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LETTER TO THE EDITOR

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

Bodily activity plays a pervasive role in memory, emotion, perception and self-related processes, supporting the view that cognitive functions are embodied (Azzalini et al., 2019). While empirical evidence has been largely obtained in wakefulness, bodily functions have been also proposed to relate to cognitive functions during sleep (Chouchou & Desseilles, 2014). An example 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 (Whitehurst et al., 2016).

Despite this knowledge, the underlying mechanisms of how cardiac activity informs sleep states has only just started to receive better understanding (Whitehurst et al., 2020). 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 analysed a recently acquired dataset showing that slow-wave sleep duration and subjective sleep quality can increase by playing relaxing words during non-rapid eye movement (NREM) sleep (Figure 1a; Beck et al., 2021). This increase was associated with an enhancement of slow-wave activity in response to relaxing words as compared with 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 inter-beat intervals of word presentation to the average inter-beat intervals without word presentation (values set to 100% for NREM without word presentation). We found that inter-beat 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 with 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 versus 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 (Raimondo et al., 2017). 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 (17.4 ms ± [−8.9, 43.7], Wilcoxon signed-rank test: $p = 0.037$), while it was not for neutral words over their reversed counterparts (−4.6 ms ± [−36.3, 27.1], $p = 0.561$), and the difference between the relaxing and control conditions was significant (relaxing versus control: 50.8 ms ± [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.

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 (Beck et al., 2021): (a) the left–right slow-wave activity (SWA) asymmetry during versus before word presentation; and (b) the SWA responses to words versus their reversed version averaged over significant time points and electrode clusters (Table 1).

Following the methodology of Whitehurst et al. (2016), we tested if continuous and evoked cardiac and brain indices contributed, in interaction or independently, to the word-induced modulation of sleep depth (Whitehurst et al., 2020). The interaction was tested by building a general linear mixed model predicting relaxing versus 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.

However, when we compared a restricted mixed model containing brain markers only with a full model containing both brain and

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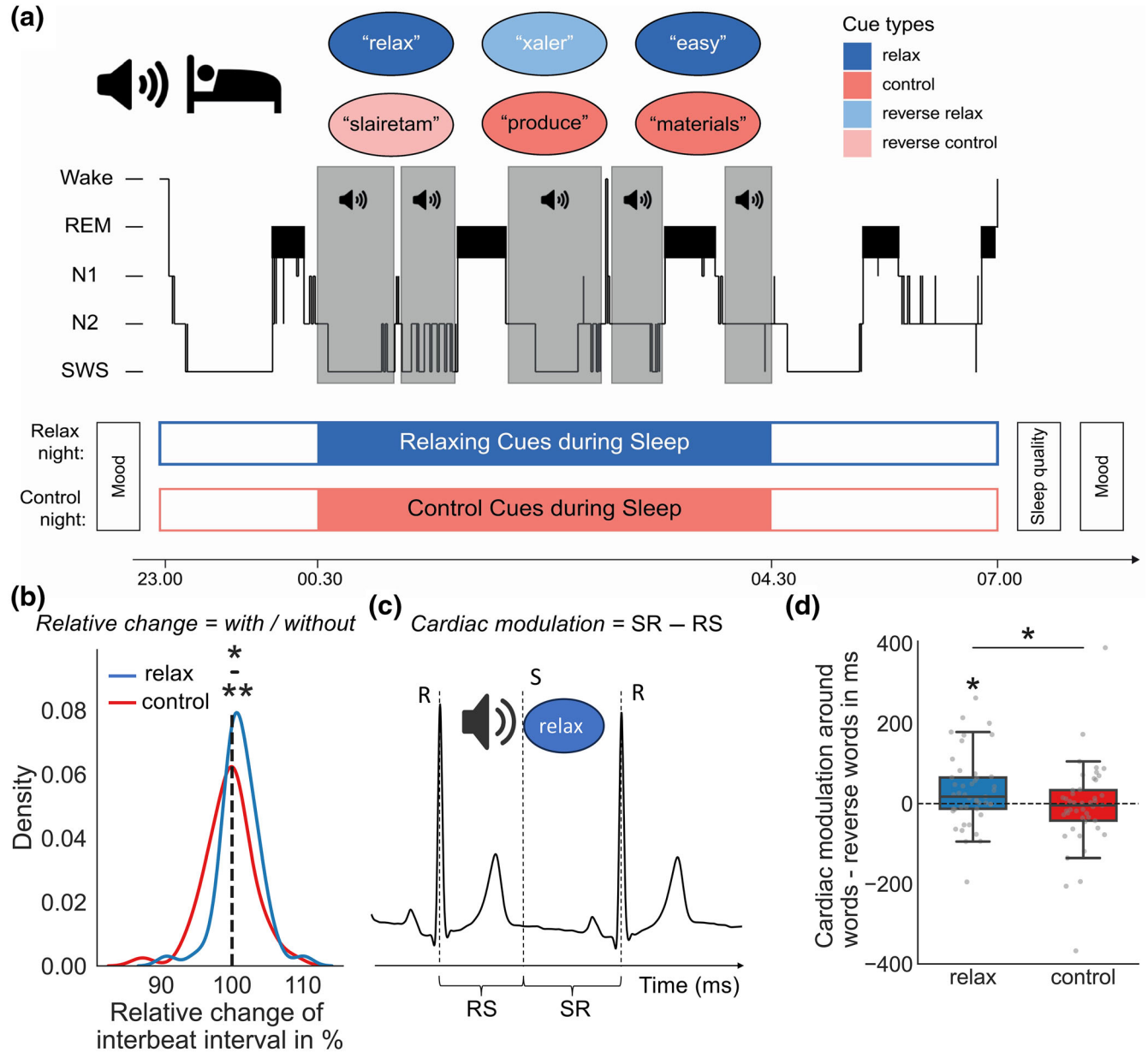

FIGURE 1 Cardiac activity slows down in response to word-induced relaxation during non-rapid eye movement (NREM) sleep. (a) Experimental protocol: by means of a within-subject design, the protocol included the presentation of relaxing words and their reversed version (blue) for 1 night (relaxing night), and the presentation of neutral words and their reversed version (red) in another night (control night). Reproduced from Beck et al. (2021). (b) Cardiac slowing (larger inter-beat 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 with 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) versus 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 versus reversed words. No such effect was observed for control words. Across all plots, statistical significance was obtained with non-parametric Wilcoxon signed-rank tests: $^{*}p < 0.05$; $^{**}p < 0.01$.

cardiac markers, we obtained a significant difference (part of variance explained computed as partial R^2 with confidence intervals for the restricted versus full model: 18% ± [11, 50] versus 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 with brain markers of sleep functions in accounting for the difference between relaxing versus control nights.

Overall, here we 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

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TABLE 1 Cardiac activity independently contributes to NREM sleep depth modulation as compared with brain activity.

Signal Type	Cardiac		Brain	
	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]			

Note: 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 (Beck et al., 2021). 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 versus control nights, as computed by partial R^2 and confidence intervals with the Part2 package in R. Wilcoxon-signed rank test: non-parametric effect sizes computed following the formula *Z*-value/√(Number of subjects).
*$p < 0.05$.**$p < 0.01$.

responses to auditory cues can be identified in the Targeted Memory Reactivation paradigm (Oudiette & Paller, 2013), 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 (Kluyver et al., 2016): 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 analyse. It has clear components, such as the heartbeat, and classical tools of dynamic 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 be recorded and analysed 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 that 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 (Park & Tallon-Baudry, 2014). Given that interoception has been highlighted as a promising avenue for sleep and sleep disorders (Wei & Van Someren, 2020), 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.

AUTHOR CONTRIBUTIONS

Matthieu Koroma: Conceptualization; investigation; writing – original draft; methodology; validation; visualization; writing – review and editing; project administration; formal analysis; software; data curation; resources; funding acquisition; supervision. **Jonas Beck:** Investigation; validation; formal analysis; data curation; visualization; writing – review and editing; methodology; resources. **Christina Schmidt:** Conceptualization; writing – original draft; methodology; validation; visualization; project administration; formal analysis; supervision; writing – review and editing; funding acquisition. **Björn Rasch:** Data curation; resources; project administration; formal analysis; visualization; validation; funding acquisition; investigation; conceptualization; supervision; methodology; writing – review and editing. **Athena Demertzi:** Supervision; conceptualization; investigation; validation; visualization; writing – review and editing; formal analysis; project administration; resources; data curation; methodology; writing – original draft; funding acquisition.

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CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in OSF at https://osf.io/jn7ar/, reference number doi:10.17605/OSF.IO/JN7AR.

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