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Original Article

Reduced sleep-associated consolidation of declarative memory in attention-deficit/hyperactivity disorder

Alexander Prehn-Kristensen [a,*], Robert Göder [b], Jochen Fischer [a], Ines Wilhelm [c], Mareen Seeck-Hirschner [b], Josef Aldenhoff [b], Lioba Baving [a]

[a] Center for Integrative Psychiatry, Department of Child and Adolescent Psychiatry and Psychotherapy, Christian-Albrechts-University School of Medicine, 24105 Kiel, Germany
[b] Center for Integrative Psychiatry, Department of Psychiatry and Psychotherapy, Christian-Albrechts-University School of Medicine, 24105 Kiel, Germany
[c] Department of Neuroendocrinology, University of Lübeck, 23538 Lübeck, Germany

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ABSTRACT

Objective: Sleep supports the consolidation of declarative memory. Patients with attention-deficit/hyperactivity disorder (ADHD) are not only characterized by sleep problems but also by declarative memory deficits. Given that the consolidation of declarative memory during sleep is supported by slow oscillations, which are predominantly generated by the prefrontal cortex, and that ADHD patients display low prefrontal brain activity, we assumed that ADHD patients show reduced sleep-associated consolidation of declarative memory.

Methods: The impact of sleep on the consolidation of declarative memory was examined with a picture recognition task. Twelve ADHD patients (10–16 years) and 12 healthy controls participated in two experimental conditions: in the sleep condition, learning was performed in the evening and picture recognition was tested after nocturnal sleep; in the wake condition, learning was conducted in the morning while retrieval took place after a day of wakefulness.

Results: Analyses of recognition accuracy revealed reduced sleep-associated enhancement of recognition accuracy in ADHD. While sleep-associated enhancement of recognition accuracy was correlated with slow oscillation power during non-REM sleep in healthy controls, no such correlations were observed in ADHD.

Conclusions: These data indicate a deficit in sleep-associated consolidation of declarative memory in ADHD. Moreover, our results suggest reduced functionality of slow oscillations in sleep-associated consolidation of declarative memory in ADHD.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most prevalent (3–6%) psychiatric disorder in children and adolescents, characterized by patterns of inattention, hyperactivity, and impulsiveness, often persisting into adulthood [1]. Neurobiological hallmarks of ADHD are reduced functionality of the prefrontal cortex (PFC), resulting in deficits of attention control and executive functions as core symptoms of ADHD [2–4].

Since cognitive functions involving the PFC are susceptible to sleep deficits and deprivation [5–7], it is proposed that sleep problems may cause core symptoms in ADHD [8]. Patients with ADHD exhibit higher daytime sleepiness, higher apnea–hypopnea index, delayed sleep onset, and lower sleep efficiency [9–11]. Sleep not only supports attention control and executive functions, but also remarkably benefits the consolidation of declarative memory [12,13]. Thus, the hypothesis emerges that declarative memory deficits in ADHD [14,15] are enhanced by sleep alteration.

In healthy adults, declarative memory is supported by slow wave sleep (SWS) [12,13]. Slow oscillations (<1 Hz) during SWS—predominantly generated by the prefrontal cortex [16,17]—have a particularly enhancing effect on sleep-associated declarative memory consolidation [18,19]. Sleep in the first half of the night is characterized by a large amount of SWS, and therefore non-REM sleep during the first sleep cycle is critically involved in sleep-associated consolidation of declarative memory [20]. Comparable to adults, non-REM sleep enhances the consolidation of declarative memory in healthy children [21–24]. The contribution of slow oscillations to sleep-associated consolidation of declarative memory in children, however, has not yet been reported.

The aim of the present study was to examine the impact of sleep on the consolidation of declarative memory in children and adolescents with ADHD. Based on the findings that (a) patients with

* Corresponding author. Address: Center for Integrative Psychiatry, Department of Child and Adolescent Psychiatry and Psychotherapy, Christian-Albrechts-University School of Medicine, Niemannsweg 147, 24105 Kiel, Germany.
E-mail address: a.prehn@zip-kiel.de (A. Prehn-Kristensen).

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ADHD display reduced prefrontal activity and that (b) forebrain structures are critically involved in declarative memory consolidation during sleep, we hypothesized that patients with ADHD show reduced sleep-associated enhancement of declarative memory due to a reduced impact of slow oscillations on memory consolidation during sleep. Additionally, we explored whether or not sleep-associated memory consolidation in ADHD is biased by emotion stimulus content.

2. Methods

2.1. Participants

ADHD patients and controls (right-handed and with normal or corrected-to-normal vision) were recruited by announcements in local schools and in our outpatient clinic. Due to the high prevalence of ADHD in males and in order to control for gender-dependent effects of emotional reactions [25], only boys were included. All participants and their parents were interviewed with a German translation of the Revised Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL) [26,27] and a standard parent-reported questionnaire (the Child Behavior Checklist, CBCL [28]) in order to assess psychiatric symptoms. ADHD patients were excluded if they displayed any comorbidity apart from oppositional defiant disorder (ODD). Controls were excluded if they displayed psychiatric abnormalities. Further exclusion criteria for all participants were a below average intelligence quotient (IQ < 85) measured by Culture Fair Intelligence Test Revised Vision (CFT-R) [29], significant memory impairments measured by Diagnosticum für Cerebralschädigung (DCS, cut-off score: <16th percentile of the reference sample) [30], or sleep-related disorders measured with an adaptation of the Pittsburgh Sleep Quality Index [31]. Due to these criteria, twelve patients and four controls were excluded after the diagnostic session. Another four patients and one control child ceased participation in the study due to motivational reasons.

The remaining 12 ADHD patients, aged 10–16, and twelve healthy controls, aged 11–14 had at least an average intelligence quotient and no significant memory impairments. Patients and healthy controls did not differ significantly in age ($p = .542$), IQ ($p = .611$) or DCS score ($p = .429$, Table 1). All patients met the criteria for ADHD according to DSM-IV [1]. Three patients with ADHD additionally exhibited an oppositional defiant disorder (ODD). Five patients took methylphenidate but discontinued medication 48 h (approximately 12 half-lives) prior to each experimental condition. Healthy controls did not exhibit psychiatric symptoms. Parents of the ADHD group reported more internalizing ($p < .001$) and externalizing ($p < .001$) symptoms in their children than parents of healthy control subjects (Table 1).

All participants and their parents gave written informed consent, and participants were reimbursed with a voucher for their participation. The study was approved by the ethics committee of the medical faculty of the University of Kiel and followed the ethical standards of the Helsinki Declaration.

2.2. Declarative memory task

A picture recognition task was used which had already been conducted in an earlier study to investigate sleep-associated memory consolidation in children [23]. In total, 360 emotional and neutral pictures were used of which 70% consisted of pictures from the International Affective Picture System [IAPS [32]; valence for emotional pictures: 3.0 ± .06 (mean ± SEM), and neutral pictures: 5.2 ± .06, $t(256) = 24.74$, $p < .001$; arousal for emotional pictures: 5.5 ± .07, and neutral pictures: 3.2 ± .08, $t(256) = 23.86$, $p < .001$]. The remaining pictures (30%) were taken from our own database and matched with IAPS picture content. Two sets of pictures were generated, both consisting of 180 pictures (50% emotional, i.e., high arousing, and 50% neutral, i.e., low-arousing). During the learning session, 120 pictures were presented randomly intermixed on a 15-in. monitor. Each trial started with the appearance of a fixation cross (500 ms), followed by the target picture (1500 ms). Then, the Self Assessment Manikin Scale for Arousal (SAM) [33] appeared on the monitor and participants were supposed to judge the degree of the picture's arousal by pressing one of nine response buttons (ranging from 1 = very low to 9 = very high). After the response was given, the next trial started.

In the recognition test, the same 120 pictures from the learning session along with 60 new pictures were presented in pseudo-randomized order. Each trial started with the fixation cross (500 ms), followed by a target picture (1500 ms). Participants were asked to indicate whether they had seen the target picture during the current learning session ("old") or not ("new") by pressing one of two response buttons. The next trial did not start until an answer was given. Stimulus presentation and response recording were conducted with E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA; http://www.pstnet.com) on an ASUS X50R notebook (monitor size: 15.4″).

2.3. Procedure

Each participant underwent two experimental conditions. The sleep condition consisted of a learning session in the evening and a retrieval session in the morning after a 10-h interval which included nocturnal sleep. In the wake condition, the learning session was conducted in the morning and the retrieval session took place after a 10-h wake interval. The order of picture sets and conditions (each being conducted at least 2 weeks apart) was counterbalanced across both groups.

At the beginning of each session, participants were requested to rate their current emotional state using the SAM scales for valence and arousal and to assess their alertness using a 10-cm analog

Table 1
Characteristics of participants.

		ADHD	Controls	ADHD vs. Controls	
		Mean ± SEM	Mean ± SEM	*t*	*p*
Age		12.99 ± .52	12.64 ± .24	.62	.542
IQ		111.67 ± 2.56	109.83 ± 2.45	.51	.611
Figural memory		51.85 ± 8.23	44.03 ± 5.12	.81	.429
CBCL (T scores)	Attention problems	67.75 ± 1.66	51.25 ± .65	9.27	**<.001**
	Delinquent rule-breaking behavior	60.25 ± 1.88	50.0 ± .0	5.44	**<.001**
	Aggressive behavior	60.67 ± 2.64	50.58 ± .43	3.77	**.001**
	Internalizing	60.92 ± 1.81	48.75 ± 2.0	4.51	**<.001**
	Externalizing	59.58 ± 2.92	45.83 ± 1.19	4.36	**<.001**

Bold values indicate a significant comparison; ADHD, attention-deficit hyperactivity disorder; CBCL, child behavior checklist.