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Sleep Disturbances and Neurobehavioral Performance in Juvenile Idiopathic Arthritis

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Abstract

Objectives—To examine the extent of polysomnographic sleep disturbances (obstructive apnea hypopnea index [OAHI], number of wake bouts, arousals, periodic limb movements) and the effect of OAHI on neurobehavioral performance in juvenile idiopathic arthritis (JIA) with OSA, JIA without OSA, and controls without OSA, adjusting for IQ, pain, medications, daytime sleepiness and wake bouts.

Methods—Children, 6-11 years, 68 with JIA and 67 controls underwent one night of polysomnography, completed self-reported daytime sleepiness surveys, multiple sleep latency tests (MSLT) for physiological sleepiness, and neurobehavioral performance tests the next day.

Results—Compared to JIA and controls without OSA, mean OAHI and arousals were significantly higher in JIA with OSA (p <.001, respectively). In comparison to JIA and controls without OSA, mean simple reaction time and sustained attention were significantly slower in JIA with OSA, adjusting for IQ, pain, any medication, daytime sleepiness, and wake bouts.

Conclusion—Elevated OAHI is suggestive of obstructive sleep apnea and a co-morbidity in JIA that may predispose JIA children to daytime sleepiness and impaired neurobehavioral performance.

Keywords

Juvenile Idiopathic Arthritis; daytime sleepiness; MSLT; polysomnography; obstructive sleep apnea; neurobehavioral performance; CANTAB

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INTRODUCTION

Sleep disturbance from obstructive sleep apnea (OSA) is a costly (1, 2) serious health concern (3) associated with negative health outcomes (e.g., daytime sleepiness, lower quality of life) (4, 5). Our previous study (6) of 73 children with juvenile idiopathic arthritis (JIA), 40% had an elevated apnea/hypopnea index suggestive of OSA, and 19% of these children showed physiological daytime sleepiness on multiple sleep latency tests. Regardless of active or inactive JIA, the apnea/hypopnea index was inversely associated with reaction time ($p < 0.001$), and the number of wake bouts (an indicator of sleep fragmentation) was inversely associated with reaction time and with the probability of making a correct response ($p < 0.05$), controlling for IQ, medications, and pain (6). These findings were the first to link physiological objective measures of sleep disturbance with validated cognitive test results in JIA. However, we did not examine whether the associations between OSA and altered neurobehavioral function were unique to JIA, JIA and OSA, or represented similar effects in healthy children.

The objectives of the current study were to examine the extent of polysomnographic sleep disturbances (obstructive apnea hypopnea index [OAHI], number of wake bouts, arousals, periodic limb movements) and the effect of OAHI on neurobehavioral performance in JIA with OSA, JIA without OSA, and controls without OSA, adjusting for IQ, maternal education, pain, medications, daytime sleepiness and wake bouts. Based on our prior findings of OSA, daytime sleepiness, and altered neurobehavioral performance in JIA, we hypothesized that JIA with OSA have increased OAHI and daytime sleepiness, slower movement time and reaction time, and decreased sustained attention compared to JIA and control without OSA.

MATERIALS AND METHODS

Recruitment and Screening

The Institutional Review Board approved this study (Seattle Children's IRB #13532). Written informed consent was obtained from parents; assent was obtained from children. All participants were recruited from Seattle Children's rheumatology clinic from October 2011 through December 2014. A research coordinator screened the clinic records for potential JIA participants. Subsequently, during a routine clinic visit, the coordinator met with eligible participants to confirm eligibility, discuss the study, and invite participation. Control children were recruited from Eastern and Western Washington via flyers, media advertisements, and from friends and/or relatives of JIA children. Interested families contacted a member of the team who screened participants via a telephone interview, confirmed eligibility, described the study, and invited participation. After agreeing to participate in the study, children and their parents were scheduled for an overnight sleep study.

Participants

A convenient sample of 143 children, 6-to-11 years, with JIA (n=68) and controls (n=75) participated in the study. Subjects were excluded if they had a diagnosis of DSM-IV-TR criteria (e.g., ADHD), diagnosed sleep disorder (e.g., OSA) by parent report or medical

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record, history of adenotonsillectomy, obesity, family history of narcolepsy, and Tanner stage ≥3. Because of the prevalence of asthma and allergies, subjects were eligible if they had no asthma or allergy exacerbations and required no medication one month prior to the study (asthma n=8 [4 JIA]; allergic rhinitis n=18 [6 JIA]). Eight control children, who met the clinical criteria for OSA, were excluded because this group is too small to conduct analysis. The final sample consisted of 135 children (JIA = 68; controls = 67).

Of the 120 JIA families screened, 52 declined to participate. Of those who declined, 53% had co-morbid conditions or were too busy. Of the 140 control families interested in the study, 65 declined to participate. Of those who declined, 65% had co-morbid conditions, 10% had a previous adenotonsillectomy, and 25% had schedule conflicts.

General Procedures

Children, accompanied by a parent, arrived at the Sleep Research Laboratory for one night of PSG, and on the next day completed a MSLT protocol and neurobehavioral performance tests.

Polysomnography

An overnight PSG was performed according to national standards (8, 9). Obstructive apnea was defined as cessation of airflow with ongoing thoracoabdominal effort for at least 2 respiratory cycles. Hypopnea was defined as a >50% reduction in airflow with ongoing thoracoabdominal effort, resulting in either an arousal or an oxyhemoglobin desaturation of >3%. Obstructive AHI (OAHI) was defined as the number of obstructive apneas and hypopneas per hour of sleep. Periodic leg movements (≥4 leg movements, of 0.5 to 5 seconds duration with an interval of 5-90 seconds), and arousals (shift to a fast EEG frequency lasting 3-15 seconds) were scored manually and expressed as an index/hour of total sleep time. Snoring time during any sleep stage was scored as an increase in the amplitude of the snore signal by >1.5 times of baseline flat line signal (6). A wake bout was defined as an awakening of at least one 30 second epoch duration and reported as the total number of bouts that occurred throughout the sleep period. A board-certified pediatric sleep physician interpreted each study and verified OSA based on the OAHI ≥1.5 (8). OSA severity was categorized according to the OAHI: 1) mild OSA = ≥1.5 to < 5; 2) moderate OSA = ≥5 to < 10; and 3) severe OSA = ≥10.

Standard sleep variables were calculated. The amount of time in NREM stages, REM stage, and wake after sleep onset were expressed as percentages of sleep period time (time from sleep onset until final awakening). Total sleep time was the amount of time in NREM stages and REM. Sleep latency was the time from lights out to first epoch of NREM stage 2. Sleep efficiency was expressed as a ratio of total sleep time/time in bed.

Multiple Sleep Latency Test

Physiological daytime sleepiness was evaluated with a MSLT protocol of 4 nap opportunities of 20 min duration conducted at 2-h intervals (09:00, 11:00, 13:00, 15:00) (10). For each nap opportunity, a child was placed in a dark quiet room and asked not to resist falling asleep. *Sleep latency* was defined as the minutes from lights out to the first

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epoch of NREM stage 1 sleep. Latency to sleep was reported for each nap opportunity and averaged over the 4 nap opportunities for each child.

Self-report Daytime Sleepiness

Child-report of daytime sleepiness was assessed before and after each nap opportunity. Children completed a visual analogue scale and placed an "X" on the line (100 mm) to express how sleepy s/he felt at the time ("extremely awake" face, an "extremely sleepy" face). Results were reported in millimeters from the "extremely awake" end of the scale. Children < 8 years were assisted by the laboratory staff to complete this scale.

Neurobehavioral Performance

Wechsler Abbreviated Scale of Intelligence—In the afternoon in between two MSLTs, a neuropsychologist administered the Wechsler Abbreviated Scale of Intelligence (WASI), a test of cognitive ability that include 3 dimensions of intelligence (verbal, performance, full IQ), standardized for age and sex (Pearson, San Antonio, TX).

Cambridge Neuropsychological Test Automated Battery—Children completed computer based neurobehavioral performance tests (CANTAB, Cambridge Cognition) (11). The test battery was administered upon arrival to the sleep laboratory as a practice session, and the following morning at 10:00 A.M. as a test session.

CANTAB test domains included: 1) *motor screening test (MOT*, a measure of movement time; 2) *reaction time*, a measure of visual scanning and processing speed with two tests (simple and 5-choice [RTI]); 3) *match to sample visual search (MTS) tests, a* measure of recall and reaction time that involves a visual search strategy to accurately identify a specific object; and 4) *rapid visual processing (RVP)*, a measure of sustained attention. CANTAB scores for each test are standardized for age and sex, and were averaged over the trials for each test.

Reaction Time (RTI was used to measure the time it takes to touch the target after the press pad has been released with 1-choice (simple) and 5-choice stimulus conditions. *Match to Sample Visual Search (MTS) test* was used to evaluate speed and visual recognition to recall patterns. MTS variables included: 1) *MTS percent correct*, the number of correctly identified responses out of a possible 48 presented and reported as the proportion of correct responses; and 2) *MTS latency to change 2*-8, the time needed to correctly identify a target presented from 2 choices versus 8 choices. *Rapid Visual Processing* was a measure of sustained visual attention (e.g., how good the participant was at detecting the target sequences). RVP variables include: 1) *probability to a hit*, the proportion of correct responses when a target sequence was presented; and 2) *probability of false alarm*, the proportion of responses when no target sequence was presented (e.g. inappropriate responses).

Demographic and Clinical Characteristics

Parents completed questionnaires about their child's age, ethnicity, and the highest level of maternal education. Children reported *pain intensity* and *number of joints* that hurt in the evening prior to the sleep study. Pain intensity was measured with the Oucher Faces Rating

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pain scale (0 = no hurt, 10 = the biggest hurt) (12). Number of joints that hurt was measured by a skeleton figure where children circled the joints that corresponded to location of the pain (13).

JIA disease duration was measured from the date the child was first diagnosed. Prior to the scheduled sleep study, a pediatric rheumatologist confirmed JIA subtype and disease activity according to: (1) physician global assessment (PGA) on a scale of "0 = no disease" to "10 = very severe disease"; and (2) the number of active joints, defined as the number of joints with active synovitis during the examination. Active disease was defined as synovitis of one or more joints, along with active uveitis, and PGA>0; inactive disease was defined as no active joints, joint synovitis, or uveitis, and a PGA=0 (7).

Medications

Parents recorded medications their child received during the study as "yes" or "no" and classified as: 1) disease modifying anti-rheumatic drugs ([DMARD], methotrexate); 2) sulfasalazine; 3) biologics (e.g. etanercept); 4) non-steroidal-anti-inflammatory drugs (NSAIDS); 5) glucocorticoids; 6) other (zinc, multivitamins); and 7) none.

Statistical Analysis

Data were analyzed using SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL, USA) and Stata version 14.1 (StataCorp LP., College Station, TX, USA). Preliminary analyses showed no differences in PSG sleep, sleep disturbances (OAHI, wake bouts, arousals, periodic limb movements), daytime sleepiness (self-report, MSLT nap opportunities), and CANTAB test domains (movement time, reaction time, sustained attention) based on active and inactive JIA; therefore, disease activity was not included in any subsequent analysis.

The first analyses tested differences on demographics and clinical characteristics. Statistical comparison tests between the groups were performed using Student's t-tests for normally distributed continuous variables, and χ^2 and Fisher's exact tests for categorical variables. Because 51% of JIA children (n=35) had an OAHI ≥1.5, the second set of analysis tested differences among JIA with OSA (n=35), JIA without OSA (n=33), and controls without OSA (n=67) on PSG sleep, sleep disturbances, neurobehavioral performance scores, and daytime sleepiness. Statistical comparison tests between the groups were performed using ANOVA's for normally distributed continuous variables, χ^2 tests for categorical variables, and *Kruskal-Wallis* tests for non-normally distributed variables.

The third analyses examined the effect of OAHI on neurobehavioral performance scores across three groups (JIA with OSA; JIA without OSA; controls without OSA). A series of regression models explored neurobehavioral performance by group (e.g., unadjusted models). Subsequently, we examined the effect of group, adjusting for covariates including IQ, maternal education, pain, medications, sleep latency for the first nap opportunity, and number of wake bouts (e.g. adjusted models). The sleep latency for the first nap opportunity was used in the regression models because sleepiness fluctuates across a day, and this nap opportunity was the most proximal to the time the neurobehavioral tests were administered to provide the best control for sleepiness.

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RESULTS

Demographic and clinical characteristics

Table 1 shows the demographics among the 3 groups; significant group differences were found for maternal education. In comparison to mothers of JIA with and without OSA, control mothers' were more highly educated (Fisher's exact test, $p < .01$). Table 2 shows the clinical characteristics between JIA children with OSA and JIA without OSA; no significant differences were found.

Polysomnographic sleep disturbances and daytime sleepiness

Table 3 shows data for PSG sleep, sleep disturbances, and daytime sleepiness for JIA with OSA, JIA without OSA, and controls without OSA. ANOVAs revealed significant differences among the 3 groups for OAHI ($\chi^2=76.8$, $p < .001$) and arousals ($F_{2,134}=8.0$, $p < .001$). Post hoc comparisons showed significantly higher OAHI and arousals in JIA with OSA compared to JIA and controls without OSA ($p < .001$, respectively). Of the JIA children with OSA, 47% had mild to moderate OSA and 4.4% had severe OSA. Self-report sleepiness and the mean of the 4 nap opportunities did not significantly differ among the groups.

WASI and neurobehavioral performance

Table 4 shows the mean scores for the WASI and the CANTAB variables with maternal education as a covariate. Adjusting for multiple comparisons ($p < .006$), ANOVAs revealed no significant differences for verbal, performance, and total IQ scores, or for any of the CANTAB variables among the 3 groups (see Table 4).

OSA and neurobehavioral performance

Bivariate correlations—Bivariate correlations showed OAHI was positively associated with pain (r = .20, $p < .02$) and any medication (r = .25, $p < .002$). Number of wake bouts was positively associated with total IQ (r = .26, $p < .002$) and RVP probability to hit a correct target sequence (r = .27, $p < .002$). Total IQ was positively associated with maternal education (r = .41, $p < .001$) and MTS percent correct (r = .19, $p < .03$), and negatively associated with any medication (r = −.21, $p < .02$) and RVP probability to hit false alarm (r = −.25, $p < .004$). Pain was positively associated with any medication (r =.33, $p < .001$) and negatively associated with maternal education (r = −.18, $p < .05$). Based on the bivariate correlations, IQ, maternal education, pain, medication, and the number of wake bouts were adjusted for in each of the regression models.

OSA and neurobehavioral performance—Among the CANTAB tests, RVP probability to hit and RTI simple reaction time were statistically significant among the groups. For RVP probability to hit scores, the effect of group was significant ($F_{2,120}= 3.9$, $p < .02$), such that JIA with OSA had a decreased probability of hitting the correct target sequence in comparison to controls without OSA (see Table 5), but RVP probability to hit scores were not significantly different between JIA with and without OSA (t = −1.0, $p= .31$). In the adjusted model for RVP probability of hit, the effect of group remained significant ($F_{2,112}= 3.4$, $p < .04$). In comparison to controls, JIA with OSA had a significantly lower

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probability to hit the correct target sequence (t = −2.5, p <.01). RVP probability to hit was similar between JIA with and without OSA, adjusting for the covariates.

For RTI simple reaction time, the effect of group was significant, ($F_{2,118}$= 3.7, p <.03), such that JIA with OSA had significantly longer reaction time than controls without OSA (t = 2.4, p <.02, see Table 5). Simple reaction time was also longer in JIA without OSA than in controls without OSA (t= 1.97, p= .051). No significant differences in reaction time were found between JIA with and without OSA. In the adjusted model, the effect of group remained significant ($F_{2,110}$= 4.4, p <.02) adjusting for covariates. In comparison to controls without OSA, simple reaction time was significantly longer in JIA with and without OSA (t = 2.9, p <.005; t = 2.5, p <.02, respectively). However, simple reaction times did not differ between JIA with and without OSA, adjusting for covariates (t = −.56, p= .58).

DISCUSSION

In JIA, an elevated OAHI was common. In comparison to controls, our findings suggest that measures of neurobehavioral performance that are considered sensitive to disturbed sleep (e.g., simple reaction time, sustained visual attention) were impaired in JIA with OSA.

Neurobehavioral Performance

We found a significant group effect for sustained visual attention and simple reaction time in the JIA with OSA. The probability to hit a correct target, a measure of sustained visual attention, was lower in JIA with OSA than controls. Mild to moderate OSA may lead to more lapses in attention with a tendency to incorrectly respond to the correct target sequence.

Prior studies in children with OSA have reported positive associations between OAHI and poor sustained attention using different neuropsychological assessments than those used in this study (14–16). However, the findings from these studies are mixed with respect to OSA severity and neurobehavioral performance (17–21). For example, Karpinski and colleagues reported positive associations between OSA severity and a working memory deficit, but Giordani and colleagues found that children with less severe OSA performed significantly worse on measures of working memory. It is possible that different types of neurobehavioral tests used in these studies would account for these inconsistent findings.

We found a significant group effect for simple reaction time. In comparison to controls without OSA, both JIA groups with and without OSA had significantly slower simple reaction times. This finding suggests that JIA disease, rather than OSA co-morbidity alone, could impact how quickly a child responds to stimuli. Although disease activity and pain levels were low, the underlying disease inflammation, physical function, and/or dexterity in the hands and wrists may contribute to this finding. JIA with OSA had slower reaction times, but the scores were not significantly different from JIA without OSA and controls. We anticipated that a breathing abnormality during sleep could be related to difficulty in responding to multiple stimuli (e.g., making slower responses), but this was not observed. Nevertheless, our finding of slower simple reaction time is similar to previous studies in children with OSA that showed negative associations between OSA and tests of speed and

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accuracy (5, 14–16, 23). We had anticipated finding significant differences in sustained visual attention and simple reaction time between JIA with and without OSA, but this was not observed. Few studies have examined OSA in JIA with PSG (22), and the impact of OSA on neurobehavioral performance, remains under studied. Longitudinal studies are needed to examine the trajectories in neurobehavioral performance as a function of OSA, which would provide new knowledge about the clinical implications of OSA in these children.

Daytime sleepiness

Self-reported sleepiness and average sleep latency for the nap opportunities in the JIA groups were similar to those reported previously (6). Contrary to our hypothesis, the nap opportunities were not significantly different among the groups. This observation was not attributed to the high proportion of OSA or other sleep measures. This finding may be explained by a change in children's daily routine during the study. For example, children remained in the sleep laboratory for several hours after the overnight sleep study, and this alteration in daily routine may have induced daytime sleepiness (e.g., boredom) for some children. Regardless of the etiology, in comparison to studies of healthy controls (10, 27–29) that report average MSLT sleep latency of 27.5 min, children in our study had much shorter latencies suggestive of some degree of daytime sleepiness. Daytime sleepiness is a common symptom of OSA (29, 31, 32), and present in JIA (6, 25, 30) that may place children at risk for poor school performance or attention problems. Daytime sleepiness is an important covariate to include in studies of OSA and neurobehavioral performance.

OSA

In JIA, an elevated OAHI, suggestive of OSA, is important for several reasons. First, the symptoms of OSA in JIA are not routinely assessed in clinical practice. Sleep disturbances are often attributed to pain, JIA-related fatigue, and/or medication side effects, without adequately screening for treatable underlying sleep disorders, such as OSA. Second, daytime sleepiness is a common symptom of OSA, and studies of otherwise healthy children who are sleepy during the day have shown to be at high risk for inattention or impulsivity, which can lead to misdiagnosis for ADHD (32, 33). Third, the average time from JIA diagnosis to the identification of OSA by PSG was 2 ½ years (data not shown), implying that some children could have been experiencing OSA for several years. Timely diagnosis and treatment is important, as JIA children may be more vulnerable to the consequences of OSA. OSA may also complicate clinical management and important health outcomes.

The high prevalence of OSA may be related to TMJ involvement and retrognathia, both common in JIA and also risk factors for OSA (22). Currently there are no screening or treatment guidelines for OSA in JIA. The Pediatric Sleep Questionnaire (PSQ), a validated, 1-page, sleep-related breathing symptom survey (34) with a clinical OSA cut-off score, may be a useful screening measure. Recent studies in control children show that the PSQ is positively associated with OAHI, and predicts improvements in key clinical outcomes including behavior, quality of life, and sleepiness before and after adenotonsillectomy (20, 35). To date, there have been no longitudinal sleep studies using PSG that examine the OSA in JIA, and whether or not OSA treatment (adenotonsillectomy) resolves OSA and changes

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in neurobehavioral function. Longitudinal studies would provide knowledge about the effect of OSA treatment on neurobehavioral function and disease-related symptoms, which would increase awareness among pediatric providers and pediatric rheumatologists of the need for systematic and routine screening for OSA.

Limitations

There are study limitations that deserve comment. First, PSG was obtained for one night. Although this is consistent with clinical practice, and enabled comparisons to previous studies, a single night may not fully characterize typical sleep. Second, medications were included as a covariate in the regression analysis because we had too few children on each type of medication to conduct a more refined analysis. To our knowledge, the cognitive effects of medication in JIA are not well-characterized. Third, although our control and JIA groups were not matched on maternal education, they fit closely on other demographic factors and we controlled for maternal education in analyses. Lastly, physical function was not measured and may contribute to the neurobehavioral test scores. However, elevated OAHI in JIA and altered neurobehavioral performance function are consistent with our prior work and supports reproducibility of the findings.

Conclusion

In summary, OSA was prevalent in JIA, and may predispose children to daytime sleepiness and impaired neurobehavioral performance. Effective detection and treatment of OSA may reduce morbidity, decrease health care costs, and improve disease management.

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Table 1

Demographics

	JIA with OSA (n=35)	JIA without OSA (n=33)	Control (n=67)	p value
Age, years	8.7 ± 1.8	8.4 ± 1.9	8.8 ± 1.6	0.52
Child Ethnicity, n (%)				0.57
White	23 (65.7%)	25 (75.8%)	46 (68.7%)	
Mixed race	7 (20.0%)	4 (12.1%)	10 (14.9%)	
Girls, n(%)	20 (57.1%)	18 (54.5%)	40 (59.7%)	0.88
Maternal Education, n (%)				0.01
High School	3 (8.6%)	1 (3.0%)	7 (10.4%)	
Some college (1–3 years)	14 (40.0%)	16 (48.5%)	9 (13.4%)	
College degree	10 (28.6%)	8 (24.2%)	25 (37.3%)	
Master's degree or higher	8 (22.9%)	8 (24.2%)	25 (37.3%)	

Data are mean ± SD or n (%)

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Table 2

Clinical characteristics

	JIA with OSA (n=35)	JIA without OSA (n=33)	p value
Disease subtype, n (%)			0.15
Oligoarticular	6 (17.1%)	13 (39.4%)	
Extended oligoarticular	7 (20.0%)	6 (18.2%)	
Polyarticular RF negative	12 (34.3%)	10 (30.3%)	
Polyarticular RF positive	0 (0%)	1 (3.0%)	
Systemic	6 (17.1%)	1 (3.0%)	
Enthesitis-related	2 (5.7%)	2 (6.1%)	
Psoriatic	2 (5.7%)	0 (0%)	
JIA Disease Activity, n (%)			0.30
Active	16 (45.7%)	11 (33.3%)	
Inactive	19 (54.3%)	22 (66.7%)	
Physician Global Rating (0–10)	1.03 ± 1.5	0.75 ± 1.5	0.76
Disease Duration, months	38.8 ± 28.7	36.6 ± 28.8	0.75
Active Joint Count, (#)	1.74 ± 3.8	1.4 ± 5.3	0.91
Pain			
Evening pain	0.86 ± 1.4	0.55 ± 1.3	0.15
Evening joint count (number)			0.51
0	25 (71.4%)	27 (81.8%)	
1	5 (14.3%)	4 (12.1%)	
2	3 (8.6%)	2 (6 %)	
3	2 (5.7%)	0 (0%)	
Medications, n (%)			
Disease modifying anti-rheumatic drugs	14 (40.0%)	18 (54.5%)	
Sulfasalazine	4 (11.4%)	1 (3.0%)	
Biologics	10 (28.6%)	6 (18.2%)	
NSAIDS	16 (45.7%)	11 (33.3%)	
Corticosteroids	1 (2.9%)	2 (6.1%)	
Other (vitamins)	19 (54.3%)	20 (60.6%)	
No medication	4 (11.4%)	6 (18.2%)	

Data are mean ± SD or n (%).

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Table 3

PSG sleep, sleep disturbances, and daytime sleepiness

	JIA with OSA (n = 35)	JIA without OSA (n=33)	Controls without OSA (n = 67)	P value[b]
Polysomnography sleep variables				
Time in Bed, min	583.6 ± 33	567.1 ± 42	567.6 ± 33	0.07
Total Sleep Time (TST), min	498.4 ± 65	491.3 ± 69	475.6 ± 58	0.18
Sleep Efficiency, %	85.4 ± 10	86.7 ± 11	83.8 ± 9	0.38
Sleep Latency Stage 2, min	32.5 ± 30	37.8 ± 32	38.0 ± 35	0.71
Wake After Sleep Onset, % SPT	9.1 ± 9.3	8.0 ± 8.8	9.4 ± 7.6	0.74
NREM (Stage 1,2,3), % SPT	72.2 ± 7	73.5 ± 8	72.2 ± 6	0.78
REM, % SPT	18.7 ± 4	19.3 ± 5	17.1 ± 5	0.26
Mean oxygen saturation, %	97.5 ± .61	97.7 ± .51	97.6 ± .59	0.23
Polysomnography sleep disturbances				
Snoring, min	287.3 ± 127	216.4 ± 118	251.1 ± 123	0.06
Arousals/h TST	10.3 ± 2.8	7.7 ± 2.4	8.8 ± 2.7	0.001
Wake bouts, (number)	19.0 ± 8.4	19.2 ± 8.2	19.8 ± 7.5	0.86
OAHI/h TST	4.7 ± 4.8	0.86 ± .38	0.99 ± .41	0.001
Periodic limb movement/h TST	2.3 ± 6.1	1.6 ± 2.9	1.6 ± 3.3	0.68
Daytime sleepiness				
Self report sleepiness, min	5.3 ± 4.4	5.5 ± 4.7	6.2 ± 5.2	0.73
Average MSLT sleep latency, min [a]	15.3 ± 4.6	15.6 ± 4	17.4 ± 3.6	0.03
MSLT # 1, min	16.3 ± 5	16.9 ± 5	18.4 ± 4	0.07
MSLT # 2, min	15.5 ± 6	17.3 ± 4	18.1 ± 4	0.04
MSLT # 3, miN	14.2 ± 7	14.7 ± 6	16.3 ± 5	0.19
MSLT # 4, min	15.0 ± 6	13.7 ± 6	16.6 ± 5	0.06

Data are mean ± SD; Bonferroni correction for multiple comparisons with $p < .002$

[a] Average MSLT sleep latency are mean of 4 nap opportunities and SD;

[b] Oneway ANOVAs used for normally distributed variables; Kruskal-Wallis tests used for AHI and Periodic limb movement

SPT- sleep period time; NREM- nonrapid eye movement; REM- rapid eye movement; OAHI-obstructive apnea hypopnea index; MSLT-multiple sleep latency

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Table 4

WASI and Neurobehavioral Performance

	JIA OSA (n=35)	JIA without OSA (n=33)	Controls without OSA (n=67)	p value
WASI				
Verbal	113.1 ± 14	106.9 ± 16	113.7 ± 16	0.30
Performance	105.6 ± 13	100.6 ± 12	110.2 ± 16	0.03
Full Score	110.4 ± 12	103.9 ± 13	113.5 ± 15	0.06
CANTAB variables				
RTI Simple Reaction Time (ms)**	436.5 ± 105	436.4 ± 133	385.8 ± 98	0.03
RTI 5-Choice Reaction Time (ms)	454.1 ± 94	439.3 ± 93	416.0 ± 105	0.20
MTS percent correct (%)	94.3 ± 7	96.8 ± 6	94.5 ± 7	0.26
MTS Mean Latency Change (2–8) (ms)	2040.9 ± 1350	2769.6 ± 1733	2113.9 ± 1533	0.07
RVP Probability to hit (p)*	0.28 ± .19	0.34 ± .21	0.40 ± .23	0.08
RVP Probability of false alarm (p)	0.03 ± .05	0.03 ± .06	0.02 ± .03	0.32

Data are mean ± SD; Bonferroni correction for multiple comparisons with $p < .006$

Maternal education included as a covariate for all outcomes

WASI: Wechsler Abbreviated Scale of Intelligence

Raw CANTAB scores. MOT = motor screening test, RTI = reaction time test, MTS = match to sample test, RVP = rpid visual information processing test, ms = milliseconds, p = probability range 0 – 1.0

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Table 5

OSA and Neurobehavioral Performance

	B	95% CI	Beta	*P*	*Adjusted R^2*
RVP Probability to hit					
Step 1 – Group [a]					0.05
JIA with OSA	−0.13	−0.22 to −0.03	−0.26	0.007	
JIA without OSA	−0.07	−0.17 to 0.02	−0.14	0.15	
Step 2 – Group + Covariates					0.17
JIA with OSA	−0.17	−0.30 to −0.03	−0.34	0.01	
JIA without OSA	−0.07	−0.20 to 0.05	−0.15	0.25	
IQ	0.00	−0.00 to 0.01	0.17	0.08	
Maternal Education [b]					
High School	−0.04	−0.22 to −.15	−0.04	0.69	
Some college (1–3 years)	−0.07	−0.17 to 0.03	−0.15	0.16	
College degree	−0.00	−0.10 to 0.10	−0.00	0.98	
Pain	0.02	−0.02 to 0.07	0.09	0.30	
Any medication	0.04	−0.08 to 0.16	0.09	0.48	
MSLT sleep latency	−0.01	−0.02 to −0.00	−0.26	0.003	
Wake bouts	0.00	−0.00 to −0.01	0.17	0.03	
RTI mean simple reaction time					
Step 1 – Group [a]					0.04
JIA with OSA	54.96	10.39 to 99.52	0.23	0.02	
JIA without OSA	46.15	−0.24 to 92.53	0.19	0.05	
Step 2 – Group + Covariates					0.07
JIA with OSA	97.3	30.4 to 164.2	0.41	0.005	
JIA without OSA	82.5	16.7 to 148.3	0.34	0.01	
IQ	0.30	−1.2 to 1.8	0.04	0.70	
Maternal Education [b]					
High School	385	−56.3 to 133.2	0.08	0.42	
Some college (1–3 years)	12.7	−39.0 to 64.3	0.06	0.63	
College degree	−33.1	−80.9 to 14.7	−0.15	0.17	
Pain	−10.5	−32.4 to 11.4	−0.09	0.34	
Any medication	−38.3	−97.9 to 21.3	−0.18	0.21	
MSLT sleep latency	5.1	1.1 to 9.1	0.23	0.01	
Wake bouts	−0.3	−2.8 to 2.1	−0.03	0.79	

[a] Controls without OSA (reference group).

[b] Master's degree of higher (reference group).