Good night, sleep tight : performance and EEG measures in primary insomnia patients and during sleep deprivation in health volunteers

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Valorization addendum

This addendum addresses the relevance and the impact of the results described in the current dissertation entitled "Performance and EEG measures in primary insomnia patients and during sleep deprivation in healthy volunteers". For this purpose, five topics are developed in relation to the **social and economic relevance** of our results, the **target groups** for whom our results are relevant, the **activities and products** that can derive from the work described in the current dissertation, the **innovative** aspect of our research, and finally, how ideas resulting from our work have been and will be **implemented**.

Social and economic relevance

Sleep disruption has become a major problem in Western society [1,2]. Among the different types of sleep disruption, we have considered sleep deprivation and chronic insomnia in the current dissertation. The latter is one of the most prevalent current health concerns [3,4]. Between 10 and 15% of adults in the general population are reported to have complaints of insomnia associated with complaints of daytime fatigue and cognitive impairments [5–7]. Insomnia is defined as a complaint of non-restorative and/or insufficient sleep associated with complaints of daytime consequences without comorbidities.

Both insomnia and sleep deprivation can lead to a range of adverse consequences on daytime performance, health, and productivity [8–14] that place a heavy economic burden on our society [14–17]. It has been estimated that, in the United States, insomnia was associated with 7.2% of all costly workplace accidents and errors [18], and the Sleep Health Foundation evaluated the indirect costs of sleep loss at 1.5 billion dollars in 2011 [14]. Cognitive and psychomotor dysfunction may hamper day-to-day operations such as driving a car. Indeed, insomnia has been indicated as an additional risk factor for traffic accidents [19–21]. Epidemiological studies have also shown that sleep deprivation leads to increased sleepiness and increased risk of traffic accidents [22–25]. Furthermore, crash risk following sleep deprivation seems most pronounced during extended driving periods when loss of vigilance is highest [26–28].

Daytime performance of insomnia patients is described in Chapters 2, 3, and 4. The current thesis explored for the first time the driving performance of untreated primary insomnia patients during simulated and on-the-road driving. We have shown that insomnia patients, even without being treated for their sleep problems, could have a driving impairment in monotonous situations in simulated driving. In contrast, on-the-road driving investigation revealed that older insomnia patients are fit to drive on the highway, meaning that it is not a simple problem. In fact, compensation mechanisms can occur in older insomnia patients or the occurrence of frequent stimuli (as is the case in real highway driving compared to simulated monotonous driving) can preserve insomnia patients from driving impairments. In addition, our results showed that insomnia patients have a vigilance decrement that seems more prominent than in good sleepers during monotonous driving and difficulties in conflict resolution. Conflict resolution is part of the executive control process that includes a large range of abilities such as initiating, planning, setting goals, and resolving conflicts that are consistently useful in day-to-day life. Because we (and previous research) have shown that insomnia patients have difficulties in complex cognitive and monotonous driving tasks, these results are in line with complaints of daytime fatigue and cognitive impairments that are often expressed by insomnia patients in daily life activities such as those done at work and/or in their personal life. Daytime difficulties may also be related to economic issues. Firstly, by being less efficient at work and by having more absenteeism than people with good sleep, insomnia patients' sleep problems contribute to costs. Secondly, if insomnia patients are more likely to have driving accidents than good sleepers, related health care costs must also be higher.

Beside these daytime deficits, the sleep spectral investigation in insomnia patients described in Chapter 6 revealed a specific cortical activity pattern in the prefrontal cortex compared to other cortical areas (i.e. parietal, occipital, and central). As the prefrontal cortex mediates sleep physiology as well as high-order cognitive abilities, it may thus be a target for sleep and cognitive performance enhancement using electrical stimulation, as described in recent studies [29–32].

We also investigated the effects of sleep deprivation over time on real monotonous driving performance and cortical activity as assessed by electroencephalography (EEG) during driving. Laboratory investigations have shown that sleep deprivation exacerbates time-on-task effects (performance decrement over time). Results described in Chapter 5 revealed that the interaction between sleep deprivation and duration of driving is present in real conditions as well. In addition, sleep EEG results revealed that, in particular, the theta EEG power, which is related to sleepiness, was increased both after sleep deprivation and by duration of driving. The deleterious effects induced by the duration of driving were exacerbated by sleep deprivation compared to the normal sleep condition. During on-the-road driving, after sleep deprivation, the time-on-task effects found in both driving performance and cortical activity differ slightly from those found in simulated driving setting. Our results did not reveal any significant correlation between EEG and driving performance measures, similar to previous driving and EEG investigations. It appears therefore that EEG is not the ideal physiological measure for predicting driving performance.

Target groups

The results described in this dissertation are relevant to many groups including the academic community, insomnia patients, clinicians, governments, and companies.

Clinicians, and by extension governments, should be aware that, even if the daytime deficits of insomnia patients are difficult to describe using classic neuropsychological tests, these patients do have daytime difficulties as revealed in part by results from Chapters 2, 3, and 4, and insomnia patients' complaints need to be heard. Therefore, sleep clinicians and general practitioners are directly concerned by results described in this dissertation. Consequently, if the current results are taken into account in creating more comprehensive care in the management of insomnia patients' daytime and sleep problems, these patients will benefit from our results. In addition, the results described in this dissertation are relevant for governments, especially in the field of prevention because it gives scientific support to epidemiological reports about both the interaction of sleep deprivation and duration of driving. Complaints of driving difficulties in insomnia patients are also supported.

Ultimately, our results may help companies develop devices dedicated to the prevention of vigilance decrement during driving, both after sleep deprivation and in insomnia patients.

Activities and products

As a first step, our results on daytime difficulties in insomnia patients may help clinicians in the management of the cognitive difficulties of insomnia patients. Cognitive therapies in particular should focus on executive control and memory, which are the cognitive domains most affected in insomnia based on our report and those of previous studies.

The prevention of driving sleepy is still in development, and our results open new opportunities for preventing traffic accidents related to sleepiness. The results described in Chapter 5 together with results from previous driving studies suggest that results from simulator driving studies, especially EEG measurements, may not be completely representative of the sleepiness state of the driver. Therefore, results from simulator driving studies should not be used as a basis for preventing sleepy-based traffic accidents. By having better knowledge about the effects of sleep deprivation on actual driving particularly throughout the driving task and not an overall view, companies will be able to improve drowsy driver detection systems. Because our study in Chapter 5 and previous driving and EEG investigations led to inconsistent results about a clear relationship between EEG and driving measures, it seems that EEG is not the ideal physiological measure to predict driving performance. Thus, new combinations of physiological measures obtained on-board and able to predict driving impairment are needed. This could be done by forming collaborative relationship between companies and researchers who can interact and exchange their knowledge. This is a good opportunity to increase contribution of public research to private companies. Such development will lead to the creation of new systems that will involve researchers and start-ups as well as international automobile companies and will thus lead to patents. The development of high order statistical models to prevent hypo-vigilance will also involve statisticians who are accustomed to working with private companies. Therefore, various fields of research will contribute and interact to develop on-board systems for preventing sleepiness and hypo-vigilance.

Electrical stimulation to improve cognitive performance is becoming increasingly popular among researchers and companies. Based on tDCS research experiment results, companies have recently developed devices that apply small electrical currents directly onto the scalp, in order to stimulate neurons. This method has been shown to improve attention and cognitive abilities. Based on this knowledge, it is tempting to think about using these devices in insomnia patients or after sleep deprivation. One may imagine that we could use tDCS to reverse the deleterious effects of insomnia or sleep deprivation on daytime performance by using electrical stimulation over the prefrontal cortex, for example. However, although this method has been said to be non-invasive, this is not necessarily the case if non-experienced persons perform the stimulation. Indeed, in order to use tDCS properly, it is important to know how long to stimulate, at what time to stimulate, and what intensity to use. Unfortunately, this knowledge is only available to clinicians or researchers in the field who have already had experience with tDCS. Consequently, one can imagine that tDCS could be used to improve daytime cognitive performance in insomnia or after sleep deprivation, but such electrical stimulation needs to be done by clinicians from the field and cannot be done by the patient himself.

Innovation

The research described in this dissertation is innovative in various aspects. Firstly, to our knowledge, this is the first time that EEG measures and on-the-road driving performance have been investigated together in insomnia patients and after total sleep deprivation in comparison to a normal night of sleep in healthy volunteers. Such experiments give new insights into the physiological basis of driving when sleepy and of daytime deficits of insomnia patients, and may help to improve driving safety. Driving experiments have high ecological validity that is particularly true for on-the-road driving. Conducting on-the-road driving studies is a scientific and technical challenge that has been possible only because of the expertise of the

Department of Neuropsychology and Psychopharmacology (Maastricht, The Netherlands) in this field of research.

Secondly, studying the driving performance of both healthy volunteers after sleep deprivation and insomnia patients in the same thesis is also innovative. Although surprising, most insomnia patients are not sleepy and have a reasonable amount of sleep. Therefore, sleep deprivation study results should not be extended to insomnia patients. The behavioral and EEG results described in this dissertation are in line with this assertion because we showed that driving performance particular as well as EEG measures over time differ between insomnia patients and healthy sleep deprived in participants.

Besides these general methodological aspects, the special feature of the statistical investigations of our results helped to highlight for the first time sleep and daytime characteristics of insomnia patients and healthy volunteers that were sleep deprived. In particular, in Chapter 6, we chose to consider all cortical areas while investigating sleep spectral analysis. This allowed us to find specific cortical activity patterns in insomnia patients that have not been highlighted before. In Chapters 3, 4, and 5, instead of considering driving performance and EEG measures in a global way, we investigated their fluctuations over time that yielded more in-depth results about driving performance deficits and cortical fluctuations over the driving task.

Timeline and implementation

As a first step, our results have already been presented at various national and international scientific and clinical conferences. In addition, the papers described in this dissertation have been published or are in revision in scientific journals that target both scientific and clinical areas of interest. Moreover, dissemination of information about our study in public journals (Inserm, Science et Santé, March 2015) and in scientific editorials [33,34] has been achieved.

In the long-term, we hope that our findings will be used to pursue efforts in the education of the general public about the risks of drowsiness on the road. Until now, less attention has been given to insomnia patients on the road than sleep deprivation or drug use. The present results underline the fact that driving safety and accident prevention should be extended to patients with sleep disorders, particularly insomnia patients. Therefore, it would be wise to include insomnia in prevention campaigns for public education on driving risks. This also raises the question of whether or not insomnia patients are indeed dangerous on the road, and public debates should be organized on this topic, during French Sleep Day or French Science Day for example. One can also imagine that, as in the case of drunk-driving, an insomnia-driving association could be created in order to encourage research and development and dissemination of information about insomnia and driving. Previous campaigns of prevention have focused on sleepy/drowsy driving. However, insomnia patients are qualified as "hyperaroused" and thus not really sleepy. Even if the question remains to be elucidate regarding the neural correlates of driving impairment in insomnia, our results emphasize the fact that not only being sleepy can be dangerous on the road.

Cognitive therapies in insomnia patients should focus specifically on executive control and memory, which are the cognitive domains most affected in insomnia based on our report and those of previous studies. More generally, sleep centers may receive additional interest and provide the opportunity for their sleep physicians to spend more time on insomnia patients, as in the case for OSAS for example. Additional effort needs to be put into finding resources (financial and human) in order to better support insomnia patients and develop the use of non-pharmacological treatment to improve sleep and performance of daily activities. In France, consultations for insomnia patients are currently considered to be too time consuming and thus not cost-effective for hospitals, so less attention is given to insomnia compared to other sleep disorders which are easier to manage. Our governments should consider the long-term consequences and understand that, although not immediately profitable, the long-term benefits of better patient management and lessening of economic burden will outweigh the benefits of short-term solutions. Insomnia is not untreatable, and these patients should be shown more consideration.

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