) = 2.86, p = .003) and after averaging for each subject the fluency index of the three objects (HR = 8.2 ± 2.4, LR = 7.2 ± 2.3, T(53) = 1.68, p = .049). Furthermore, they also reported a significantly greater number of rare uses. The effect was significant for the pen (HR = 3.1 ± 1.7, LR = 2.2 ± 1.8, T(53) = 1.88, p = .033), the mug (HR = 3.8 ± 2.5, LR = 2.8 ± 1.8, T(53) = 1.72, p = .045) and after averaging for each subject the rare uses index of the three objects (HR = 3.1 ± 1.6, LR = 2.3 ± 1.5, T(53) = 1.77, p = .042).

Functional connectivity

The mean DMN functional connectivity was higher in HR than in LR (HR = 0.64 ± 0.14, LR = 0.56 ± 0.16, T(52) = 1.81, p = .038; Fig 1B). The DMN connectivity matrices for

Table 2. Behavioral results of the cognitive and personality traits (n=55, 28 HR, 27 LR). BFI = Big Five Inventory, STAI = State-trait Anxiety Inventory, PQSI = Pittsburgh Sleep Quality Index. All p-values derived from two-sided T-tests.

Test	High recallers	Low recallers	T	P-value
BFI				
- Openness to experience	3.8 ± 0.6	3.7 ± 0.5	0.52	0.61
- Conscientiousness	3.3 ± 0.7	3.6 ± 0.6	-1.39	0.17
- Extraversion	3.4 ± 0.8	3.3 ± 0.7	0.54	0.59
- Agreeableness	4.0 ± 0.6	3.7 ± 0.6	1.87	0.07
- Neuroticism	2.9 ± 0.8	2.5 ± 0.9	1.34	0.19
STAI				
- State anxiety	33.5 ± 8.9	29.9 ± 8.6	1.55	0.13
- Trait anxiety	39.7 ± 10.6	36.9 ± 9.0	1.03	0.31
MEM-III				
- Immediate recall	29.4 ± 4.9	28.9 ± 7.2	0.30	0.76
- Delayed recall	31.8 ± 5.1	31.7 ± 6.9	0.05	0.96
PQSI	4.8 ± 2.6	4.3 ± 1.9	0.78	0.44
Digit span	17.6 ± 3.0	18.4 ± 3.6	-0.9	0.37

each group with pairwise connectivity color coded by strength are presented in Fig 1C. Between group comparisons of the connectivity matrices indicated a greater connectivity between the MPFC and right LP (effect size = 0.16, T(52) = 2.70, p-FDR = .028, p-unc = .009).

Discussion

This study reports for the first time the brain functional connectivity correlates of DRF in healthy subjects. The results presented above indicate that HR have an increased brain functional connectivity within the DMN, notably between the MPFC and TPJ. In addition HR scored higher than LR on measures of creative-idea generation, without any further between group differences in cognitive or memory abilities.

With regards to functional connectivity, our results are remarkably consistent with a previous PET study from our team that showed, in an unrelated sample of 41 participants, a higher rCBF in HR compared to LR in these two same regions during both sleep and wakefulness (Eichenlaub et al., 2014b). Both these studies are in accordance with clinico-anatomical reports showing that lesions in the TPJ and the MPFC lead to a cessation of dream recall (Solms, 1997). Our results provide therefore strong evidence that the ability to recall dreams is linked to rCBF and functional connectivity in these two brain regions.

Furthermore, our findings confirmed previous studies reporting a positive link between creativity and DRF (Fitch and Armitage, 1989; Schredl, 1995; Schredl et al., 2003b). This

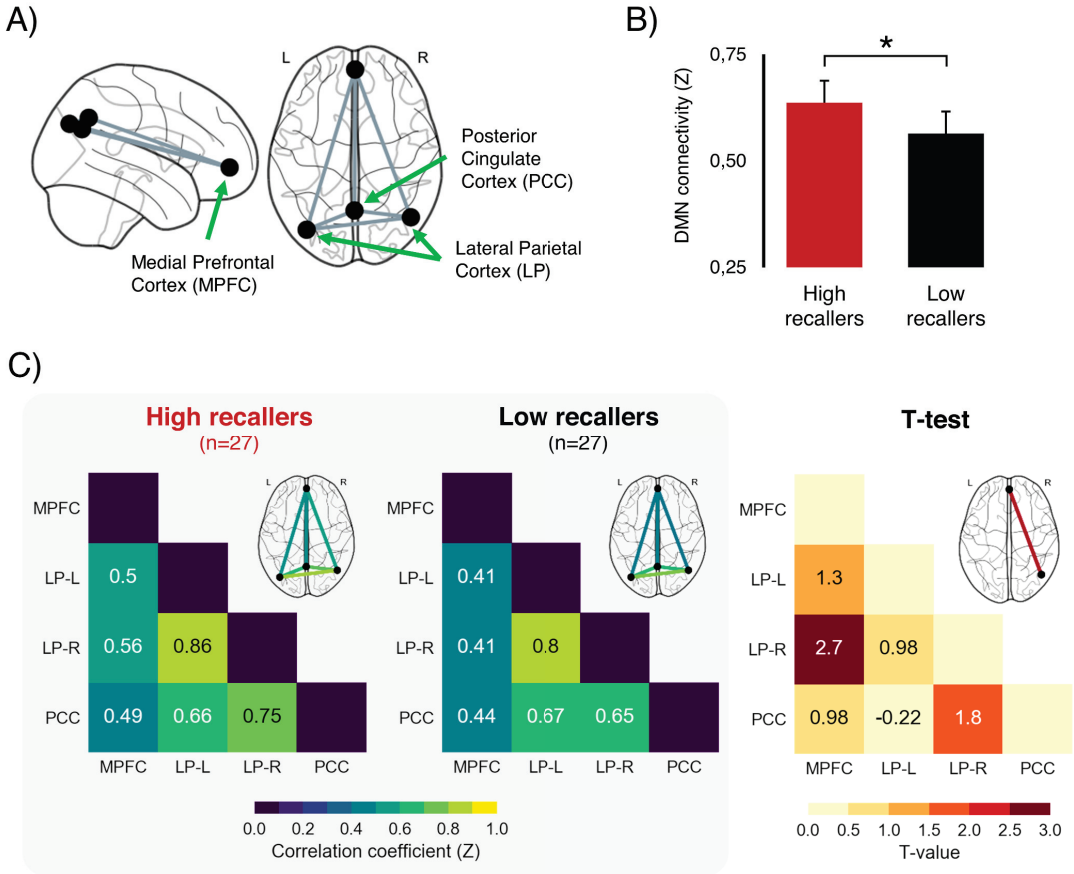

Fig 1. Increased default mode network connectivity in High dream recallers (HR) compared to Low dream recallers (LR). (A) Schematic illustration of the four main nodes of the default mode network (DMN) included in further connectivity analysis. (B) Mean pairwise connectivity of the DMN for HR (red) and LR (black), obtained by averaging for each subject all the pairwise correlation values within the default network. The average DMN connectivity was significantly higher in HR than in LR. Error bars represent 95% confidence intervals. (C) Left grey panel. Functional connectivity matrix representing the mean pairwise correlation coefficient between regions of the DMN in HR and LR. Right. Between-group statistical comparison (two-sided T-test corrected for multiple comparisons using the false discovery rate). The connectivity between the right lateral parietal and medial prefrontal cortex was significantly higher in HR than in LR.

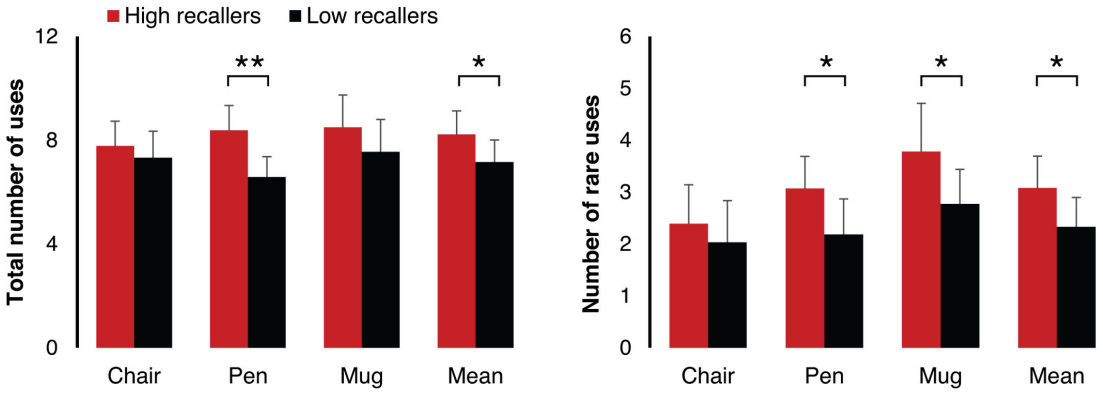

Fig 2. Higher creativity in High dream recallers (HR) than in Low dream recallers (LR). *Left*. Group means for the total number of uses found by HR (red) and LR (black) during the Guildford's alternate uses task. HR reported significantly more uses than LR for the "pen" object and in average ("mean" column). *Right*. Group means for the number of uses reported by 5 or less participants (i.e. top 10% rarest uses). HR reported significantly more rare uses than LR for the "pen" and "mug" objects, as well as in average ("mean" column). Error bars represent 95% confidence intervals. *p<.05.

is of particular interest given that the generation of creative ideas is thought to be also supported by a preferential recruitment of regions of the DMN, and particularly of the MPFC (Dietrich and Kanso, 2010; Ellamil et al., 2012; Jung, 2013; Beaty et al., 2014; Mok, 2014; Beaty et al., 2015). This large overlap of brain regions involved in dreaming and creativity was noticed by Christoff et al. (2016) who postulated that creative thought and dreaming are best understood as members *"of a family of spontaneous-thought processes"*. This idea was put slightly differently by Barrett (2017) who stated that *"dreaming is essentially our brain thinking in another neurophysiologic state—and therefore it is likely to solve some problems on which our waking minds have become stuck"*. Several studies have indeed reported that dream content *per se* often contains solutions of unsolved problems and can be a source of insight (Dement and Kleitman, 1957; Barrett, 1993; Maquet and Ruby, 2004; Edwards et al., 2013)).

Taking this line of thought further, we argue here that high frequency dream recallers have a specific cognitive and functional profile, involving greater baseline activity in regions of the DMN, which might in turn promote in these individuals creativity and dreaming abilities. Further evidence that HR and LR have a differential neurophysiological profile is provided by recent works from our team showing that HR demonstrated a larger amplitude of brain responses to auditory novel stimuli than LR during both a night of polysomnographically recorded sleep and wakefulness, as well as an increased duration of intra-sleep wakefulness (15 min more on average) and nocturnal awakenings, whatever of the previous sleep stage, and without any other differences in the micro- or macro-structure of sleep (Eichenlaub et al., 2014a; Vallat et al., 2017).

Along with the consistent positive association between DRF and creativity, studies have often reported a substantial correlation between DRF and personality traits, such as openness to experience (Schredl et al., 2003a), thinner boundaries (i.e. propensity to being more open, trustworthy, vulnerable, and sensitive; Hartmann, 1989; Schredl et al.,

1996), and anxiety (Schonbar, 1959; Tart, 1962). None of these variables were statistically different between HR and LR in the present study but it is noteworthy that HR scored higher for all of these variables and some of them were close to significance. Since the above-mentioned correlations have often been reported on larger samples, one can assume that the group differences on these variables would have been significant if our study involved a larger sample of participants. The general idea that differential DRF is linked to traits factors was first introduced by Schonbar (1965) in her so-called *"life-style"* hypothesis. While she did not explained the underlying mechanisms, she postulated that high dream recall is part of a general life style characterized by *"creativity, rich fantasy, introversion, introspection, field independence and divergent thinking"* (Schredl, 1999). Our findings argue in favor of this model and provide a brain mechanism for it, i.e. an increased activity in the DMN promoting dreaming and creativity.

Our results suggest that the activity in the DMN should also predict intra-individual variability in DRF across time. This prediction will have to be tested in future studies. DRF enhancing methods (such as keeping a dream diary; Schredl, 2002) could be indeed used to test whether an increased DRF would result in increased creativity scores and DMN functional connectivity in post compared to pre-training measures within the same individuals (preferentially a group of LR). If true, DRF enhancement methods could become a creativity enhancement method.

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Study 4. Sleep and dream habits in a sample of French students

Sleep and dream habits in a sample of French students

Under review at *Journal of Sleep Research*

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Summary

Several authors have drawn the attention to the risk of sleep difficulties during college years. However, sleep and dream habits have been scarcely documented in young adults. We collected such information in a sample of 1137 French college students (411 males). In average, the participants reported spending roughly 8 hours in bed during weekdays, 9 hours during the weekends, and 90.9% reported no difficulty to fall asleep. The mean sleep agitation score reported was 3.3 ± 1.7 (1-to-10 scale). Less than 0.4% of students reported to have sleep-walking episodes regularly but nearly 7% reported regular sleep-talking episodes. About 10% reported to often take a nap. In average, participants mentioned 3 dream reports per week, 14% said they had frequent lucid dreams and 6% reported frequent recurrent dreams. The clarity of dream memory was positively correlated with dream recall frequency. An academic field effect (humanities, science, medicine) has been found for sleep duration. By contrast, no DRF differences were observed between disciplines. We observed the well-known negative correlation between age and dream recall frequency despite a limited age range, as well as a gender effect for several sleep and dream parameters. As compared to men, women spent more time in bed and reported slightly more dreams. These results (1) suggest that the great majority of French college students do not suffer from sleep disturbances, (2) show a gender difference for several sleep parameters and (3) provide supplementary arguments in favor of a small but consistent gender effect regarding dream recall frequency.

Keywords Sleep habits, dream recall frequency, students, survey, epidemiology, gender differences

Introduction

Recent years have witnessed a renewed interest in sleep and dreaming (Dijk, 2015). However, epidemiological investigations in healthy subjects combining questions on both sleep and dream habits are relatively rare. Such surveys are yet necessary to establish and keep up to date sleep and dream norms in the general population. Of particular

interest is the college population, which is more at risk of suffering from sleep difficulties than the general population (Buboltz et al., 2001; Curcio et al., 2006; Forquer et al., 2008; Lund et al., 2010). Yet, there are few, up-to-date, data available on sleep habits of college students. This is especially true for the European college population since most epidemiological studies have been carried out on Americans (e.g. Lund et al., 2010). By contrast, dream habits of college students have been more investigated, especially by Mickael Schredl who extensively reported the dream patterns of German students. Yet, most surveys on dream habits were conducted on psychology students (Schredl et al., 2003b), and are therefore not necessarily representative of the student population since there is a great majority of women in this academic field. This point is not negligible given that several studies suggest a gender effect in sleep and dream habits (Beck et al., 2013; Schredl and Reinhard, 2008). It is important to note however, that regarding DRF the effect was not always reproduced and the overall effect size is small.

The originality of our study is to provide recent (2016) sleep and dream habits from a large sample (n = 1137) of French college students (Lyon University) pertaining to various academic fields (i.e. humanities, sciences, medicine), and composed for one third by males (n = 411). The web questionnaire asked about habitual time of light extinction and awakening during the week and the week-end, ability to fall asleep, sleep agitation, nap frequency, sleepwalking, sleep-talking, dream recall frequency, clarity of dream content, frequency of lucid and recurrent dreams. In addition to the descriptive aim of the study, we expected to reproduce results reported in previous surveys such as the correlation between age and DRF (Schredl, 2008), or between DRF and the clarity of the dream memory, and a gender effect on sleep and dream parameters.

Methods

Data were collected in 2016 using an online questionnaire for the recruitment phase of an fMRI sleep study. The subjects were informed of the study through an announcement sent to several mailing lists of Lyon University. Among with basic sociodemographic variables (age, gender, height, weight, education, academic discipline), the online survey included the following questions:

1. What time do you usually go to bed and get up during weekdays?
2. What time do you usually go to bed and get up during weekends?
3. In general, you fall asleep: very easily, easily, quite easily, with difficulty or with great difficulty?
4. On a scale of 1 to 10, how much agitated is your sleep? (1 = not at all agitated, 10 = very agitated)
5. How often do you experience sleepwalking episode? (never, rarely, sometimes, often)
6. How often do you talk during your sleep? (never, rarely, sometimes, often)
7. How often do you take daytime nap? (never, rarely, sometimes, often)
8. How many days per week do you usually wake up with a dream in mind?

9. How many days per month do you usually wake up with a dream in mind?
10. How often do you have lucid dream(s) (i.e. dreams in which you are aware that you are dreaming)? (never, rarely, sometimes, often)
11. How often do you have recurrent dream(s) (i.e. dream experienced repeatedly)? (never, rarely, sometimes, often)
12. In general, how clear is the memory of your dream content? (very vague, vague, clear, very clear)

We collected 1262 completed questionnaires (459 M, age range = 18 - 61 yr., mean age ± SD = 22.75 ± 3.94 yr.). In order to be representative of a student population, participants older than 30 years were removed, leading to a final sample size of 1137 (411M - 726 F, mean age ± SD = 22.23 ± 2.36 yr., height = 170.2 ± 11.4 cm, weight = 64.1 ± 11.6 kg, education = 3.3 ± 1.8 years after high school). A binomial logistic regression was performed to investigate the gender differences in sleep and dream habits. In order to be entered in the model, the frequency of sleepwalking and sleep-talking episodes, and the frequency of lucid and recurrent dreams were recoded as follows: Never → 0, Rarely → 1, Sometimes → 2, Often → 3. The dream clarity scale was recoded using: Very vague → 0, Vague → 1, Clear → 2, Very clear → 3. The level of ease or difficulty to fall asleep was recoded using: very easily → 0, easily → 1, quite easily → 2, with difficulty → 3, with great difficulty → 4. Finally, we compared the sleep and dream habits of students as a function of the academic discipline. We partitioned the sample in three broad categories, namely sciences (i.e. hard sciences and technology, n = 432 students), humanities (i.e. social sciences, literature, psychology, educational science, law school, n = 417 students) and medicine (i.e. medical and dental studies, n = 190). The 98 remaining students of the sample were not included in the analysis because they were issued from heterogeneous academic and/or professional environment.

Results

Sleep habits

The average time in bed was 7.90 ± 0.96 hours (range = 3.5 - 12 hours) during weekdays and 9.10 ± 1.13 hours (range = 4 - 13 hours, paired t-test = <.001) during weekends. Sleep schedules during weekdays and weekends are reported in Fig 1. The peak bedtime was between 11 and 11.59 pm (43.4%) during weekdays and between 0 and 0.59 am during weekends (33.57%). The peak waking time was between 7 and 7.59 am during weekdays (42.33%) and between 10 and 10.59 am during weekends (29.96%).

Only 4 respondents (0.35%) reported having great difficulty falling asleep. Conversely, 429 students (37.7%) reported falling asleep easily and 184 (16.18%) reported falling asleep very easily. The mean sleep agitation score reported was low (3.3 ± 1.7). Regarding sleepwalking, only 4 students (0.35%) reported having regular episodes, while 986 (86.72%) of them reported never having episodes. The percentage of students reporting regular episodes of sleep-talking was higher (75 students, 6.6%), and only 315 respondents

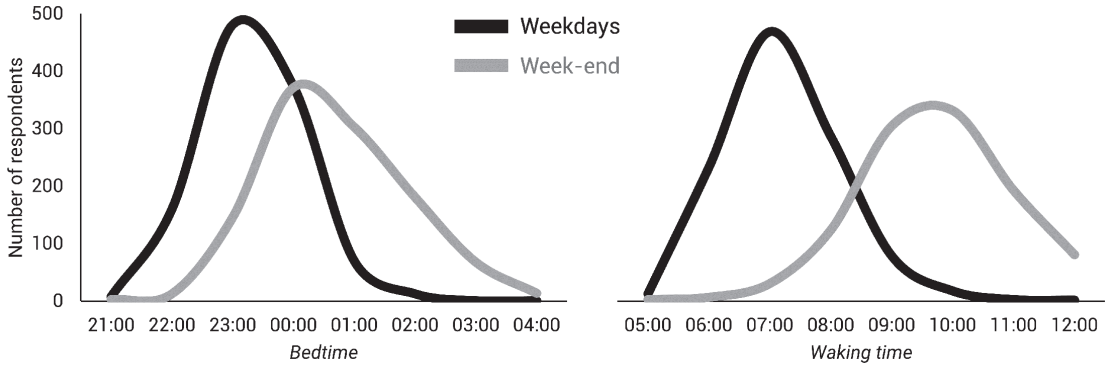


Fig 1. Bedtime (left) and waking time (right) distribution during weekdays (black lines) and weekends (grey lines).

(27.7%) declared never having sleep-talking episodes. Finally, a total of 113 participants (9.94%) reported that they often took nap, while 196 respondents (17.24%) reported that they never took nap. Frequencies of nap, sleepwalking, sleep-talking, recurrent dreams and lucid dreams are reported in Fig 2.

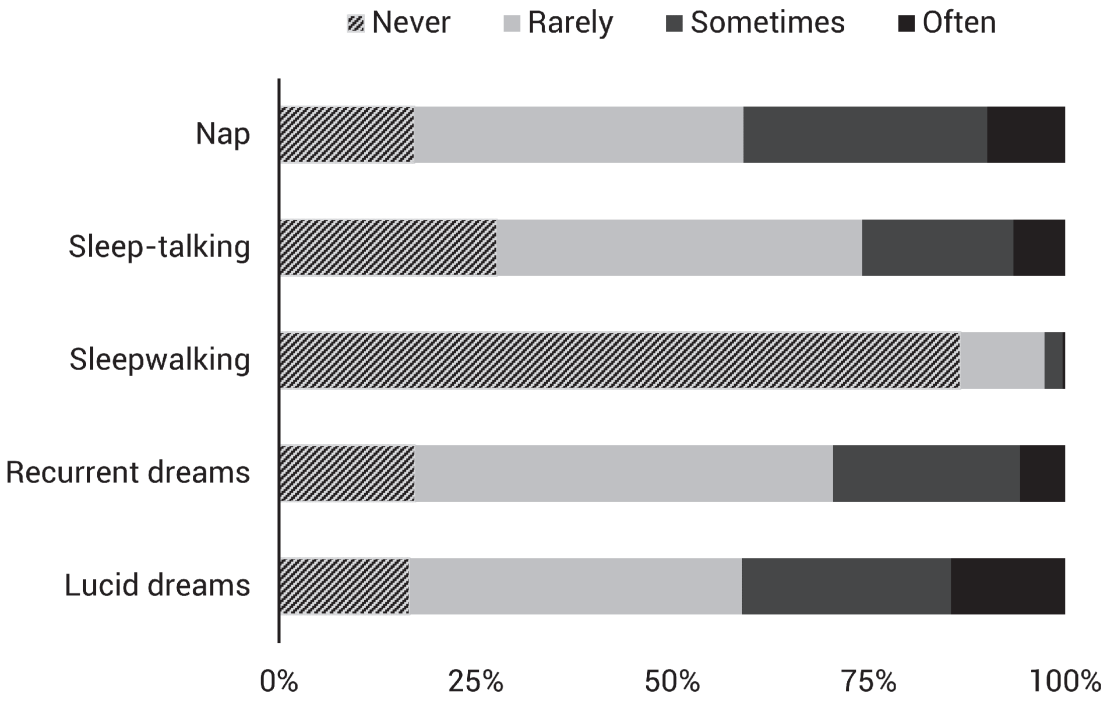


Fig 2. Frequencies of nap, sleep-talking, sleepwalking, recurrent dreams and lucid dreams in the sample.

Dream recall frequency

The mean dream recall frequency (DRF) was 3.12 ± 1.78 days per week (i.e. the participants recalled a dream in average 3 mornings per week) and 12.84 ± 7.51 days per

month. Fifty-eight participants (5.10%) reported not recalling any dream per week and 9 participants (0.79%) reported not recalling any dream per month. On the opposite, 34 participants (2.99%) reported recalling a dream 7 mornings per week and 29 participants (2.55%) reported recalling a dream every morning of the month.

Despite the narrow age range of our sample (18 to 30 years old), we were able to evidence the negative correlation between DRF (weekly estimation) and age (Fig 3A) evidenced in previous studies with a larger range (e.g. Schredl, 2008). Weekly DRF was positively correlated with the frequency of lucid dreams (Fig 3C), as could be expected from previous results (Stepansky et al., 1998; Schredl and Erlacher, 2004; Schredl and Erlacher, 2011). Weekly DRF was also positively correlated with the clarity of dreams (Fig 3D) and the level of agitation during sleep (Pearson $r = 0.08$, $p = 0.008$). We observed neither an effect of the academic field on DRF, nor a significant correlation between DRF and the education level (Fig 3B). These findings are consistent with two studies that reported no association between DRF and the education level and DRF and the socioeconomic status (Schredl, 2007; Schredl, 2008).

Clarity of dreams Thirty-five participants (3.08%) reported that the usual clarity of their dreams was very vague. By contrast, 75 participants (6.60%) reported that their dreams were usually very clear. The great majority of respondents (n=705, 62.0%) reported that their dreams were usually clear.

Frequency of lucid dreams A lucid dream is a dream during which the dreamer is aware of dreaming. In our sample, 165 participants (14.51%) reported that they often had lucid dreams, while 189 participants (16.62%) reported that they never had a lucid dream (Fig 2). From these figures, it could be inferred that approximatively 83% of the participants have already experienced a lucid dream at least once. This number is remarkably consistent with those from other studies focusing on student population (e.g. 82% in Schredl and Erlacher, 2004). However, it should be noted that the definition of lucid dreaming given in the questionnaire did not include the ability to control the dream characters and narratives, but simply to be aware of dreaming during the dream. It is generally admitted that control over the dream represents the full extent of lucid dreaming and is more difficult to attain than the mere awareness of dreaming (Purcell et al., 1986; LaBerge and Rheingold, 1991). Consequently, the proportion of participants having already experienced a lucid dream would probably be lower if the definition of lucid dreaming involved the ability to exert some degree of control over the dream.

Frequency of recurrent dreams A recurrent dream is a dream which is experienced repeatedly. In our sample, 65 participants (5.72%) reported that they often had recurrent dreams, while 197 participants (17.33%) reported that they never had a recurrent dream (Fig 2), meaning that roughly a little more than 80% of the participants had already experienced recurrent dreams at some point in their lives. Again, this figure is consistent with several studies that reported a prevalence of 60% to 75% of recurrent dreams in college students and young adults (Zadra, 1996).

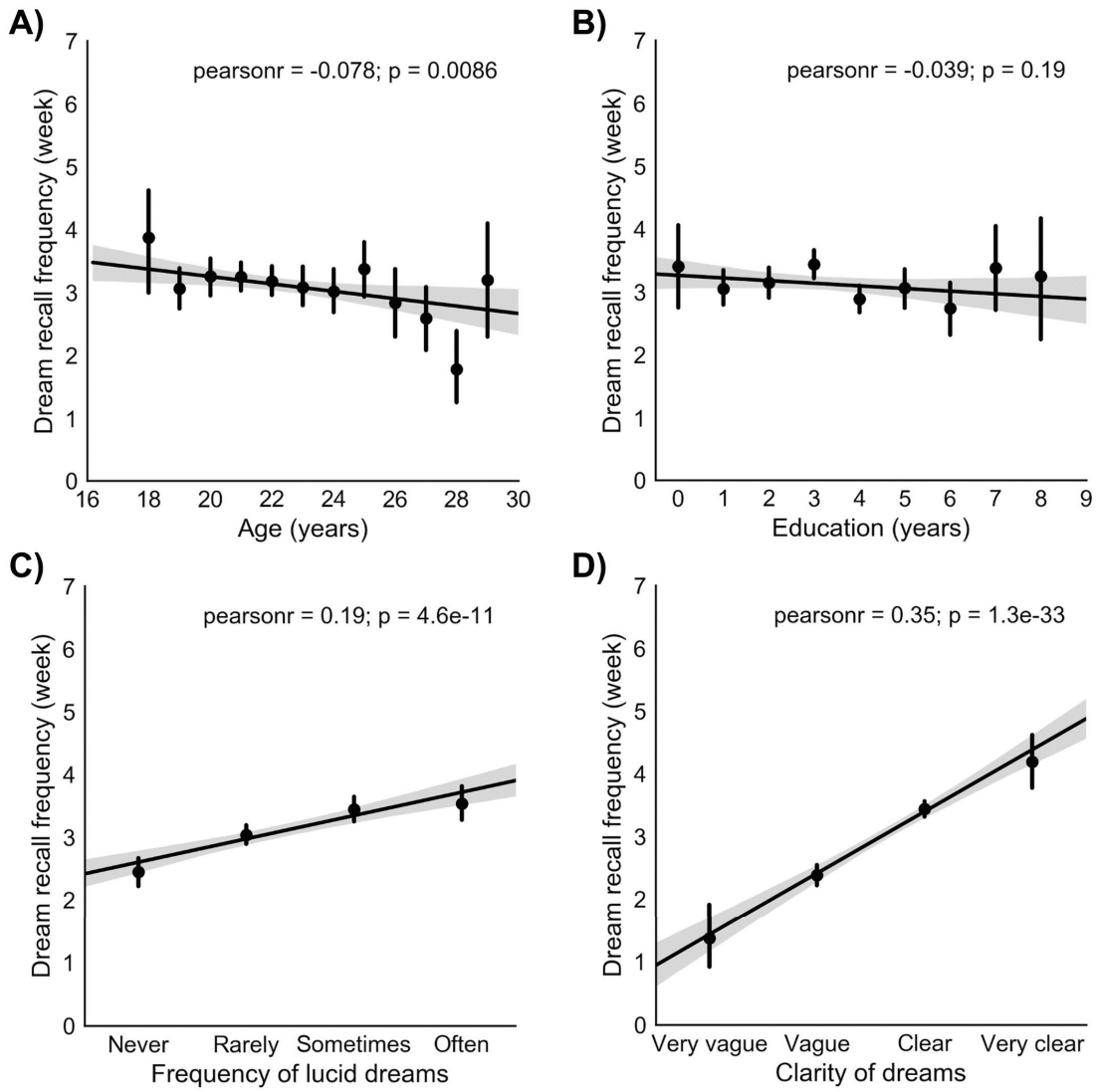


Fig 3. Correlations between dream recall frequency (number of mornings per week with a dream in mind) and (A) age (B) education level (C) frequency of lucid dreams (D) clarity of dream memory. Error bars represent 95% confidence intervals.

Gender differences

Table 1 depicts the summary of the binomial logistic regression for gender differences. In our sample, as compared to men, women spend more time in bed (during both weekdays and weekends), take naps more often, are more susceptible to have episodes of sleepwalking, and have a higher weekly-estimated DRF. Women tend also to have a more agitated sleep and to report more difficulties to fall asleep. Finally, the frequency of lucid dreams tends to be higher in men, while the frequency of recurrent dreams tends to be higher in women.

Table 1. Binomial logistic regression for gender differences in sleep and dream habits (n=1137). SE = standardized estimate, DRF = dream recall frequency. Frequencies of nap, sleepwalking, sleep-talking, recurrent dreams and lucid dreams are expressed using a recoded scale ranging from 0 (Never) to 3 (Often). Sleep agitation is scored on a 1-to-10 scale where 1 means no agitation at all during sleep and 10 means a very agitated sleep. Difficulty falling asleep is expressed using a recoded scale ranging from 0 (very easy to fall asleep) to 4 (very difficult to fall asleep). For sleep agitation and difficulty to fall asleep, higher scores indicate more disturbances.

Variable	Men	Women	SE	X^2	p
Sleep					
Time in bed (weekdays)	7.70 ± 1.0	8.02 ± 0.9	0.31	28.92	.001
Time in bed (weekends)	8.93 ± 1.2	9.19 ± 1.1	0.13	5.14	.023
Difficulty falling asleep	1.35 ± 0.9	1.42 ± 0.9	0.14	3.61	.057
Sleep agitation	3.13 ± 1.6	3.39 ± 1.8	0.07	2.87	.090
Frequency of nap	1.24 ± 0.9	1.39 ± 0.8	0.23	9.31	.002
Frequency of sleepwalking	0.12 ± 0.4	0.19 ± 0.5	0.33	4.02	.045
Frequency of sleep-talking	1.04 ± 0.9	1.05 ± 0.8	-0.11	0.61	0.43
Dream					
DRF (weekly)	2.83 ± 1.7	3.29 ± 1.8	0.10	15.50	.001
DRF (monthly)	11.60 ± 7.3	13.54 ± 7.5	0.01	0.18	.663
Dream clarity	1.69 ± 0.6	1.74 ± 0.6	-0.04	0.16	.689
Frequency of recurrent dreams	1.09 ± 0.8	1.23 ± 0.8	0.14	2.77	.096
Frequency of lucid dreams	1.40 ± 0.9	1.38 ± 0.9	-0.16	3.83	.050

Academic fields differences

Table 2 depicts the results of the ANOVA testing an academic disciplines effect on sleep and dream variables (Science, n=432; Humanities, n=417; Medicine, n=190). First, the time in bed during weekdays was significantly different between the three groups. Post-hoc tests (two-sided T-tests) showed that humanities students reported a longer time in bed duration than students in sciences ($T = 6.31$, $p < .001$) or medicine ($T = 2.81$, $p = .005$). Second, medicine student reported less recurrent dreams than humanities ($T = 2.49$, $p = .013$) or sciences students ($T = 2.27$, $p = .023$).

However, there results should be taken cautiously considering that the average age of the students was slightly lower in the Science group (i.e. science students were significantly younger than humanities, T = 3.91, p < .001; and medicine students, T = 2.65, p = .008) and that a sex ratio difference has been observed between the three academic fields. Specifically, the proportion of females was higher in humanities than in science (Z = 15.02, p < .001) or medicine (Z = 6.29, p < .001), and was also higher in medicine than in science (Z = 7.23, p < .001). Since we have previously seen that women reported a higher time in bed duration and tended to have a higher frequency of recurrent dreams, the finding that humanities student spend more time in bed could be as least partly explained by a higher proportion of women in this academic discipline. Apart from the frequency of recurrent dreams, no difference was found regarding the other dream variables.

Table 2. Sleep and dream habits differences between academic disciplines (Science, Humanities and Medicine). Differences between disciplines were assessed using one-way ANOVAs. Sex ratio difference between disciplines was assessed using a chi-squared test. DRF = dream recall frequency. Frequencies of nap, sleepwalking, sleep-talking, recurrent dreams and lucid dreams are expressed using a recoded scale ranging from 0 (Never) to 3 (Often). Sleep agitation is scored on a 1-to-10 scale where 1 means no agitation at all during sleep and 10 means a very agitated sleep. Difficulty to fall asleep is expressed using a recoded scale ranging from 0 (very easy to fall asleep) to 4 (very difficult to fall asleep). For sleep agitation and difficulty to fall asleep, higher scores indicate more sleep disturbances.

Variable	Humanities	Science	Medicine	X^2/F	p
Sex ratio (F/M)	3.8	1.1	1.7	67.5	.001
Age	22.4 ± 2.4	21.8 ± 2.0	22.3 ± 2.4	8.0	.001
Sleep					
Time in bed (weekdays)	8.1 ± 1.0	7.7 ± 0.9	7.9 ± 0.8	21.1	.001
Time in bed (weekends)	9.1 ± 1.2	9.1 ± 1.2	9.1 ± 1.0	0.1	.921
Ease/Difficulty to fall asleep	1.4 ± 0.9	1.4 ± 0.8	1.3 ± 0.9	1.7	.191
Sleep agitation	3.3 ± 1.8	3.3 ± 1.7	3.1 ± 1.7	0.7	.522
Frequency of nap	1.3 ± 0.9	1.3 ± 0.9	1.4 ± 0.9	1.0	.379
Frequency of sleepwalking	0.2 ± 0.5	0.2 ± 0.5	0.2 ± 0.4	0.2	.808
Frequency of sleep-talking	1.0 ± 0.9	1.1 ± 0.9	1.0 ± 0.9	0.9	.409
Dream					
DRF (weekly)	3.2 ± 1.8	3.1 ± 1.8	3.1 ± 1.8	0.3	.733
DRF (monthly)	12.9 ± 7.6	12.9 ± 7.6	12.6 ± 7.2	0.2	.851
Dream clarity	1.7 ± 0.6	1.8 ± 0.7	1.7 ± 0.6	0.9	.424
Frequency of recurrent dreams	1.2 ± 0.8	1.2 ± 0.8	1.0 ± 0.7	3.4	.035
Frequency of lucid dreams	1.4 ± 0.9	1.4 ± 0.9	1.4 ± 1.0	0.2	.825

Discussion

Regarding sleep habits and patterns, our findings suggest that French college students have little or unfrequent sleep disturbances. For instance, the average time in bed during weekdays is almost one hour more in our study (7 h 54 min) than the one reported in a representative sample of Taiwanese students (6 h 59; Tsai and Li, 2004), and is equivalent to two studies based on American students habits (8 h 2 min in Buboltz et al., 2001; 7 h 45 min in Lund et al., 2010). Note however that only the time in bed could be extracted from the participants' answers (time spent in bed, both awake and sleeping). It follows that the sleep duration may be overestimated in our survey, even if probably not that much since the large majority of students (90.9%) reported no difficulty to fall asleep. Consistent with several studies, we have found that the average time in bed was longer of more than one hour during weekends as compared to weekdays, suggesting that, to some extent, students suffer from sleep deprivation during the weekdays. Nevertheless, it is important to note that the average time in bed during both weekdays and weekends fall in the range that is considered as normal (i.e. 7-9 hours/night; Hirshkowitz, 2004).

Women self-reported a longer time in bed, during weekdays (19 min more than men on average) and weekends (16 min more than men on average) as could be expected from a previous survey which assessed the French general population sleep habits (Beck et al., 2013). Reyner and Horne (1995) reported results close to ours experimentally recording sleep with home-recorded logs in 400 British adults, i.e. an 18-min longer total sleep time in women. It is however interesting to note that in their sample, this effect was not significant in the *"young"* group (20-34 years) but appeared only in the older groups. In the same study, they also observed that women had a poorer subjective sleep quality and an increased intra-sleep wakefulness. A possible explanation for an increased time in bed in women could thus be that they spend more time in bed to compensate for increased intrasleep awakenings. In coherence with this hypothesis, in our sample women reported more difficulties to fall asleep, more agitation during sleep and a higher frequency of daytime naps.

Regarding dream recall, in average students reported having a dream 3 mornings per week, which is higher than what was observed in a representative sample of the German adult population (Schredl, 2008), but similar to the figures reported in several studies with German student samples composed of a great majority of women (3.5 dream recalls per week in Schredl and Fulda, 2005, N = 196 (138 women), age = 24.8 ± 5.9; 2.75 in Schredl et al., 2003b, N = 444 (376 women), age = 23.5 ± 5.70). The fact that the averaged DRF is not that much different in our sample with a more balanced sex ratio is probably due to the fact that the effect size of gender difference in DRF, when this effect is found, is generally small. Regarding the DRF discrepancy between student and the general adult population it is probably at least partly explained by the well-known negative correlation between DRF and age, which we were able to replicate in this study despite a narrow age range (18 to 30 years old). We also found a significant correlation between the clarity of the dream memory and DRF. This result is consistent with previous ones (e.g. Schredl, 2000b) showing a significant correlation between dream report length and DRF and suggest that the more often you recall dreams the clearer they are.

Regarding gender difference, our results add to the numerous studies reporting a higher DRF in women than in men. This difference was reported to be lower during childhood, an observation that led (Schredl and Reinhard, 2008) to explain adults gender difference in DRF by a gender-specific dream socialization process. Their hypothesis is that girls are encouraged more often than boys to talk about their dreams, which could explain the gender effect since the interest in dream is known to increase DRF (Schredl et al., 2003b). However, there is currently a lack of longitudinal studies to support this hypothesis. Another explanation could relate to gender differences in sleep patterns. Indeed, we have mentioned previously that women tend to have increased intra-sleep wakefulness and poorer sleep quality. According to the arousal-retrieval model of dream recall (Koulack and Goodenough, 1976), the occurrence of a period of wakefulness immediately following dreaming is necessary to encode the dream content into long term memory. This model implies that nocturnal awakenings are positively associated with DRF, an idea that has been experimentally supported using retrospective evaluation (Schredl et al., 2003b) and polysomnographic measures in high and low dream recallers (Eichenlaub et al., 2014a; Vallat et al., 2017). Therefore, according to this model an increased intra-sleep wakefulness in women can explain an increase in dream recall frequency. It is nonetheless interesting to stress that when found, the gender difference in dream recall between men and women is small (Schredl and Reinhard, 2008). It is the case in our study (the DRF was 0.45 points higher in women when estimated in number of mornings per week). Importantly, in our sample when participants estimated their DRF in number of days per month, no significant gender difference was found anymore. One possible explanation is that the weekly measure may have encouraged the participants to round the figures which could have led to artificially increase the discrepancy between men and women. This explanation seems however unlikely since whatever the measure and the group, the average women DRF is always above the one of men (S1 Fig). It seems thus more likely that the better memory availability of recent events induces a more precise DRF assessment at the week scale than at the month scale, which could explain the absence of significant gender effect in DRF for the measure assessed at the month scale. On another note, the higher frequency of recurrent dreams in women than in men has previously been reported (see Zadra, 1996) but is not yet clearly understood. Similarly, the finding that men have a higher frequency of lucid dreams than women should be taken cautiously as the effect size is small, and other studies reported either the opposite effect (Schredl and Erlacher, 2011) or no gender difference (Schredl and Erlacher, 2004; Stepansky et al., 1998).

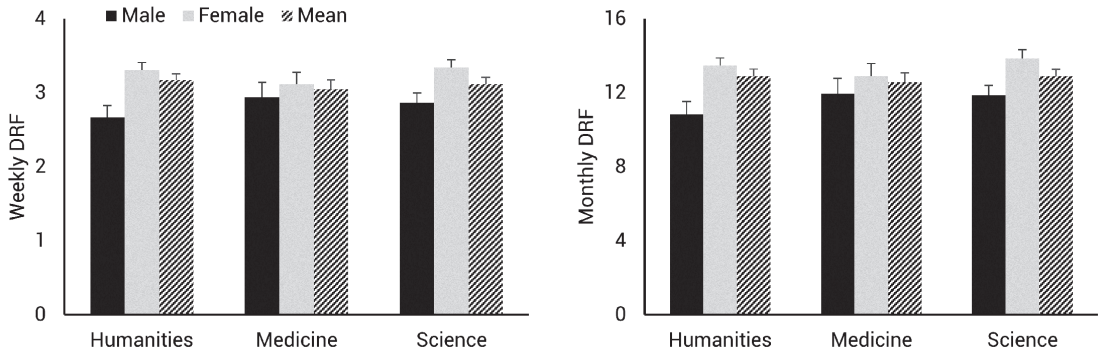
Noteworthy, we also observed sleep differences between academic fields. The longer time in bed in Humanities students may be explained by the fact that a great majority are women known to sleep longer than men (e.g. Beck et al., 2013). It could also be explained by a lower number of courses per week and/or a different morning schedule of classes in Humanities and/or by a less involving, challenging and stressful system of evaluation. Indeed, in the Medicine and the Science academic field, students often have competitive examination, whereas in humanities students more often have a level-checking evaluation. An average personality trait difference between academic fields could also at least partly explain the sleep duration differences between groups (Hartmann, 1989). Further studies will be needed to confirm this academic field effect and to better understand why Humanities students sleep longer than the ones in Science and Medicine.

Limitations and conclusions

Limitations arise from the fact that the survey was designed for the recruitment phase of an fMRI sleep study. For this reason the survey only included a limited number of questions regarding sleep and dreams but had also the advantage to ask unusual ones (recurrent dreams, lucid dreams, agitation during sleep, sleep talking). In addition, the announcement for the fMRI sleep study explicitly mentioned that the participants would be asked to sleep in an MRI scanner. As a consequence participants with subjectively disturbed or difficult or light or short sleep may have spontaneously censored themselves from answering the survey. We indeed cannot exclude that our sample is biased towards students with no or little sleep disturbances. Further investigations are needed to get a comprehensive overview of sleep and dream patterns in college students. It would be interesting for example to study the prevalence of nightmares or bad dreams in student population. Further studies are also needed to deepen our understanding of the gender differences found in both sleep and dream habits.

Author contribution R.V and P.R designed the survey, RV collected, analyzed the data and wrote the first draft. All authors were involved in the writing process.

Supplementary materials



S1 Fig. Dream recall frequency as a function of gender and academic disciplines. Left: weekly DRF (number of mornings per week with a dream in mind), Right: monthly DRF (number of mornings per month with a dream in mind). Error bars represent standard error.

12

Study 5. The relationship between waking life and dream content

PLOS ONE

RESEARCH ARTICLE

Characteristics of the memory sources of dreams: A new version of the content-matching paradigm to take mundane and remote memories into account

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Citation: Vallat R, Chatard B, Blagrove M, Ruby P (2017) Characteristics of the memory sources of dreams: A new version of the content-matching paradigm to take mundane and remote memories into account. PLoS ONE 12(10): e0185262. https://doi.org/10.1371/journal.pone.0185262

Editor: Raffaele Ferri, Associazione OASI Maria SS, ITALY

Received: January 19, 2017

Accepted: September 8, 2017

Published: October 11, 2017

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This work was supported by the LABEX CORTEX (ANR-11-LABX-0042) of Université de Lyon, within the program "Investissements d'Avenir" (ANR-11-IDEX-0007) operated by the French ANR. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Abstract

Several studies have demonstrated that dream content is related to the waking life of the dreamer. However, the characteristics of the memory sources incorporated into dreams are still unclear. We designed a new protocol to investigate remote memories and memories of trivial experiences, both relatively unexplored in dream content until now. Upon awakening, for 7 days, participants identified the waking life elements (WLEs) related to their dream content and characterized them and their dream content on several scales to assess notably emotional valence. Thanks to this procedure, they could report WLEs from the whole life-span, and mundane ones before they had been forgotten. Participants (N = 40, 14 males, age = 25.2 ± 7.6) reported 6.2 ± 2.0 dreams on average. For each participant, 83.4% ± 17.8 of the dream reports were related to one or more WLEs. Among all the WLEs incorporated into dreams dated by the participants (79.3 ± 19%), 40.2 ± 30% happened the day before the dream, 26.1 ± 26% the month before (the day before excluded), 15.8 ± 21% the year before the dream (the month before excluded), and 17.9 ± 24% happened more than one year before the dream. As could be expected from previous studies, the majority of the WLEs incorporated into dreams were scored as important by the dreamers. However, this was not true for incorporated WLEs dating from the day before the dream. In agreement with Freud's observations, the majority of the day residues were scored as mundane. Finally, for both positive and negative WLEs incorporated into dreams, the dreamt version of the WLE was rated as emotionally less intense than the original WLE. This result, showing that dreams tend to attenuate the emotional tone of waking-life memories towards a more neutral one, argues in favor of the emotional regulation hypothesis of dreaming.

Competing interests: The authors have declared that no competing interests exist.

Introduction

A way to progress in our understanding of the possible functions of dreaming is to investigate the parameters constraining or influencing dream content. An extensive amount of research has investigated the memory sources of dreams and has demonstrated that dream content very rarely replays an episodic memory as it is remembered [1,2], although it is often related to some elements of the waking life of the dreamer (for reviews [3–5]). This has led to the so-called "continuity hypothesis of dreaming" which simply states that dreams reflect waking life experiences [6]. In 2010, Michael Schredl reported that according to results from studies using various methods (assessing temporal references of dream elements retrospectively, experimental manipulation of the pre-sleep situation, field studies, fluctuations over time within persons, differences between persons), the five following factors influence the incorporation of a waking life element (WLE) into dreams:

- Time (the more remote the WLE, the less incorporated into dreams, e.g. [7,8])
- Emotion intensity (the more emotional the WLE, the more incorporated into dreams, e.g. [9,10])
- Type of experience (e.g. working with a computer is less often incorporated into dreams than is chatting with friends, e.g. [11])
- Personality traits of the dreamer (field dependence and thin boundaries may moderate the magnitude of the continuity between waking and dreaming, e.g. [12])
- Time of the night (dreams of the second part of the night comprise more elements of the distant past, while dreams of the first part of the night incorporate mostly recent daytime experiences, e.g. [13,14]).

However some characteristics of dream content do not fit with this modelling of the data. Firstly, some body injuries—be it congenital or acquired—such as amputation, paraplegia and deafness, are less incorporated into dream reports than this model would predict considering how highly emotional and central to the person's life they are [15–17]. Secondly, the available results show that WLEs incorporated into dreams are more emotionally intense than are WLEs that are not incorporated into dreams [9,10], while day residues (WLEs from the day before the dream), which are known to be a great part of the WLEs incorporated into dreams [18–23], are often mundane, as noticed by Freud [24].

Even if they are not necessarily contradictory with Freud's observation, results showing a bias towards the incorporation of emotional elements into dreams may be explained by the method used in experimental studies so far, i.e. the content matching paradigm. It requires the participants to rate a posteriori (i.e. at the end of the 14 days of the experiment) similarities between a day diary and a dream diary completed for 14 days [9,10]. Such a method has the advantage of controlling for retrospective availability of memories for elements when participants relate dream content to WLEs, but it has the drawback of missing mundane experiences that are not recorded in the diary. As a consequence, previous studies could not assess whether mundane WLEs were incorporated into dreams.

The present study aims to investigate more exhaustively than previously achieved the characteristics of the WLEs incorporated into dreams, notably by assessing their remoteness on a life-time scale and by taking mundane WLEs into account. To do so, instead of asking dreamers to keep a day diary, we asked participants to report and characterize the WLEs related to their dreams immediately upon awakening. This strategy presents several advantages regarding previous methods. Firstly, any remembered WLE at any timescale can be considered. This

method offers then the possibility of investigating the incorporation of WLEs across the whole life span, which has been rarely attempted until now [8,25]. Secondly, as the reported memory sources of a dream are dependent on the delay between the dream and the task to report memory sources, the sooner the task after the dream, the more chances we have to identify the true memory sources of the dream [26]. Thirdly, as the connections between elements of waking life and dream content are assessed when the memories of the preceding days are still fresh, this method enables the recall of trivial WLEs from at least the few days before the dream. Using this new approach, we are able to test whether emotional WLEs are still preferentially incorporated into dream reports when trivial WLEs are taken into account and to investigate the emotionality and significance of WLEs incorporated into dreams as a function of their remoteness. The results will be discussed regarding previous literature and current hypotheses about dream function, notably those attributing a role to dreaming in emotion regulation [27,28] and memory consolidation [29–31].

Material and methods

Participants

An announcement describing the study was sent by emails to students and staff of Lyon University. The inclusion criteria were (1) a habitual dream recall frequency of at least 3 mornings per week with a dream in mind, (2) the agreement for reporting all recalled dreams exhaustively without censorship and (3) the agreement for sleeping at habitual hours without excessive consumption of alcohol during the 7 days of the experiment. Forty participants (14 males, age = 25.2, SD = 7.6) were recruited accordingly. The study conformed with French regulation and ethics regarding research in humans and approval was granted by the "Centre National de Recherche Scientifique, Cellule Informatique et Liberté". Subjects gave written informed consent according to the Declaration of Helsinki and were paid for their participation.

Procedure and questionnaires

The recruited participants were asked to come to the lab for a 30 minutes meeting. At this occasion, the experimenters described the study requirements, gave instructions and answered any questions of the participants. Experimenters explained that the aim of the study was to identify the possible links between waking life experiences and dream content and that participants were expected to report without censorship any kind of waking life elements related to their dreams (episodes, objects or characters, whether recent or old, important or trivial).

The participants were also given a questionnaire designed for the study that they had to fill in before starting reporting their dreams. This questionnaire asked about various aspects of the participant's lives (age; gender; habitual dream recall frequency; habitual sleep time and duration; education; work; first names of siblings, parents, children, current and previous partners, closest friends and any deceased friends or family members; hobbies; possible experiences with a high emotional load in the last 4 weeks; a list of the most personally important places of habitation or vacation; a list of the most important current concerns). This questionnaire was designed to identify the personally important aspects of the participant's life, to enable us to score their possible appearances in dream content.

Next, participants were requested to report their dreams using a voice recorder immediately upon awakening for seven consecutive days. They were asked to describe their dream content in as much detail as possible without adding interpretations. After each dream was reported participants completed a questionnaire about possible links between the dream content and their waking life. Participants had to tell whether they felt that parts of their dream were obviously related to some features of their waking lives. It was made clear during the initial

interview that any kind of waking life feature could be considered (e.g., places, characters, actions, events, objects, thoughts) even if trivial. If so, for each link that was made the participant had to: 1) score the emotional valence of the element of the dream that reminded them of an element of their waking life, 2) describe the waking life element incorporated into their dream with written words, dating it when possible and rating it on various scales (from 1 to 10) to assess its familiarity, frequency, emotional valence, importance, personal versus professional dimension, social dimension, how much a concern it was, and how similar it was to the corresponding dream content. If several waking life elements were incorporated into a dream, participants had to describe and rate each of them separately.

The questionnaire also asked participants to quantify several aspects of dream content. Dreamers had to: 1) rate the emotional intensity (scales from 1 to 10) and the emotional valence (scale from 1 very negative, to 10 very positive) of the dream and to report the emotions encountered during the dream (primary emotions, i.e. joy, sadness, fear, anger, disgust, surprise were proposed as possible answers as well as a blank field for other possible emotions), 2) count the number of characters in the dream, and report for each character whether they are familiar in their waking life (and if so, their name or relationship to the participant), unknown in their waking life, or with mixed characteristics, 3) report the number of places in the dream and whether these places are familiar in their waking life (and if so, their name), unknown in their waking life or with mixed characteristics. This questionnaire was designed for the study with the objective of complying with two contradictory aims: minimizing the time to fill in the questionnaire each morning and maximizing the quality and quantity of information on the dream and on the WLEs related to the dream. A preliminary study with 10 subjects was used to optimize the questionnaire (those subjects were not included in the main study). At the end of the experiment participants were asked whether they had experienced a strongly emotional event or new concern during the 7 days of the experiment.

Note that the main aim of the study was to identify the temporal and emotional characteristics (among others) of the WLEs incorporated into dreams. We did not aim to investigate the memory type of the WLEs reported (episodic, autobiographic and semantic). Future studies will be needed to investigate the interaction between the factors we studied and memory type.

Data analysis and scoring of dream content

Word count. Audio reports were transcribed from audio to written language by the company TranscribeMe! (http://transcribeme.com/) and were subsequently checked by the experimenters before word count.

Characters and settings. Crowds counted as one person if individuals were not explicitly specified, following the Hall & Van de Castle rating system [32]. Among the existing characters, close family members and close friends were counted by RV and BC using the names mentioned *a priori* in the initial questionnaire. Similarly, among the known places, RV and BC counted the significant ones, defined as those mentioned in the initial questionnaire by the participants. RV and BC conducted scorings independently and, in case of disagreement between scores, reached a consensus after discussion.

Emotional valence and intensity. For each dream the emotional valence of the WLE(s) incorporated into the dream and the emotional valence of the dream were compared. If several WLEs were incorporated into one dream their average valence was considered.

The emotional intensity of WLEs incorporated into dreams was derived from the rating of emotional tone by a transposition of the initial valence scale (1 = very negative, 10 = very positive) to an intensity scale of zero to four (0, neutral; 1, feebly intense; 4, very intense; irrespective of the positive or negative tone of the WLE). We considered as low emotional intensity the

ratings 4, 5 or 6 on the 1-to-10 scale. Medium intensity was attributed to ratings of 2, 3, 7 or 8 and high intensity to a rating of 1 or 9–10. In other words, positive and negative WLE were re-rated on a 1 to 4 scale where 1 means feeble positive/negative and 4 means very positive/negative.

Temporal remoteness of WLEs incorporated into dreams. First, to assess the predominant temporal origin of the WLEs incorporated into dreams, we compared the proportion of WLEs in each of the 3 following categories: day before (day-residues), month before (day before the dream excluded) and older than one month. Secondly, to test whether we reproduce the dream lag effect (i.e. as compared to what would be expected according to memory decay with time, some studies reported an overrepresentation in dreams of the WLEs that happened approximately one week before the dream), we compared the proportion of WLEs in each of the 4 following categories: day before, 2 to 5 days before, 6 to 9 days before and 10 to 14 days before the dream. We chose for the analysis temporal categories according to the time scale of the maximum of the effect previously reported (6 days before the dream, [22]; 7 days before the dream, [21,23]; 9 days before the dream, Jouvet [33] quoted in [34]), and of equal durations (4 days), i.e. WLEs that happened 2 to 5 days and 6 to 9 days before the dream.

Concerns. Concerns listed in the initial questionnaire were grouped into 7 thematic categories (Work/Study, Family/Friends, Leisure (i.e., extra-professional or extra-scholar activity), Everyday life, Romantic relationship, Self-related and Health) by RV and BC. The assessment of whether or not a concern listed in the initial questionnaire was incorporated into a dream was not done at awakening by the participants but *a posteriori* by two scorers. Scorers used the concerns listed in the initial questionnaire to assess whether the WLEs incorporated into dreams could be considered as part of the current concerns of the dreamers. RV and BC conducted scorings independently and, in case of disagreement between scores, reached a consensus after discussion.

Re-occurrence of a WLE in several dreams. As it has been shown that some memories may be iteratively processed across subsequent nights (e.g. [35]), for all participants, RV and BC assessed whether some WLEs were incorporated into several dreams during the time of the experiment (in case of disagreement, they reached a consensus after discussion).

Statistics. Except when specified, values reported are always grand means (mean of each participant's mean) and standard deviation. Statistical testing were made using repeated measures ANOVA, followed by Tukey HSD pairwise comparisons in case of significance (alpha level = 0.05).

Results

A total of 247 dreams were reported, ranging from 16 to 3691 words (average per participant, 543 ± 262 words). On average the participants reported 6.2 ± 2 dreams in the 7 days of the experiment (range = 3–14; 8 participants reported at least once, more than one dream per morning, leading to 14 mornings with multiple dream reports). Among all the dreams reported 207 have been related to a WLE (83.8%). For each participant, 1) on average, 83.4% ± 17.8 of their dream reports were related to one or more WLEs, 2) on average 1.8 ± 1.6 incorporations per dreams were reported (2.1 ± 1.5 considering only dream reports with incorporation of WLE, maximum per dream = 19). Dream reports for which dreamers reported a link with one or several WLEs were in average longer than dream reports that were not related to WLEs (576.0 ± 280.1 vs 411.9 ± 118.4 words; paired t-test = 0.04). S1 Table provides examples of WLEs incorporated into dreams.

Emotions in the dreams

The average emotional intensity of the reported dreams (scale from 1, low to 10, high) was 5.65 ± 1.55. In average, for each subject 30.1% ± 27.2 of the dreams were of low emotional intensity (score inferior to 5), 13.5 ± 16.6 were neutral (score equal to 5) and 56.4 ± 29.6 were of high emotional intensity (score superior to 5). The average emotional valence of the reported dreams (scale from 1, highly negative to 10, highly positive) was 4.79 ± 0.91. In average, for each subject 42.7 ± 27.2 of the dreams were negative (score inferior to 5), 30.4 ± 24.7 were neutral (score equal to 5) and 26.9 ± 20.2 were positive (score superior to 5). The mean number of emotions per dream was 1.82 ± 0.69. The most frequent emotion reported by participants was surprise (present in 29.96% of the dream reports), followed by fear (26.72%), joy (25.10%), anger (20.65%) and sadness (16.59%).

A t-test revealed that WLEs incorporated into dreams were rated as significantly more positive (5.61 ± 2.2) than the dreams in which they had been incorporated into (4.81 ± 1.9; paired t-test $p < .001$, $n = 247$). Moreover, in average WLEs incorporated into dreams were rated as significantly more positive (5.74 ± 2.4,) than the element of the dream related to that WLE (5.30 ± 2.2; paired t-test on the emotional ratings of the WLE and the ones of the dreamt version of the WLE, $p < .001$, $n = 492$). Interestingly, when we ran the analysis separately for positive, neutral and negative WLEs (Fig 1A), we found that positive WLEs (valence > 5) were rated as more positive (8.0 ± 1.4) than the element of the dream related to that WLE (6.5 ± 2.4; paired t-test $p < .001$, $n = 214$), and that negative WLEs (valence < 5) were rated as more negative (2.78 ± 1.1) than the element of the dream related to that WLE (3.5 ± 1.6; paired t-test $p < .001$, $n = 129$). For neutral WLEs we found no significant difference between the valence of the WLE (valence = 5) and the valence of the element of the dream related to that WLE

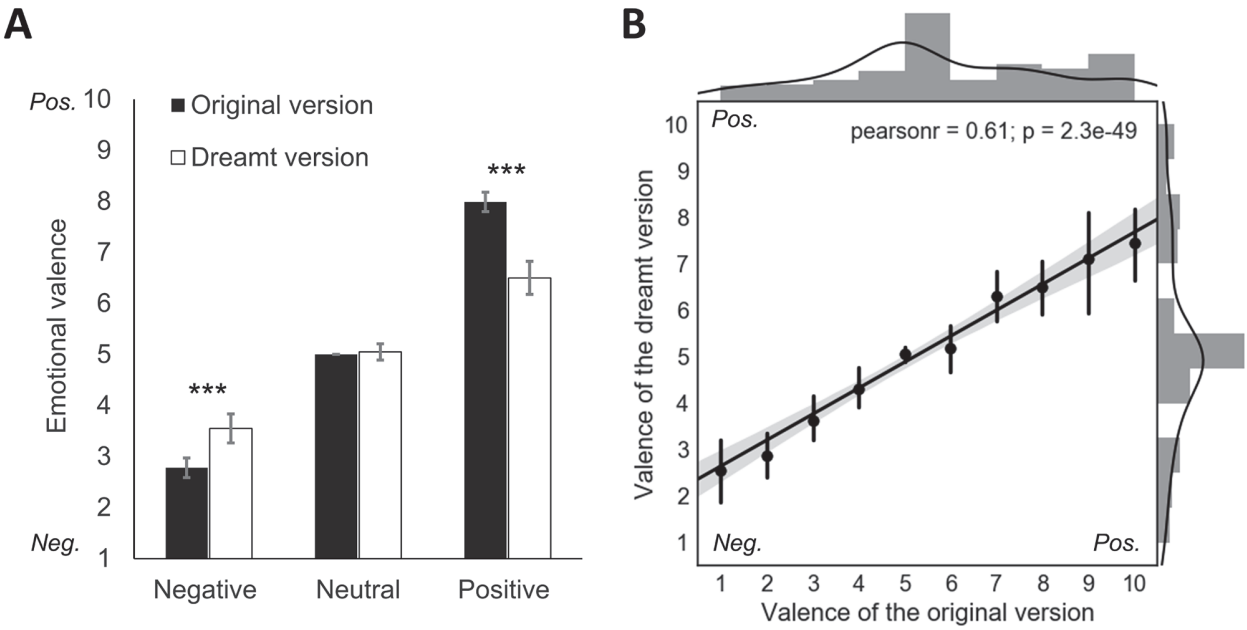

Fig 1. Emotional valence of the dreamt version and the original version of the WLEs incorporated into dreams. A) Emotional valence of the dreamt version (white bars) and the original version (black bars) of the WLEs incorporated into dreams for positive (rating > 5), neutral (rating = 5) and negative (rating < 5) elements. The dreamt version was scored as more neutral than the original version of the WLEs. B) Significant positive correlation between the emotional valence ratings of the original and the dreamt versions of the WLEs incorporated into dreams. Gray bars indicate the distribution of the ratings for the original and the dreamt version of the WLEs incorporated into dreams. Error bars represent 95% confidence intervals. *** p <.001.

https://doi.org/10.1371/journal.pone.0185262.g001

(5.05 ± 1.0; paired t-test p = .53, n = 140). A correlation analysis further showed the grouping of the emotional valence grades toward the 5 (neutral) grade for the dreamt version of the WLE as compared to its original one (Pearson, r = 0.61, p < .001) (Fig 1B).

Places and characters of the dreams

The mean number of characters per dreams was 4.7 ± 2.3. At least one character was reported in 96.55% of the dream reports. As illustrated in Fig 2, the majority of the dreamed characters existed in waking life (54% ± 18), and 11% ± 11 had mixed attributes (e.g. in the dream the dreamer knows that a character is someone that he knows even if he/she has modified physical attributes, or the other way around). About one third of the dreamed characters were unknown to the dreamer (36% ± 18). Among the existing characters, close family members and close friends (i.e. those mentioned *a priori* in the initial questionnaire) accounted each for 28% ± 20 and 27% ± 20 of the dreamt characters. The remaining (45% ± 25) included existing but less close persons such as distant relatives, distant friends and work colleagues.

There was an average of 2.3 ± 1.5 places per reported dream. Nearly half (47% ± 23) of the dreamed places were unknown to the participant and the remaining places were either existing (26% ± 10) or with mixed attributes (27% ± 18). Among the existing places, 38% ± 30 had been reported as significant in the initial questionnaire by the participants (Fig 2).

Incorporation of the current concerns of the dreamer into the dreams

On average participants listed 4.7 ± 1.2 concerns in the initial questionnaire. A great majority of the participants (70%) incorporated at least one waking life element related with their current concerns (i.e. those listed in the initial questionnaire) during the 7 days of the experiment. In average, 23% ± 21 of the dream reports of each subjects incorporated a current concern.

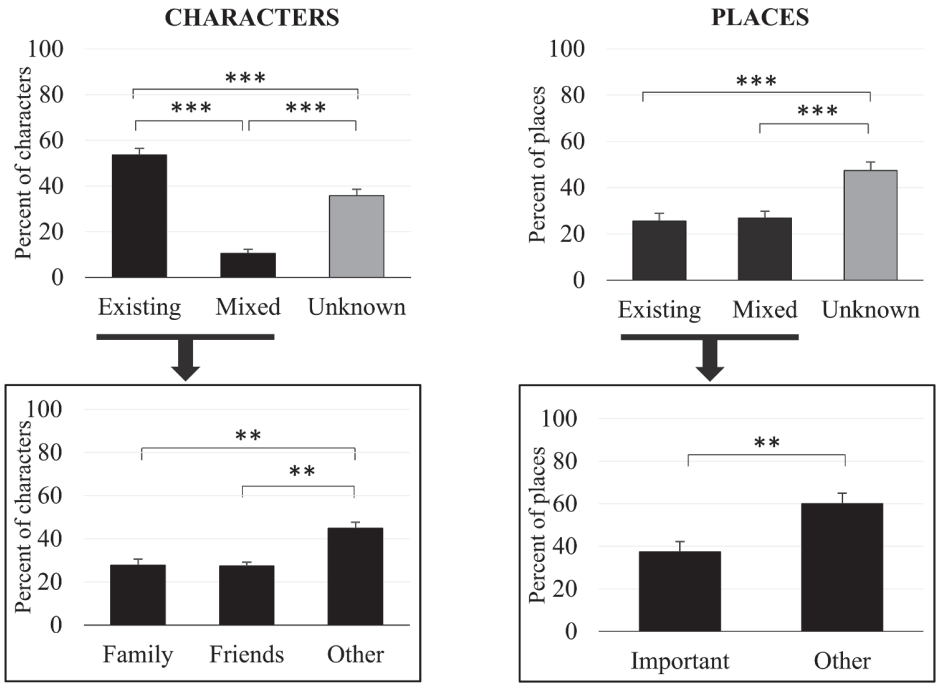

Fig 2. Characters and places of the dreams. Error bars represent standard error of the mean. ***p<.01* ****p<.001*.

https://doi.org/10.1371/journal.pone.0185262.g002

Table 1. Examples of concerned incorporated into a dream.

Subject	Concern	Dream report
S29	Concern n°1: *"My aunt passed away recently and I miss her terribly. I know she will not come back, but some days I still hope it will happen."*	Day 6: *"I descend into another world to pick up my aunt and realize that it is not possible—I feel a deep anguish and I am cold"*
S4	Concern n°1: *"My girlfriend suffers from anorexia. She is much stressed and vomits almost everything she eats. I am trying to help her relax and regain self-confidence."*	Day 5: *"My girlfriend threw up what she had eaten after a big meal. I comfort her."*
S28	Concern n°2: "*To succeed in my university studies"*	Day 1: *"It was the day of publication of the 1st semester's results. We were in the tramway. The teachers were within the tramway (which was also the classroom). I was waiting for the teachers to tell us our results. But nobody told us and they just gave us the corrections instead. I felt very impatient."*

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Finally, for each subject among all the concerns listed in the initial questionnaire an average of 25% ± 22 were incorporated into a dream report during the 7 days of the experiment (see Table 1 for examples). The category with the greatest number of concerns happened to be the Work/Study one. The distribution of concerns according to each category and the percentages of concerns in each category incorporated into dreams are illustrated in S1 Fig.

Re-occurrence of a WLE in several dreams

Re-occurrence of a WLE in several dreams was found for only 6/40 participants and only one of them mentioned explicitly that it was a re-occurrence. For all six we found a WLE incorporated in two different dreams and, for one of them, a WLE incorporated in 3 different dreams. The WLEs re-occurring in several dreams were related to current or emotional concerns (e.g. preparation of a journey abroad, awaiting the results of university exams, grand-mother in hospital for a recent accident, fear of succumbing to a morally reprehensible desire, meeting with the new boyfriend of his ex-girlfriend) or to recent hobbies (a TV show, a role play, hiking with friends).

Characteristics of WLEs incorporated into the dreams

Average scores. The averages scores given by the dreamer at awakening for various dimensions of the WLEs incorporated into their dream reports are presented in Table 2 and

Table 2. Averaged scores given by the dreamers at awakening to describe the WLEs incorporated into their dreams.

Characteristics	All WLEs	Day-residues	*p-value*
Frequency *(1: Rare—10: Daily)*	4.5 ± 1.5	4.4 ± 2.2	*0.6*
Familiarity *(1: New—10: Familiar)*	6 ± 1.5	5.2 ± 2.4	**0.03*
Personal dimension *(1: Professional—10: Personal)*	7.8 ± 1.4	8.3 ± 1.9	*0.2*
Social dimension *(1: Not social—10: Social)*	5.7 ± 1.8	5.1 ± 2.4	*0.2*
Emotional valence *(1: Negative—10: Positive)*	5.7 ± 1.3	5.9 ± 1.9	*0.1*
Emotional intensity *(0: None—4: Very intense)*	1.9 ± 0.8	1.6 ± 1.2	*0.08*
Importance *(1: Not important—10: Important)*	5.5 ± 1.5	4.6 ± 2.2	**0.01*
Current concern *(1: Not a concern—10: Concern)*	4.1 ± 1.6	3.9 ± 2.2	*0.9*
Similarity with dream *(1: Not similar—10: Identical)*	6.3 ± 1.5	6.3 ± 1.7	*0.6*

Scores for all WLEs and day-residues only are presented (*p-values* of the t-test comparing the scores in the two categories are presented).

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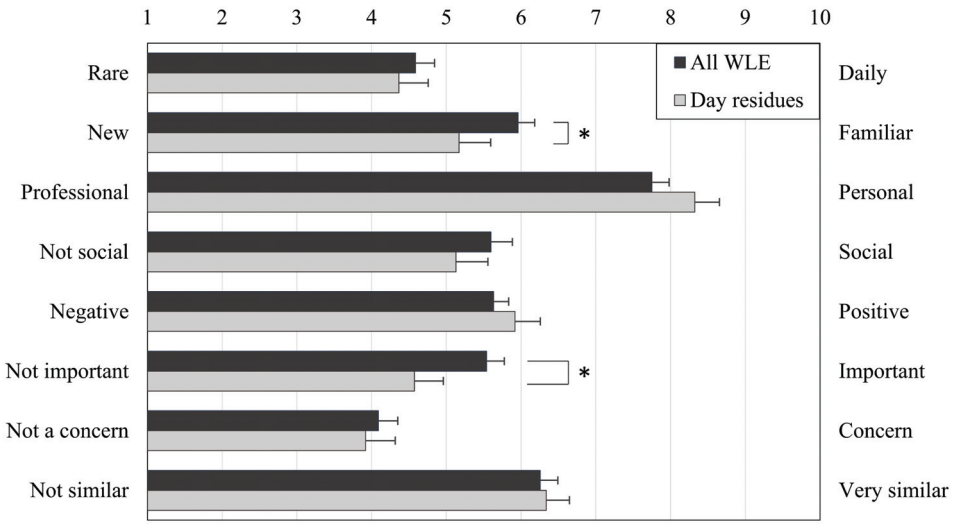

Fig 3. Characteristics of waking life elements incorporated into dreams. All waking life elements (black) and day residues only (grey). Error bars represent standard error of the mean. *$p<.05$.

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Fig 3. T-tests revealed that as compared to all WLEs, day-residues were scored as less familiar, less important and tended to be scored as less emotionally intense. The distribution of WLEs with a rating inferior, equal and superior to 5 can be found in S1 File and S2 Fig.

Proportions of the WLEs incorporated into dreams as a function of their temporal remoteness. In average 79.3 ± 19 percent of the WLEs incorporated into dreams were dated by the participants. Table 3 and Fig 4 show the distribution of dated waking life experiences incorporated into dreams as a function of their date of occurrence in the waking life of the dreamer. Using a one-way repeated measures ANOVA, we observed no significant differences between the proportions of WLEs in the 3 following categories: day before (day-residues), month before (day before the dream excluded) and older than one month. For the analysis focusing on the 15 days before the dreams, a one-way repeated measures ANOVA yielded a significant main effect of time ($F(3,39) = 32.3$, $p < .001$). Post-hoc comparisons using the Tukey HSD test indicated that the proportion of WLEs which occurred the day before the dream (59.7% ± 36.9) was significantly larger than the proportions of WLEs that occurred 2 to 5 days (11.2% ± 15.3), 6 to 9 days (15.3% ± 25.8) and 10 to 14 days before the dream (6.3 ± 13.2; $p < .001$ for all comparisons). No significant differences was found between the other categories. The characteristics (scores averages and distributions) of the WLEs incorporated into dreams that occurred between 6 and 9 days before the dream are presented in S3 Table.

Table 3. Percentage of the dated WLEs incorporated into dreams as a function of their temporal remoteness.

	1 day	2 to 5 days	6 to 9 days	10 to 14 days	15 to 31 days	2 to 12 months	More than 1 year
Mean	40.2	7.3	8.1	4.3	6.4	15.8	17.9
SD	30	9	12	9	13	21	24

The time elapsed between the occurrence of the dream and the occurrence of the WLE is used to date WLEs incorporated into dreams. The WLEs from the "1 day" category occurred the day before the dream.

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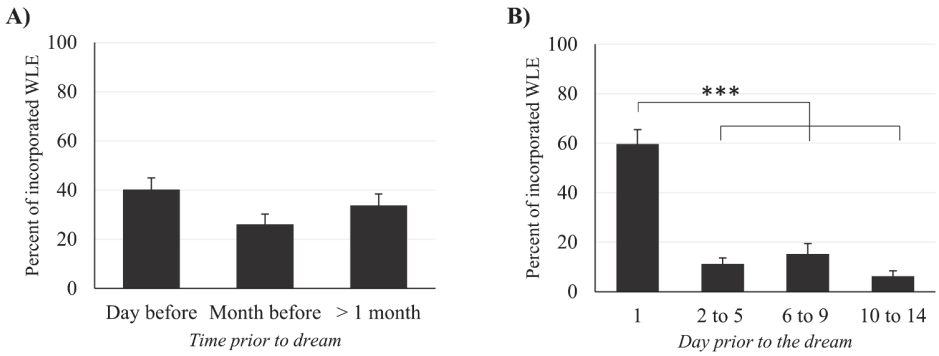

Fig 4. Distribution of the dated WLEs incorporated into dreams as a function of their remoteness. (A) Distribution of all the WLEs incorporated into dreams when 3 categories of remoteness are considered. (B) Distribution of the WLEs incorporated into dreams which happened between 1 day to 14 days when 4 categories of remoteness are considered. Error bars represent standard error of the mean. ***$p < .001$.

https://doi.org/10.1371/journal.pone.0185262.g004

Interactions between remoteness and emotion/importance. We tested for a possible interaction between remoteness and either emotional tone or emotional intensity or importance. To that purpose, the 492 incorporated WLEs were divided in 3 temporal categories: from the day before, from the month before (day before excluded), and from more than 1 month. For each of the three temporal categories, the means across all incorporated WLEs were computed for importance, emotional intensity and emotional tone (see Table 4 and Fig 5).

First, a one-way ANOVA yielded a significant effect of remoteness on the importance ratings of incorporated WLEs ($F(2,352) = 10.4$, $p < .001$). Tukey post hoc revealed that incorporated WLEs that happened a month or more before the dream were scored as more important than the ones that happened the day before the dream (respectively 5.6 ± 0.2 vs 4.2 ± 0.2; p = .001 and 5.9 ± 0.2 vs 4.2 ± 0.2; p = .000). Incorporated WLEs that happened during the month preceding the dream (day before the dream excluded) were not rated as more or less important as compared to incorporated WLEs that happened more than one month before the dream (p = .86).

Secondly, there was also a significant effect of remoteness on the emotional intensity rating of the WLEs incorporated into dreams ($F(2,389) = 15.4$, $p < .001$). According to Tukey post hoc, incorporated WLEs that happened more than one month before the dream were rated as significantly more intense emotionally (2.4 ± 0.1) than the ones that happened the month before (day before the dream excluded, 1.7 ± 0.1; $p < .001$) or the day before the dream (1.4 ± 0.1; $p < .001$)$p < .001$.

Third, a one-way ANOVA showed a significant effect of remoteness on the rating of the emotional tone of the WLEs incorporated into dreams for the negative subscale ($F(2,96) = 3.4$, p = .04). Indeed, incorporated WLEs that happened more than one month before the dream were rated as more negative (2.6 ± 0.1) than the ones experienced the day before the dream

Table 4. Rating (Mean+SD) of the dated WLEs incorporated into dreams as a function of their remoteness.

	Day before	Month before	Older than a month	*F*	*p*
Importance *1-to-10 scale*	4.2 ± 3.1	5.6 ± 3	5.9 ± 3.1	10.4	*.00*
Emotional intensity *0-to-4 scale*	1.4 ± 1.5	1.7 ± 1.4	2.4 ± 1.4	15.4	*.00*
Positive *1-to-4 scale*	2.7 ± 1.1	2.5 ± 1.1	3 ± 1	1.23	*.29*
Negative *1-to-4 scale*	1.9 ± 1.1	2.1 ± 1.2	2.6 ± 1.1	4.29	*.02*

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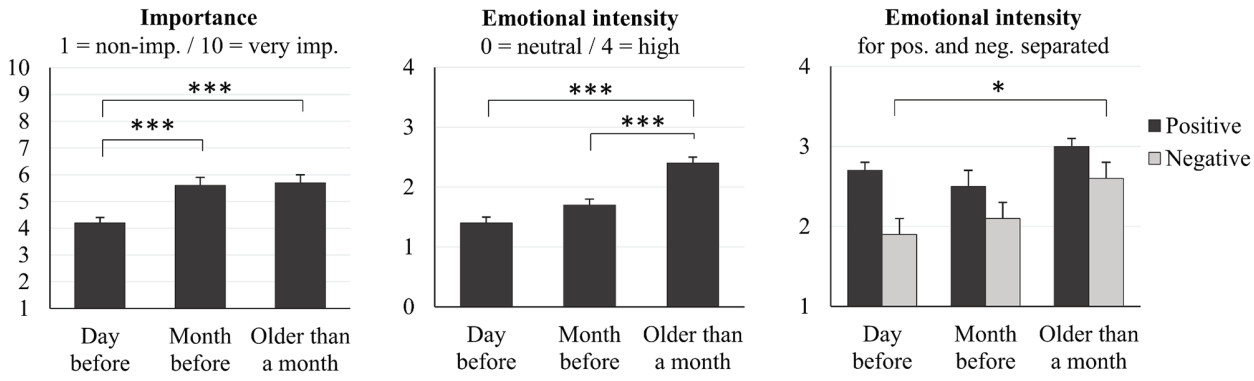

Fig 5. Emotionality of the dated WLEs incorporated into dreams as a function of their remoteness. (A) Importance scores of the WLEs incorporated into dreams as function of their remoteness. (B) Emotional intensity as a function of remoteness. (C) Emotional tone as a function of remoteness. Error bars represent standard error of the mean. *$p<.05$—**$p<.01$—***$p<.001$.

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(1.9 ± 0.1; p = .03). There was no significant effect of remoteness on the rating of emotional tone for the positive subscale.

Finally, to ensure that mundane WLEs did not all date form the day before the dream, the distribution of mundane WLEs incorporated into dreams according to their temporal remoteness was calculated and is presented in S4 Table.

Discussion

The present study aimed to investigate the characteristics of the waking life experiences that are incorporated into remembered dreams upon morning awakenings at home. Subjects were asked to report and characterize WLEs incorporated into their dreams immediately upon awakening during 7 consecutive days. By contrast with most previous studies, such an approach enabled us to consider WLEs from the whole lifespan of the participants and also mundane ones. Only the main results are discussed below. Discussion of the remaining results is available in S2 File (incorporation of familiar characters and places, and current concerns in dreams).

The percentage of dreams with incorporation of WLEs

In 84% of all the dreams (N = 247) and in 83% ± 18 of the dreams of each subjects, the dreamer identified at least one obvious waking life source in his or her dream. Asking participants to draw connections between 14-days day and dream diaries, Schredl [10] reported that 41% of 254 dreams had been related to at least one WLE, while in Fosse [1] it was the case for 65% of 299 dreams. Thanks to a survey Botman & Crovitz [7] observed that 83% of 124 dreams incorporated somebody or something from the past while Malinowski and Horton found that 95% of the 186 dream reports contained an element either weakly or strongly related to an autobiographical memory [36]. According to our study, and previous ones which most probably underestimated the percentage of dreams related to waking life features (i.e. either by considering only a small part of the subject's waking life by using a day diary or asking the subjects to report only the WLEs obviously related to dream content), the incorporation of WLEs into dreams appears to be extremely frequent if not to suppose systematic. Moreover, an average of 1.9 WLE were incorporated per dream in our study which is similar to the results of Marquardt [25] who reported an average of 1.3 WLE per dream using a comparable approach. These results highlight WLEs as a core feature of dream content.

The emotionality of the WLEs incorporated into dreams

Using a paradigm that takes trivial experiences into account we observed that 46% of all WLEs incorporated into dreams were scored as non-important or neutral by the dreamers and 42.5% as feebly emotionally intense. This result supports our claim that mundane experiences are a significant part of the WLEs incorporated into dreams and that the proportion of emotionally intense WLEs was probably overestimated in previous studies [9,10]. According to our results, trivial WLEs (be it recent or remote, see S4 Table) are largely represented in dreams (S2 Fig).

Coherently with this idea, we found that on average the dreamers scored the WLEs incorporated into their dreams as moderately important and emotionally intense (Table 2). The distribution of the scores show that a slight majority of the WLEs incorporated into dreams were scored as important (i.e. with a score above 5) and as moderately or highly emotionally intense (S2 Table, S2 Fig), as suggested by previous studies [9,10]. However, as we hypothesized, we also observed that the majority of day-residues were scored as feebly emotionally intense and as feebly or neutrally important. This result does justice to Freud who wrote at the end of the 19th century in his book the Interpretation of Dreams [24] (http://psychclassics.yorku.ca/Freud/Dreams/dreams.pdf, p.176, emphasis added) "*Although the foregoing remarks have restricted the significance of the day-residues for the dream, they are none the less deserving of some further attention. For they must be a necessary ingredient in dream-formation, inasmuch as experience reveals the surprising fact that every dream shows in its content a connection with a recent waking impression, often of the most indifferent kind*".

According to the hypothesis of a preferred incorporation of emotionally intense experiences into dreams [9,10], one would expect to observe more important and emotionally intense WLEs than trivial ones among day-residues. As a consequence, our results question the hypothesis that important and emotionally intense waking life experiences are generally more represented in dreams than are trivial ones.

Regarding the valence of the WLEs incorporated into dreams we observed that a large majority were scored as positive or neutral and that less than 30% were reported as negative. Interestingly, we also found that the valence of the dreamt version of the WLEs was on average experienced as less positive than in waking life. Separate analyses for positive, negative and neutral WLEs further revealed that the valence of the dreamt version of the WLEs was experienced as less positive than in waking life for positive WLEs, as less negative than in waking life for negative WLEs and as as neutral as in waking life for neutral WLEs. The possible implications for dream functions are further discussed below.

The temporal remoteness of the WLEs incorporated into dreams

Among all the dated WLEs incorporated into dreams we found that 40% were day residues i.e. from the day before the dream (Fig 4A). This is very similar to the 44% reported by Marquardt [25] using a similar procedure as ours but it is widely lower than the 94% reported by Hartmann [18] after he analyzed 800 of his own dreams. Using a different approach (a survey comprising 340 students), Botman & Crovitz [7] reported that 63% of the 103 dreams which had incorporated WLEs, presented a day-residue. All together these results highlight a very important influence of the day before the dream on dream content, as observed by Freud a century ago [24] (see quotation above). However, this study has also highlighted, as hypothesized, the large participation of remote WLEs in dream content. WLEs which happened more than one month before the dream represent approximately one third of all the WLEs incorporated into dreams, and those that happened more than one year before the dream represent nearly 20% (Fig 4A and Table 3).

Regarding the dream lag effect (S3 Table) we found that the percentage of WLEs that happened 6 to 9 days prior to the dreams was not significantly different from the percentages of WLEs that happened 2 to 5 days or 10 to 14 days prior to the dreams. These results question the existence of a dream lag effect in our data.

A remarkable finding of this study is the significant interactions that we have found between temporal remoteness and each of importance, emotional intensity and valence (Fig 5). One can see on Fig 5A and 5B that, as we hypothesized, day residues were scored significantly lower than older WLEs incorporated into dreams on the importance and the emotional intensity scales. In addition the day residues were scored as less negative than the oldest incorporated experiences (Fig 5C). In other words, the oldest incorporated memories were found to be more emotionally intense, more important and more negative than day residues. Interestingly, this effect was also partially reported by Hartmann [18] who found that *"the relatively rare earlier waking experiences from more than 1 day before the dream were more likely to be important."* These results raise several questions with regards to the current hypotheses about dream function.

Implication for the hypothesis of a role of dreaming in emotional regulation

A current mainstream hypothesis proposes that dreams participate in emotional regulation, through an active moderation of waking life affects [27,28,37–39]. If so, one may expect 1) that dreams incorporate more emotional experiences than non-emotional experiences, 2) that the majority of incorporated WLEs have a negative valence, 3) that the most negative WLEs incorporated into dream date from recently before the dream. Our data do not verify the first prediction since 73% of the WLEs incorporated into dreams were rated as feebly or moderately emotionally intense. The second prediction is not verified either since 72% of the WLEs incorporated into dreams were neutral or positive. This result is coherent with previous ones showing that the average valence of WLEs incorporated into dreams is positive and not significantly different from that of WLEs not incorporated into dreams [10]. Finally, the third prediction is also overruled by our results since we found that the most negative WLEs incorporated into dreams were also the oldest ones. A precaution needs however to be taken regarding this result since it may be at least partly explained by the relatively rare frequency of very negative events in the lives of our participants (young healthy French students) and by the short duration of the study (7 days). Given that our results did not support the 3 above predictions, they may, as a consequence, be interpreted against a role of dreaming in emotional regulation. However an alternative interpretation could be that our predictions were inadequate and that dreaming may participate in emotional regulation through another mechanism.

Interestingly, although 45% of the WLEs incorporated into dreams had a positive valence, 40% of dreams were found to have a negative emotional tone. Even more interesting, we found that in average, for positive and negative WLEs, the emotional tone of the dreamt version of the WLE was rated as less intense than its original version (Fig 1A). Positive WLEs were less positive in the dream, negative WLEs were less negative in the dream and neutral WLEs remained neutral in the dream. Dreams seem thus to attenuate the emotional intensity of emotional memories and somehow modulate their emotional tone towards a more neutral one. This effect cannot be explained by a general effect of moderation of emotional intensity in dreams since the range of the emotional gradation of the dream content was maximum (range: 1–10). It is also important to note that participants rated the emotional valence of the original WLE and its dreamt version at the same time, the intensity difference cannot thus be explained

by a delay between the two notations. The very significant correlation between the emotional grades of the original WLEs and the emotional grades of the dreamt WLEs further shows that the dreams linearly decrease the emotional intensity of WLEs towards neutrality (Fig 1B). The dreams even seem to normalize the distribution of emotional grades, since the distribution of the grades of the original WLEs is dissymmetric (higher frequency of very positive than very negative WLEs, Fig 1B) whereas the distribution of the grades of the dreamt version is not. Our results suggest that dreams participate to emotional regulation through a relative neutralization of the emotional intensity of both negative and positive WLEs incorporated into dreams. The gradation of similarity between the original version and the dreamt version of the WLEs shows that the original WLEs are recognizable but transformed (average gradation ~ 6/10, Fig 3). The dream seems thus to keep the WLE recognizable and to also modify it (e.g. changing the context, the plot) just enough to diminish its emotional intensity. This mechanism may have a significant impact since the majority of the WLEs incorporated into dreams are important for the dreamer, a lot are of high emotional intensity (mean percentage of WLEs with an emotional rating > 8 or $< 3 = 31.5 \pm 23.7\%$) and a significant proportion are concerns (S2 Fig) of the daily life (e.g. work-, relatives-, love- related, S1 Fig). These findings are the first strong experimental arguments in favor of the emotional regulation hypothesis of dreaming, and are consistent with the numerous experimental results showing a modulation of affective neural systems and the (re)processing of recent emotional experiences during sleep [40,41]. Interestingly, our results suggest that the mechanism by which the emotional regulation is made during dreaming does not require that the dream is recalled to be efficient i.e. they suggest that whether or not the dream is recalled, the dreamt WLE is experienced with diminished emotional intensity.

Implication for the hypothesis of a role of dreaming in memory consolidation

Some researchers have suggested that dreaming reflects the physiological process of consolidating novel memories and assimilating them into a large memory network [29–31,42]. One proposed mechanism is that emotional intensity is the parameter triggering the selection of memories for consolidation into long term memory [9,43]. In our data, the most emotionally intense experiences incorporated into dreams were the oldest ones and day residues were rather trivial (with low scores of importance and emotional intensity). This result does not really fit with the idea of emotional intensity tagging the recent memory traces to be consolidated during sleep. In addition the WLEs incorporated into dreams were scored as rather familiar, and they were rarely repeatedly incorporated into dreams across the week. This result comes against the hypothesis that dreaming consolidates novel memory traces. An alternative hypothesis might be that dream content reflects the physiological down-regulation of recent useless memories [44,45]. This would explain the great proportion of day residues of low importance and low emotional intensity in dream reports. In the light of the above discussion, the link between dreams and memory consolidation is still unclear and would need further testing. Notably, the role of mundane day residues would need to be better understood and taken into account in a memory consolidation model of dreaming.

Conclusion

Important contributions of this study are to provide significant arguments in favor of the emotional regulation hypothesis of dreaming and to show the importance of day residues in dream content and their tendency to be mundane. In addition, our results clearly show that dreams mix various and opposite elements of waking life which are all incorporated in significant

proportions, i.e. recent and old, emotionally loaded and emotionless, positive and negative, rare and occurring daily, familiar and new, important and insignificant, concerns and non-concern issues.

A possible explanation of the heterogeneity and diversity of WLEs incorporated into dream content could be that dreams are an open window on the cognitive processes taking place during sleep. According to our current understanding, sleep is indeed involved in various cognitive processes such as memory consolidation, forgetting, emotional regulation, creativity and stimuli processing [40,41,44,46–50].

One may speculate according to our results and previous ones that sleep classifies and reprocesses mainly the information processed during the day before, while also processing the incoming information. Indeed a great part of the WLEs incorporated into dreams are from the day before the dream. Some of the remaining ones may have been considered as more remote because participants forgot that they thought about these WLEs the day before the dream (thoughts may be more difficult to recall than actions and perceptions) and the other remaining ones may be related to the day-residues, as already proposed by Marquardt [25]. Dreams would thus be the witnesses of sleep working at reprocessing what has been processed during the previous day, consolidating some information, incorporating it in a larger network of memories, forgetting other information, regulating emotions, promoting creativity and processing stimuli all together. If so, it would explain the great heterogeneity and lack of coherence of dream content mixing all together information to be erased or consolidated, information to be down-regulated at the emotional level and even old memories to be related to newly consolidated information. Emotion could in this case be the tag which decides how each items of information is processed during sleep. The strength of this proposition is to encompass and explain most of the characteristics of dream content and not only some of them, as it has been the case for previous hypotheses until now (see [5] for a review).

Limitations

This study aimed at investigating dream content obtained in naturalistic conditions which implied that participants slept at home, without electroencephalographic recordings, and that they had to report one dream per night in the morning. As a consequence we have investigated only dreams from the end of the sleep period, and our results apply only to this type of dream. Results may have been different if we had collected dreams from the beginning of the night. Indeed, some studies have shown that the remoteness of memory sources of dreams may increase from the beginning to the end of the night [13,14]. However other studies suggest a continuity in the thematic content of dreams across the night [51,52].

Given our protocol we do not know which sleep stage dreams occurred in. However, there is an approximately equal likelihood that morning awakenings occur in REM or N2 sleep [53], and the differences between the contents of N2 and REM sleep dreams become less marked in the second half of the night [54]. As a consequence, it seems likely that our results are valid for both N2 and REM sleep dreams of the end of the night.

However, as previous studies have shown that the mean percentage of episodic memory sources is significantly greater for NREM than for REM dreams whatever the time of the night [55], it would be worth testing in future studies whether the results presented here can be reproduced for NREM and REM dreams separately.

Note that the protocol was not designed to dissociate episodic, autobiographic and semantic memories among the memory sources of the dream [36,55,56]. This point would be worth investigating in future studies, carried out with explicit rules to be applied by external judges to classify type, emotionality and remoteness of dream memory sources.

Supporting information

S1 Table. Examples of waking life elements incorporated into dreams.
(DOCX)

S2 Table. Distribution of the score given to WLEs incorporated into dreams, for all WLEs (bold) and day-residues only.
(DOCX)

S3 Table. Characteristics of the WLEs incorporated into dreams that happened 6 to 9 days before the dreams (n = 36).
(DOCX)

S4 Table. Distribution (%) of mundane WLEs incorporated into dreams according to their temporal remoteness.
(DOCX)

S1 Fig. Concerns reported in the initial questionnaire. Concerns were distributed in 7 thematic categories. The number of concerns per categories are represented in pink. Red bars illustrate the percentage of concerns from one category that were incorporated into dreams during the 7-days experiment.
(TIF)

S2 Fig. Distribution of the scores for all the WLEs incorporated into dreams and day-residues only (see S2 Table for the figures).
(TIF)

S1 File. Supp_discussion.
(DOCX)

S2 File. Supp_results.
(DOCX)

Acknowledgments

We thank all the participants for having shared their dreams and for their morning time during the study. We thank Lancelot Hamelin for triggering fascinating interdisciplinary discussions about dreaming at the Villa Medicis in April 2017 in Rome leading to important ideas regarding the analysis of the data. Finally we thank the reviewers for their helpful comments on the previous version of the manuscript.

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References

1. Fosse MJ, Fosse R, Hobson JA, Stickgold RJ. Dreaming and episodic memory: a functional dissociation? J Cogn Neurosci. 2003; 15: 1–9. https://doi.org/10.1162/089892903321107774 PMID: 12590838
2. Nielsen TA, Stenstrom P. What are the memory sources of dreaming? Nature. 2005; 437: 1286–1289. https://doi.org/10.1038/nature04288 PMID: 16251954
3. Schredl M. Characteristics And Contents Of Dreams. In: McNamara AC and P, editor. International Review of Neurobiology. Academic Press; 2010. pp. 135–154. http://www.sciencedirect.com/science/article/pii/S0074774210920072 PMID: 20870066
4. Blagrove M, Pace-Schott EF. Trait And Neurobiological Correlates Of Individual Differences In Dream Recall And Dream Content. International Review of Neurobiology. Elsevier; 2010. pp. 155–180. http://linkinghub.elsevier.com/retrieve/pii/S0074774210920084 PMID: 20870067
5. Ruby P. Experimental Research on Dreaming: State of the Art and Neuropsychoanalytic Perspectives. Front Psychol. 2011; 2. https://doi.org/10.3389/fpsyg.2011.00286 PMID: 22121353
6. Schredl M, Hofmann F. Continuity between waking activities and dream activities. Conscious Cogn. 2003; 12: 298–308. https://doi.org/10.1016/S1053-8100(02)00072-7 PMID: 12763010
7. Botman HI, Crovitz HF. Dream reports and autobiographical memory. Imagin Cogn Personal. 1990; 9: 213–224.
8. Grenier J, Cappeliez P, St-Onge M, Vachon J, Vinette S, Roussy F, et al. Temporal references in dreams and autobiographical memory. Mem Cognit. 2005; 33: 280–288. PMID: 16028583
9. Malinowski J, Horton CL. Evidence for the preferential incorporation of emotional waking-life experiences into dreams. Dreaming. 2014; 24: 18–31. https://doi.org/10.1037/a0036017
10. Schredl M. Factors Affecting the Continuity Between Waking and Dreaming: Emotional Intensity and Emotional Tone of the Waking-Life Event. Sleep Hypn. 2006; 8: 1–5.
11. Schredl M. Continuity between waking life and dreaming: are all waking activities reflected equally often in dreams? Percept Mot Skills. 2000; 90: 844–846. https://doi.org/10.2466/pms.2000.90.3.844 PMID: 10883763
12. Schredl M, Kleinferchner P, Gell T. Dreaming and personality: Thick vs. thin boundaries. Dreaming. 1996; 6: 219–223.
13. Verdone P. Temporal Reference of Manifest Dream Content. Percept Mot Skills. 1965; 20: 1253–1268.
14. Stenstrom P, Fox K, Solomonova E, Nielsen T. Mentation during sleep onset theta bursts in a trained participant: A role for NREM stage 1 sleep in memory processing? Int J Dream Res. 2012; 5: 37–46.
15. Voss U, Tuin I, Schermelleh-Engel K, Hobson A. Waking and dreaming: Related but structurally independent. Dream reports of congenitally paraplegic and deaf-mute persons. Conscious Cogn. 2011; 20: 673–687. https://doi.org/10.1016/j.concog.2010.10.020 PMID: 21147002
16. Saurat M-T, Agbakou M, Attigui P, Golmard J-L, Arnulf I. Walking dreams in congenital and acquired paraplegia. Conscious Cogn. 2011; 20: 1425–1432. https://doi.org/10.1016/j.concog.2011.05.015 PMID: 21704532
17. Bekrater-Bodmann R, Schredl M, Diers M, Reinhard I, Foell J, Trojan J, et al. Post-Amputation Pain Is Associated with the Recall of an Impaired Body Representation in Dreams—Results from a Nation-Wide Survey on Limb Amputees. Longo M, editor. PLOS ONE. 2015; 10: e0119552. https://doi.org/10.1371/journal.pone.0119552 PMID: 25742626
18. Hartmann E. The day residue: Time distribution of waking events. Psychophysiology. 1968; 5: 222.
19. Strauch I, Meier B. Dem Traum auf der Spur: Zugang zur modernen Traumforschung. Aufl Bern Hans Huber. 2004;
20. Nielsen TA. Chronobiological features of dream production. Sleep Med Rev. 2004; 8: 403–424. https://doi.org/10.1016/j.smrv.2004.06.005 PMID: 15336239
21. Nielsen TA, Kuiken D, Alain G, Stenstrom P, Powell RA. Immediate and delayed incorporations of events into dreams: further replication and implications for dream function. J Sleep Res. 2004; 13: 327–336. https://doi.org/10.1111/j.1365-2869.2004.00421.x PMID: 15560767
22. Blagrove M, Fouquet NC, Henley-Einion JA, Pace-Schott EF, Davies AC, Neuschaffer JL, et al. Assessing the Dream-Lag Effect for REM and NREM Stage 2 Dreams. Tsakiris M, editor. PLoS ONE. 2011; 6: e26708. https://doi.org/10.1371/journal.pone.0026708 PMID: 22046336
23. Blagrove M, Henley-Einion J, Barnett A, Edwards D, Heidi Seage C. A replication of the 5–7day dream-lag effect with comparison of dreams to future events as control for baseline matching. Conscious Cogn. 2011; 20: 384–391. https://doi.org/10.1016/j.concog.2010.07.006 PMID: 20739193
24. Freud S. Die Traumdeutung. Leipzig und Wien: Deuticke; 1899 (English translation:The Interpretation of Dreams. Standard Edition, voll. 4–5. London: Hogarth Press; 1953).

25. Marquardt CJ, Bonato RA, Hoffmann RF. An empirical investigation into the day-residue and dream-lag effects. Dreaming. 1996; 6: 57–65.

26. Cavallero C. Dream sources, associative mechanisms, and temporal dimension. Sleep. 1987; 10: 78–83. PMID: 3563251

27. Cartwright RD. Dreams that work: The relation of dream incorporation to adaptation to stressful events. Dreaming. 1991; 1: 3–9.

28. Nielsen T, Levin R. Nightmares: a new neurocognitive model. Sleep Med Rev. 2007; 11: 295–310. https://doi.org/10.1016/j.smrv.2007.03.004 PMID: 17498981

29. Llewellyn S. Such stuff as dreams are made on? Elaborative encoding, the ancient art of memory, and the hippocampus. Behav Brain Sci. 2013; 36: 589–607. https://doi.org/10.1017/S0140525X12003135 PMID: 24304746

30. Wamsley EJ. Dreaming and Offline Memory Consolidation. Curr Neurol Neurosci Rep. 2014; 14: 433. https://doi.org/10.1007/s11910-013-0433-5 PMID: 24477388

31. Schredl M. Is Dreaming Related to Sleep-Dependent Memory Consolidation? In: Axmacher N. and Rasch B. (eds.), Cognitive Neuroscience of Memory Consolidation. Springer; 2017. pp. 173–182.

32. Hall CS, Van de Castle RL. The content analysis of dreams. New York: Appleton-Century-Crofts; 1966.

33. Jouvet M. Mémoire et 'cerveau dédoublé'au cours du rêve a propos de 2525 souvenirs de rêve. L'année Prat. 1979; 29: 27–32.

34. Nielsen TA, Powell RA. The day-residue and dream-lag effects: A literature review and limited replication of two temporal effects in dream formation. Dreaming. 1992; 2: 67–77.

35. Kramer M, Roth T, Arand D, Bonnet M. Waking and dreaming mentation: A test of their interrelationship. Neurosci Lett. 1981; 22: 83–86. PMID: 7219895

36. Malinowski JE, Horton CL. Memory sources of dreams: the incorporation of autobiographical rather than episodic experiences. J Sleep Res. 2014; 23: 441–447. https://doi.org/10.1111/jsr.12134 PMID: 24635722

37. Cartwright RD. The twenty-four hour mind: The role of sleep and dreaming in our emotional lives. Oxford University Press New York, NY; 2010.

38. Cartwright R, Luten A, Young M, Mercer P, Bears M. Role of REM sleep and dream affect in overnight mood regulation: a study of normal volunteers. Psychiatry Res. 1998; 81: 1–8. PMID: 9829645

39. Cartwright R, Agargun MY, Kirkby J, Friedman JK. Relation of dreams to waking concerns. Psychiatry Res. 2006; 141: 261–270. https://doi.org/10.1016/j.psychres.2005.05.013 PMID: 16497389

40. Walker MP, van der Helm E. Overnight therapy? The role of sleep in emotional brain processing. Psychol Bull. 2009; 135: 731–748. https://doi.org/10.1037/a0016570 PMID: 19702380

41. Perogamvros L, Schwartz S. The roles of the reward system in sleep and dreaming. Neurosci Biobehav Rev. 2012; 36: 1934–1951. https://doi.org/10.1016/j.neubiorev.2012.05.010 PMID: 22669078

42. Payne JD, Nadel L. Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol. Learn Mem. 2004; 11: 671–678. https://doi.org/10.1101/lm.77104 PMID: 15576884

43. Payne JD, Stickgold R, Swanberg K, Kensinger EA. Sleep preferentially enhances memory for emotional components of scenes. Psychol Sci. 2008; 19: 781–788. https://doi.org/10.1111/j.1467-9280.2008.02157.x PMID: 18816285

44. Hardt O, Nader K, Nadel L. Decay happens: the role of active forgetting in memory. Trends Cogn Sci. 2013; 17: 111–120. https://doi.org/10.1016/j.tics.2013.01.001 PMID: 23369831

45. Tononi G, Cirelli C. Sleep and the Price of Plasticity: From Synaptic and Cellular Homeostasis to Memory Consolidation and Integration. Neuron. 2014; 81: 12–34. https://doi.org/10.1016/j.neuron.2013.12.025 PMID: 24411729

46. Rauchs G, Desgranges B, Foret J, Eustache F. The relationships between memory systems and sleep stages. J Sleep Res. 2005; 14: 123–140. https://doi.org/10.1111/j.1365-2869.2005.00450.x PMID: 15910510

47. Maquet P, Ruby P. Psychology: insight and the sleep committee. Nature. 2004; 427: 304–305. https://doi.org/10.1038/427304a PMID: 14737153

48. Cai DJ, Mednick SA, Harrison EM, Kanady JC, Mednick SC. REM, not incubation, improves creativity by priming associative networks. Proc Natl Acad Sci. 2009; 106: 10130–10134. https://doi.org/10.1073/pnas.0900271106 PMID: 19506253

49. Eichenlaub J-B, Bertrand O, Morlet D, Ruby P. Brain Reactivity Differentiates Subjects with High and Low Dream Recall Frequencies during Both Sleep and Wakefulness. Cereb Cortex. 2014; 24: 1206–1215. https://doi.org/10.1093/cercor/bhs388 PMID: 23283685

50. Perrin F, Bastuji H, Garcia-Larrea L. Detection of verbal discordances during sleep. Neuroreport. 2002; 13: 1345–1349. PMID: 12151800

51. Cipolli C, Baroncini P, Fagioli I, Fumai A. The thematic continuity of mental sleep experience in the same night. Sleep. 1987; 10: 473–479. PMID: 3685755

52. Cipolli C, Fagioli I, Baroncini P, Fumai A, Marchió B, Sancini M. The thematic continuity of mental experiences in REM and NREM sleep. Int J Psychophysiol. 1988; 6: 307–313. https://doi.org/10.1016/0167-8760(88)90018-9 PMID: 3225207

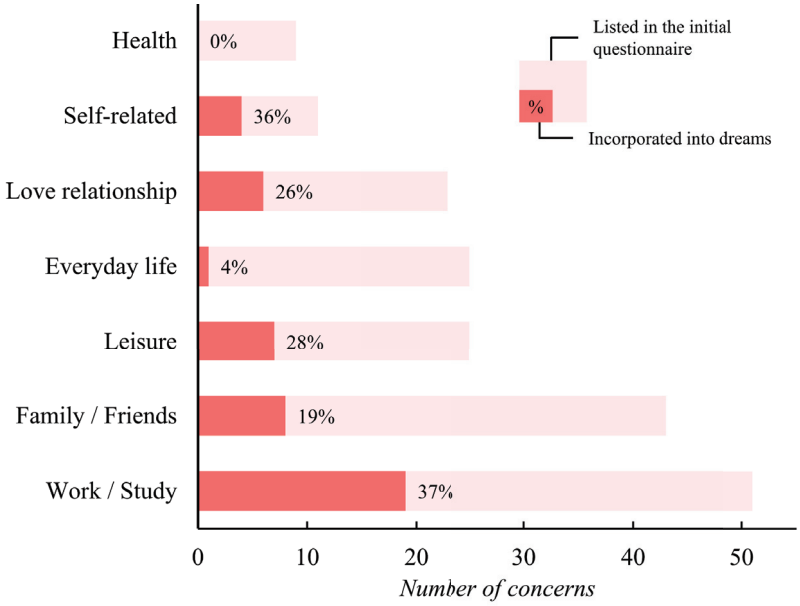
53. Webb WB, Kersey J. Recall of dreams and the probability of stage 1-REM sleep. Percept Mot Skills. 1967; 24: 627–630. https://doi.org/10.2466/pms.1967.24.2.627 PMID: 6040240

54. Pivik T, Foulkes D. NREM mentation: relation to personality, orientation time, and time of night. J Consult Clin Psychol. 1968; 32: 144. https://doi.org/10.1037/h0025489 PMID: 5654189

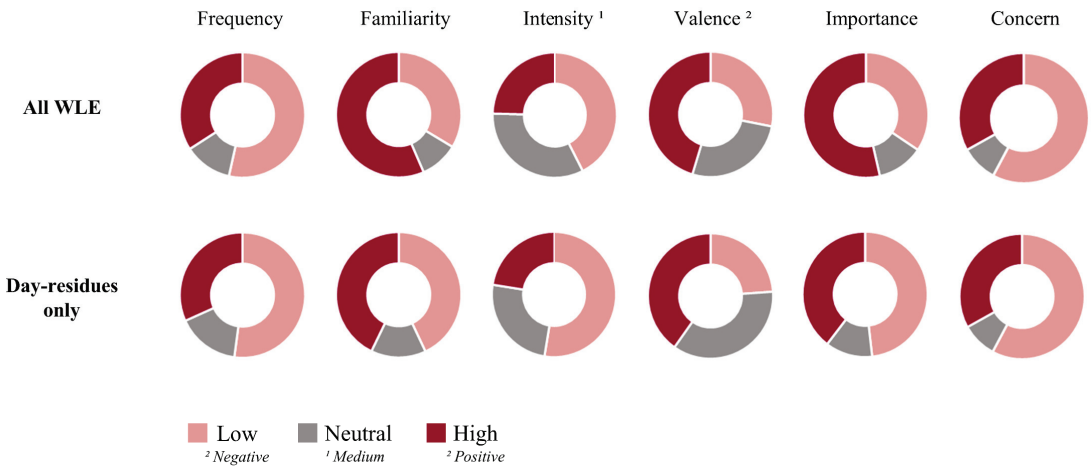
55. Baylor G, Cavallero C. Memory Sources Associated with REM and NREM Dream Reports Throughout the Night: A New Look at the Data. Sleep. 2001; 24: 165–170. PMID: 11247052

56. Cicogna P, Cavallero C, Bosinelli M. Differential access to memory traces in the production of mental experience. Int J Psychophysiol. 1986; 4: 209–216. https://doi.org/10.1016/0167-8760(86)90017-6 PMID: 3793564

Supplementary materials



S1 Fig. Concerns reported in the initial questionnaire. Concerns were distributed in 7 thematic categories. The number of concerns per categories are represented in pink. Red bars illustrate the percentage of concerns from one category that were incorporated into dreams during the 7-days experiment.



S2 Fig. Distribution of the scores for all the WLEs incorporated into dreams and day-residues only (see S2 Table for the figures).

S1 Table. Examples of waking life elements incorporated into dreams.

Old, important and emotionally negative WLE

S1 | Valence = 2 ; Importance = 7 ; Dream valence = 5
Dream report: *"I am with an ex-girlfriend in my dream, we get along together very well"*
WLE description: *"We broke up several years ago in a difficult situation and none of us had given sign of life since."*

S29 | Valence = 2 ; Importance = 10 ; Dream valence = 1
Dream report: *"I descend into another world to pick up my aunt and realize that it is not possible - I feel a deep anguish and I am cold"*
WLE description: *"My aunt passed away 3 months ago and I miss her terribly. I know she will not come back, but some days I still hope it will happen."*

S35 | Valence = 2 ; Importance = 10 ; Dream valence = 3
Dream report: *"In my dream I saw my ex-girlfriend and her new partner. Suddenly, I felt really angry and started to push them down the stairs. They fell down and I shout at them."*
WLE Description: *"Three years ago I bumped into them in the streets and was particularly unkind to them."*

Old, important and emotionally positive WLE

S6 | Valence = 10 ; Importance = 10 ; Dream Valence = 10
Dream report: *"I was comforting two twins sisters that just got fired from the religious association I was working in several years ago."*
WLE description: *"It reminded me of the responsibility I used to have there."*

S19 | Valence = 10 ; Importance = 10 ; Dream Valence = 10
Dream report: *"I am working at my shop with my employee and my friend F* with whom I get along very well"*
WLE description: *"F* is an old school friend. At the time we were always together and for me he was almost part of the family"*

Mundane and feebly emotional day-residues

S3 | Valence = 5 ; Importance = 1 ; Dream valence = 6
Dream report: *"I was in an unknown house with two friends and a talking Koala."*
WLE description: *"It reminded me of the talking raccoon in the movie Guardian of the Galaxy that I watched the day before."*

S15 | Valence = 5 ; Importance = 1 ; Dream valence = 5
Dream report: *"I am in the supermarket looking for a dishwasher."*
WLE description: *"Yesterday I saw on the internet a picture of the proper way to load dishes in a dishwasher."*

S25 | Valence = 5 ; Importance = 1 ; Dream valence = 5
Dream report: *"In my dream I was creating magical creatures in order to destroy something"*.

WLE description: *"The creatures reminded me of the ones in the video game I played for several hours the day before."*

S38 | Valence = 5 ; Importance = 1 ; Dream valence = 5
Dream report: *"I was in a house with a small swimming-pool."*
WLE description: *"The swimming-pool was very similar to the one I saw yesterday in a park. The shape, depth and color were the same."*

Important and emotionally intense day-residues
S40 | Valence = 1 ; Importance = 10 ; Dream Valence = 1
Dream report: *"I was at work, struggling to fix several mistakes made by my boss. At the end of the day, I took the blame and got fired."*
WLE description: *"Yesterday there was a problem in my company after a client requested a sudden change."*

S33 | Valence = 2 ; Importance = 8 ; Dream Valence = 4
Dream report: *"My father offers me a sewing machine. I realize that I already have this model."*
WLE Description: *"My father is a recurring concern and we talked yesterday about his health. Also, yesterday I thought that I should sew this week-end."*

S29 | Valence = 10 ; Importance = 10 ; Dream Valence = 10
Dream report: *"I was talking to several persons at the university and each time I tried to say only positive things in order to make them happy."*
WLE description: *"Yesterday I thought that I should really stop being always negative and doubtful. In my dream it felt as if I put into practice this."*

S19 | Valence = 10 ; Importance = 10 ; Dream Valence = 10
Dream report: *"In my dream there was this cartoon character that I really like."*
WLE description: *"Yesterday I watched a really good new cartoon movie."*

Supplementary results: distribution of the scores

For each characteristic, the percentage of WLEs with a rating inferior, equal and superior to 5 was computed. A visual inspection of S2 Table shows that if we compare the distribution of the scores for all the WLEs incorporated into dreams and day-residues only, the distributions differ for familiarity, importance, and emotional valence and intensity. As compared to all WLEs incorporated into dreams, for day-residues only we observed a greater percentage of WLEs scored as feebly familiar, emotionally neutral, feebly important and feebly emotionally intense (S2 Fig).

S2 Table. Distribution of the score given to WLEs incorporated into dreams, for all WLEs (bold) and day-residues only. For emotional valence, Low = negative and High = positive. Emotional intensity is rated on a 1-to-4 scale (see Methods). Neutral = medium emotional intensity.

Characteristics	Low (%)	Neutral (%)	High (%)
Frequency (Rare – Daily)	**53.5 ± 22.3**	**12.4 ± 11.4**	**34.2 ± 24.2**
	52.1 ± 33	16.2 ± 25	31.7 ± 35
Familiarity (New – Familiar)	**33.6 ± 21.7**	**9.9 ± 14.5**	**56.5 ± 23**
	43 ± 37	14.2 ± 25	42.9 ± 37
Emotional valence (Neg. – Pos.)	**28.1 ± 20.9**	**26.6 ± 25.3**	**45.3 ± 26.2**
	23.9 ± 28	35.9 ± 34	40.2 ± 37
Importance	**34.4 ± 23.6**	**12 ± 12.7**	**53.5 ± 22.9**
	48.2 ± 37	12.2 ± 25	39.6 ± 38
Current concern	**56.6 ± 25.1**	**9 ± 13.8**	**34.4 ± 21.6**
	57.8 ± 37	9.1 ± 21	33.1 ± 33
Emotional intensity	**42.5 ± 25.4**	**32.9 ± 24.4**	**24.6 ± 23.4**
	52.6 ± 38	24.9 ± 32	22.5 ± 33

Supplementary discussion

The concern-related dimension of WLEs incorporated into the dreams According to the dreamers' scoring, the WLEs incorporated into dreams are not predominantly concern-related (Table 2). This result is coherent with the experimenters' assessment of the incorporation of current concerns into dreams taking the initial questionnaire into account. We found that in average 23% of the dream reports of each subjects incorporated a current concern. Reciprocally, on average for each subject only 25% of the concerns listed in the initial questionnaire were incorporated into a dream report during the 7 days of the experiment. Previous studies reported a larger percentage of dreams in relation with the

S3 Table. Characteristics of the WLEs incorporated into dreams that happened 6 to 9 days before the dreams (n=36). Except for emotional intensity, Neutral (%) refers to the percentage of WLEs with a score of 5. For emotional valence, Low = negative and High = positive. Emotional intensity is rated on a 1-to-4 scale (see Methods). Neutral = medium emotional intensity.

Characteristics	Mean Score	Low (%)	Neutral (%)	High (%)
Frequency (Rare – Daily)	4.1 ± 2.9	49.3 ± 48	18.6 ± 37	32.1 ± 42
Familiarity (New – Familiar)	5.2 ± 3.0	38.1 ± 43	25.2 ± 42	36.7 ± 42
Emotional valence (Neg. – Pos.)	5.4 ± 2.1	24.6 ± 36	22.5 ± 39	52.9 ± 46
Importance	5.7 ± 3.0	21.9 ± 34	19.5 ± 31	58.6 ± 39
Current concern	5.1 ± 3.4	39.3 ± 40	8.6 ± 27	52.1 ± 40
Emotional intensity	1.4 ± 1.3	56.1 ± 46	31.8 ± 41	12.1 ± 29

S4 Table. Distribution (%) of mundane WLEs incorporated into dreams according to their temporal remoteness. Each time category mutually excludes the previous ones (e.g. month before excludes day before the dream).

	Day before	Month before	More than a month	Not dated
Importance < 5, n=196	43.4	19.9	20.4	16.3
Importance = 1, n=96	52.1	17.7	17.7	12.5
Importance = 1 and emotional intensity = Low, n=70	60	20	8	12

dreamers' current concerns. For example, Schwartz and Maquet (2002), who used an automatic analysis of words on 1770 dreams of the first author found that 35% of the dreams were considered related to current concerns. The great heterogeneity between studies may come from different definitions of the term *concerns* and from different methods (if close friends and family were considered as concerns, the % of dreams related to concerns would be much higher in our study). Our results show that when listed a priori (i.e. before dreams content analysis), current concerns are not as represented in dreams as would be expected from the dominant hypothesis saying that *"much of it tends to revolve around a relative handful of personal concerns"* (Domhoff and Schneider, 2008b).

The characters and places incorporated into the dreams At least one external character was reported for nearly all remembered dreams. The mean number of characters per dream was slightly above with the norm (2.6 in Hall and Van de Castle, 1966). This results is most likely due to several methodology differences: in Hall & Van de Castle system, rating was done a posteriori by an external judge, who would consider groups of characters not individually named (e.g. a couple, a group of 3 children) as one character. In our study, the number of characters was assessed by the dreamer and considering each characters of the dreams as one individual. Regarding familiar existing persons (Fig 2) our results even if a little higher, are also coherent with the norm (familiar characters, 45% in males and 58% in females in Hall and Van de Castle, 1966). However, in our data close family and friends appeared to be more represented than in the normative study (family, 9% in males, 14% in females; relatives, 2% in males, 4% in females in Hall and Van de Castle, 1966)

Regarding places, in our study participants reported nearly twice as much places (2.3 ± 1.5) as in the norm (average n° of settings per dream, 1.3 in Hall and Van de Castle, 1966) and nearly half of these places were unknown (Fig 2) which is far more than the norm (unfamiliar, 14% Hall and Van de Castle, 1966). Finally, we observed a little less familiar places (familiar, 33% Hall and Van de Castle, 1966) and a little less mixed places (questionable, 40% Hall and Van de Castle, 1966). It is important to keep in mind that in our study the dreamers rated their own dreams while in Hall and Van de Castle (1966) an external rating was used. The two methods may yield divergent results (Sikka et al., 2014).

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Study 6. An open-source software for sleep reading and analysis

frontiers in Neuroinformatics

METHODS
published: 21 September 2017
doi: 10.3389/fninf.2017.00060

Sleep: An Open-Source Python Software for Visualization, Analysis, and Staging of Sleep Data

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OPEN ACCESS

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Received: *03 July 2017*
Accepted: *06 September 2017*
Published: *21 September 2017*

Citation:
Combrisson E, Vallat R, Eichenlaub J-B, O'Reilly C, Lajnef T, Guillot A, Ruby PM and Jerbi K (2017) Sleep: An Open-Source Python Software for Visualization, Analysis, and Staging of Sleep Data. Front. Neuroinform. 11:60. doi: 10.3389/fninf.2017.00060

We introduce Sleep, a new Python open-source graphical user interface (GUI) dedicated to visualization, scoring and analyses of sleep data. Among its most prominent features are: (1) Dynamic display of polysomnographic data, spectrogram, hypnogram and topographic maps with several customizable parameters, (2) Implementation of several automatic detection of sleep features such as spindles, K-complexes, slow waves, and rapid eye movements (REM), (3) Implementation of practical signal processing tools such as re-referencing or filtering, and (4) Display of main descriptive statistics including publication-ready tables and figures. The software package supports loading and reading raw EEG data from standard file formats such as European Data Format, in addition to a range of commercial data formats. Most importantly, Sleep is built on top of the VisPy library, which provides GPU-based fast and high-level visualization. As a result, it is capable of efficiently handling and displaying large sleep datasets. Sleep is freely available (http://visbrain.org/sleep) and comes with sample datasets and an extensive documentation. Novel functionalities will continue to be added and open-science community efforts are expected to enhance the capacities of this module.

Keywords: polysomnography, electroencephalography, automatic detection, graphoelements, hypnogram, scoring, graphical user interface, opengl

INTRODUCTION

Polysomnography provides a comprehensive recording of the major physiological changes associated with sleep and is hence the gold standard for modern sleep analysis, both in research and clinical settings. At its simplest, it consists of monitoring at least 2 electroencephalogram (EEG), an electro-oculogram (EOG), and a submental electromyogram (EMG), providing sufficient information to identify sleep stages (sleep scoring) according to standard international established guidelines. A first set of rules were published by Rechtschaffen and Kales (1968) and proposed to divide sleep into 5 stages with distinct electrophysiological properties, named rapid-eye movement (REM) and non-REM (NREM) stages 1, 2, 3, 4. This nomenclature was updated in 2007 by the American Academy of Sleep Medicine (Iber et al., 2007) and sleep stage 3 and 4

have been merged into stage N3. In humans, a normal night of sleep consists of a repetition of four or five cycles in which sleep stages tend to follow each other in a particular order. Sleep staging is generally done visually by inspecting consecutive polysomnographic segments of 30 s. It results in a hypnogram which represents the succession of sleep stages across time. Apart from being time-consuming, visual sleep scoring is subject to both inter and intra-rater variability and is thus far from being optimal. By contrast, automatic sleep scoring has the advantage of being fast, reproducible and with generally good agreement with visual scoring (Berthomier et al., 2007; Lajnef et al., 2015a), yet its usage is far from being widespread and most sleep laboratories still rely on visual scoring, using either commercial softwares or in-house packages. In many cases, these software tools come with their own data and hypnogram file formats, and this heterogeneity can represent a substantial obstacle for sharing of sleep data across laboratories or clinics. Some of the very few existing open sources graphical user interface (GUI) for reading and scoring sleep include Phypno[1], written in Python, and the MATLAB-based toolboxes sleepSMG[2] or SpiSOP[3].

With this in mind, we developed *Sleep*, an intuitive and efficient open-source GUI dedicated to the visualization of polysomnographic recordings and scoring of sleep stages. *Sleep* supports a range of data file formats and provides several scoring aid including the detection of essential features of NREM and REM sleep such as spindles, K-complexes, slow waves, and REM. *Sleep* was written in Python, an easy-to-learn high-level programming language widely used in the scientific community. We developed *Sleep* on top of VisPy[4] (Campagnola et al., 2015), a Python scientific library based on OpenGL which offloads graphics rendering to the graphics processing unit (GPU) in order to provide fast and high-quality visualization, even under heavy loads as is the case with large dataset. *Sleep* therefore benefits from the high performances provided by VisPy alongside Python's inherent qualities such as its portability and ease of use.

METHODS

Scientific visualization often consists of finding the best possible way to explore the data and to illustrate results in an intuitive and straightforward manner. The huge variety of neuroscientific data types and acquisition modalities naturally requires a wide range of specific visualization tools. Ideally, software packages needed for the various applications should be free and capable of handling several types of brain data recordings. In this context, we are currently developing a Python package we called Visbrain[5] distributed under a BSD license, which provides and centralizes a number of useful brain data visualization utilities. Given the lack of software solutions that wrap together a portable and user-friendly interface for polysomnographic data visualization and edition, we set out to develop an open-source module (included within the Visbrain package) and named Sleep.

The Choice of Python and the Project Vision

The choice of the programming language naturally turned to Python as this high-level and open-source language benefits from many libraries, an extensive documentation and a dynamic community. From data analysis to the production of high-definition paper figures, Python offers all the tools needed by scientists, with the comfort of a clean and easy to read syntax. *Sleep* is a pure Python software built on top of NumPy, VisPy, PyQt4[6] and uses a limited number of functions from SciPy and Matplotlib. Thanks to the Python portability, the software can be installed and used on any platform. One of the initial objectives of the project was to provide a user-friendly and intuitive interface capable of loading and displaying large sleep dataset. To this end, we paid a particular attention to avoid deep data copy and display only what is necessary. Therefore, even very large recordings with a consequent number of channels can be handled by *Sleep* on any modern laptop with snappy GUI response. From a programming perspective, we did our best to provide a clean, commented and high-quality code, with a NumPy style documentation and using static analysis tool, as recommended by PEP 8. *Sleep* is hosted on GitHub and we encourage Python programmers and sleep scientists to collaborate in order to collectively improve this software by extending its functionalities and data compatibilities.

Hardware Accelerated Graphics

In addition to ergonomic considerations and providing a portable interface, a further important goal was to use a plotting library which would allow our *Sleep* module to support and process large sleep data. Using Matplotlib was an option we considered, but although it is particularly convenient to produce publication quality figures, it is not the best option when it comes to plotting and interacting in real-time. In contrast, VisPy is a scientific visualization library based on NumPy and OpenGL and was primarily designed to provide both high performances with real-time interactions and publication quality figures. VisPy provides a bridge between the intuitive Python syntax and modern shader-based OpenGL pipeline allowing the graphical rendering cost to be offloaded to the GPU. This package has been well-designed and is built on four levels, from a Matplotlib oriented one to the lowest-level (closer to OpenGL) which makes it more flexible and efficient at the cost of a potentially slower learning curve. Because all *Sleep* graphical elements are primitive 2D objects (line, points, and images) it was not a necessity to go down to the lowest level of VisPy (vispy.gloo). Indeed, all required objects were already implemented into the Visual library. Hence, any modern computer equipped with a GPU should see the benefits of the hardware accelerated graphics implemented in *Sleep*.

[1]https://github.com/gpiantoni/phypno
[2]http://sleepsmg.sourceforge.net/
[3]http://spisop.org/
[4]http://vispy.org/
[5]https://github.com/EtienneCmb/visbrain
[6]https://riverbankcomputing.com/software/pyqt/intro

Portable GUI through Python

Currently, among the major cross-platform GUI toolkits that interface with Python, wxWidgets[7] (wxPython), Tcl/Tk[8] (TkInter), and Qt[9] (PyQt/PySide) are probably the most known and used. We chose PyQt which is a python binding for the C++ Qt toolkit, and we used Qt Designer to design the GUI.

Taken together, VisPy provides high-performance rendering graphics that are well-integrated in a portable, modular and responsive Qt GUI using Python PyQt package. The use of this library is therefore one of the major strengths of this open-source module, and is particularly important when it comes to handling large multi-dimensional brain data, such as full-night sleep EEG recordings.

Automatic Events Detection

One of the main objectives of *Sleep* was to provide a complete and easy-to-use interface for analyzing and staging sleep data. To this purpose, we implemented several algorithms for the automatic detection of sleep features, and embedded them within the software ("Detection" panels). This includes detection of spindles, K-complexes, slow waves, rapid-eye movements, muscle twitches, and signal peaks. With the exception of the latter, all these features are often used as landmarks of specific sleep stages and can be very helpful to guide experts in their identification of specific sleep stages within a period of sleep, i.e., sleep scoring or sleep staging (see **Figure 1**). The main characteristics of each of these features are summarized below.

- Sleep spindles refer to burst of 12–14 Hz waves predominant over central scalp electrodes and lasting between 0.5 and 2 s (Rechtschaffen and Kales, 1968). These bursts of oscillatory activity have been known as a defining characteristics of N2 sleep (although there is an increasing number of studies that analyze spindles in N3 stages). Several automatic spindle detection algorithms have been developed in recent years (reviews in Devuyst et al., 2011; Warby et al., 2014). The algorithm implemented in *Sleep* is based on a wavelet transform followed by amplitude threshold and duration criteria. The default algorithm parameters (duration, frequency, and power threshold) were chosen according to previously published detection methods (Devuyst et al., 2011). The consecutive steps of the spindles automatic detection algorithm implemented in *Sleep* are detailed in **Figure 2**.
- K-complexes are defined as sharp negative waves followed by a positive component, prominent over frontal scalp electrodes and lasting more than 0.5 s. Along with spindles, they constitute one landmark of N2 sleep. Briefly, the algorithm implemented in *Sleep* comprises the following steps: (1) bandpass filtering of the signal in the delta frequency band (2) amplitude thresholding of the Teager-Keaser Energy Operator (Erdamar et al., 2012; Parekh et al., 2015) of the filtered signal (3) computation of the probability of detecting true K-complexes based on morphological criteria (duration and amplitude) and the presence of spindles in the vicinity.
- Slow-waves (or delta waves) are high-amplitude ($>75\,\mu V$) and low-frequency (<3 Hz) oscillations that are present during the deepest NREM sleep stage, i.e., N3 sleep. According to the standard international guidelines, N3 sleep is defined by the presence of 20% or more slow waves in a given epoch. As period of N3 sleep are marked by a high delta power and low power in the other frequency bands (theta, alpha, beta), the algorithm implemented in *Sleep* is based on a thresholding of the delta relative band power.
- As its name suggests, REM sleep is characterized by rapid eye movements easily observable on the EOG channels. They consist of conjugate, irregular and sharply peaked eye movements, similar to some extent to those exhibited during wakefulness. The algorithm implemented for the detection of REMs is detailed elsewhere (Vallat et al., 2017).
- Another fundamental aspect of REM sleep is its muscle atonia, as revealed by a low EMG activity. However, some transient muscle activity or muscle twitchings (MTs) can also be observed. These short irregular bursts of EMG activity are superimposed on the background of low EMG activity. The automatic detection of MTs is based on a thresholding of the Morlet's complex decomposition of the EMG signal followed by morphological criteria (duration and amplitude).
- Finally, *Sleep* implements a signal peak detection algorithm that is useful for example to calculate the heart rate, provided that an ECG channel is present. The algorithm implemented in *Sleep* searches for the highest point around which there are points lower by a certain duration on both sides[10].

Altogether, the set of detectors implemented in our software offers a valuable help for scoring sleep stages through the identification of the main features of each sleep stages. Detections can also be used for a more in-depth analysis of the sleep microstructure (e.g., Vallat et al., 2017). Comparisons of performances between our detections and visual scoring are reported for K-complexes and spindles in the Results section.

Signal Processing Tools

In addition to the automatic detections presented above, *Sleep* also provides a wide range of basic and advanced signal processing tools such as signal demeaning, detrending, and a filtering. The latter can be done either with Butterworth or Bessel filters and four filter designs are currently available: lowpass, highpass, bandpass, or bandstop. Importantly, further information can be extracted from the Morlet's wavelet complex decomposition (Tallon-Baudry et al., 1996) such as time-resolved and band-specific amplitude, power or phase. Critically, each one of these signal processing tools are reversible and can therefore be activated and deactivated without altering the original data and without any memory-intensive data copy. Finally, loaded data can be re-referenced directly from the interface by either re-referencing to a selected single channel or common-average (frequently used for scalp EEG datasets) or by using bipolarization, which consists of subtracting neural activity

[7]https://www.wxwidgets.org/
[8]http://www.tcl.tk/
[9]https://www.qt.io/
[10]https://github.com/DiamondLightSource/auto_tomo_calibration-experimental/blob/master/old_code_scripts/peak_detect.py

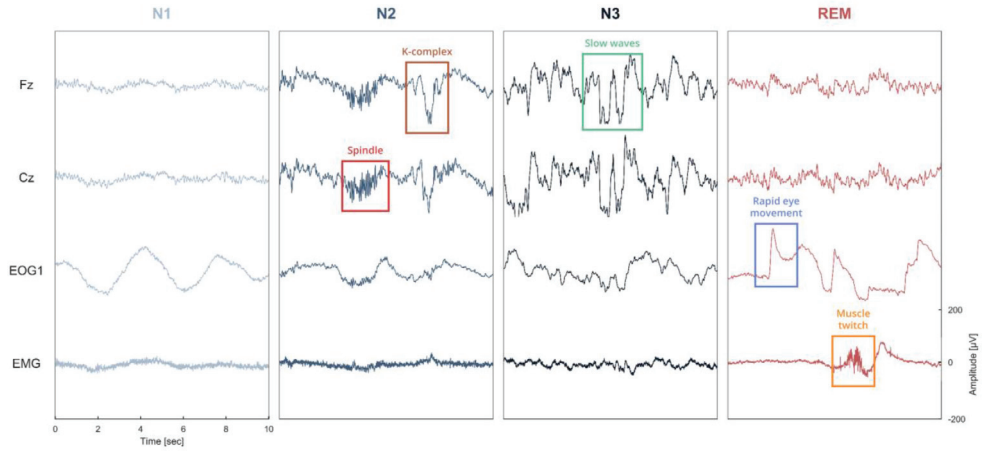

FIGURE 1 | Illustration of the different sleep features observed in a polysomnographic recording of one individual. To see examples of automatic detection actually performed by our software, see **Figure 4**. Spindles and K-complexes are landmarks of N2 sleep. Slow waves are present during N3 sleep (sometimes referred to as slow wave sleep). Rapid eye movements, observed in the EOG channel, and muscle twitches, observed on the EMG channel, are two essential features of rapid eye movement (REM) sleep.

from consecutives sites (classically used in intracranial EEG, see Jerbi et al., 2009).

Documentation and Examples

Sleep comes with a detailed step-by-step documentation, built with Sphinx[11] and hosted on GitHub[12]. This documentation include a description of the graphical components and the main functionalities of the software. A PDF version of the documentation can also be downloaded from the "Help" contextual menu of the software. We also provide anonymized and free-to-use sample datasets, including the corresponding loading scripts. This will help users test the *Sleep* module and get familiar with its functionalities before trying it on their own data. Finally, we also implemented an interactive documentation using the tooltips provided by PyQt to describe each element of the interface.

RESULTS

In the following we overview the current GUI and software functionalities of Sleep and provide details on hypnogram editing and event detection validation results.

Graphical User Interface

The *Sleep* GUI is currently subdivided into six distinct components (**Figure 3**): (*1*) settings panel, (*2*) navigation bar, (*3*) hypnogram, (*4*) electrophysiological time series, (*5*) spectrogram canvas, (*6*) topographic map. As the user interface is built up in a modular way, each of these components can be hidden or displayed, depending on whether the user prefers a light or fully-featured interface. Using the contextual menu, users can save and subsequently load the current display properties in order to easily retrieve and continue working on a previous session.

Settings Panel and Navigation Bar

All controls and properties are grouped in a settings panel. This panel is subdivided into five thematic tabs:

- Panels: manage the visibility and properties of each plotted canvas.
- Tools: bundle of signal processing tools.
- Infos: basic informations of the current recording (name, sampling rate) and sleep statistics computed using the hypnogram (sleep stage duration, latency, etc.). Note that the statistics can be exported in *.csv or *.txt file and are automatically updated when the hypnogram is edited.
- Scoring: scoring table that can be used to inspect and edit where each stage starts and end. This panel represents one of the three methods available within the software to edit the hypnogram (see hypnogram edition section) and may be useful for example to score long periods of continuous and homogenous sleep by just providing the starting and ending times.
- Detection: perform and manage the automatic detection of several sleep features.
- Annotations: add notes or comments to specific time points within the recordings. Annotations can be saved and loaded using the File contextual menu or can be passed as an input parameter. Each annotation is then referenced in a table comprising the start and end time (in seconds) and the corresponding text. Selecting a row in the table centers the main window around it. This latter feature enables a quick access to annotated events for a faster navigation. Annotated events are also identified in the time axis as a green triangle.

[11] http://www.sphinx-doc.org/en/stable/
[12] http://visbrain.org/sleep.html

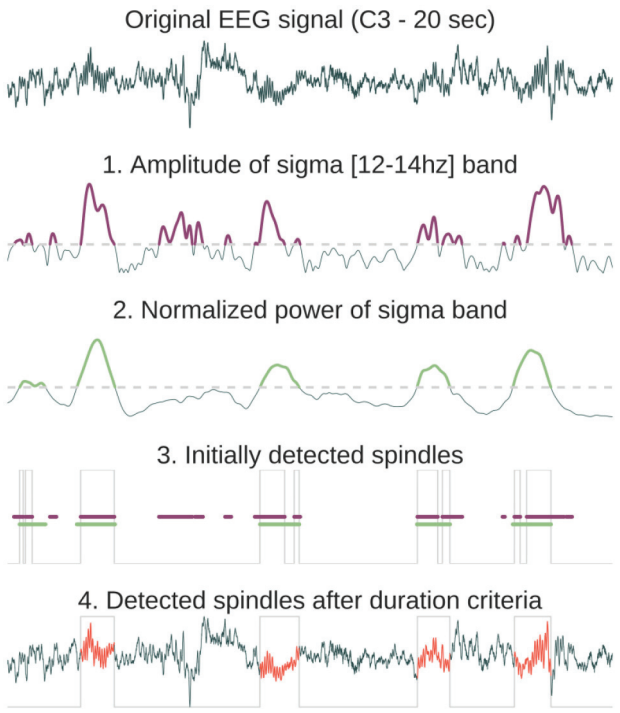

FIGURE 2 | Method description for the automatic sleep spindles detection. First, the original signal is convoluted with a Morlet wavelet centered in the spindles frequency band [12–14 Hz]. From the resulting complex decomposition, we only keep the amplitude and find time indices where the amplitude exceeds the threshold (purple in 1). Then, we compute the normalized power in the sigma band and detect again time indices where the power exceeds a threshold (green in 2). The normalized sigma power is obtained by first computing absolute power in four frequency bands (delta = [0.5–4 Hz], theta = [4–8 Hz], alpha = [8–12 Hz], sigma = [12–16 Hz]) and then dividing each of them by the sum of these powers. As a result, for each time point the sum of powers in the four frequency bands equals 1. The time location of the initial detected spindles (gray line in 3) is the result of the intersection of exceeding both the amplitude index (purple line) and the power index (green line). Finally, time gaps are filled only for neighboring detected events (<500 ms) and a final duration criteria is applied in order to suppress events with a duration inferior to 500 ms or superior to 2,000 ms (these thresholds can be set within *Sleep* interface, 4).

In addition to this setting panel, *Sleep* provides a navigation bar that can be used to set several temporal properties, such as the length of the current time window, time step between each window, time units and the use, if provided, of the absolute time of the current recording. This navigation bar also includes a *grid toggle* button that can either hide or display the grid, as well as a *magnify* option to enlarge short events (see **Figure 4**).

Electrophysiological Time Series

Sleep offers a dynamic control of the displayed polysomnographic time series and most of the settings are in the "Panels" tab. Indeed, each channel can be added or removed from the list of the currently displayed canvas. By default, *Sleep* displays the time series by frames of 30 s, which is a standard duration for stage scoring (Iber et al., 2007), but this value can be changed directly from the navigation bar. Furthermore, the amplitude of each channel can either be set independently, using a same range across all channels, or automatically adjusted according to the minimum/maximum of the currently displayed signals.

Time-Frequency Representation

The visibility and amplitude of each channel can be controlled from the GUI (see **Figure 3**). The same applies for the spectrogram, which corresponds to a time-frequency representation of the entire recording performed on one channel. Among the definable parameters of the spectrogram are the channel on which it is computed, lower and upper limit frequencies, length and overlap of the fast Fourier transform and colormap properties. Finally, a topographic map based on the Source Connectivity Toolbox (SCoT) and the Magnetoencephalography and Electroencephalography (MNE) toolbox implementations (Gramfort et al., 2013; Billinger et al., 2014) can also be embedded inside the GUI for full data inspection. The topological plot depicts the mean values computed from the time window currently displayed. This channel-space 2D topographical functionality provides a convenient and versatile tool to visualize various data types, including the raw data, the amplitude or power in specific frequency bands.

Shortcuts

Navigation and operations inside a software can be sometimes repetitive. For that reason, *Sleep* comes with numerous native shortcuts to facilitate the visualization and stage scoring. For a complete list we refer the reader to the "Shortcuts" paragraph of the documentation[13].

Supported Electrophysiological and Hypnogram Data Formats

Sleep natively supports several standard electrophysiological file formats, including European Data Format (EDF *.edf), Micromed (*.trc), Brain Vision (*.eeg), and Elan (*.eeg). In addition, it is possible to load directly NumPy array or Matlab file using the command-line parameters.

The hypnogram of the corresponding dataset can also be loaded and then edited directly from the GUI. Accepted hypnogram file formats are *.txt, *.csv, or *.hyp. There is a great heterogeneity among sleep laboratories with respect to hypnogram format. This represents an obvious barrier for data sharing. To overcome this problem, *Sleep* allows the user to specify the hypnogram format in a separate text file. This file should contain the names and integer values assigned to each sleep stage in the hypnogram file, as well as the number of values per second. During loading, the hypnogram file will be converted to *Sleep* native hypnogram format described in the documentation[14]. An example description file can be found in the documentation[14].

[13]http://visbrain.org/sleep.html#shortcuts
[14]http://visbrain.org/sleep.html#hypnogram

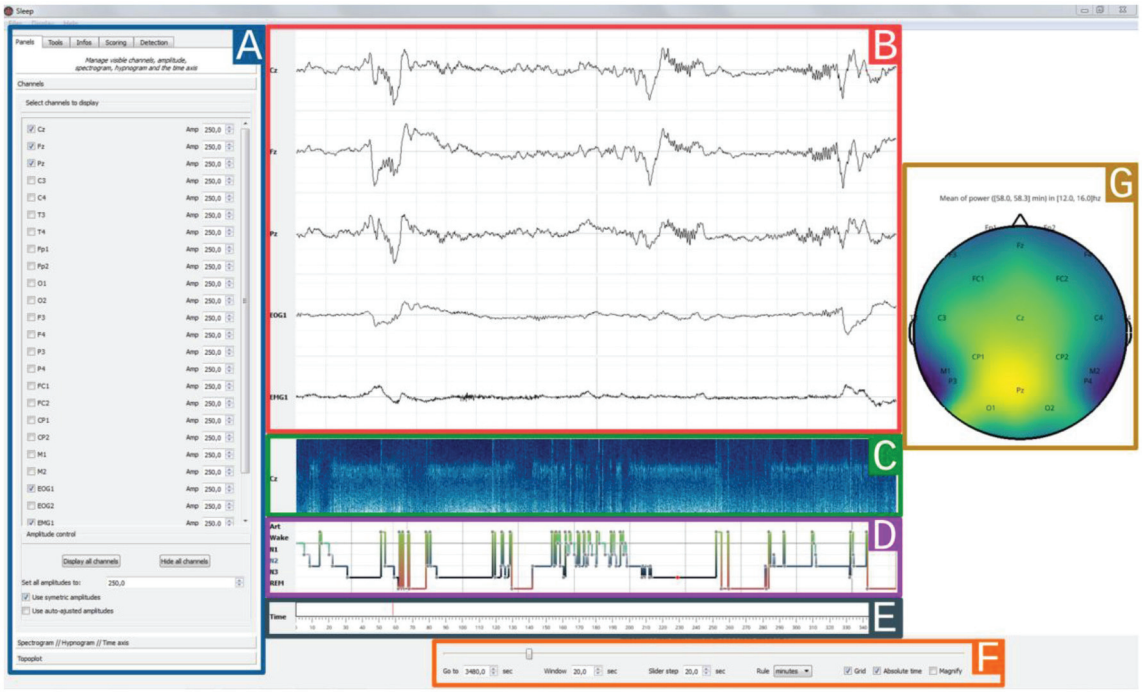

FIGURE 3 | *Sleep* main interface. Each element of the graphical user interface can either be displayed or hidden, **(A)** Settings panel containing all *Sleep* controls and parameters. The current displayed tab can be used to toggle channel visibility and to adjust individual amplitudes, **(B)** 30 s time window of electrophysiological data. Here, only 5 channels are currently displayed (Cz, Fz, Pz, EOG1, EMG1), **(C)** The spectrogram displays the time-frequency representation of a specific channel for the entire recording, and can be useful to identify global changes in the spectral properties of the signal often associated with changes in sleep stages. Any channel can be picked and further time-frequency controls are available in the settings panel, **(D)** Hypnogram with one specific color per stage. The stage order can be changed from the default *Artefact, Wake, REM, N1, N2, N3,* **(E)** Time axis with visual indicator, **(F)** Navigation bar with time settings: window length and step size, unit (seconds/minutes/hours), **(G)** Topographic data representation.

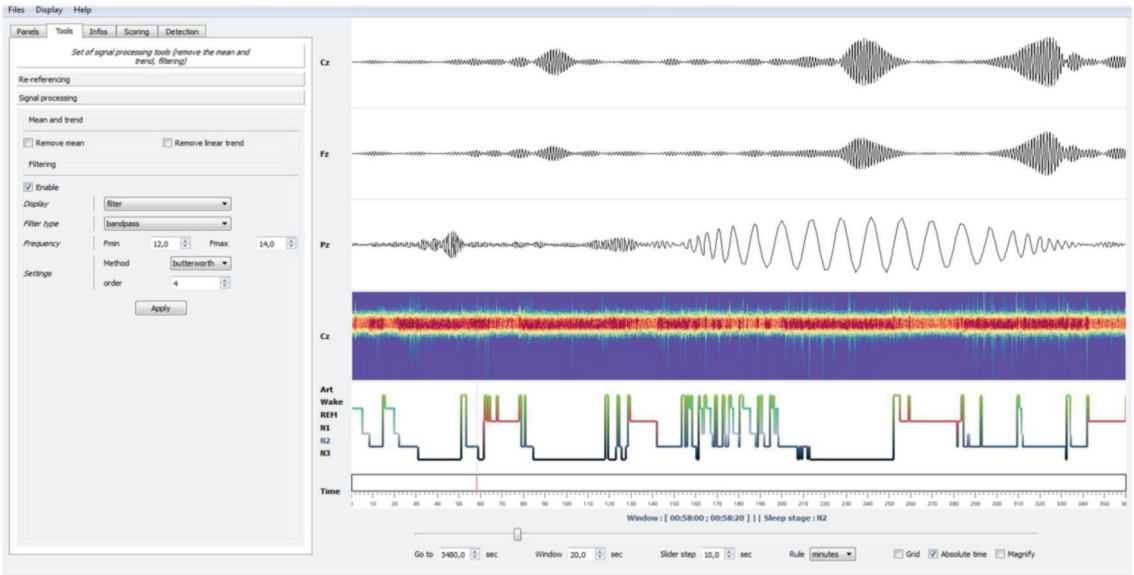

FIGURE 4 | Example of bandpass filtering. Using the Tools panel (**left**), the EEG signals have been bandpass-filtered in the spindles frequency band (12–14 Hz, Butterworth filter). Using the "Enable" checkbox of the panel, this filtering operation can be disabled at any moment to retrieve the original EEG signals. Finally, by left-clicking on a specific time point in a channel or selecting the Magnify tools (**bottom**), users can enlarge events. This was used in this example to enlarge a sleep spindle observed on channel Pz.

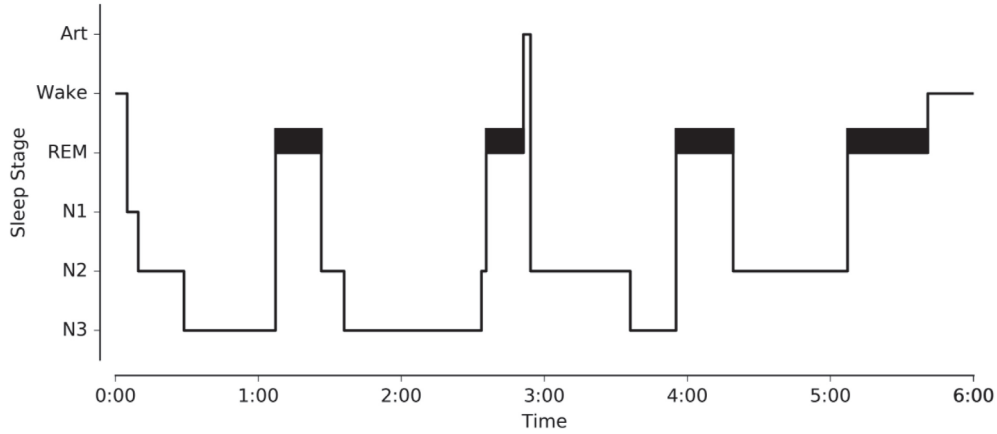

FIGURE 5 | Example of publication-ready hypnogram figure exported using *Sleep* GUI.

Editing the Hypnogram

The hypnogram can be edited either from scratch or from an existing hypnogram file. There are three methods to edit the hypnogram using *Sleep* GUI:

- Using intuitive keyboard shortcuts. When a new stage is entered, the next window is shown.
- Using a table where each stage can be specified by it starting and ending time point.
- Using a drag and drop operation directly on the hypnogram canvas.

At any moment, the user can export the hypnogram or save it as a black and white (or color) publication-ready figure using the contextual menu (**Figure 5**).

GUI Integration and Validation of Automatic Events Detection

The automatic events detection can be performed on any selected or visible channel. When the detection is completed, detected events are depicted directly on the selected channel using a specific color-code for each feature. In addition, the starting point, duration and stage of occurrence of each one of the detected events are reported in the "Location table." Users can then easily navigate between the detected events by clicking on a row, which automatically sets the time so that the event is centered on the screen. Furthermore, this table can be exported to a *.csv or *.txt file. Users can perform an unlimited number of detections in a row on a single channel and then switch from one to another using the "Location" panel. Last but not least, the location of each detected event is reported on the hypnogram using specific visual cues for each detection types. Integration of the detection inside the GUI is shown in **Figure 6**.

To test how these detections performed on real datasets, we measured performances of the spindle and K-complex detection methods using visually-annotated EEG segments of N2 sleep collected from full-night polysomnographic recordings of 14 participants (Eichenlaub et al., 2012, 2014; Ruby P. et al., 2013; Ruby P. M. et al., 2013). Spindles and K-complexes were visually scored by an expert (JBE) as part of a previous work that focused specifically on the detection of these sleep features using machine-learning (Lajnef et al., 2015a).

To perform the detection methods using *Sleep* algorithm, all N2-sleep EEG segments were concatenated into a single file of 210 min with a single channel (C3) and with a sampling rate of 100 Hz (native downsampling frequency of *Sleep*). Then, to evaluate the performances of our detection, we used two standards metrics: the sensitivity *(1)*, which measures the proportion of correctly identified detected events and the False Detection Rate (FDR) *(2)* which assess the proportion of incorrectly detected events.

$$Sensitivity = \frac{True\ Positive}{True\ Positive + False\ Negative} \quad (1)$$

$$False\ Detection\ Rate = \frac{False\ Positive}{False\ Positive + True\ Positive} \quad (2)$$

where True Positive refers to the events scored by the expert and correctly detected by our methods, False Negative refers to the events scored by the expert but not detected by our method and False Positive refers to the events detected by our methods but not scored by the expert.

Performances of the detection algorithm implemented in *Sleep* are reported in **Figure 7.** For both spindles and K-complexes, we used 25 different thresholds ranging from 0 to 5 with 0.2 steps. The optimal threshold was defined as the one that maximizes the difference between sensitivity and FDR (Lajnef et al., 2015a). Regarding spindles, the best performance of our algorithm was obtained at a threshold of 2.4 standard deviations, yielding a sensitivity of 77.2% and a FDR of 40.1%. Regarding K-complexes, a threshold of 1.0 resulted in the best performances with a sensitivity of 70.7% and a FDR of 27.2%. These results are similar to those of previous detection methods (Devuyst et al., 2011; Lajnef et al., 2015a). Moreover, the time of execution of these two algorithms are very fast.

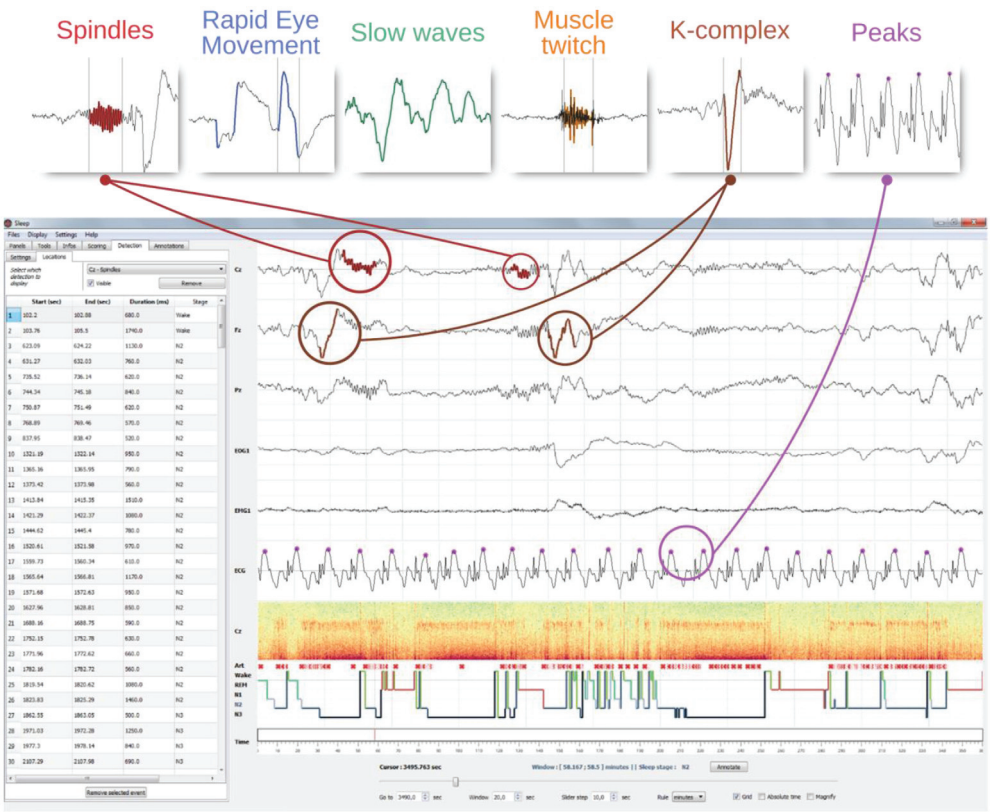

FIGURE 6 | GUI integration of the automatic event detection. The top row illustrate examples of typical graphoelements detected with *Sleep* including spindles, K-complexes, rapid eye movements, slow-waves, muscle twitches, and peaks. The window below illustrate how detections of such events are visually integrated into the interface. First, each detected event are highlighted into the channel time-series. Then, all the detected events are displayed on top of the hypnogram (identified using different symbols and colors per detection type) and reported into a table embedded into the settings panel. A mouse click on a line centers the corresponding event on the screen. This table can be exported into a *.csv or a *.txt file.

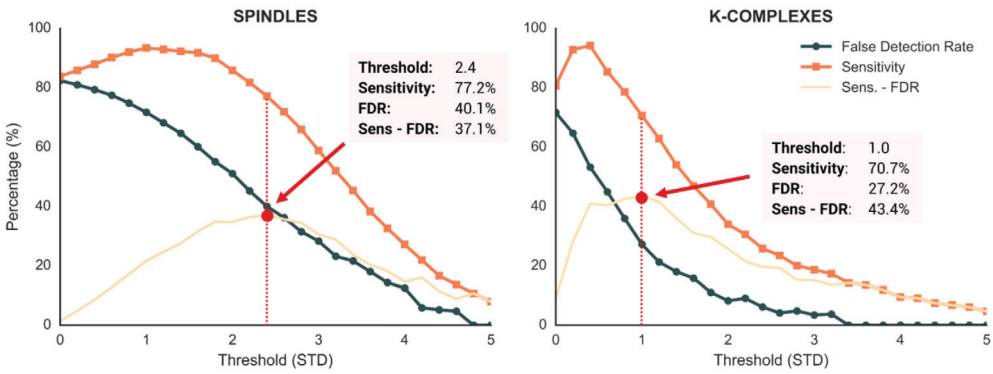

FIGURE 7 | Performance metrics of the *Sleep* spindle and K-complex detection methods evaluated at 25 different thresholds (range = 0–5, step = 0.2). Dark orange and blue lines depict the sensitivity and false detection rate (FDR), respectively. Light orange lines show the difference between sensitivity and FDR. Red dotted lines depict the threshold values that maximized this difference.

Sleep Class Inputs and Code Example

From a programming point of view, the high-level interface with our software is provided by the *Sleep* class. This class can take into account a few input arguments. Hence, loading sleep data can be assessed in three ways adapted to a range of users, from non-programmers to advanced users. As shown in the **Code Snippet 1**, running *Sleep* without further input arguments will ask the user to specify the path to a supported sleep dataset (*.eeg,

*.edf, or *.trc). In addition, the user can either use an existing hypnogram or start a new one from scratch. Alternatively, instead of using the interface to select the files, they can be directly passed as input arguments (**Code Snippet 2**). In this example, we also demonstrate how to change the default order of the sleep stages in the hypnogram using a simple command-line option. If this option is not specified, the default display of *Sleep* is as follows: *Art, REM, Wake, N1, N2, N3.* Finally, several others file formats such as EEGLab, Neuroscan, EGI, GDF, and BDF can be loaded using MNE Python package[15]. We report in **Code Snippet 3** a method to pass data to *Sleep* after loading them using MNE python.

Code Snippet 1 | Simplest way to launch Sleep from a Python interpreter. This will open a window asking the user to select the EEG data and corresponding hypnogram.

```
# Load the Sleep module from visbrain:
from visbrain import Sleep
# Open the default Sleep window:
Sleep().show()
```

Code Snippet 2 | In this example, the paths to the EEG data and hypnogram are entered as inputs arguments of the main Sleep function, resulting in the software opening directly with the dataset and hypnogram loaded. We also show how to change the default display order of the hypnogram by changing the href argument of *Sleep* main function. The sleep stages will be displayed in the order defined in *norder* variable, with N3 on top and Art on bottom.

```
# Import the Sleep module from visbrain:
from visbrain import Sleep
# Define where the data are located:
dfile = '/home/perso/myfile.eeg'
# Define where the hypogram is located:
hfile = '/home/perso/hypno.hyp'
# hfile = None # Eventually, start from a fresh one
# Inverse the default sleep stage order:
norder = ['n3', 'n2', 'n1', 'rem', 'wake', 'art']
# Finally, pass both file to the class:
Sleep(file=dfile, hypno_file=hfile, href=norder).show()
```

Code Snippet 3 | This example shows a method to pass data to *Sleep* after loading them using MNE-Python package (see http://martinos.org/mne/dev/manual/io.html for a full list of the data formats supported by MNE)

```
# Import the Sleep module and MNE:
import numpy as np
from visbrain import Sleep
from mne import io, Annotations
# - Biosemi Data Format (BDF)
raw = io.read_raw_edf('mybdffile.bdf', preload=True)
# - EGI format
# raw = io.read_raw_egi('myegifile.egi', preload=True)
# - EEGLab
# raw = io.read_raw_eeglab('myeeglabfile.set',
preload=True)
# Extract data, sampling frequency and channels names
data, sf, chan = raw._data, raw.info['sfreq'],
raw.info['ch_names']
# Define annotations for this file:
onset = np.array([145., 235., 1045.]) # Onset of each
event (sec)

dur = np.array([1., 5., 2.5]) # Duration (sec)

description = np.array(['First event', # Description

'Second event',

'Third event'

])

annot = Annotations(onset, dur, description)

# Now, pass all the arguments to the Sleep module:

Sleep(data=data, sf=sf, channels=chan, annotation_file=
annot).show()
```

[15]https://martinos.org/mne/stable/manual/io.html#importing-eeg-data

DISCUSSION

This paper introduces an open-source software module called Sleep which provides a user-friendly and efficient GUI dedicated to visualization, scoring and analysis of sleep data. This proposed module is part of a larger ongoing open-source Python project by our group called *Visbrain* dedicated to the visualization of neuroscientific data. The design and functionalities of *Sleep* are specifically geared toward scientists and students involved in sleep research.

Sleep comes with a GUI in which we embedded high-quality plots with graphical rendering offloaded to the GPU. As a result, plotting and user interactions can be processed in real-time. The software is capable of loading several widely-used sleep data files format, such as European Data Format and BrainVision, and to stream efficiently all of the polysomnographic channels, even on an average modern laptop. On top of that, *Sleep* also provides the possibility to display time-frequency (spectrogram) and topographic representations of the data, with several adjustable parameters for each. Regarding sleep staging and hypnogram editing, *Sleep* offers intuitive manual scoring functionalities, signal processing tools and automatic detection of sleep features in order to facilitate this fastidious process. Once completed, users can export sleep statistics, or publication-ready high-quality figure of the hypnogram in one click.

Comparison with Other Solutions

First, it is noteworthy that the scope and functionalities of the present module differs from a previous MATLAB tool we have released, called *Spinky* (Lajnef et al., 2017) and which aims specifically to provide a joint spindle and K-complex detection framework using the tunable Q-factor wavelet transform (TQWT) (Selesnick, 2011). In addition with being written entirely in Python, *Sleep* allows for a wide range of functionalities, such as sleep scoring, fast raw and spectral data visualization, edition and creation of hypnogram and annotation files, and automatic detection of several sleep features. *Spinky* and *Sleep* subserve distinct purposes and are thus highly complementary. Second, there are currently only a few freewares for human sleep scoring and analysis. The Python package Phypno and MATLAB-based toolbox SpiSOP both provide a GUI for scoring sleep stages, and include several other command line features to perform automatic detections and compute

sleep statistics. However, one of the advantages of *Sleep* in comparison with these two solutions is the dynamic integration of these features into the GUI, which we believe will allow our software to be understood and accessible by users with no or little programming knowledge. Finally, *Sleep* offers several advantages compared to the numerous existing commercial solutions, the most obvious one being that it is free and therefore more easily accessible to students or small sleep laboratories. Also, the fact that it is open-source allows more easily the community to contribute to its extension and development. Furthermore, special emphasis was given to ensure compatibility with several electrophysiological and hypnogram file formats and thus liberate the data from proprietary formats that are dependent upon specific software. We firmly believe that this, in addition with the possibility to save and load automatic detection or configuration files, will promote and facilitate data sharing across sleep laboratories.

Performance of the Automatic Detections

Regarding the automatic detections, *Sleep* includes 6 robust algorithms for detecting some of the most prominent features of each sleep stage, including spindles, K-complexes, slow waves, REM, and muscle twitches. Spindle and K-complex detection algorithms were validated on a visually scored dataset including 210 min of N2 sleep from 14 participants and resulted in performances similar to those reported in recent publications. Last but not least, these detections are implemented inside the GUI in an ergonomic and intuitive manner. We think that these detections may represent a valuable help not only in the process of staging sleep, but also for researchers that are interested in the microstructure of sleep. The automatic detection algorithms proposed in *Sleep* can be used as a starting point for a semi-automatic procedure where users can correct or adjust the output of the detector. Beyond saving a lot of time, this approach has generally been shown to yield reliable and robust detection (O'Reilly and Nielsen, 2015).

FUTURE DIRECTIONS AND CONCLUSION

We are considering to extend the list of the default supported files and we encourage programmers or sleep scientists interested by this project to collaborate on it. Regarding sleep analysis we are working on an automatic scoring function based on machine-learning algorithms, inline with our previous work (Combrisson and Jerbi, 2015; Lajnef et al., 2015b; Combrisson et al., 2017). Finally, as different users have different needs, we are constantly improving the interface and functionalities of the software thanks to the feedback we receive.

With the release of *Sleep,* we offer a portable and cross-platform software, installable and usable on most configuration. While there is still room for improvement, *Sleep* already provides a complete and intuitive interface designed by and for scientists involved in sleep research. We hope this software will be used and further developed by many like-minded students and researchers with a strong commitment to open science and to high quality open-source software.

AUTHOR CONTRIBUTIONS

EC and RV contributed equally in the development of this software and writing of the article. JE provided visual scoring for the validation of K-complex and spindles detection. JE, CO, TL, AG, PR, and KJ actively helped in the writing process and with software testing.

FUNDING

EC acknowledges support through a PhD Scholarship awarded by the Ecole Doctorale Inter-Disciplinaire Sciences-Santé (EDISS), Lyon, France, and by funding via a Natural Sciences and Engineering Research Council of Canada (NSERC). RV acknowledges support through a PhD scholarship awarded by the Ecole Doctorale NsCo, Lyon, France, and by funding via the framework LABEX CORTEX (ANR-11-LABX-0042) of Université de Lyon, within the program ANR-11-IDEX-0007. KJ acknowledges funding from the Canada Research Chairs program, NSERC Discovery Grant [grant number RGPIN-2015-04854] and FRQNT New Researcher Grant [RQT00121].

REFERENCES

Berthomier, C., Drouot, X., Herman-Stoïca, M., Berthomier, P., Prado, J., Bokar-Thire, D., et al. (2007). Automatic analysis of single-channel sleep EEG: validation in healthy individuals. *Sleep* 30, 1587–1595. doi: 10.1093/sleep/30.11.1587

Billinger, M., Brunner, C., and Müller-Putz, G. R. (2014). *SCoT: a Python Toolbox for EEG Source Connectivity*. Available online at: https://pdfs.semanticscholar.org/b196/7f587fbea9ecf4cb6be3f757a8136fc60ca8.pdf

Campagnola, L., Klein, A., Larson, E., Rossant, C., and Rougier, N. P. (2015). "VisPy: harnessing the GPU for fast, high-level visualization," in *Proceedings of the 14th Python in Science Conference*. Available online at: https://hal.inria.fr/hal-01208191/ (Accessed May 23, 2017).

Combrisson, E., and Jerbi, K. (2015). Exceeding chance level by chance: the caveat of theoretical chance levels in brain signal classification and statistical assessment of decoding accuracy. *J. Neurosci. Methods* 250, 126–136. doi: 10.1016/j.jneumeth.2015.01.010

Combrisson, E., Perrone-Bertolotti, M., Soto, J. L., Alamian, G., Kahane, P., Lachaux, J.-P., et al. (2017). From intentions to actions: neural oscillations encode motor processes through phase, amplitude and phase-amplitude coupling. *Neuroimage* 147, 473–487. doi: 10.1016/j.neuroimage.2016.11.042

Devuyst, S., Dutoit, T., Stenuit, P., and Kerkhofs, M. (2011). Automatic sleep spindles detection—overview and development of a standard proposal assessment method. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* 2011, 1713–1716. doi: 10.1109/IEMBS.2011.6090491

Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Ruby, P. (2014). Brain reactivity differentiates subjects with high and low dream recall frequencies during both sleep and wakefulness. *Cereb. Cortex* 24, 1206–1215. doi: 10.1093/cercor/bhs388

Eichenlaub, J.-B., Ruby, P., and Morlet, D. (2012). What is the specificity of the response to the own first-name when presented as a novel in a passive oddball paradigm? An ERP study. *Brain Res.* 1447, 65–78. doi: 10.1016/j.brainres.2012.01.072

Erdamar, A., Duman, F., and Yetkin, S. (2012). A wavelet and teager energy operator based method for automatic detection of K-complex in sleep EEG. *Expert Syst. Appl.* 39, 1284–1290. doi: 10.1016/j.eswa.2011.07.138

Gramfort, A., Luessi, M., Larson, E., Engemann, D. A., Strohmeier, D., Brodbeck, C., et al. (2013). MEG and EEG data analysis with MNE-Python. *Front. Neurosci.* 7:267. doi: 10.3389/fnins.2013.00267

Iber, C., Ancoli-Israel, S., Chesson, A. L., and Quan, S. F. (2007). *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications.* Westchester, IL: American Academy of Sleep Medicine.

Jerbi, K., Ossandón, T., Hamamé, C. M., Senova, S., Dalal, S. S., Jung, J., et al. (2009). Task-related gamma-band dynamics from an intracerebral perspective: review and implications for surface EEG and MEG. *Hum. Brain Mapp.* 30, 1758–1771. doi: 10.1002/hbm.20750

Lajnef, T., Chaibi, S., Eichenlaub, J.-B., Ruby, P. M., Aguera, P.-E., Samet, M., et al. (2015a). Sleep spindle and K-complex detection using tunable Q-factor wavelet transform and morphological component analysis. *Front. Hum. Neurosci.* 9:414. doi: 10.3389/fnhum.2015.00414

Lajnef, T., Chaibi, S., Ruby, P., Aguera, P.-E., Eichenlaub, J.-B., Samet, M., et al. (2015b). Learning machines and sleeping brains: automatic sleep stage classification using decision-tree multi-class support vector machines. *J. Neurosci. Methods* 250, 94–105. doi: 10.1016/j.jneumeth.2015.01.022

Lajnef, T., O'Reilly, C., Combrisson, E., Chaibi, S., Eichenlaub, J.-B., Ruby, P. M., et al. (2017). Meet spinky: an open-source spindle and K-complex detection toolbox validated on the open-access Montreal Archive of Sleep Studies (MASS). *Front. Neuroinform.* 11:15. doi: 10.3389/fninf.2017.00015

O'Reilly, C., and Nielsen, T. (2015). Automatic sleep spindle detection: benchmarking with fine temporal resolution using open science tools. *Front. Hum. Neurosci.* 9:353. doi: 10.3389/fnhum.2015.00353.

Parekh, A., Selesnick, I. W., Rapoport, D. M., and Ayappa, I. (2015). Detection of K-complexes and sleep spindles (DETOKS) using sparse optimization. *J. Neurosci. Methods* 251, 37–46. doi: 10.1016/j.jneumeth.2015.04.006

Rechtschaffen, A., and Kales, A. (1968). *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. Washington, DC: United States Government Printing Office.

Ruby, P., Blochet, C., Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Bidet-Caulet, A. (2013). Alpha reactivity to complex sounds differs during REM sleep and wakefulness. *PLoS ONE* 8:e79989. doi: 10.1371/journal.pone.0079989

Ruby, P. M., Blochet, C., Eichenlaub, J.-B., Bertrand, O., Morlet, D., and Bidet-Caulet, A. (2013). Alpha reactivity to first names differs in subjects with high and low dream recall frequency. *Front. Psychol.* 4:419. doi: 10.3389/fpsyg.2013.00419

Selesnick, I. W. (2011). Wavelet transform with tunable Q-factor. *IEEE Trans. Signal Proc.* 59, 3560–3575. doi: 10.1109/TSP.2011.2143711

Tallon-Baudry, C., Bertrand, O., Delpuech, C., and Pernier, J. (1996). Stimulus specificity of phase-locked and non-phase-locked 40 Hz visual responses in human. *J. Neurosci.* 16, 4240–4249.

Vallat, R., Lajnef, T., Eichenlaub, J.-B., Berthomier, C., Jerbi, K., Morlet, D., et al. (2017). Increased evoked potentials to arousing auditory stimuli during sleep: implication for the understanding of dream recall. *Front. Hum. Neurosci.* 11:132. doi: 10.3389/fnhum.2017.00132

Warby, S. C., Wendt, S. L., Welinder, P., Munk, E. G. S., Carrillo, O., Sorensen, H. B. D., et al. (2014). Sleep-spindle detection: crowdsourcing and evaluating performance of experts, non-experts and automated methods. *Nat. Methods* 11, 385–392. doi: 10.1038/nmeth.2855

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Part IV

GENERAL DISCUSSION

14 Neurophysiological and behavioral factors associated with a high DRF

14.1 Summary of the results

One of the major objectives of the present thesis was to investigate the neurophysiological and behavioral correlates of inter-individual variability in dream recall frequency (DRF). Based on previous findings, we hypothesized that DRF is associated with a specific psychological and physiological functioning during both sleep and wakefulness. To test this hypothesis, we conducted several experiments to compare the brain activity, sleep parameters, cognitive abilities and personality traits of high and low dream recallers (HR and LR, respectively). The main findings of our experiments are summarized in Fig 14.1.

14.1.1 DRF is positively associated with increased brain reactivity and longer intra-sleep awakening

In Study 1, we performed an in-depth investigation of the sleep macro and micro-structure of HR and LR by re-analyzing the polysomnographic recordings of Eichenlaub et al. (2014a). First, we did not find any significant between-group differences in any of the sleep microstructural features considered (e.g. arousals, spindles, K-complexes, REMs). Our interpretation of these findings is that, most probably, sleep microstructural features are not crucial factors to explain DRF variability. By contrast, we observed that full awakenings (i.e > 15 seconds) were longer in all sleep stages in HR as compared to LR (roughly 2 vs 1 min respectively). Noteworthy, the number of awakenings was not different between the two groups.

These observations led us to propose that among sleep parameters, the duration of intra-sleep wakefulness seems to be the most critical predictor of inter-individual differences in DRF. This result provides a strong evidence in favor of the arousal-retrieval model (see section 2.4.4, Koulack and Goodenough, 1976), which states that a short period of wakefulness has to occur immediately after dreaming in order to transfer the dream content from short to long term memory. Our findings constitute an important contribution to this model by demonstrating, using objective measurements, a link between intra-sleep awakening and DRF. These results also extended this model by showing that the duration of awakenings is more critical to dream recall than the number of awakenings. We proposed that awakenings must be of sufficient duration to allow successful encoding of dreams into memory. Based on our results and previous ones (Campbell and Webb, 1981), we suggested that 2 minutes might be the threshold duration for a successful encoding.

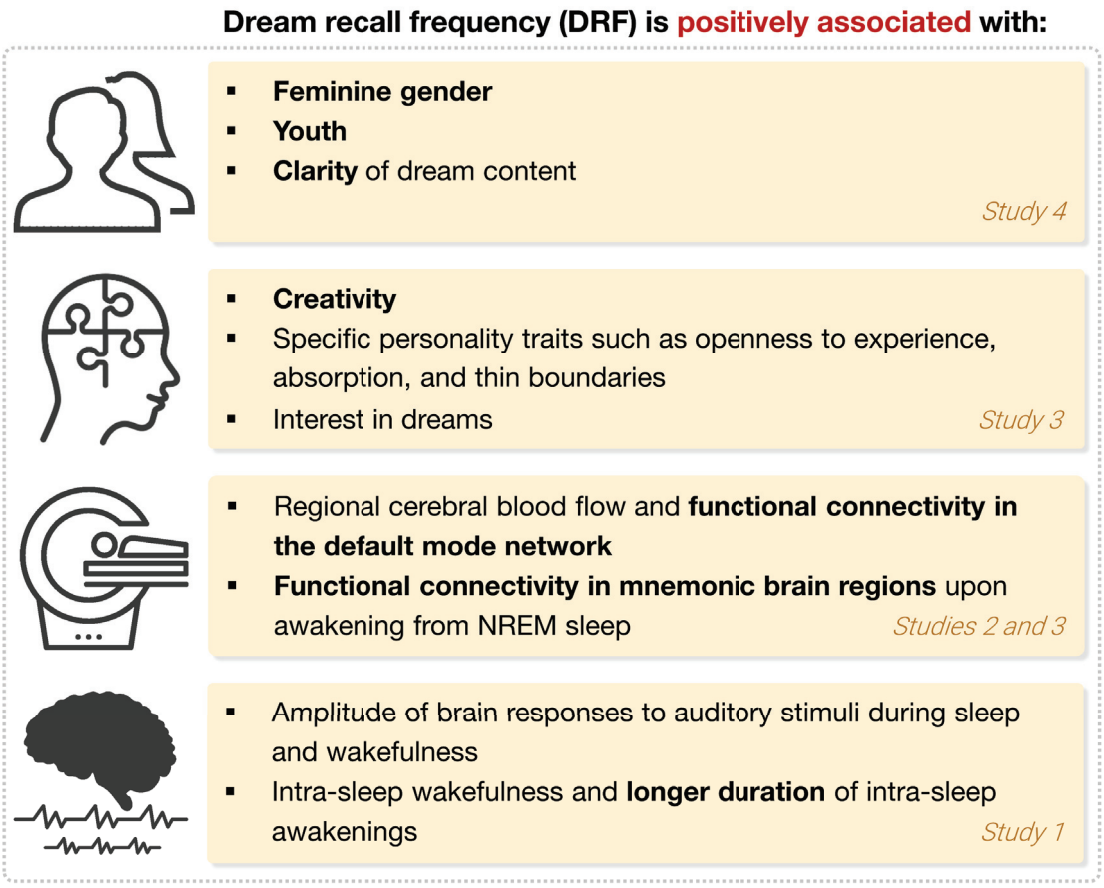

Fig. 14.1 **Summary of the differences observed between high and low dream recallers.** The findings of the present thesis are written in bold. By opposition, DRF was not associated with memory abilities or the density of certain sleep microstructural events such as rapid eye movements, muscle twitches, spindles and K-complexes.

On this point, it should be noted that the author of the present thesis contributed to an ongoing study aiming at investigating, by means of human intra-cortical EEG, the temporal dynamic of reactivation of brain regions involved in memory processing during arousals (ranging from 3 sec to 2 minutes). Preliminary results showed that the spectral composition of hippocampal EEG signal during these arousals was intermediate between that of sleep and wakefulness activities in NREM and REM sleep, and that this activation was modulated by the awakening duration (Eskinazi et al., *in preparation*, see Publications list). Furthermore, we observed that hippocampus activity during these arousals was different during NREM and REM sleep, a finding particularly relevant considering the well-known dichotomy between these two sleep stages with regards to dream recall and, more broadly, memorization processes (Nielsen, 2000; Conduit et al., 2004).

The visual scoring of arousals allowed us to address another issue, which is related to the finding of differential brain reactivity to auditory stimuli in high and low dream recallers (see section 2.3.4). Eichenlaub et al. (2014a) has suggested that there might be a causal link between the larger brain responses to auditory stimuli and greater intra-sleep wakefulness during sleep in HR as compared to LR. In other words, the amplitude

of brain responses to auditory stimuli could be predictive of subsequent awakening or arousal reactions, an observation that has been previously reported for nociceptive stimuli Bastuji et al. (2008). To test this hypothesis, we computed the auditory evoked potentials to arousing stimuli (i.e. inducing either an arousal or awakening within the next 15 sec) or non-arousing stimuli (i.e. stimuli that do not induce a disruption of the PSG signal within the next 15 sec). This comparison was not possible without the tedious and time-consuming visual scoring of arousals, given that arousals are far more frequent than awakenings in a normal night of sleep, and are therefore needed to compute reliable and statistically valid evoked potentials. Consistent with our hypothesis, we have shown that brain responses to auditory stimuli, in N2 sleep, were larger when followed by a subsequent arousing reaction. Importantly, this increase in the amplitude of the brain responses seemed to be truly related to the stimulus since the amplitude was larger when arousing reactions were within 5 seconds after the stimulus compared to when they were between 5 and 15 seconds. Although it was not possible to compare the brain responses to arousing stimuli between HR and LR (because of too few subjects in each group having a sufficient number of arousing stimuli), behavioral results showed that HR elicited a significantly greater proportion of arousing reaction than LR, thus confirming the idea of a greater brain reactivity to external stimuli in HR (Eichenlaub et al., 2014a). It is important to note that these findings may also suggest differential attentional processes between HR and LR. This hypothesis was recently tested in an EEG study in which the author of the present thesis contributed (Ruby et al., *in preparation*, see Publications list). Preliminary findings showed an increase of both top-down and bottom-up attentional processes in HR and LR during wakefulness, thus reinforcing the idea of a differential cognitive and brain functioning between the two groups.

In sum, our findings argue for the existence of a causal link between intra-sleep awakening and the brain reactivity to stimuli during sleep. As compared to LR, a greater brain reactivity during sleep in HR could promote intra-sleep awakening which could in turn promote dream recall. Our hypothesis is that if these awakenings are of sufficient duration to allow for the reactivation of the memory encoding abilities of the brain (and notably the hippocampus), then the dream content can be successfully encoded into long-term memory and therefore successfully recalled in the morning. That said, it should be taken into account, however, that DRF variability is unlikely to be explained fully through this one mechanism, since studies have shown that even when awakened at specific moment during the night and under controlled laboratory condition, LR still report significantly less dreams than HR (Goodenough et al., 1959, also replicated in Study 2 of this thesis). Consequently, it is reasonable to assume that some other factors mediate the forgetting and recalling of dreams. A factor that has been proposed but surprisingly never experimentally tested until now is the brain and cognitive functioning during the transition from sleep to wakefulness (i.e. sleep inertia).

14.1.2 DRF is positively associated with brain functional connectivity upon awakening

In Study 2, we tested the hypothesis of a differential sleep inertia between HR and LR. To this aim, we designed an EEG-fMRI sleep study to compare specifically the brain functional connectivity and cognitive performances of these two groups following awakening from a daytime nap. To our knowledge, this was the first study to experimentally test the relationship between sleep inertia and DRF. Our predictions were that HR would show less cognitive impairments and brain functional alterations than LR at awakening, therefore allowing them to better encode dream content upon awakening from sleep.

While we were not able to evidence significant behavioral between-group differences at awakening (discussed in section 9.2), our results showed on a differential brain functional organization associated with DRF in the minutes following awakening from sleep. We found that at 5 min-post-awakening, HR exhibited a greater functional connectivity within the default mode network and regions involved in memory retrieval, such as the medial prefrontal cortex (MPFC), the precuneus, the left medial temporal lobe (MTL) and the left dorsolateral prefrontal cortex (DLPFC). Remarkably, these are almost exactly the same regions found to be involved in episodic memory encoding and retrieval (reviewed in Spaniol et al., 2009). Our interpretation of these results is that the higher functional connectivity in mnemonic brain regions observed in HR could facilitate in these participants the retrieval of dream content, by preventing the loss of the short-term dream memory during the sleep-wake transition. Inversely, LR could fail to recall their dreams because of greater functional connectivity alterations during the first minutes following awakening. More broadly, our results argue in favor of a differential functional awakening process between HR and LR that could explain inter-group differences in dream recall.

On another topic, it is important to note that this study was also the first to investigate simultaneously the brain and cognitive alterations of sleep inertia in healthy subjects (part 1 of Study 2). Using measures of arithmetic performances at pre-sleep, 5 min and 25 min post-awakening, we replicated the finding of reduced cognitive performances just after awakening as compared to before sleep or 25 min after awakening. Furthermore, we provided a brain mechanism for these cognitive impairments, by showing a global loss of brain functional *segregation* following awakening from N2 and N3 sleep. Consistent with the well-known link between the severity of sleep inertia and the prior sleep stage (Tassi and Muzet, 2000), we found that awakening from N3 sleep was associated with the most severe and robust changes in the brain functional connectivity. Among the perspectives for future studies, it would be interesting to extend these data to N1 sleep and REM sleep, which are known to induce less sleep inertia than N2 or N3 sleep. However, REM sleep is very difficult to observe in an MRI setting, unless applying a severe and specific REM sleep deprivation in the night(s) before (Duyn, 2012), which is of course not ideal to study functional connectivity given the huge impact of severe sleep deprivation on the brain functional connectome (De Havas et al., 2012; Yeo et al., 2015; Krause et al., 2017).

14.1.3 DRF is positively associated with creative-thinking abilities and default mode network connectivity

There is a rising consensus that dreaming, or at least dream recall, could be subserved by regions of the default mode network (DMN). In Study 3, we re-analyzed the fMRI data of Study 2 to specifically investigate the relationship between DRF and the DMN. Our results show that, during rest and compared to LR, HR exhibit a higher functional connectivity within the DMN (1) in average and (2) specifically between the MPFC and TPJ. These results are remarkably consistent with previous ones showing a higher rCBF in HR between these two same regions during sleep and wakefulness (Eichenlaub et al., 2014b), and a cessation of dream reporting following focal lesions in these brain areas (Solms, 1997). Based on all these observations, one can reasonably argue that the TPJ and the MPFC are two critical regions when it comes to the ability to recall dreams. The question remains yet pending whether these regions are only involved in dream recall during wakefulness, or also in the production of dreams during sleep. It would be premature to answer that question given that we still have no other means than awakening the participants to assess whether he or she was dreaming.

The second goal of this study was to compare the cognitive abilities (e.g. memory, creativity) and personality traits of HR and LR. We found that HR scored higher than LR on measures of creative-idea generation, without any further between group differences in memory or cognitive abilities. Regarding personality traits, we found that HR tended to score higher on several big five dimensions such as neuroticism, agreeableness and openness-to-experience. These differences were however not significant. This could be due, in part, to the number of participants (n=55), which despite being great for a typical neuroimaging study (especially involving simultaneous EEG-fMRI recordings), is rather low for behaviorally assessing subtle differences in personality traits (e.g. n=981 in Hartmann, 1989). The finding of a higher creativity in HR than in LR, which has already been reported in several studies (Fitch and Armitage, 1989; Schredl, 1995; Schredl et al., 2003b), is particularly interesting given that creative-thinking has also been associated with the recruitment of the DMN (Ellamil et al., 2012; Jung, 2013; Beaty et al., 2014; Mok, 2014; Beaty et al., 2015; Christoff et al., 2016). As such, these findings are consistent with the emerging view that creative-thinking and dreaming share some phenomenological and neurophysiological properties (Christoff et al., 2016).

Altogether, these results argue in favor of Schonbar's claim (1965) that high or low DRF can be explained by the *"life-style"* of individuals (among which are creative-thinking abilities and personality traits). Our findings go one step further by suggesting that this life-style is related to a specific brain functioning, characterized notably by an increased functional connectivity in the DMN. As we will discuss in section 14.2, the question remains to whether there is a causal link between all these variables, and notably whether personality traits, life-style and DRF variations can significantly influence and modify the brain functional properties (and reciprocally).

14.1.4 DRF is associated with age, gender, and clarity of dream content

We took advantage of the recruitment questionnaire of the EEG-fMRI study on sleep inertia to perform an epidemiological survey of the sleep and dream habits of a large sample of French college students from Lyon University. The survey included several questions regarding DRF. Remarkably, we were able to evidence a negative correlation between DRF and age, even on the tight age range of our sample (i.e. from 18 to 30 years old), as well as a positive correlation between DRF and the clarity of dreams. Furthermore, we were able to replicate the finding of a higher DRF in women than in men (Schredl and Reinhard, 2008). Many factors could explain, at least partly, this gender difference in DRF. For instance, Schredl and Reinhard (2008) proposed that it was the result of a gender-specific dream socialization process during childhood. According to them, girls are encouraged more often than boys to talk about their dreams during their childhood, and might therefore develop a stronger interest in dreams, a factor consistently reported to be positively associated with DRF (Schredl et al., 2003b). Another possible explanation could be the higher proportion of intra-sleep wakefulness reported in women as compared to men (Reyner and Horne, 1995), which could give them more opportunities to encode dreams into memory according to the arousal retrieval-model (Koulack and Goodenough, 1976). Finally, drawing from Schonbar's life-style hypothesis (1965), one can argue that the higher DRF in women could be the result of differential personality and cognitive traits between men and women. This observation is supported by studies showing higher levels of neuroticism, extraversion, agreeableness, and conscientiousness in women compared to men, as well as a tendency for higher creativity (reviewed in Schmitt et al., 2009; Baer and Kaufman, 2008).

Remarkably, age, gender and clarity can all be related to a specific functioning of the default mode network (DMN). For instance, women tend to exhibit a higher functional connectivity in the DMN (Bluhm et al., 2008). Similarly, in comparison with younger subjects, older people were consistently found to exhibit a global lower functional connectivity within the DMN (Damoiseaux et al., 2008; Koch et al., 2010), a finding well in line with the observation of reduced mind-wandering abilities in older people (Jackson and Balota, 2012). Finally, there is a rising consensus that DMN may be involved in visual imagery process (Andrews-Hanna et al., 2010), thus suggesting that a high DMN activity could be causally linked to an increased clarity of the dream content. By extension, this could mean that DMN activity is directly related to the salience of dream content. We will discuss further these interactions between DMN functioning and other factors related to DRF in the next section, in which we propose an integrative model of dream recall based on all these findings.

14.2 An integrative model of dream recall

How can we combine the above findings on DRF variability to the previously existing knowledge on dream recall? The results of the present thesis led us to propose a comprehensive and integrative model of dream recall, depicted in Fig 14.2.

The main assumption of this model is that successful dream recall requires two successive steps, namely the *survival* of the dream content during the sleep wake-transition and the *encoding* of the dream content from short to long term memory. As such, our model draws from the arousal-retrieval model (Koulack and Goodenough, 1976), which states that the encoding of dream content into long-term memory is not possible during sleep but only during wakefulness. This model has received support from several experimental studies, including the Study 1 of the present thesis in which we observed a positive association between DRF and the duration of intra-sleep awakenings. Our results led us to propose that there might be a threshold duration to allow the full reactivation of the memory encoding abilities of the brain, which we estimated to be around two minutes. Furthermore, our ERPs results suggest that intra-sleep awakenings might be causally linked to the brain reactivity to auditory stimuli. Based on these findings, we propose that the encoding of the dream content from short to long term memory is dependent of the duration of intra-sleep awakenings, which is in turn linked to the processing of external stimuli during sleep. In addition, our model incorporates, on the psychological side, the interference hypothesis of Cohen and Wolfe (1973), who proposed that the dream memory trace remains so long as there is no distraction or interferences in the encoding process.

Second, we postulate that in order to be successfully encoded into a long-term memory, the dream content first needs to survive the sleep-wake transition. Indeed, we have seen in the Study 2 of the present thesis that the brain undergoes dramatic changes during the transition from sleep to wakefulness. We found notably that awakening from N3 sleep induces more severe brain functional alterations than awakening from N2 sleep, thus suggesting a causal link between sleep depth and the severity of the functional alterations at awakening. With regards to dream recall, we observed a higher functional connectivity in HR in the first minutes following awakening. This result suggests that the severity of brain alterations at awakening is causally linked to dream recall, an idea well in line Koukkou and Lehmann (1983)'s stage-shift hypothesis according to which the forgetting of dreams is a function of the magnitude of the difference between the pre- and post-awakening brain state. Given that awakening from N3 sleep induces the most severe changes in the brain functional organization, it is not surprising therefore that awakening from N3 sleep has been consistently associated with the lowest frequency of dream recall. Another, more psychological, factor that, according to our model, plays a crucial role in the survival of the dream content during the sleep-wake transition is the salience of the dream content. This idea was first proposed by Cohen and MacNeilage (1974) and received further support from experimental studies since then (Cipolli et al., 1993; Schredl and Doll, 1998). Put it simply, this hypothesis states that the more salient a dream is (e.g. vivid, bizarre, emotionally intense), the more likely it will be recalled. In sum, we propose that two conditions are necessary for dream content to survive the sleep-wake transition. First,

the awakening must preferentially occur in a brain state functionally close to wakefulness (typically REM sleep), in order to limit the magnitude of the brain functional alterations upon awakening. Second, the dream content must contain salient features.

Drawing from Schonbar (1965)'s life-style hypothesis, we further propose that all these state factors might be influenced by psychological and cognitive traits factors. For instance, the level of interference during the encoding process might be related to the interest in dreams, which has been consistently found to be positively associated with DRF (Schredl et al., 2003b). One explanation could be that individuals highly interested in their dreams might make a voluntarily effort upon awakening to *grasp* the dream memory and consequently reduce interferences in the encoding process. This mechanism could also explain why DRF is known to be significantly enhanced by keeping a dream diary (Schredl, 2002). Similarly, the salience of dream content might also be related to some traits factors, including creative-thinking abilities, life-style, and personality traits.

One of the key finding of the present thesis is that this differential psychological profile between high and low dream recallers is also associated with a specific neurophysiological profile, characterized notably by a higher functioning of the default mode network (DMN) in high dream recallers. According to our model, this neurophysiological profile could be interdependently linked with psychological parameters, and exerts as such an influence on all the state factors involved in the process of dream recall. For instance, a higher DMN functioning could be related to creative-thinking abilities, which could determine in turn the salience of dream content. Second, higher DMN functioning in HR during sleep could reduce brain functional alterations at awakening, therefore facilitating the survival of dream content during the sleep-wake transition, and at the same time promote the brain reactivity to external (and internal) stimuli, leading to increased intra-sleep wakefulness and thus more opportunities to encode dream content into memory. Lastly, age and gender have been both related to changes in DRF (see Study 4), and changes in psychological and neurophysiological traits. Our model propose therefore that age and gender could mediate several factors related to the dream recall process. For instance, reduced cognitive and DMN functioning in older people could prevent a successful encoding of dream recall into memory and explain the well-known negative correlations between age and DRF. Similarly, specific personality traits in women, associated with a higher DMN functioning, could result in an increased salience of dream content and greater intra-sleep wakefulness, therefore explaining the small but consistent gender effect found in DRF.

14.3 Conclusions and perspectives

In summary, the different studies on DRF of the present thesis improved our knowledge of the factors and their interactions contributing to the process of dream recall. Based on the latests experimental findings, we proposed an integrative model of dream recall which can hopefully serve as a basis for future work. Among possible future axes of research, it seems promising to test whether DMN activity could also predict intra-individual variability in DRF across time. To this aim, one could use DRF enhancing methods (such as keeping a dream

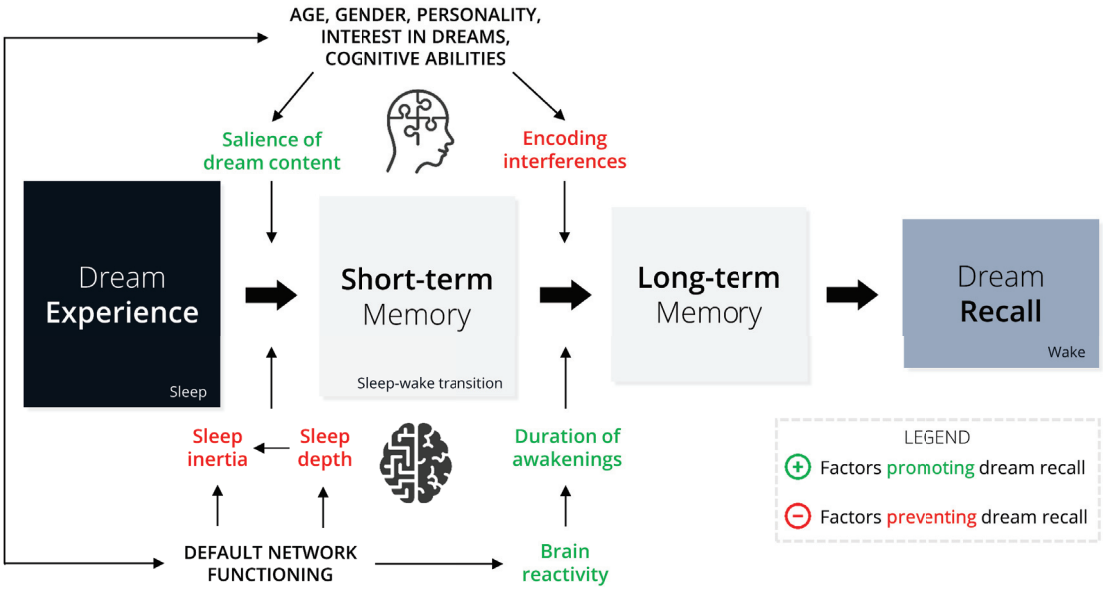

Fig. 14.2 An integrative model of dream recall.

diary; Schredl, 2002) to test whether an increased DRF would result in increased creativity scores and DMN functional connectivity in post compared to pre-training measures within the same individuals (preferentially an initial group of low dream recallers).

15

The relationship between waking life and dream content

15.1 Such stuff as dreams are made on

We are such stuff,
As dreams are made on; and our little life,
Is rounded with a sleep

— **William Shakespeare**
The Tempest. 1611

Through an extensive investigation of the relationship between waking-life and dream content, Study 5 significantly improved our knowledge of the *stuff that dreams are made on*. We asked participants to record and describe, over a period of one week, the obvious connections that they could make between their waking-life and dream content. By specifically investigating the characteristics of waking-life experiences (WLE) incorporated into dreams, we enhanced our understanding of the filter that dreaming applies to waking life.

We observed that the *"dream mixture"*, as Freud called it, is composed of several types of WLE which are all incorporated in significant proportions, i.e. recent and old, emotionally loaded and emotionless, positive and negative, important and insignificant, concerns and non-concern issues, to name but a few. Remarkably, we also found a significant interaction between the temporal remoteness of WLE and their emotional intensity. Older memories were scored by the subjects as the most emotionally intense and important, by opposition with memories of the day before (i.e. day-residues) that were mainly self-rated as non-important and emotionally neutral. However, it should be noted that this effect could be partly explained by the generally low-frequency of emotionally intense WLE. Indeed, none of the participants experienced a highly emotional experience during the 7 days of the experiment. Taken together, the observations of this study led us to support Payne and Nadel (2004)'s claim that dream content reflects certain memory processes taking place during sleep. Notably, the selective consolidation and/or forgetting of new memories during sleep (i.e. *"memory triage"*, Stickgold and Walker, 2013) could be function of the adaptive relevance and the emotional intensity of these memories (Schwartz, 2003; Malinowski and Horton, 2014b; Saletin et al., 2011).

15.2 A role of dreaming in emotional regulation

The questionnaires that the participants had to fill in each morning after awakening included questions regarding the emotional tone of the waking-life memories, not only as they were experienced originally, but also as they were experienced within the dream content. Remarkably, we found that the dreamed version of the WLE was emotionally down-regulated compared to its waking-life counterpart form. Both emotionally positive and negative WLE were rated as less emotionally intense within dreams as compared to their original occurrence in waking-life.

These results suggest the existence of a down-regulation of emotional waking memories during dreaming (i.e. attenuation of the emotional intensity of waking memories toward a more neutral tone), and provide as such one of the very few experimental evidences supporting the emotional regulation theory of dreaming (Cartwright et al., 1998a; Cartwright et al., 1998b; Perogamvros and Schwartz, 2012), which claims that dreaming may actively moderate mood overnight in healthy individuals (see section 4.2.4). Taking up the idea of dreams as an open-window on the cognitive processes occurring during sleep, this down-regulation of emotional waking memories observed in dream content could be the result of an overnight modulation of affective neural system and reprocessing of emotional experiences (Walker and van der Helm, 2009; Goldstein and Walker, 2014). Noteworthy, well in line with our observations, a recent ERP study suggested a dissociation between the informational and emotional components of memories during REM sleep, which might, according to the author, result in a strengthening of the informational core of the memories combined with a reduction of the affective tone (Groch et al., 2013). Furthermore, in addition with being involved in mood regulation, this recombination of memories during sleep may also lead to creative insights and new ideas (Maquet and Ruby, 2004; Payne and Nadel, 2004; Edwards et al., 2013; Barrett, 2017). All the more reason, then, to believe that Hamlet was right to say *"to sleep, perchance to dream"* (Shakespeare, Hamlet, 1603).

15.3 Perspectives

Several open questions remain following this work. For instance, several studies demonstrated that time of night affects wake–dream continuity (Roffwarg et al., 1978; Malinowski and Horton, 2014c), with notably a preferential incorporation of memories from the recent past in the beginning of the night, and a preferential incorporation of memories from the distant past in the end of the night. This suggests the thought-provoking idea that consolidation and regulation processes of waking memories follows a sequential pattern throughout the night. Accordingly, novel and salient waking memories from the recent past could be prioritized and processes earlier in the night than old memories. It would be thus interesting to test, using our protocol, whether we could find differences between the characteristics of the WLE observed from spontaneous awakening (i.e. at the end of the night) and those of the WLE observed earlier in the night (for example, by asking participants to put an alarm clock 2 or 3 hours after going to bed).

Another, perhaps more theoretical issue, relates to whether the dream does really incorporate both day-residues and old memories, or rather that these old memories are somehow linked to day-residues. This latter idea was proposed by Freud (1900) who noticed that *"references to earlier episodes in life may also be incorporated [into dreams], but these episodes were always linked somehow to the dream-day and were therefore, day-residues. For example, they could have been recalled during the dream-day or perhaps reflect the same concern as the day-residue"* (Marquardt et al., 1996). This problem has also been raised by Grenier et al. (2005) who proposed that *"it would be interesting to examine the profile of references [i.e. WLE] that were identified as having been recently thought of or talked about, and to trace the life period to which they refer in terms of the last time seen or experienced in reality"*. The issue remains, however, as to whether the participants would be able to remember all their daily thoughts, words and deeds.

Finally, it should be added that the author of the present thesis contributed to a study which aimed at investigating the putative role of dreaming in memory consolidation (see section 4.2.3). To this aim, we tested whether recalling a dream related to a recent experience is associated with improved post-sleep memory performance (Plailly et al., *in preparation*, see Publications list), using an ecological non-explicit visuo-olfactory learning task (Saive et al., 2013). Participants were presented with a visuo-olfactory environment (odors presented at precise locations of a landscape image) during 7 minutes for 3 consecutive days. They were also asked to record their dreams during the 3 nights following the learning (subjects were selected as high dream recallers). Memory for the multi-sensory episodes was tested on the fourth day of the experiment. Both between-subjects and intra-subjects comparisons revealed no significant effect of dream content on odor recognition and episodic retrieval. In other words, we found no significant effect of the incorporation of the learning phase into dream reports on memory performance. Our results therefore do not argue for the hypothesis of a link between the incorporation of a task into dream report and the subsequent memory of this task. As pointed out by Schredl (2017), *"the research in this area is, however, just at its beginning"*, and further studies are needed to either replicate or refute these findings.

Methodological development 16

16.1 A state-of-the-art open-source software

SLEEP is a free, cross-platform and open-source graphical user interface dedicated to sleep reading, scoring and analysis. Initially designed for a personal use, it soon extended into a fully developed and comprehensive software thanks to a close collaboration with a fellow PhD student, Etienne Combrisson. SLEEP has many advantages over other existing solutions. First, and perhaps most importantly, it is free and open-source. Second, it leverages the graphics processing unit to deliver cutting edge graphical performances. Third, it natively supports several commercial and public data file formats, thus making it accessible to the greatest possible number of people. Fourth, it implements several signal processing tools, as well as several automatic detections of sleep microstructural features. Fifth, it comes with an extensive documentation, a chat room and a peer-reviewed publication. In view of all these functionalities, one can reasonably conclude that SLEEP represents a state-of-the-art software in sleep research which should consequently benefit many. Furthermore, as the development of the software is still ongoing, novel functionalities will continue to be added. Some of these future perspectives are detailed in the section below.

16.2 Future directions

SLEEP includes so far 5 algorithms for detecting some of the most prominent features of each sleep stage, namely spindles, K-complexes, slow waves, rapid eye movements and muscle twitches. Two of these detections (spindles and K-complexes) were compared against a visual scoring reference and showed overall good performances. Yet, there are still opportunities for further enhancements and the detection algorithms were improved since the initial, published, version. An example of the updated spindles detection pipeline can be found in Fig 16.1.

Furthermore, perhaps one of the most challenging issue in sleep research is the scoring of sleep stages. Currently, the gold standard remains visual scoring by an expert, which is time-consuming and subject to high inter-rater variability. There is therefore a crucial need for reliable and time-efficient algorithms capable of detecting sleep stages in healthy and patients alike. With this in mind, we are currently working on two distinct automatic sleep scoring methods, based respectively on spectral feature extraction / microstructural detection (Fig 16.2), and on machine-learning algorithms. Preliminary results based on the former method show a 81% agreement with a manually scored standard reference, a

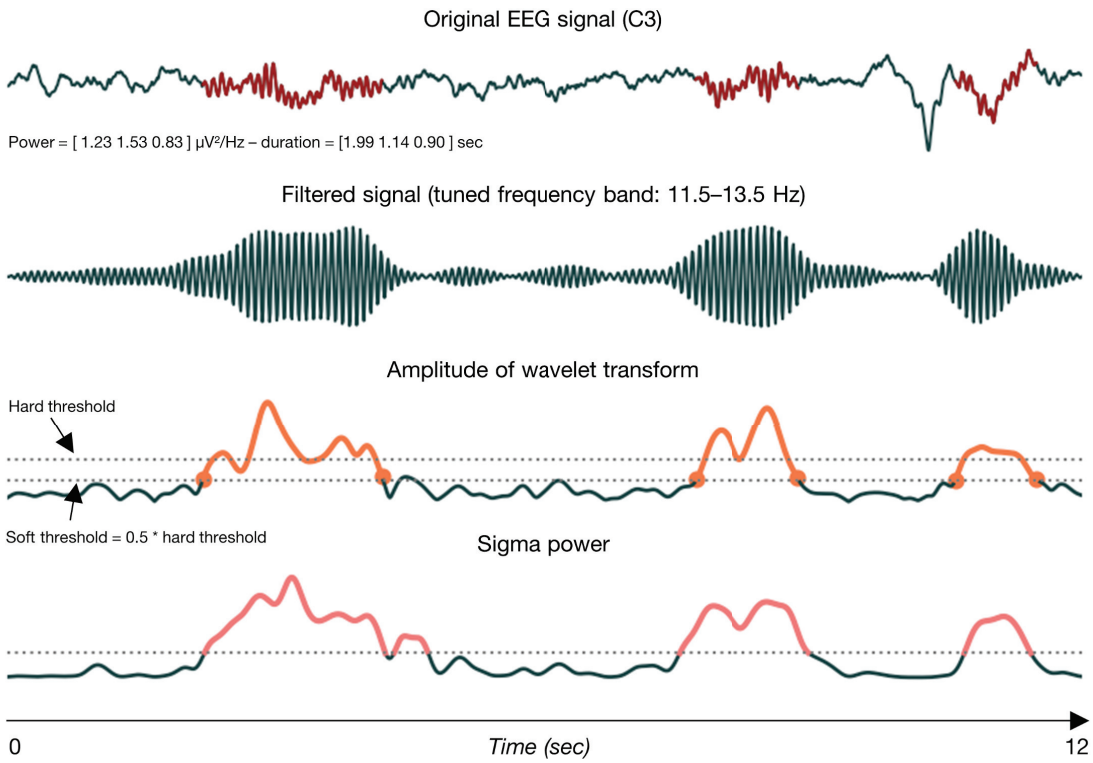

Fig. 16.1 **Improved spindles detection algorithm.** Compared to the initial algorithm (presented in chapter 13), the new spindles detection has several improvements. First, we implemented a data-driven tuning of the spindle frequency band by finding the peak spectral power within the sigma range. This step, described by Berthomier et al. (2007), allows to accommodate for inter-individual variability of EEG signals, and is particularly useful when analyzing patients who tend to exhibit higher variability. Second, we now use both a hard and a soft threshold on the amplitude of the wavelet transform to determine more precisely the beginning and the end of each spindle. Finally, to allow users to better understand how the detection algorithm works, we implemented a function to plot the current figure for each desired time window.

figure comprised within the range of human inter-scorer agreements (generally between 80 and 90%, see Silber et al., 2007). A similar agreement was obtained using the second, machine-learning based automatic sleep scoring method. Future developments will be needed to get the most out of these two methods and ultimately provide a state-of-the-art algorithm.

Finally, it is also important to consider that SLEEP is part of a larger package, in which the author of the present thesis is a main contributor, entitled Visbrain. Visbrain is a high-performance open source visualization suite dedicated to neuroscientific data at large. It currently includes 6 visualization modules, among which the three most prominent are SLEEP, BRAIN and SIGNAL. The BRAIN module is dedicated to EEG, magneto-encephalographic (MEG) and intra-cranial recordings, and allows notably the visualization of connectivity, sources and regions of interests on a 3D brain template. The SIGNAL module is dedicated to the visualization of uni- or multi-dimensional time-series arrays, and offers as such a convenient way to inspect datasets, locate artifacts and quickly analyze time-frequency properties of time-series. We are currently working on connecting the SIGNAL and the SLEEP module, notably through the visualization of automatically

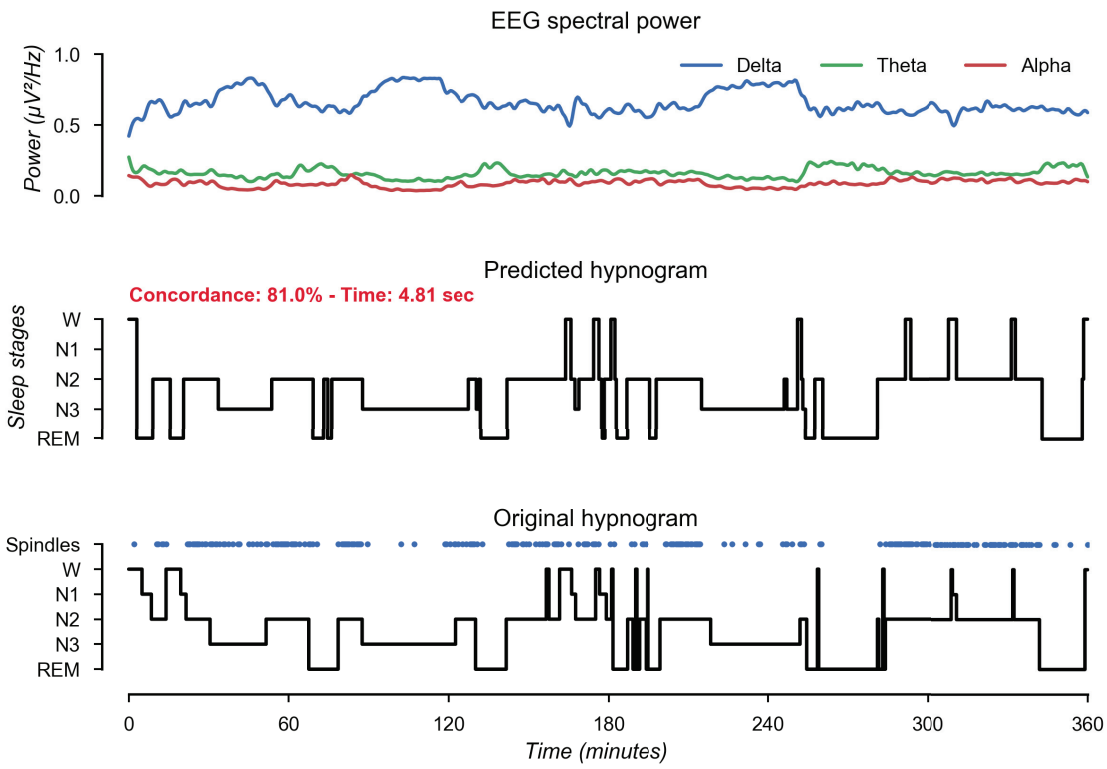

Fig. 16.2 **Preliminary results of the automatic sleep scoring algorithm.** The algorithm is based on a combination of spectral features extraction (Top) and automatic detection of microstructural features (e.g. spindles, blue dots). Preliminary tests on a single EEG channel (C3) of one healthy individual yielded 81% agreement between the predicted and the manually scored full night hypnogram (with a running time inferior to 5 seconds).

detected microstructural sleep events (e.g. spindles) inside the SIGNAL module. This will provide the users an interface to identify, at a glance, the false-positive events, and allow them to further investigate the time-frequency properties of each or all events.

17 General conclusion

Throughout this work, we have addressed several unresolved issue related to the nature, the physiological correlates, and the function of dreaming. A large part of the present thesis was devoted to comparing cognitive and neurophysiological variables in high and low dream recallers, in an effort to understand *"what cause sleepers sometimes dream, and sometimes do not"* (Aristotle, On Sleep and Sleeplessness, 350 B.C., see section 2). Our results revealed that the ability to recall dream is positively associated with (1) a longer duration of intra-sleep awakenings during sleep, (2) the strength of functional connectivity in specific areas of the brain during sleep, wakefulness, and notably the period following awakening and (3) creative-thinking abilities. Based on all these findings, we proposed a new model of the dream recall process integrating the contribution of all these factors as well as their interactions. A second aspect of our work was to better understand the relationship between waking life and dream content, through an exhaustive analysis of the characteristics of waking-life memories incorporated into dreams. Our findings, in addition with providing insights on the *stuff that dreams are made on*, remarkably suggest the existence of a down-regulation of emotional waking memories during dreaming. Finally, we have been committed to developing a free and comprehensive software dedicated to sleep analysis, which will hopefully represent an important step forward in sleep research by providing students, researchers and engineers a common and portable platform for their analyses. Therefore, and although much works remain to be done, the present thesis opened up a new chapter in the understanding of this fascinating phenomenon that is dreaming. The experimental, theoretical and methodological contributions of the present work could serve as a basis for future research, in the hope that someday, we will be able to fully apprehend dreaming, in all its richness and diversity.

Part V

REFERENCES

Translations

18

[1] Free translation to English: *"The science of dreams holds an intermediate position between history and biology. It is a science of observation, considering the essential role that observation plays in it, but it is also an historical science in that the elapsed dream can never be reenacted and is therefore investigated, not directly, but through memory"*. —Yves Delage. Le rêve. Etude psychologique, philosophique et littéraire. 1920

[2] Free translation from French: *"Le rêve, à t-on dit, est la pensée du sommeil. A-t-on jamais songé à mettre en doute l'exactitude de cette formule? Je pense qu'il convient de la modifier, et de dire : Le rêve dont on se souvient est la pensée du réveil."* —Edmond Goblot. Le souvenir des rêves. 1896

[3] Free translation from French: *"La mémoire bannit rapidement les rêves, parce qu'ils n'ont pas de conséquences dans la réalité et qu'il n'y a que profit à les oublier."* —Roger Caillois. L'incertitude qui vient des rêves. 1956

[4] Free translation to English: *"To assimilate dreams as mere thoughts or images of the imagination, is to show a lack of reflection or loyalty; because obviously they differ from it specifically. The images of the imagination are feeble, languid, incomplete, partial, and so fleeting that one can scarcely fix in his memory for a few seconds the features of an absent, and that even the most lively play of the imagination cannot be compared to the palpable reality that dreams bring before our eyes."* —Schopenhauer. Parerga und Paralipomena. 1851

[5] English translation: *"Dreamed indeed I have, and that right lustily; but I could take along with me no more thereof that I did goodly understand."* —François Rabelais. Pantagruel. 1532

[6] Free translation to English: *"Dreaming is undoubtedly one of the phenomenon, which, better than the sun or the rain, places men of any climate, of any time and any condition in front of identical problems"* —Roger Caillois. L'incertitude qui vient des rêves. 1956

Bibliography

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Abel, G. G., W. D. Murphy, J. V. Becker, and A. Bitar (1979). “Women’s vaginal responses during REM sleep”. In: *Journal of sex & marital therapy* 5.1, pp. 5–14 (cit. on p. 6).

Aguera, P.-E., K. Jerbi, A. Caclin, and O. Bertrand (2011). “ELAN: A Software Package for Analysis and Visualization of MEG, EEG, and LFP Signals”. en. In: *Computational Intelligence and Neuroscience* 2011, pp. 1–11 (cit. on p. 50).

American Sleep Disorders Association (1992). “EEG arousals: scoring rules and examples”. In: *Sleep* 15, pp. 74–101 (cit. on p. 8).

Andrews-Hanna, J. R., J. S. Reidler, J. Sepulcre, R. Poulin, and R. L. Buckner (2010). “Functional-Anatomic Fractionation of the Brain’s Default Network”. en. In: *Neuron* 65.4, pp. 550–562 (cit. on pp. 56, 194).

Andrillon, T. (2016). “The sleeping brain at work: perceptual processing and learning in human sleep”. PhD thesis. Paris Sciences et Lettres (cit. on pp. 5, 52).

Aserinsky, E. and N. Kleitman (1953). “Regularly occurring periods of eye motility, and concomitant phenomena, during sleep”. In: *Science* 118.3062, pp. 273–274 (cit. on p. 10).

Baer, J. and J. C. Kaufman (2008). “Gender differences in creativity”. In: *The Journal of Creative Behavior* 42.2, pp. 75–105 (cit. on p. 194).

Balkin, T. J., A. R. Braun, N. J. Wesensten, et al. (2002). “The process of awakening: a PET study of regional brain activity patterns mediating the re-establishment of alertness and consciousness”. eng. In: *Brain: A Journal of Neurology* 125.Pt 10, pp. 2308–2319 (cit. on pp. 82, 97).

Barrett, D. (1993). “The" committee of sleep": A study of dream incubation for problem solving.” In: *Dreaming* 3.2, pp. 115–122 (cit. on p. 129).

– (2017). “Dreams and creative problem-solving: Dreams and creative problem-solving”. en. In: *Annals of the New York Academy of Sciences* (cit. on pp. 129, 200).

Bastuji, H., C. Perchet, V. Legrain, C. Montes, and L. Garcia-Larrea (2008). “Laser evoked responses to painful stimulation persist during sleep and predict subsequent arousals”. eng. In: *Pain* 137.3, pp. 589–599 (cit. on pp. 39, 191).

Bastuji, H. and L. García-Larrea (1999). “Evoked potentials as a tool for the investigation of human sleep”. In: *Sleep medicine reviews* 3.1, pp. 23–45 (cit. on p. 52).

Bastuji, H., L. García-Larrea, C. Franc, and F. Mauguière (1995). “Brain processing of stimulus deviance during slow-wave and paradoxical sleep: a study of human auditory evoked responses using the oddball paradigm.” In: *Journal of Clinical Neurophysiology* 12.2, pp. 155–167 (cit. on p. 52).

Bastuji, H., F. Perrin, and L. Garcia-Larrea (2003). “Event-related potentials during forced awakening: a tool for the study of acute sleep inertia”. In: *Journal of sleep research* 12.3, pp. 189–206 (cit. on p. 52).

Beaty, R. E., M. Benedek, R. W. Wilkins, et al. (2014). “Creativity and the default network: A functional connectivity analysis of the creative brain at rest”. en. In: *Neuropsychologia* 64, pp. 92–98 (cit. on pp. 120, 129, 193).

Beaty, R. E., M. Benedek, S. Barry Kaufman, and P. J. Silvia (2015). “Default and Executive Network Coupling Supports Creative Idea Production”. en. In: *Scientific Reports* 5.1 (cit. on pp. 120, 129, 193).

Beck, F., J. B. Richard, and D. Leger (2013). “Insomnia and total sleep time in France: prevalence and associated socio-demographic factors in a general population survey”. In: *Revue neurologique* 169.12, pp. 956–964 (cit. on pp. 134, 141, 142).

Beckmann, C. F., M. DeLuca, J. T. Devlin, and S. M. Smith (2005). “Investigations into resting-state connectivity using independent component analysis”. en. In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 360.1457, pp. 1001–1013 (cit. on p. 59).

Behzadi, Y., K. Restom, J. Liau, and T. T. Liu (2007). “A component based noise correction method (CompCor) for BOLD and perfusion based fMRI”. In: *Neuroimage* 37.1, pp. 90–101 (cit. on pp. 86, 110, 124).

Berger, H. (1929). “Über das elektrenkephalogramm des menschen”. In: *European Archives of Psychiatry and Clinical Neuroscience* 87.1, pp. 527–570 (cit. on p. 49).

Berger, R. J. (1961). “Tonus of extrinsic laryngeal muscles during sleep and dreaming”. In: *Science* 134.3482, pp. 840–840 (cit. on p. 10).

Berthomier, C., X. Drouot, M. Herman-Stoïca, et al. (2007). “Automatic analysis of single-channel sleep EEG: validation in healthy individuals”. In: *Sleep* 30.11, p. 1587 (cit. on p. 204).

Biswal, B., F. Zerrin Yetkin, V. M. Haughton, and J. S. Hyde (1995). “Functional connectivity in the motor cortex of resting human brain using echo-planar mri”. In: *Magnetic resonance in medicine* 34.4, pp. 537–541 (cit. on p. 54).

Blagrove, M. (2011). “Distinguishing continuity/discontinuity, function and insight when investigating dream content”. In: *International Journal of Dream Research* 4.2, pp. 45–47 (cit. on p. 36).

Blagrove, M. and E. F. Pace-Schott (2010). “Trait And Neurobiological Correlates Of Individual Differences In Dream Recall And Dream Content”. en. In: *International Review of Neurobiology*. Vol. 92. Elsevier, pp. 155–180 (cit. on pp. 19, 28).

Blagrove, M., J. Henley-Einion, A. Barnett, D. Edwards, and C. Heidi Seage (2011a). “A replication of the 5–7day dream-lag effect with comparison of dreams to future events as control for baseline matching”. en. In: *Consciousness and Cognition* 20.2, pp. 384–391 (cit. on p. 30).

Blagrove, M., N. C. Fouquet, J. A. Henley-Einion, E. F. Pace-Schott, A. C. Davies, J. L. Neuschaffer, and O. H. Turnbull (2011b). “Assessing the Dream-Lag Effect for REM and NREM Stage 2 Dreams”. en. In: *PLoS ONE* 6.10. Ed. by M. Tsakiris, e26708 (cit. on p. 30).

Bluhm, R. L., E. A. Osuch, R. A. Lanius, K. Boksman, R. W. Neufeld, J. Théberge, and P. Williamson (2008). “Default mode network connectivity: effects of age, sex, and analytic approach”. In: *Neuroreport* 19.8, pp. 887–891 (cit. on p. 194).

Bonnet, M. H. (1983). “Memory For Events Occurring During Arousal From Sleep”. en. In: *Psychophysiology* 20.1, pp. 81–87 (cit. on pp. 113, 114).

Bonnet, M. H. and D. L. Arand (2007). “EEG arousal norms by age”. eng. In: *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 3.3, pp. 271–274 (cit. on p. 8).

Bonnet, M. H., K. Doghramji, T. Roehrs, et al. (2007). “The scoring of arousal in sleep: reliability, validity, and alternatives”. eng. In: *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 3.2, pp. 133–145 (cit. on p. 8).

Borbély, A. A. (1982). “A two process model of sleep regulation.” In: *Human neurobiology* (cit. on p. 4).

Botman, H. I. and H. F. Crovitz (1990). “Dream reports and autobiographical memory”. In: *Imagination, Cognition and Personality* 9.3, pp. 213–224 (cit. on p. 30).

Boveroux, P., A. Vanhaudenhuyse, M.-A. Bruno, et al. (2010). “Breakdown of within-and between-network resting state functional magnetic resonance imaging connectivity during propofol-induced loss of consciousness”. In: *The Journal of the American Society of Anesthesiologists* 113.5, pp. 1038–1053 (cit. on p. 95).

Braun, A. R., T. J. Balkin, N. J. Wesenten, et al. (1997). “Regional cerebral blood flow throughout the sleep-wake cycle. An H2 (15) O PET study.” In: *Brain: a journal of neurology* 120.7, pp. 1173–1197 (cit. on p. 12).

Bryant, P. A., J. Trinder, and N. Curtis (2004). “Sick and tired: does sleep have a vital role in the immune system?” In: *Nature Reviews Immunology* 4.6, pp. 457–468 (cit. on p. 5).

Buboltz, W. C., F. Brown, and B. Soper (2001). “Sleep Habits and Patterns of College Students: A Preliminary Study”. en. In: *Journal of American College Health* 50.3, pp. 131–135 (cit. on pp. 43, 134, 141).

Buckner, R. L., F. M. Krienen, and B. T. T. Yeo (2013). “Opportunities and limitations of intrinsic functional connectivity MRI”. In: *Nature Neuroscience* 16.7, pp. 832–837 (cit. on pp. 56, 57).

Bullmore, E. and O. Sporns (2009). “Complex brain networks: graph theoretical analysis of structural and functional systems”. In: *Nature Reviews Neuroscience* 10.3, pp. 186–198 (cit. on p. 59).

Buysse, D. J., C. F. Reynolds, T. H. Monk, S. R. Berman, and D. J. Kupfer (1989). “The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research”. en. In: *Psychiatry Research* 28.2, pp. 193–213 (cit. on p. 122).

Caillois, R. (1956). *L’incertitude qui vient des rêves*. Vol. 488. Gallimard (cit. on p. 24).

Calkins, M. W. (1893). “Statistics of dreams”. In: *The American Journal of Psychology* 5.3, pp. 311–343 (cit. on p. 27).

Campbell, S. S. and W. B. Webb (1981). “The perception of wakefulness within sleep”. eng. In: *Sleep* 4.2, pp. 177–183 (cit. on p. 189).

Cartwright, R., A. Luten, M. Young, P. Mercer, and M. Bears (1998a). “Role of REM sleep and dream affect in overnight mood regulation: a study of normal volunteers”. In: *Psychiatry Research* 81.1, pp. 1–8 (cit. on pp. 31, 36, 200).

Cartwright, R., M. A. Young, P. Mercer, and M. Bears (1998b). “Role of REM sleep and dream variables in the prediction of remission from depression”. In: *Psychiatry Research* 80.3, pp. 249–255 (cit. on pp. 36, 200).

Cartwright, R., M. Y. Agargun, J. Kirkby, and J. K. Friedman (2006). “Relation of dreams to waking concerns”. In: *Psychiatry Research* 141.3, pp. 261–270 (cit. on pp. 30, 31).

Cartwright, R. D. (1991). “Dreams that work: The relation of dream incorporation to adaptation to stressful events.” In: *Dreaming* 1.1, pp. 3–9 (cit. on p. 31).

Cavallero, C. (1987). “Dream sources, associative mechanisms, and temporal dimension.” In: *Sleep* 10.1, pp. 78–83 (cit. on p. 44).

Cavallero, C. E. and D. E. Foulkes (1993). *Dreaming as cognition.* Harvester Wheatsheaf (cit. on p. 29).

Chellappa, S. L., S. Frey, V. Knoblauch, and C. Cajochen (2011). “Cortical activation patterns herald successful dream recall after NREM and REM sleep”. en. In: *Biological Psychology* 87.2, pp. 251–256 (cit. on pp. 15, 16, 120).

Christoff, K., Z. C. Irving, K. C. R. Fox, R. N. Spreng, and J. R. Andrews-Hanna (2016). “Mind-wandering as spontaneous thought: a dynamic framework”. In: *Nature Reviews Neuroscience* 17.11, pp. 718–731 (cit. on pp. 15, 42, 56, 58, 89, 95, 106, 120, 129, 193).

Cipolli, C., R. Bolzani, C. Comoldi, R. D. Beni, and I. Fagioli (1993). “Bizarreness effect in dream recall”. In: *Sleep* 16.2, pp. 163–170 (cit. on pp. 24, 195).

Cohen, D. B. and P. F. MacNeilage (1974). “A test of the salience hypothesis of dream recall.” In: *Journal of Consulting and Clinical Psychology* 42.5, p. 699 (cit. on pp. 24, 195).

Cohen, D. B. and G. Wolfe (1973). “Dream recall and repression: Evidence for an alternative hypothesis.” In: *Journal of Consulting and Clinical Psychology* 41.3, p. 349 (cit. on pp. 23, 195).

Colrain, I. M. and K. B. Campbell (2007). “The use of evoked potentials in sleep research”. en. In: *Sleep Medicine Reviews* 11.4, pp. 277–293 (cit. on p. 52).

Combrisson, E., R. Vallat, J.-B. Eichenlaub, et al. (2017). “Sleep: an open-source python software for visualization, analysis and staging of sleep data”. In: *Frontiers in Neuroinformatics* 11, p. 60 (cit. on pp. 86, 109).

Conduit, R., S. G. Crewther, and G. Coleman (2004). “Poor recall of eye-movement signals from Stage 2 compared to REM sleep: Implications for models of dreaming”. en. In: *Consciousness and Cognition* 13.3, pp. 484–500 (cit. on pp. 19, 25, 40, 106, 113, 114, 190).

Connor, G. N. and W. Boblitt (1970). “Reported frequency of dream recall as a function of intelligence and various personality test factors”. In: *Journal of clinical psychology* 26.4, pp. 438–439 (cit. on p. 19).

Curcio, G., M. Ferrara, and L. De Gennaro (2006). “Sleep loss, learning capacity and academic performance”. en. In: *Sleep Medicine Reviews* 10.5, pp. 323–337 (cit. on pp. 43, 134).

Damoiseaux, J., C. Beckmann, E. S. Arigita, et al. (2008). “Reduced resting-state brain activity in the “default network” in normal aging”. en. In: *Cerebral Cortex* 18.8, pp. 1856–1864 (cit. on p. 194).

De Gennaro, L., M. Ferrara, and M. Bertini (2001). “EEG arousals in normal sleep: variations induced by total and selective slow-wave sleep deprivation”. eng. In: *Sleep* 24.6, pp. 673–679 (cit. on p. 8).

De Gennaro, L., C. Marzano, F. Moroni, G. Curcio, M. Ferrara, and C. Cipolli (2010). “Recovery sleep after sleep deprivation almost completely abolishes dream recall”. In: *Behavioural Brain Research* 206.2, pp. 293–298 (cit. on pp. 19, 106).

De Havas, J. A., S. Parimal, C. S. Soon, and M. W. Chee (2012). “Sleep deprivation reduces default mode network connectivity and anti-correlation during rest and task performance”. en. In: *NeuroImage* 59.2, pp. 1745–1751 (cit. on pp. 56, 82, 95, 97, 114, 192).

De Koninck, J. (2012). “Sleep, dreams and dreaming”. In: *Oxford handbook of sleep and sleep disorders*, pp. 150–171 (cit. on pp. 13, 28, 29, 33).

Delorme, A. and S. Makeig (2004). “EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis”. In: *Journal of neuroscience methods* 134.1, pp. 9–21 (cit. on p. 50).

Dement, W. and N. Kleitman (1957). “The relation of eye movements during sleep to dream activity: an objective method for the study of dreaming.” In: *Journal of experimental psychology* 53.5, p. 339 (cit. on pp. 10, 129).

Dement, W. and E. A. Wolpert (1958). “The relation of eye movements, body motility, and external stimuli to dream content.” In: *Journal of experimental psychology* 55.6, p. 543 (cit. on pp. 10, 31).

Diekelmann, S. and J. Born (2010). “The memory function of sleep”. In: *Nature Reviews Neuroscience* (cit. on pp. 5, 35).

Dietrich, A. and R. Kanso (2010). “A review of EEG, ERP, and neuroimaging studies of creativity and insight.” en. In: *Psychological Bulletin* 136.5, pp. 822–848 (cit. on p. 129).

Dijk, D.-J. (2015). “Dreaming, memory, insomnia and the exploding attention for sleep”. en. In: *Journal of Sleep Research* 24.4, pp. 359–359 (cit. on p. 133).

Dinges, D. F. (1990). “Are you awake? Cognitive performance and reverie during the hypnopompic state”. In: *Sleep and cognition. Washington, DC: American Psychological Association*, pp. 159–75 (cit. on p. 113).

Dinges, D. F., M. T. Orne, and E. C. Orne (1985). “Assessing performance upon abrupt awakening from naps during quasi-continuous operations”. In: *Behavior Research Methods, Instruments, & Computers* 17.1, pp. 37–45 (cit. on pp. 84, 85, 94, 108, 114).

Domhoff, G. W. (2001). “A new neurocognitive theory of dreams”. In: *Dreaming* 11.1, pp. 13–33 (cit. on p. 29).

– (2011). “The neural substrate for dreaming: Is it a subsystem of the default network?” en. In: *Consciousness and Cognition* 20.4, pp. 1163–1174 (cit. on pp. 15, 106, 120).

– (2013). *Finding meaning in dreams: A quantitative approach*. Springer Science & Business Media (cit. on p. 28).

Domhoff, G. W. and K. C. Fox (2015). “Dreaming and the default network: A review, synthesis, and counterintuitive research proposal”. en. In: *Consciousness and Cognition* 33, pp. 342–353 (cit. on p. 15).

Domhoff, G. W. and A. Schneider (2008a). “Similarities and differences in dream content at the cross-cultural, gender, and individual levels”. en. In: *Consciousness and Cognition* 17.4, pp. 1257–1265 (cit. on p. 29).

– (2008b). “Studying dream content using the archive and search engine on DreamBank.net”. en. In: *Consciousness and Cognition* 17.4, pp. 1238–1247 (cit. on p. 171).

Dresler, M., R. Wehrle, V. I. Spoormaker, et al. (2012). “Neural correlates of dream lucidity obtained from contrasting lucid versus non-lucid REM sleep: a combined EEG/fMRI case study”. eng. In: *Sleep* 35.7, pp. 1017–1020 (cit. on pp. 9, 14).

Duyn, J. H. (2012). “EEG-fMRI Methods for the Study of Brain Networks during Sleep”. In: *Frontiers in Neurology* 3 (cit. on pp. 59, 87, 113, 192).

Edwards, C. L., P. M. Ruby, J. E. Malinowski, P. D. Bennett, and M. T. Blagrove (2013). “Dreaming and insight”. In: *Frontiers in Psychology* 4 (cit. on pp. 129, 200).

Eichenlaub, J.-B., O. Bertrand, D. Morlet, and P. Ruby (2014a). “Brain Reactivity Differentiates Subjects with High and Low Dream Recall Frequencies during Both Sleep and Wakefulness”. en. In: *Cerebral Cortex* 24.5, pp. 1206–1215 (cit. on pp. 20, 21, 38, 39, 105, 106, 110, 113, 120, 129, 142, 189–191).

Eichenlaub, J.-B., A. Nicolas, J. Daltrozzo, J. Redouté, N. Costes, and P. Ruby (2014b). “Resting brain activity varies with dream recall frequency between subjects”. eng. In: *Neuropsychopharmacology* 39.7, pp. 1594–1602 (cit. on pp. 21, 106, 113, 120, 127, 193).

Ellamil, M., C. Dobson, M. Beeman, and K. Christoff (2012). “Evaluative and generative modes of thought during the creative process”. en. In: *NeuroImage* 59.2, pp. 1783–1794 (cit. on pp. 120, 129, 193).

Ellman, S. J. and J. S. Antrobus (1991). *The mind in sleep: Psychology and psychophysiology*. Vol. 166. John Wiley & Sons (cit. on p. 10).

Esposito, M. J., T. A. Nielsen, and T. Paquette (2004). “Reduced Alpha power associated with the recall of mentation from Stage 2 and Stage REM sleep”. en. In: *Psychophysiology* 41.2, pp. 288–297 (cit. on pp. 14, 16, 120).

Evans, F. J. and M. T. Orne (1975). *Recovery from Fatigue.* Tech. rep. DTIC Document (cit. on pp. 84, 94, 108).

Faraut, B., T. Andrillon, M.-F. Vecchierini, and D. Leger (2016). “Napping: A public health issue. From epidemiological to laboratory studies”. en. In: *Sleep Medicine Reviews* (cit. on pp. 40, 82, 83, 94).

Ferrara, M., G Curcio, F Fratello, F Moroni, C. Marzano, M Pellicciari, and L Gennaro (2006). “The electroencephalographic substratum of the awakening”. en. In: *Behavioural Brain Research* 167.2, pp. 237–244 (cit. on pp. 82, 95).

Fisher, C., J. Gross, and J. Zuch (1965). “Cycle of penile erection synchronous with dreaming (REM) sleep: preliminary report”. In: *Archives of General Psychiatry* 12.1, pp. 29–45 (cit. on p. 6).

Fitch, T. and R. Armitage (1989). “Variations in cognitive style among high and low frequency dream recallers”. In: *Personality and Individual Differences* 10.8, pp. 869–875 (cit. on pp. 19, 120, 127, 193).

Forquer, L. M., A. E. Camden, K. M. Gabriau, and C. M. Johnson (2008). “Sleep patterns of college students at a public university”. In: *Journal of American College Health* 56.5, pp. 563–565 (cit. on pp. 43, 134).

Fosse, M. J., R. Fosse, J. A. Hobson, and R. Stickgold (2003). “Dreaming and episodic memory: a functional dissociation?” In: *Journal of Cognitive Neuroscience* 15.1, pp. 1–9 (cit. on p. 30).

Foulkes, D. (1982). *Children’s dreams: Longitudinal studies*. John Wiley & Sons (cit. on p. 28).

Foulkes, D., M. Hollifield, B. Sullivan, L. Bradley, and R. Terry (1990). “REM dreaming and cognitive skills at ages 5-8: A cross-sectional study”. In: *International Journal of Behavioral Development* 13.4, pp. 447–465 (cit. on p. 28).

Foulkes, W. D. (1962). “Dream reports from different stages of sleep.” In: *The Journal of Abnormal and Social Psychology* 65.1, p. 14 (cit. on p. 10).

Fox, M. D. and M. E. Raichle (2007). “Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging”. In: *Nature Reviews Neuroscience* 8.9, pp. 700–711 (cit. on p. 56).

Fox, M. D., A. Z. Snyder, J. L. Vincent, M. Corbetta, D. C. Van Essen, and M. E. Raichle (2005). “The human brain is intrinsically organized into dynamic, anticorrelated functional networks”. In: *Proceedings of the National Academy of Sciences of the United States of America* 102.27, pp. 9673–9678 (cit. on p. 56).

Freud, S. (1900). *The Interpretation of Dreams. SE, 4–5*. London: Hogarth (cit. on pp. 23, 30, 33, 44, 201).

Germain, A., T. A. Nielsen, M. Khodaverdi, P. Bessette, B. Faucher, and I. Raymond (1999). “Fast frequency EEG correlates of dream recall from REM sleep”. In: *Sleep* 22.Suppl 1, p. 131 (cit. on p. 16).

Goblot, E. (1896). “Le souvenir des rêves”. In: *Revue Philosophique de la France et de l’Étranger* 42, pp. 288–290 (cit. on p. 9).

Goldstein, A. N. and M. P. Walker (2014). “The Role of Sleep in Emotional Brain Function”. en. In: *Annual Review of Clinical Psychology* 10.1, pp. 679–708 (cit. on pp. 5, 200).

Goodenough, D. R., A. Shapiro, M. Holden, and L. Steinschriber (1959). “A comparison of" dreamers" and" nondreamers": Eye movements, electroencephalograms, and the recall of dreams.” In: *The Journal of Abnormal and Social Psychology* 59.3, p. 295 (cit. on pp. 10, 18, 106, 191).

Gorgoni, M., M. Ferrara, A. D’Atri, G. Lauri, S. Scarpelli, I. Truglia, and L. De Gennaro (2015). “EEG topography during sleep inertia upon awakening after a period of increased homeostatic sleep pressure”. en. In: *Sleep Medicine* 16.7, pp. 883–890 (cit. on pp. 82, 95).

Grenier, J., P. Cappeliez, M. St-Onge, et al. (2005). “Temporal references in dreams and autobiographical memory”. In: *Memory & cognition* 33.2, pp. 280–288 (cit. on pp. 30, 44, 201).

Groch, S., I. Wilhelm, S. Diekelmann, and J. Born (2013). “The role of REM sleep in the processing of emotional memories: Evidence from behavior and event-related potentials”. en. In: *Neurobiology of Learning and Memory* 99, pp. 1–9 (cit. on p. 200).

Guildford, J. P., P. R. Christensen, P. R. Merrifield, and R. C. Wilson (1978). “Alternate uses: Manual of instructions and interpretation”. In: *Orange, CA: Sheridan Psychological Services* (cit. on pp. 42, 123).

Gusnard, D. A. and M. E. Raichle (2001). “Searching for a baseline: functional imaging and the resting human brain”. In: *Nature Reviews Neuroscience* 2.10, pp. 685–694 (cit. on p. 120).

Guénolé, F. (2009). “À quel moment le rêve se produit-il au cours d’une nuit de sommeil ? Une revue des données psychophysiologiques”. fr. In: *Médecine du Sommeil* 6.2, pp. 56–64 (cit. on pp. 3, 4).

Guénolé, F. and A. Nicolas (2010). “Le rêve est un état hypnique de la conscience : pour en finir avec l’hypothèse de Goblot et ses avatars contemporains”. fr. In: *Neurophysiologie Clinique/Clinical Neurophysiology* 40.4, pp. 193–199 (cit. on p. 9).

Guénolé, F., G. Marcaggi, and J.-M. Baleyte (2013). “Do dreams really guard sleep? Evidence for and against Freud’s theory of the basic function of dreaming”. In: *Frontiers in Psychology* 4 (cit. on p. 34).

Hall, C. S. and R. L. Van de Castle (1966). *The content analysis of dreams.* New York: Appleton-Century-Crofts (cit. on pp. 27, 28, 35, 171).

Hall, C. S., G. W. Domhoff, K. A. Blick, and K. E. Weesner (1982). “The dreams of college men and women in 1950 and 1980: A comparison of dream contents and sex differences”. In: *Sleep* 5.2, pp. 188–194 (cit. on p. 27).

Hartmann, E. (1996). “We do not dream of the Three R’s: a study and implications”. In: *Sleep Research* 25, p. 136 (cit. on p. 30).

Hartmann, E. (1989). “Boundaries of dreams, boundaries of dreamers: Thin and thick boundaries as a new personality measure.” In: *Psychiatric Journal of the University of Ottawa* 14, pp. 557–560 (cit. on pp. 19, 120, 129, 142, 193).

– (2007). “The nature and functions of dreaming”. In: *The New Science of Dreaming: Content, Recall and Personality Correlates*, pp. 171–192 (cit. on p. 29).

– (2008). “The central image makes" big" dreams big: The central image as the emotional heart of the dream.” In: *Dreaming* 18.1, pp. 44–57 (cit. on p. 29).

Hayasaka, S. and P. J. Laurienti (2010). “Comparison of characteristics between region-and voxel-based network analyses in resting-state fMRI data”. en. In: *NeuroImage* 50.2, pp. 499–508 (cit. on p. 59).

Hirshkowitz, M. (2004). “Normal human sleep: an overview”. en. In: *Medical Clinics of North America* 88.3, pp. 551–565 (cit. on pp. 5, 6, 141).

Hobson, J. A. (1988). *The dreaming brain*. Basic Books (cit. on p. 13).

Hobson, J. A., E. F. Pace-Schott, R. Stickgold, and D. Kahn (1998). “To dream or not to dream? Relevant data from new neuroimaging and electrophysiological studies”. In: *Current opinion in neurobiology* 8.2, pp. 239–244 (cit. on pp. 11, 34).

Hobson, J. A., E. F. Pace-Schott, and R. Stickgold (2000). “Dreaming and the brain: Toward a cognitive neuroscience of conscious states”. In: *Behavioral and Brain Sciences* 23.6, pp. 793–842 (cit. on p. 13).

Horovitz, S. G., A. R. Braun, W. S. Carr, D. Picchioni, T. J. Balkin, M. Fukunaga, and J. H. Duyn (2009). “Decoupling of the brain’s default mode network during deep sleep”. In: *Proceedings of the National Academy of Sciences* 106.27, pp. 11376–11381 (cit. on pp. 56, 82, 106).

Iber, C. (2007). *The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications*. American Academy of Sleep Medicine (cit. on pp. 5, 109).

Jackson, J. D. and D. A. Balota (2012). "Mind-wandering in younger and older adults: Converging evidence from the sustained attention to response task and reading for comprehension." en. In: *Psychology and Aging* 27.1, pp. 106–119 (cit. on p. 194).

John, O. P. and S. Srivastava (1999). "The Big Five trait taxonomy: History, measurement, and theoretical perspectives". In: *Handbook of personality: Theory and research* 2.1999, pp. 102–138 (cit. on pp. 42, 122).

Jouvet, M. (1979). "Mémoire et 'cerveau dédoublé'au cours du rêve a propos de 2525 souvenirs de rêve". In: *L'année du praticien* 29, pp. 27–32 (cit. on p. 34).

– (1991). "Le sommeil paradoxal: Est-il le gardien de l'individuation psychologique?" In: *Canadian Journal of Psychology/Revue canadienne de psychologie* 45.2, p. 148 (cit. on p. 34).

Jouvet, M., F. Michel, and J. Courjon (1959). "Sur un stade d'activité électrique cérébrale rapide au cours du sommeil physiologique". In: *CR Soc Biol* 153, pp. 1024–1028 (cit. on p. 10).

Jung, R. E. (2013). "The structure of creative cognition in the human brain". In: *Frontiers in Human Neuroscience* 7 (cit. on pp. 120, 129, 193).

Kales, A. and A. Rechtschaffen (1968). *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. US Department of Health, Education, Welfare, Public Health Service, National Institutes of Health, National Institute of Neurological Diseases, and Blindness, Neurological Information Network (cit. on p. 5).

Kaufmann, T., T. Elvsåshagen, D. Alnæs, et al. (2015). "The brain functional connectome is robustly altered by lack of sleep". en. In: *NeuroImage* (cit. on pp. 82, 97).

Key, A. P. (2016). "Human Auditory Processing: Insights from Cortical Event-related Potentials". In: (cit. on p. 52).

Klem, G. H., H. O. Lüders, H. H. Jasper, C. Elger, and others (1999). "The ten-twenty electrode system of the International Federation". In: *Electroencephalogr Clin Neurophysiol* 52.3, pp. 3–6 (cit. on p. 50).

Koch, W., S. Teipel, S. Mueller, et al. (2010). "Effects of aging on default mode network activity in resting state fMRI: Does the method of analysis matter?" en. In: *NeuroImage* 51.1, pp. 280–287 (cit. on p. 194).

Koukkou, M. and D. Lehmann (1983). "Dreaming: The functional state-shift hypothesis. A neuropsychophysiological model". en. In: *The British Journal of Psychiatry* 142.3, pp. 221–231 (cit. on pp. 24, 114, 195).

Koulack, D. and D. R. Goodenough (1976). "Dream recall and dream recall failure: An arousal-retrieval model." In: *Psychological Bulletin* 83.5, pp. 975–984 (cit. on pp. 19, 24, 38, 106, 142, 189, 194, 195).

Krause, A. J., E. B. Simon, B. A. Mander, S. M. Greer, J. M. Saletin, A. N. Goldstein-Piekarski, and M. P. Walker (2017). "The sleep-deprived human brain". In: *Nature Reviews Neuroscience* 18.7, pp. 404–418 (cit. on pp. 95, 114, 192).

Krueger, J. M. and S. Takahashi (1997). "Thermoregulation and Sleep". In: *Annals of the New York Academy of Sciences* 813.1, pp. 281–286 (cit. on p. 5).

LaBerge, S. and H. Rheingold (1991). *Exploring the world of lucid dreaming*. Ballantine Books New York (cit. on pp. 9, 14, 137).

Larson-Prior, L. J., J. M. Zempel, T. S. Nolan, F. W. Prior, A. Z. Snyder, and M. E. Raichle (2009). "Cortical network functional connectivity in the descent to sleep". In: *Proceedings of the National Academy of Sciences* 106.11, pp. 4489–4494 (cit. on p. 56).

Larson-Prior, L. J., J. D. Power, J. L. Vincent, et al. (2011). “Modulation of the brain’s functional network architecture in the transition from wake to sleep”. en. In: *Progress in Brain Research*. Vol. 193. Elsevier, pp. 277–294 (cit. on pp. 56, 82, 95, 106).

Leclair-Visonneau, L., D. Oudiette, B. Gaymard, S. Leu-Semenescu, and I. Arnulf (2010). “Do the eyes scan dream images during rapid eye movement sleep? Evidence from the rapid eye movement sleep behaviour disorder model”. In: *Brain* 133.6, pp. 1737–1746 (cit. on p. 10).

Legrand, D. and P. Ruby (2009). “What is self-specific? Theoretical investigation and critical review of neuroimaging results.” In: *Psychological review* 116.1, p. 252 (cit. on p. 106).

Lehmann, D., G. Dumermuth, B. Lange, and C. A. Meier (1981). “Dream recall related to EEG spectral power during REM periods”. In: *Sleep Research* 10, p. 151 (cit. on p. 16).

Llewellyn, S. (2013). “Such stuff as dreams are made on? Elaborative encoding, the ancient art of memory, and the hippocampus”. en. In: *Behavioral and Brain Sciences* 36.06, pp. 589–607 (cit. on p. 44).

Logothetis, N. K. (2008). “What we can do and what we cannot do with fMRI”. In: *Nature* 453.7197, pp. 869–878 (cit. on p. 53).

Luck, S. J. (2014). *An introduction to the event-related potential technique*. MIT press (cit. on p. 50).

Lund, H. G., B. D. Reider, A. B. Whiting, and J. R. Prichard (2010). “Sleep Patterns and Predictors of Disturbed Sleep in a Large Population of College Students”. en. In: *Journal of Adolescent Health* 46.2, pp. 124–132 (cit. on pp. 43, 134, 141).

Malinowski, J. and C. L. Horton (2014a). “Evidence for the preferential incorporation of emotional waking-life experiences into dreams.” en. In: *Dreaming* 24.1, pp. 18–31 (cit. on pp. 30, 43, 44).

Malinowski, J. E. and C. L. Horton (2014b). “Memory sources of dreams: the incorporation of autobiographical rather than episodic experiences”. en. In: *Journal of Sleep Research* 23.4, pp. 441–447 (cit. on pp. 30, 199).

– (2014c). “The effect of time of night on wake–dream continuity.” In: *Dreaming* 24.4, pp. 253–269 (cit. on pp. 30, 200).

Maquet, P. and P. Ruby (2004). “Psychology: insight and the sleep committee”. In: *Nature* 427.6972, pp. 304–305 (cit. on pp. 129, 200).

Maquet, P., J.-M. Péters, J. Aerts, G. Delfiore, C. Degueldre, A. Luxen, and G. Franck (1996). “Functional neuroanatomy of human rapid-eye-movement sleep and dreaming”. In: *Nature* 383.6596, pp. 163–166 (cit. on p. 12).

Maquet, P., P. Ruby, A. Maudoux, et al. (2005). “Human cognition during REM sleep and the activity profile within frontal and parietal cortices: a reappraisal of functional neuroimaging data”. en. In: *Progress in Brain Research*. Vol. 150. DOI: 10.1016/S0079-6123(05)50016-5. Elsevier, pp. 219–595 (cit. on pp. 13, 15).

Marquardt, C. J., R. A. Bonato, and R. F. Hoffmann (1996). “An empirical investigation into the day-residue and dream-lag effects.” In: *Dreaming* 6.1, pp. 57–65 (cit. on pp. 30, 44, 201).

Marzano, C., M. Ferrara, F. Mauro, et al. (2011). “Recalling and Forgetting Dreams: Theta and Alpha Oscillations during Sleep Predict Subsequent Dream Recall”. In: *The Journal of Neuroscience* 31.18, pp. 6674–6683 (cit. on pp. 14, 16, 82, 95, 120).

Maury, L. F. (1865). *Le sommeil et les rêves* (cit. on p. 9).

Mazza, S., C. Perchet, M. Frot, G. A. Michael, M. Magnin, L. Garcia-Larrea, and H. Bastuji (2014). “Asleep but aware?” en. In: *Brain and Cognition* 87, pp. 7–15 (cit. on p. 52).

Moffitt, A. (1982). “Individual differences among pre-and post-awakening EEG correlates of dream reports following arousals from different stages of sleep.” In: *Psychiatric Journal of the University of Ottawa* (cit. on p. 16).

Mok, L. W. (2014). “The interplay between spontaneous and controlled processing in creative cognition”. In: *Frontiers in Human Neuroscience* 8 (cit. on pp. 120, 129, 193).

Morel, C. R., R. F. Hoffmann, and A. R. Moffitt (1991). “The electrophysiological correlates of dream recall and nonrecall from Stage 2 sleep.” In: *Canadian Journal of Psychology/Revue canadienne de psychologie* 45.2, p. 140 (cit. on p. 16).

Nielsen, T. A. (2000). “A review of mentation in REM and NREM sleep:“covert” REM sleep as a possible reconciliation of two opposing models”. In: *Behavioral and Brain Sciences* 23.06, pp. 851–866 (cit. on pp. 10, 19, 95, 96, 106, 114, 190).

Nielsen, T. A. and R. A. Powell (1992). “The day-residue and dream-lag effects: A literature review and limited replication of two temporal effects in dream formation.” In: *Dreaming* 2.2, pp. 67–77 (cit. on p. 30).

Nielsen, T. A. and P. Stenstrom (2005). “What are the memory sources of dreaming?” In: *Nature* 437.7063, pp. 1286–1289 (cit. on p. 30).

Nielsen, T. A., A. L. Zadra, V. Simard, S. Saucier, P. Stenstrom, C. Smith, and D. Kuiken (2003). “The Typical Dreams of Canadian University Students.” In: *Dreaming* 13.4, pp. 211–235 (cit. on p. 29).

Nir, Y. and G. Tononi (2010). “Dreaming and the brain: from phenomenology to neurophysiology”. en. In: *Trends in Cognitive Sciences* 14.2, pp. 88–100 (cit. on p. 13).

Noreika, V., K. Valli, H. Lahtela, and A. Revonsuo (2009). “Early-night serial awakenings as a new paradigm for studies on NREM dreaming”. In: *International Journal of Psychophysiology* 74.1, pp. 14–18 (cit. on p. 10).

Ogilvie, R. D. and I. Simons (1992). “Falling asleep and waking up: a comparison of EEG spectra”. In: *Sleep, arousal and performance*, pp. 73–87 (cit. on pp. 82, 95).

Pagel, J. F., M. Blagrove, R. Levin, R. Stickgold, and S. White (2001). “Definitions of dream: A paradigm for comparing field descriptive specific studies of dream.” In: *Dreaming* 11.4, pp. 195–202 (cit. on p. 3).

Parke, A. R. and C. L. Horton (2009). *A re-examination of the interference hypothesis on dream recall and dream salience*. Universitätsbibliothek der Universität Heidelberg (cit. on p. 24).

Payne, J. D. and L. Nadel (2004). “Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol”. In: *Learning & Memory* 11.6, pp. 671–678 (cit. on pp. 199, 200).

Perogamvros, L. and S. Schwartz (2012). “The roles of the reward system in sleep and dreaming”. en. In: *Neuroscience & Biobehavioral Reviews* 36.8, pp. 1934–1951 (cit. on pp. 36, 200).

– (2013). “Sleep and Emotional Functions”. In: *Sleep, Neuronal Plasticity and Brain Function*. Ed. by P. Meerlo, R. M. Benca, and T. Abel. Vol. 25. DOI: 10.1007/7854_2013_271. Berlin, Heidelberg: Springer Berlin Heidelberg, pp. 411–431 (cit. on p. 36).

Perrin, F., H. Bastuji, and L. Garcia-Larrea (2002). “Detection of verbal discordances during sleep”. In: *Neuroreport* 13.10, pp. 1345–1349 (cit. on p. 52).

Peter-Derex, L., M. Magnin, and H. Bastuji (2015). “Heterogeneity of arousals in human sleep: A stereo-electroencephalographic study”. en. In: *NeuroImage* 123, pp. 229–244 (cit. on p. 8).

Picchioni, D., J. H. Duyn, and S. G. Horovitz (2013). “Sleep and the functional connectome”. en. In: *NeuroImage* 80, pp. 387–396 (cit. on pp. 56, 82, 87).

Plaisant, O., R. Courtois, C. Réveillère, G. A. Mendelsohn, and O. P. John (2010). “Validation par analyse factorielle du Big Five Inventory français (BFI-Fr). Analyse convergente avec le NEO-PI-R”. In: *Annales Médico-psychologiques, revue psychiatrique*. Vol. 168. Elsevier, pp. 97–106 (cit. on p. 122).

Popper, K. (2014). *Conjectures and refutations: The growth of scientific knowledge*. routledge (cit. on p. 34).

Purcell, S., J. Mullington, A. Moffitt, R. Hoffmann, and R. Pigeau (1986). “Dream self-reflectiveness as a learned cognitive skill”. In: *Sleep* 9.3, pp. 423–437 (cit. on p. 137).

Raichle, M. E., A. M. MacLeod, A. Z. Snyder, W. J. Powers, D. A. Gusnard, and G. L. Shulman (2001). “A default mode of brain function”. In: *Proceedings of the National Academy of Sciences* 98.2, pp. 676–682 (cit. on pp. 56, 106, 120).

Rasch, B., C. Buchel, S. Gais, and J. Born (2007). “Odor Cues During Slow-Wave Sleep Prompt Declarative Memory Consolidation”. en. In: *Science* 315.5817, pp. 1426–1429 (cit. on p. 35).

Rechtschaffen, A., M. A. Gilliland, B. M. Bergmann, and J. B. Winter (1983). “Physiological correlates of prolonged sleep deprivation in rats”. In: *Science* 221.4606, pp. 182–184 (cit. on p. 5).

Rechtschaffen, A., B. M. Bergmann, C. A. Everson, C. A. Kushida, and M. A. Gilliland (1989). “Sleep deprivation in the rat: X. Integration and discussion of the findings”. In: *Sleep* 12.1, pp. 68–87 (cit. on p. 5).

Revonsuo, A. (2000). “The reinterpretation of dreams: An evolutionary hypothesis of the function of dreaming”. In: *Behavioral and Brain Sciences* 23.06, pp. 877–901 (cit. on p. 35).

Revonsuo, A., J. Tuominen, and K. Valli (2015). “The avatars in the machine: Dreaming as a simulation of social reality”. In: *Open MIND*. Open MIND. Frankfurt am Main: MIND Group (cit. on p. 35).

Reyner, A. and J. A. Horne (1995). “Gender-and age-related differences in sleep determined by home-recorded sleep logs and actimetry from 400 adults”. In: *Sleep* 18.2, pp. 127–134 (cit. on pp. 141, 194).

Rochlen, A., R. Hoffmann, and R. Armitage (1998). “EEG correlates of dream recall in depressed outpatients and healthy controls.” en. In: *Dreaming* 8.2, pp. 109–123 (cit. on p. 16).

Roffwarg, H. P., J. H. Herman, C. Bowe-Anders, and E. S. Tauber (1978). “The effects of sustained alterations of waking visual input on dream content”. In: *The mind in sleep*, pp. 295–349 (cit. on pp. 30, 200).

Ruby, P. (2011). “Experimental Research on Dreaming: State of the Art and Neuropsychoanalytic Perspectives”. In: *Frontiers in Psychology* 2 (cit. on pp. 13, 17, 19, 28, 30, 34, 95, 96, 114, 119).

Ruby, P., C. Blochet, J.-B. Eichenlaub, O. Bertrand, D. Morlet, and A. Bidet-Caulet (2013). “Alpha reactivity to first names differs in subjects with high and low dream recall frequency”. In: *Frontiers in Psychology* 4 (cit. on p. 21).

Saive, A.-L., N. Ravel, M. Thévenet, J.-P. Royet, and J. Plailly (2013). “A novel experimental approach to episodic memory in humans based on the privileged access of odors to memories”. en. In: *Journal of Neuroscience Methods* 213.1, pp. 22–31 (cit. on p. 201).

Saletin, J. M., A. N. Goldstein, and M. P. Walker (2011). “The Role of Sleep in Directed Forgetting and Remembering of Human Memories”. en. In: *Cerebral Cortex* 21.11, pp. 2534–2541 (cit. on p. 199).

Sastre, J.-P. and M. Jouvet (1979). “Le comportement onirique du chat”. In: *Physiology & Behavior* 22.5, pp. 979–989 (cit. on p. 10).

Scarpelli, S., C. Marzano, A. D’Atri, M. Gorgoni, M. Ferrara, and L. De Gennaro (2015). “State- or trait-like individual differences in dream recall: preliminary findings from a within-subjects study of multiple nap REM sleep awakenings”. In: *Frontiers in Psychology* 6 (cit. on pp. 16, 120).

Scarpelli, S., A. D’Atri, A. Mangiaruga, et al. (2017). “Predicting Dream Recall: EEG Activation During NREM Sleep or Shared Mechanisms with Wakefulness?” en. In: *Brain Topography* (cit. on p. 16).

Schenck, C. H. and M. W. Mahowald (2002). “REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP.” In: *Sleep: Journal of Sleep and Sleep Disorders Research* (cit. on p. 10).

Schmitt, D. P., A. Realo, M. Voracek, and J. Allik (2009). “"Why can’t a man be more like a woman? Sex differences in big five personality traits across 55 cultures": Correction to Schmitt et al. (2008).” en. In: *Journal of Personality and Social Psychology* 96.1, pp. 118–118 (cit. on p. 194).

Schonbar, R. A. (1959). “Some manifest characteristics of recallers and nonrecallers of dreams.” In: *Journal of Consulting Psychology* 23.5, p. 414 (cit. on pp. 19, 130).

– (1965). “Differential dream recall frequency as a component of" life style".” In: *Journal of Consulting Psychology* 29.5, p. 468 (cit. on pp. 23, 120, 130, 193, 194, 196).

Schredl, M. (1995). “Creativity and dream recall”. In: *The Journal of creative behavior* 29.1, pp. 16–24 (cit. on pp. 19, 120, 127, 193).

– (1999). “Dream recall: research, clinical implications and future directions”. In: *Sleep and Hypnosis* 1.2, pp. 72–81 (cit. on pp. 17, 18, 23, 25, 130).

– (2000a). “Continuity between waking life and dreaming: are all waking activities reflected equally often in dreams?” In: *Perceptual and Motor Skills* 90.3, pp. 844–846 (cit. on p. 30).

– (2000b). “The relationship between dream recall and dream content: Negative evidence for the salience hypothesis.” In: *North American Journal of Psychology* 2.2, pp. 243–246 (cit. on pp. 24, 141).

– (2002). “Questionnaires and diaries as research instruments in dream research: Methodological issues.” In: *Dreaming* 12.1, pp. 17–26 (cit. on pp. 17, 18, 130, 196, 197).

– (2006). “Factors Affecting the Continuity Between Waking and Dreaming: Emotional Intensity and Emotional Tone of the Waking-Life Event”. In: *Sleep and Hypnosis* 8.1, pp. 1–5 (cit. on pp. 30, 43, 44).

– (2007). “Dream recall frequency by socioeconomic status of Chinese students”. In: *Perceptual and motor skills* 105.2, pp. 636–638 (cit. on p. 137).

– (2008). “Dream recall frequency in a representative German sample”. In: *Perceptual and motor skills* 106.3, pp. 699–702 (cit. on pp. 18, 19, 134, 137, 141).

– (2010a). “Characteristics And Contents Of Dreams”. In: *International Review of Neurobiology*. Ed. by A. C.a. P. McNamara. Vol. 92. Academic Press, pp. 135–154 (cit. on pp. 28–30).

– (2010b). “Dream content analysis: Basic principles”. In: *International Journal of Dream Research* 3.1, pp. 65–73 (cit. on p. 27).

– (2017). “Is Dreaming Related to Sleep-Dependent Memory Consolidation?” In: *Cognitive Neuroscience of Memory Consolidation*. Springer, pp. 173–182 (cit. on pp. 35, 201).

Schredl, M. and E. Doll (1998). “Emotions in diary dreams”. In: *Consciousness and cognition* 7.4, pp. 634–646 (cit. on pp. 24, 195).

Schredl, M. and D. Erlacher (2004). “Lucid dreaming frequency and personality”. en. In: *Personality and Individual Differences* 37.7, pp. 1463–1473 (cit. on pp. 137, 142).

– (2010). *Is sleep-dependent memory consolidation of a visuo-motor task related to dream content?* Universitätsbibliothek der Universität Heidelberg (cit. on p. 35).

– (2011). “Frequency of Lucid Dreaming in a Representative German Sample”. en. In: *Perceptual and Motor Skills* 112.1, pp. 104–108 (cit. on pp. 137, 142).

Schredl, M. and S. Fulda (2005). “Reliability and Stability of Dream Recall Frequency.” en. In: *Dreaming* 15.4, pp. 240–244 (cit. on pp. 18, 141).

Schredl, M. and F. Hofmann (2003). “Continuity between waking activities and dream activities”. In: *Consciousness and Cognition* 12.2, pp. 298–308 (cit. on pp. 30, 43).

Schredl, M. and A. Montasser (1996). “Dream recall: State or trait variable? Part I: Model, theories, methodology and trait factors”. In: *Imagination, Cognition and Personality* 16.2, pp. 181–210 (cit. on p. 23).

Schredl, M. and I. Reinhard (2008). “Gender differences in dream recall: a meta-analysis”. en. In: *Journal of Sleep Research* 17.2, pp. 125–131 (cit. on pp. 19, 134, 142, 194).

Schredl, M., P. Kleinferchner, and T. Gell (1996). “Dreaming and personality: Thick vs. thin boundaries.” In: *Dreaming* 6.3, pp. 219–223 (cit. on pp. 29, 120, 129).

Schredl, M., A. T. Funkhouser, C. M. Cornu, H.-P. Hirsbrunner, and M. Bahro (2001). “Reliability in Dream Research: A Methodological Note”. en. In: *Consciousness and Cognition* 10.4, pp. 496–502 (cit. on p. 18).

Schredl, M., P. Ciric, S. Götz, and L. Wittmann (2003a). “Dream recall frequency, attitude towards dreams and openness to experience.” In: *Dreaming* 13.3, pp. 145–153 (cit. on pp. 19, 120, 129).

Schredl, M., L. Wittmann, P. Ciric, and S. GÖtz (2003b). “Factors of home dream recall: a structural equation model”. In: *Journal of sleep research* 12.2, pp. 133–141 (cit. on pp. 17–19, 25, 40, 106, 120, 127, 134, 141, 142, 193, 194, 196).

Schredl, M., P. Ciric, S. Götz, and L. Wittmann (2004). “Typical dreams: stability and gender differences”. In: *The journal of psychology* 138.6, pp. 485–494 (cit. on p. 29).

Schwartz, S. (1999). “Exploration statistique et neuropsychologique des phénomènes oniriques au travers des textes et des images de rêves”. PhD thesis. Ph. D. thesis, University of Lausanne, Lausanne, 375 (cit. on pp. 27, 28).

– (2003). “Are life episodes replayed during dreaming?” In: *Trends in cognitive sciences* 7.8, pp. 325–327 (cit. on pp. 30, 199).

Schwartz, S. and P. Maquet (2002). “Sleep imaging and the neuro-psychological assessment of dreams”. In: *Trends in cognitive sciences* 6.1, pp. 23–30 (cit. on pp. 4, 13, 171).

Schwartz, S., T. T. Dang-Vu, A. Ponz, S. Duhoux, and P. Maquet (2005). “Dreaming: a neuropsychological view”. In: *Schweiz Arch Neurol Psychiatr* 156, pp. 426–39 (cit. on pp. 3, 4, 11, 12, 119).

Sestieri, C., M. Corbetta, G. L. Romani, and G. L. Shulman (2011). “Episodic Memory Retrieval, Parietal Cortex, and the Default Mode Network: Functional and Topographic Analyses”. en. In: *Journal of Neuroscience* 31.12, pp. 4407–4420 (cit. on p. 106).

Siclari, F., B. Baird, L. Perogamvros, et al. (2017). “The neural correlates of dreaming”. In: *Nature Neuroscience* 20.6, pp. 872–878 (cit. on pp. 15, 16, 120).

Sikka, P., K. Valli, T. Virta, and A. Revonsuo (2014). “I know how you felt last night, or do I? Self- and external ratings of emotions in REM sleep dreams”. en. In: *Consciousness and Cognition* 25, pp. 51–66 (cit. on pp. 27, 171).

Silber, M. H., S. Ancoli-Israel, M. H. Bonnet, et al. (2007). “The visual scoring of sleep in adults”. eng. In: *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine* 3.2, pp. 121–131 (cit. on p. 204).

Smitha, K., K Akhil Raja, K. Arun, P. Rajesh, B. Thomas, T. Kapilamoorthy, and C. Kesavadas (2017). “Resting state fMRI: A review on methods in resting state connectivity analysis and resting state networks”. en. In: *The Neuroradiology Journal* 30.4, pp. 305–317 (cit. on p. 55).

Solms, M. (1997). *The neuropsychology of dreams: A clinico-anatomical study*. L. Erlbaum (cit. on pp. 11, 106, 110, 120, 127, 193).

– (2000). “Dreaming and REM sleep are controlled by different brain mechanisms”. In: *Behavioral and Brain Sciences* 23.6, pp. 843–850 (cit. on pp. 11, 106).

Spaniol, J., P. S. Davidson, A. S. Kim, H. Han, M. Moscovitch, and C. L. Grady (2009). “Event-related fMRI studies of episodic encoding and retrieval: Meta-analyses using activation likelihood estimation”. en. In: *Neuropsychologia* 47.8-9, pp. 1765–1779 (cit. on pp. 113, 192).

Spielberger, C. D., R. L. Gorsuch, and R. E. Lushene (1970). “Manual for the state-trait anxiety inventory”. In: (cit. on p. 122).

Spoormaker, V. I., P. M. Gleiser, and M. Czisch (2012). “Frontoparietal Connectivity and Hierarchical Structure of the Brain’s Functional Network during Sleep”. In: *Frontiers in Neurology* 3 (cit. on p. 82).

Stampi, C, J. Mullington, M Rivers, J. Campos, and R. Broughton (1990). “Ultrashort sleep schedules: Sleep architecture and the recuperative value of multiple 80- 50- and 20-min naps”. In: *Sleep 90’*. Pontagenel Press. Bochum: J. Horne, pp. 71–74 (cit. on pp. 84, 94, 108).

Stepansky, R., B. Holzinger, A. Schmeiser-Rieder, B. Saletu, M. Kunze, and J. Zeitlhofer (1998). “Austrian dream behavior: Results of a representative population survey.” In: *Dreaming* 8.1, pp. 23–30 (cit. on pp. 18, 137, 142).

Stickgold, R. and M. P. Walker (2013). “Sleep-dependent memory triage: evolving generalization through selective processing”. In: *Nature Neuroscience* 16.2, pp. 139–145 (cit. on p. 199).

Strauch, I. and B. Meier (2004). “Dem Traum auf der Spur: Zugang zur modernen Traumforschung”. In: *Aufl. Bern: Hans Huber* (cit. on p. 30).

Sutin, A. R., L. L. Beason-Held, S. M. Resnick, and P. T. Costa (2009). “Sex differences in resting-state neural correlates of openness to experience among older adults”. In: *Cerebral Cortex* 19.12, pp. 2797–2802 (cit. on p. 23).

Sämann, P. G., C. Tully, V. I. Spoormaker, T. C. Wetter, F. Holsboer, R. Wehrle, and M. Czisch (2010). “Increased sleep pressure reduces resting state functional connectivity”. en. In: *Magnetic Resonance Materials in Physics, Biology and Medicine* 23.5-6, pp. 375–389 (cit. on pp. 82, 95, 97).

Sämann, P. G., R. Wehrle, D. Hoehn, et al. (2011). “Development of the Brain’s Default Mode Network from Wakefulness to Slow Wave Sleep”. en. In: *Cerebral Cortex*, bhq295 (cit. on pp. 82, 95, 106).

Takeuchi, T., R. D. Ogilvie, T. I. Murphy, and A. V. Ferrelli (2003). “EEG activities during elicited sleep onset REM and NREM periods reflect different mechanisms of dream generation”. In: *Clinical Neurophysiology* 114.2, pp. 210–220 (cit. on p. 16).

Tart, C. T. (1962). “Frequency of dream recall and some personality measures.” In: *Journal of Consulting Psychology* 26.5, p. 467 (cit. on p. 130).

Tassi, P and A Muzet (2000). “Sleep inertia”. en. In: *Sleep Medicine Reviews* 4.4, pp. 341–353 (cit. on pp. 9, 25, 40, 81–83, 94, 96, 106, 113, 192).

Tassi, P., A. Nicolas, G. Dewasmes, et al. (1992). “Effects of noise on sleep inertia as a function of circadian placement of a one-hour nap”. eng. In: *Perceptual and Motor Skills* 75.1, pp. 291–302 (cit. on p. 97).

Tononi, G. and C. Cirelli (2014). “Sleep and the Price of Plasticity: From Synaptic and Cellular Homeostasis to Memory Consolidation and Integration”. en. In: *Neuron* 81.1, pp. 12–34 (cit. on p. 5).

Trotti, L. M. (2016). “Waking up is the hardest thing I do all day: Sleep inertia and sleep drunkenness”. en. In: *Sleep Medicine Reviews* (cit. on pp. 9, 25, 81, 82, 85, 94, 97, 106, 111).

Tsai, L.-L. and S.-P. Li (2004). “Sleep patterns in college students”. en. In: *Journal of Psychosomatic Research* 56.2, pp. 231–237 (cit. on p. 141).

Tsai, P.-J., S. C.-J. Chen, C.-Y. Hsu, et al. (2014). “Local awakening: Regional reorganizations of brain oscillations after sleep”. en. In: *NeuroImage* 102, pp. 894–903 (cit. on pp. 82, 96).

Tüshaus, L., J. H. Balsters, A. Schläpfer, D. Brandeis, R. O'Gorman Tuura, and P. Achermann (2017). "Resisting Sleep Pressure: Impact on Resting State Functional Network Connectivity". en. In: *Brain Topography* (cit. on pp. 82, 97).

Vallat, R., T. Lajnef, J.-B. Eichenlaub, C. Berthomier, K. Jerbi, D. Morlet, and P. M. Ruby (2017). "Increased Evoked Potentials to Arousing Auditory Stimuli during Sleep: Implication for the Understanding of Dream Recall". In: *Frontiers in Human Neuroscience* 11.132 (cit. on pp. 105, 120, 129, 142).

Valli, K., A. Revonsuo, O. Pälkäs, K. H. Ismail, K. J. Ali, and R.-L. Punamäki (2005). "The threat simulation theory of the evolutionary function of dreaming: Evidence from dreams of traumatized children". en. In: *Consciousness and Cognition* 14.1, pp. 188–218 (cit. on pp. 18, 35).

Valli, K., B. Frauscher, V. Gschliesser, et al. (2012). "Can observers link dream content to behaviours in rapid eye movement sleep behaviour disorder? A cross-sectional experimental pilot study". In: *Journal of sleep research* 21.1, pp. 21–29 (cit. on p. 10).

Van Rijn, E., J.-B. Eichenlaub, P. A. Lewis, M. P. Walker, M. G. Gaskell, J. E. Malinowski, and M. Blagrove (2015). "The dream-lag effect: Selective processing of personally significant events during Rapid Eye Movement sleep, but not during Slow Wave Sleep". ENG. In: *Neurobiology of Learning and Memory* (cit. on p. 30).

Van den Heuvel, M. P. and H. E. Hulshoff Pol (2010). "Exploring the brain network: A review on resting-state fMRI functional connectivity". en. In: *European Neuropsychopharmacology* 20.8, pp. 519–534 (cit. on p. 54).

Van Dijk, K. R. A., T. Hedden, A. Venkataraman, K. C. Evans, S. W. Lazar, and R. L. Buckner (2010). "Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization". eng. In: *Journal of Neurophysiology* 103.1, pp. 297–321 (cit. on pp. 54, 56).

Verdone, P. (1965). "Temporal Reference of Manifest Dream Content". In: *Perceptual and Motor Skills* 20.3_suppl, pp. 1253–1268 (cit. on p. 44).

Voss, U., R. Holzmann, I. Tuin, and J. A. Hobson (2009). "Lucid dreaming: a state of consciousness with features of both waking and non-lucid dreaming". In: *Sleep* 32.9, p. 1191 (cit. on p. 14).

Voss, U., R. Holzmann, J. A. Hobson, W. Paulus, J. Koppehele-Gossel, A. Klimke, and M. A. Nitsche (2014). "Induction of self awareness in dreams through frontal low current stimulation of gamma activity". In: *Nature Neuroscience* 17.6, pp. 810–812 (cit. on p. 14).

Walker, M. P. and E. van der Helm (2009). "Overnight therapy? The role of sleep in emotional brain processing." en. In: *Psychological Bulletin* 135.5, pp. 731–748 (cit. on p. 200).

Wamsley, E. J. and R. Stickgold (2010). "Dreaming and offline memory processing". In: *Current Biology* 20.23, R1010–R1013 (cit. on p. 35).

Wang, C., J. L. Ong, A. Patanaik, J. Zhou, and M. W. L. Chee (2016). "Spontaneous eyelid closures link vigilance fluctuation with fMRI dynamic connectivity states". en. In: *Proceedings of the National Academy of Sciences* 113.34, pp. 9653–9658 (cit. on p. 95).

Wechsler, D. (2001). *MEM-III: échelle clinique de mémoire de Wechsler*. Éditions du Centre de psychologie appliquée (cit. on pp. 42, 122).

Weissenbacher, A., C. Kasess, F. Gerstl, R. Lanzenberger, E. Moser, and C. Windischberger (2009). "Correlations and anticorrelations in resting-state functional connectivity MRI: A quantitative comparison of preprocessing strategies". en. In: *NeuroImage* 47.4, pp. 1408–1416 (cit. on pp. 87, 110, 124).

Whitfield-Gabrieli, S. and A. Nieto-Castanon (2012). "Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks". eng. In: *Brain Connectivity* 2.3, pp. 125–141 (cit. on pp. 86, 123).

Williamson, P. C., A. Csima, H. Galin, and M. Mamelak (1986). "Spectral EEG correlates of dream recall". In: *Biological Psychiatry* 21.8, pp. 717–723 (cit. on p. 16).

Windt, J. M. (2015). *Dreaming: A conceptual framework for philosophy of mind and empirical research*. MIT Press (cit. on pp. 28, 34).

Wittmann, L., C. Palmy, and M. Schredl (2004). "NREM sleep dream recall, dream report length and cortical activation". In: *Sleep and Hypnosis* 6, pp. 54–58 (cit. on pp. 16, 120).

Wollman, M. C. and J. S. Antrobus (1987). "Cortical arousal and mentation in sleeping and waking subjects". In: *Brain and cognition* 6.3, pp. 334–346 (cit. on p. 16).

Wu, C. W., P.-Y. Liu, P.-J. Tsai, et al. (2012). "Variations in Connectivity in the Sensorimotor and Default-Mode Networks During the First Nocturnal Sleep Cycle". en. In: *Brain Connectivity* 2.4, pp. 177–190 (cit. on pp. 56, 82, 96).

Yeo, B. T. T., F. M. Krienen, J. Sepulcre, et al. (2011). "The organization of the human cerebral cortex estimated by intrinsic functional connectivity". en. In: *Journal of Neurophysiology* 106.3, pp. 1125–1165 (cit. on p. 56).

Yeo, B. T., J. Tandi, and M. W. Chee (2015). "Functional connectivity during rested wakefulness predicts vulnerability to sleep deprivation". en. In: *NeuroImage* 111, pp. 147–158 (cit. on pp. 82, 97, 114, 192).

Zadra, A. (1996). "Recurrent dreams and their relation to life events and well-being". In: *Trauma and dreams*, pp. 231–247 (cit. on pp. 137, 142).

Zadra, A. and D. C. Donderi (2000). "Nightmares and bad dreams: their prevalence and relationship to well-being." In: *Journal of abnormal psychology* 109.2, p. 273 (cit. on p. 29).

Zadra, A., M. Pilon, and D. C. Donderi (2006). "Variety and intensity of emotions in nightmares and bad dreams". In: *The Journal of nervous and mental disease* 194.4, pp. 249–254 (cit. on p. 29).

Zald, D. H., D. L. Mattson, and J. V. Pardo (2002). "Brain activity in ventromedial prefrontal cortex correlates with individual differences in negative affect". In: *Proceedings of the National Academy of Sciences* 99.4, pp. 2450–2454 (cit. on p. 23).

Colophon

This thesis was typeset with LaTeX 2_ε. It uses the *Clean Thesis* style developed by Ricardo Langner (http://cleanthesis.der-ric.de/).