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Pre-schoolers suffering from psychiatric disorders show increased cortisol secretion and poor sleep compared to healthy controls

Martin Hatzinger [a,b,*], Serge Brand [b], Sonja Perren [c], Anges von Wyl [d], Stephanie Stadelmann [e], Kai von Klitzing [e], Edith Holsboer-Trachsler [b]

[a] Psychiatric Services Solothurn, Department of Adult Psychiatry, Solothurn, Switzerland
[b] Psychiatric Hospital of the University of Basel, Depression and Sleep Research Unit, Wilhelm Kleinstr. 27, 4012 Basel, Switzerland
[c] Jacobs Center for Productive Youth Development, University of Zurich, Switzerland
[d] Institute of Psychology, University of Zurich, Switzerland
[e] Department of Child and Adolescent Psychiatry, Psychotherapy, and Psychosomatics, University of Leipzig, Germany

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ABSTRACT

Background: Various studies of child cortisol secretion and sleep show a close association between poor sleep, deterioration of the HPA axis and unfavorable psychological functioning. However, there is little evidence as to whether these associations are clearly present in pre-school children suffering from psychiatric disorders.

Method: A total of 30 pre-schoolers suffering from psychiatric disorders (anxiety, adjustment disorders, emotional and attachment disorder; hyperactivity or oppositional disorder) and 35 healthy controls took part in the study. Saliva cortisol secretion was assessed both at baseline and under challenge conditions. Sleep was assessed via activity monitoring for seven consecutive days and nights, using a digital movement-measuring instrument. Parents and teachers completed questionnaires assessing children's cognitive, emotional and social functioning. The Berkeley Puppet Interview provided child-based reports of cognitive–emotional processes.

Results: Compared to healthy controls, children suffering from psychiatric disorders had much higher cortisol secretion both at baseline and under challenge conditions. Sleep was also more disturbed, and parents and teachers rated children suffering from psychiatric disorders as cognitively, emotionally and behaviorally more impaired, relative to healthy controls. Children with psychiatric disorders reported being more bullied and victimized.

Conclusions: In five-year old children the presence of psychiatric disorders is reflected not only at psychological, social and behavioral, but also at neuroendocrine and sleep-related levels. It is likely that these children remain at increased risk for suffering from psychiatric difficulties later in life.

1. Introduction

More than 50% of psychiatric disorders emerge before the age of 15 years (Paus et al., 2008; Giedd, 2008). In Germany, hospitalizations of children and adolescents diagnosed with psychiatric disturbances increased by 38.1% between 2000 and 2007 (Holtmann et al., 2010). Thus, it would appear that psychiatric disorders in children and adolescents (that is, severe emotional, cognitive, behavioral and social difficulties) are becoming more common and constitute a growing concern for children, parents, teachers, and for the public health system.

Additionally, there is virtually no psychiatric disorder which is not also associated with poor sleep. To give a few examples, in adults, impaired sleep has been observed in patients suffering from depressive disorders (Schüle et al., 2001; Pillai et al., 2011), anxiety disorders (Koffel and Watson, 2009), specific phobias (Brand et al., 2011a), posttraumatic stress disorders (McLay et al., 2010), and bipolar disorders (Murray and Harvey, 2010; Smith et al., 2005). Similarly, an association between poor sleep and poor psychological functioning is also apparent in infants suffering from infantile colic (Brand et al., 2011b), healthy pre-schoolers (Hatzinger et al., 2008, 2010), children (Gregory and Sadeh, 2011), children with ADHD (Kirov et al., 2007; Cortese et al., 2006), adolescents (Lund et al.,

* Corresponding author. Psychiatric Adult Services of Solothurn, Switzerland. Tel.: +41 32 627 14 50; fax: +41 32 627 14 66.
E-mail address: martin.hatzinger@spital.so.ch (M. Hatzinger).

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2010), and adolescents suffering from bipolar disorders (Heiler et al., 2011; Lorberg et al., 2010), alcohol abuse (Gromov and Gromov, 2009; Lorberg et al., 2010) and depressive disorders (Lofthouse et al., 2009; see Brand and Kirov 2011; Kirov and Brand, 2011; Ivanenko, 2008 for overview). Of note, restorative and adequate sleep is fundamental to brain plasticity (Dang-Vu et al., 2006) and brain development (Peiraro and Algarin, 2007). Thus, chronic sleep disturbances and neuronal loss during childhood seem to be causally related (Jan et al., 2010). Importantly, data from longitudinal studies indicate that for instance sleep difficulties between the ages three and five years predict early onset of any use of alcohol, marijuana, and illicit drugs, as well as early onset of occasional or regular use of cigarettes by age 12 to 14 (Wong et al., 2004). Likewise, 9-year old children reporting chronic insomnia were at increased risk of developing adverse physical and mental health consequences five years later, along with maladaptive lifestyle coping strategies such as smoking and alcohol consumption (Zhang et al., 2011). Moreover, Gregory et al. (2005, 2009) were able to show that sleep problems during childhood increased the risk of developing anxiety and depressive disorders in adulthood. These studies, therefore, suggest that severe sleep problems in pre-schoolers and older children do persist and predict poor mental health not only in early and mid-adolescence, but also in early adulthood.

In addition to evidence of a relation between sleep and psychological functioning, current concepts suggest that psychophysiological arousal is related to poor sleep. In this regard, one of the most studied and investigated outcome variables of psychophysiological arousal is cortisol secretion, reflecting hypothalamus–pituitary–adrenocortical-axis activation (HPA AA). There is evidence that poor sleep is associated with increased cortisol secretion (Buckley and Schatzberg, 2005; Steiger, 2007) both in healthy adults (Hori et al., 2011) and adults suffering from specific phobias (Brand et al., 2011a), but also much earlier in life, in infants suffering from infantile colic (Brand et al., 2011b), in healthy though sleep-deprived pre-schoolers (Hatzinger et al., 2008, 2010; Raikkönen et al., 2010), and in sleep-deprived healthy adolescents (Zeiders et al., 2011).

Moreover, there is compelling evidence that HPA AA is compromised among those with mental disorders (for review, see Holsboer and Ising, 2010; Jezova and Hlavacova, 2008; Wolkowitz et al., 2010; de Kloet et al., 1998). For example, elevated cortisol levels have been observed in adults suffering from major depressive disorders (Schüle et al., 2001; Pillai et al., 2011; Heim et al., 2008), posttraumatic stress disorders (McFarlane et al., 2011), specific phobias (Brand et al., 2011a), and bipolar disorders (Steen et al., 2011). HPA AA has also been observed to vary with psychological functioning and psychiatric disorders in children and adolescents. However, the direction of association seems more complex. A *de*crease in HPA AA has been observed in boys with attention-deficit/hyperactivity disorder and disruptive behavior problems (Stadler et al., 2011), in children with ADHD (Pesonen et al., 2011), and more generally in children with externalizing problems, (i.e., aggressive or other antisocial behavior; Flinn and England, 1997; Moss et al., 1995; Haltigan et al., 2011). In contrast, Hatzinger et al. (2007) were able to show that in 5-years old boys with hyperactivity/impulsivity and emotional problems HPA system activity was significantly *in*creased. Furthermore, cross-sectional studies have shown task-related increases in salivary cortisol to be linked to a pattern of negative control-related beliefs (that is, low self-perceived ability to cope with stressful situations; Granger et al., 1996) as well to with internalizing symptoms, which are typically related to disturbances in mood and anxiety (Zahn-Waxler et al., 2000). Similarly, high basal levels of cortisol (particularly in the early morning) and heightened stress responses (that is, strong behavioral reactions to unfamiliar events) have been noted in young children described as behaviorally inhibited and shy (Kagan et al., 1988; Schmidt et al., 1997; Nachmias et al., 1996; Watamura et al., 2003). Greatly increased HPA AA has also been observed in children suffering from separation anxiety disorders, relative to healthy controls (Brand et al., 2011c), as well as in children suffering from social phobia when starting school (Russ et al., in press). Finally, studies of depression in childhood lend support to the view that depressive symptoms and increased HPA AA are closely related in pre-schoolers (Luby et al., 2003; see Lopez-Duran et al., 2009 for review).

Taken together, numerous publications suggest that poor sleep is related to poor mental functioning and psychophysiological hyperarousal as reflected in raised cortisol secretion. Data from longitudinal studies further indicate that untreated sleep difficulties during early and mid-childhood predict poor mental development. However, no data related to mental health and sleep are concomitantly available from pre-schoolers suffering from psychiatric disorders. But given the high risk of these young children reporting psychological difficulties in later life, we believe that basic data on psychoendocrinology (i.e., cortisol secretion), mental health and sleep are essential for both intervention and prediction.

The following four hypotheses were formulated. First, following Luby et al. (2003), Lopez-Duran et al. (2009), Russ et al. (in press), Kagan et al. (1988), Schmidt et al. (1997), Nachmias et al. (1996) Watamura et al. (2003) and Brand et al. (2011c), we expected higher cortisol secretion both at baseline and during a challenge condition in children with psychiatric disorders as compared to healthy controls. Second, following Kirov et al. (2007), Räikkönen et al. (2010), Hatzinger et al. (2008, 2010), Hori et al. (2011), and Zeiders et al. (2011), we anticipated poor sleep patterns in children with psychiatric disorders as compared to healthy controls. Third, by definition, we expected to find greater emotional and behavioral difficulties in children with psychiatric disorders as compared to healthy controls. Last, we anticipated that unfavorable psychological functioning, poor sleep and increased HPA AA would be associated in the sample of children with psychiatric disorders.

2. Methods

2.1. Participants

A total of 35 of children suffering from emotional and behavioral difficulties were referred from residents and pediatricians to the Department of Child and Adolescent Psychiatry, University of Basel (Switzerland) for further diagnoses and treatment. Parents of 30 children consented to participation in the study. Average age was 4.84 years (SD = .49); 7 were girls and 23 were boys (gender ratio: 7/23 = .30). Based on ICD-10 codifications, the following diagnoses were made: F40.9: Phobic anxiety disorders, unspecified ($n = 2$); F41.9: Anxiety disorder, unspecified ($n = 2$); F43: Reaction to severe stress, and adjustment disorders ($n = 4$) (clustered to and termed as anxiety and adjustment disorders; $n = 8$); F90: Hyperkinetic disorder ($n = 3$); F91: Conduct disorder ($n = 5$) (clustered to and termed as behavioral disorders; $n = 8$); F93.9: Childhood emotional disorder, unspecified ($n = 3$); F94.9: Childhood disorder of social functioning, unspecified ($n = 6$) (clustered to and termed as emotional and social disorders; $n = 9$); F98.9: Unspecified behavioral and emotional disorders with onset usually occurring in childhood and adolescence ($n = 5$) (clustered to and termed as other psychiatric disorders; $n = 5$).

To provide a comparison group of healthy controls, data were used for 35 children from a larger sample of 102 (see Hatzinger et al., 2007, 2008, 2010 for a detailed description of the entire sample). The selected group consisted of nine girls and 26 boys (gender ratio: 9/26 = .34), and mean age was $M = 4.91$ years (SD = .48). For selection,