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Sleep and neurocognitive functioning in children with eczema

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ABSTRACT

Sleep disruption in childhood is associated with clearly defined deficits in neurocognition and behaviour. Childhood eczema is also a potent cause of sleep disruption though it is unknown whether it too results in neurocognitive deficits. To test this hypothesis, neurocognitive (WISC-IV), parental-reported sleep quality (Sleep Disturbance Scale of Children (SDSC)) and overnight polysomnographic (PSG) data were collected in 21 children with eczema and 20 healthy controls (age range 6–16 years). Children with eczema had worse sleep quality on both PSG (notably increased nocturnal wakefulness, a higher number of stage shifts and a longer latency to REM onset) and parental report. In addition, they demonstrated significant neurocognitive deficits (especially verbal comprehension, perceptual reasoning and to a lesser extent working memory) with a composite Full Scale IQ 16 points lower than controls. Parental reported sleep problems but not PSG parameters were correlated with reduced neurocognitive performance. However, hierarchical regression analyses revealed that eczema status was predictive while sleep fragmentation (parental or PSG) was not predictive of neurocognitive performance. As this is the first study to systematically examine neurocognitive functioning in children with eczema and given the finding of significant deficits it merits replication especially given the prevalence of the condition. The unanswered question is whether these cognitive deficits normalise with effective eczema treatment and if this is mediated by improvements in sleep architecture.

1. Introduction

A frequently reported symptom in children with eczema is disturbed sleep typically characterised by poor sleep initiation and frequent and prolonged awakenings, which are thought to be related to nocturnal itching and the subsequent scratch response (Bartlet et al., 1997; Chamlin et al., 2005a, 2005b; Dahl et al., 1995; Daud et al., 1993; Emerson et al., 2000; Fennessy et al., 2000; Lawson et al., 1995; Long et al., 1993; Monti et al., 1989; Reid and Lewis-Jones, 1995; Reuveni et al., 1999; Stores et al., 1998). In otherwise healthy children, disturbed sleep has been associated with behavioural deficits (e.g., hyperactivity, aggression, anxiety, etc.) (Buckhalt et al., 2009; Hiscock et al., 2007; Huang et al., 2004; O'Brien et al., 2003; Owens et al., 2000; Sadeh et al., 2002; Willoughby et al., 2008) and reduced neurocognitive performance (e.g., lower IQ, impaired memory, reduced academic performance, reduced attentional capacity, etc.) (Buckhalt et al., 2009; Hiscock et al., 2007; Randazzo et al., 1998; Sadeh et al., 2002). In children with eczema, disturbed sleep has also been associated with behavioural deficits (e.g., irritability, oppositional behaviour and Attention Deficit Hyperactivity Disorder) (Camfferman et al., 2010a; Dahl et al., 1995; Romanos et al., 2010) but to date, its impact on neurocognitive performance is unknown. Given the findings that eczema disturbs sleep and, moreover, the association between disturbed sleep and reduced neurocognitive performance in otherwise healthy children, we predict that neurocognitive performance would be reduced in children with eczema and, moreover, the greater the sleep deficit the worse the neurocognitive performance. Therefore, the aims of the present study are to examine the neurocognitive profile of children with eczema compared to controls and to evaluate the relationship between sleep and neurocognitive performance.

2. Materials and method

2.1. Participants

Parents and their children with eczema (n = 21) (aged 6–16 years) attending Allergy and Dermatology clinics at the Women's and Children's Hospital, a tertiary referral centre for the state of South

Abbreviations: IQ, intelligence quotient; EEG, electroencephalography; EMG, electromyography; EOG, electrooculography; ECG, electrocardiography; ISSAC, International Study of Asthma and Allergies in Childhood; LTE_4, leukotriene E_4; NART-R, National Adult Reading Test Revised; NREM, Non rapid eye movement sleep; OAHI, Obstructive Apnoea Hypopnoea Index; PSG, polysomnography; REM, rapid eye movement sleep; SCORAD, Scoring of Atopic Dermatitis Index; SDB, Sleep disordered breathing; WISC-IV, Wechsler Intelligence Scale for Children.

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Australia, were recruited to the study and compared to healthy case controls without eczema (n = 20) (aged 6–16 years) recruited from advertisements within the hospital. Children with eczema were diagnosed by using standardised clinical criteria (Hanifin, 1984). We excluded children with a history of cranio-facial abnormality, cleft palate, neurological disorder, muscular dystrophy, cardio-respiratory conditions associated with hypoxia, intellectual delay, prematurity, developmental delay and behaviour disorder. The study was approved by the relevant Hospital and University Human Research Ethics Committees and written informed consent was obtained from all participating families. These participants overlap with those in a larger study examining behaviour and self-reported sleep in children with eczema (Camfferman et al., 2010a).

2.2. Procedure

An omnibus questionnaire was used to assess child demographics (including birth weight, Body Mass Index (Keys, 1972) and socio-economic status which was assessed utilising postcode and the Australian Bureau of Statistics Socio-Economic Indices for Areas (Pink, 2006)). General health, self-reported sleep, daytime functioning and the presence of an atopic disorder (eczema, asthma and rhinitis) were also assessed. Children underwent one night of polysomnography (PSG) on a non-school day at the Adelaide Women's and Children's Sleep Disorder Unit, followed by neurocognitive testing the following morning.

Prior to the overnight PSG, eczematous children provided a urine sample which was refrigerated at −80 °C for later analysis of leukotriene E_4 (LTE_4), a biological marker of inflammation associated with atopic activity (Rabinovitch, 2007).

2.3. Material and methods

2.3.1. Eczema assessment

Eczema severity was assessed by using the Scoring of Atopic Dermatitis Index (SCORAD) (European Task Force on Atopic Dermatitis, 1993; Oranje et al., 1997) and the following recommended cut-off points for objective SCORAD were used for disease severity: mild <15; moderate 15–40; and severe >40 (Holm et al., 2006; Kunz et al., 1997).

2.3.2. Leukotriene E_4

LTE_4 is a biomarker of total body cysteinyl leukotriene production and excretion (Rabinovitch, 2007) and is reported to be elevated in children with severe eczema (median; and 1st–4th quartiles:140; 66–166 μg/mmol creatinine) compared to healthy controls (52; 30–90, $p<.05$ Oymar and Aksnes, 2005). The LTE_4 EIA kit was used to assess LTE_4 concentration in the urine of children with eczema. To control for urine dilution, measurements are reported as picogram per milligram of urinary creatinine (pg/mg creatinine) (McEntagart et al., 2000). Prior to analysis, urine specimens were purified by using the Cysteinyl Leukotriene Affinity Sorbent methodology with an 86% recovery after purification (Meaney and Butler, 1987).

2.3.3. Asthma and allergic rhinitis

A yes/no response format was used to assess the presence of asthma and rhinitis using the following questions from the International Study of Asthma and Allergies in Childhood (ISSAC) Phase 1 Core questionnaire: "In the last twelve months has your child had wheezing or whistling in the chest?" and "In the last twelve months, has your child had a problem with sneezing or a runny or blocked nose when he/she did not have a cold or flu?" (Asher et al., 1995). The following ISAAC questions were used to assess the impact of asthma and rhinitis on sleep: "In the last 12 months, how often, on average, has wheezing disturbed your child's sleep?" (1 = "never woke with wheezing", 2 = "less than one night per week" and 3 = "one or more nights per week") and "In the last twelve months, how often, on average, has your child been kept awake by this nose problem?" (1 = "never in the last twelve months", 2 = "less than one night per week" and 3 = "one or more nights per week").

2.3.4. Parental-reported sleep problems

Sleep problems were assessed by using the Sleep Disturbance Scale for Children (SDSC) (Bruni et al., 1996). The SDSC contains two items assessing sleep quality using a five point scale (total sleep time 1 = 9–11 h to 5 = <5 h; and latency to sleep onset 1 = <15 min to 5 = >60 min) and 24 items assessing the frequency of sleep disorder symptoms also rated on a five point scale (1 = never to 5 = always). The SDSC provides normed T-scores (mean = 50 and SD = 10) for six scales: Disorders of Initiating and Maintaining Sleep (e.g., sleep duration, sleep latency, night awakenings, etc.), Sleep Breathing Disorders (e.g., snoring, etc,), Disorders of Arousal (e.g., sleepwalking, sleep terrors, nightmares, etc.), Sleep–Wake Transition Disorders (e.g., rhythmic movements, hypnogogic jerks, sleep talking, bruxism, etc.), Disorders of Excessive Somnolence (e.g., difficulty waking up, morning tiredness, etc.), and Sleep Hyperhydrosis (e.g., nocturnal sweating, etc.) and a composite Total Sleep Problem score. The reliability and validity of the SDSC have been well evaluated and supported (Bruni et al., 1996; Ferreira et al., 2009). Additional questions on the average timing of sleep onset and offset on a typical school weekday were also collected.

2.3.5. Polysomnography

A standard polysomnographic montage was used to collect the following measures; electroencephalography, electrooculography, electromyography, intercostal electromyography, thermistor (air flow), nasal cannula (nasal pressure), leg leads (limb movement), respiratory bands (respiratory and abdominal movements), electrocardiography and oximetry. The signals were digitised and stored by using the Compumedic's S-Series Sleep System (Melbourne, Australia).

Studies were scored according to standard criteria by an experienced sleep technician blinded to child status (Iber et al., 2007). The following variables were collected: total sleep time, sleep efficiency, latency to REM (Rapid Eye Movement) onset, percentage of slow wave sleep, percentage of REM sleep, number of sleep stage shifts, arousal index, spontaneous arousals, wake after sleep onset time, obstructive apnea hypopnea index (OAHI) (defined as the total number of obstructive apneas, mixed apneas and obstructive hypopneas divided by the total sleep time) and central apnea hypopnea index (CAHI) (defined as the total number of central apneas and central hypopneas divided by the total sleep time). Spontaneous and respiratory arousals were scored according to the American Academy of Sleep Medicine criteria (Iber et al., 2007).

2.3.6. Neurocognitive assessment

The Wechsler Intelligence Scale for Children (WISC-IV) was used to assess cognitive functioning (Wechsler, 2003). The WISC-IV contains ten tests which generate four composite indices: Verbal Comprehension Index, Perceptual Reasoning Index, Processing Speed Index and Working Memory Index and a global composite, Full Scale Intelligence. Verbal Comprehension assesses children's ability to listen to a question, draw upon learned information from both formal and informal education, reason through an answer, and express their thoughts aloud. Perceptual Reasoning assesses children's ability to examine a problem, draw upon visual–motor and visual–spatial skills, organise their thoughts, create solutions, and then test them. Processing Speed assesses children's abilities to focus attention and, as well, to quickly scan and discriminate and sequentially order visual information. Success on the Processing Speed subtests requires persistence and planning ability, but is sensitive to motivation, difficulty working under a time pressure, and motor coordination. Finally, Working Memory assesses children's ability to memorise new information, hold it in short-term memory, concentrate, and manipulate that information to problem