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Original Article

Working memory impairment and its associated sleep-related respiratory parameters in children with obstructive sleep apnea

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ABSTRACT

Study Objective: Working memory deficits in children with obstructive sleep apnea (OSA) have been reported in previous studies, but the results were inconclusive. This study tried to address this issue by delineating working memory functions into executive processes and storage/maintenance components based on Baddeley's working memory model.

Methods: Working memory and basic attention tasks were administered on 23 OSA children aged 8–12 years and 22 age-, education-, and general cognitive functioning-matched controls. Data on overnight polysomnographic sleep study and working memory functions were compared between the two groups. Associations between respiratory-related parameters and cognitive performance were explored in the OSA group.

Results: Compared with controls, children with OSA had poorer performance on both tasks of basic storage and central executive components in the verbal domain of working memory, above and beyond basic attention and processing speed impairments; such differences were not significant in the visuo-spatial domain. Moreover, correlational analyses and hierarchical regression analyses further suggested that obstructive apnea–hypopnea index (OAHI) and oxygen saturation (SpO_2) nadir were associated with verbal working memory performance, highlighting the potential pathophysiological mechanisms of OSA-induced cognitive deficits.

Conclusions: Verbal working memory impairments associated with OSA may compromise children's learning potentials and neurocognitive development. Early identification of OSA and assessment of the associated neurocognitive deficits are of paramount importance. Reversibility of cognitive deficits after treatment would be a critical outcome indicator.

1. Introduction

Obstructive sleep apnea (OSA) is a frequently diagnosed nocturnal breathing disorder, with a prevalence rate of around 1%–3% in the western pediatric populations [1,2]. In the Hong Kong population, the prevalence of childhood OSA has been found to affect 5% of school-aged children [3]. Childhood OSA is characterized by snoring associated with sleep fragmentation, exaggerated upper airway resistance, obstructive breathing, intermittent hypoxia, hypercapnia, and repeated arousals [4].

It was well documented that children with OSA experience difficulties on a wide cognitive spectrum, including vigilance, sustained attention, visual sequencing, and memory, as well as executive functions such as planning and organization, inhibition, mental flexibility, metacognition, and working memory [5–13]. Among the cognitive functions previously studied in OSA populations, executive functions and, in particular, working memory have been highlighted [14–16]. Working memory deficits measured by the n-back task have been demonstrated in adult OSA populations [17] and have been shown to persist even after treatment [18]. Neurocognitive outcomes, especially working memory functions in childhood OSA, are less clear. Halbower et al. [19] reported deficits in verbal executive functioning measured by sentence span and word fluency tasks. Kohler et al. [20] identified poor working memory functions in both verbal and nonverbal domains in sleep-disordered breathing children on standardized test batteries, such as the Developmental

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NEuroPSYchological Assessment (NEPSY) and the Standford–Binet Intelligence Test [20]. Biggs et al. [14] assessed working memory in children with sleep-disordered breathing using both parent-rating and neuropsychological tests. Although working memory deficits were reported by parents, no significant impairments were identified on the objective tests. The authors attributed the lack of significant objective deficits to possible sampling bias and the lack of sensitivity of the digit span test as a working memory task. Other studies also reported working memory performance in children with OSA comparable to that of controls [7,21,22]. On the other hand, some treatment studies have demonstrated that impaired neurocognitive functions could mostly be reversed after adenotonsillectomy or tonsillectomy [7,13,23]. However, changes in executive function in these studies were measured only by test batteries or combinations of stand-alone neuropsychological tests, such as digit span, verbal fluency tests, and cancellation tests, none of which sufficiently differentiate the contribution of basic cognitive processes in executive tasks. Taken together, there has been a lack of systematic and theory-driven studies on working memory functions in pediatric OSA, leading to inconsistent findings. Specifically, a closer look at the methodology of the studies reporting null findings revealed that these studies treated the executive controller and the underlying basic cognitive processes (ie, maintenance capacity/speed) of working memory as a whole, without delineating the individual components [18]. In addition, most previous childhood OSA studies measured only the verbal domain of working memory, rendering the visuo-spatial domain understudied. Therefore, a comprehensive model of working memory encompassing both the verbal and the visuo-spatial domains that could be captured by well-validated tests was called for, to shed light on the complex questions regarding working memory functioning in children with OSA.

The application of Baddeley's working memory model has been shown to be fruitful in previous studies in western [18] as well as in Chinese [17] adult OSA populations. Elucidating potential deficits in working memory in childhood OSA is critical, given its underlying role in a wide range of complex cognitive processes, including reading comprehension, mathematic ability, planning, reasoning, and problem solving, which are regarded as pivotal to children's learning and development [24]. The working memory model involves a supervisory (executive) attention system that controls the processes of two domain-specific storage components responsible for maintaining verbal (phonological loop) and visuospatial information (visuospatial sketchpad), and also an episodic buffer that provides a limited capacity multi-modal interface between systems [24,25]. By adopting the multi-component model of working memory proposed by Baddeley and Hitch [25], our experimental tasks were specifically developed to distinguish the basic and the higher-ordered functions in both verbal and visuo-spatial domains of working memory, respectively [26].

In terms of the underlying mechanisms of the OSA-related cognitive deficits, intermittent hypoxia and sleep disruption have been proposed to be the two major pathways [5]. Previous studies have suggested the role of stage 1 sleep, rapid eye movement (REM) sleep, and movement-related arousals in neurocognitive deficits in sleep-disordered children [21,27,28]. Other studies have investigated the associations between oxygen saturation, REM sleep, arousal index on cerebral oxygenation, and endothelial functions in sleep-disordered breathing [29–31]. However, other studies have shown that sleep disruptions alone were sufficient to result in neurobehavioral deficits [32]. A more recent study reported the associations of executive deficits with nocturnal hypoxemia levels in children with OSA [15]. Working memory, as one of the executive functions, might also be susceptible to respiratory disturbances during sleep. Therefore, an exploration of potential respiratory predictors of working memory functioning in children with OSA would be warranted.

To our knowledge, the present study was the first attempt to isolate the basic storage from the executive processes within each domain (verbal and visuospatial) of the working memory system in comparing children with and without OSA. It was also the first to investigate the correlations between objective sleep-related respiratory parameters with specific working memory components in this population. We hypothesized that Chinese children with OSA would perform worse than controls on working memory tests. Tasks of basic attention and vigilance would be included to control for their potential contribution to performance on working memory tasks. We also tested whether respiratory parameters would predict working memory performance in the OSA group.

2. Methods

2.1. Participants and design

This study was prepared in accordance with the Declaration of Helsinki and approved by the Chinese University of Hong Kong and Hospital Authority New Territories East Cluster Clinical Research Ethics Committee. Altogether 51 children (23 children with OSA and 28 controls) aged 8–12 years were recruited. The children with suspected OSA were from the Pediatric Respiratory Sleep Disorder and Obesity Clinic at the Prince of Wales Hospital of Hong Kong, whereas the age-matched controls were recruited from a population-based study conducted by one of our colleagues [33]. The test administrator was blinded to the background of the participants. Exclusion criteria comprised neurological co-morbidity such as history of head injury, an intercurrent upper respiratory tract infection within four weeks of recruitment, craniofacial anomalies, syndromic disorders such as Down syndrome, history of other sleep pathologies including primary snoring, prior upper airway surgery, and obesity (body mass index [BMI] > 30). Children who were diagnosed with developmental or psychiatric disorders (eg, autism, attention-deficit/hyperactivity disorder (ADHD), and specific learning disability) and/or who were on medications that could affect cognitive functions were also excluded. Written consent from parents and assent from children were obtained. Individual participants were first given the test battery consisting of experimental tasks, a general cognitive functioning screening tool (Raven's Standard Progressive Matrices), and standardized paper-and-pencil neuropsychological tests. Together with their parents, the children were then asked questions regarding their health condition. Afterward, the children underwent standard single-night polysomnography (PSG) at the hospital with the PSG montage detailed below.

2.2. Measures

2.2.1. Polysomnographic assessment

In this study, a standardized sleep study was carried out using Siesta ProFusion III PSG monitor (Compumedics Telemed, Abbotsford, Victoria, Australia). The following parameters were measured: electroencephalogram (EEG), left and right electrooculogram (EOG), electromyogram (EMG) (chin and bilateral anterior tibialis muscle), and electrocardiogram (ECG). Respiratory movements of the chest and abdomen were measured by piezo crystal effort belts. Arterial oxyhemoglobin saturation (SaO_2) was measured by a built-in oximeter with finger probe. Respiratory air-flow pressure signal was measured via nasal catheter placed at the anterior nares and connected to a pressure transducer. An oronasal thermal sensor was also used to detect any absence of airflow. Snoring was measured by a snoring microphone placed near the throat. Body position was monitored via a body position sensor. All computerized sleep data were manually scored by registered PSG technologists according to standardized criteria [34]. Obstructive apnea–hypopnea index (OAHI) was defined as the total number of obstructive and mixed apneas