**INTRODUCTION**

Good morning everyone,

Before starting my presentation, I would like to thank all of you for being here, and particularly the professors Sophie Schwartz, Michael Schredl and Yves Rossetti for accepting to be members of my PhD jury. I also want to thank my thesis advisor Perrine Ruby, without whom none of the work I will present today would have been possible.

The general outline of my presentation is shown here. First I will introduce dreaming and some of the main issues related to its scientific study. Secondly, I will detail several studies that we have conducted in the aim of understanding the mechanism of dream recall. In the third section, I will describe a study which aimed at characterizing the relationship between waking-life and dream content and in the fourth section, I will briefly describe an open-source software that I co-developed dedicated to the visualization and analysis of sleep data. Finally, I will end with some general conclusions and future perspectives.

To begin with, I would like to start by stating some open questions related to dreaming that I will use as a support for introducing this vast phenomenon. These questions are: what is dreaming? When does it occur during sleep? Does it have a functional effect? And why is there such variability in dream recall?

There are many ways to answer the first question of what is dreaming, or in other words, what is a definition of dreaming. In this presentation, I will use the definition and framework proposed by Fabian Guénolé which simply states that “dreaming is a mental experience during sleep which can be recalled and reported at wake”. In this model, the dreaming phenomenon is separated in three successive steps, namely the dream experience, the dream recall and finally the dream report. The dream experience takes place during sleep and refers to the dream as it is originally experienced. Upon awakening, the dream experience can be recalled, or forgotten, depending on whether one is able to encode the dream experience into memory or not. Finally, the dream can be reported using either words or pictures. Importantly, there is a loss of information between each of these three steps, in part because of forgetting, reconstruction mechanisms, censorship and description difficulties.

The second question was when does dreaming occur during sleep. Before answering that question, I would like first to introduce some basic notions of sleep and the methods to study it. Sleep is not a passive and homogenous state but rather an evolving process during which the brain pass through several distinct states, or sleep stages. The gold standard for the identification of sleep stages is polysomnography, which refers to the simultaneous recording of brain activity (EEG or electroencephalography), eye movements (EOG or electrooculography) and muscle activity (EMG or electromyography). Using those information the identification of sleep stages is then performed visually by inspecting consecutive segments of polysomnographic recordings. The five sleep stages are Wakefulness, N1 sleep, N2 sleep, N3 sleep and REM sleep. They all have distinctive electrophysiological properties. For instance, resting wakefulness is characterized by a predominance of the alpha rhythm and a high muscular activity, whereas N3 sleep, sometimes called deep sleep is characterized by large amplitude slow waves.

A normal night of sleep consists of a repetition of four or five ninety minutes long cycle in which sleep stages follow each other in a specific order. On this figure, you can see a hypnogram, which represents in one person the succession of sleep stages across time.

Back to our question of when does dreaming occur during sleep. I want to say first that, contrarily to what was believed for several decades, we know today that dreaming is not specific to REM sleep, but can in fact occur during any sleep stages. That said, there is a higher rate of dream recall after awakening from REM sleep than NREM sleep (about 80% of recall versus twenty to fifty percent), but again I want to emphasize that it does not mean as a fact that people dream more in REM sleep, but maybe it could just mean that the recall is easier after awakening from REM sleep than non REM sleep. Because dreaming is not specific to a single brain state, there is no electrophysiological signature of dreaming, and this represents a fundamental impediment to the study of the cerebral correlates of dreaming because one can never be sure whether someone asleep is dreaming or not unless awakening him or her. And even after asking the sleeper, we cannot be sure that failure to recall a dream means that the sleeper was not dreaming before.

Moving to the next question, which was “does dreaming have a functional effect”. On this point, numerous assumptions have been made over the centuries. For example, in ancient times dreams were believed to be omens or messages from deities. Freud believed in the beginning of the twentieth century that they were the guardians of sleep. More recently, dreams have been proposed to play a role in psychological individualism, emotional regulation, memory consolidation, threat or social simulation. However, there are still few evidences either supporting or refuting these hypotheses. One of the best way to better understand the potential function of dreaming is by looking closely at dream content and the rules organizing dream content. In the part 3 of this presentation, I will describe a study in which we looked specifically at the relationship between waking life and dream content, in order to understand the filter that dreaming applies to waking experiences.

Finally, a question which will take up a great deal of our attention relates to why there is such variability in dream recall. To introduce this point I would like to borrow the words of Aristotle who wrote more than two thousand years ago in his famous treatise on sleep: “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.”

Indeed, Aristotle was right to point out that there is a large variability in the dream recall frequency (or DRF, an acronym that I will use a lot throughout this presentation), both among a single person, but, above all, between people. One method to find, as wanted by Aristotle, an explanation for this variability is to compare psychological, sleep and neurophysiological parameters between individuals who recall their dreams every day, or High recallers, and individuals who almost never recall a dream, or Low recallers.

Doing so, decades of research have shown that several factors are positively associated with dream recall frequency. First, if we look at psychophysiological parameters, we know that women recall their dreams better than men, and young people better than older people. People with specific personality traits, such as increased openness to experience or anxiety, recall their dreams more often than others. People with higher creative-thinking abilities recall their dreams more often.

Second, if we look at sleep parameters between high and low dream recallers, one factor that is strongly associated with dream recall is the frequency and duration of nocturnal awakenings. And previous results from the lab have shown in a sample of 36 subjects that high recallers have in average 15 min more intra-sleep wakefulness than low recallers. A second critical factor, as I said before, is the sleep stage prior to awakening, with awakening from REM sleep inducing more dream recall than awakening from non-REM sleep.

However, these two factors does not explain everything because even when awakened in the same sleep stage, as verified by polysomnography, and asked whether they have a dream in mind or not, low recallers still recall less dream than high recallers. So there must be others factors at play. One hypothesis, that has never been tested, is that successful dream recall can be function of the post-awakening brain functioning. In that case, one could expect that low recallers have a higher sleep inertia, or say more simply, more difficulty awakening than high recallers. This is the central idea of an EEG-fMRI study that was the central study of my PhD and that I am going to present you right after. A second hypothesis that has never been tested until now is that maybe others sleep parameters are at play, and notably microstructural features such as arousals, sleep spindles, K-complexes. We tested that by re-analyzing the sleep data of Jean-Baptiste Eichenlaub and I will present you this after the sleep inertia study.

Finally, there are also some neurophysiological differences between high and low dream recallers. A previous study conducted in the lab showed that high recallers have a higher brain reactivity to auditory stimuli during both sleep and wakefulness. Now if you remember I said just before that High recallers have also more wakefulness during sleep, and this suggests the idea that there is a causal link between brain reactivity and increased wakefulness. Using PET scan, Jean-Baptiste and Perrine have also showed that high recallers have a higher spontaneous regional cerebral blood flow in specific brain regions during both sleep and wakefulness. These two regions are namely the medial prefrontal cortex and the temporo-parietal junction, and what is interesting is that lesions in these two areas are known to induce a cessation of dream recall. This means that these regions are critical for dream recall. These regions are also among the core nodes of the default mode network, which is a brain network highly activated during internal mental processes such as future thinking, mind-wandering and introspection. Some authors have postulated that the default mode network could be the neural substrate of dreaming.

The conclusion to be drawn from all these findings is that dream recall frequency is associated with a specific psychological and neurophysiological profile. High dream recallers tend to have higher creativity and anxiety, greater baseline activity in the default mode network, more intra-sleep wakefulness, higher brain reactivity and so on… Yet there are still several unresolved issues, such as the influence of sleep inertia and microstructural parameters on dream recall, and one of the major goal of my PhD was to investigate these issues.

**RESULTS: INERTIA**

Now that I have introduced the literature and our main objectives, I will move to the results section. The most substantial part of my presentation will focus on the EEG-fMRI study that we conducted to investigate the effect of sleep inertia on dream recall. This study was the central work of my thesis and it took us more than one year to acquire the data for the 55 participants.

So, just to put a bit of context, as I said before, the first minutes following awakening are marked by sleep inertia, which corresponds to impaired cognitive and physical performances, reduced vigilance, a strong desire to return to sleep, and a rapid vanishing of dream content. Surprisingly, while sleep inertia is a phenomenon that we all experience at different level each morning, still very little is known about the brain alterations during this period. Even more relevant to us during this thesis is the fact that sleep inertia could be an important factor to explain inter and intra individual variability in DRF but this hypothesis has never been tested. We therefore designed a combined EEG-fMRI study to measure the brain alterations during sleep inertia, and test the influence of sleep inertia on dream recall.

For this study, we recruited a total of 55 participants, among which 28 were high dream recallers, meaning that they usually recalled more than 6 dream per weeks. 27 were low dream recallers, recalling about one dream per month. The two groups were paired in age, gender, education level and habitual sleep duration.

The major points of the protocol are the followings. Participants were asked to sleep for about 45 minutes inside an MRI scanner. We monitored the sleep stages online and awakened them if possible in N3 sleep. Our protocol was designed to maximize sleep inertia, for that participants were partially sleep deprived on the night before, and they took a nap during the circadian low of early afternoon. We also measured the cognitive impairments during sleep inertia using a validated task, namely the descending subtraction task in which subjects were asked to subtract backwards 9 then 8 then 7 and so on to a three digits number for two minutes.

The full protocol of the study is shown here. Subjects arrived at the sleep unit of Alain Nicolas in the Vinatier Hospital at 8 pm. During two hours, I stayed with them and made them perform several behavioral and cognitive tasks to assess for example creativity, arithmetic and memory abilities. They stayed from about 11pm to 5 am under the supervision of night nurses and were asked to go to sleep at 5 am in the morning until 8 am, meaning that they slept a total of 3 hours in the night. After lunch at noon, subjects were led to the CERMEP neuroimaging center and they were set up with EEG electrodes in order to monitor online the sleep stages. They then performed the behavioral arithmetic task, DST, and their brain was scanned for 6 minutes during which they were just told to stay awake and focus on a fixation cross. We then switch off the light and told them that they could sleep if they wanted to. About 45 minutes later, we awakened them, if possible in N3 or deep sleep, and we immediately scanned their brain and performed again a behavioral task. And we did the same thing again about 25 minutes after awakening. So for both the cognitive performances and the brain functioning, we had three measurements points, before sleep, 5 min post-awakening and 25 min post-awakening. Our general hypothesis is that we should observe a reduction of arithmetic performances and brain alterations specifically at 5 minutes post-awakening compared to pre-nap and 25 minutes post awakening, because it corresponds to the moment where sleep inertia is at its maximum.

I will now present three different articles that we wrote with this study, starting with the first one that is currently under review at NeuroImage, and in which we described the brain alterations upon awakening from sleep, regardless of the effect on dream recall. Indeed, because of our large number of participants, which is 55 if we pool both high and low dream recallers, our study offers a unique opportunity to measure the brain and cognitive functioning during sleep inertia. Furthermore, and because not all the subject were able to reach and maintain deep sleep, we were able to separate our sample in two groups, namely participants who were awakened in N3 sleep and participants who were awakened in N2 sleep. The analysis we did in this study was to compute the functional connectivity within and between the main brain functional networks at 5 min post-awakening compared to pre-sleep and 25 min post-awakening. Here you can see the networks and their main regions of interests that were included in the analysis.

We found that

**RESULTS: AROUSAL**

**RESULTS: WLE**

We know that dream content is somehow related to the waking-life of the dreamer. However, the factors that mediate the incorporation of waking-life experiences into dream content are still poorly known.

**SOFTWARE**

We now arrive to the fourth section, in which I am going to present you a software that I developed during the last year of my PhD, and I want to emphasize that it was not intended originally in my PhD and it started more as a personal project. The motivation for this software came when I started working with sleep data and realized that there were few free and open source solutions that were dedicated to sleep research. So in early 2017 I started to work on a simple Matlab prototype that was intended for my personal use and which allowed me to visualize and score the sleep stages. And one day I showed this software to my fellow PhD student Etienne Combrisson and we decided to rewrite it in Python and implement it into the package he was currently developing at the time, entitled Visbrain, and which is intended as a multi-purpose and broad package for neuroscientific analysis. We worked together for several months and quite quickly we obtained a full interface with many features. In September of this year, we released a stable version of this software, called SLEEP, and at the same time we published it into a peer reviewed journal, frontiers in Neuroinformatics.

Here you can see the main interface of the software. It is comprised of several different modules. On the top center are the polysomnographic signals in which it is possible to navigate, they are displayed by default by epochs of 30 seconds but you can adjust that windows on the bottom of the software. One of the important specifications of this software was that it should be able to read natively several commercial and public file formats. In its current version, the software is capable of handling all the main international file formats, including for example Brainvision, European data format, Micromed, and so on. Below the polysomnographic signals is the spectrogram, which is the time frequency representation of the full recording, and which is useful to see at a glance variation in spectral properties of the signal. Below that is the hypnogram that you can of course edit from an existing one or create from scratch and then save in several possible file formats again. On the left side of the software is the setting panel which allows the user to perform several actions, such as changing the visibility and amplitude of the channels, running a bunch of signal processing tools, computing sleep statistics, and one particular aspect I want to emphasize, running automatic detection of phasic events, such as spindles, K-complexes, rapid eye movements and so on. And I think that one of the strength of this software is that these detections are directly embedded within the interface, both on the signals but also on the hypnogram.

To finish, I would like to mention that the development of this software is still ongoing and we are currently implementing a function to automatically identify and score the sleep stages. I am happy to say that we obtain so far very good performances, with a percentage of agreement between our algorithm and a human visual scoring of about 80%. This is a nice result given that it took less than 5 seconds to our software to compute this hypnogram, while for an expert human it would take at least 2 to 3 hours!

**CONCLUSION**