Letter to the Editor

Probing the embodiment of sleep functions: Insights from cardiac responses to word-induced relaxation during sleep

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Bodily activity plays a pervasive role in memory, emotion, perception, and self-related processes, supporting the view that cognitive functions are embodied [1]. While empirical evidence has been largely obtained in wakefulness, bodily functions have been also proposed to relate to cognitive functions during sleep [2]. An example of such kind is the importance of cardiac activity in accounting for overnight memory improvements, above and beyond classically used sleep indices, such as sleep stages duration and sleep spindles [3].

Despite this knowledge, the underlying mechanisms of how cardiac activity informs sleep states only now starts to receive a better understanding [4]. Indeed, electrocardiography (ECG) is standardly acquired along with electroencephalography (EEG) in classical polysomnography but its analysis has been usually neglected. Here, we advocate for considering bodily signals in the understanding of sleep functions, by showing that cardiac activity during polysomnography holds valuable information about perceptual processing during sleep and its impact on sleep functions.

To this end, we analyzed a recently acquired dataset showing that slow-wave sleep (SWS) duration and subjective sleep quality can increase by playing relaxing words during NREM sleep (Figure 1A) [5]. This increase was associated with an enhancement of slow-wave activity in response to relaxing words as compared to the same words played in reverse (relaxing night), while the effect was not found for neutral words (control night). At this time, the authors hypothesized that words were semantically processed during sleep in an embodied way, explaining how word processing during sleep led to effective physiological changes.

Here, we directly tested the embodiment hypothesis by looking at how word presentation would modulate ECG activity during NREM sleep. To do so, for both night conditions, we defined a relative change index by normalizing the average interbeat intervals of word presentation to the average interbeat intervals without word presentation (values set to

100% for NREM without word presentation). We found that interbeat intervals were longer while words were played in relaxing nights (median ± 95% confidence interval = 100.8%±[100.0, 101.6], Wilcoxon signed-rank test compared to 100%: p=0.001), but not in control nights (100.0%±[99.0, 101.0], p=0.418), with a significant difference between the two night conditions (relaxing vs. control: 1.6%±[0.20, 2.84], p = 0.022; Figure 1B). This shows that the presentation of relaxing words, but not control words, was accompanied during NREM sleep with a slowdown of cardiac activity.

We further investigated how heartbeats were modulated around each word's presentation. For this, we compared the interval between the words' onset (S) with the timing of the heartbeat (R) coming before and after the word presentation, as in previous work [6]. We found that the interval between heartbeats and sound onset was modulated according to whether the word was relaxing or not, played in reverse or not, and the interval with the heartbeat was coming before (RS) or after (SR) the word's onset (linear mixed-model effects: triple interaction, t(380,49)=2.17, p=0.031, no other significant effect).

To investigate the origin of this effect, we defined a cardiac modulation index by subtracting SR from RS for each word presentation and by averaging this value across word types for each participant (Figure 1C). In line with our hypothesis, we found that cardiac modulation was larger for relaxing words over their reversed counterparts (17.4ms±[-8.9, 43.7], Wilcoxon signed-rank test: p=0.037), while it was not for neutral words over their reversed counterparts (-4.6ms±[-36.3, 27.1], p=0.561), and the difference between the relaxing and control conditions was significant (relaxing vs. control: 50.8ms±[8.2, 93.5], p=0.040; Figure 1D). Overall, these results demonstrate that the slowdown of cardiac activity in relaxing nights directly resulted from the embodied processing of relaxing words.

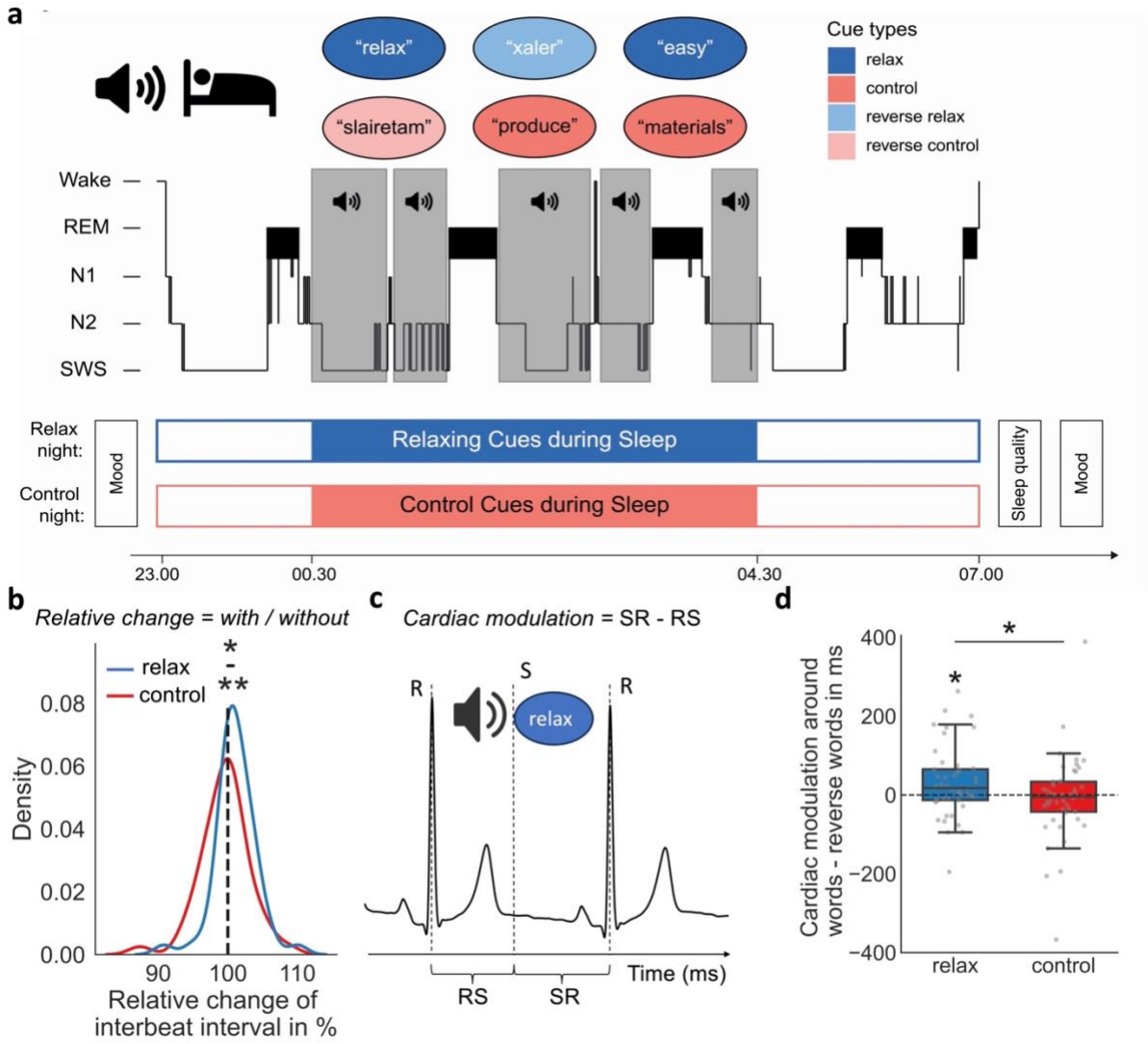

Figure 1. Cardiac activity slows down in response to word-induced relaxation during NREM sleep. (A) Experimental protocol: By means of a within-subject design, the protocol included the presentation of relaxing words and their reversed version (blue) for one night (relaxing night), and the presentation of neutral words and their reversed version (red) in another night (control night). Reproduced from [5] (B) Cardiac slowing (larger interbeat intervals) was observed during word presentation in relaxing but not control nights: Kernel Density Estimate of the relative change in cardiac activity for NREM periods with word presentation as compared to periods without word presentation, set at 100%. (C) Cardiac modulation index was defined as the difference between the word's onset (S) and the heartbeat (R) coming after (SR) *vs.* before (RS) the word's presentation. Positive index values indicate cardiac activity deceleration; negative index values indicate cardiac acceleration. (D) The cardiac modulation index was higher for relaxing words over their reversed counterpart for both relaxing and control nights, showing a slowing down of cardiac activity in response to the presentation of relaxing vs. reversed words. No such effect was observed for control words. Notes: across all plots, statistical significance was obtained with non-parametric Wilcoxon signed-rank tests, *: $p<0.05$, **: $p<0.01$.

Finally, in order to test whether cardiac activity carries independent information about sleep depth modulation in comparison to brain activity, we matched the relative change and cardiac modulation indices with two cerebral indices that significantly differ between relaxing and control nights from the original study [5]: a) the left-right slow-activity activity (SWA) asymmetry during vs. before word presentation, and b) the SWA responses to words vs. their reversed version averaged over significant time points and electrode clusters (Table 1).

Following the methodology of Whitehurst and colleagues (2016), we tested if continuous and evoked cardiac and brain indices contributed, in interaction or independently, to the word-induced modulation of sleep depth [4]. The interaction was tested by building a general linear mixed model predicting relaxing vs. control nights based on the selected brain and cardiac indices. We found no significant differences when adding or removing interaction effects from the model (model comparison test: $p=0.412$), suggesting that interactions between brain and cardiac indices do not play a role in sleep depth modulation.

Table 1. Cardiac activity independently contributes to NREM sleep depth modulation as compared to brain activity. We matched relative change and cardiac modulation with one continuous and one evoked brain index differing significantly during relaxing and control nights: slow-wave activity (SWA) asymmetry and SWA response [5]. Then, we built mixed models with cardiac or brain indices as predictors and subjects as random effects. Cardiac and brain indices each explained parts of variance in the difference between relaxing vs. control nights, as computed by partial R^2 and confidence intervals with the Part2 package in R. Notes: *: $p<0.05$, **: $p<0.01$; Wilcoxon-signed rank test: non-parametric effect sizes computed following the formula Z-value /√(Number of subjects).

Signal	Cardiac		Brain	
Type	Continuous	Evoked	Continuous	Evoked
Indices	Relative change	Cardiac modulation	SWA asymmetry	SWA response
Effect size	0.33 *	0.29 *	0.41 **	0.37 **
Variance explained	10% ± [2,47]		18% ± [11, 50]	
	28% ± [20, 55]			

However, when we compared a restricted mixed model containing brain markers only with a full model containing both brain and cardiac markers, we obtained a significant difference (part of variance explained computed as partial R^2 with confidence intervals for the restricted vs. full model: 18% ± [11, 50] vs. 28% ± [20, 55], model comparison test: p=0.027, Table 1). This confirms that cardiac activity holds an irreducible part of the variance as compared to brain markers of sleep functions in accounting for the difference between relaxing vs. control nights.

Overall, we here aimed at providing a proof-of-concept to promote the study of embodied stimulus processing during sleep. This approach can be used for various purposes. For example, cardiac responses to auditory cues can be identified in the Targeted Memory Reactivation paradigm [7], extending correlates of memory consolidation from the brain to the body. To encourage the investigation of the cardiac correlates of sleep functions, the here described methodology is openly accessible as a step-by-step introductory guide to the analysis of time-locked ECG signals using Python and R in Jupyter-lab [8]: https://gitlab.uliege.be/Matthieu.Koroma/cardiac_relaxation_beck/.

With these tools, cardiac activity can be easily (re)analysed in already acquired datasets: ECG is indeed a low-dimensional signal relatively simple to analyze. It has clear components, such as the heartbeat, and classical tools of dynamical signal processing can be applied. Cardiac activity can also be easily considered for new experimental acquisitions: most classical EEG setups for polysomnography have external channels acquiring and amplifying ECG. Simpler recording devices, like sleep wristbands or rings, can also extract heart rate based on pulse, facilitating its acquisition outside laboratory contexts. Overall, cardiac signals can thus be recorded and analyzed at a low cost across a wide range of experimental practices and ecological settings.

In conclusion, by promoting the study of cardiac responses in sleep research, we wish to foster a more comprehensive approach which includes bodily effects in the investigation of sleep functions. Cardiac activity might indeed uncover irreducible aspects of sleep as compared to brain activity and has even been proposed to constitute part of the subjective dimension of cognition [9]. Given that interoception has been highlighted as a promising avenue for sleep and sleep disorders [10], we hope that the analysis of cardiac activity will highlight the role of bodily signals in our understanding of sleep functions and their modulation by sensory stimulation.

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