Laterality of the sleep onset process: Which hemisphere goes to sleep first?

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Abstract
This study aims to assess whether the hemispheric asymmetry inversion observed in the wake-sleep transition can also be revealed by the latency of inter tapping intervals /C212.5 s for each hand and the latency of theta burst /C212.5 s in symmetrical loci of the two hemispheres during the sleep onset process. Data collected from 16 right-handed subjects showed a hemispheric asymmetry in the sleep onset latency with both behavioural and EEG indices. For the first time, a hemispheric asymmetry in the sleep onset latency was found considering a visual analysis of EEG. Results suggest that the hemispheric pattern found during sleep onset can be considered a steady characteristic of the transition from wake to sleep, relatively independent of homeostatic and time of night effects. These results are interpreted as being consistent with the hypothesis concerning an advantage of the right hemisphere in sustaining vigilance.

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Cerebral areas are known to fall asleep at different times. The sleep onset process follows an anterior–posterior direction. Thus, when frontal areas have just fallen asleep, central areas are only drowsy and occipital areas are still awake (Wright et al., 1995; Tanaka et al., 1997). And what happens in the two hemispheres? Do they go to sleep together?

EEG data have shown that the average amplitude of the left–right hemisphere difference in the beta/delta EEG ratio decreases gradually to zero at 400-s after sleep onset (Merica et al., 1991; Merica and Gaillard, 1992). By analyzing EEG during the transition from wakefulness to sleep, other studies have found a decrease in interhemispheric coherence during sleep onset (Boldyrev a and Zhavoronkova, 1991; Zhavoronkova and Trofimova, 1997, 1998; Wright et al., 1995). In fact, during the sleep onset period (SOP) all bands, except beta, reverse to predominate in the right hemisphere (Boldyrev a and Zhavoronkova, 1991; Zhavoronkova and Trofimova, 1997, 1998).

These data indicate that there is a shift in hemispheric asymmetry on sleep onset. However, hemispheric EEG amplitude differences during sleep do not necessarily reveal whether the sleep onset process happens at the same time or in the same way in both hemispheres.

Electrophysiologically, the sleep onset process is defined by a slowing of the EEG activity (Loomis et al., 1935) and by the appearance of theta rhythms, followed by sleep spindles and K complexes (Dement and Kleitman, 1957). The current literature shows that, during the transition from wakefulness to sleep, EEG variations evolve at different velocities in the two hemispheres, but a different slowing in EEG activity does not mean that the two hemispheres fall asleep at different times.

The French psychologist Henry Piéron (1913) was among the first to suggest that sleep may be described as a temporary suspension of sensorimotor activities. Therefore, the sleep onset process can also be defined by behavioural criteria: impairment in the capacity to respond to external stimuli (Ogilvie and Wilkinson, 1984) and to produce self-generated motor responses—i.e., performing a Finger tapping task (FTT) (Casagrande et al., 1997).

Thus, shifts in hemispheric functional asymmetries could be revealed by lateralized behavioural tasks performed by subjects when sleepy or attempting to fall asleep. However, is it possible to test behavioural performances while subjects are...
an attempt to fall asleep, without disrupting the sleep onset process?

It has repeatedly been shown that reaction times (RT) can be used as a behavioural index to supplement or substitute polygraphic measures of sleep onset (e.g., Ogilvie and Wilkinson, 1984). According to the literature, a failure to press a button in response to faint tones indicates sleep; furthermore, during the transition from wakefulness to sleep, there is a lengthening of RT, which provides a behavioural measure of drowsiness. It has been also shown that a FTT, in which subjects are required to repeatedly press a button while falling asleep, provides the same information as RT tasks and interferes less with the sleep onset process (Casagrande et al., 1997).

Using these behavioural techniques (RT and FTT) it was found that there are systematic variations of hemispheric functioning when falling asleep (Casagrande et al., 1995). A stronger impairment of the right hand (left hemisphere) both in reacting to external stimuli (auditory reaction time task) and in sustaining endogenous motor programs (FTT), indicating a repatterning of hemispheric asymmetry at the SOP. Furthermore, during the transition from wakefulness to sleep, the right hand stops responding before the left hand in the RT task and in the FTT, showing that the left hemisphere falls asleep earlier than the right hemisphere.

The FTT should provide an adequate index of cerebral variations during the transition from wakefulness to sleep, since the subject’s control of the finger movements required for tapping depends on central pre-programming (Schmidt, 1975), and the rate of finger tapping is a sensitive behavioural index of brain damage (Reitan and Davison, 1974). Furthermore, Anliker (1963) found that a reduction in integrated EEG alpha was accompanied by an increase in inter-response intervals during a tapping task. Finally, positron emission tomography shows that index finger tapping depends on a significant activation of the controlateral sensorimotor cortex (Blinken-berg et al., 1996).

Even more recent data showed that performance in a FTT revealed a repatterning of the relative hemispheric activity during the transition from wake to sleep and even upon awakenings from REM and NREM sleep and during morning awakening. This reversal of hemispheric dominance on sleep onset was independent of time of night (Casagrande and Bertini, submitted). Since a reduction in integrated EEG alpha was paralleled by an increase in inter-response intervals during a FTT (Anliker, 1963) and since there was a strong correlation between cessation of response to the FTT and the appearance of stage 1 sleep (Casagrande et al., 1997), this study aims to assess whether the hemispheric asymmetry inversion observed in the wake-sleep transition can be observed by considering the latency of inter-tapping intervals (ITI) ≥ 2.5 s for each hand and the latency of theta burst ≥ 2.5 s in symmetrical loci (C3 and C4) of the two hemispheres. In this way, it will be possible to evaluate whether the two hemispheres have different sleep onset times by considering standard EEG criteria and behavioural criteria, i.e., the inability to self-generate motor responses.

1. Methods

1.1. Subjects

Sixteen strongly right-handed male undergraduates, with Hand Preference ≥.95, as assessed by a Lateral Preference Questionnaire (Salmaso and Longoni, 1985), aged 20–27, signed an informed consent before participating as paid volunteers in the study. For 1 week, subjects were required to fill in a sleep questionnaire at home daily upon morning awakening. Only subjects that reported normal sleep duration (7.5–8.5 h per day) and schedule (going to sleep at 11.30 p.m. ± 60 min and waking up at 7.30 a.m. ± 60 min) and who reported no sleep, medical, or psychiatric disorders were included in the study. The subjects themselves were unaware of the purpose of the experiment.

1.2. Apparatus

1.2.1. Poligraphic recordings

A “Beckman R 611” polygraph set at a paper speed of 10 mm/s was used for polygraphic recordings.

The EEG activity was recorded from electrodes fixed to the scalp at central, frontal, and occipital locations over each hemisphere. EEG recordings were unipolar (C3-A2, C4-A1) with a time constant of 0.3 s. Bipolar horizontal eye movements were recorded from electrodes placed above and below the right eye pupil. Both were recorded at a time constant of 1 s. Submental electrodes were employed for recording bipolar EMG, with a time constant of 0.03 s. All recordings were in AC.

The subjects were required to tap on the push button with their index finger of each hand quickly. The ITI and the times from light out to each ITI were recorded for each hand. During SOP and upon awakening from REM and stage 2 sleep, data were recorded for 1 h from light out or until stage 3 was scored for at least 1 min. During the wakeful condition (in morning and evening periods) and upon morning awakening, data were recorded for 14 min.

1.3. Procedure

Subjects spent six consecutive nights each in a sound attenuated air-conditioned sleep-room. Only the last night is considered in this study. Each subject came to the Sleep Lab the afternoon before the first night of the study (which was for adaptation) and received instructions on the experimental procedures. From the second night to the sixth night subjects were awakened twice, once from REM and once from NREM (stage 2) sleep; eight subjects were awakened 5 min after the beginning of the second NREM period and 5 min after the onset of the third REM period. The other eight subjects were first awakened 5 min following the onset of the second REM and 5 min after the onset of the fourth NREM. The order of the awakenings from REM and NREM sleep was counterbalanced across the subjects. On the sixth night, after each awakening, subjects spent 45 min performing cognitive tasks and then they were required to fall asleep again. On each night subjects fell asleep performing the FTT and after each awakening, they were required to fall asleep again performing the FTT.

During each sleep onset period the FTT was performed in the dark with the subject lying on the bed; in wakeful conditions the FTT was performed under a dim light with the subject sitting on a chair at one time and with the subject lying on the bed at another time. The first sleep onset was at 23.30 h (± 30 min). The mean time of the second sleep onset period was 3.00 h (± 30 min) and the mean time of the third sleep onset period was 6.30 h (± 30 min).
1.4. Data analysis

Scoring of polysomnographic recordings was based on the standard criteria (Rechtschaffen and Kales, 1968). Behavioural sleep onset latencies were measured with respect to the cessation of the FTT for more than 2.5 s. EEG sleep onset latencies were measured as the time for the appearance of the first theta burst lasting more than 2.5 s. EEG channels were scored blind: i.e., when C4 was scored, the other EEG channels were hidden from the scorer and vice-versa. Behavioural measures were obtained by means of the same software that recorded ITI.

Theta burst scoring was carried out by two independent scorers and interscorer reliability was computed using Cohen’s K with the following results: K = 0.96.

For data analysis, a repeated measure sleep onset (1st, 2nd, 3rd) by measure (EEG, FTT) by hemisphere (right, left) ANOVA was carried out. The Duncan test was used for post hoc analysis of the means.

2. Results

A significant effect for the measure factor ($F_{1,15} = 16.66; p < .001$) was found, indicating a shorter latency for the FTT (mean: 180 ± 177.04 s) as compared to the theta burst latency (mean: 600 ± 582.11 s). A significant effect for hemisphere ($F_{1,15} = 8.78; p < .01$) was also present, revealing shorter sleep onset latency in the left hemisphere (mean = 385.26 ± 376.12 s) with respect to the right hemisphere (mean = 399.90 ± 386.36 s). No other effect or interaction were observed ($F < 1$). Fig. 1 shows theta burst latencies for both hemisphere and FTT latencies for both hands.

3. Discussion

The results reveal shorter sleep onset latencies for the left hemisphere, considering both behavioural (cessation of the FTT for more than 2.5 s) and EEG sleep onset latencies (first theta burst lasting more than 2.5 s). These results were obtained by analysing central areas (C3 and C4) and one can speculate that the same EEG asymmetrical pattern may also characterize frontal areas since they are close to the ones involved in FTT performance, but this hypothesis is harder to test with an EEG visual analysis because frontal EEG channels are more affected by ocular artefacts and this could influence theta detection.

The results confirm our previous findings (Casagrande et al., 1995, 1999; Casagrande and Bertini, submitted) and show that hemispheric asymmetry in the behavioural sleep onset latency is also found when a very early index of falling asleep ($IIT \geq 2.5$ s) is considered. For the first time, a hemispheric asymmetry in the sleep onset latency was observed by adopting an EEG visual analysis. The latter result confirms the strong relationship between the FTT and EEG (Anliker, 1963; Casagrande et al., 1997). Although both behavioural and EEG measures show that the left hemisphere falls asleep earlier than the right hemisphere, a shorter latency for the FTT as compared to the theta burst latency was found, showing a temporal dissociation between behavioural and EEG sleep, as far as the two indices used in this study are concerned: in fact, behavioural sleep develops before EEG sleep. This finding confirms previous results (Blood et al., 1997; Casagrande et al., 1997; Ogilvie and Wilkinson, 1988; Ogilvie et al., 1989) and it is in keeping with the partial independence of the neurophysiological systems that control behavioural and electrophysiological aspects of wake and sleep (Feldman and Waller, 1962). On the other hand, this dissociation between behavioural and EEG indices of activation is also in line with data found with monkeys, revealing an asynchronous development of sleep in cortical areas; even if an inverse electrophysiological–behavioural pattern was observed in these animals. In fact, in drowsy animals, visual responses in the extrastriate cortex may be reduced or even completely blocked with the background activity changed to the burst-pause pattern typically seen in sleep, while the animals continue to perform in a visual task (Pigarev et al., 1997).

The hemispheric pattern found during sleep onset seems to depend on the hemispheric dominance of the subjects tested, who were all right-handed. In fact, when we compared the hemispheric pattern during sleep onset in both right- and left-handed subjects, who fell asleep performing the FTT, we found an asymmetrical hemispheric pattern only in the right-handed subjects; while left-handed ones showed only a tendency to a reversed hemispheric pattern. The latter result appears consistent with the greater variability in cerebral organization characterizing the left-handed subjects with respect to the right-handed ones (Casagrande et al., 1999).

The hemispheric pattern found during sleep onset did not vary with time of night. Since it is known that homeostatic sleep pressure decreases through the night, one could suggest that the steady asymmetrical brain pattern detected during sleep onset in the early, middle and last part of the night seems unaffected by sleep pressure. Such a result would lead us to suggest that it could be a steady characteristic of the transition from wake to sleep, although the current research design was not aimed at manipulating homeostatic drive. Further, this conclusion agrees with other data indicating a greater right-sided cerebral activation during the transition from wake to sleep also when sleep onset is during rapid eye movement (REM) sleep (Asenbaum et al., 1995).
In conclusion, we found a greater alerting state in the right hemisphere when the brain is sleepy and is falling to sleep. These results are in keeping with data showing the advantage of the right hemisphere in the control of vigilance (e.g., Whitehead, 1991) and in responding to warning stimuli (e.g., Heilman and Van Den Abele, 1980). It is known that a noradrenergic fronto-parietal-thalamic-brainstem network subserving vigilance is located in the right hemisphere (Bench et al., 1993; Deutsch et al., 1988; Posner and Rafal, 1987; Raz, 2004; Sturm et al., 1999; Weis et al., 2000). This right-hemisphere network also seems to be activated when all the brain is sleepy. In other words, the right hemisphere, as compared to the left, seems to have greater levels of "wakeability" or "vigilanceability" when the vigilance state is very low and the brain is going to sleep. The latter is a conclusion in keeping with data showing an increased activation in the prefrontal cortex and parietal lobes, particularly in the right hemisphere, following total sleep deprivation (Drummond et al., 2001; Szelenger et al., 2005).

In the same way as dolphins show periods of deep slow-wave sleep in either the right or the left hemisphere alone (Mukhametov, 1987), revealing that – for them – good environmental adaptation requires unilateral sleep, the human brain may require an asymmetrical activation of the cerebral hemispheres during the sleep onset process. Probably, this asymmetrical pattern also remains in the following sleep, as recently suggested by findings revealing a right-hemispheric predominance in a frequency range (4–8 Hz) close to the theta band and a left-side dominance in the frequency range of sleep spindles (Roth et al., 1999). These results agree with those revealed by non-linear analysis of the EEG, indicating that the right hemisphere appears to be more complex than the left hemisphere during sleep stages 1 and 2 (Pereda et al., 1999). In addition, it is interesting to note that the finding of an asymmetrical theta burst latency agrees with EEG and PET data indicating, in an alert resting state, positive correlations between theta density and cerebral metabolism in right fronto-temporal regions, including the right middle and superior frontal gyri, and the right middle and temporal frontal gyri (Pizzagalli et al., 2003).

The lateralization of the function is a marker of increasing complexity in the evolutionary development of biological systems. Thus, the laterality of the sleep onset process might be considered as an important biological requirement for an adequate environmental adaptation that easily allows people to experience the pleasure of dreaming while the right hemisphere maintains greater vigilance that is useful in order to alert people when some environmental stimuli make it necessary to do so, as also shown by reaction time data recorded during sleep onset (Casagrande et al., 1995).

References

Casagrande, M., Bertini, M., submitted for publication. Night-time right hemisphere superiority and daytime left hemisphere superiority: a repatterning of laterality across wake-sleep-wake states.
Casagrande, M., Curcio, G., Bertini, M., 1999. Hemisphere asymmetry in the sleep onset process: differences between right- and left-handed subjects. Sleep Research Online 2 (Sup. 1), 224.

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