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Ashworth, A.

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1

The importance of sleep: Attentional problems in school-aged children with Down syndrome and Williams syndrome

Short title: Sleep and attention in children with DS and WS

Anna Ashworth, PhD*[1], Catherine M. Hill, MD[2] Annette Karmiloff-Smith, PhD[3],

and Dagmara Dimitriou, PhD[1]

[1]Department of Psychology and Human Development, Institute of Education, Bedford Way, London WC1H 0AL, UK

[2]Division of Clinical Neuroscience, School of Medicine, University of Southampton, University Road, Southampton, SO17 1BJ, UK

[3]Centre for Brain and Cognitive Development, Birkbeck University of London, Malet Street, London, WC1E 7HX, UK

*Address for correspondence to Dagmara Dimitriou, d.dimitriou@ioe.ac.uk

2

Abstract

In typically developing (TD) children, sleep problems have been associated with day-time attentional difficulties. Children with developmental disabilities often suffer with sleep and attention problems, yet their relationship is poorly understood. The present study investigated this association in school-aged children with Down syndrome (DS) and Williams syndrome (WS). Actigraphy and pulse oximetry assessed sleep and sleep disordered breathing respectively, and attention was tested using a novel visual Continuous Performance Task (CPT).

Attentional deficits were evident in both disorder groups. In the TD group higher scores on the CPT were related to better sleep quality, higher oxyhaemoglobin saturation (SpO_2) and fewer desaturation events. Sleep quality, duration and SpO_2 variables were not related to CPT performance for children with DS and WS.

Key words: Sleep, attention, Down syndrome, Williams syndrome

Words (excluding references): 6284

Introduction

Attention is a core cognitive process involved in most higher-order cognitive tasks. The ability to selectively concentrate on important stimuli whilst ignoring other competing aspects of the environment is a necessary life-skill and a precursor to learning. It is therefore a critical aspect of a child's development. Attentional abilities generally improve with age but with great individual variability (Scerif, 2010). The domain of attention encompasses a number of separate components including vigilance or sustained attention, inhibition, shifting of attention and selective attention (e.g., Manly et al., 2001). Tasks used to test these constructs generally involve recording participants' ability to attend and respond to a repetitive and unrewarding task, often over a prolonged period of time. For example, the often-used computerized Continuous Performance Task (CPT), which requires sustained and selective attention to respond to an infrequently occurring target whilst inhibiting the response to non-targets (Steele, Karmiloff-Smith, Cornish, & Scerif, 2012; Sullivan et al., 2007).

Although attention is one of the most widely researched domains in the field of cognitive psychology, relatively little research has explored its relationship with sleep in children with developmental disorders. These children often suffer from chronic sleep problems and also have difficulties with attention (Beresford, Stuttard, Clarke, Maddison, & Beecham, 2012). This paper focuses on the relationship between sleep problems, sustained attention and inhibition in children with Down syndrome (DS), Williams syndrome (WS) and a typically developing (TD) control group. We first provide a summary of sleep problems and their relationship with attention in TD children, followed by a brief characterization of the two syndromes and the sleep difficulties which have been reported.

Around one third of children experience some kind of sleep problem (Owens, Spirito, McGuinn, & Nobile, 2000). These range from behaviorally-based problems such as behavioral insomnia, to physiological problems like sleep disordered breathing (SDB) and

periodic limb movement disorder (PLMD). Parasomnias such as nocturnal enuresis (bed wetting), somnambulism (sleep walking), bruxism (grinding teeth) or sleep terrors are also common but are generally outgrown by mid childhood. Sleep serves a vital function for both physiological and psychological optimization of the human body; thus sleep disruptions can lead to behavioral and cognitive problems, including attentional deficits (Archbold, Giordani, Ruzicka, & Chervin, 2004; Pocket & Kirk, 2006).

Snoring is a common problem thought to affect around 11% of school-aged children (Ali, Pitson, & Stradling, 1993; Gozal, 2008). It is one of the primary symptoms of obstructive sleep apnea syndrome (OSAS), a condition where the upper airway becomes occluded during sleep during intermittent apneic (cessation of breathing) or hypopnea (abnormally shallow or slow breathing) events. There is often an associated decrease in oxygen levels (hypoxia) and increased circulation of carbon dioxide (hypercarbia) in the blood, which may or may not lead to arousal. OSAS affects around 1 to 3% of children (Brunetti, 2001; Sogut et al., 2005). Problems with sustained and selective attention as well as impulsivity have often been noted in children who snore, with these problems being specifically linked to oxygen desaturations and associated night wakings (Archbold et al., 2004; Blunden, Lushington, Lorenzen, Martin, & Kennedy, 2005; Kennedy et al., 2004).

SDB and its associated cognitive deficits often improve after adenotonsillectomy, but with some residual long-lasting effects that may reflect damage to the frontal lobes caused by prolonged apneic episodes and disruption to sleep architecture during the critical stages of neural development (Blunden et al., 2005; Gozal, 2008).

Sleep duration, too, has been linked with attentional abilities. Gruber et al. (2012) found that objectively-measured, habitual shorter sleep duration was significantly associated with teacher-reported cognitive problems and inattention, with 27% shared variance, as well as problems with learning, memory and organization but not hyperactivity or impulsivity. In

contrast, following a single night where sleep was restricted to four hours, 45 TD children aged 8 to 15 years were still able to maintain attention and inhibit incorrect responses on a nine-minute visual CPT. They did, however, show objective and subjective evidence of sleepiness as well as observer-ratings of sleepy behaviors and inattention (Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001). Attentional difficulties are also not seen following three consecutive nights of minor (mean 41 minutes) sleep restriction (Sadeh et al., 2003). Together, the findings suggest that acute sleep restriction is not sufficient to disrupt attention in otherwise well-rested children with intellectual abilities in the normal range. Attention problems must therefore arise from long-term sleep disturbance such as chronic sleep restriction or disorders that disrupt sleep continuity such as PLMD or SDB. The application of the current findings to healthcare and sleep education would be beneficial to students, parents and teachers, since optimizing sleep could have advantageous effects on attention and school performance.

Down syndrome

DS is the most common chromosomal anomaly, affecting around 1 in 800 live births and usually caused by a trisomy of chromosome 21. Individuals with DS have distinctive physical characteristics and impaired cognitive ability, with an average IQ of around 50, but with great variability between individuals (Roizen & Patterson, 2003).

Almost all individuals with DS experience sleep disturbances. The most common cause of these is OSAS, which is thought to affect up to 80% of people with DS (Dyken, Lin-Dyken, Poulton, Zimmerman, & Sedars, 2003; Ng et al., 2006) and is likely to be attributed to other features of DS, such as craniofacial and upper airway abnormalities, obesity, tonsil and adenoid encroachment, and generalized hypotonia (Churchill, Kieckhefer, Landis, & Ward, 2011). Problems with settling, sleep maintenance, early morning waking and daytime

sleepiness have also been reported (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2013;

Breslin, Edgin, Bootzin, Goodwin, & Nadel, 2011; Carter, McCaughey, Annaz, & Hill, 2009;

Stores, Stores, Fellows, & Buckley, 1998).

Attentional difficulties are regularly reported in children with DS across most, if not all,

areas. For example, Munir, Cornish and Wilding (2000) found difficulties in selective,

divided and sustained attention as well as in inhibition in a group of 25 boys with DS aged 7

to 15 years (mean 11.17). Particular problems have also been noted in visual, as opposed to

auditory, attention in children with DS (Trezise, Gray, & Sheppard, 2008).

Williams syndrome

WS is a rare neurodevelopmental disorder affecting around 1 in 20,000 live births (Morris,

Demsey, Leonard, Ditts, & Blackburn, 1988) and caused by a deletion of around 28 genes on

one copy of chromosome 7 at q11.23. Individuals with WS tend to have distinctive physical

features along with cardiovascular and musculoskeletal abnormalities. They are inclined to be

overly sociable and perform relatively well on some language tasks, despite having an

average IQ of 56 (range: 50 to 70) (see Donnai & Karmiloff-Smith, 2000 for an overview).

Previous data on sleep in WS have mainly been acquired from questionnaire studies and have

reported settling problems at bedtime, long sleep latencies and frequent night wakings as well

as bed wetting, getting up for the bathroom, body pain and sleep anxiety (Annaz, Hill,

Ashworth, Holley, & Karmiloff-Smith, 2011; Ashworth et al., 2013; Sarimski, 1996; Udwin,

Yule, & Martin, 1987). Objective measures have shown problems with long sleep latencies

(Ashworth et al., 2013), PLMS (Arens et al., 1998; Goldman, Malow, Newman, Roof, &

Dykens, 2009), decreased rapid eye movement and increased slow wave sleep (Gombos,

Bódizs, & Kovács, 2011; Mason et al., 2011).

Attention difficulties are common in WS, including selective and sustained attention (Menghini, Addona, Costanzo, & Vicari, 2010) as well as ability to shift focused attention (Rhodes, Riby, Park, Fraser, & Campbell, 2010). Problems with attention have been reported by parents and healthcare practitioners to be worse in preschool and early school-age children and to decline in adolescence (Carrasco, Castillo, Aravena, Rothhammer, & Aboitiz, 2005).

In spite of this evidence, to our knowledge, no studies have hitherto investigated the association between sleep and attention in children with DS or WS.

The present study addresses this void by using objective measures of actigraphy and pulse oximetry to assess sleep patterns and nocturnal oxyhaemoglobin (SpO$_2$) saturation (as a marker of OSAS) in children with DS and WS. We investigate the relationship between these measures and attention using a visual CPT. It is predicted that 1) sleep problems in DS and WS will be syndrome-specific; 2) children with DS and WS will perform less well than TD children on the visual CPT; 3) performance on the task will be age-related, with older children showing better attentional control; 4) longer sleep duration, better sleep quality and/or higher SpO$_2$ will be related to better performance on the task across the groups.

Methods

Participants

Twenty-two children with DS (11 male), 22 children with WS (10 male) and 41 TD children (19 male) took part in the study. Details of the final sample are shown in Table 1. Analysis of Variance (ANOVA) and Chi-square tests respectively yielded no significant age ($F(2,81)=.14$, $p=.87$, $\eta_p^2=.003$) or sex differences ($\chi^2(2,84)=.02$, $p=.99$, phi=.02) between the three groups. Table 1 also shows mental age scores as measured by Raven's Colored Progressive Matrices (RCPM, described later).

TD children were recruited through local primary schools in London, UK. Parents of children with DS were contacted through local groups and schools for children with special needs. All parents were informed in writing that the study was investigating sleep patterns and attention and were invited to respond to the school or to the researcher if they wished to take part. The Williams Syndrome Foundation, UK assisted with recruitment of children with WS; parents were given study information over the telephone and later in writing. Parents confirmed that all children with DS had previously tested positively for trisomy of chromosome 21. , whereas children with WS had been diagnosed by the *fluorescence in situ hybridization* test for microdeletion of genes at the elastin locus (7q11.22-23). Children whose parents reported co-morbid disorders, psychiatric or current medical conditions and those taking any hypnotic medication were excluded. All children were physically well at the time of study. Ethical approval was granted by the Institute of Education, University of London Research Ethics Committee and supported by Down Syndrome Education International and The Williams Syndrome Foundation, UK. Both parental informed consent and the child's verbal assent were obtained prior to participation.

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Table 1 about here

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Materials

Actigraphy

Sleep patterns were measured using actigraphy, a reliable and valid method for assessing sleep and wake, which shows more than 80% agreement with overnight polysomnographic

laboratory-based studies but can be used to measure activity levels in a naturalistic setting over a prolonged period of time (Sadeh, Hauri, Kripke, & Lavie, 1995).

Each child was requested to wear an Actiwatch Mini (CamNTech, Cambridge, UK) on the non-dominant wrist continuously for one week (Acebo et al. 1999). The sampling rate was one second and data were analyzed in one-minute epochs using Sleep Analysis 7 (CamNTech, Cambridge, UK). In addition, parents completed a sleep log to support analyses of actigraphy data.

Actigraphy variables were selected to give a broad overview of sleep parameters that have previously been associated with children's cognitive performance (Gruber et al., 2012; Holley, 2009; Sadeh, Gruber, & Raviv, 2002). These related to sleep duration: bed time, getting up time, assumed sleep time (total time from falling asleep to waking up) and actual sleep time (assumed sleep minus any periods of wake) as well as sleep quality: sleep efficiency (percentage of time spent asleep from sleep onset to wake up), sleep latency (time from lights out, as reported by parents, to sleep onset), number and mean duration of night wakings, and fragmentation (an indication of restlessness where a higher figure indicates increased restlessness based on nocturnal wakings rather than subtle limb movements associated with PLMD where the participant may not wake up).

Masimo pulse oximetry

Heart rate and SpO_2 were measured in the child's home using Masimo Radical 8 monitors. Recordings were taken through an infrared sensor attached to the toe (usually the second toe). Parents were shown how to use the device correctly and were given an opportunity to ask any questions. They were requested to use the monitor overnight for three consecutive nights. Devices were set to a two-second averaging time and sampled SpO_2 saturation at 1 Hz. Data were analyzed using Visi-Download software (Stowood Scientific Instruments, Oxford, UK).

They were visually screened prior to analysis and artifacts such as low signal strength or periods of instability were removed from the analysis. The program was set to automatically detect and remove artifacts where there was too much ambient light, low signal, low perfusion, interference, no pulse, and when the sensor was defective, disconnected or not on the patient. It is recommended that at least five hours of artifact-free data from one night be analyzed since apneas often occur in rapid eye movement sleep which is greater in the latter part of the night, so it is important to obtain some recording from this time (Urschitz et al., 2003).

Pulse oximetry variables were selected that have been demonstrated in previous studies to be indicators of sleep apnea (Urschitz, Brockmann, Schlaud, & Poets, 2010). These were mean SpO_2, median SpO_2, SpO_2 dips per hour greater than 4%, percentage of time spent below 90% SpO_2, and delta 12 (an index of SpO_2 variability over each 12-second epoch where a higher figure indicates increased variability).

Raven's Colored Progressive Matrices

Raven's Colored Progressive Matrices (RCPM; Raven, Raven, & Court, 1998) is a popular, standardized test of fluid intelligence that is often used to give a non-verbal reasoning score for children. This correlates well with IQ in TD children so can be used to give a child's non-verbal mental age (MA). This is necessary when researching with developmental disorder groups whose MA is discordant with their chronological age (CA) and, because it is non-verbal, children with language difficulties are able to complete the task. The RCPM is designed for use with children aged 3 to 12 and has also been used successfully with children with DS (Laws, Buckley, Bird, Macdonald, & Broadley, 1995) and WS (Van Herwegen, Farran, & Annaz, 2011). The test consists of 36 abstract figures, each with a section missing. Children were presented with each figure individually and asked to choose the piece which

would fit the pattern from a selection of six pieces. The task was conducted according to the manual, with no time limits, and it was ensured that all children understood the instructions before progressing.

Continuous Performance Attention Task

In order to assess children's sustained and selective attention and impulsivity, a visual CPT was designed based upon other CPTs that have been used with young children and children with developmental disorders (Manly et al., 2001; Steele et al., 2012; Trezise et al., 2008). The task was developed using DMDX (Forster, 2009), a Win32-based system that can be used to present stimuli and accurately record reaction times (RTs). It was presented on a Dell Vostro laptop with 15.5 inch screen and a viewing distance of around 45cm. The task required the child to respond to an infrequently occurring target whilst ignoring competing non-targets. Stimuli were attractive, colored images of zoo animals where the targets were two different monkeys amongst eight other distracter animals (lion, tiger, anteater, leopard, giraffe, elephant, hippo and octopus; see Figure 1).

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Figure 1 about here

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Stimuli were presented sequentially for 300ms each in a randomized order in the center of a white background with an inter-stimulus interval of 2000ms. There were 200 trials so the total task duration was 7:36 minutes. The study instructions were presented on screen and read aloud by the researcher: "*In this game you will see some pictures. You need to catch the naughty monkeys. Click every time you see a monkey*". They were presented with images of the target monkeys, and were told to press the left touchpad button to 'catch' the monkeys.

Children were asked and shown to rest the index finger of their dominant hand on the response key and, if necessary, were reminded to do so throughout. There was a practice session of 20 trials to ensure that children understood the instructions before completing the full test. During the test they were given verbal appraisals by the researcher (e.g., *"Well done"*) when they clicked the target, and were reminded to *"Only catch the monkeys"* if they clicked non-targets. This was similar to the procedure used by Steele et al. (2012), where the computer made a 'reward' or 'error' sound in response to hits or incorrect clicks.

Omission errors (where children missed targets), commission errors (incorrect hits) and RTs were recorded.

Procedure

Parents were contacted by telephone to ensure that children met inclusion criteria, were in good health, and to arrange a suitable time for each child to participate in the study. Schools were also contacted by telephone to arrange testing sessions. The researcher visited all families at home where they were provided with the actiwatch and pulse oximetry devices. Parents gave written informed consent for their child to take part in the study and children gave their verbal assent. During the following week children were visited in the morning at school where they individually completed the CPT followed by the RCPM between 9 and 10 o'clock in a quiet room. This was always during school term time in order to avoid irregular routines and sleep schedules that may occur during school holidays. Sometimes children with DS and WS were accompanied by their learning support assistant who sat quietly without intervening with the testing.

Statistical Analyses

Data were analyzed using IBM Statistical Package for Social Sciences V.20. Outlying scores were identified using Cook's distance. Analyses where the significance of results changed after excluding outliers will be explicitly mentioned by denoting 'OR' (Outliers Removed) beside the variable. In all other instances outliers were not excluded (see Thomas et al., 2009).

Data for actigraphy, pulse oximetry and CPT performance were investigated using one-way between-groups ANOVA tests to compare the TD, DS and WS groups. For all ANOVAs, Levene's test was used to assess the assumption of homogeneity of variance. This is sometimes violated when studying atypical groups however ANOVAs were still used to avoid losing power associated with nonparametric tests. The Bonferroni correction was used in post hoc analysis except where equal variances could not be assumed then the Games-Howell test was used, as recommended by Field (2005). We then explored the effects of age on CPT performance using linear regression to plot the developmental trajectory of each dependent variable (scores on CPT task) against increasing CA and MA (independent variables).

Finally we used hierarchical multiple regression to examine the relationship between sleep parameters and performance on the CPT. CA and MA (based on RCPM total score) were controlled for in the first block of the model. The second and third blocks respectively included actigraphy variables relating to sleep duration (actual sleep time) and quality (sleep efficiency, number of night wakings, mean duration of night wakings). These actigraphy variables were selected based on previous research and that they did not strongly correlate with one another so that the assumption of no multicollinearity was not violated (all $<.7$) (Field, 2005). The order of blocks here was important. Firstly, it was necessary to control for CA and MA due to their influences on task performance and sleep parameters in some groups. Second, it was necessary to control for sleep duration before investigating sleep

quality because a physiological compensatory mechanism works to improve or reduce sleep quality in response to shorter or longer sleep duration respectively (Sadeh et al., 2003).

SpO_2 variables were not included in the model due to missing data. Instead, a second model was created, also controlling for CA and MA in block 1, then including mean SpO_2, dips per hour >4%, delta 12 index, and % time spent below 90% SpO_2 in block 2. Again, the assumption of no multicollinearity was not violated.

Results

Actigraphy

With the exception of one TD child who refused to wear the actiwatch, all children had four or more days and nights of actigraphy data and the majority (78%) had seven or more, as requested. One-way between-groups ANOVA showed no significant difference in compliance between the three groups (F (2, 94) = 1.72, p = .19, ηp^2 = .04). Children in the TD group had the latest bedtimes. Children with DS had the most night wakings and restless sleep and therefore lower sleep efficiency, whilst children with WS had the longest sleep latencies. Interestingly, although the mean assumed sleep time was considerably longer for children with DS relative to the other two groups, the actual sleep time of all three groups was remarkably similar, varying by only four minutes. The results are presented in Table 2.

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Table 2 about here

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Pulse Oximetry

Pulse oximetry data were not available for all children. In the cases of six TD children (20%) this was due to lack of equipment and for two cases data on the machine was corrupted. Three children (14%) with DS and ten with WS (45%) refused to wear the pulse oximeter probe due to fear of the equipment. Further, data were removed for five children with DS (23%) and two with WS (9%) who did not achieve at least five hours of recording on any one night (Urschitz et al., 2003). Hence the final sample was 33 TD children (80%), 14 children with DS (64%) and 10 children with WS (45%). These drop-out rates for home pulse oximetry recordings are a common occurrence when working with children with disabilities due to known difficulties with hypersensitivity and anxiety (e.g., Davies, Udwin, & Howlin, 1998; Morris, 2006; Myers & Pueschel, 1991). There was no difference between groups for the total amount of artifact-free recording time that was analyzed ($F(2,56)=1.65$, $p=.21$, $\eta p^2=.06$).

One way between groups ANOVAs showed greater evidence of possible SDB in the children with DS, with lower SpO_2, more dips per hour and a higher delta 12 index. The WS group had a significantly higher heart rate than the other two groups (Table 3).

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Table 3 about here

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Group differences on tasks

One-way between-groups ANOVAs were computed to investigate group differences on the CPT task for number of correct hits and commission errors as well as RTs for hits and errors. Data from one child with DS were removed as he did not adhere to the instructions of the CPT. Significant group differences were evident, with the two disorder groups performing

significantly less well than TD children on all variables. In addition, children with DS

achieved significantly fewer hits and their RT for errors was significantly slower than both

other groups (Table 4).

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Table 4 about here

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Developmental effects on the CPT task

Linear regression was used to investigate CA- and MA-related changes in performance scores

for correct hits, commission errors, and RTs for hits and errors.

Chronological age

In the TD group but not the DS or WS groups there was a significant positive relationship

between CA and number of correct hits (TD: R^2=.11, $F(1,39)$=4.80, p=.04; DS: R^2=.14,

$F(1,19)$=2.4, p=.14; WS: R^2=.04, $F(1,20)$=2.56, p=.13) and between increased CA and

reduced number of commission errors (TD: R^2=.10, $F(1,39)$=4.21, p<.05; DS: R^2=.03,

$F(1,19)$=.62, p=.44; WS: R^2=.02, $F(1,20)$=.35, p=.56).

In the TD and WS groups but not the DS group, increased CA was significantly related to

faster RT for correct hits (TD: R^2=.69, $F(1,39)$=35.81, p<.001; DS: R^2=.12, $F(1,19)$=2.51,

p=.13; WS: R^2=.48, $F(1,20)$=18.53, p<.001) and to faster RT for commission errors (TD:

R^2=.14, $F(1,36)$=5.99, p=.02; DS: R^2=.09, $F(1,17)$=1.57, p=.23; WS: R^2=.33, $F(1,20)$=9.85,

p=.01).

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Figures 2 and 3 about here

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Mental age

In the TD group but not the DS or WS groups, increased RCPM total was significantly related to increased correct hits on the CPT (TD: R^2=.22, $F(1,39)$=11.07, p=.002; DS: R^2=.10, $F(1,17)$=1.95, p=.18; WS: R^2=.003, $F(1,20)$=.06, p=.82).

In the TD and WS groups but not the DS group, increased MA was significantly related to faster RT for correct hits on the CPT (TD: R^2=.69, $F(1,39)$=35.81, p<.001; DS: R^2=.12, $F(1,19)$=2.51, p=.13; WS: R^2=.48, $F(1,20)$=18.53, p<.001).

MA was not significantly related to number of or RT for commission errors for any group.

Relationship between sleep and attention

Hierarchical multiple regression was used to examine the relationship between actigraphy variables, SpO$_2$ and CPT performance. Omission errors, commission errors and their RTs on the CPT were entered individually as dependent variables.

The first model (actigraphy) included CA and MA in block 1, actual sleep time in block 2 (sleep duration block), and sleep efficiency, number of night wakings and mean duration of night wakings in block 3 (sleep quality block). After controlling for CA and MA, significant findings in the TD group showed that block 3 (sleep quality) was able to predict 16% of the variance in number of correct hits (R^2 change=.16, F change (3,30)=2.97, p=.046) and 27% of the variance for RT errors (R^2 change=.27, F change(3,30)=5.07, p=.01). Children with better sleep quality achieved more correct hits on the task and had quicker RTs for commission

errors. The model was not able to significantly predict performance on the task for the DS or WS groups.

The second model included SpO_2 variables (mean SpO_2, dips per hour >4%, delta 12 index, and % time spent below 90% SpO_2) in block 2. In the TD group, the SpO_2 variables block explained almost half of the variance in number of commission errors (R^2 change=.48, F change $(2,30)$=7.30, $p<.001$). TD children with better (higher and less variable) SpO_2 saturation made fewer commission errors on the tasks than children with poorer SpO_2. The model was not able to significantly predict performance on the task for the DS or WS groups.

Discussion

The present study used a novel visual CPT and objective sleep measures to investigate the relationship between sleep and attention in children with DS and WS compared to TD children.

Actigraphy and pulse oximetry data were consistent with previous reports of sleep problems in children with DS and WS (e.g., Annaz et al., 2011; Carter et al., 2009). These sleep characteristics were syndrome-specific. Children with DS had increased night wakings and fragmented sleep as well as lower SpO_2, increased SpO_2 dips and higher delta 12 indices (SpO_2 variability) compared to TD children. These data are suggestive of OSAS, which is known to be common in DS (Churchill et al., 2011; Dyken et al., 2003; Ng et al., 2006), though cannot be determined by pulse oximetry alone as it has relatively low sensitivity: 64% when compared to polysomnography for accurate detection of OSAS related SpO_2 desaturations. Children with WS had long sleep latencies, consistent with previous parental reports and actigraphy data (Annaz et al., 2011; Ashworth et al., 2013; Udwin et al., 1987), although night wakings and sleep efficiency were comparable to the TD group, which is in contrast with some earlier reports (Annaz et al., 2011; Ashworth et al., 2013). We also found

that children with WS had a lower mean and median SpO_2 than the TD group which, to our knowledge, has not been previously reported. Children with WS also had a significantly higher heart rate during sleep than both other groups, and children with DS had a higher heart rate than TD children, possibly due to known cardiovascular problems in these groups (Donnai & Karmiloff-Smith, 2000; Roizen & Patterson, 2003). The pulse oximetry data for our TD group are analogous to reference values reported by Urschitz et al. (2003) in a large random sample of 100 healthy TD children, so we can assume that these children form a representative comparison group.

The findings from the CPT attention task support previous research showing that children with DS and WS suffer problems with attention (Munir et al., 2000; Trezise et al., 2008), as they displayed clear deficits across all elements of the task, achieving fewer hits, more commission errors and longer RTs. Particular problems were noted in the DS group, who performed significantly less well than both other groups on their ability to respond to the target, achieving ten fewer hits than the WS group, and 18 fewer than the TD children.

In general, children tended to improve on all areas of the CPT with increasing CA and MA, though this was not always statistically significant. TD children showed the strongest age-related effects on the task with a significant relationship with CA on all variables, and significant association with MA for number and RT of correct hits. There was more variability in CPT performance in the DS and WS groups, shown by the increased standard deviations, so it is no surprise that the strength of developmental trajectories was weaker in these two groups. Interestingly, although in the WS group children's hit and error rates did not significantly improve with age, the RTs for hits and commission errors become faster for the TD and WS groups, supporting previous research that RT decreases with age (Steele et al., 2012). The TD group also had a significantly faster mean RT for commission errors than the other two groups. Fast RTs for incorrect responses often indicate reduced inhibition.

However, in this case we suspect that this is due to better motor skills in this group and motor speed has developed with age in TD and WS. It is not proposed that the TD group were actually less inhibited than the DS and WS groups because their absolute number of commission errors was fewer.

Sleep parameters assessing sleep duration, sleep quality and SpO_2 variables were examined for possible influences on task performance using hierarchical multiple regression controlling for effects of CA and MA. The models showed that performance was not related to sleep or SpO_2 in the DS or WS groups; however, in the TD group, children with better sleep quality and higher, less variable SpO_2 had improved performance on the task compared to children with poorer sleep quality and SpO_2. For the TD group, these results support our hypothesis that better task performance will be related to improved sleep quality or duration. Specifically, better sleep quality was related to more correct hits and faster RT for commission errors. This is in contrast with other research which has reported that reduced sleep time, rather than sleep quality, is related to inattention (Gruber et al., 2012; Holley, 2009). Others, however, have reported similar findings to the current study, namely, that children with disrupted sleep architecture suffer problems in the attentional domain (Blunden et al., 2005; Herrera et al., 2006). The present study also found that higher, less variable SpO_2 was associated with fewer commission errors, accounting for almost half (48%) of the variance in commission errors in the TD group. This directly supports previous reports that children who snore have problems with sustained and selective attention, which were related to SpO_2 desaturations and associated night wakings (Archbold et al., 2004; Kennedy et al., 2004).

The fact that the multiple regression models were not able to predict CPT performance for the DS or WS groups was somewhat surprising since, in general, the DS group had the poorest sleep quality and also the lowest performance on the CPT. Hence it was expected that there

would be a strong relationship between sleep and performance. This is the first study to investigate this area in children with DS and WS, including a cross-syndrome comparison; thus it paves the way for future research to investigate in further detail the precise factors that may contribute to attentional control and whether it is sleep-related in children with DS and WS. In two complex disorders with a spectrum of behavioral and cognitive problems, it is likely that other confounding factors were not accounted for in the present study, such as motor ability, motivation or environmental factors. For example, some children with DS and WS attended special schools for children with learning difficulties where they may be less used to having to sustain attention compared with children attending mainstream schools. In addition, all but two children with DS and all with WS were from different schools throughout the UK, relative to only three London schools for the TD group. These differences in learning environments may help to explain some of the variability in the results of the DS and WS groups. It is also possible that characteristics of the syndrome affect sleep and attention in different ways, so masking their relationship. One example is the issue of motivation to complete a repetitive and unrewarding task. Although TD children appeared to be motivated by a desire to perform well on the task, it is unlikely that all children with intellectual delay were motivated in this way, especially the DS group, who had the lowest MA. Perhaps the promise of a tangible reward for good performance would have better served to encourage them. Future studies could attempt to control for behavioral characteristics that may confound the results.

It is unfortunate that some pulse oximetry data were necessarily missing. Group sizes were therefore smaller in the DS and WS groups (14 and 10 respectively) thus power was reduced. Nevertheless, others have found significant effects with such sample sizes (e.g., Archbold et al., 2004; Blunden et al., 2005). In fact, the sample size in this study is larger than much other research in the field and effect sizes were generally good. However, it is probable that it would have benefitted from more participants in order to add power to analyses where

significant effects were expected but not found. Nevertheless, our use of actigraphy meant that detailed information on sleep quality and duration could still be gathered from all children. Although actigraphy provides a useful and cost-effective method of gathering data, the Actiwatch Mini has not yet been validated against PSG or other devices, and norms in typical populations are not available. However, our use of a TD group gives a useful comparison in this study so results are still meaningful.

An issue with the CPT task was that it was subject to a ceiling effect in the TD group, with 19 children (46%) making no omission errors. This can often be a problem with researching attention, as tasks often need to be quite long or more demanding in order to avoid ceiling effects in the most able children. However, standard CPT tests have been found to be unsuitable for testing children with developmental delay as they are too long or difficult so many children lose interest and do not or cannot complete the task, thus data are not meaningful (Knox et al., 2012; Sullivan et al., 2007). At 7:36 minutes, the present task was already longer than some other CPTs that have been used with children with disorders (e.g., Trezise et al., 2008; 6:20 minutes with 7 to 18 year olds with DS). Despite the ceiling effect in the TD group, the CPT task is still useful for understanding attentional skills in children with DS and WS. The fact that these children did not reach the test ceiling shows atypical development of sustained/selective attention.

A final point to note is that we cannot rule out the possibility of a selection bias in the TD and DS groups. Although parents were told that the study was investigating normal sleep patterns, it is conceivable that parents whose children experienced sleep problems were more inclined for their children to participate. Nevertheless, our findings in these groups were consistent with previously reported data (Churchill et al., 2011; Urschitz et al., 2003) so we can assume that these were representative groups. Selection bias was not thought to be a problem in the

WS group as parents were contacted initially by telephone and only two families declined to take part due to current family circumstances.

In conclusion, significant attentional difficulties were found in the two disorder groups, with children with DS experiencing the greatest problems. In the TD group, better performance on the CPT was related to better sleep quality and higher, less variable SpO_2. In the DS and WS groups it is likely that attention was influenced by other confounding factors that were not accounted for in the present study such as environmental aspects, motivation or other syndrome characteristics. Nevertheless, it should not be ruled out that improved sleep would be beneficial. Attention is an important aspect of normal healthy development, affecting the way in which an individual interacts with their environment and therefore learns from it. In light of these findings, as well as the known physiological and psychological benefits of sleep, it should be ensured that children obtain adequate sleep in order to maximize attention and achieve optimum cognitive performance. This study is unique in investigating relationships between sleep and attention in children with DS and WS, it reveals the problems associated with assessment of attention in these groups and opens the way for future research to investigate what the precise contributions to attention are, and whether sleep has any influence.

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Table 1

Participant details

Group	Chronological age (mean (SD))	Age range	RCPM raw score (mean (SD))	Mental age equivalent	Mental age range
TD (n=41)	9.44 (1.70)	6.19 – 12.90	27.68 (5.35)	11	6.25 – Over 12
DS (n=22)	9.42 (1.98)	6.09 – 12.23	12.60 (3.53)	Under 5	Under 5 – 8
WS (n=22)	9.24 (2.13)	6.08 – 12.58	14.64 (3.02)	6	Under 5 – 8.75

Table 2.

Mean scores (SD) and group differences using ANOVA for selected actigraphy variables

	TD (n = 40)	DS (n = 22)	WS (n = 22)	F	p	η_p^2
Bed time (hh:mm)	21:18 (0:42)	20:30 (0:37)	20:48 (0:38)	10.74	<.001[ab]	.21
Getting up time (hh:mm)	7:33 (0:31)	7:06 (0:37)	7:04 (0:41)	6.08	<.01[ab]	.13
Assumed sleep time (hh:mm)	9:28 (0:42)	10:06 (0:43)	9:21 (1:01)	5.82	<.01[ac]	.13
Actual sleep time (hh:mm)	8:19 (0:37)	8:22 (0:50)	8:18 (0:55)	.06	.94	.01
Sleep efficiency (%)	87.66 (3.61)	82.99 (5.45)	88.79 (3.28)	13.03	<.001[ac]	.24
Sleep latency (mm:ss)	27:40 (11:11)	23:23 (15:53)	46:30 (37:34)	3.44	.04[c]	.08
Number of night wakings	31.91 (7.97)	39.50 (9.19)	28.00 (6.10)	12.30	<.001[ac]	.23
Mean night waking duration (mm:ss)	2:08 (0:24)	2:35 (0:30)	2:14 (0:26)	7.60	.001[ac]	.16
Fragmentation index	29.70 (8.14)	41.77 (8.74)	31.84 (6.31)	17.26	<.001[ac]	.30

a = Significant difference between TD and DS (p < .05)

b = Significant difference between TD and WS (p < .05)

c = Significant difference between DS and WS (p < .05)

Table 3.

Mean scores (SD) and group differences using ANOVA for SpO$_2$ saturation variables

	TD (n = 33)	DS (n = 14)	WS (n = 10)	F	p	η_p^2
Time analysed (hh:mm)	28:22 (10:59)	24:09 (8:27)	22:43 (8:36)	1.65	.21	.06
Mean SpO$_2$ OR	97.81 (.71)	96.80 (0.84)	96.83 (.71)	10.12	<.001[ab]	.31
Median SpO$_2$ OR	98.03 (.72)	97.00 (0.77)	96.88 (.83)	12.27	<.001[ab]	.35
SpO$_2$ dips per hour >4% OR	1.96 (1.26)	4.35 (1.37)	2.36 (.34)	16.70	<.001[ac]	.42
% time SpO$_2$ below 90 %	0.79 (2.00)	2.22 (5.14)	0.96 (.54)	1.06	.36	.04
Delta 12	0.41 (.13)	0.52 (0.12)	0.43 (.12)	4.02	.02[a]	.13
Pulse OR	73.37 (4.52)	79.24 (4.22)	85.63 (.84)	22.28	<.001[abc]	.51

a = Significant difference between TD and DS (p < .05)

b = Significant difference between TD and WS (p < .05)

c = Significant difference between DS and WS (p < .05)

Table 4.

Group differences using ANOVA for correct hits, commission errors and reaction times on the CPT

	TD (n = 41)	DS (n = 21)	WS (n = 22)	F	p	ηp^2
Correct hits (/40)	37.79 (3.87)	19.58 (11.51)	30.05 (8.87)	35.13	<.001[abc]	.48
Commissions (/160)	8.58 (9.19)	21.00 (18.27)	18.82 (17.53)	6.21	<.01[ab]	.14
RT hits	619.18 (69.90)	837.60 (179.23)	786.35 (148.73)	23.16	<.001[ab]	.38
RT errors	484.06 (80.34)	714.70 (146.13)	615.11 (110.60)	31.10	<.001[abc]	.45

a = Significant difference between TD and DS (p < .05)

b = Significant difference between TD and WS (p < .05)

c = Significant difference between DS and WS (p < .05)
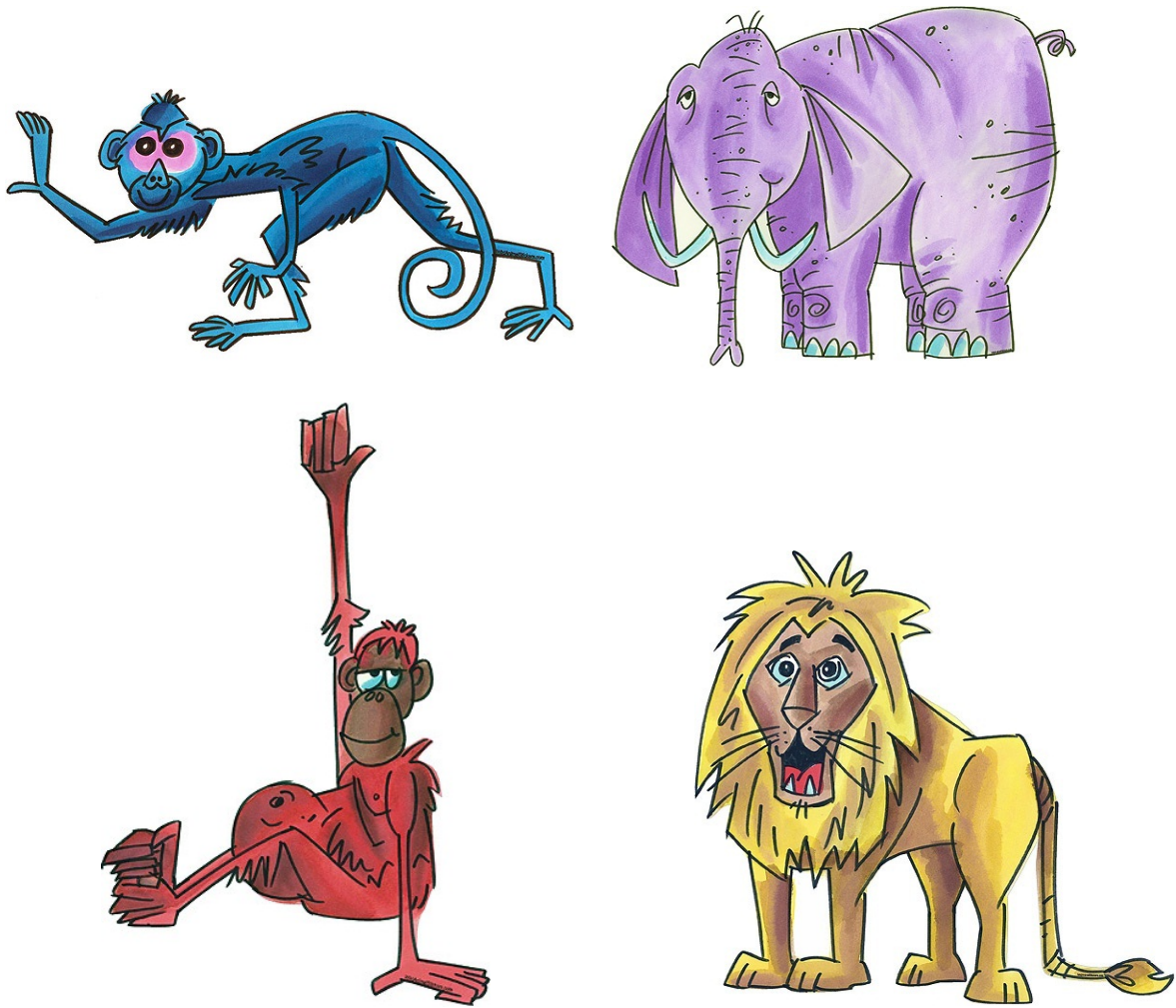
Figure 1. Example of stimuli used in the CPT task, including two target monkeys.
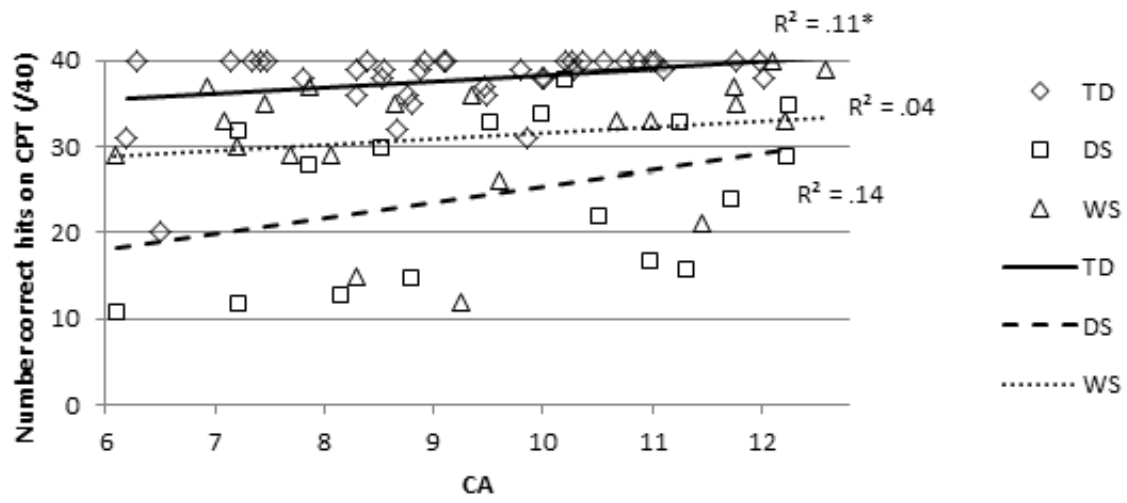
Figure 2. Developmental trajectories for the TD, DS and WS groups for correct hits on the CPT. * =
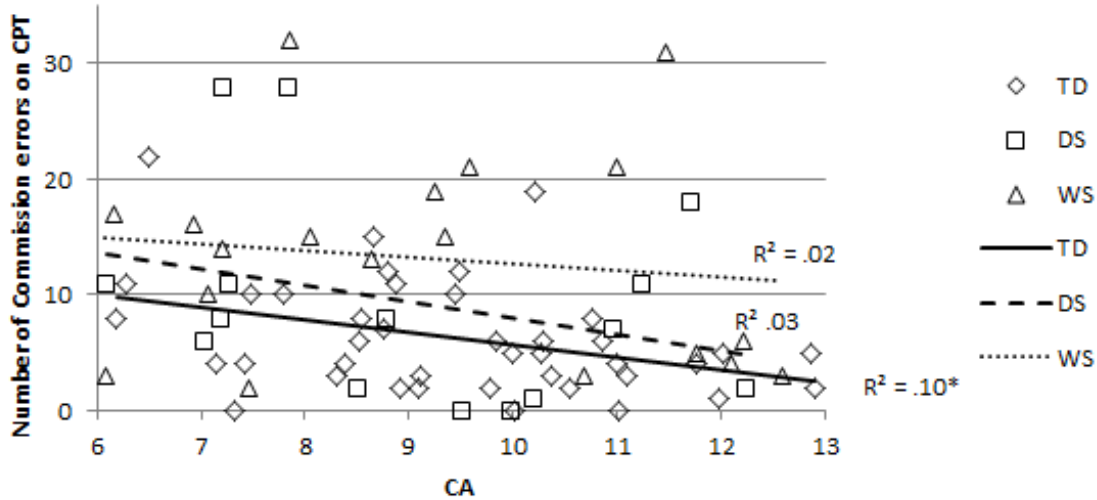
significant effect.

Figure 3. Developmental trajectories for the TD, DS and WS groups for commission errors on the

CPT. * = significant effect.