Temperature, sleep and aging
Heidi Danker-Hopfe

**Outline**

Temperature

- Is there an age specific variation in what temperature has to do with sleep?
- What has temperature to do with sleep?

Sleep

- Why sleep?
- Sleep regulation

Aging

- How does sleep change with aging?
One of the most consistent findings is an effect of RF-EMF exposure on brain activity as assessed by powerspectra of the EEG during sleep.
Objective assessment of sleep

assignment of (sleep) stages (for every 30 sec)
based on specific combinations of EEG, EMG and EOG

graphic representation of scoring results ➔ hypnogram

 fundamentally different physiological states

NREM stages (N1, N2, and N3) ➔ REM sleep (R)
**Objective assessment of sleep**

Sleep latency *(Rechtschaffen & Kales 1968 standard)*: time from lights out to the occurrence of the first three consecutive stages S1 or first occurrence of S2 (or REM sleep) – whatever is shorter.

**Quantitative description of the sleep EEG**

Powerspectrum: quantitative description of the EEG

*Bryant et al. Nature Reviews Immunology 4, 457-467 (June 2004)*
Sleep promoting neurons

Brain regions (cluster of neurons) and neurotransmitter involved in S-W regulation

The sleep switch: hypothalamic control of sleep and wakefulness

VLPO: ventrolateral preoptic area

Fig. 1. The ascending arousal system sends projections from the brainstem and posterior hypothalamus throughout the forebrain. Neurons of the lateral preoptic area (blue circles) project to many forebrain targets, including the thalamus, which then regulates cortical activity. Atrial natriuretic peptide (ANP) neurons (green circles) diffuse throughout much of the forebrain, regulating the activity of cortical and hypothalamic targets directly. Neurons of the lateral hypothalamic nucleus (LH) contain histamine (HIST), neurons of the ventral tegmental area (VTA) contain serotonin (5-HT) and neurons of the locus coeruleus (LC) contain norepinephrine (NA). Sleep-promoting neurons of the ventrolateral preoptic nucleus (VLPO, red circle) contain GABA and galanin (Gal).

Temperature and sleep

What has temperature to do with sleep?

- Ambient temperature
- Body core temperature
- Brain temperature
- Skin temperature
Temperature and sleep: anecdotal knowledge

Experiencing difficulty to fall asleep in a very hot or cold environment is a common phenomenon
difficulty falling asleep with cold feet; easier to fall asleep following a warm bath in the evening
more than anecdotal knowledge?

Thermoregulation

Thermoregulation refers to the process required to maintain the core body temperature within a narrow set range essential for cell functioning

Core temperature: regulated at about 37 °C
Shell temperature: largely depends on ambient temperature and varies with part of the body

Ambient temperature
23 °C: distal parts (hand and feet) 7-8 °C below core temperature
35 °C: distal parts (hand and feet) 3-4 °C below core temperature
Gilbert et al. (2004) Sleep Medicine Reviews 8:81-93
The primary factor driving $T_c$ and sleep onset is the circadian control.

Humans sleep when their core temperature is low and are awake when core body temperature is high. Sleep initiation coincides with the decrease in core body temperature. Sleep is consistently terminated on the ascending portion of the $T_c$ curve.

Information about environmental temperature is registered by receptors of the skin.

Cold receptors: detect changes in the order of 20 - 30 °C.

Warm receptors: detect temperature changes above 30 °C.
Thermoregulation

Pre-optoc area / anterior hypothalamus (PoAH)

Information from these receptors is integrated at several levels, the main integrator of thermal information is a region in the hypothalamus.

Lesions in this region lead to impaired thermoregulatory responses to changes in ambient temperatures.

Mechanisms:
Existence of a set point PoAH generates an error signal that is proportional to the difference between the set point and the measured temperature.

Regions involved in temperature and sleep-wake regulation

Ventricular part of the preoptic area: VLPO known to be involved in sleep-wake regulation.
Temperature and sleep regulation: possible mechanism

The VLPO contains warm- and cold sensitive neurons (40% of all neurons).

The warm sensitive neurons of the preoptic area are not only involved in sleep but also in thermoregulation.

The WS neurons increase firing following heating of the peripheral skin (Gilbert et al. 2004).
Temperature and sleep regulation: possible mechanism

**Summary:**

- A mild increase in brain temperature may differentially drive different brain areas towards a more sleep-like or a more wake-like firing pattern. Complex relationships make an unequivocal sleep promoting effect of mild increases in brain temperature unlikely.

- A mild increase in skin temperature seems to drive different brain regions towards a more sleep-like firing rate.

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- Sleep
  - Why sleep?
  - Sleep regulation
- Aging
  - How does sleep change with aging?
Sleep and aging: changes in the macrostructure of sleep

Pace-Schott and Spencer (2011) Prog Brain Res; 191: 75-89

Comparatively stable:
- Sleep latency
- REM-sleep latency

Decrease:
- Total sleep time (during the night)
- Sleep efficiency
- Slow wave sleep
- Stage R sleep (stage N2 sleep)

Increase:
- Wake stage N1 sleep


EU funded project
SIESTA
Sleep and aging: changes in powerspectra

Power spectra – sleep EEG

Cross-sectional study:

Thin line: Young subjects
Thick line: Elderly subjects

Analysis showed a significant (p < 0.001) age group by trend interaction.

Sleep and aging: slow wave activity

Slow Wave Activity as a correlate of the homoestatic process declines with age.

Aging and core body temperature

- Older subjects (n=43)
- Younger subjects (n=97)

Aging is associated with a reduced circadian modulation of core temperature as indicator of changes in the circadian rhythms regulation mechanisms

sleep and cold feet: more than anecdotal knowledge!

Table 3
Sleep-onset latency by treatment condition per group

<table>
<thead>
<tr>
<th>Treatment Condition</th>
<th>Young adults free from sleep complaints</th>
<th>Elderly free from sleep complaints</th>
<th>Poorly sleeping elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutral SOCKPRE (baseline)</td>
<td>15.69±3.47</td>
<td>11.19±3.32</td>
<td>10.50±2.87</td>
</tr>
<tr>
<td>Warm SOCKPRE</td>
<td>12.94±3.21</td>
<td>9.81±2.71</td>
<td>9.38±3.41</td>
</tr>
<tr>
<td>Neutral FBPRE</td>
<td>15.13±3.29</td>
<td>9.50±2.26</td>
<td>11.81±3.02</td>
</tr>
<tr>
<td>Warm FBPRE</td>
<td>15.56±3.45</td>
<td>8.13±1.45</td>
<td>8.06±1.69</td>
</tr>
<tr>
<td>Neutral SOCKBED</td>
<td>11.38±3.31*</td>
<td>8.00±1.83*</td>
<td>7.63±1.57</td>
</tr>
<tr>
<td>Warm SOCKBED</td>
<td>11.25±3.77*</td>
<td>10.56±2.33</td>
<td>8.31±1.25</td>
</tr>
</tbody>
</table>

Values are means±SE.

*Significantly different from baseline.


SOCKPRE
Socks prior to going to bed

SOCKBED
Socks in bed

FBPRE
Footbath prior to going to bed

Temperature and sleep regulation: experimental evidence

Skin temperature causally contributes to sleep onset latency within the range of its normal nocturnal fluctuations.

Experimental studies (with thermosuits and cooled vs. warmed foods and drinks) aiming at manipulating core and skin temperatures within the comfortable range showed that a proximal skin temperature difference on (only) 0.8 ± 0.03 °C (mean ± SEM) around a mean of 35.1 ± 0.1 °C changed sleep onset latency by 26%.


The induction of changes in core temperature (δ = 0.2 ± 0.02 °C) and distal skin temperature (δ = 0.7 ± 0.05 °C) was not effective.
Temperature and sleep regulation: experimental evidence

Table 3 Summary of the main effects of temperature manipulations on sleep stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Young adults</th>
<th></th>
<th>Elderly without sleep complaints</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{suit \ prox}$</td>
<td>OR (95% CI) P</td>
<td>$T_{suit \ dist}$</td>
<td>OR (95% CI) P</td>
</tr>
<tr>
<td>Wake</td>
<td>0.84 (0.77–0.92)$^{***}$</td>
<td></td>
<td>0.77 (0.73–0.81)$^{***}$</td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>0.80 (0.73–0.89)$^{***}$</td>
<td></td>
<td>0.86 (0.81–0.92)$^{***}$</td>
<td></td>
</tr>
<tr>
<td>S2</td>
<td>1.04 (1.01–1.08)$^{a}$</td>
<td></td>
<td>1.04 (1.01–1.08)$^{a}$</td>
<td></td>
</tr>
<tr>
<td>SWS</td>
<td>1.08 (1.03–1.13)$^{a}$</td>
<td></td>
<td>1.25 (1.19–1.32)$^{a}$</td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Skin temperature differences:** $\approx 0.4 ^\circ C$

**Core body temperature:** virtually unchanged

Raymann et al., Brain, 131: 500-5134 (2008)
Evidence from experimental human studies shows that skin temperature manipulations (in the thermoneutral range, i.e. without changes in core body temperature) have an effect on sleep as reflected by changes in sleep latency and sleep stages and power spectra of the sleep EEG.

There is a mechanism which can link the observations from the experimental studies. The warm and cold sensitive neurons of the ventrolateral preoptic area respond to changes in skin temperature and are involved in sleep regulation.

Limitation: small sample sizes
Skin temperature and sleep

Are there implications of these observations for the interpretation of effects on the sleep EEG seen in RF-EMF exposure studies?

Implications for effects observed under RF-EMF exposure

The insulation and the electrical power dissipation lead to statistically significant rises in the skin temperature, while the RF exposure did not.


### TABLE 3. The Mean Value of the Temperature Rise of the Mobile Phone Surface Areas “Cheek” and “Ear” after 15 and 30 min with the Phone Transmitting at the MIN and MAX Output Power

<table>
<thead>
<tr>
<th>Time of exposure (min)</th>
<th>Mobile phone “cheek” area</th>
<th>Mobile phone “ear” area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIN LOAD</td>
<td>MIN RFE</td>
</tr>
<tr>
<td>15</td>
<td>2.6</td>
<td>2.7</td>
</tr>
<tr>
<td>30</td>
<td>3.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

LOAD: combined effect of insulation and electrical heating; RFE: “normal” use of mobile phone with RF

Implications for effects observed under RF-EMF exposure


Mean temperature patterns for sham (●), 1.5 W/kg (●) and 6 W/kg (●) exposure during the 30 min trial measured at sensor 1. Each measurement point was standardized by subtracting it from the basic value at time point zero.
Implications for effects observed under RF-EMF exposure

NREM power

Stage N2 power

Open questions

Given: Thermosuit studies manipulate distal (hand and feet) and/or proximal (body and limbs) skin temperature over larger body areas.

- Can a locally focussed, exposure related increase in skin temperature of the head (ear, cheek) explain the observed CNS effects during sleep?

Schmid et al. 2012, Bioelectromagnetics 33:594-603

Fronczek et al. 2008 J Neurol Neurosurg Psychiatry 79:1354-7

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Open questions

To answer this question we would need a study with a sham, a verum and a heated sham condition.

Thank you for your attention