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TRAIT-LIKE INDIVIDUAL DIFFERENCES IN THE HUMAN SLEEP ELECTROENCEPHALOGRAM

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Abstract—We aimed to examine whether commonly observed individual differences in sleep architecture and the sleep electroencephalogram reflect individual traits, which are amenable to a genetic investigation of human sleep. We studied intra-individual stability and inter-individual variation in sleep and sleep electroencephalogram spectra across four baseline recordings of eight healthy young men. A similarity concept based on Euclidean distances between vectors was applied. Visually scored sleep variables served as feature vector components, along with electroencephalogram power spectra in non-rapid-eye-movement and rapid-eye-movement sleep. The distributions of similarity coefficients of feature vectors revealed a clear distinction between high within-subject similarity (i.e. stability), and low between-subject similarity (i.e. variation). Moreover, a cluster analysis based on electroencephalogram spectra in both non-rapid-eye-movement and rapid-eye-movement sleep segregated all four baseline nights of each individual into a distinct cluster. To investigate whether high and low sleep pressure affects the similarity coefficients, normalized non-rapid-eye-movement sleep electroencephalogram spectra of the first and second half of the recordings were compared. Because the electroencephalogram changes systematically in the course of the night, within-subject variation no longer differed from between-subject variation. In conclusion, our data provide evidence for trait-like characteristics in the sleep electroencephalogram. Further studies may help to identify distinct phenotypes to search for genes underlying functional aspects of undisturbed human sleep. © 2005 Published by Elsevier Ltd on behalf of IBRO.

Key words: Euclidean distance, feature vector, hierarchical cluster analysis, sleep regulation, similarity, variation.

It has long been noticed that even a complex phenomenon such as the electroencephalogram (EEG) is partly under genetic control (Lennox et al., 1945; Vogel, 1958). For example, early twin studies revealed that the EEG characteristics of quiet wakefulness and sleep have much higher resemblance between monozygotic (MZ) twins than between dizygotic (DZ) twins and unrelated persons (Vogel, 1958). Subsequent studies corroborated the importance of genetic factors for spontaneous waking-EEG activity (Stassen et al., 1987; van Beijsterveldt and Boomsma, 1994; van Beijsterveldt et al., 1998), and found a high test–retest correlation for spectral power in distinct EEG frequency bands (Gasser et al., 1985; Stassen, 1985). It was estimated that the heritability of activity in delta, theta, alpha and beta frequencies is over 80% (van Beijsterveldt et al., 1996), which demonstrates that the waking EEG is among the most-heritable traits in humans.

The possible heritability of EEG activity during human sleep has attracted much less attention. Nevertheless, certain aspects of sleep architecture and the sleep EEG are also likely to be under genetic control (Rétey et al., 2005; for recent overviews see Toth, 2001; Tafti and Franken, 2002; Shaw and Franken, 2003; Dauvilliers et al., 2005; Van Dongen et al., 2005). Zung and Wilson (1966) reported concordance of the temporal sequence of sleep stages in MZ twins. Later polysomnographic studies indicated that a significant proportion of the variance in stage 2, stage 4, slow wave sleep (SWS; i.e. combined stages 3 and 4), and the density of rapid eye movements in rapid-eye-movement (REM) sleep are in part genetically determined (Merica and Gaillard, 1985; Linkowski et al., 1989, 1991). Furthermore, certain sleep disorders such as narcolepsy and sleep walking also show genetic influences (reviewed by Hublin et al., 1996; Franken and Tafti, 2003; Dauvilliers et al., 2005). These insights from studies in healthy human subjects and patients are consistent with studies in inbred mice, which revealed that differences in sleep duration and sleep structure, as well as in the spectral patterns of the sleep EEG, show high estimates of heritability (for recent reviews see Franken and Tafti, 2003; Dauvilliers et al., 2005).

Inter-individual differences in human sleep characteristics not only offer the prospects to identify genetic aspects of sleep, but they are also interesting for many additional reasons. First, a functional relationship between distinct EEG markers of sleep regulation in waking and sleep was recently established based on inter-individual variation (Finelli et al., 2000). Second, sleep spindles show strikingly distinct and reproducible individual patterns with little night-to-night variation, yet considerable variation between individuals (Werth et al., 1997; De Gennaro et al., 2005). Third, the topographic distribution of EEG power in non-REM sleep appears to reflect an individual "fingerprint" (Finelli et al., 2001; De Gennaro et al., 2005). Finally, individual differences in habitual sleep duration may be associated with accumulated sleep debt in young adults (Klerman and Dijk, 2005). These examples highlight the importance of scrutinizing inter-individual differences as a

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Abbreviations: EEG, electroencephalogram; MZ, monozygotic; REM, rapid-eye-movement; SWS, slow wave sleep.

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Table 1. Sleep variables derived from visual scoring

Sleep variables	Mean	SEM
Time in bed	479.7	0.0
Total sleep time	454.8	1.9
Sleep efficiency	94.8	0.6
Waking after sleep onset	7.8	1.7
Movement time	8.1	0.6
Stage 1	42.1	5.3
Stage 2	220.5	10.5
Stage 3	47.0	5.5
Stage 4	39.4	9.1
SWS	86.4	10.6
Non-REM sleep	306.9	7.5
REM sleep	105.8	5.9
Latency to stage 2	8.7	1.5
REM sleep latency	69.6	5.4

Mean values ($n=8$) and standard errors of the mean (SEM) are in minutes, with the exception of sleep efficiency, which represents the percentage of total sleep time per time in bed. Mean values were first calculated within subjects prior to averaging across subjects.

powerful approach to tackle basic questions in sleep research and sleep medicine (Van Dongen et al., 2005).

The aim of this study was, therefore, to examine intra-individual stability and inter-individual variation in sleep architecture and spectral components of the sleep EEG. As a new approach in sleep research similarity and hierarchical cluster analyses were performed. Specific questions included whether certain characteristics are particularly stable within a subject and especially variable between subjects, and whether the similarity measures depend on homeostatic (i.e. sleep–wake dependent) influences.

EXPERIMENTAL PROCEDURES

Subjects and study design

The baseline data of a selective REM sleep deprivation study (Endo et al., 1998) were analyzed. Eight healthy, right-handed men (mean age: 24.1±0.6 years) participated in the study, which consisted of two sessions of nine consecutive nights. In each session, an adaptation night was followed by two baseline nights and six experimental nights (Endo et al., 1998). The two sessions were 28 days apart, except in subject six with only 23 days between the sessions. Bedtimes were scheduled from 23:00–7:00 h. The local ethical committee for research on human subjects approved the study protocol, and written informed consent was obtained from the subjects prior to the study.

Sleep variables and sleep EEG power spectra

Sleep stages were visually scored for 20-s epochs (C3A2 derivation) according to standard criteria (Rechtschaffen and Kales, 1968). Sleep onset was defined as the first occurrence of stage 2. Power spectra of consecutive 20-s epochs were computed using a Fast Fourier Transform routine (Hanning window, average of five 4-s epochs). The frequency resolution was 0.25 Hz, and frequencies up to 20 Hz were included in the analyses. The lowest two frequency bins (0.25–0.5 Hz) were excluded because of their sensitivity to artifacts. Twenty-s epochs with artifacts were identified and excluded by visual inspection and by a semi-automatic procedure based on power in the 0.75–4.5 Hz and 20–40 Hz bands. Artifact-free EEG spectra of 20-s epochs were matched with the corresponding sleep scores, and absolute all-night power spectra were computed for non-REM sleep (stage 2, 3 and 4) and REM sleep. In addition, average non-REM sleep EEG power

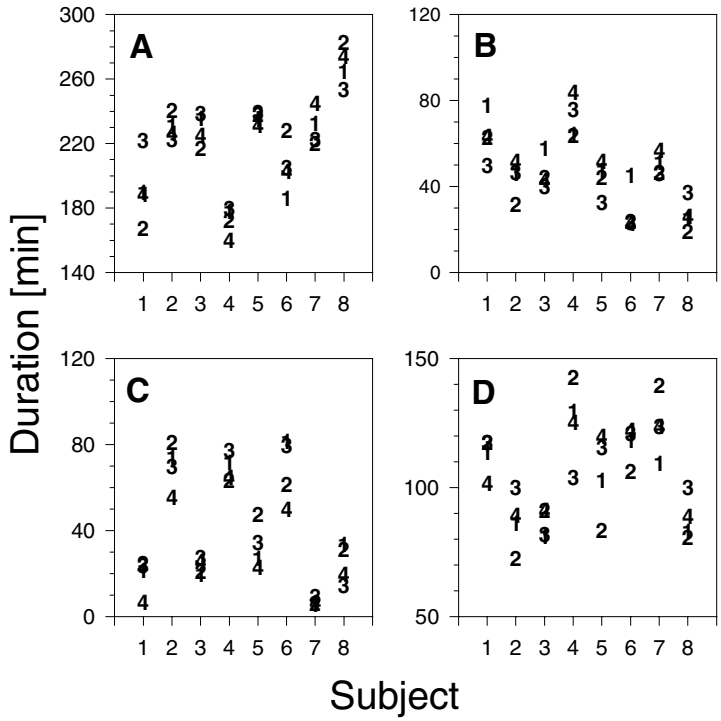

Fig. 1. Individual duration (minutes) of non-REM sleep stages 2 (A), 3 (B), 4 (C), and REM sleep (D) in baseline nights 1–4.