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Skin temperature and vigilance: from association to application

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Summary

The present thesis focuses on interactions between the regulation of body temperature and the regulation of sleep and vigilance in humans. Skin blood flow, and consequently its temperature, changes with many factors that have shown to affect vigilance, including environmental light, anxiety or stress and one's posture. Even under thermoneutral conditions, skin temperature is not fixed, but fluctuates. Previous studies have shown that experimentally induced changes in skin temperature affect sleep and alertness. The induction of a somewhat higher skin temperature, yet within the thermoneutral range, resulted in increased sleepiness; slower responses on sustained attention tasks; faster sleep onset; and deeper sleep. However, so far it has not been studied whether *naturally occurring* fluctuations in skin temperature within the thermoneutral zone are similarly associated with vigilance. The present thesis aimed to evaluate whether naturally occurring fluctuations in skin temperature are related to fluctuations in vigilance, and whether such association is still present after sleep deprivation. Furthermore, the thesis addressed brain mechanisms that could be involved in the link between fluctuations in vigilance and skin temperature. Finally, the thesis addressed whether the link can be utilized by adding skin temperature assessment to devices that aim to unobtrusively assess the sleep-wake state from wrist movements, and thus improve the performance of these devices.

In the **second chapter**, we examined whether fluctuations in skin temperature are associated with those in vigilance level, under conditions similar to everyday-life situations requiring sustained attention. Eight healthy participants participated in a two-day protocol during which vigilance and skin temperature were assessed 4 times per day in a silent dimly-lit, temperature-controlled room. Out of the three measured locations, distal, proximal and intermediate, especially the spontaneous fluctuations in proximal temperature were negatively associated with fluctuations in response speed, and positively with lapse rate on the vigilance task. We therefore concluded that a higher proximal skin temperature was associated with decreased vigilance.

Since the previous study was limited to the study of temperature and vigilance under well-rested conditions, in the **third chapter**, we set out to obtain a detailed view on the effect of sleep deprivation on the profile of human skin temperature gradients over the body, as well as on their association with sustained attention. Eight healthy young adults participated in a repeated-measures constant routine design, in which skin temperatures were assessed continuously from 14 locations while performance was assessed using a reaction time task, including eyes-open video monitoring, performed five times a day for two days, following a normal

sleep or sleep deprivation night. Mixed-effect regression models were used to evaluate the effect of sleep deprivation on skin temperature gradients of the upper (ear-mastoid), middle (hand-arm) and lower body (foot-leg), and on the association between fluctuations in performance and temperature gradients. Sleep deprivation induced a marked dissociation of thermoregulatory skin temperature gradients, indicative of attenuated heat loss from the hands co-occurring with enhanced heat loss from the feet. Sleep deprivation moreover attenuated the association between fluctuations in performance and temperature gradients; the association was best preserved for the upper body gradient. Therefore, we concluded that sleep deprivation disrupts coordination of fluctuations in skin temperature gradients. The dissociation of middle and lower body temperature gradients may therefore be pursued as a possible marker for sleep debt, and the upper body gradient as possible aid in vigilance assessment when sleep debt is unknown. Importantly, our findings suggest that sleep deprivation affects the coordination between skin blood flow fluctuations and the baroreceptor-mediated cardiovascular regulation that prevents venous pooling of blood in the lower limbs when there is the orthostatic challenge of an upright posture. The finding is important because it suggests limited generalizability of lab studies on the effects of sleep deprivation on human physiology when participants are only studied in a supine position.

Following up on the studies that assessed the association of skin temperature with behavioural indicators of vigilance, we set out to study the association of skin temperature with neurophysiological indicators of vigilance. The **fourth chapter** described how fluctuations of skin temperature are associated with changes in the electroencephalographic power spectrum and event related potentials, recorded during a sustained attention task both under well-rested and sleep-deprived conditions. Simultaneous measurement of activity in the central nervous system (CNS), the autonomous nervous system (ANS), and behavior allowed us to determine whether the association between skin temperature and vigilance is not only visible in *performance*, but in *cerebral* activity as well. Correlating event related potentials elicited by stimuli in a reaction task to temperature measured at the ear, we have shown that a higher skin temperature is associated with a longer latency of the P300 evoked potential, which has previously been shown to indicate decreased vigilance. A practical consequence of this finding is that the sensitivity of ERP studies might increase if skin temperature would be co-registered and included in the statistical analysis as a nuisance variable. Furthermore, after sleep deprivation, fluctuations in the 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, which has previously been interpreted as compensatory efforts in order to maintain vigilance.

To investigate brain structures involved in the link between skin temperature and vigilance, the **fifth chapter** focused on the relationship between skin temperature and sleep onset in subjects with hypothalamic damage. The hypothalamus is crucially involved in the circadian timing of the sleep-wake rhythm, and also accommodates the most important thermoregulatory neuronal network. We have shown before that adults with pituitary insufficiency and history of chiasm compression due to a tumor with suprasellar extension fall asleep later and sleep shorter than those without such history, and presume hypothalamic involvement. To further evaluate the hypothesized hypothalamic involvement in the association between vigilance and thermoregulation, we investigated whether hypothalamic impairment also affects skin temperature and its association with sleep onset. In a case-control study in fifty patients with pituitary insufficiency, thirty-three of which had a history of chiasm compression, ambulatory distal and proximal skin temperatures were assessed continuously for 24 hours. Sleep parameters were assessed by questionnaires. Group differences in mean skin temperature, calculated over the wake and sleep periods separately, and group differences in the strength of association between pre-sleep skin temperature and sleep onset latency were compared. Results showed that patients with a history of chiasm compression had a lower proximal skin temperature during the day ($34.1 \pm .7$ vs. $34.6 \pm .7$ °C, $p = .045$). Additionally, the typical association between sleep onset latency and pre-sleep distal-to-proximal skin temperature gradient was absent in these patients ($r = -.01$, $p = .96$), while it was unimpaired in those without chiasm compression ($r = -.61$, $p = .02$). Thus, patients with a history of chiasm compression show impaired skin temperature regulation in association with disturbed sleep.

The **sixth chapter** focused on the practical application of the knowledge acquired on the association between skin temperature, sleep and vigilance. Due to its low invasiveness and costs, actigraphy is widely used as an alternative to polysomnography (PSG) to measure sleep wake rhythms in human subjects. However, although actigraphy and PSG correspond relatively well during sleep, actigraphy has problems detecting wake during immobility. Since skin temperature is closely correlated to vigilance and sleep under so many conditions and in so many populations, we considered the possibility that it could increase the accuracy of sleep/wake classification. Under normal daily routine conditions, 52 subjects either without sleep disorder or diagnosed with sleep disorders such as OSAS, insomnia, and PLMS, were monitored using ambulatory EEG, an actigraph and skin temperature sensors. The congruency of actigraphic sleep estimates with PSG-defined sleep was calculated before and after the use of wrist temperature to reclassify actigraphic sleep estimates. Results showed that skin temperature was lower during epochs that actigraphy falsely classified as sleep than during epochs that actigraphy correctly classified as sleep. Also, skin temperature was higher during epochs that actigraphy falsely classified as wake than during epochs that actigraphy correctly classified as wake. However, using

temperature as additional information in the actigraphy scoring algorithm did not significantly alter the percentage of misclassified epochs. We propose that the sluggish response of the sensor and/or skin to changes in skin perfusion may have interfered with the possibility to exploit the systematic skin temperature differences. Infrared temperature sensing or even perfusion sensing may be required to improve actigraphic sleep estimates.

Taken together, the findings in this thesis demonstrate that naturally occurring fluctuations in skin temperature are related to fluctuations in vigilance. We have shown that higher proximal skin temperature is associated with lower alertness under well-rested conditions (chapter 2). Furthermore, this correlation is still present after a vigilance-challenging occurrence such as an entire night of sleep deprivation (chapter 3). As a first step towards elucidating the brain mechanisms involved in the coupling of infraslow fluctuations in skin temperature and alertness, the present work showed that they also coincide with fluctuations in the latency of an event related potential, the P300 (chapter 4). As a second step towards understanding brain mechanisms involved in the coupling we showed that it is compromised in patients with hypothalamic damage (chapter 5). Finally, the correlation between naturally occurring skin temperature fluctuations and vigilance was used in an attempt to improve movement-based sleep-wake assessment (chapter 6). The findings presented in this thesis may also have relevance for the field of environmental ergonomics. Because the skin is rather poikilotherm, its manipulation by means of environmental temperature in combination with clothing could make the difference between being alert and being sleepy. This contention is indeed supported by the skin temperature manipulation studies.