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## Neurofeedback to improve wakefulness maintenance ability

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**[Instructions:** The extended abstract content should not be more than 1000 words (excluding references and figures/tables). This extended abstract should clarify the research question, the research performed and methods applied, results and findings, as well as the inferences and conclusions of the authors. The text can be supplemented by up to two figures or two tables (or one figure and one table) with separate captions. These figures/tables and their captions do not count towards the word limit. The structure of the extended abstract should include the following section: synopsis, background, methods, results, discussion, disclosures (if any), and references.]

**Synopsis** [i.e., a short abstract of the work, maximum 1000 characters. This synopsis should be the same as the abstract written on CMT during the submission]

The aim of this study was to evaluate the effect of an EEG-based neurofeedback (NF) program on the ability to maintain wakefulness in healthy subjects, after a controlled one-night complete sleep debt condition. The Maintenance Wakefulness Test (MWT), which assesses objective wakefulness maintenance abilities, and the Karolinska Sleepiness Scale (KSS), which assesses subjective wakefulness maintenance abilities, were administered to a group of healthy sleep-deprived subjects (n=16) before (V1) and after (V2) eight neurofeedback sessions on  $\beta/(\theta-\alpha)$  EEG spectral bands activities target. Mean sleep latency on the MWT and mean KSS scores increased significantly between V2 and V1 ( $p = 0,001$ ). This proof-of-concept study is the first step towards developing cognitive remediation strategies using EEG neurofeedback targeting sleep complaints in patients with residual hypersomnolence. Further research is needed to confirm the efficacy and benefits of this type of non-pharmacological therapy.

### Background

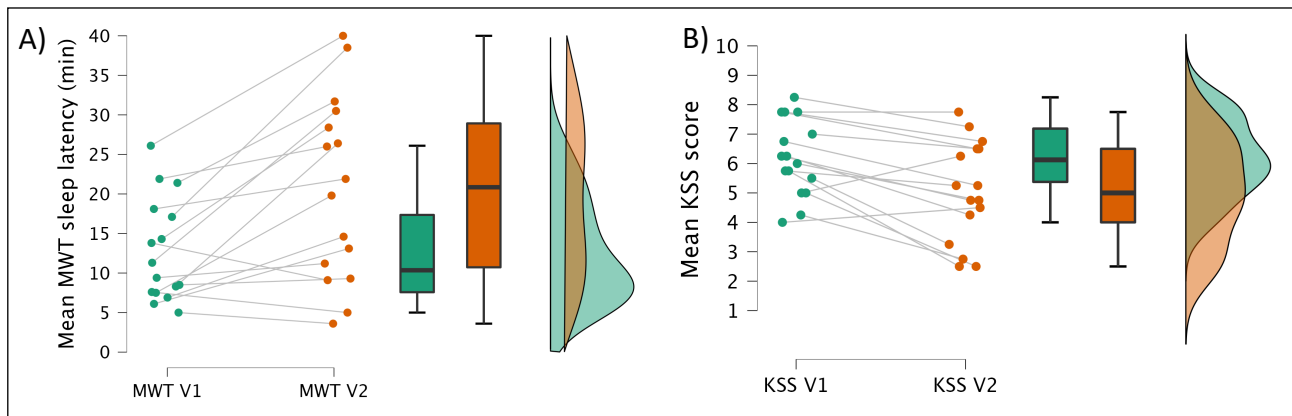
Excessive Daytime Sleepiness (EDS) is a common symptom of sleep disorders, and is the consequences of reduced wakefulness maintenance ability. This reduced ability has an impact on quality of life and results in functional impairments (Waldman et al., 2020). The persistence of EDS in certain pathologies, such as Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS), led to the development of new treatments, including non-pharmacological ones. EEG Neurofeedback (NFB) is an innovative technique for treating EDS that looks promising : an initial preliminary study on a small group of subjects demonstrated the possibility of using a NFB training targeting beta and theta-alpha EEG spectral bands activities to modify brain activity (Monseigne et al., 2019). Today, larger-scale studies are needed to better determine the effectiveness of this type of protocol in subjects with EDS, and the factors predictive of success in learning neurofeedback, in order to optimize treatment (Ros et al., 2020). This proof-of-concept study is the first step towards developing cognitive remediation strategies using EEG neurofeedback targeting sleep complaints in patients with residual hypersomnolence.

## Methods

The Maintenance Wakefulness Test (MWT), which assesses objective wakefulness maintenance abilities (at 10h, 12h, 14h and 16h), and the Karolinska Sleepiness Scale (KSS), which assesses subjective wakefulness maintenance abilities, were administered to a group of healthy sleep-deprived subjects (n=16) before (V1) and after (V2) eight neurofeedback sessions on  $\beta/(\theta-\alpha)$  EEG spectral bands activities target, which is the combination of a marker of homeostatic sleep pressure (power of the spectral band  $\theta-\alpha$  (6,25-9Hz) in Cz) and a marker of vigilance (power of the spectral band  $\beta$ , which decrease with sleepiness). During both visits (V1 and V2), subjects are deprived of a full night's sleep in a controlled manner according to an acute sleep deprivation model. MWT and KSS were measured after the full night's sleep debt. Objective and subjective sleepiness measures obtained during the two visits (before, V1 and after, V2) are compared using a Student's t test.

## Results

Mean sleep latency on the MWT and mean KSS scores increased significantly between V2 and V1. Average latencies increase from 12,7 min (V1) to 20,5 min (V2) on the MWT with a p-value of 0,001. The sleep latency curve over the course of the day (10h, 12h, 14h and 16h) is similar between V1 and V2. The mean KSS score increase from 6,1 (V1) to 5,0 (V2) with a p-value of 0,001.



**Figure 1 :** **A)** Mean sleep latency (in min) at first visit V1 (before 8 NF sessions) and second visit V2 (after 8 NF sessions) on group (n=16, Student's t-test with p=0.001). The mean sleep latency corresponds to the average time taken by subjects to fall asleep during the MWT realized after a full night's sleep debt. **B)** Mean KSS score at first visit V1 (before 8 NF sessions) and second visit V2 (after 8 NF sessions) on group (n=16, Student's t-test with p=0.001). The mean KSS score latency corresponds to the average score from the four KSS assessment at V1 and V2 after a full night's sleep debt.

## Discussion

A neurofeedback training targeting EEG  $\beta/(\theta-\alpha)$  activities seems to be of interest to improve objective and subjective wakefulness maintenance abilities and decrease EDS after a full night's

sleep debt. It is worth noting that we find a significant intra- and inter-individual variability, which is often observed in neurofeedback studies. The next step is to understand this variability by looking for differences between those who respond to NF training (responders) and those who do not (non-responders). We might be able to identify factors predictive of learning. In the future, it will be necessary to carry out a randomized, controlled, double-blind study to better control bias and assess the real effectiveness of this training. Further research is needed to confirm the efficacy and benefits of this type of non-pharmacological therapy for patients suffering from EDS in the context of sleep disorders.

## References

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