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The association between prolonged sleep onset latency and heart rate dynamics among young sleep-onset insomniacs and good sleepers

Hsin-Jung Tsai [a,b,1], Terry B.J. Kuo [a,b,c,d,e], Yu-Cheng Lin [a,b,1], Cheryl C.H. Yang [a,b,c,d,*]

[a] Sleep Research Center, National Yang-Ming University, Taipei, Taiwan
[b] Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan
[c] Brain Research Center, National Yang-Ming University, Taipei, Taiwan
[d] Department of Education and Research, Taipei City Hospital, Taipei, Taiwan
[e] Department of Biomedical Sciences and Engineering, National Central University, Taoyuan, Taiwan

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ABSTRACT

A blunting of heart rate (HR) reduction during sleep has been reported to be associated with increased all-cause mortality. An increased incident of cardiovascular events has been observed in patients with insomnia but the relationship between nighttime HR and insomnia remains unclear. Here we investigated the HR patterns during the sleep onset period and its association with the length of sleep onset latency (SOL). Nineteen sleep-onset insomniacs (SOI) and 14 good sleepers had their sleep analyzed. Linear regression and nonlinear Hilbert-Huang transform (HHT) of the HR slope were performed in order to analyze HR dynamics during the sleep onset period. A significant depression in HR fluctuation was identified among the SOI group during the sleep onset period when linear regression and HHT analysis were applied. The magnitude of the HR reduction was associated with both polysomnography-defined and subjective SOL; moreover, we found that the linear regression and HHT slopes of the HR showed great sensitivity with respect to sleep quality. Our findings indicate that HR dynamics during the sleep onset period are sensitive to sleep initiation difficulty and respond to the SOL, which indicates that the presence of autonomic dysfunction would seem to affect the progress of falling asleep.

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1. Introduction

It has been reported that approximately 25% of the general Taiwanese adult population and approximately 21% of Taiwanese teenagers have at least one symptom of insomnia (Kao et al., 2008). In addition, an elevation in mortality and an increased in the incidence of cardiovascular diseases such as hypertension have been observed among patients with insomnia. Previous studies have demonstrated that nighttime heart rate (HR) plays a more important role in predicting cardiovascular events than daytime HR (Palatini et al., 2013); moreover, a smaller HR reduction during sleep has been found to be independently associated with all-cause mortality (Ben-Dov et al., 2007). An elevated nighttime HR and an alternation in HR variability have been reported to be present in patients with insomnia (de Zambotti et al., 2011; Spiegelhalder et al., 2011; Stein and Pu, 2011; de Zambotti et al., 2013) and this has been used as a basis of a hyperarousal theory of insomnia (Bonnet and Arand, 1997; Riemann et al., 2010; Bonnet et al., 2014; de Zambotti et al., 2014).

In order to determine changes in HR during wake-to-sleep transitions, a number of different calculations have been used including averaged HR, differential values from wake-HR to sleep-HR, using frequency domain analysis or using time domain analysis. However, findings based on these various analytical approaches have been inconsistent across a number of studies (Freedman and Sattler, 1982; Stepanski et al., 1994; Bonnet and Arand, 1998; Varkevisser et al., 2005; de Zambotti et al., 2011; Spiegelhalder et al., 2011), especially when targeting the sleep onset period.

Issues associated with variations in sleep onset duration have also been put forward as a key factor when investigating HR dynamics. A possible way to eliminate the effect of sleep onset duration would be slope analysis. In addition to using linear analysis of the HR slope, using nonlinear analysis of the HR slope is another possible approach when investigating HR fluctuations; the latter approach is useful because HR dynamics are supposed to be unpredictable in healthy humans. The nonlinear Hilbert Huang transform (HHT) approach has been put forward as a useful method when analyzing non-stationary data and is believed to be able to reflect the intrinsic physiological trends present in such data (Huang et al., 1998). The HHT approach can easily and

* Correspondence to: Sleep Research Center and Institute of Brain Science, National Yang-Ming University, No. 155, Section 2, Li-Nong St., Taipei 11221, Taiwan.
E-mail address: cchyang@ym.edu.tw (C.C.H. Yang).
[1] The authors contributed equally to this paper.

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reasonably decompose any complex raw data via a sifting process into a number of intrinsic mode functions (IMFs) and also produces a final non-oscillation trend. The final intrinsic non-oscillation trend should then correctly correspond to the trend's intrinsic variation within the high complexity of the physiological dataset. This method has been widely applied in a number of studies when analyzing physiological signals (Ur Rehman et al., 2010; Lin and Zhu, 2012; Thuraisingham et al., 2012). Based on the above, it was expected to be able to isolate a range of confounding factors, such as motion artifacts, respiration artifact and measurement noises, all of which are known to affect oscillations in HR. Therefore, in order to catch the HR fluctuation during the sleep onset period correctly, the nonlinear approach was also used.

In this study, we hypothesized that a reduction in HR fluctuation during the sleep onset period is a feature of sleep initiation difficulty and that this phenomenon should be able to be observed by both the linear and nonlinear approaches; we postulated that this reduction in HR fluctuation will be associated with the length of sleep onset latency. Thus, we investigated the role of HR in relation to sleep onset period among individuals with sleep-onset insomnia (SOI) and among individuals who were good sleepers (GS) using both linear regression analysis and the nonlinear HHT method. These were used to estimate the slope of the HR, and to explore HR fluctuations during the sleep onset period. Indices of the linear and nonlinear slopes were quantified based on the regression line and extracted non-oscillation trends, respectively.

2. Method

2.1. Participants

To recruit study participants, information on the study was posted on University notice-boards and the internet. The age range of the subjects was between 20 to 25 years old, and the body mass indices (BMI) of the participants were within the normal range, from 18.5 to 24.5 kg/m^2. All participants had a regular evening bedtime as well as a regular morning waking time. None of the participants had a reported medical history that included psychiatric, neurological or cardiovascular illness. Furthermore, the subjects indicated that they had no history of sleep disorders, such as sleep apnea periodic limb movement disorder, substance abuse or sedative/hypnotic drug use. This study was conducted at the Sleep Center of the Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan. The procedures used in this study were approved by the Institutional Review Board of National Yang-Ming University.

2.2. Procedures

All 33 participants filled in the Pittsburgh Sleep Quality Index (Buysse et al., 1989) questionnaire to evaluate their subjective sleep quality. Daytime sleepiness was also measured by Epworth Sleepiness Scale (Johns, 1991). These questionnaires were used to identify the SOI participants (6 male and 13 female, $n=19$), who consisted of individuals with a PSQI total score of >5, and who had specifically reported having difficulty falling asleep greater than 20–30 min on more than 3 days within one week over six months; such difficulties having caused daytime consequences and impaired their quality of life. The participants of SOI group were further defined as individuals with psychophysiological insomnia based on the objective findings. The control group consisted of individuals who formed the GS participants (9 male and 5 female, $n=14$); these individuals had a reported PSQI total score ≤ 5, had experienced less than 1 week of sleep disturbance in the last month and who were satisfied with their sleep quality. All participants were required to keep a written sleep log for seven days to record their life schedule and sleep habits. This log included the time of morning waking, the time they went to bed, drug use, caffeine intake and alcohol intake.

After completing their sleep logs, all participants were evaluated by miniature polysomnography over two consecutive nights in order to assess their objective sleep quality. The participants arrived at the sleep laboratory between 6:00 p.m. to 8:00 p.m. for miniature polysomnography setup, which was conducted by a research assistant, and then participants went home. The first night was utilized for adaption and to minimize the first-night effect; the second night was utilized for the subsequent analyses.

2.3. Data collection

Electrophysiological signals were recorded using miniature polysomnography equipment (TD1, Taiwan Telemedicine Device Company, Taiwan) (Kuo and Yang, 2009; Kuo et al., 2012) that was carried by each participant. The small size ($5.2 \times 3.1 \times 1.2$ cm^3) and light weight (11 g) of the recorder resulted in minimal interference/stress for the participants. The electrophysiological signal recordings were a simplified version of standard sleep monitoring and four electrophysiological signals, namely electrooculogram, EOG; electromyogram, EMG; electroencephalogram, EEG, and electrocardiogram, ECG, were recorded. In addition, accelerometers on three axes were implemented within the device to allow bodily movement detection.

The EEG was recorded from the C3 point with a reference point at A2 (Yang et al., 2002). The EOG was recorded from a pair of differential electrodes placed 1 cm above the right outer canthus and 1 cm below the left outer canthus. The EOG recording was able to detect both horizontal and vertical movements of the eye ball in one single channel of recording and is widely used in current sleep research. Since the EOG was high-pass filtered, it was sensitive to changes in the position of the cornea. The EMG was recorded from a pair of differential electrodes in the submental area. The ECG was recorded from the V5 site on the chest.

The EEG, EOG, EMG, and ECG signals were amplified 2000-fold, 1000-fold, 1000-fold, and 250-fold, respectively. The EEG was filtered at 0.34–53 Hz; the EOG was filtered at 0.034–53 Hz, the EMG at 16–113 Hz and the ECG at 1.6–113 Hz. Finally the EEG, EOG, EMG, and ECG signals were synchronously digitized at a 12-bit resolution using different sampling rates (125, 125, 250, and 500 Hz, for the EEG, EOG, EMG, and ECG, respectively). All of the signals were then truncated into 64-sec time segments with 50% (32-sec) overlap. The acquired dataset was stored on a flash memory device for subsequent offline analysis.

2.4. Sleep analysis

The data file was converted into the European Data Format (Kemp et al., 1992) and then imported into a commercial sleep analysis software program (Somnologica 3.1.2, Embla, USA). The lights-off and lights-on were firstly checked from sleep log that participant had provided. The physical activity recorded by accelerometers was automatically estimated before- and after that time. If a 5-min interval without detected excessively body movement was found, the first 32-s of this 5-min interval was then identified as the lights off. Likewise, the continuous 5-min interval of awaking before lights on was identified as the end of sleep. The last 32-s of this 5-min was recognized as lights on. The sleep analysis was carried out according to the standard sleep-stage scoring criteria, as defined by the American Academy of Sleep Medicine (Iber et al., 2007), using standard 30-sec epochs to score the various sleep stages (Wake, non-rapid eye movement (NREM) stage 1, NREM stage 2, NREM stage 3 and REM sleep).

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