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Original Article

Association between sleep parameters and cognitive function in drug-naïve children with attention-deficit hyperactivity disorder: a polysomnographic study

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Objective: Sleep problems are common among patients with attention-deficit hyperactivity disorder (ADHD), and are considered major causes of behavioral and cognitive dysfunction in ADHD patients. In the present study, we investigated the relationship between sleep parameters and cognitive function in drug-naïve children with ADHD.

Methods: Twenty-eight patients were recruited to participate in the study, and a polysomnography was used to measure sleep parameters of the subjects. Cognitive measurements were collected, utilizing the Wechsler Intelligence Scale for Children-III (WISC-III), and the Matching Familiar Figure Test for Korean Children (MFFT-KC), while behavioral characteristics of the subjects were assessed using Conners' Global Index-Parent version (CGI-P). Descriptive statistics were calculated for demographic data, sleep parameters, and neurocognitive characteristics of ADHD patients. Spearman's correlation analyses were performed to determine the association between sleep parameters and neurocognitive measures. Moreover, multiple regression analyses were used to identify the best predictors of cognitive function among the various sleep parameters.

Results: The regression analyses revealed several meaningful correlations, suggesting that slow wave sleep, stage 2 sleep, REM sleep, and limb movement index with arousals (LMAs) as predictors of cognitive function in ADHD patients.

Conclusion: Based on our study results, sleep parameters and cognitive function were closely associated in ADHD patients; further research should be directed at clarifying this crucial link.

1. Introduction

Attention-deficit hyperactivity disorder (ADHD) is a highly common psychiatric disease among children and adolescents, with a worldwide prevalence rate as high as 6% [1]. Symptom clusters of ADHD include inattention, hyperactivity, and impulsivity, which can lead to behavioral problems, emotional dysregulation, and poor academic performance when left untreated [2]. Due to its notoriously debilitating clinical course, ADHD has attracted special clinical attention for many years. Recent research has focused on identifying predictors or endophenotypes that can aid early identification and intervention pertaining to this disorder, thereby preventing long-term detrimental consequences in children and adolescents [3–6].

Sleep patterns of subjects with ADHD have been extensively studied with the aim of explaining the possible role of sleep problems as predictors or endophenotypes of ADHD [7–9]. High prevalence rates of sleep problems in ADHD subjects have been identified, and up to 70% of ADHD patients report some type of sleep problems, with varying degrees of severity [10]. Moreover, many studies suggesting phenotypic similarities between ADHD symptoms and primary sleep disorders such as restless leg syndrome (RLS), periodic limb movement disorders (PLMDs), and obstructive sleep apnea (OSA) have been published [11,12]. Furthermore, it has been proposed that sleep problems do not originate solely as consequences of stimulant medications in ADHD patients [13]. Consequently, several studies have explored the unique sleep patterns of ADHD patients compared with controls. Objective measurements have included polysomnography, actigraphy, multiple sleep latency test, and infrared video camera [14], resulting in varied and inconclusive findings regarding discrepancies in the sleep patterns between ADHD patients and controls [15–17].

The effects of sleep problems on cognitive function in ADHD patients have been replicated in several studies. In recent studies, sleep

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problems in ADHD resulted in significant inattention and deficits in executive functioning [18], and aggravation of ADHD symptoms in patients with sleep problems has been observed [19,20]. Furthermore, reaction time on the Continuous Performance Test was affected in ADHD children with low sleep efficiency [21]. Sleep not only helped enhance procedural memory [22], but also played an integral role in the consolidation of emotional memory in ADHD children [23]. Consequently, many studies to date have hypothesized that there is a close association between cognitive and behavioral problems in ADHD and sleep.

The most significant limitation of previous studies focusing on the sleep problems of ADHD patients is that the majority of subjects participating in the studies were on medication to control ADHD symptoms, which may be a potent confounding factor complicating the results. Identifying the unique sleep patterns of ADHD patients under the effects of medication is difficult, since psychostimulants commonly prescribed for controlling ADHD symptoms can significantly affect sleep initiation and maintenance as well as sleep duration [19]. Psychostimulants can decrease total sleep time and increase sleep latency, which may complicate sleep measurements in ADHD patients [24]. Moreover, many recent studies have focused on the cognitive enhancing effect of psychostimulants and their direct effect on the prefrontal cortex [25,26]. Two existing studies have attempted to overcome these limitations using actigraphy to demonstrate the relationship between neurobehavioral characteristics of ADHD and sleep parameters [27,28]. Although easily implemented and cost-effective, such measures of sleep parameters fail to delineate detailed information regarding sleep, while excluding integral parameters evaluating rapid-eye movement (REM) sleep abnormalities or sleep-disordered breathing (SDB). There has been a previous polysomnographic study that included drug-naïve subjects, but it mainly focused on the first night effect on sleep variables in ADHD children [16].

To overcome the aforementioned methodological limitations, all of the participants in the present study were drug-naïve to exclude the effects of medication, and every subject in the study underwent polysomnography, one of the most objective tests to determine sleep problems. Moreover, cognitive test results and data pertaining to behavioral characteristics of the participants were obtained to closely investigate the relationship between neurocognitive and behavioral characteristics of ADHD and sleep. We hypothesized that sleep parameters are associated with neurocognitive and behavioral measures of ADHD patients, and that they would have significant clinical implications regarding their roles as predictors of ADHD symptoms.

2. Methods

2.1. Participants

Twenty-eight drug-naïve patients (22 males, six females) diagnosed with ADHD using the Diagnostic and Statistical Manual of Mental disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria [29] were recruited among 6- to 12-year-old patients who visited the St Vincent's Hospital Child and Adolescent Psychiatry outpatient clinic at the Catholic University of Korea. Physical and neurological disorders were excluded based on a thorough physical and neurological examination, and history taken from parents by a trained psychiatrist. Psychiatric disorders other than ADHD, and primary sleep disorders (eg, PLMS, RLS, and OSA), were excluded based on mental status examination, involving interviews conducted by a trained psychiatrist and nocturnal polysomnography. All neurocognitive tests were performed during the daytime before the overnight polysomnography took place. This study was conducted in accordance with the Declaration of Helsinki. The study protocol followed the rules of the Institutional Review Board of St Vincent's Hospital at the Catholic University of Korea, and the contents and procedures of the study were thoroughly explained to the participants and their parents; written informed consent was obtained from each participant.

2.2. Procedures

2.2.1. Conners' Global Index-Parent version (CGI-P)

Conners' global index (CGI; previously known as hyperactivity index) is a 10-item ADHD rating scale most commonly used for its clinical convenience [30]. CGI scores may be collected from either parents or teachers, with separate versions provided for each group [30]. The Korean version of CGI-Parent version (CGI-P) has exhibited high reliability and validity in a large-scale study, with a Cronbach's alpha of 0.82 [31]. The scale reflects the degree of emotional lability, restlessness, and impulsivity in ADHD children, with higher scores indicating greater severity of symptoms [30]. Among ADHD patients of 8–9 years of age, mean CGI-P scores were 7.36 ± 4.57 for males and 6.15 ± 4.20 for females [31]. In this study, all the parents of the ADHD patients completed the scale.

2.2.2. Wechsler Intelligence Scale for Children-III (WISC-III)

The Korean version of the Wechsler Intelligence Scale for Children-III (K-WISC-III) [32] was used to measure cognitive function in ADHD patients. The K-WISC-III consists of three parts including full-scale IQ (FSIQ), verbal IQ (VIQ), and performance IQ (PIQ). Subtests included in the measurement of VIQ are digit span, arithmetic, information, similarities, comprehension, and vocabulary. The PIQ subtests include block design, picture completion, picture arrangement, coding, object assembly, maze, and symbol search. FSIQ represents the sum of scale scores from verbal and performance subtests, with tables of scores from standardized samples utilized in the process. The subtests of the WISC-III have been shown to be effective predictors for discriminating ADHD patients from normal subjects [33–35], and the role of IQ scores obtained on the WISC-III in representing academic achievements in ADHD children has been elucidated [36].

2.2.3. Matching Familiar Figure Test for Korean Children (MFFT-KC)

The Matching Familiar Figure Test for Korean Children (MFFT-KC) consists of a set of 12 main pictures such that each main picture is shown with six variants [37,38]. MFFT-KC has exhibited high reliability and validity in a standardization study conducted in Korea, with a Cronbach's alpha of 0.9294 [39]. In the MFFT-KC, participants are instructed to select one variant picture that is most identical to the main picture. Subjects with shorter times to a first response and high error counts are considered impulsive, whereas those with longer times to a first response and low error counts are considered reflective [37,38]. Reportedly, results from the Matching Familiar Figure Test show good correlation with ADHD symptoms [40,41]. In this study, we recorded the time to a first response (RL_T) and response errors (RE_N) in ADHD subjects, and estimated the percentile of response errors along with the percentile of response latency (RL_P; percentile increasing with the shortening of time to the first response). Times of less than 154.69 s for 9-year-old males and 166.44 s for 9-year-old females indicated higher than moderate impulsivity, while more than nine response errors for 9-year-old males and ten errors for 9-year-old females indicated higher than moderate impulsivity [39]. (A 9-year-old group was selected for reference considering the average age of our participants.)

2.2.4. Polysomnography

Every participant underwent polysomnography at night using the EMBLA® S7000 System (Embla Systems, Inc., Broomfield, CO, USA) and Somnologica version 3.3.1. Sleep stages were classified based on electroencephalogram, electrooculogram, and electromyogram for chin