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Principal component analysis of the EEG spectrum can provide yes-or-no criteria for demarcation of boundaries between NREM sleep stages

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ABSTRACT

Human sleep begins in stage 1 and progresses into stages 2 and 3 of Non-Rapid-Eye-Movement (NREM) sleep. These stages were defined using several arbitrarily-defined thresholds for subdivision of albeit continuous process of sleep deepening. Since recent studies indicate that stage 3 (slow wave sleep) has unique vital functions, more accurate measurement of this stage duration and continuity might be required for both research and practical purposes. However, the true neurophysiological boundary between stages 2 and 3 remains unknown. In a search for non-arbitrary threshold criteria for distinguishing the boundaries between NREM sleep stages, scores on the principal components of the electroencephalographic (EEG) spectrum were analyzed in relation to stage onsets. Eighteen young men made 12–20-minute attempts to nap during 24-hour wakefulness. Single-minute intervals of the nap EEG records were assigned relative to the minute of onsets of polysomnographically determined stages 1, 2, and 3. The analysis of within-nap time courses of principal components scores revealed that, unlike any conventional spectral EEG index, score on the 4th principal component exhibited a rather rapid rise on the boundary between stages 2 and 3. This was mostly a change from negative to positive score. Therefore, it might serve as yes-or-no criterion of stage 3 onset. Additionally, similarly rapid changes in sign of scores were exhibited by the 1st and 2nd principal components on the boundary of stages 2 and 1 and on the boundary between stage 1 and wakefulness, respectively.

1. Introduction

Scientific study of human sleep has been initiated by the discovery that sleep progresses through a series of stages in which different brain wave patterns are displayed (e.g., [6]). Indeed, visual analysis of most of polysomnographic sleep records reveals that human sleep begins in stage 1 (N1) and progresses into stages 2 (N2) and 3 (N3) of Non-Rapid-Eye-Movement (NREM) sleep. The conventional methodology of such subdivision of the sleep records into intervals each of

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which is allocated to one of a few all-or-nothing variables called "sleep stages" has been first introduced in 1968 in the publication of the standard sleep scoring rules [20]. Since some of these rules, especially with respect to stage boundaries, are difficult to follow, this standard system of sleep description faces practical problems of definition and demarcation of sleep stages [24,23]. Nevertheless, the criteria for distinction between stages 1 and 3 of NREM sleep had remained almost unchanged after rare attempts to revise these criteria [3,24].

One of the major shortcomings of the standard scoring rules is their relying on arbitrarily-defined thresholds for separation of NREM sleep stages. For instance, the most powerful component of the electroencephalographic (EEG) signal, delta activity (slow waves with frequencies 0.5–4.5 Hz), exhibits a gradual increase in the course of sleep deepening that starts with a short transitional interval known as stage 1 (N1), continues through the following much longer interval of stage 2(N2) that is viewed as the first unequivocal stage of sleep and reaches its peak during stage 3 (N3) that is usually named slow wave sleep (SWS) due to predominance of relatively high-voltage (more than 75 μV) low-frequency waves (0.5–2.0 Hz). The arbitrarily-defined threshold criteria that were recommended for defying stage 3 (N3 or SWS) include three (amount, frequency and amplitude) thresholds, i.e., more than 20% of <2 Hz activity with amplitude >75 μV during a given epoch of sleep [20,3]. Therefore, subjective assessment of the EEG epochs is necessary and this can lead to unreliable results and poor agreement between scorers [4]. Particularly, Norman et al. [10] reported that stages N1 and N3 are most prone to disagreement, and that, overall, 88.4% of the scoring disagreements are associated with scoring adjacent stages (wake/N1, N1/N2, and N2/SWS).

Until recently, SWS and slow-wave activity have been simply viewed as useful objective markers of sleep deepness and intensity. However, most recent studies showed that they might be of particular importance for analysis of the sleep process due to their unique vital functions. For example, these studies point to their essential role in learning and memory (e.g., [7,19,5,26,25]). Since the presence and integrity of SWS was found to be linked to the ability to form and retain memories, the diminished levels of conventionally scored stage 3 sleep can explain some cognitive impairment in primary insomnia and older age (e.g., [1,9]). Therefore, one of the questions that need to be answered in the light of such recent findings might be: where is the true neurophysiological boundary between stages 2 and 3 (N2/N3)?

Earlier we showed that principal component structuring of the EEG spectrum provides a theoretically sound method of relating the quantitative descriptions of spectral power densities to quantitative changes (i.e., from negative to positive) in scores on the largest principal components of the EEG spectrum [11–15,17,16,18]. It was hypothesized that the rise of the 1st score reflects the switch-like change in the sleep-promoting processes that usually delays relative to the change in the wake-promoting processes represented by the decline of the 2nd score [11,16]. Consequently, stage 1 sleep might be viewed as "no man's land" between the opponent driving forces for wake and sleep [14,15]. It was also shown that, like it occurs during diurnal sleep-wake transitions, the 1st and 2nd components of the EEG spectrum might also represent alternations between competing drives for sleep and wakefulness throughout the whole episode of all-night sleep, whereas time courses of the next pair of component scores (3rd and 4th) might reflect the within-sleep alternations between sub-sates of light and deep sleep, respectively [11,12]. At least, the time course of the 4th score during each ultradian sleep cycle pointed to its link to deep sleep, i.e., its rapid raise always delayed relative to changes in the 1st and 2nd scores in the beginning of the first sleep cycle, but its maximum was reached already in the middle of the cycle, and its fall during the second half of the cycle occurred earlier compared to changes in other scores [11,12].

However, it remains unclear whether the rapid rise of the 4th principal component score precedes or coincides with or follows the transition from stage 2 to stage 3 sleep. Empirical support of the suggestion of stable phase relationship of such a rise with the conventionally scored onset of stage 3 can open a perspective of identification of non-arbitrary (i.e., neuro-physiologically meaningful) boundaries between stages 2 and 3. Therefore, the present analysis was aimed on testing the hypothesis that the rapid rise of the 4th principal component score coincides with the transition to stage 3, whereas the rapid changes in the 1st and 2nd scores are not associated with this transition but, instead, linked to the boundaries of two earlier NREM sleep stages.

2. Methods

The experimental study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki. Its protocol was approved by the Ethics Committee of the Siberian Branch of the Russian Academy of Medical Sciences (#2/07.06.2009). Informed written consent was obtained from each study participant. The analyzed data set contains spectra of the EEG signals recorded from 18 male cadets of the Novosibirsk military high school. Their ages ranged from 18 to 22 years. Their regular sleep prior to the experiments occurred within 7-hour interval between the rising and bedtimes scheduled on 06:30 and 23:30, respectively. The experiments were carried out in the laboratory complex on 9 weekends, between Saturday morning and Monday morning, with 2 participants studied during each weekend. They both were kept continuously awake until 23:00, and then one of them was allowed to sleep in the sleep laboratory until 06:00 h. The other was kept awake for the whole night. The next 24 h were organized in 12 wake–sleep cycles each consisting of 100-minute wakefulness followed by 20-minute nap with polysomnographic recordings. A participant was asked to sleep lying in bed in a sound-attenuated and completely darkened room of the sleep laboratory during a 20-minute span with closed eyes. Then he was taken out of the sleep laboratory to stay in other rooms together with experimenters for the whole time interval between consecutive napping attempts. To prevent unintended sleep, he was constantly engaged in research activities and social interactions.

Polysomnographic sleep recordings were performed using a standard monitoring montage that included 5 EEG channels, two electro-oculogram channels, and one chin electromyogram channel. Data were collected via an 8-channel Medicor polygraph (EEG8S, Micromed, Hungary). Since the central derivations were recommended for visual scoring of sleep stages