CORTICAL EXCITABILITY TRANSIENTLY INCREASES DURING ATTENTIONAL LAPSES

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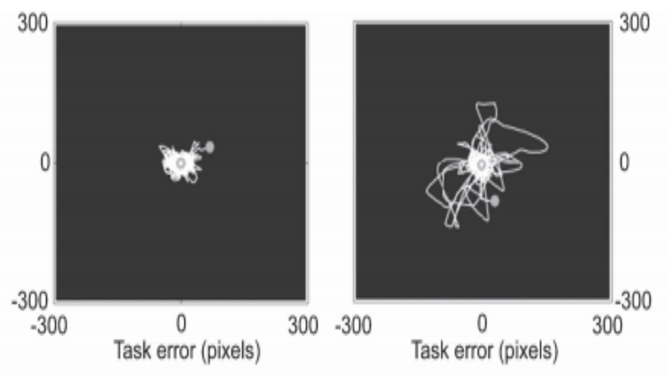
BACKGROUND

- Cortical excitability reflects the reaction of the cortex to a stimulation. It is related to neuron **response selectivity**.
- Cortical excitability is affected by sleep-wake history, circadian rhythmicity and conscious state: it increases during prolonged wakefulness, decreases in the evening due to circadian influence and it is maximum when unconscious (i.e. during sleep, anesthesia or altered state of consciousness) *(Massimini et al., 2005; Huber et al., 2013; Ly et al., 2016)*
- **Attentional lapses heavily** depend on sleep-wake history and circadian phase *(Gaggioni et al., 2018)*. They may be considered as a transient altered state of consciousness where stimulation processing does not trigger optimal behavioral response.
- ***Whether cortical excitability is altered during attentional lapses is unknown.***

METHODS

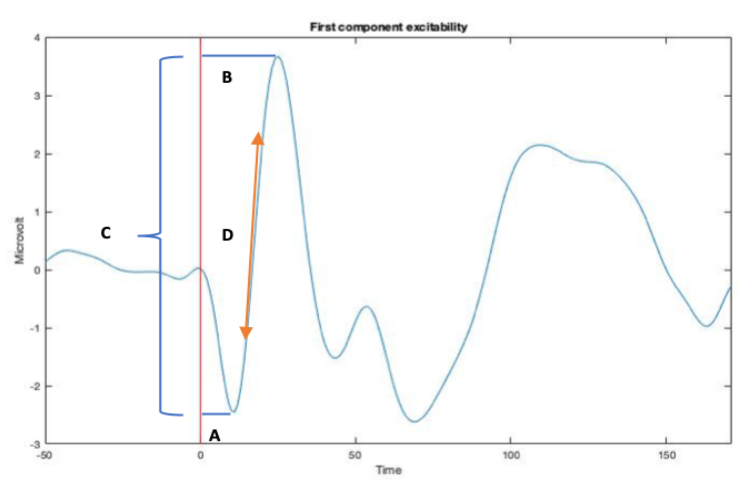
- Retrospective analysis on 3 prolonged wakefulness constant routine protocols, including night time sessions (lasting from 20h to 36h).
- **Cortical excitability** was assessed based on EEG recordings of **TMS Evoked Response** over the **superior frontal gyrus** in 13 younger (age: 22 +/- 2.5; 2 women) and 13 older (age: 60+/- 6.5; 7 woman) healthy individuals.
- Attention lapse detection was based on a **visual Compensatory Tracking Task (CTT)**, carried out during TMS-EEG recordings (Figure 1)
- One night time session (either ~2 AM or ~7 AM) was selected in each study.
- To be included subjects had to have at least 20 lapses in the chosen session.
- Measures of interest were based on the **first component (0-30 ms) of the TMS-EEG Evoked Potential**: Slope, Amplitude, Latency of positive peak and latency of the negative one (Figure 2)

FIGURE 1: Attentive Task – Compensatory Tracking Task (CTT)



A constantly moving cursor gets away from the target, the subject has to center it. A lapse is a episode of the cursor being outside of the central 200 by 200 pixels box surrounding the target after >500ms from the last trackball movement.

FIGURE 2: Cortical Excitability



A) Latency of the negative peak **B)** Latency of the positive peak **C)** Peak to Peak amplitude **D)** Slope of the curve. Here, represented the tangent at the inflection point.

DATA PROCESSING AND ANALYSES

- TMS-EEG data pre-processing were computed using the SPM12 software package (Statistical Parametric Mapping 12, http://www.fil.ion.ucl.ac.uk/spm/) implemented in Matlab. Recordings were re-referenced to the average of all good channels, low-pass filtered at 80 Hz, resampled from 1450 to 1000 Hz, and high-pass filtered at 1 Hz, split into epochs between –100 and 300 ms around TMS pulses, and baseline corrected (-100 to -1 ms pre-TMS). Robust averaging was applied to compute the mean evoked response of each session.
- Statistical analyses were performed with SAS version 9.4 (SAS Institute). The time-course of all variables was examined with a Generalized Linear Mixed Model (PROC GLIMMIX) including age, sex, education and TMS pulse characteristics to test whether measures of interest differed between attentional lapse and no-lapse.

RESULTS

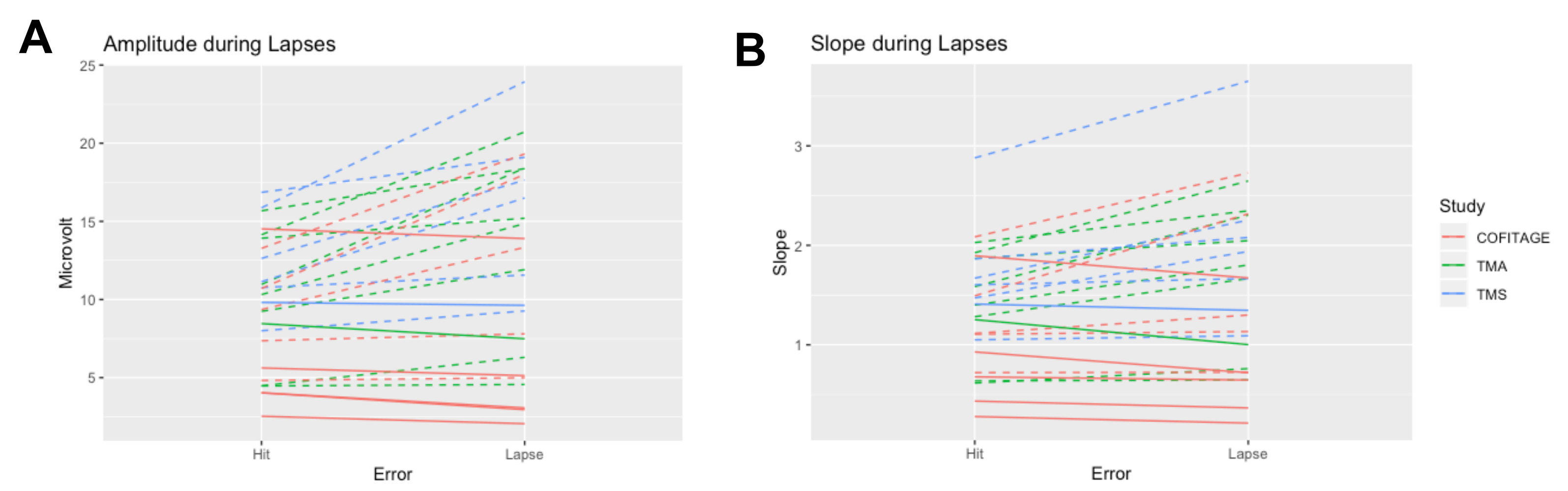
- **Slope, Amplitude and latency of positive peak** of TMS evoked responses **increased** during lapse compared to no-lapses (Table 1).
- **Latency of negative peak** of TMS evoked responses **decreased** during lapse vs. no-lapses.
- No impact of age.

TABLE 1: Results and effect size of excitability

Measure	F-Value	Adjusted *p*-value	R-squared beta star
Amplitude	12.03	0.002	0.34
Slope	7.02	0.014	0.23
Negative Latency	12.66	0.002	0.36
Positive Latency	8.12	0.009	0.26

All the results with relative F-Value and adjusted *p*-value. Effect size for GLMM was calculated as indicated by Jaeger and colleagues (2017) to have a comparable R^2.

FIGURE 3: Single subject level plot – Amplitude and Slope



Plot for Amplitude (A) and Slope (B) of TMS evoked potential for no-lapse (left) and attentional lapses (right).

DISCUSSION

- This is the first evidence of **transient increase of cortical excitability** during attention lapses.
- It is uncertain whether it is a **sleep related-phenomenon**, such as an epiphenomenon of probability to falling asleep or local sleep, or rather a **specific brain state** related to error making.
- More research is needed to untangle the generalization of such findings.
- No confounding effect of any demographic factor or session characteristic.
- This suggest promising future intervention to decrease the probability to make errors with online brain-state dependent stimulation.

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Bibliography:
- Huber, R. *et al. Cereb. Cortex* **23**, 332–338 (2013).
- Ly, J. Q. M. *et al. Nat. Commun.* **7**, 11828 (2016).
- Jaeger, B. C., Edwards, L. J., Das, K. & Sen, P. K.. *J. Appl. Stat.* **44**, 1086–1105 (2017)
- Gaggioni, G. *et al. Neuroimage* **175**, 354–364 (2018).
- Massimini, M., Ferrarelli, F., Huber, R. & Esser, S. K.. *Science (80-.).* **309**, 2228–2233 (2005)