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Coupling of infraslow fluctuations in autonomic and central vigilance markers: Skin temperature, EEG beta power and ERP P300 latency

Jennifer R. Ramautar [a,1], Nico Romeijn [a,1], Germán Gómez-Herrero [a], Giovanni Piantoni [a], Eus J.W. Van Someren [a,b,c,*]

[a] Department of Sleep and Cognition, Netherlands Institute for Neuroscience, an institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands
[b] Department of Integrative Neurophysiology, Center for Neurogenomics and Cognitive Research (CNCR), Neuroscience Campus Amsterdam, VU University and Medical Center, Amsterdam, The Netherlands
[c] Department of Medical Psychology, Center for Neurogenomics and Cognitive Research (CNCR), Neuroscience Campus Amsterdam, VU University and Medical Center, Amsterdam, The Netherlands

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ABSTRACT

Even under thermoneutral conditions, skin temperature fluctuates spontaneously, most prominently at distal parts of the body. These fluctuations were shown to be associated with fluctuations in vigilance: mild manipulation of skin temperature during nocturnal sleep affects sleep depth and the power spectral density of the electroencephalogram (EEG), and fluctuations in skin temperature during daytime wakefulness are related to sleep propensity and task performance. The association of daytime skin temperature fluctuations with EEG markers of vigilance has not previously been investigated. Therefore, the present study aimed to evaluate the association between daytime fluctuations in skin temperature with those in two quantitative EEG measures: the power spectral density of background EEG, and the event related potential (ERP) elicited by visual stimuli.

High-density EEG and skin temperature were obtained in eight healthy adults five times a day while they performed a visual sustained-attention task. Assessments were made after a night of normal sleep and after the challenge of a night of total sleep deprivation.

Fluctuations in the distal-to-proximal skin temperature gradient measured from the earlobe and mastoid were associated with fluctuations in parieto-occipital high beta band (20–40 Hz) power of the pre-stimulus background EEG, but only after sleep deprivation. The temperature fluctuations were moreover associated with fluctuations in the latency of the P300 elicited by the stimulus.

The findings demonstrate close association between fluctuations in an autonomic correlate of the vigilance state (i.e. the distal-to-proximal skin temperature gradient), and fluctuations in central nervous system correlates of the vigilance state (i.e. background EEG and ERP). The findings are of theoretical and practical relevance for the assessment and manipulation of vigilance.

1. Introduction

The temperature of the skin of the human body shows spontaneous fluctuations, even under thermoneutral conditions (Romanovsky, 2007). Especially the skin of the distal extremities fluctuates considerably, for example over a range of about 2 °C for the finger, measured under strictly controlled conditions (Huizenga et al., 2004; van Marken Lichtenbelt et al., 2006). Both in controlled laboratory settings (Kräuchi and Wirz-Justice, 1994) and in everyday life (Van Someren, 2006), the most pronounced fluctuation in skin temperature is a rhythm of 24-hour. Body temperature rhythms are among the first rhythms to appear during early development and are driven by the hypothalamic suprachiasmatic nucleus, the biological clock of the brain (Swaab et al., 1996). Skin temperature also shows ultradian fluctuations that are associated with variability in subjective, physiological and behavioral indices of sleep propensity and vigilance (Fronczek et al., 2006; Romeijn and Van Someren, 2011; Romeijn et al., 2012). Vigilance may be most strongly associated with the distal-to-proximal gradient, i.e. the temperature gradient between distal skin areas of the extremities relative to proximal skin areas (DPG, Kräuchi et al., 1999, 2000). This association is most reliably found if the gradient is measured between the ear lobe (distal) and the nearby mastoid (proximal) (Romeijn et al., 2012). The gradients reflect sympathetic regulation of distal blood flow (Rubinstein and Sessler,

Abbreviations: BSRT, Brief-Stimulus Reaction Time Task; DPG, Distal-to-Proximal Gradient; EEG, Electroencephalogram; ERP, Event-Related Potential; NS, Normal Sleep; P300, P300 component; SD, Sleep Deprived.

* Corresponding author at: Department of Sleep and Cognition, Netherlands Institute for Neuroscience, Meibergdreef 47, 1105 BA Amsterdam, The Netherlands. Tel.: +31 20 5665500; fax: +31 20 5666121.
E-mail address: e.van.someren@nin.knaw.nl (E.J.W. Van Someren).

[1] Authors contributed equally.

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1990) and thus provide a window on the activity of the autonomic nervous system. It has been proposed that the association is mediated by signaling of skin thermoreceptors to thermosensitive neurons in the preoptic area–anterior hypothalamus (POAH) and other areas that are involved in the regulation of sleep and vigilance (Van Someren, 2006).

A number of studies provide behavioral and physiological support for the proposed causal contribution of fluctuations in skin temperature to variability in sleep and vigilance.

When applied during sleep, mild skin warming affects the macrostructure of sleep, in the sense that it increases the percentage of time spent in deep sleep (Fronczek et al., 2008a; Raymann et al., 2008). Additionally, mild skin warming during sleep changes quantitative sleep measures: the electroencephalogram (EEG) power spectrum shows enhancement of the lower delta and theta oscillations that are typical of sleep, as well as suppression of the higher beta oscillations that are associated with arousal (Raymann et al., 2008).

When applied during wakefulness, mild skin warming accelerates sleep onset latency (Fronczek et al., 2008b; Raymann et al., 2005). It also deteriorates the performance on sustained attention tasks, as indicated by reaction time slowing and an increase in the number of lapses (Raymann and Van Someren, 2007). However, it is not known whether daytime fluctuations of skin temperature are associated with quantitative changes in the background EEG, or in event-related potentials (ERPs). The hypothesis of skin temperature affecting vigilance regulation in the central nervous system would be strongly supported by a covariation with electrophysiological markers of the vigilance state. The present study therefore aimed to evaluate the presence of an association between daytime fluctuations in skin temperature and those in two quantitative EEG measures: the power spectral density of background EEG and the P300 component of the ERP elicited by visual stimuli.

Spectral changes in background EEG in association to changes in vigilance have been demonstrated in numerous studies, often using sleep deprivation as a tool to manipulate vigilance level. Fluctuations in vigilance have been associated with resting-state EEG power fluctuations in the alpha band (8–12 Hz) (Corsi-Cabrera et al., 1996, 1992, 2003; Ferreira et al., 2006; Galliaud et al., 2008; Gast et al., 2011; Strijkstra et al., 2003), theta band (4–8 Hz) (Caldwell et al., 2003; Ferreira et al., 2006; Galliaud et al., 2008; Hoedlmoser et al., 2010) and delta band (Ferreira et al., 2006; Hoedlmoser et al., 2010). Similar findings were reported in studies that assessed sleep deprivation-induced changes in EEG during task performance instead of during relaxed wakefulness (Caldwell et al., 2003; Corsi-Cabrera et al., 1996; Hoedlmoser et al., 2010). Sleep deprivation has also been reported to increase beta band (13–30 Hz) power (Smulders et al., 1997). Because beta band power is mostly regarded as indicating excitatory cortical activity and a state of high arousal, the increase after sleep deprivation has been interpreted as a compensatory effort to maintain vigilance (Smulders et al., 1997; Tsuno et al., 2002).

With respect to changes in ERPs associated with fluctuations in vigilance during normal wakefulness or extended wakefulness (i.e. following sleep deprivation), several studies reported associations with P1, N1 and P300 amplitude or latency (Corsi-Cabrera et al., 1999; Gosselin et al., 2005; Hoedlmoser et al., 2010; Trujillo et al., 2009). These potentials are thought to reflect sensory and higher order processing and are sensitive to modulations in attention and arousal. Sleep deprivation may most consistently affect the P300. A sleep deprivation-induced delay in P300 peak latency has been interpreted as indicating either a slower processing speed or a reduced allocation of attention (Lee et al., 2003). A sleep deprivation-induced attenuation of P300 peak amplitude has been interpreted as a reduction in the resources allocated either to attention or to stimulus evaluation processes, depending on the nature of task used (Corsi-Cabrera et al., 1999; Cote et al., 2008; Gosselin et al., 2005). Other interpretations include lapses, general fatigue, and changes in alertness (Morris et al., 1992). An increase in effort to successfully perform the task ameliorates the effects of sleep deprivation on the peak latency and amplitude of the P300 (Colrain and Campbell, 2007).

The response of background EEG and ERPs to changes in temperature has been studied less extensively. Morris et al. (1992) reported that sleep deprivation-induced changes in the P300 correlate with core body temperature. We are not aware of previous studies that have investigated associations of EEG or ERPs with skin temperature. It would be of interest to evaluate whether central nervous system markers of vigilance (EEG and ERPs) covary with an autonomic nervous system marker of vigilance (distal-to-proximal skin temperature gradient). The present study therefore assessed whether these quantitative EEG markers of vigilance vary in synchrony with daytime fluctuations in skin temperature. It was hypothesized that these central nervous system readout variables indicate lower vigilance during periods of a more elevated distal-to-proximal skin temperature gradient. The association was evaluated both in a well-rested state after a normal night of sleep, and in a state of challenged vigilance induced by a night of sleep deprivation.

2. Methods

2.1. Participants

Eight healthy adults (3 females) gave their written informed consent to participate. Their age ranged from 20 to 26 years (mean = 22.0, sd = 1.77). All were right-handed and had normal or corrected-to-normal vision. Participants received money for their participation. All procedures complied with the declaration of Helsinki and medical ethical approval was obtained from the medical ethical committee of the Academic Medical Center of the University of Amsterdam and the Medical Ethics Committee of the VU University.

2.2. Inclusion criteria

All subjects were non-smokers and free of any medication known to affect sleep or the circadian system, cardiovascular medication, and psychotropic medication. None of the subjects had a history of sleep-related disorders. All subjects were reported to be in good health and free of any physical or mental disorder. None of the female subjects used hormonal contraceptives and they all participated between day 4 and day 13 of the menstrual cycle (follicular phase).

2.3. Study design and procedure

The design and procedure have been described in detail previously (Romeijn et al., 2012). Subjects were instructed to keep a regular sleep–wake pattern by minimizing variability in bedtime and wake-up time in the week before the experiment, which was screened using a sleep diary and actigraphy (Actiwatch, Cambridge Neuro-Technology, Cambridge, UK). Subjects were also instructed to refrain from caffeine, alcohol, heavy medicine, and intensive physical exercise for 12 h before arriving at the sleep laboratory, and to refrain from eating for at least 4 h before arrival.

The experiment consisted of a series of tasks and assessments on two days: after a night of normal sleep (NS) and, in counterbalanced order, after a night of total sleep deprivation (SD). The interval between the two assessment days allowed for at least two nights of normal sleep in between. On assessment days, subjects arrived at the sleep laboratory at 08.30 for setup and EEG preparation. From 10:00 until 17:30 h, participants completed 5 identical experimental blocks while seated under dim-light conditions (<15 lx). Assessments during these blocks included an EEG-ERPs participants, comfortably seated, performed a simple reaction time sustained attention task, the Brief-Stimulus Reaction Time Task (BSRT, Romeijn and Van Someren, 2011), which commenced at 10:35, 12:05, 13:35, 15:05, and 16:35 h.

2.4. Brief-Stimulus Reaction Time Task (BSRT)

Using E-Prime software (Psychology Software Tools Inc., Pittsburgh, USA), brief stimuli were presented at the center of a 17-inch screen with a refresh rate of 60 Hz at a distance of approximately 90 cm. Participants were instructed to fixate at a black crosshair displayed on a gray background and to respond as fast as possible if the plus sign changed into a hyphen (a minus sign) by pressing a button with the index finger of their dominant hand. The hyphen was presented only very briefly (25 ms) at a quasi-random interstimulus interval (ISI) of 4–14 s. If participants did not respond within 1000 ms after presentation of the stimulus, a lapse was recorded. The BSRT task comprised of 120 stimuli and lasted 19 min per session. Participants completed five sessions on each assessment day, rendering 600 trials for both the normal sleep condition and the sleep deprivation condition.

2.5. Skin temperature assessment

The ear-to-mastoid gradient was calculated as the difference between the temperatures measured by two thermistors (P-8432, ICBT, Tokyo, Japan) attached to the earlobe and the nearby mastoid skin area and connected to a HOBO U12-06 data logger (Onset Computer Corporation, Massachusetts, USA) sampling at 30-second intervals with a resolution of 0.03 °C.

2.6. EEG recording

High-density EEG was assessed using an EEG cap with 64 equidistant sintered Ag–AgCl electrodes (Easycap, Herrsching, Germany) referenced to the vertex and connected to an SD LTM 64 digital recorder (Micromed, Treviso, Italy). The EOG was recorded from sites above and below one eye and from electrodes lateral to both eyes. The electrode closest to AFz served as ground. Electrode impedance was kept below 5 KΩ. Signals were band-pass filtered between 0.15 and 70 Hz and digitized at 1024 Hz.

2.7. EEG pre-processing

EEG was analyzed using EEGLAB version 12 [http://www.sccn.ucsd.edu/eeglab, Delorme and Makeig, 2004] running under Matlab 7.11.0 (The MathWorks, Natick, MA). Preprocessing consisted of down-sampling to 256 Hz and correcting for artifacts including eye blinks and eye movements using RUNICA (Delorme and Makeig, 2004; Jung et al., 2000), an implementation of the logistic infomax independent component analysis algorithm of Bell and Sejnowski (1995). Artifacts were identified by visual inspection of the spatial and temporal representation of the independent components. Approximately ten artifactual components per subject were identified. Artifact-free signal was recomposed from the reduced component mixing matrix that consisted of all independent components except for those identified as representing artifacts. The artifact-free signals were low-pass filtered at 40 Hz and re-referenced to linked mastoids. Trials that did not include a response within 1000 ms (lapses) were discarded and epochs containing signal exceeding 200 μV were considered artifactual and omitted from the analysis.

2.8. Predictive value of skin temperature for power spectral density of the background EEG

For analysis of pre-stimulus background EEG, epochs of −3000 to 0 ms preceding the stimulus presentation were extracted, multiplied by a Hanning taper, and subjected to a Fast Fourier Transform algorithm implemented in FieldTrip [http://www.ru.nl/neuroimaging/fieldtrip, Oostenveld et al. (2011)]. For each epoch and every channel, the average power in the frequency bands delta (1–4 Hz), theta (4–7 Hz), alpha (8–12 Hz) beta1 (13–20 Hz), and beta2 (20–40 Hz) was used as dependent variable. On each of the recording days, i.e. after a night of normal sleep and after a night of sleep deprivation, 5 blocks of 120 trials were recorded. This resulted, after omission of lapses, in at most 600 pre-stimulus EEG epochs, each paired with the distal-to-proximal skin temperature gradient value. The test of whether skin temperature was predictive of the power in the baseline period was conducted on each frequency band of interest separately. For each subject, a linear regression analysis estimated the regression coefficient of power as function of the DPG at each electrode. If the regression coefficient across all participants is significantly different from zero, assessed using a one-sample *t*-test with $p \leq 0.05$, an association between skin temperature and power is inferred for a given electrode. Correction of multiple comparisons over the electrodes was subsequently achieved by clustering adjacent electrodes showing a significant association, and assessing the corrected P-value at the cluster level using a cluster-based non-parametric randomization procedure (Maris and Oostenveld, 2007) implemented in Fieldtrip, as described below. Adjacent electrodes that were significant and had the same sign (t-values < -1.96 or t-values > 1.96) were clustered together. Each cluster was associated with the corresponding sum of the t-values of its constituent electrodes. To evaluate the significance of the cluster-sum of t-values, a reference probability distribution for cluster-summed t-values was created using a Monte Carlo approach. Namely, in 10,000 Monte Carlo repetitions, the sign of the t-value of each electrode was either kept or swapped (− to +, + to −), with a probability of 0.5. The largest cluster-sum of t-values is obtained from the resulting matrix and added to build the reference distribution. A cluster was considered significant if its cluster-sum of t-values was above the 95% threshold of the reference distribution. All the p-values reported here refer to the p-value of the clusters computed using this procedure and are thus corrected for multiple comparisons. The regressions and cluster analyses were performed two times; on the data acquired after normal sleep, and on the data acquired after sleep deprivation. This procedure was repeated for all the frequency bands of interest.

2.9. Predictive value of skin temperature for the P300 of the ERP

For analysis of ERPs, epochs of −200 ms preceding to 700 ms following the stimulus presentation onset were extracted and baseline corrected (−200 to 0 ms). The linear regression analysis described above for the analysis of pre-stimulus background EEG cannot be replicated for the analysis of ERPs. Because of the poor signal-to-noise ratio of single-trial ERP parameters (peak amplitude and latency), ERPs have to be constructed by averaging over multiple epochs. In order to evaluate whether ERPs differed depending on the distal-to-proximal skin temperature gradient, four ERPs were calculated, each corresponding to one quartile of the range of recorded temperatures within an individual.

On each of the recording days, i.e. after a normal night of sleep and after a night of sleep deprivation, 5 blocks of 120 trials were recorded. This resulted, after omission of lapses, in at most 600 ERP epochs per condition, each paired with a most recently assessed distal-to-proximal skin temperature gradient value. For each individual participant, the range of these DPG values was assigned to quartiles, each representing one fourth of the total number of available artifact-free trials. Average ERPs were obtained for each DPG quartile. For each DPG quartile, the amount of trials was sufficient to create clear ERP waveforms, both for the day after normal sleep (NS: mean = 124. 12, sd = 36.46) and for the day after sleep deprivation (SD: mean = 69.24, sd = 26.04). Each of the resulting four DPG-quartile ERP waveforms was subjected to automated P300 peak detection analysis within the time window of 350 to 650 ms after stimulus presentation. The peak amplitudes and latencies of the P300 component retrieved from average ERP waveforms at Pz were subjected to statistical analyses.

The predictive effect of skin temperature fluctuations for the peak latency and amplitude of the P300 was evaluated using linear mixed-effect

regression analysis (MLwiN 2.02, Institute of Education, London, UK) to account for hierarchical dependency in the data structure. Significance was assessed using the Wald test. For every participant, there were two days with each four DPG-quartile P300 amplitudes and latencies, paired with the corresponding DPG average in that quartile.

3. Results

3.1. Actigraphic verification of sleep deprivation compliance

Actigraphic recordings were inspected closely to verify compliance with the sleep deprivation protocol. As described in detail elsewhere (Romeijn et al., 2012), cumulative distributions of immobility bout durations confirmed good compliance with the sleep deprivation protocol in all participants included in the present analysis.

3.2. The effect of sleep deprivation on the distal-to-proximal skin temperature gradient

Fig. 1 shows an example of daytime fluctuations of the ear-to-mastoid DPG in a single participant after normal sleep and after sleep deprivation. As reported elsewhere (Romeijn et al., 2012), sleep deprivation did not significantly alter the ear-to-mastoid DPG, which was -3.91 ± 0.17 °C after a normal night's sleep and -4.09 ± 0.33 °C after sleep deprivation ($p = 0.51$).

3.3. Predictive value of skin temperature for power spectral density of the pre-stimulus background EEG

Fig. 2A shows the one-sample t-values, across subjects, of the predictive effect of DPG fluctuations for spectral power after a night of normal sleep. For graphic purposes, the surface in between electrodes is interpolated to create scalp maps. Electrodes with significant t-values are indicated in red. One scalp map is shown for each of the five frequency bands (delta, theta, alpha, beta1, and beta2). Higher DPG values appeared significantly associated with lower alpha on two frontocentral electrodes. After cluster correction, however, the cluster did not reach the 95% threshold of the cluster reference distribution.

Fig. 2B shows the one-sample t-values, across subjects, of the predictive effect of DPG fluctuations for spectral power after a sleep deprived night. Higher DPG values are significantly associated with lower beta1 power on one right parietal electrode and with lower beta2 power on three adjacent right parieto-occipital electrodes. The latter cluster was significant after correction for multiple comparisons ($p = 0.03$).

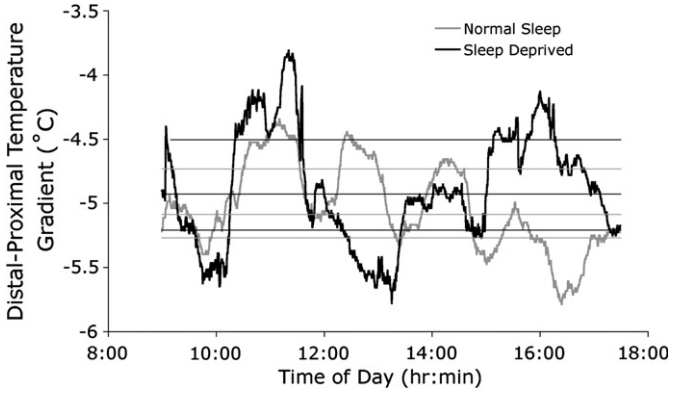

Fig. 1. Example of daytime fluctuations of the ear-to-mastoid distal-to-proximal skin temperature gradient (DPG) in a single participant after normal sleep (gray trace) and after sleep deprivation (black trace). Horizontal lines illustrate borders of the individually determined DPG quartile borders after normal sleep (gray lines) and after sleep deprivation (black lines).

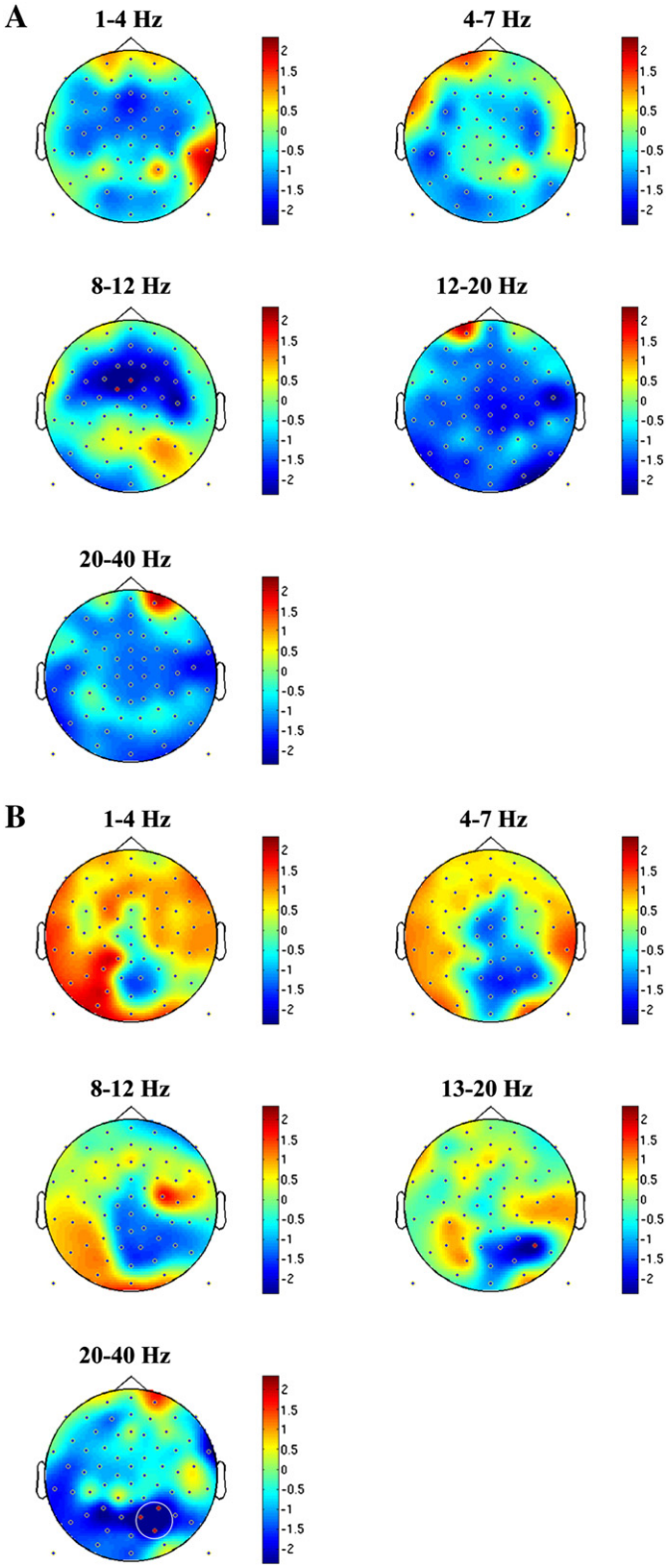

Fig. 2. A. Topographical maps of one-sample t-values reflecting whether there is linear regression of fluctuations in pre-stimulus EEG power on fluctuations in DPG showed a consistent deviation from zero across all participants after a normal night of sleep. Maps are shown for the delta (1–4 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta1 (13–20 Hz), and beta 2 (20–40 Hz) power bands. Electrodes where absolute t-values exceeded 2.34 are shown as red dots. Warm colors indicate positive associations. Subsequent correction for multiple comparisons indicated that no cluster met the significance threshold. B. Same convention as panel A, for the recordings after sleep deprivation. Subsequent correction for multiple comparisons indicated that one cluster met the significance threshold of a corrected p-value of 0.01, as indicated by the white circle. In this cluster including O2, PO4, and PO6, higher values of the distal-to-proximal skin temperature were consistently associated with lower values of beta2 power.

3.4. The effect of sleep deprivation on the P300 of the ERP

Fig. 3A shows the parietal ERPs evoked by the BSRT stimuli averaged over all trials that the participants responded to, both for the day after a normal night of sleep and the day following a sleep deprived night. A P300 is clearly evoked on both days, most evidently at the parietal lead (Pz), as shown in the topographical maps of the P300 peak amplitude (Fig. 3B).

3.5. Predictive value of skin temperature for the P300 of the ERP

Both after normal sleep and after sleep deprivation, four ERPs were obtained, representing the average parietal response elicited by stimuli presented when the DPG was in the low, mid-to-low, mid-to-high, or high quartiles of an individual's range of DPG values. Mixed effect linear regression analysis showed a significant predictive value of DPG for the peak latency of the P300. The P300 peak latency increased by 13.5 ± 6.4 ms per °C increase in DPG ($p = 0.04$) after a normal night's sleep and tended to increase by 8.6 ± 5.0 ms per °C increase in DPG ($p = 0.08$) after sleep deprivation. Fig. 4 shows the average DPG and corresponding P300 latency for each of the four DPG quartiles on both days. Fluctuations in DPG did not significantly predict fluctuations in P300 amplitude (all $p > 0.98$).

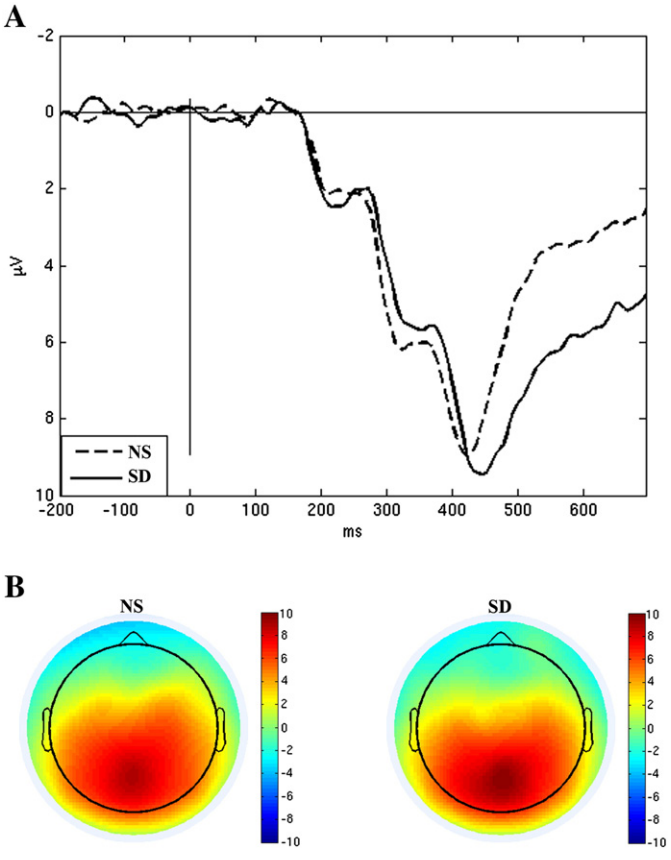

Fig. 3. A. Event-related potentials (ERPs) evoked at the parietal lead Pz by stimuli presented during the Brief-Stimulus Reaction Time Task. The broken line shows the ERP after a normal night of sleep (NS, broken line) and the solid lind the ERP after a sleep deprived night (SD, solid line). Note that positive is plotted downwards, following the convention in the ERP literature. B. Maps representing topographical differences in the peak amplitude of the P300 component show a clear parietal focus both after a normal night of sleep (NS, left panel) and after a sleep deprived night (SD, right panel). Warmer colors indicate larger amplitudes.

4. Discussion

The present study aimed to evaluate whether the spontaneous fluctuations in skin temperature that occur even under thermoneutral conditions are associated with fluctuations in EEG potentials evoked by visual stimuli and with fluctuations in the background EEG measured immediately prior to presentation of the stimuli. Whereas several previous studies indicated associations of skin temperature with sleep onset latency (Fronczek et al., 2008b; Raymann et al., 2005) and performance on sustained attention tasks (Raymann and Van Someren, 2007; Romeijn and Van Someren, 2011; Romeijn et al., 2012), it had not been previously evaluated whether daytime fluctuations in skin temperature are associated with fluctuations in quantitative electrophysiological markers of the vigilance state of the central nervous system. The association between fluctuations in an autonomic correlate of the vigilance state (i.e. the distal-to-proximal skin temperature gradient) and fluctuations in central nervous system correlates of the vigilance state (i.e. background EEG and ERPs) was evaluated both after a normal night of sleep and after sleep deprivation. Sleep deprivation was applied to challenge vigilance-regulating systems.

The pre-stimulus background EEG findings indicate that, after the challenge of sleep deprivation, right parieto-occipital power in the high beta band (20–40 Hz) is significantly lower when the distal to proximal gradient reaches higher values. ERP findings indicate that, especially after a normal night of sleep, the P300 response to a simple visual stimulus shows a longer latency for higher values of the distal to proximal skin temperature gradient, indicating a reduction in the sympathetic outflow that vasoconstricts the distal skin vasculature (Rubinstein and Sessler, 1990).

The pre-stimulus background EEG findings of the present study show, for the first time, that a reduction in sympathetic outflow of the autonomic nervous system is associated with central nervous system markers that indicate a reduction in excitatory cortical activity and arousal. Higher proximal skin temperature is associated with a decrease in parieto-occipital EEG power in the high beta band, which is thought to reflect excitatory processes in the central nervous system (Tsuno et al., 2002). It is worthwhile to discuss two studies that reported, counter intuitively at first sight, an increase in beta power after sleep deprivation. In a study by Smulders et al. (1997), sleep deprivation increased power in the high beta range (22.7–29.7 Hz) during a reaction time task that applied variable interstimulus intervals, similar to the task applied in the present study. The effect was most noticeable at Fz and

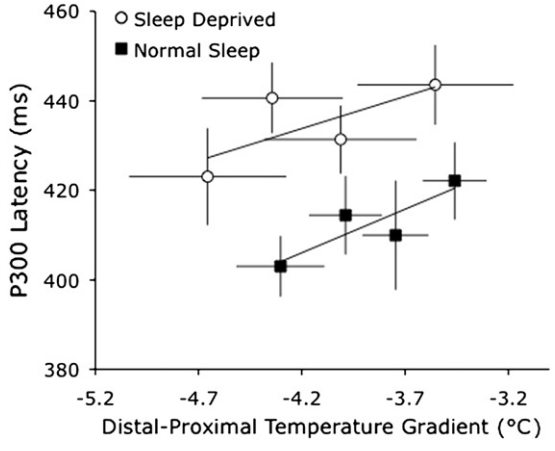

Fig. 4. Group means (±between-subject standard error of the mean, s.e.m.) of the P300 latency plotted against the distal-to-proximal skin temperature gradient group means (±s.e.m.) in each of the four quartiles covering the range of observed temperature values. Closed squares represent values obtained after a normal night of sleep, and open circles represent the values obtained after sleep deprivation. Linear regression lines illustrate the increased P300 latencies at higher DPG values, reaching significance on the day following normal sleep ($p = 0.04$) and representing a trend after sleep deprivation ($p = 0.08$).

Oz but also significant at Cz and Pz. Beta power in this range also increased with time on task. In a sleep deprivation study by Dumont et al. (1999), the diurnal time course of subjective sleepiness correlated strongly ($r = 0.85$) with the power in a high beta range (18.0–24.8 Hz). Dumont et al. (1999) suggested that the high beta range could reflect the increasing effort made by subjects to perform the task as the duration without sleep deprivation lengthened. This suggestion is also supported by the findings of Smulders et al. (1997). According to this interpretation, the present results suggest that a reduction in thermoregulatory sympathetic outflow of the autonomic nervous system to the distal vasculature (as indicated by an elevated distal-to-proximal skin temperature gradient) is paralleled by a decrease in compensatory efforts of the central nervous system to maintain vigilance.

The P300 findings of the present study show, for the first time, that a reduction in sympathetic outflow of the autonomic nervous system is associated with a central nervous system marker indicating slower processing speed: fluctuations in the distal-to-proximal skin temperature gradient were associated with fluctuations in P300 latency. A longer P300 latency has been observed when vigilance decreases (Lee et al., 2003; Morris et al., 1992). Fluctuations in the distal-to-proximal skin temperature gradient were, however, not associated with fluctuations in the amplitude of the P300, while previous studies found an association between P300 amplitude and vigilance (Gosselin et al., 2005; Lee et al., 2003; Morris et al., 1992). The selective pairing of skin temperature with the P300 latency, but not amplitude, suggests that the autonomic–central nervous system association mostly concerns processing speed or the time required to detect the stimulus. The absence of a correlation of skin temperature with P300 amplitude suggests that the autonomic–central nervous system association does not concern allocation of attentional resources. However, the absence may also be due to the very low processing demands of the Brief-Stimulus Reaction Time Task. Paired fluctuations in skin temperature and P300 might surface during more demanding tasks.

The P300 elicited by the brief stimuli in the implemented simple reaction time task clearly displayed a parietal focus, similar to the 'target' P300 with its origin in the temporal–parietal junction that is typically evoked in oddball paradigms (Polich, 2007). The enhanced target response is thought to reflect activity of noradrenergic neurons located in the locus coeruleus that project to the cerebral cortex and basal forebrain(Aston-Jones and Cohen, 2005; Nieuwenhuis et al., 2005; Nieuwenhuis et al., 2011 Rajkowski et al., 1994). Animal studies, moreover, indicate that the application of noradrenaline to cholinergic cells in the basal forebrain produces a dose-dependent increase in the power of high beta and low gamma (30–58 Hz) oscillations in the EEG and, simultaneously, a decrease the power of delta (1.5–4 Hz) oscillations (Cape and Jones, 1998).

In agreeement with these previous findings, it may be hypothesized that the reduction in sympathetic outflow to the vasculature of the distal skin that results in an elevated distal-to-proximal skin temperature gradient, coincides with a reduction in noradrenergic activity that results in a delayed P300, a decrease in high beta power, and an increase in delta power. Although not significant, the topographic maps of Fig. 3b suggest a widespread increase in delta power in association with an increase in the distal-to-proximal skin temperature gradient. Indeed, delta power in the wake EEG is inversely related to the level of vigilance (Cajochen et al., 2002).

In summary, the present study provides further support for an association between fluctuations in skin temperature and vigilance by demonstrating associations with markers of vigilance in the background EEG and the P300 response to visual stimuli.

Conflict of interest

The authors have no conflict of interest.

Acknowledgments

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