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REVIEW ARTICLES

The impact of sleep problems on functional and cognitive outcomes in children with Down syndrome: a review of the literature

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Study Objectives: The aim of this review was to summarize the existing literature on the association between sleep problems and cognition, function, and behavior in children with Down syndrome.

Methods: Embase, PubMed, CINAHL, and PsychINFO databases were searched to retrieve all studies published between 1990 and 2018 that evaluated the relationship between sleep and cognition, function, or behavior in children with Down syndrome.

Results: Fifteen articles were included, which were mostly of a cohort or case-controlled design. Five articles addressed sleep and cognition only, 6 reported on sleep and behavior, and only 1 reported on sleep and functional ability. Three papers evaluated sleep and both cognition and behavior. Findings varied across studies with methodological differences, making it difficult to directly compare results. The association between sleep and behavior or cognition in children with Down syndrome remains uncertain, but a large study in 110 children provides strong evidence of a negative impact of sleep disorders on the accomplishment of daily life habits.

Conclusions: The impact of coexisting sleep disorders in children with Down syndrome has not been widely studied, with only 15 relevant studies found through an extensive literature review. Large well-designed studies are required to fully understand this relationship further. This is important as sleep-disordered breathing and difficulties with sleep patterns and routines are highly prevalent in children with Down syndrome. Sleep may be one of the few treatable factors that can assist in improving long-term outcomes in this population.

Keywords: pediatrics, Down syndrome, cognition, behavior, function

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INTRODUCTION

Children with Down syndrome (DS) have been shown to have different sleep architecture compared with those without DS and to have a high prevalence of sleep problems.[1] Anatomic considerations such as hypotonia, macroglossia, and midface hypoplasia result in an increased risk for obstructive sleep apnea (OSA), and central sleep apnea also occurs, possibly secondary to neurological factors.[2,3] Family dynamics, medications, and coexisting medical conditions may also contribute to poor sleep quality.

OSA results from repetitive upper airway obstruction during sleep and can lead to snoring, intermittent hypoxia, hypercarbia, restless sleep, and increased awakenings.[4] The prevalence of OSA in children with DS is estimated to be between 31% and 79%,[5-9] which is approximately 6 times higher than in the general pediatric population. OSA severity peaks during early childhood, subsiding with growth and improved tone during school years. A resurgence of symptoms often occurs with the onset of obesity in adolescent years, with an estimated risk ratio of 2.4.[10]

Comorbidities found in children with DS can be associated with significantly disrupted sleep.[11] In a recent large-cohort study, 78% of children with DS with pulmonary hypertension were found to have coexisting OSA. Other common coexisting conditions, such as gastroesophageal reflux disease, hypothyroidism, and lower airway abnormalities, may further exacerbate OSA.[12]

Behavioral characteristics of DS are an important contributor to disrupted sleep. Common sleep problems include bedtime resistance, sleep anxiety, night waking, parasomnia, daytime sleepiness, and periodic limb movements.[1,13-16] These problems place a significant burden on caregivers as well as impacting on their own sleep quality. The pressures of raising a child with intellectual disability often influence parenting strategies, including the ability to cope with their child's sleep problems. Other medical problems are often a priority over establishing sleep routines, and further disruption of sleep can occur with repeated or prolonged hospital admissions. Combined with the intellectual and communication limitations seen in children with DS, it is not surprising that this population has difficulties acquiring good sleep habits and achieving quality sleep.

The spectrum of intellectual disability in DS ranges from profound to borderline intellectual functioning.[17-19] Studies evaluating IQ (intelligence quotient) have universally shown that decline occurs over time and that cognitive development in children with DS proceeds at a slower rate.[20] Verbal domains are consistently affected, with attainment of verbal abilities

decelerating with age. Temperament, maternal education, medical conditions, and school experiences have all been shown to be associated with cognitive differences in children with DS.[21] Individual phenotype still remains highly variable, and existing literature has been unable to ascertain the expected age-related trajectory for this population versus slowing or acceleration of function that has been impacted by other factors. More work is required to determine if there are ages at which interventions to enhance specific cognitive domains may be less or more effective.[20]

Children with DS do show increased behavior problems compared with children without developmental disabilities.[22] Studies have demonstrated a pattern of predominantly externalizing behaviors (dominant, opposing/refusing impulsiveness, inattention, and increased motor activity) in younger school-aged children and increased internalizing behaviors (shy/insecure, low self-confidence, decreased motor activity) in adolescents and adults.[19,23-25] Attention-deficit/hyperactivity disorder and autistic spectrum disorder have been found to coexist in children with DS, with prevalence estimates of 6–8% and approximately 10%, respectively.[26] Behavioral difficulties are often exacerbated by intellectual disability and frustration developing from communication issues.

There is now significant evidence regarding the negative impact of sleep deprivation[27] and sleep-disordered breathing[28-33] on cognition and behavior in healthy children. Whether children with DS, in whom sleep problems are so common, are more at risk for these negative effects of poor sleep remains to be determined; in children with DS, the crucial period of development is likely to be longer than in healthy children and sleep problems may also receive less attention, due to priority being given to coexisting health issues.[34] These factors, combined with existing intellectual disability and behavioral phenotype, may contribute to increased vulnerability in this group.

The present study reviews existing literature regarding cognitive, behavioral, and functional outcomes in children with DS and coexisting sleep problems. This area has not been widely studied. We aimed to examine whether there is evidence to support an association between sleep problems and (1) cognition, (2) behavior, and (3) function in children with DS.

METHODS

The current systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines. [35]

Search strategy

A literature search was conducted using the following databases: EMBASE, PubMed, CINAHL, and PsychINFO. The search was limited to studies published between 1 January 1990 and 31 December 2018. The following MeSH (medical subject heading) terms and related subheadings were combined iteratively to generate our search strategy: "Down syndrome," Down's syndrome," "Trisomy 21," "T21 to define the population, "sleep," "sleep problems," "sleep disorders," AND "cognition," "cognitive function," "cognitive outcomes," "IQ," "Intellectual Ability" OR "behaviour," behavior," "behavioural outcomes,' "behavioral outcomes," "temperament," OR "function," "functional ability," "functional outcomes," "activities of daily living," "ability".

Inclusion criteria

All studies in children with DS (0–18 years) that evaluated a relationship between sleep and any of (1) cognition, (2) behavior, or (3) functional ability were included in the search. Only English-language studies published between 1 January 1990 and 31 December 2018 were included.

Exclusion criteria

Exclusion criteria included the following: (1) studies not written in English; (2) studies published outside of 1 January 1990 to 31 December 2018; (3) studies pertaining to adults with DS (classed as >18 years); (4) papers focusing on sleep interventions and outcomes; and (5) clinical reviews, case reports, abstracts, and editorials/commentaries. To our knowledge there are no studies that have specifically looked at the effectiveness of sleep therapies on cognitive, behavioral, and functional outcomes.

Study selection

All studies were managed using the EndNote X9 program (Clarivate Analytics, Philadelphia, PA). Duplicates were removed by hand and using the automatic duplicate removal process in EndNote. Remaining results were screened first by title and abstract for relevance and then by the full article. To ensure reliability of the screening process, 2 authors completed the screening independently.

In total, the 4 database searches yielded 605 results. After removal of duplicates, 408 results remained. A total of 376 were excluded as being irrelevant to the study question after review of title and abstracts, and a further 4 were excluded because the articles were abstracts only. Twenty-eight articles were screened by full-article review. One was excluded as a clinical review published after 31 December 2018. Thirteen articles related to sleep in children with DS but did not address function, behavior, or cognition and therefore were excluded from analysis. A total of 15 papers were included in the final review. The detailed filtering and selection process is summarized in **Figure 1**.

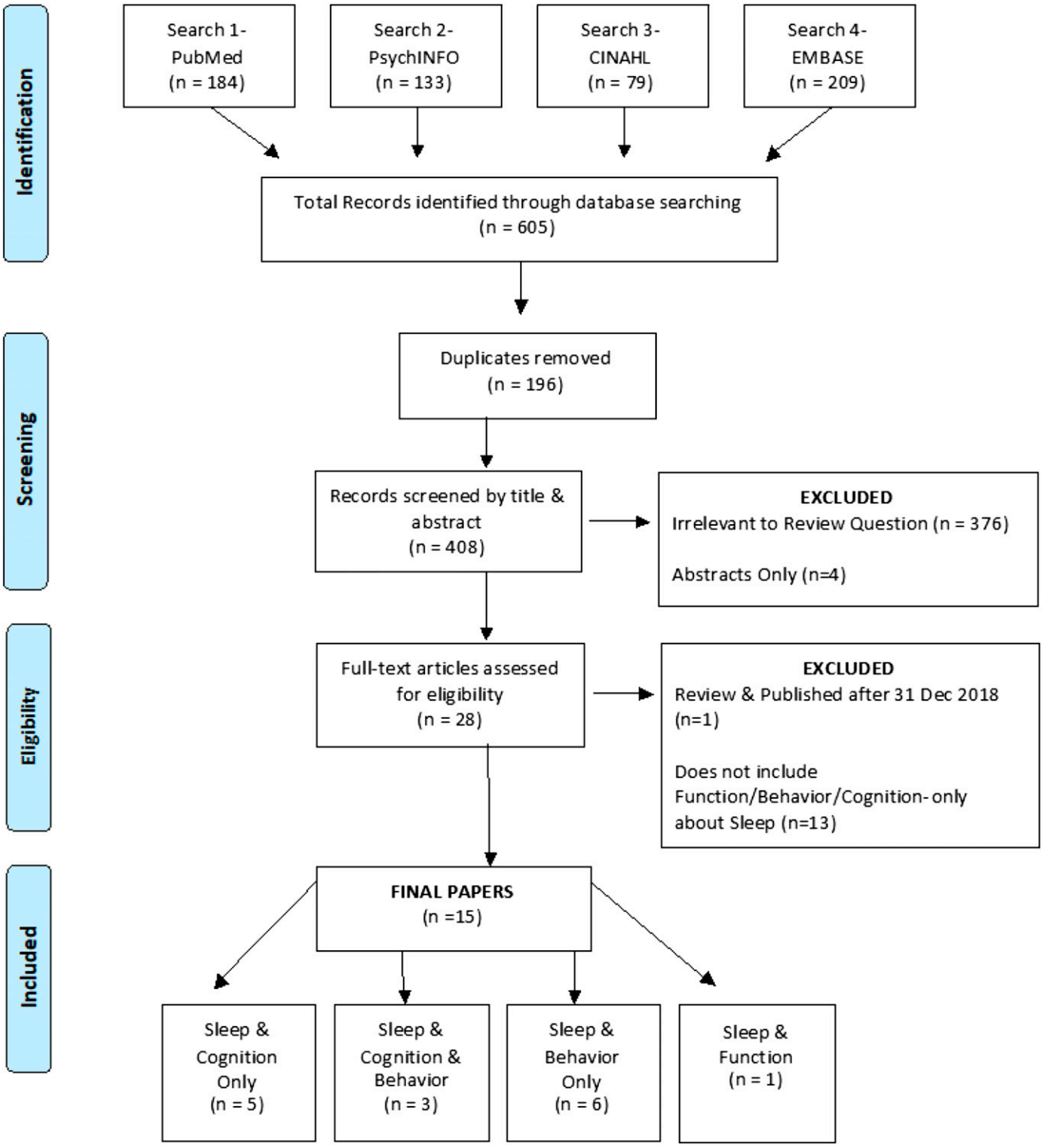
RESULTS

Fifteen relevant articles were identified for inclusion in this review. Some of these studies were found to include the evaluation of participants with DS in addition to children with other disabilities or typically developing (TD) children. These were still believed to be significantly relevant to the study questions. Five articles addressed sleep and cognition only, 6 addressed sleep and behavior, and only 1 article addressed sleep and functional ability. Three papers evaluated sleep and both cognition and behavior. These were evaluated from both aspects separately.

Sleep and cognition in DS

Studies in children with DS that have assessed the relationship between cognitive deficits and sleep-disordered breathing have

Figure 1—Flow chart of the study screening and selection process.



Adapted from the PRISMA 2009 flow diagram. PRISMA = Preferred Reporting Items for Systematic Review and Meta-Analyses.

been mixed, with some studies strongly suggesting an association and others not.[36-43] This is perhaps not surprising considering that this has been a difficult association to ascertain even in the TD healthy population.

Table 1 summarizes the existing evidence in this area, with only 8 articles to date addressing this topic. All of these articles have been published within the last decade, with 50% of them in the last 4 years. However, direct comparison of these studies is difficult due to their heterogenous nature. Most of the studies have concentrated on school-age children, with those that have focused on the preschool-age group showing different results. An example of this is in the studies by Breslin et al[38] and Edgin et al,[39] which found contrasting results with sleep disruption and executive function in the 2 age groups; Breslin et al concluded

Table 1—Studies evaluating sleep and cognitive measures in children with DS.

First Author	Year	n	Cohort and Mean Age, y	Sleep Assessment	Cognitive Test	Findings	Comments
Chen[36]	2013	29	Adolescents and young adults with low OSA, 20.26 (n = 13); high OSA, 22.44 (n = 16)	Sleep questionnaire assessment of OSA and sleep disturbances in general	Choice Reaction Time Test, Verbal Fluency Test, Knock Tap Test	Features of OSA significantly associated with poor verbal fluency and attention	Self-reported measure of sleep disturbance and OSA only
Breslin[38]	2014	31	School age, 9.7	PSG defined: OSA = 19, no OSA = 12	Arizona Cognitive Test Battery	Verbal IQ 9 points lower in those with OSA	Arizona Cognitive Test Battery specifically designed and validated to assess the cognitive phenotype in DS
						Executive function also less good in those with OSA	
						No difference in full-scale and verbal IQ	
Brooks[37]	2015	25	School age, 10.2	PSG defined: OSA = 10, no OSA = 15	Battery of neuropsychological tests including Stanford Binet Intelligence Scale, Woodcock Johnson Tests of Achievement	No independent associations of SDB with any of the neuropsychological tests	—
						No difference in any of the neuropsychological tests between those who had OSA and those who did not	
						Positive relationship seen between total sleep time and % slow-wave sleep and cognitive function	
Edgin[39]	2015	DS = 29, TD = 20	Preschool, 3.5	Actigraphy, CSHQ	The MacArthur-Bates CDI, LENA digital processor, BRIEF-P	Significant proportion of young children with DS showed disturbed sleep (66%)	—
						DS group with poor sleepers showed specific difficulties with expressive language compared with DS good sleepers	
						No difference in executive function	
Nixon[42]	2016	30	School age, 9.1	SDB measured by PSG	The Adaptive Behavior Assessment System Parent/ Primary Caregiver Form (ABAS-II)	General adaptive composite score not statistically different between OSA severity groups but generally low	Self-reported questionnaire assessment
						Conceptual score—specifically communication skill area significantly correlated with OAHI; lower with higher OAHI	No control group without SDB to compare – referred sample

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Table 1—Studies evaluating sleep and cognitive measures in children with DS. (continued)

First Author	Year	n	Cohort and Mean Age, y	Sleep Assessment	Cognitive Test	Findings	Comments
Joyce[40]	2017	TD = 22, DS = 22	Preschool: TD = 3.25, DS = 3.05	SDB measured by PSG	Mullen Scales of Early Learning	SDB in TD children associated with poorer cognitive but same not found in DS group	Only mild SDB in both groups
					MacArthur Communicative Development Inventory		
Ashworth[43]	2017	DS = 20, WS = 22, TD = 33	School age, 9.59	Measured sleep-dependent learning testing task ability after periods of wake and sleep	Novel Animal Names Task to assess learning of declarative information	In DS, learning did not appear to be dependent on sleep	Novel testing technique and novel test
						Trend toward improvement in wake-sleep group after sleep, suggesting learning may be better in mornings for children with DS	Quality of sleep periods not objectively assessed
Esbensen[41]	2018	30	School age, 11.68	Sleep disturbances assessed by actigraphy and parent-reported questionnaire (CSHQ)	Kaufmann Brief Intelligence Test-2	Parent reports of restless sleep behavior but not actigraphy reports of short sleep duration or poor sleep efficiency were predictive of executive dysfunction	No objective measure of OSA specifically
					Stanford Binet-5–Working Memory		
					Scales of Independent Behavior–Revised	No measures of sleep problems were predictive of children's performance on neuropsychological tests	
					BRIEF		

BRIEF = Behavior Rating Inventory of Executive Function; BRIEF-P = Behavior Rating Inventory of Executive Function-Preschool; CDI = communicative development inventories; CSHQ = Child Sleep Habits Questionnaire; DS = Down syndrome; LENA = Language Environment Analysis; OAHI = obstructive apnea-hypopnea index; OSA = obstructive sleep apnea; PSG = polysomnography; SDB = sleep-disordered breathing; TD = typically developing; WS = Williams syndrome.

that school-age children with DS and OSA had poorer executive function than those without OSA. In their study, Edgin et al demonstrated no difference in executive function between poor sleepers and good sleepers in the preschool-age group, although language development was worse in the poor sleepers. In their conclusions, the authors provided several valid reasons for the difference in results from published studies in older children, including highlighting the difficulty of testing in the preschool population. Methodologically, a major strength of both these studies was the use of objective measures of sleep (polysomnography [PSG] and actigraphy, respectively) compared with many other studies that have used parent-reported sleep questionnaires. However, this could potentially also explain the different results, as although both use objective sleep measures, actigraphy and PSG evaluate different aspects of sleep. Actigraphy is unable to discriminate whether sleep disruption occurs as a result of OSA or from other nonrespiratory sleep problems but provides an overall pattern of sleep quality, usually in the home environment. In contrast, PSG can diagnose OSA but only evaluates sleep quality over 1 night in a laboratory setting. Therefore, it is possible that the differing results from these 2 studies reflect different underlying sleep problems contributing to the sleep disruption. Before any conclusions can be drawn regarding the relationship between sleep and executive function in children of any age with DS, further work is required to develop more reliable measures of cognitive function, particularly in the younger age group, and ideally studies should include the use of multiple sleep measures to understand the exact sleep condition for the children included. This is particularly important in this subgroup of children in whom respiratory and nonrespiratory sleep problems commonly coexist.

Another difficulty in comparing published studies is that the choice of cognitive test has also varied from study to study. Cognitive measures have ranged from a battery of tests, including several aspects of cognition, to specifically looking at certain fields such as language or executive function. The reliability and interpretation of such testing in children with existing intellectual disability are also uncertain. Most neuropsychological assessments have not been validated in children with known developmental disabilities. Special challenges are associated with testing individuals who have intellectual and developmental disorders, including substantial floor effects and the confounding effects of impaired language and attention.[44] This is particularly relevant to children with DS as many are nonverbal, adding to the complexity of testing.

Despite these challenges there are, however, some striking findings that support an association between sleep disturbance and worse cognitive function in children with DS. In the previously mentioned study by Breslin et al[38] verbal IQ was 9 points lower in children with DS and coexisting OSA compared with those without OSA. This study included the largest subset of school-age children with DS and used a previously validated cognitive test battery designed specifically for use in children with DS.[44]

Edgin et al[39] found that only 31.6% of preschool children in their DS poor-sleepers group were combining words, compared with 80% of those in the DS good-sleepers group. Confounding factors such as the presence of behavioral problems may have influenced these results, but the significance of such striking findings cannot be overlooked when drawing conclusions regarding the potential impact of sleep problems on certain aspects of cognitive function in children with DS. It also highlights the need for well-designed, large-scale studies to evaluate this relationship more effectively in this population of children.

Sleep and behavior in DS

One of the difficulties in examining sleep and its impact on behavior is the number of potential confounding environmental factors that may also influence behavior, such as diet, parenting methods, and medications. This area has not been widely studied in children with DS, with only 9 studies that have evaluated the relationship between sleep and behavior in children with DS[37,38,40,45-50] found through the search strategy (**Table 2**). Included in this are 3 studies that examined both cognitive and behavioral measures, therefore having some overlap with **Table 1** and subject to the same limitations.[37,38,40]

The largest study, by Kelmanson,[46] evaluated 34 children with DS aged 9–15 years and 34 TD controls of the same age. This study found sleep problems to be a predictor of behavioral and emotional difficulties in both children with DS and TD children, with the total sleep disturbance score on the Child Sleep Habits Questionnaire being a significant predictor of the child attention-deficit/hyperactivity score. Although only self-reported sleep assessment was undertaken with parental Child Sleep Habits Questionnaire completion, the study findings are perhaps strengthened using teacher rather than parent reports of behavior.

Esbensen et al[49] also suggest a positive relationship between sleep and poor behavior. Interestingly, in this study, parent reports of restless sleep behaviors on the Child Sleep Habits Questionnaire but not actigraph-measured sleep efficiency were predictive of parent and teacher behavioral concerns. Looking at daytime parent-reported inattention, both actigraph-measured sleep period and parent-reported sleep duration were found to be predictive. However, for hyperactivity/impulsivity, only actigraph-measured sleep period was predictive. This is one of the only studies to have used both a self-reported and objective measure of sleep efficiency and demonstrates poor correlation in these 2 measures in this population. This could be explained by multiple reasons, including potential difficulties with actigraphy in this group of children, but it highlights that utility of multiple sleep measures may, in the future, help us improve our understanding of the complex relationship between poor sleep and behavioral problems.

Breslin et al included 2 measures of attention in their study of 38 school-age children with DS and did not find poorer attention in those with OSA on PSG compared with those without.[38] This study used both a self-reported parent-rated measure of attention as well as an independent examiner-rated score of participant attention. Children with and without OSA were matched by age, body mass index, and background health status to add strength to the study design. The directly contrasting results with the previous 2 studies cannot be easily explained. All 3 studies were carefully designed and all were subject to similar limitations. A possible explanation is that the tests used in each study concentrate on different aspects of the child's behavior. To further understand this, larger trials are required with the use of a standard battery of assessments that evaluate different aspects of behavior.

Table 2—Studies evaluating sleep and behavioral measures in children with DS.

First Author	Year	n	Cohort and Mean Age, y	Sleep Assessment	Behavior/Attention Tests	Findings	Comments
Cotton[50]	2010	DS = 12, PWS = 12, autism = 34, unknown ID = 24, TD = 33	DS group, 8.7	Sleep diary over 14 days	Daytime behavior rated on a visual analog scale (excitability, energy levels, and general behavior)	Significant correlation between sleep and day behavior	Main aim was to examine 24-hour sleep patterns in all groups
							Small group only and not a validated behavior scale
Capone[45]	2013	DS + depression = 28, DS controls = 9	Adolescents and young adults with DS + depression, 21.0; controls, 19.8	PSG defined: DS + depression: OSA = 24, no OSA = 4; controls: OSA = 4, no OSA = 5	RSCDD	High prevalence of OSA in adolescents and young adults with DS and depression	Limited by small numbers and unable to comment on any specific relationship between OSA and presence of depression in DS
					ABC Caregiver Questionnaire		
Breslin[38]	2014	31	School age, 9.7	PSG defined: OSA = 19, no OSA = 12	Connors-3 ADHD Index Scales of Independent Behavior–Revised	No difference in parent-reported ADHD scores or experimenter-reported ratings of attention between those with and without OSA	—
Ashworth[48]	2015	DS = 22, WS = 22, TD = 41	School age, 9.42	Actigraphy	Continuous Performance Attention Task	Performance was not related to sleep parameters in the DS or WS groups	Novel Continuous Performance Attention Task—designed for study
				Masimo pulse oximetry		In TD children better sleep quality and higher, less variable SpO_2 had improved performance compared with those with poorer sleep quality and SpO_2	Oximetry low sensitivity for diagnosis of OSA
Brooks[37]	2015	25	School age, 10.2	PSG defined: OSA = 10, no OSA = 15	CBCL–Parent & Teacher	No difference between children who did and did not have OSA	Improvement in attention seen following successful treatment of OSA
					Conners Hyperactivity Index–Parent & Teacher		
					Vineland Adaptive Behavior Scales		
Kelmanson[46]	2017	TD = 34, DS = 34	School age, 9-15	CSHQ	Teacher Achenback Child Behavior Checklist	Increased ADHD score with increased sleep disturbance score	Self-reported measure of sleep disorders only
					Diagnostic Adaptive Behavior Scale	Higher sleep disturbance scores predictors of poorer adaptive skills	
Joyce[40]	2017	TD = 22, DS = 22	Preschool: TD = 3.25, DS = 3.05	SDB measured by PSG	Strengths & Difficulties Questionnaire	SDB in TD children associated with poorer behavioral functioning but same not found in DS group	Only mild SDB in both groups

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Table 2—Studies evaluating sleep and behavioral measures in children with DS. (continued)

First Author	Year	n	Cohort and Mean Age, y	Sleep Assessment	Behavior/Attention Tests	Findings	Comments
Lukowski[47]	2017	TD = 20, DS = 19	TD = 20 months, DS = 33 months	Abbreviated version of CSHQ	Short Form of Early Childhood Behavior Questionnaire	Children with DS and sleep problems have reduced effortful control and inhibitory control compared with TD children	—
Esbensen[41]	2018	30	School age, 11.68	Sleep disturbances assessed by actigraphy and parent-reported questionnaire (CSHQ)	Nisonger Child Behavior Rating Score–Parent & Teacher, Vanderbilt ADHD Rating Scales–Parent & Teacher	Parent-reported poor sleep quality but not actigraph-measured activity during sleep was predictive of increased conduct problems, insecure and anxious behaviors, and daytime hyperactivity/impulsivity	No objective measure of OSA specifically; tests used considered appropriate for children with intellectual and developmental disabilities
						Parent and actigraph-measured shortened sleep was predictive of daytime inattention	
						Actigraph-measured sleep period predictive of hyperactivity/impulsivity as reported by both parents	

ABC = Aberrant Behavior Checklist; ADHD = attention-deficit/hyperactivity disorder; CBCL = Child Behavior Checklist; CSHQ = Child Sleep Habits Questionnaire; DS = Down syndrome; ID = intellectual disability; OSA = obstructive sleep apnea; PSG = polysomnography; PWS = Prader-Willi syndrome; RSCDD = Reiss Scale for Children's Dual Diagnosis; SDB = sleep-disordered breathing; SpO_2 = oxygen saturation; TD = typically developing; WS = Williams syndrome.

Table 3—Studies evaluating sleep and functional ability in children with DS.

First Author	Year	n	Cohort and Mean Age, y	Sleep Disturbance	Assessment of Functional Ability	Findings	Comments
Churchill[51]	2015	DS = 110, TD = 29	DS = 11.05, TD = 12.52	CSHQ	Life-Habit Questionnaire (Life-H)	Sleep disturbances are negatively associated with the accomplishment of daily activities in DS 0.06–0.12-point decrease in the accomplishment score for every point increase in the total CSHQ score	Self-reported sleep measure

CSHQ = Child Sleep Habits Questionnaire; DS = Down syndrome; TD = typically developing.

Two studies evaluated children with DS alongside children with other syndromes and TD children[48,50]; Cotton and Richdale[50] examined sleep and behavior patterns in children with autism, Prader Willi syndrome, DS, and other disabilities and TD children. They did demonstrate some positive correlations between sleep and behavioral parameters in children with DS, but the study was aimed more at describing and comparing patterns within the different groups of children rather than specifically evaluating the relationship between sleep and behavior.

Ashworth et al[48] assessed children with DS, William syndrome, and TD children. They used continuous pulse oximetry over 3 nights as a surrogate marker for OSA, using oxygen saturation (SpO_2) dips and variability to predict OSA presence. This is a limitation of the study as oximetry is generally regarded as a screening tool rather than as being diagnostic for OSA. Additionally, very few participants in the DS and William syndrome groups had complete oximetry data. Ashworth et al were unable to demonstrate a relationship between sleep and attention problems in either the DS or William syndrome groups. However, it is likely that results were affected by the study design and limitations pointed out by the authors in their discussion.

Lukowski and Milojevich[47] found more-mixed results in their study of younger children; this group did not find significant associations between sleep and temperament in their correlation analysis, but their mediation analyses to assess for causality suggested a bidirectional relationship between the 2 variables. It remains unanswered whether the impact of sleep is greater on behavior or vice versa.

Joyce and Dimitriou[40] are the only other group to have specifically studied preschool children, with some unexpected findings. To examine behavior, this study used the Strengths and Difficulties Questionnaire for 2–4 years and compared 22 TD children with 22 children with DS. All children underwent a cardiopulmonary PSG study. Results showed that TD children with higher apnea-hypopnea indices had worse behavioral scores, but the same relationship was not seen in children with DS. Interestingly, total sleep duration was longer in the children with DS than the TD children and the authors hypothesized that this could have been protective, improving behavior and cognitive scores for this group. This is in keeping with the findings of Brooks et al,[37] who did not find a difference in behavior between school-age children with DS with and without OSA but did demonstrate a positive relationship between total sleep time, percentage of slow-wave sleep, and cognitive function.

An interesting study in an older age group of adolescents and young adults with DS suggests a potential link between depression and the presence of comorbid OSA.[45] This is the only study to have looked at mood disturbance, specifically depression, in a group of young people with DS and demonstrated a high prevalence of comorbid OSA in those experiencing a major depressive episode. The main criticism of this study is that the control group consisted of a much smaller number of participants, with only 9 in this group compared to 28 in the group with depression. The mean age of the participants in this study was 21.8 years, making it perhaps less relevant to adolescents. Therefore, the results should be interpreted with caution and are limited by these factors.

In summary, at present it is difficult to make any conclusions regarding the impact of sleep on behavior in children with DS. Taken together, the published literature suggests that there is an association between sleep and certain aspects of behavior, but with the variability in study design and measures used by individual groups the exact relationship remains poorly understood. The difficulty in controlling for other environmental factors that may affect behavior also needs to be taken into consideration.

Sleep and functional ability in DS

Although functional ability and independence is one of the most important outcome measures to families only 1 study has focused on this in children with DS, particularly relating the impact of sleep on these poor outcomes. **Table 3** summarizes the 1 study undertaken in this area.[51] Churchill et al[51] provide strong evidence to suggest that sleep disturbances are negatively associated with the accomplishment of daily activities in children with DS, undertaking the largest community-based study to date involving 110 children with DS. The authors suggest that improvement in sleep problems such as sleep-disordered breathing could potentially translate to significantly improved quality of life in children with DS. To date, however, no studies have evaluated the effect of treatment of sleep problems on such outcomes.

DISCUSSION

At present, there is limited evidence relating to the relationship between sleep and cognitive, behavioral, and functional

outcomes in children with DS, with only 15 relevant studies found through an extensive literature review. Most of these have included no more than 30–35 children with DS, making it difficult to extrapolate findings to the wider population. Some have examined community-based populations, whereas others have studied referred populations. The majority have been undertaken in school-age children, with very few assessing the younger or adolescent populations. Analysis of the combined findings of these studies is also limited by the heterogeneous methodology and varied outcome measures utilized, which may also account for mixed results.

It seems likely from the evidence available that sleep does influence certain aspects of cognitive, behavioral, and functional progress in children with DS, but before any firm conclusions can be reached larger well-designed studies using a standardized battery of assessments are required and should ideally include children with DS with and without sleep disorders. It is important also that the specific sleep disorders are defined with objective measures as both sleep duration and sleep quality appear to be relevant. Age-related changes also need to be considered as the phenotype of DS is often evolving through childhood and will contribute to changes seen in cognitive and behavioral parameters. Patterns of change with age are not entirely predictable in DS and this may make it more difficult to attribute lack of skills to a sleep problem specifically. Studies that use assessment of trajectories, focusing on change over time, may be more useful, comparing those with and without sleep problems and evaluating the rate of change over time in these 2 groups.

Understanding whether treatment of sleep disorders leads to improvements in outcomes is an important area of study; research in this area may help to strengthen our knowledge of the association between sleep and cognitive, behavioral, and functional outcomes in children with DS. However, studies in this area will need to include objective re-evaluation of sleep problems to ensure resolution before assessing benefit of therapy as treatment is often challenging in this group. For OSA, adenotonsillectomy remains the first-line treatment option in children with DS but is acknowledged to be less successful than in TD children, with approximately 50% of children continuing to have residual OSA postsurgery.[52] Continuous positive airway pressure therapy is often attempted for the management of persisting OSA and is sustained in approximately 60% in the home.[53] Additional surgical procedures, including uvulopalatopharyngoplasty, lingual tonsillectomy, supraglottoplasty, partial midline glossectomy, and tongue suspension with or without lingual tonsillectomy have been suggested as surgical options, but there is currently limited evidence to support the routine use of these procedures.[54] Therefore, with the treatment options currently available, a significant number of children with DS may have residual sleep-disordered breathing and for this reason research study design will need to include evaluation of response to therapy for the specific sleep problem in order to accurately evaluate the effect on other outcomes. For OSA, this would mean ensuring re-evaluation with PSG after any treatment is undertaken, thus allowing comparison of those with and without residual disease.

The high prevalence of sleep disorders in children with DS and the increasing body of evidence relating to negative effects of sleep disorders on cognitive and behavioral outcomes in TD children make further study in this area important despite the mentioned challenges. In order to direct management pathways for sleep problems in children with DS further understanding of the impact on longer-term outcomes is essential and may help us advocate for priority treatment for this population.

ABBREVIATIONS

DS, Down syndrome
OSA, obstructive sleep apnea
PSG, polysomnography
TD, typically developing

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