



# Memory consolidation of socially relevant stimuli during sleep in healthy children and children with attention-deficit/hyperactivity disorder and oppositional defiant disorder: What you can see in their eyes

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## ABSTRACT

Children with attention-deficit/hyperactivity disorder (ADHD) display deficits in sleep-dependent memory consolidation, and being comorbid with oppositional defiant disorder (ODD), results in deficits in face processing. The aim of the present study was to investigate the role of sleep in recognizing faces in children with ADHD+ODD. Sixteen healthy children and 16 children diagnosed with ADHD+ODD participated in a sleep and a wake condition. During encoding (sleep condition at 8 p.m.; wake condition at 8 a.m.) pictures of faces were rated according to their emotional content; the retrieval session (12 h after encoding session) contained a recognition task including pupillometry. Pupillometry and behavioral data revealed that healthy children benefited from sleep compared to wake with respect to face picture recognition; in contrast recognition performance in patients with ADHD+ODD was not improved after sleep compared to wake. It is discussed whether in patients with ADHD+ODD social stimuli are preferentially consolidated during daytime.

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## 1. Introduction

Recognizing individuals and their emotional state by their face is essential for appropriate social interaction (Adolphs & Birmingham, 2011; Gobbi & Haxby, 2007). Humans are inherently social, and the ability to detect faces or to recognize face identity can already be seen in newborn infants (Hoehl & Peykarjou, 2012; Simion & Giorgio, 2015; Wilmer et al., 2010). However, children's ability to recognize faces is also clearly influenced by learning and experience (da Silva Ferreira, Crippa, & de Lima Osorio, 2014; Goodman et al., 2007; Macchi Cassia, Luo, Pisacane, Li, & Lee, 2014; Proietti, Macchi Cassia, dell'Amore, Conte, & Bricolo, 2015). On the other hand, deficits in identifying faces can lead to serious social consequences as seen in prosopagnosia. (Susilo & Duchaine, 2013; Yardley, McDermott, Pisanski, Duchaine, & Nakayama, 2008). Also, several childhood and adult psychiatric disorders are accompanied by deficits in recognizing facial

identities or emotional expressions which may amplify aberrant social behavior (Bortolon, Capdevielle, & Raffard, 2015; Collin, Bindra, Raju, Gillberg, & Minnis, 2013; Ventura, Wood, Jimenez, & Hellemann, 2013). With a prevalence of 5.7%, disruptive behavior disorders are one of the most prevalent psychiatric diseases in childhood and adolescence (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015) and are characterized by profound deficits in socio-emotional development (American Psychiatric Association, 2013). Disruptive behavior disorders include oppositional defiant disorder (ODD) or conduct disorder (CD) which are highly comorbid with attention-deficit/hyperactivity disorder (ADHD) (Waschbusch, 2002). Particularly, childhood ADHD in combination with ODD is a high risk factor for later antisocial behavior often resulting in young adult delinquency. Patients with disruptive behavior disorder display defiant performance when it comes to recognizing faces and their emotional states (Aspan, Bozsik, Gadoros, & Nagy, 2014; Cadesky, Mota, & Schachar, 2000; Downs & Smith, 2004) and show altered brain activity in emotion-related brain regions (amygdala, prefrontal cortex) while processing social stimuli such as faces (Jones, Laurens, Herba, Barker, & Viding, 2009;

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Lozier, Cardinale, VanMeter, & Marsh, 2014; Marsh et al., 2008; White et al., 2012).

Sleep supports the consolidation of various memory systems: post-learning sleep benefits the integration of newly encoded, fragile memory information into more stable, long-term memory traces (Diekelmann & Born, 2010; Rasch & Born, 2013; Wilhelm, Prehn-Kristensen, & Born, 2012). Recently, we observed that children with ADHD display altered sleep-dependent memory consolidation; i.e. sleep in children with ADHD benefits procedural memory more than in healthy children (Prehn-Kristensen, Göder et al., 2011; Prehn-Kristensen, Molzow et al., 2011), and sleep in ADHD supports declarative memory less than in healthy children (Prehn-Kristensen, Göder et al., 2011; Prehn-Kristensen, Molzow et al., 2011; Prehn-Kristensen et al., 2014, 2013). We assumed that in ADHD the sleep-dependent consolidation of declarative memory is disturbed due to dysfunctional prefrontal brain activity during sleep (Wilhelm et al., 2012). There is a whole body of evidence that sleep supports the memory for emotional events (Wagner, Gais, & Born, 2001; Wagner, Hallschmid, Rasch, & Born, 2006) or scenes (Hu, Stylos-Allan, & Walker, 2006; Payne, Stickgold, Swanberg, & Kensinger, 2008; Prehn-Kristensen et al., 2009). The question of whether or not sleep modulates the affective tone of learned emotional stimuli, however, is still under debate: Some authors emphasize that the affective tone of learned emotional stimuli is attenuated after sleep (Walker & van der Helm, 2009), while others have not found support for the hypothesis that sleep tunes down the affective tone of consolidated stimulus material (Baran, Pace-Schott, Ericson, & Spencer, 2012; Deliens, Neu, & Peigneux, 2013; Groch, Wilhelm, Diekelmann, & Born, 2013; Wiesner et al., 2015).

Studies in healthy adults have reported that sleep also benefits the memory recognition of social stimuli such as pictures of faces with neutral or emotional expressions (Mogras, Guillem, & Godbout, 2008; Mogras, Godbout, & Guillem, 2006; Wagner, Hallschmid, Verleger, & Born, 2003; Wagner, Kashyap, Diekelmann, & Born, 2007). A recent study of young patients with autism spectrum disorder (ASD) reported that sleep in ASD patients amplified altered recognition of neutral faces (Tessier, Lambert, Scherzer, Jemel, & Godbout, 2015). Autism is characterized by profound difficulties in communication and social interactions (American Psychiatric Association, 2013) and is associated with deficits in face processing (Harms, Martin, & Wallace, 2010; Nomi & Uddin, 2015). To date, no information – neither in healthy nor in diseased children – is available about whether or not sleep modulates the affective tone of learned social stimuli such as faces.

The aim of the present study is to investigate the influence of sleep on the picture recognition of emotional faces and their affective regulation in children with ADHD and comorbid ODD (ADHD+ODD) in comparison to healthy children. Based on our previous studies, we hypothesize that healthy children benefit more from sleep with respect to the recognition of faces compared to children with ADHD+ODD. Besides behavioral responses, we use pupillometry as an objective measurement to assess recognition performance on a psychophysiological level (Goldinger, He, & Papesh, 2009; Laeng, Sirois, & Gredeback, 2012; Papesh, Goldinger, & Hout, 2012). Since emotional face expression might influence the sleep-related face recognition performance, different emotional conditions (happiness, fear, anger, and neutral) are introduced on an explorative level. The question of whether or not sleep regulates affective tone is still under debate. Therefore, we do not have any specific hypothesis about the impact of sleep on the emotional assessment of consolidated pictures.

## 2. Methods

### 2.1. Participants

Sixteen male children diagnosed with ADHD and ODD aged between 8 and 11 years ( $M = 11.4$ ,  $SD = 1.5$ ) and 16 healthy male children aged between 9 and 11 years

( $M = 11.1$ ,  $SD = 1.1$ ) participated in this study. Patients and controls did not differ in age, pubertal stage, or IQ (see Table 1). All children and their parents were interviewed using a German translation of the Revised Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (Kiddie-SADS-PL; Delmo et al., 2000; Kaufman et al., 1997). A standardized questionnaire, the Child Behavior Checklist (CBCL; Achenbach, 1991), was filled out by parents to assess any psychiatric symptoms of their children. According to the DSM-IV-TR, all patients met the criteria for ADHD (13 x combined type, 3 x inattentive type) and comorbid oppositional defiant disorder (ODD). In addition, one patient suffered from nocturnal enuresis. Controls were excluded if they displayed any psychiatric abnormalities. Exclusion criteria for all participants were: below average intelligence quotient ( $IQ < 85$ ), as measured by the Culture Fair Intelligence Test 20-Revised Version (CFT 20-R; Weiß & Osterland, 2013), or profound memory impairment, as measured by a figural learning test to assess cerebral dysfunctions (Diagnostikum für Cerebralschädigung, DCS; Lamberti & Weidlich, 1999; cut-off score: 16th percentile of the reference sample).

According to the Sleep-Self-Report questionnaire (SSR; Owens, Spirito, McGuinn, & Nobile, 2000; critical score:  $>24$ ) patients rated themselves as having more sleep problems than healthy controls [ADHD: Median: 23.5, Range: 21–40,  $M = 25.4$ ,  $SD = 4.8$ ; healthy controls: Median: 20.5, Range: 18–28,  $M = 20.9$ ,  $SD = 2.5$ ; ADHD vs. controls:  $t(30) = 3.4$ ,  $p = 0.002$ ]; the same was true for parental ratings on the Children Sleep Habit Questionnaire [CSHQ; Owens, Spirito, & McGuinn, 2000; critical score  $>41$ ; ADHD: Median: 42.5, Range: 36–60,  $M = 43.9$ ,  $SD = 5.9$ ; healthy controls: Median: 38.5, Range: 33–45,  $M = 38.6$ ,  $SD = 4.0$ ; ADHD vs. controls:  $t(30) = 2.9$ ,  $p = 0.006$ ]. The ratings of seven patients and two controls were above the critical SSR score; parents of ten patients and three controls rated the sleep habits of their children above the critical CSHQ score. All participants had normal or corrected-to-normal vision. To control for possible group differences in emotional face processing, patients and controls completed the computer-based program for the training and testing of facial affect recognition (Frankfurter Test und Training fazialen Affekts, FEFA; Bolte et al., 2002). Although patients performed worse than controls in general [FEFA sum score patients:  $M = 69.7\%$ ,  $SD = 2.9$ ; controls:  $M = 79.2$ ,  $SD = 7.5$ ; patients vs. controls:  $t(30) = 2.75$ ,  $p = 0.01$ ] and made more errors regarding neutral pictures ( $M = 90.2\%$ ,  $SD = 16.3$ ; controls:  $M = 99.0$ ,  $SD = 3.7$ ; patients vs. controls:  $t(29) = 2.06$ ,  $p = 0.048$ ), the affect recognition performances concerning angry, fearful, or happy faces were not different between groups ( $p > 0.147$ ). According to self-reports, all participants were free of any neurological, immunological, or endocrinological diseases. Parental reports revealed that no participant took any medication except for methylphenidate in eleven ADHD patients; however, these patients discontinued medication 48 h (approximately twelve half-lives) prior to each experimental condition.

All participating children and their parents gave written, informed consent and 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. Procedure

Each participant took part in a sleep and a wake condition. The sleep condition consisted of an encoding phase in combination with a baseline measurement in the evening at 8 p.m. and a retrieval session in the morning after a 12-h interval which included nocturnal sleep. In the wake condition, the encoding session and baseline measurement were conducted in the morning at 8 a.m.; the retrieval session took place after a 12-h wake interval. The order of conditions (each being conducted at least two weeks apart) was counterbalanced across both groups. All experimental sessions were carried out under laboratory conditions: Children were seated in a comfortable EEG chair; the distance between the children's eyes and the monitor was constantly kept at 60 cm; and the room illumination was the same for all participants.

At the beginning of each session, participants rated their current emotional state using the Self-Assessment Manikin (SAM; Bradley & Lang, 1994) scales for valence and arousal and their tiredness using a 10-cm analog scale (0 = very tired; 10 = very alert). In addition, the current alertness was measured by a computer-based alertness test (KITAP subtest "Alertness"). In the evening sessions, participants were asked to report on whether or not they slept during the daytime or intake of any medication.

### 2.3. Picture recognition paradigm

A total of 320 black and white pictures of faces were used showing different kinds of emotional expressions (80 angry, 80 fearful, 80 happy, 80 neutral faces). Pictures of faces were taken from the following databases: Database of facial expressions in young, middle-aged, and older women and men FACES (Ebner et al., 2010), NimStim set of Facial Expressions (Tottenham et al., 2009), 3D Facial Emotional Stimuli (Gur et al., 2002), Karolinska Directed Emotional Faces Systems (KDEF; Lundqvist et al., 1998), and Productive Aging Laboratory Face Database (Minear & Park, 2004). Prior to the experiment, a preselection of 180 pictures of females and 177 pictures of males were presented to a group of 12 healthy children (aged 9–12 yrs., 7 girls) and 12 healthy adults (aged 25–48 yrs., 6 women) in order to be able to remove pictures which depicted ambiguous emotional face expression. 160 female and 160 male

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