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by

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A thesis submitted for the Degree of Doctor of Philosophy

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Abstract

Eczema affects up to 20% of children in western industrialised countries. Chronic childhood eczema has significant morbidity characterised by physical discomfort, emotional distress, reduced child and family quality-of-life and, of particular note, disturbed sleep. Sleep disturbance, characterised by frequent and prolonged arousals, affects up to 60% of children with eczema, increasing to 83% during exacerbation. Even in clinical remission, children with eczema demonstrate more sleep disturbance than healthy children. Disturbed sleep in otherwise healthy children is associated with behavioural and neurocognitive deficits. Preliminary evidence suggests that disturbed sleep in children with eczema is also associated with behavioural deficits while the impact on neuropsychological functioning remains unexplored.

Two major studies were undertaken to examine the sleep of children with eczema and possible secondary deficits due to poor sleep. Parents of children (6-16y) with eczema (n = 77) and healthy controls (n = 30) completed a validated omnibus questionnaire which included items which assessed sleep, behaviour, general health, quality-of-life and additional items assessing eczema, asthma, rhinitis and demographics. Structural Equation Analyses revealed that the effect of eczema on the behavioural variables of Hyperactivity, ADHD Index and Oppositional behaviours were mediated through sleep with no direct effect of eczema on behaviour. A similar relationship between sleep and behaviour was observed for the comorbid atopic disorders of rhinitis and asthma.

In the second study, children (aged 6-16y) with eczema (n = 24) and controls (n = 19) were assessed through polysomnography to provide data on their sleep quality. Eczema severity was evaluated using SCORAD ratings scales and eczematous children provided a urine sample for analysis for Leukotriene E₄, a biological marker of atopic inflammation.

Scratching was assessed using infra-red camera. Distal and Proximal body temperature was measured to ascertain potential deficits in homeostatic processes and actigraphy was employed to record nocturnal activity. To evaluate neurocognitive ability all children underwent IQ testing with eczematous children undergoing additional children attention and reading age measurements.

Polysomnographic data on children with eczema showed that they had a longer REM onset latency, higher percentage stage 3 & 4 sleep, longer Wake After Sleep Onset and a lower Sub Cortical Arousal Index than controls. Higher Leukotriene E₄ levels was strongly associated with longer Wake after Sleep Onset. In addition, Wake after Sleep Onset also exhibited a trend toward higher itch and sleep loss ratings of the SCORAD. Increased Leukotriene E₄ levels also demonstrated associated trends in lower Sleep Efficiency, longer REM Onset Latency, a lower percentage of REM and fewer Stage Shifts. Using infra-red video contiguous with polysomnography, scratching was found to occur during sleep in all sleep stages. The SCORAD variable of Erythema, which is the redness or inflammation of the skin that is the result of dilation of superficial capillaries was found to be strongly associated with nocturnal scratching.

Actigraphic data demonstrated that children with severe eczema had more nocturnal activity and for longer periods of time than either mild to moderate eczema patients or controls.

Actigraphy variables were also associated with the frequency that asthma and rhinitis disturbed sleep as well as eczema severity and Leukotriene E4 levels in children with eczema. The actigraphic variables of Sleep Efficiency and Awakenings were moderately associated with the polysomnographic variables of Total Sleep Time, Sleep Efficiency and Sleep Onset Latency.

Sleep Onset temperatures were similar between eczema and control groups, however the skin temperature profile of children with eczema differed markedly from control subjects thereafter. Distal skin temperature in eczematous children was found to be significantly lower than controls for approximately a third of the night. Overnight trends in eczema subject's Distal temperature indicated that the heat loss usually associated with nocturnal sleep was markedly greater than controls.

Eczema children scored significantly lower on Full Scale IQ, Verbal Comprehension and Perceptual Reasoning scores than controls. On the WISC-IV subtests, scores of similarities, comprehension, picture concepts and letter-number sequencing were also significantly lower in children with eczema than controls. After controlling for the impact of snoring, asthma and rhinitis disturbing sleep, our findings suggest that lower neurocognitive performance in children with eczema is related to their sleep quality.

In conclusion, eczema was found to affect the sleep of children with longer periods of awake during the night and with more nocturnal movement than controls. The sleep architecture of children with eczema was also found to be associated with behavioural and neurocognitive deficits. Nocturnal scratching was found to occur during sleep and further, produce arousal from sleep, however the lack of associations between itch and sleep variables indicate that itch is also not a primary cause of sleep disturbance in children with eczema. The role of skin temperature in nocturnal thermoregulation appears to be disturbed in this patient group with eczema children showing evidence of a greater and more rapid heat loss than controls. It is also suggested that these rapid changes in temperature are associated with sleep disturbance. While the findings of a case study indicating that treatment improving sleep quality is also associated with neurocognitive and behavioural improvements, further study is required to determine the mechanism associating sleep fragmentation with daytime functioning.

Declaration

Name: Danny Camfferman

Program: PhD in Medicine

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Publications in support of thesis

Publications

Camfferman D, Kennedy JD, Gold M, Martin AJ, Lushington K. (2010) Eczema and sleep and its relationship to daytime functioning in children. Sleep Medicine Reviews, 14 (6), 359-369.

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List of Abbreviations

Acetylcholine (Ach)

Arteriovenous-anastomoses (AVAs)

Attention Deficit Hyperactivity Disorder (ADHD).

Brain-Derived Neurotrophic Factor (BDNF)

Childhood Atopic Dermatitis Impact Scale (CADIS)

Child Health Questionnaire-Parent Form (CHQ-PF-28)

Children's Dermatology Life Quality Index (CDLQI)

Circulatory Temperature Index (CTI)

Dermatitis Family Impact questionnaire (DFI)

Eczema Area Severity Index (EASI)

Immunoglobulin E (IgE)

Infants' Dermatology Quality of Life Index (IDQoLI)

International Study of Asthma and Allergies in Childhood (ISSAC)

Leukotriene E₄ (LTE₄)

Macrophage-Derived Chemokine (MDC)

Nottingham Eczema Severity Score (NESS)

Polysomnography (PSG)

Rapid Eye Movement (REM)

SCORing Atopic Dermatitis (SCORAD)

Socio-Economic Indexes For Areas (SEIFA)

Sleep Disordered Breathing (SDB)

Sleep Disturbance Scale for Children (SDSC)

Suprachiasmatic nucleus (SNC)

T-cell attracting cytokine (CTACK)

Temperature environment (Te)

Temperature rectal (Tr)

Temperature skin (Ts)

The German Health Interview and Examination Survey for Children and Adolescents (KiGGS)

Thymus and Activation Regulated Chemokine (TARC)

Visual Analogue Scale (VAS)

Wechsler Intelligence Scale for Children (WISC-IV)