Obstructive sleep apnoea in Down syndrome

*Current knowledge and future directions*

BACCH 2017
Southampton

Dr Cathy Hill

Associate Professor of Child Health & Consultant in Sleep Medicine
OSA is a relatively new concept!

The stupid-lazy child who frequently suffers from headaches at school, breaths through his mouth instead of his nose, snores and is restless at night, and wakes up with a dry mouth in the morning, is well worthy of the solicitous attention of the school medical officer. BMJ 1889

• 1962 first report of obstructive apnoeas in sleep in obese adults (called Pickwickian syndrome)

• 1976, first description of paediatric OSA was published describing 8 children ‘with a sleep apnea syndrome similar to that seen in adults’.
Obstructive sleep apnoea (OSA)

- Negative intraluminal pressure in pharynx with inspiration NOT counterbalanced by dilator muscles
- Continued respiratory effort against a blocked upper airway in sleep
- Characterised by both complete (apnoea) or partial (hypopnoea) obstruction of the upper airway
- Causes combination of intermittent hypoxia, hypercapnia and brief arousals from sleep that restore airway patency, but fragment sleep.
The landscape of sleep

Risk of OSA in 2nd half of sleep
Sleep and the upper airway

- **N2**: Muscle tone drops
- **REM**: Skeletal muscle atonia
- **EOG**
- **EEG**
- **CHIN**
- **EMG**

Drowsy but awake
Causes in children

- Adeno-tonsillar hypertrophy in pre-school years
Causes of OSA:

One in five children in Reception is overweight or obese

One in three children in Year 6 is overweight or obese

• OSA risk 16-36% for obese children
Causes of OSA: cranio-facial anatomy/tone

• Small chin or mid-face
• Large tongue
• Low muscle tone
• Children with Down syndrome – perfect storm of multiple risk factors
Why worry about OSA?

In otherwise healthy typically developing children:
- Impairment of daytime attention
- Worse school performance
- Behavioural problems
- High blood pressure
- Faltering growth
- Reduced quality of life
- Increased health care utilization

In children with Down syndrome:
- Poverty of research data (more on this later!)
Why does OSA affect the brain?
Pre-frontal model for neurocognitive deficit in Sleep Disordered Breathing

Sleep disruption

- Disruption of restorative Properties of sleep

Intermittent hypoxia/hypercarbia

- Disruption of cellular homeostasis

Prefrontal cortical dysfunction

Dysfunction of cognitive executive system
How do we diagnose OSA?
1. Symptoms

- During sleep
  - snoring
  - pauses in breathing followed by gasp
  - restless sleep
  - enuresis
  - sweating
  - unusual sleeping positions
  - Headache and dry mouth on waking

- In the day
  - Learning and development non-specific!
  - Behavioural problems
Questionnaire tools

• Only one fulfils psychometric quality criteria (Pediatric sleep questionnaire\(^9\)) but includes questions about BEHAVIOUR so poor specificity in a DS population:

  *My child often...*

• *does not seem to listen when spoken to directly*
• *has difficulty organising tasks and activities*
• *is easily distracted by extraneous stimuli*
• *fidgets with hands or feet or squirms in seat*
• *is “on the go” or often acts as if “driven by a motor”*
• *interrupts or intrudes on others (e.g. butts into conversation)*
The development of a screening questionnaire for obstructive sleep apnea in children with Down syndrome

Emma Sanders¹, Catherine Mary Hill¹,², Hazel Jean Evans¹,²† and Catherine Tuffrey¹,³†

• 14 item questionnaire
• Question items developed using expert consensus to generate a content validity index and parent cognitive interviews confirmed readability and relevance of questions¹⁰
• Psychometric properties evaluation underway
Physical examination

- BMI
- Dysmorphic features
- ENT exam
- Chest wall deformity
- Disorders affecting muscle tone
- Evidence of pulmonary hypertension

A systematic review of in 2004 concluded that clinical history and examination are poor at predicting OSA in children and have limited utility\(^{11}\).
European respiratory taskforce guideline on investigation and management of OSA in 2-18 y olds\textsuperscript{12}

- Defines child at risk of OSA as having $>1$ of following:
  - Symptoms
  - Clinical findings OR neuromuscular disorders and syndromes known to be at risk e.g. Down syndrome
  - Diagnostic findings e.g. lateral neck XR/MRI

- Recommended investigation
  - Polysomnography
  - Polygraphy

- IF not available
  - Home PSG or polygraphy
  - Pulse oximetry
International diagnostic standards

- Based on the number of EVENTS per hour of sleep: the apnoea/hypopnoea index (OAHI)

- **Hypoponea** = reduced airflow by >30% from baseline ONLY scored if assoc. with >3% desat. OR EEG arousal

- **Apnoea** – cessation or airflow

- Each event must last at least 2 breath cycles

- ALWAYS with continued effort to breathe

- OAHI >/=2 events per hour = OSA

- OAHI >/=5 events per hour = risk of morbidity treatment indicated
Full polysomnography (gold standard)

- Measures sleep and wake and identifies stage of sleep
- EEG (min. 3 leads), EOG, EMG (chin)
- Respiration – movements (RIP)
- Respiration – airflow
- ECG
- Gas exchange – SpO2 and CO2
- Snoring
- Body position
- +/- limb EMG
Commonest test in the UK: respiratory polygraphy

- Respiration – movements
- Respiration – airflow
- ECG
- Gas exchange – O$_2$ and CO$_2$
- Snoring
- Body position
- Sensitivity of 90.9% and a specificity of 94.1% to detect obstructive apnoea/hypopnoea index $> 5.6$/hr compared to a gold standard = polysomnography
Children who benefit from treatment include those with:

- AHI >5/hr OR AHI 1–5/hr + other factors predicting persistence
- Complex conditions (e.g. Down syndrome)

**Stepwise treatment approach**

- Weight loss if overweight or obese
- Nasal anti-inflammatory treatment
- Adenotonsillectomy
- Rapid maxillary expansion or orthodontic appliances
- CPAP therapy
UK expert consensus report in 2009\textsuperscript{13}

• Down syndrome: ‘based on the 197 children reported, sleep related breathing disorders occurs in 58% and between one-third and three-fifths of children with Down syndrome have desaturation below 90% while asleep’.

• Recommended SCREENING as follows:
  • Oximetry once in infancy then annually to 3-5 yrs
  • Children with abnormalities on screening, or a clinical suspicion of a false negative screening test, should have respiratory polysomnography

• BUT ACKNOWLEDGED LACK OF EVIDENCE
Screening practice DSMIG members

(Hill CM and Evans HE, 2012)

Location of 29 respondents

- Scotland
- N Ireland
- S Ireland
- Wales
- N England
- Midlands
- London
- S England
Adherence to RCPCH guidelines

- Only 5 had a screening programme
- 4 followed RCPCH guidelines
- 1 used cardiorespiratory PG as first line

19/25 routinely offer pulse oximetry at HOME
Pulse Oximetry

**Advantages**
- Widely available
- Well tolerated

**Disadvantages**
- Sensitivity & specificity unknown
- Child may be awake
- Central apnoea causes dips in oxygen
Known gaps in research evidence

• Accurate prevalence data – how common is it in DS?

• What is the best way to test for it and how often should children be screened?

• Natural history of condition treated/untreated

• Effects on cognition

• Best way to treat it
Very limited research on OSA and cognition in children with DS$^{14}$

- 38 children with DS (15 males aged 7–12y).
- Arizona Cognitive Test Battery: psychometric measures designed and validated for this population
- Home polysomnography.
- Mean Verbal IQ score ($p=0.006$) was 9 points lower in those with OSA (AHI >1.5) than in those without OSA
- Performance on measures of cognitive flexibility was poorer ($p=0.03$)
- Those with OSA showed increased light-stage sleep ($p=0.009$) at the expense of slow-wave sleep ($p=0.04$)
OSA in young children with DS

Primary aim

• To determine the diagnostic test accuracy of pulse oximetry to predict OSA in children with DS as measured against respiratory polygraphy

Secondary aims

• To study the association between OSA and neurobehavioral measures

• To establish a cohort of children to map the natural history of OSA in DS and offer future intervention studies
Recruitment

- Aimed to recruit 180
- Multi-modal recruitment approach:
  - Regional community paediatricians, respiratory and cardiology services
  - Parent support groups and word of mouth
  - DSMIG

Inclusion criteria

- Children with Down syndrome aged 6 months to 6\textsuperscript{th} birthday
- No cardiorespiratory polygraphy in the past 3 months
- Not using home oxygen or CPAP
- Family able to travel to centre
Measures: OSA

One night each of home pulse oximetry and respiratory polygraphy
Measures: Behavior Rating of Executive Function (P)

It yields 5 sub-scales:
- Inhibit
- Shift
- Emotional control (EC)
- Working memory (WM)
- Plan/organise (PO)

- 3 broader indexes
  - Inhibitory self-control (ISCI)
  - Flexibility (FI)
  - Emergent metacognition (EMI)
- Global executive composite (GEC)

Scores of 65 or more are considered clinically significant
Results 1: demographics

- 202 children recruited of whom 188 had a successful respiratory polygraphy study
- No differences between centres in any of the core variables

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>mean (SD) min-max</th>
<th>36.3 (20.6) 6-71</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>male</td>
<td>100 (53%)</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>88 (47%)</td>
</tr>
<tr>
<td>BMI (3 missing)</td>
<td>mean (SD) min-max</td>
<td>16.9 (1.5) 13.0-21.2</td>
</tr>
</tbody>
</table>
Prevalence of OSA$^{15, 16}$

- Male gender and habitual snoring predicted OSA but did not have independent predictive power in the presence of the other factors.
- Age, BMI centile and tonsillar size did not predict OSA.
How did pulse oximetry perform as a screening tool?

• The best OSA predictor was delta 12s index. This is a marker of oxygen saturation variability. In our analysis values >0.555 predicted clinically significant OSA with sensitivity 92% and specificity 65%

• 23/25 TRUE positives were correctly detected

• In a clinical validation sample sensitivity was retained with only slight loss of specificity (63%)

• We recommend that ALL positives are then confirmed with respiratory polygraphy. This approach could HALVE the number of children needing detailed studies
BRIEF-P and OSA

- BRIEF-P were completed for 80/96 children (50 male) aged 3+ yrs.
- 5 were completed inconsistently were excluded.
- 69/75 had successful respiratory polygraphy
- OSA was defined as OAHI ≥1.5 (n=41) and absent if OAHI ≤1.49 (n=28) consistent with Arizona data.
- To assess whether OSA predicted poorer executive function behaviours, multivariate regression models with OSA group as the predictor and BRIEF-P T-scores as dependent measures.
Pairwise comparisons: relative to other scales, children performed most poorly on working memory (WM) (all $p < .005$) and plan/organise (p < .001).
Does OSA predict BRIEF-P?

• Children with OSA experienced greater difficulties with Shift ($B=.21$, $R^2=.04$, $p=.04$) and Working Memory ($B=.27$, $R^2=.07$, $p=.01$), indicating deficits in transitioning smoothly between activities or attentional focus, and ability to hold information in mind whilst working on a response.

• Children with OSA also experienced greater difficulties with Inhibitory self-control ($B=.20$, $R^2=.04$, $p=.04$) and Emergent Metacognition ($B=.23$, $R^2=.06$, $p=.02$), suggesting that OSA contributes to difficulties with self-regulating behaviour and emotions, and active problem solving.
Summary

• High prevalence of OSA in young children with Down syndrome supporting the need for regular screening

• Pulse oximetry could provide an accessible screening method for OSA and halve the number of children needing detailed studies

• We report for the first time that presence of OSA predicts greater deficits in executive function behaviours in preschool children with Down syndrome

• Greatest deficits observed in working memory and shift sub-scales namely: transitioning smoothly between activities or attentional focus, and ability to hold information in mind whilst working on a response
Conclusions

• Life expectancy in DS has dramatically improved - today's children will live to middle age and beyond
• Children with DS and OSA have limited cognitive reserve to compensate for OSA related neural insult and OSA may be a risk factor for the development of dementia in later life
• Screening programmes should be implemented as recommended in 2009
• Importantly OSA in this population is amenable to treatment
• Treatment trials are urgently needed to evidence benefit from current UK first line practice of adeno-tonsillectomy
Final acknowledgement

Children and families who supported the study 100% of whom have signed to our research registry
Thank you for listening! Any questions?
Sleep training for professionals

We have a proven track record in delivering high quality practical training courses for professionals in the UK and abroad. Our teaching is firmly grounded in evidence-based practice, and is constantly informed by our clinical experience and research findings. We are proud to have clinical staff who enjoy teaching and sharing their knowledge.

Our training courses

Our courses are suitable for all professionals who regularly work with children who have sleep problems. You may be working within the NHS, children’s services or education.

The courses we offer are:

- Managing children’s sleep disorders in clinical practice (three and five day options)
- Essentials of sleep medicine for the paediatrician (one day course)
- Sleep update and case study day (one day course)

For more information please email southamptonsleeptaining@uhs.nhs.uk

Feedback from our training courses

‘Thank you for a really excellent course last week. The content and clarity of presentations was outstanding and I feel more confident in my clinical work having attended’ - consultant paediatrician

‘I would not hesitate to recommend this course to any of my colleagues’ - health visitor

‘Thank you so much for the really excellent training course last week. I really enjoyed it and it has inspired me to ‘think sleep’ throughout my practice’ - consultant child psychiatrist

‘Looking forward to putting my newly learned skills into practice’ - therapist.
References


13. Sleep physiology and respiratory control disorders in childhood. Royal College of Paediatrics and Child Health. 2009. rcpch.ac.uk

