**INTRODUCTION**

Good morning everyone and thank you all for being here today,

I would like to express my sincere thanks to 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. In the second and most substantial part of my talk, 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.

I would like to start by asking some questions related to dreaming that I will use as a support for introducing this vast phenomenon. What is dreaming? When does it occur during sleep? Does it have a functional effect? And why is there such variability in dream recall?

A simple definition of dreaming is that it is a “mental experience which occurs during sleep”. Upon awakening, the content of the dream can be memorized and thus recalled or it can be forgotten. And finally, the dreamer can report his or her dream using either words or pictures and therefore communicate it to others. Between each of these three steps, the dream as it is experienced during sleep, the recall of the dream and the dream report, there is a substantial loss of information notably because of forgetting, reconstruction mechanisms, censorship and description difficulties.

We now move to the second question which 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 consists of simultaneously recording 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.

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.

Does dreaming have a functional effect? This question has fascinated mankind since the dawn of time. In ancient Egypt and Greece, dreams were believed to have a religious or mystical signification. Then, the father of psychoanalysis, Sigmund Freud, proposed in the beginning of the twentieth century that each dream is a wish fulfillment during which unconscious desires come to awareness, but in a distorted form to avoid sleep disturbances. More recently, and in a more psycho-cognitive view, 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, and which was already asked by Aristotle more than two thousand years ago, relates to why is there a large variability in dream recall, both among one person over time, but also, between individuals. And on this point I am pretty sure that in this room today there are people who remember their dreams every day, and people who almost never recall their dreams. One of the central focus of my thesis was to explore why there is such differences. To explore that, the general method that Perrine has used in the lab since about ten years, and that I used during my thesis is to compare psychological, sleep and neurophysiological parameters between high recallers, people who recall their dreams every day, and low recallers, people who almost never recall a dream.

By doing so, several decades of research have shown that high recallers and low recallers differ on several parameters. In their personality, high recallers tend to have specific personality traits, such as higher openness to experience and anxiety, they tend to have higher creative-thinking abilities, and they generally also report an overall higher interest in their dreams.

Second, Perrine and Jean Baptiste Eichenlaub, who was a PhD student at the lab several years ago, compared the sleep parameters of 36 high and low dream recallers who slept in the lab with polysomnographic set-up. They found that high recallers had in average longer awakening during sleep, namely 2 minutes in average versus 1 minute for low-recallers. This finding is consistent with the arousal-retrieval model proposed by Koulack and Goodenough in the seventies which postulate that a period of wakefulness must occur immediately after dreaming in order to successfully encode dream content into long term memory and therefore remember it on the following morning.

Third, Jean Baptiste and Perrine also investigated for the first time the neurophysiological differences between high and low dream recallers. They found that the amplitude of brain responses to auditory stimuli was higher in high recallers in both wakefulness and sleep. Furthermore, they observed using PET imaging that high recallers had a higher activity in two specific brain regions, the medial prefrontal cortex, and temporo parietal junction, which have been previously described as critical for dream recall. Indeed, lesions within one or both of these regions induce a global cessation of dream recall. This is interesting because these regions are also among core regions of the default mode network, a brain network that is highly activated during internal mental processes such as memory retrieval, mind wandering. Based on these findings, some authors have speculated that the default mode network could be the neural substrate of dreaming. To sum up, these results are interesting because they show that in addition with having some differences in their personality, high and low dream recallers have also differences in the functioning of their brains.

Following from these studies, there were several unresolved issues that we tried to answer during my thesis. First, I said that high recallers have a higher brain reactivity to stimuli during sleep, as well as increased wakefulness. This suggest a causal link between these two findings, namely the increased brain reactivity to stimuli could promote wakefulness in high dream recallers. This was the topic of my master 2 during which I re-analyzed the EEG data of Perrine and Jean Baptiste in order to compute auditory evoked potentials to stimuli which were followed or not by an awakening or an arousal. By arousal here, I am talking about short wakefulness-like activation during sleep with a duration comprised between 3 to 15 seconds, arousals are normal component of sleep and present in all sleep stages. To do this analysis, we had first to visually score the arousals in all subjects, and we took that opportunity to do at the same time an in-depth analysis of the sleep microstructure between high and low dream recallers.

The second unresolved issues relates to whether dream recall could in fact depend on the post-awakening brain state rather on the pre-awakening state. I could not find a better introduction to this issue than the discussion of a paper by Conduit and collaborator: 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.

The core study of my thesis was to test this hypothesis. And for that we designed a combined EEG-fMRI study to assess the post-awakening brain functioning in high and low dream recallers, and at the same time provide an overview of the awakening brain.

**RESULTS: INERTIA**

I am now going to move to the result, and I will start by detailing the EEG-fMRI study. 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.

Immediately upon awakening, the brain is in a transient state between sleep and wakefulness that is called sleep inertia. Sleep inertia is characterized by 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.

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**

I will now move to the third part of my talk in which I will present a behavioral study that we conducted to specifically look at the relationship between waking-life and dream content.

This study was recently published in the journal Plos One.

To put this study in context, we know both by subjective experience and scientific study that dream content is somehow related to the waking-life of the dreamer. However, the characteristics of the waking life experiences incorporated into dreams are still poorly known, and we don’t know precisely the filters that dreaming applies to waking-life. Yet, a better understanding of that filter could be of crucial importance to improve our knowledge of the possible function of dreaming.

The classic paradigm that is used to investigate the relationship between dreaming and waking life is the content matching paradigm, in which people are asked to write down everything they did during the day on a day diary, and everything they dreamed of during the night on a dream diary, and typically they do that for about fifteen days. After that period of time, either the participant or an external person will rate the level of matching between the days and dream diaries. Yet, one of the obvious problem with this method is that it is unlikely that the participants will be able to write down every single actions or thoughts he or she had during the day, and therefore there might be a bias towards highly emotional waking-life experiences and fewer mundane events. In addition, one of the inherent limitation of this paradigm is that it limits the span of the matching between waking life and dream content to the fifteen days or so of the experiment. And I think we have all already re-experienced in our dreams some situations that dated from several months or several years ago.

Therefore, we decided to do a new version of this paradigm that would overcome these limitations. We asked 40 participants to record their dreams immediately upon awakening during 7 consecutive days, and to subsequently report any connections they could make between their waking-lives and their dreams. After recording their dreams with a Dictaphone, participants had to fill in the first questionnaire, displayed on the left side, to quantify and qualify some general aspects of the dream, including the number of characters, emotional intensity and so on. And the last question of that questionnaire related to whether some elements of their dream made them think about an experience that they had during their waking-lives. And if they could see one or more, they had to fill in another form for each incorporated waking life elements. In this form they had to describe the element as it was originally experienced in waking life, as it was experienced within the dream, and for both they had to quantify some aspects of it on a scale of 1 to 10.

For example, I will show you the dream report and associated waking life elements of one subject of the study. His dream report was as follows: “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 shouted at them”. For him it was clear that this part of the dream was related to one situation that he experienced three years ago, during which he bumped into his ex-girlfriend and her new partner, and he was particularly rude and unkind to them.” And for him this waking life experience was mostly negative, it was also very rare because it only happened one time, it was something very personal, very important, and that he considered as personal concern, and even three years after his encounter with his ex-girlfriend.

If we now look at all the participants, we obtained a total of 247 dreams, or around 6 dreams per participants during the 7 days of the experiment, a figure which is high but was expected given that one of the inclusion criteria for this study was being a high dream recallers. About 80% of the dream reports were related to one or more waking life experiences and we obtained nearly 500 waking life experiences incorporated into dreams.

In agreement with our hypothesis, we found that the majority of the incorporated WLE were either from the day before or from the distant past, and it seems therefore that dreams incorporate in an almost equal proportion events from the day before or from several years ago. Another key result of this study is that dreaming attenuate the intensity of waking emotional memories. If we go back to the example I showed you before, if you remember the participants rated the emotional intensity of its original encounter with his ex-girlfriend as something very negative (2 out of ten). But, interestingly, if we looked at how he rated the emotional intensity of the encounter within the dream, you can see that it is slightly higher, meaning that he perceived as less emotionally negative within the dream than within waking-life. And if we look at all the participants, we have the same pattern, negative waking life experiences tend to be perceived as a bit less negative within the dream, and positive waking life experiences tend to be perceived as a bit less positive, while neutral experiences stay at the same level. This is one of the first experimental evidence supporting the emotional regulation theory of dreaming, which postulates that dreaming is involved, or at least reflects, emotional regulation processes.

These results led us to propose that dreaming can be best understood as an open window on several cognitive processes taking place at the same time during sleep. These processes involve emotional regulation, memory consolidation of relevant experiences, or forgetting of insignificant experiences. And notably the emotional intensity of an experience could be the tag to decide whether this specific waking memories should be consolidated or forgotten. In turn, this reorganization of the global memory schema could explain the creative insights and problem solving frequently observed in dreams.

One of the limitation of this study is that it only includes morning dream reports, and we know that there is a time of the night effect on the relationship between dreaming and waking-life, with for instance more references to the day before on the first part of the night. So it would be interesting to evaluate this time of the night effect using our protocol. Secondly, while our study provide a strong argument for the emotional regulation role of dreaming, there is currently very few evidence that dreaming is associated with memory consolidation processes. During my PhD I helped in a study designed by Jane Plailly and Perrine, which aimed at assessing whether recalling a dream related to a recent learning experiences could help memory consolidation, however we did not find a significant effect and therefore future research are needed.

**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**