IMPACT OF MORNING CORTISOL AND EVENING MELATONIN SECRETION ON SLEEP QUALITY

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INTRODUCTION Sleep is crucial for the regeneration of all body systems and for physical health. Poor sleep has been shown to impair brain function and is linked to an increased risk of heart disease and stroke, depression and inflammatory diseases and is associated with an increased risk of weight gain and obesity. To investigate sleep quality, perceived sleep grade derived from questionnaires can be complemented by the assessment of certain biomarkers. Two biomarkers are closely linked to the circadian regulation: the sleep-promoting neurohormone **Melatonin** is the best circadian phase marker and a reliable means to estimate the timing of the internal circadian clock [1]. The dim-light melatonin onset (**DLMO**) reflects an approximation of the onset of melatonin synthesis and secretion (about 2 to 3 hours prior to habitual sleep, [2]) and is used to assess individual's synchronization to their internal circadian clock. The second important biomarker is the glucocorticoid hormone **Cortisol**, that provides energy to the body and is a counterpart of melatonin. Therefore, cortisol should be low in the evening and during the first hours of the night with a pronounced increase at awakening (the so called Cortisol Awakening Response, **CAR**, [3, 4]). For restful sleep, a well-defined and balanced ration of the two hormones is important.

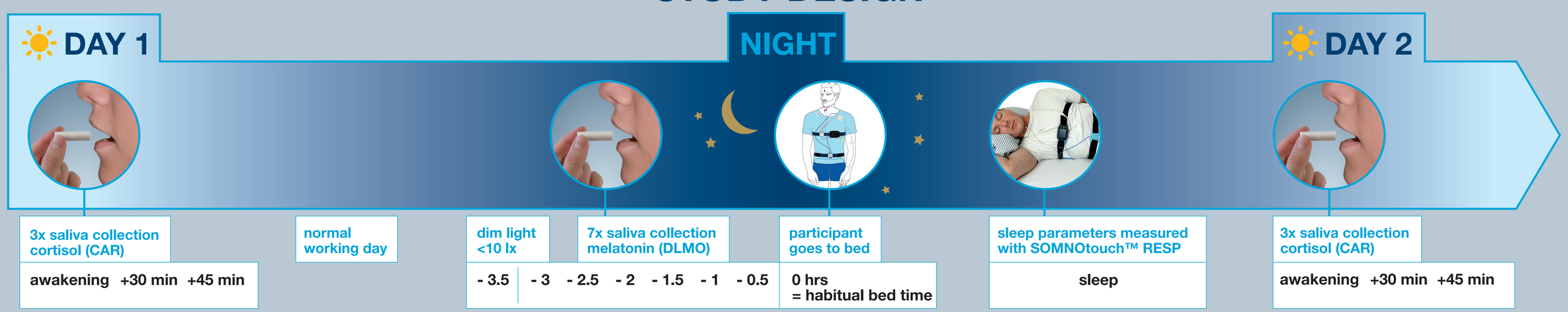
RATIONAL Is it feasible to combine DLMO and CAR assessment with a polygraphy device for home assessment of sleep quality? Are design and methods suited to detect an association between evening melatonin levels and cortisol awakening response? Do the biomarkers melatonin and cortisol predict sleep quality?

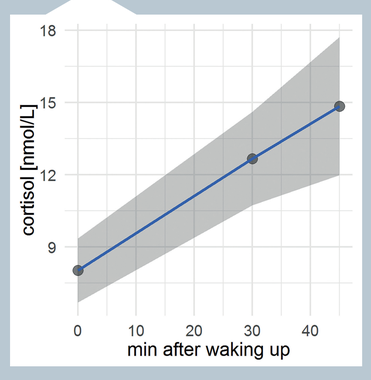
METHODS Participants: N=16 individuals (8 females, 8 males, mean age 33.3 years, mean weight 76.8 kg, mean height 1.74 m, mean BMI 25.2 kg/m²)

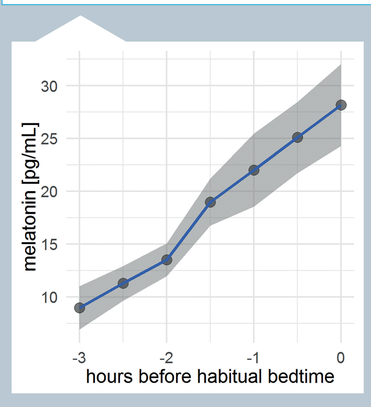
Participants collected 3 morning saliva samples to asses the CAR on two consecutive days. On the evening of the first collection day, they collected 7 saliva samples for melatonin assessment starting 3 hours prior to habitual sleep time (previously determined with a one-week sleep diary). The DLMO was calculated using a variable threshold calculated at 2SD above the average baseline samples (mean plus 2SD of 3 low daytime samples in the morning or afternoon [5]). In addition, as an approximation to the DLMO, the AUC with respect to increase (AUCi) was calculated for melatonin. A higher value indicated an earlier DLMO. Further, participants wore an ambulatory portable polygraphy device SOMNOtouch™ RESP for home measurement of sleep quality (including sleep scoring according to AASM, EEG, EOG, ECG, SpO2, pulse rate, blood pressure, PLM detection, movement and body position) and were asked to fill out questionnaires regarding perceived stress level and sleep behaviour.

LABORATORY Salivary melatonin and cortisol levels were determined at daacro's Saliva Lab Trier using competitive enzyme immunoassay kits manufactured by Salimetrics, LLC, USA. All samples were analyzed in duplicate. The calculations for determining the melatonin and cortisol concentration of each sample were carried out following the kit manufacturer's instructions and using the Gen5 v.2.04 software. Analyses were performed according to the quality and safety guidelines of the laboratory. Assay quality was measured by calculating the intra-assay coefficient of variation (CV). Inter-assay variability was checked with the low and high controls on each microplate. The intra and inter-assay CV for melatonin were 4,13 % and 22,54 %, respectively. The intra- and inter-assay CV for cortisol were 3,11 % and 7,18 %, respectively.

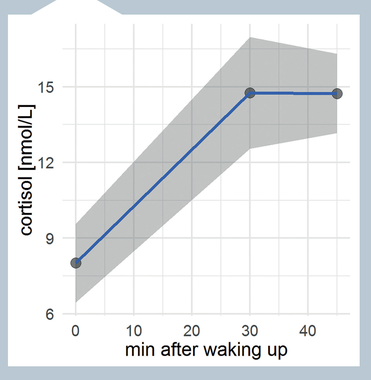
STUDY DESIGN



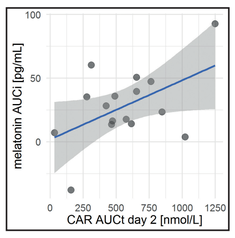




	Sleep duration [min]	Efficiency [%]	Latency [min]	REM [%]	Light sleep [%]	Deep sleep [%]
Mean	342.24	80.91	21.94	19.21	58.34	22.43
Median	356.50	83.70	12.40	19.00	58.05	22.65
SD	64.02	11.31	20.85	7.37	10.94	7.49
Min	190.00	58.20	1.80	6.50	44.20	7.90
Max	431.00	98.00	80.40	31.60	82.10	35.10

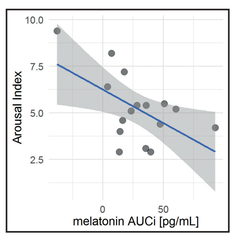


RESULTS



MELATONIN AND CORTISOL AWAKENING RESPONSE

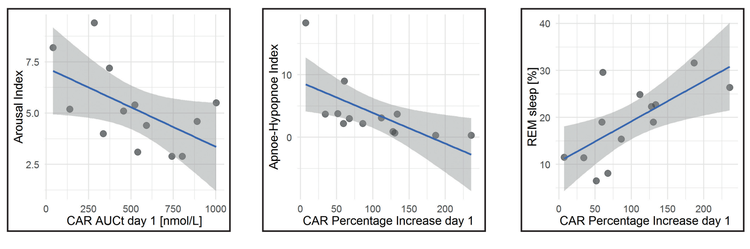
- positive correlation between melatonin AUCi and cortisol AUCt of the second day (r=0.50, p=0.047)
- more pronounced CAR response in participants that showed an earlier DLMO



MELATONIN AND SLEEP QUALITY

- negative correlation between melatonin AUCi and arousals (r=-0.56, p=0.023)
- higher levels of melatonin associated with fewer arousals during sleep

CORTISOL AWAKENING RESPONSE AND SLEEP QUALITY



Several associations between the CAR of day 1 and sleep quality:

- higher CAR AUCt → fewer arousals during sleep (r=-0.55, p=0.0495)
- higher CAR AUCi (r=-0.60, p=0.030), cortisol absolute increase (r=-0.69, p=0.009), cortisol percentage increase (r=-0.769, p=0.002) → lower Apnoe-Hypopnoe-Index (AHI)
- greater cortisol percentage increase → higher proportion of REM (r=0.68, p=0.011) and lower proportion of light sleep (r=-0.55, p=0.049)

SUMMARY

- **Melatonin and cortisol production are closely connected**
- **An earlier increase of melatonin in the evening implies less disrupted sleep during the night**
- **More pronounced CAR response implies better sleep quality in the following night**
- **An ambulant setting combining DLMO and CAR measurement with a polygraphy medical device is suited well for home assessment of sleep quality.**

REFERENCES

[1] Benloucif, S., et al. (2008). „Measuring melatonin in humans." Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine 4(1): 66-69.

[2] Burgess, H. J., et al. (2015). „Home Circadian Phase Assessments with Measures of Compliance Yield Accurate Dim Light Melatonin Onsets." Sleep 38(6): 889-897.

[3] Hellhammer, J., et al. (2007). „Several daily ymeasurements are necessary to reliably assess the cortisol rise after awakening: state- and trait components." Psychoneuroendocrinology 32(1): 80-86.

[4] Stalder, T., et al. (2016). „Assessment of the cortisol awakening response: Expert consensus guidelines." Psychoneuroendocrinology 63: 414-432.

[5] Molina, T. A. and H. J. Burgess (2011). „Calculating the dim light melatonin onset: the impact of threshold and sampling rate." Chronobiol Int 28(8): 714-718.

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