SUPPLEMENTAL RESULTS AND DISCUSSION

Is melatonin's effect on the EEG spectra independent of its effect on NREM sleep duration?
In Figure 2 we have shown that melatonin treatment resulted in changes in the NREM sleep EEG spectrum during the last 6 h of the daytime sleep opportunity. We tested whether the hormone induced changes in the EEG independently of an effect on NREM sleep duration. To this end, spectra were computed for the maximal NREM sleep time common to both conditions (238.1 ± 9.6 min), and subjected to a mixed model ANOVA with Condition (MEL, PL) and EEG Frequency bin (fifty 0.5-Hz bins in the range of 0.25-25 Hz) as fixed factors, and Subject as a random factor. This analysis revealed significant effects for Condition ($P=0.0014$) and EEG Frequency bin ($P<0.0001$), but not for their interaction ($P=0.77$), similar to the results presented in Figure 2. Taken together, it is concluded that the effects on the EEG spectra are not simply a consequence of the hormone's influence on NREM sleep duration and associated dissipation of sleep pressure, but may represent at least in part a direct effect of melatonin on EEG generation mechanisms.

Is melatonin's effect on the EEG spectra independent of its effect on body temperature?
Because melatonin had a small hypothermic effect, and since it was proposed that even small changes in brain temperature could affect the spectral composition of the EEG,[1] correlation analyses were performed: we correlated the melatonin-induced changes in core body temperature with normalized EEG power densities (MEL as % of PL) during NREM sleep in the last 6 hours of the daytime sleep episode for each 0.5-Hz bin in the range of 0.25-25 Hz. The mean temperature decrease was small (0.05°C). No significant correlations with EEG power densities were found ($P>0.16$ in all cases, $N=7$). Thus, it is unlikely that body temperature played a substantial role in mediating melatonin's effect on the NREM sleep EEG.

Alertness and attention after patch removal
Despite the fact that plasma melatonin levels remained elevated following the end of the sleep episode, alertness and attention were not compromised (Figure S1). Taken together with similar findings in other studies[2,3] it appears that physiological levels of plasma melatonin in the presence of low homeostatic sleep pressure do not negatively affect alertness and attention. In contrast, a pharmacological dose of melatonin (e.g. 5 mg orally) can reduce alertness and attention even if sleep pressure is low,[4] and a physiological dose can have similar effect in the presence of moderate levels of sleep pressure.[5] Thus, it is important to consider the interaction of dose and anticipated sleep pressure when devising a treatment with melatonin. As shown here and by Sharkey,[3] if enough time is allowed for sleep pressure to discharge, "hangover" effects in the presence of remaining physiological levels of melatonin can be avoided.

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4. Graw, P. *et al.* Early morning melatonin administration impairs psychomotor vigilance. *Behav. Brain Res.* **121**, 167-172 (2001).

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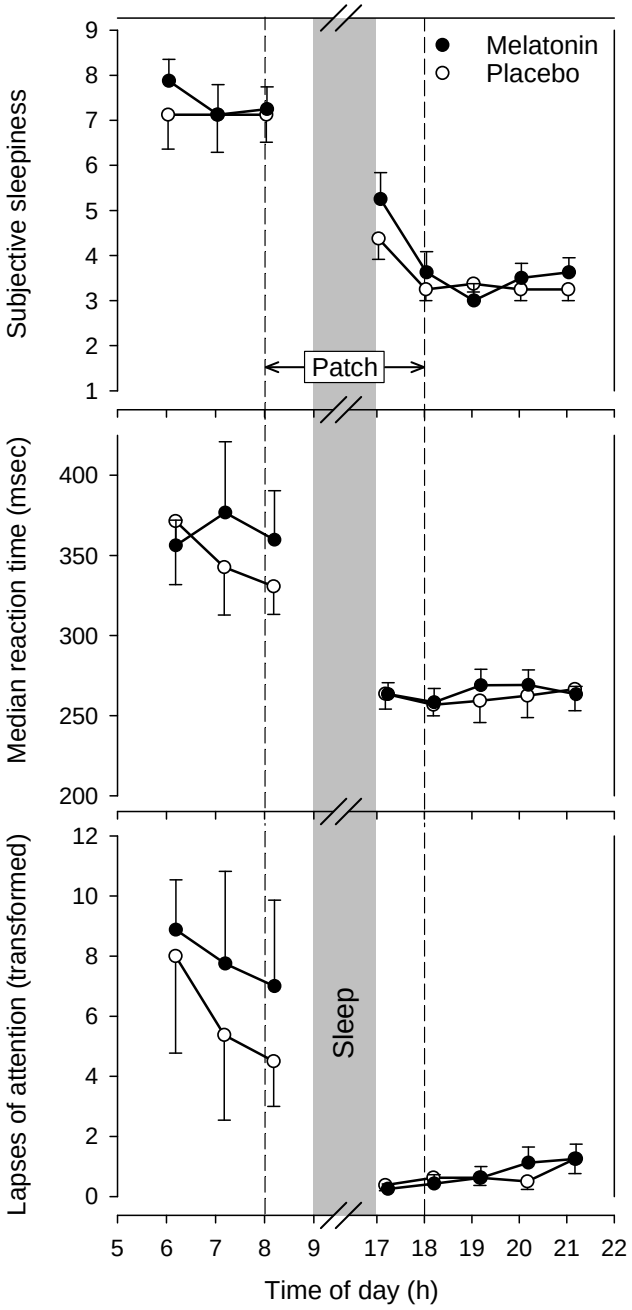

Figure S1. Subjective sleepiness (*top*), reaction time *(middle)*, and lapses of attention *(bottom)* before and after transdermal melatonin administration. Data represent mean (± SEM, N=8)) scores on the Karolinska Sleepiness Scale (KSS), means of the median reaction time and square-root transformed number of lapses (reaction times >0.5 s) in hourly 5-min Psychomotor Vigilance Tasks. Application and removal of the dermal patch are indicated by dashed vertical lines. Note break in the abscissa for representation of 8-h daytime sleep opportunity (09:00-17:00 h). No effect of melatonin on subjective sleepiness (mixed-model ANOVA on hourly KSS scores: Condition P=0.12; Time P=0.0001; Condition x Time P=0.37), log-transformed median reaction time (Condition P=0.40; Time P=0.88; Condition x Time P=0.91) and square-root transformed number of lapses (Condition P=0.82; Time P=0.21; Condition x Time P=0.81) was detected after end of daytime sleep.