Understanding the role of REM sleep continuity in emotional memory and emotional reactivity through a new methodological approach

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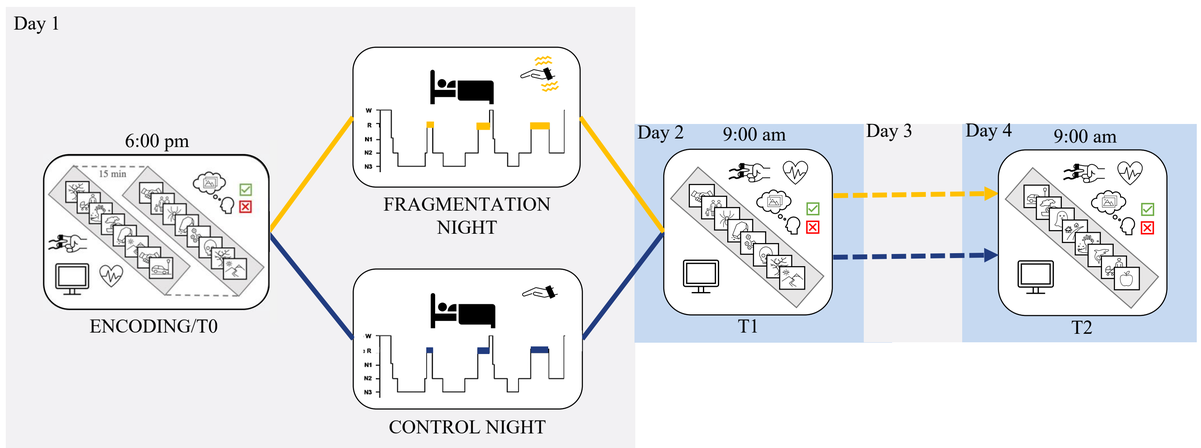
eSLEEP EUROPE
October 4-6, 2023 | Virtual Congress

INTRODUCTION

Several evidence supports the role of REM sleep in emotional processing and consolidation of emotional memories. Besides REM duration, it has been recently proposed that REM sleep continuity supports amygdala adaptation to emotional events in subjects with a wide range of insomnia severity. However, sleep features in clinical populations include other macrostructural alterations that limit the generalizability of the findings. Our study aims to understand the role of REM sleep fragmentation in the psychophysiological reactivity to emotional stimuli, experimentally manipulating the continuity of REM sleep in healthy individuals while minimizing sleep macrostructure alterations.

METHODS

Figure 1: Timeline of the experimental procedure



12 participants were involved in two experimental sessions in a counterbalanced order consisting of:

- The baseline assessment of emotional reactivity to 28 emotional pictures (14 negative; 14 neutral) and the encoding phase with the immediate test of the memory recognition for emotional pictures (40 negative; 40 neutral) at 6:00 pm (T0, Day 1);
- A polysomnography (PSG) recording with 64-channel high-density EEG of the nocturnal sleep with (Fragmentation Night) or without (Control Night) vibrotactile stimulation;
- The post-sleep assessment of emotional reactivity and emotional memory at 9:00 am (T1, Day 2);
- A delayed assessment of emotional reactivity and emotional memory 48 hrs later, at 9:00 am (T2, Day 4).

Emotional reactivity was assessed by collecting psychophysiological responses (Heart Rate Deceleration, HRD; Skin Conductance Responses, SCR) to emotional stimuli.

Emotional memory was evaluated by an Old/New paradigm by calculating the discrimination index (d') that measures the ability to distinguish between Old/New stimuli.

Linear mixed-model analyses on HRD, SCR, and d' were performed using the condition (Control, CTR; Fragmentation, FRG), the session (T0, T1, T2), the emotional valence of the stimuli (Negative, Neutral), and their interaction as factors. Statistical significance was set at $P<0.05$, Bonferroni post hoc tests were performed in the case of significant main effects or interaction effects.

Sleep before and after nocturnal polysomnography was monitored using actigraphy in CTR and FRG conditions.

Figure 2: Arousal induction procedure

Cortical arousals were induced by vibrotactile stimulation (max duration: 3s) during REM sleep. In case of no cortical response, the stimulation was repeated 3s later, increasing the vibration power. Experimentally induced cortical arousal was conceived as an abrupt shift of EEG frequency including alpha, theta and/or frequency greater than 16Hz, but not spindles, that lasts at least 3 second, with at least 10 seconds of stable sleep preceding the change.

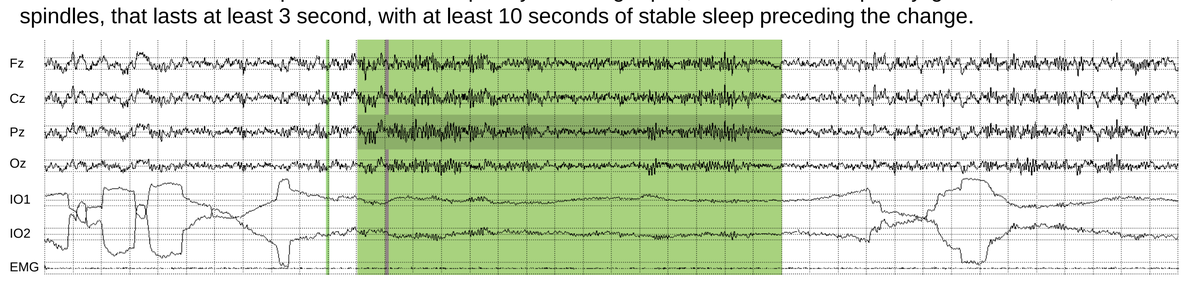
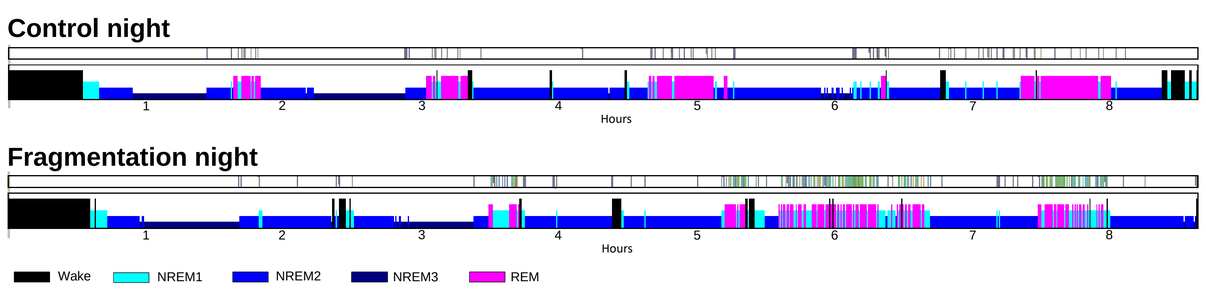


Figure 3: Example of Sleep macrostructure

Representative example of sleep macrostructure in CTR and FRG condition. The band above each hypnograms contain vertical bars that represent cortical arousal. Grey vertical bars indicate spontaneous cortical arousal, while other vertical bar colours represent experimentally induced cortical arousal at different stimulation power intensities.



RESULTS

Table 1: Sleep parameters

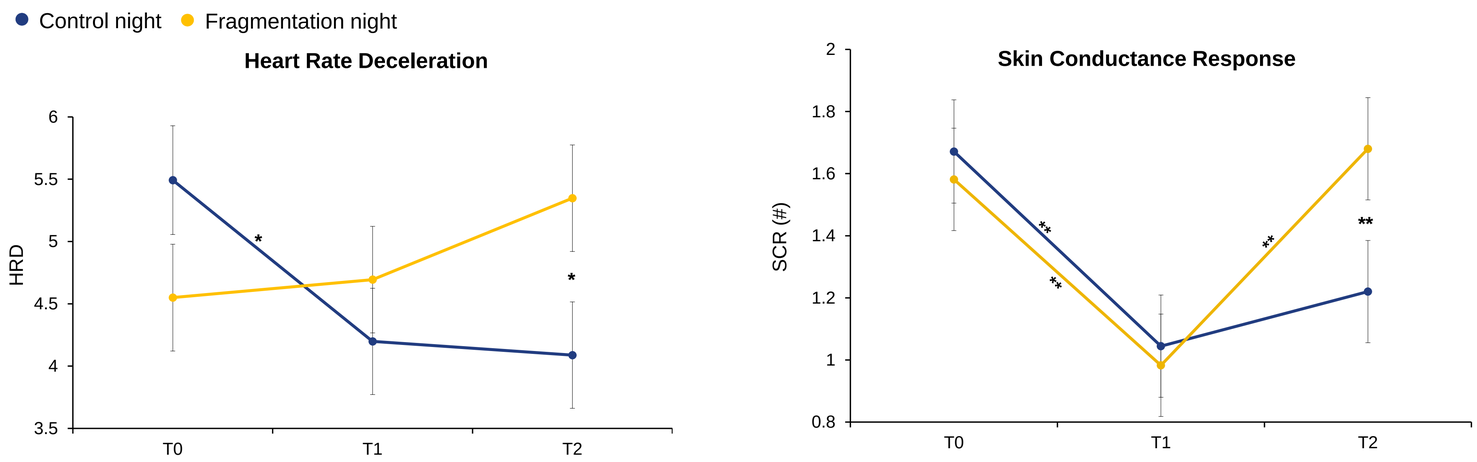
Means ± SD of sleep macrostructure variables in the CTR and FRG condition, and their statistical comparisons (paired sample t-test).

SLEEP PARAMETERS	CTR	FRG	t_{11}	p value
SOL (min)	18.7 ± 13.0	20.0 ± 11.7	-0.4	0.715
WASO (min)	60.2 ± 35.6	48.0 ± 22.9	1.6	0.146
TST (min)	427.3 ± 31.2	426.7 ± 27.1	0.1	0.953
SE%	84.8 ± 7.6	86.2 ± 3.8	-0.8	0.434
NREM1%	**8.5 ± 2.0**	**15.4 ± 4.7**	**-7.0**	**<0.001**
NREM2%	52.3 ± 6.2	50.2 ± 5.7	1.0	0.336
NREM3%	20.2 ± 4.3	21.8 ± 5.1	-1.7	0.125
REM%	**19.0 ± 3.0**	**12.5 ± 2.4**	**5.6**	**<0.001**
REM Sleep Fragmentation Index	**8.6 ± 2.6**	**23.6 ± 3.6**	**-11.4**	**<0.001**
REM continuity MAX (min)	**15.6 ± 5.7**	**4.5 ± 1.5**	**6.1**	**<0.001**
REM continuity MEAN (min)	**6.2 ± 2.0**	**1.3 ± 0.5**	**7.6**	**<0.001**

Notes: REM Sleep fragmentation index is the total number of bouts of NREM1 sleep and Wakefulness that interrupted REM episodes, divided by the total duration of REM episodes.

Figure 4: Emotional reactivity

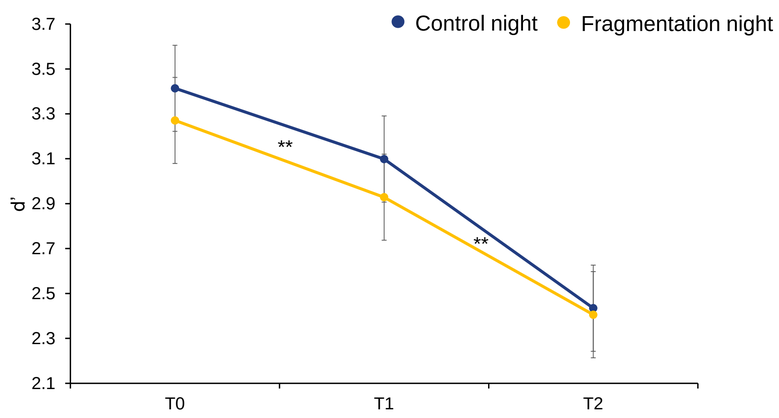
Mean and standard error of HRD and SCR values. Asterisks indicate significative Bonferroni post hoc comparisons (*p<0.05, **p<0.001).



Analyses showed no effects of the *condition* × *session* × *valence* interaction for HRD ($F_{(2,1952)}$=0.1, p=0.923) and SCR values ($F_{(2,1952)}$=1.1, p=0.339). However, *condition* × *session* interaction was significant for both HRD ($F_{(2,1953)}$=8.3, p=<0.001) and SCR values ($F_{(2,1952)}$=10.6, p=<0.001).
Post hoc comparisons indicated that HRD decreased between T0 and T1 (t_{1929}=3.3, p=0.014) in CTR condition, stabilizing at T2 (t_{1926}=0.3, p=1.000). No variations in HRD response were measured in FRG condition over sessions (all p=1.000). HRD response at T2 was higher in FRG condition than CTR condition (t_{1926}=-3.3, p=0.015).
For the SCR, post hoc comparisons indicated that SCR decreased between T0 and T1 in both conditions (both p<0.001). SCR stabilized at T2 in the CTR condition (t_{1926}=-1.8, p=0.948), while increased in the FRG condition (t_{1926}=-7.4, p<0.001) exhibiting values similar to T0 (t_{1926}=-1.0, p=1.000). SCR at T2 was higher in the FRG condition than CTR condition (t_{1926}=-4.8, p<0.001).

Figure 5: Emotional memory

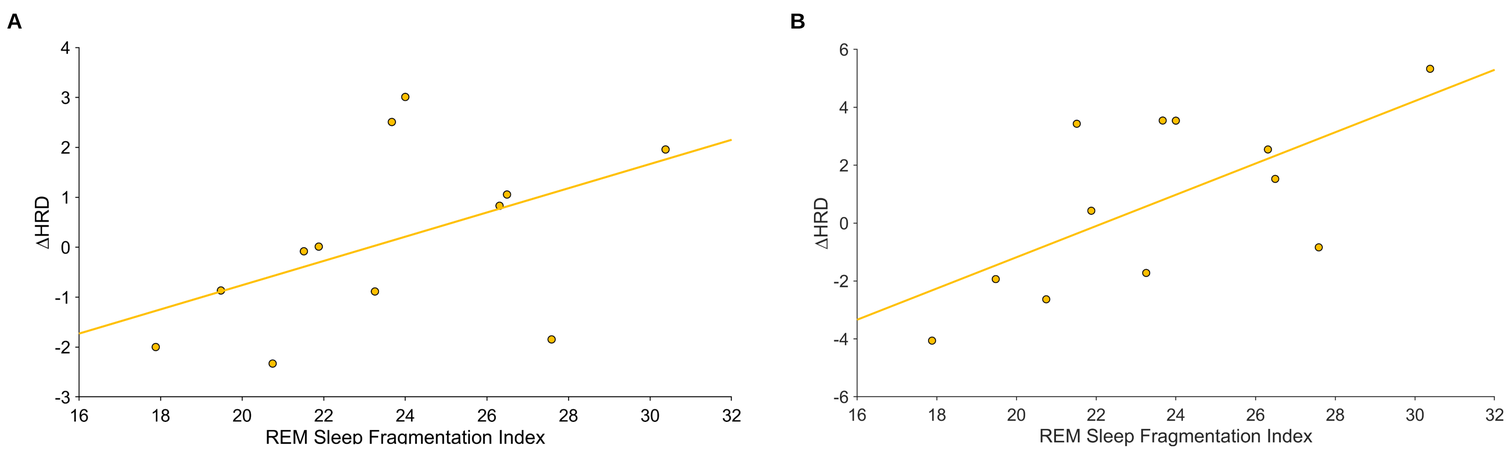
Mean and standard error of the discrimination index in CTR and FRG condition. Asterisks indicate significant Bonferroni post hoc comparisons (**p<0.001).



Analyses showed no effects of the *condition* × *session* × *valence* interaction ($F_{(2,121)}$=1.4, p=0.245). *Condition* × *session* interaction was also not significant ($F_{(2,121)}$=0.4, p=0.685). A significant effect of the *session* factor was highlighted ($F_{(2,121)}$= 59.3, p<0.001). Post hoc comparisons indicated declined memory performance overs sessions.

Figure 6: Correlation between REM Sleep Fragmentation Index and changes in HRD across nights

Explorative Pearson's r correlation analyses in FRG condition between T0 and T1 (A), and between T0 and T2 (B).



Analyses showed a significant association between REM Sleep fragmentation index and changes in HRD between T0 and T2 (r=0.65, p=0.022), and a trend to a significant correlation between T0 and T1 (r=0.49, p=0.107) in FRG condition. No significant correlation was reported between REM Sleep fragmentation Index and changes in SCR between sessions (all p>0.300).

TAKE HOME MESSAGE

- REM sleep continuity seem to play a role in the psychophysiological habituation response to neutral and negative stimuli over time.
- Inducing arousal via brief vibrotactile stimulation leads to increased NREM1 duration and reduced REM duration without affecting WASO and TST.
- REM sleep fragmentation did not affect time-dependent memory performance decay.

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