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Original Article

Hearing loss mediates executive function impairment in sleep-disordered breathing

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A B S T R A C T

Background: Sleep-disordered breathing (SDB) is often co-morbid with conductive hearing loss in early childhood due to a shared aetiology of adenotonsillar hypertrophy. Hearing loss is independently associated with impairment of executive function and behavioural difficulties. We hypothesised that these impairments in children with SDB may be mediated through hearing loss.

Methods: Fifty-eight children including 37 snorers awaiting adenotonsillectomy and 21 healthy non-snoring controls, aged 3–5 years, were assessed with pure tone audiometry, Strengths and Difficulties (SDQ), Behaviour Rating of Executive Function (BRIEF-P), and Childhood Middle Ear Disease and Hearing questionnaires. Polysomnography in snoring children generated an obstructive apnoea/hypopnea index (OAHI). Two regression models examined the effect of SDB and the mediating impact of hearing loss on BRIEF and SDQ.

Results: Snoring children had significantly poorer hearing, greater past exposure to hearing loss, and higher total SDQ and BRIEF-P scores than non-snoring controls. The first regression model, including all children, demonstrated that the impact of snoring on BRIEF_P, but not SDQ, was entirely mediated by a history of hearing loss exposure but not same-day audiometry. The second model examined snoring children only, categorising the group into 12 with obstructive sleep apnoea (OSA) (OAHI $\geq$ 5) and 25 without OSA. OSA had a direct effect on SDQ scores, but this was not mediated by a history of hearing loss.

Conclusion: In early childhood, conductive hearing loss mediates the relationship between SDB, irrespective of severity, and parent report of executive function but not behaviour. Treatment of hearing loss in pre-school SDB might improve executive function.

1. Introduction

Obstructive sleep-disordered breathing (SDB), from simple primary snoring to obstructive sleep apnoea (OSA), affects up to 10% and 5.7% children, respectively [1,2]. Childhood SDB is associated with impaired cognitive function, general intelligence, learning, school performance, language skills and behaviour [3–5]. Furthermore, recent data from a cross-sectional study of over 1000 children have suggested a 'dose–response' relationship between SDB and cognitive and behavioural function [5]. The prefrontal cortex sub-serving executive function (EF) appears to be

Abbreviations: CMEDHQ, childhood middle ear disease and hearing questionnaire; dB, decibels; ECG, electrocardiogram; EEG, electroencephalogram; EF, executive function; EMG, electromyogram; GEC, global executive composite; OAHI, obstructive apnoea/hypopnea index; OSA, obstructive sleep apnoea; RMSEA, Root Mean Square Error of Approximation; SDB, sleep-disordered breathing; SDQ, strengths and difficulties questionnaire.

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particularly vulnerable to the sleep fragmentation and intermittent hypoxia that characterize OSA [6,7].

Upper airway lymphoid hypertrophy is a key cause of SDB in otherwise healthy, non-obese, pre-school children. Hence, the first-line treatment is adenotonsillectomy [1]. However, adenotonsillar hypertrophy also causes Eustachian tube dysfunction and otitis media with effusion [8,9], a leading cause of conductive hearing loss, affecting up to 20% of 2 year olds and 8% of 8 year olds [10]. Not surprisingly, given this shared aetiology, hearing loss is a recognised co-morbidity in SDB [11]. Children aged 2–12 years with OSA have a five-fold risk of otitis media with effusion compared to non-snoring controls [12], while habitual snorers have a 1.3-fold risk [13].

Notably, hearing loss in childhood is independently associated with behavioural and EF impairment. Parent reported EF was significantly worse than normative data in 214 children (5–18 years) with hearing impairment [14]. Similarly, meta-analysis confirms greater behavioural difficulties in children with hearing loss, including those with sensorineural hearing loss unrelated to Eustachian tube dysfunction [15]. With regard to conductive hearing loss, 4–5-year-old children with recurrent otitis media are more than twice as likely as healthy peers to have abnormal/borderline Strengths and Difficulties questionnaire (SDQ) scores [16], and their total difficulties scores are approximately 25% higher [17]. Furthermore, behavioural difficulties in children with hearing loss are the greatest in those with greater language impairment [18].

We aimed to explore the extent to which hearing loss contributes to parent report of EF and behavioural problems in typically developing but otherwise healthy young children with SDB. We hypothesised that the impact of SDB on EF and behaviour would be either wholly or partially mediated by hearing loss.

2. Patients and methods

Setting: Children aged 3–5 years inclusive with a history of snoring were recruited from Southampton Children's Hospital and Queen Alexandra Hospital, Portsmouth, UK. Children were listed for adenoidectomy and/or tonsillectomy. Non-snoring, similar aged, control children with no otolaryngology history were recruited from pre-school nurseries. Children were assessed at the NIHR Wellcome Trust Clinical Research Facility, Southampton.

Children with cranio-facial abnormalities, moderate or severe learning disabilities, attention deficit hyperactivity disorder, chronic respiratory/cardiac conditions or significant allergy or where parents were not conversant in English were excluded.

The study was approved by the UK National Research Ethics committee (06/Q1702/12), and parents signed a consent form on behalf of their child.

2.1. Measures

Socio-economic status: Mothers reported age of completion of education in four categories: completed secondary education to age 16 years; ‘A’ levels (to 18 years) or a college diploma, undergraduate degree or post-graduate degree.

The Behaviour Rating of Executive Function-Preschool questionnaire (BRIEF-P): This questionnaire comprises 86 parent-rated items based on a three-point scale (never, sometimes and often). Sub-scales reflect core domains of EF (inhibition, working memory, emotional control, shift and plan/organise) and generate a global executive composite (GEC), where clinically significant T scores are >65 [19].

The SDQ: This 25-item behavioural screener, with established reliability and validity [20], comprises five subscales (emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and pro-social behaviour), each with five questions answered with a three-point rating scale (0, not true; 1, somewhat true and 2, certainly true). A total difficulties score is generated by summing all subscales, except prosocial behaviour. Total scores of 0–13 are considered normal, 14–16 borderline and 17–40 abnormal.

The Childhood Middle Ear Disease and Hearing Questionnaire (CMEDHQ) [21] comprises 19 questions about life-time hearing problems and treatment. Eleven questions generate a total score (maximum 79). The questionnaire was developed by the UK Medical Research Council Hearing Institute as a screening tool. Compared to standard, pure-tone audiometry, it has a sensitivity of 77.3% versus 89.7% and specificity of 70.9% versus 71.5% to predict hearing loss requiring intervention with a threshold score of ≥18 indicative of a past history of significant hearing loss [21].

Assessment of snoring: Snorers were actively recruited from surgical waiting lists based on a positive snoring history. Snoring status was further confirmed using a question in the CMEDHQ ‘Has your child snored?’ with potential responses ‘Only with colds, never, rarely, often or always’. Children were considered snorers if they snored ‘often or always’ and non-snorers if they snored rarely or never or only with colds.

Pure tone audiometry: Children who are able to cooperate were tested using an abbreviated SWEEP test (Grayson-Stadler, MN) according to British Society of Audiology guidelines. Pure tones were presented unilaterally through headphones in sequence: 1000, 2000, 4000, 500 and 250 Hz, initially at 40 dB. If a positive response was achieved, the child's hearing threshold was determined by sequentially reducing the tones by 10 dB. Conversely, if no response was achieved, sound levels were increased to the maximum of 80 dB. The best sound level detected with confidence in the speech range was recorded in each ear. Hearing impairment is defined by the World Health Organisation as a hearing loss with thresholds higher than 25 dB in one or both ears.

Polysomnography: All snorers had a single night of polysomnographic evaluation using computerised systems (Alice 5 – Respironics, Chichester UK) according to recognised standards [22]. Montage included EEG (C3/A2, O1/A2, C4/A1 and O2/A1), right and left EOG, bipolar submental EMG, thoracic and abdominal excursions, nasal airflow (Protech, Mukilteo, WA), finger pulse oximetry (Masimo Inc, Irvine, CA), ECG and synchronous video-recording. Sleep staging [23] and respiratory events [24] were scored according to standard criteria using Alice 5 Sleepware. Specifically, obstructive apnoea was defined by >90% drop in airflow for two breaths or more and hypopnoea as >50% drop in airflow for two breaths or more accompanied by either ≥4% oxygen desaturation or an EEG arousal, in both cases accompanied by continued respiratory effort. The obstructive apnea/hypopnea index (OAHI) was defined as the number of obstructive apnoeas, hypopnoeas and mixed apnoeas per hour of total sleep time.

Anthropometric assessment: Height and weight were measured, and body mass index was computed.

2.2. Statistical methods

Continuous variables were inspected for normality. Group differences were explored using *t*-tests or Mann–Whitney U tests, according to data distribution. Two mediation models examined the effect of hearing on the relationship between SDB and EF and behavioural measures, using the Mplus v7.4 (Muthén & Muthén, Los Angeles, CA) indirect regression method [25]. The maximum likelihood estimator was used, and bootstrapping analysis was used to calculate 90% bias corrected confidence intervals (CI) using 10,000 bootstrap samples. Model fit was evaluated with chi square,