

Neurocognitive and behavioral abnormalities in Indian children with sleep-disordered breathing before and after adenotonsillectomy

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ABSTRACT

Objectives: Children with untreated sleep-disordered breathing (SDB) have impaired intellectual ability and behavioral effects. Timely treatment of SDB by adenotonsillectomy (AT) may prevent this morbidity. This study was designed to assess the prevalence of neurocognitive and behavioral dysfunction in Indian children with SDB and to evaluate the impact of AT. **Methods:** Children recruited underwent diagnostic polysomnography (PSG), a detailed neurocognitive and behavioral assessment using a battery of validated instruments – the Malin’s Intelligence Scale (MIS) for Indian children, Modified Wisconsin’s Card Sorting Test, Parent Conners’ Scale, and the Childhood Behavior Checklist (6–18). These children then underwent AT and subsequent reassessment at 3 and 6 months. **Results:** Neurocognitive impairment was common among the 33 enrolled children (mean age 9 [\pm 2.97] years; 78.8% males). There was a significant correlation between the lowest O₂ saturation and the “categories completed” ($r = -0.379$; $P = 0.029$); and the lowest O₂ saturation and the “failure to maintain sets” ($r = 0.386$; $P = 0.026$) of the Modified Wisconsin’s Card Sorting Test. Postsurgery, although apnea–hypopnea index (AHI) significantly decreased after surgery, 15 children still had SDB. Mean scores of most of the tested neurocognitive and behavioral domains showed improvement, although residual deficits were prevalent even after 6 months. Patients with a baseline AHI >5/h and those who had complete resolution of SDB (postoperative AHI <1/h) showed improvement in more subscales than patients with baseline AHI <5/h and patients with incomplete resolution of SDB. **Conclusion:** The decreased neurocognitive performance related to SDB may be a result of hypoxemia, rather than the frequency of SDB events. Despite AT, residual disease is common and such patients may require further treatment.

KEY WORDS: Adenotonsillectomy, behavioral assessment, neurocognitive assessment, oxygen desaturation, pediatric sleep-disordered breathing, polysomnography

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INTRODUCTION

Literature on sleep-disordered breathing (SDB) in children, a hitherto neglected disorder, has proliferated substantially

over the last few decades. SDB is now considered to be one of the most prevalent pediatric disorders.^[1-5] It is known to have

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an adverse effect on the cardiovascular system, on the growth of children, and on their quality of life.^[6-8] Studies have also revealed involvement of one or more neurocognitive parameters. Children with untreated SDB have been shown to have impairment of intellectual ability and significant neurocognitive effects such as deficits in attention and executive function.^[9-13] Assessments of behavioral functions have shown increased morbidity in these children.^[14,15] Some studies have also suggested a correlation between the severity of SDB and neurocognitive impairment^[16-20] although this has not been shown in all the studies.^[15,21,22]

Early diagnosis of SDB and its prompt treatment are thought to prevent this morbidity in otherwise healthy children. Adenotonsillectomy (AT) has been the treatment of choice in affected children.^[23] Studies assessing neurocognitive and behavioral morbidity in such children have shown improvement in the verbal and performance intelligence and reduction in hyperactivity (HA), aggression/oppositional behavior, and somatic complaints. While most of the studies have shown a favorable effect of AT on neurocognitive dysfunctions,^[15,21,24-27] others have also shown significant residual impairments.^[28,29] The CHAT study,^[30] a randomized controlled trial, had shown that compared to a strategy of watchful waiting, surgical treatment for the SDB in school-age children did not significantly improve attention or executive function at 7 months but did reduce symptoms and improve secondary outcomes of behavior, quality of life, and polysomnographic (PSG) findings, thus providing evidence of beneficial effects of early AT.^[30]

Most studies, assessing neurocognitive and behavioral improvement following AT, are limited by methodological issues. Some early studies evaluated only limited domains of neurocognition and behavior and lacked objective assessment using validated instruments. Very few studies have used good-quality attended PSGs both before and after AT. Moreover, children in most of these studies have not been followed up for long periods after surgery. We also noticed a paucity of such studies from India. The present study was designed keeping in view the above lacunae and limitations in the available literature. We wanted to assess the prevalence of neurocognitive and behavioral dysfunction in Indian children with SDB and evaluate the impact of AT.

METHODS

The present prospective observational study was conducted in the Department of Pulmonary, Critical Care, and Sleep Medicine in collaboration with the Department of Otorhinolaryngology, Vardhman Mahavir Medical College and Safdarjung Hospital (VMMC&SJH), New Delhi. We enrolled consecutive children from November 2013 to June 2015, referred to our sleep clinic for symptoms suggestive of SDB to using the following inclusion and exclusion criteria:

Inclusion criteria

- Age <18 years
- Considered appropriate for AT by otorhinolaryngologists.

Exclusion criteria

- Patient with a history of asthma or allergies
- Existing neurological disorders (epilepsy, cerebral palsy, etc.)
- Prior AT or other surgical procedure for SDB, e.g., mandibular advancement surgery
- Undergoing continuous positive airway pressure therapy for SDB
- Refusal for surgery
- Presence of bony deformities such as deviated nasal symptoms requiring specific therapy other than AT.

Approval of the Institutional Human Ethics Committee was obtained. Patients were enrolled only after taking informed, written consent from parents. All children and their caregivers underwent a detailed interview about their symptoms and socioeconomic and educational status, and this was recorded in a predesigned questionnaire. A detailed examination was done by a single otolaryngologist; the neck circumference, the tonsil size, the modified Mallampati grade, and the presence of retrognathia and high-arched palate were recorded.

As a baseline, all children underwent diagnostic PSG and detailed neurocognitive and behavioral assessment using a battery of validated instruments designed specifically for this age group. Children then underwent AT and were followed up 3 and 6 months after surgery in addition to regular checkups. The sleep assessment (which included the PSG) was repeated after 3–4 months of surgery. Neurocognitive and behavioral assessment was repeated using the same instruments 3 and 6 months after surgery. The sleep assessment and neurocognitive/behavioral assessment were done within a day or two of each other as per the convenience of the child and parents.

Sleep assessment

Pediatric Daytime Sleepiness Scale

The Pediatric Daytime Sleepiness Scale (PDSS) is an eight-item, self-reported Likert-type questionnaire that measures daytime sleepiness in school-age populations, with possible scores ranging from 0 to 32. Higher PDSS scores indicate greater daytime sleepiness.^[31]

Polysomnography

Diagnostic PSG was done before AT and repeated 3–4 months after surgery using the Alice 6 Diagnostic Sleep System of the Philips Respironics at the Department of Pulmonary, Critical Care, and Sleep Medicine, VMMC&SJH. Each child underwent a fully attended in-laboratory whole-night level-I PSG performed for 7–8 h by a trained technologist. The time of sleep study and total recording time were guided by the previous week's sleep-wake diary. The following parameters were measured: three channels each for electroencephalography, electrooculography,

electromyography with submental electrodes, and electrocardiography; airflow recording through nose and mouth using a thermistor and nasal pressure cannula; thoracic and abdominal efforts by piezoelectric bands; oxygen saturation using pulse oximetry; and snoring with neck microphone. There was continuous video monitoring during recording time.

The apnea-hypopnea index (AHI) and the oxygen desaturation index (ODI) were scored as per the Update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events.^[32] Obstructive apnea was scored (using an oronasal thermal sensor) when there was a drop in the peak signal excursion by $\geq 90\%$ of the pre-event baseline, lasting for at least two breaths during baseline breathing, and associated with respiratory effort throughout the entire period of absent airflow. A respiratory event was scored as a hypopnea if the peak signal excursions dropped by $\geq 30\%$ of pre-event baseline using nasal pressure, lasting for at least two breaths, and associated with $\geq 3\%$ desaturation from pre-event baseline, or the event was associated with an arousal.

Neurocognitive and behavioral assessment

Malin's Intelligence Scale for Indian children

It is an individual intelligence test scale for Indian children comprising 11 subtests divided into two groups; verbal (consisting of information, comprehension, arithmetic, similarities, vocabulary, and digit span) and performance (consisting of picture completion, block designing, object assembly, coding, and mazes). The points or raw scores for each test are totaled and converted into intelligence quotients (IQs). IQs of all subtests are averaged to generate a verbal IQ and a performance IQ. Total IQ is generated by averaging the verbal and performance IQs. Children were classified as normal (≥ 75) and abnormal (< 75) in a subtest on the basis of a cutoff score.^[33]

Modified Wisconsin's Card Sorting Test

It is a test of executive function requiring use of working memory, planning, attention flexibility, and response inhibition to solve problems.^[34,35] Modified Wisconsin's Card Sorting Test (MWCST) consists of a total of 48 response cards and four key cards. Children are presented with response cards and told to match those with any of the key cards on the basis of color, form, or any other quality. The participant is told to match the cards but not how to match; however, he or she is told whether a particular match is right or wrong. Whatever method of matching the child chooses first becomes the first category. Subsequently, the child is told to change the rule of matching the cards after he/she correctly classifies six cards without telling the exact rule. If the child chooses a second and third rule correctly, these become the second and third category, respectively. The child then repeats matching cards as per the three categories again in the same order as earlier. The child is scored for categories completed, total errors, perseverative errors, nonperseverative errors, categorization efficiency, and

failure to maintain sets. Children were classified as abnormal in parameters of categories completed and categorization efficiency on the basis of a cutoff score of 30 or less. A cutoff value of 65 (with values < 65 classified as normal) was used to classify the parameters of total errors, perseverative errors, nonperseverative errors, and failure to maintain sets.^[35]

Parent Conners' Scale

We used "The Conners' 3-Parent" version – a validated instrument for assessing parent-reported behavioral dysfunction.^[36] It evaluates parent-reported inattention, HA, impulsivity, learning problems, executive functioning, aggression, and peer relations. It also evaluates for the presence and severity of symptoms of conduct disorder and oppositional defiance disorder according to the Diagnostic and Statistical Manual for the evaluation of Mental Disorders (DSM) IV. Parents respond to questions about their children which are scored on a Likert scale. The total score of a domain corresponds with a *t*-score provided. Children scoring 65 or greater in a particular domain were classified as abnormal and those scoring less classified as normal.

Childhood Behavior Checklist (6-18)

It is a component in the Achenbach System of Empirically Based Assessment.^[37] This questionnaire, containing 120 questions, measures emotional, behavioral, and social aspects of life. The total scores for each domain are calculated by adding the scores for all questions in that domain. These total scores are used to find *t*-scores for that individual domain. Children scoring 65 or greater in problem scores were classified as abnormal, and the rest were classified as normal. Children scoring less than 30 in any activity score were considered to be abnormal, except for total activity score where this cutoff was 37.

Statistical analysis

The data were analyzed as per appropriate statistical tools to compare variables we used the *t*-test for continuous variables with a normal distribution and Mann-Whitney U-test for continuous variables not normally distributed. Binomial data before and after surgery were compared using the McNemar test of equality of paired proportions. The correlation coefficient between the neurocognitive and behavior scores and the sleep parameters was calculated. All *P* values are two-tailed, with statistical significance determined at $\alpha = 0.05$.

RESULTS

Thirty-three children were enrolled (mean age 9 ± 2.97 years, 78.8% males, mean body mass index of $17.24 [\pm 2.83]$ kg/m²). One child (3.0%) had retrognathia and 4 (12.1%) had a high-arched palate (12.12%) [Table 1]. Baseline PSG, neurocognitive, and behavioral assessment was done. Fifteen children (45.5%) had an AHI of $< 5/h$ while 18 (54.5%) had an AHI of $\geq 5/h$. All patients

underwent AT within a week of the baseline assessment. One child did not come for follow-up after AT, and his postoperative assessment was not available. After surgery, 17 patients had complete resolution of SDB while 15 patients still had an AHI of >1/h. Another patient dropped out after the postoperative PSG; postoperative neurocognitive assessment was available for only 31 patients [Figure 1].

Snoring, reported in 84.8% of the children, was the most common symptom seen at baseline. Witnessed choking at night (57.6%), difficulty in morning awakening (48.5%), nocturnal drooling of saliva (33.3%), and nocturnal enuresis (33.3%) were also common. Most symptoms were ameliorated within 3 months of surgery. Difficulty in morning awakening and nocturnal drooling of saliva persisted in at least half of the subjects even after 6 months of treatment [Table 2].

Sleep parameters: Before and after surgery

All PSG parameters (AHI and ODI) showed significant decrease after surgery. However, significant residual

abnormalities remained in most children. The success of AT was 53.1%; out of 32 children, 15 still had SDB (defined as AHI ≥ 1/h) while two patients (6.3%) had a postoperative AHI of >5/h [Supplementary Table S1].

Baseline neurocognitive assessment and its correlation with sleep parameters

In the Malin's Intelligence Scale (MIS), 48.5% of children scored less than normal in object assembly, a measure of performance intelligence. Information (33.3%) and vocabulary (27.3%), which are domains of verbal IQ, were also common areas of impairment. In the MWCST,

Table 1: Baseline characteristics of patients

Characteristics	Study group (n=33)	AHI <5 (n=15)	AHI ≥5 (n=18)
Age	9.00±2.97	9.13±2.97	8.89±3.05
Gender			
Males [#]	26 (78.8)	11 (73.3)	15 (83.3)
Female [#]	7 (21.2)	4 (26.7)	3 (16.7)
Height (m)	1.27±0.21	1.28±0.19	1.27±0.23
Weight (kg)	29.53±13.03	28.80±10.99	30.14±14.81
BMI (kg/m ²)	17.24±2.83	16.83±2.64	17.58±3.01
BMI-Z score	-0.14±2.03	-0.19±1.35	-0.10±2.50
Neck circumference (inch)	10.46±1.08	10.21±1.08	10.68±1.06
Tonsils size grading*			
Modified	2.58±0.87	2.67±0.90	2.50±0.86
Mallampatti Grade			
Retrognathia [#]	1 (3.0)	0	1 (5.5)
High-arched palate [#]	4 (12.1)	2 (13.3)	2 (11.1)

*The size of the tonsils was graded as follow: Grade 0: The tonsils are fully inside the pillars, Grade 1: Tonsils found to be enlarged and out of its pillars, Grade 2: Tonsils extend just up to half the distance of the uvula, Grade 3: Tonsils extend to the level of the uvula, Grade 4: Tonsils almost in contact with each other; [#]Expressed as n (%). Rest of the data is expressed as mean±SD. SD: Standard deviation, BMI: Body mass index, AHI: Apnea-hypopnea index

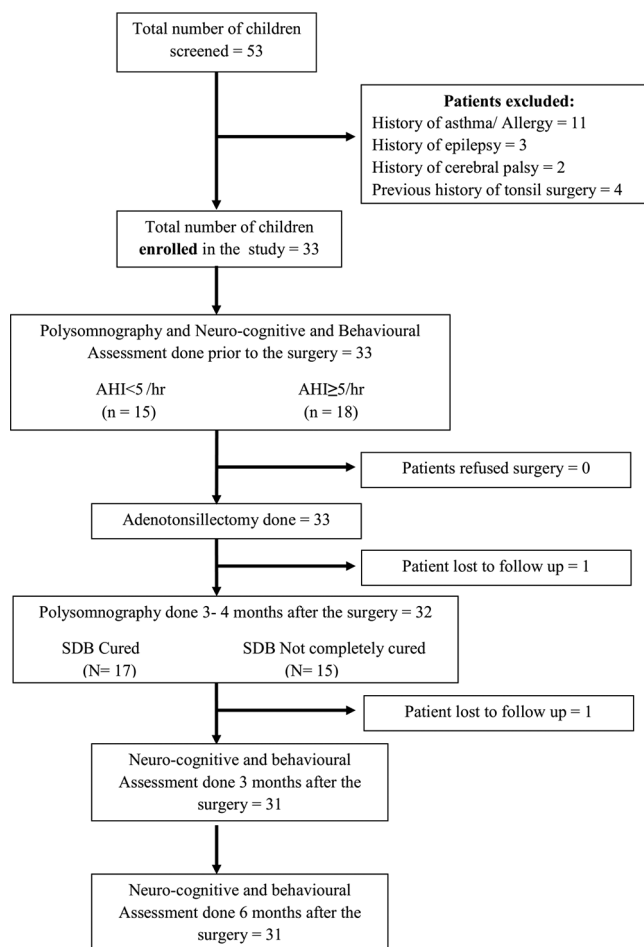


Figure 1: Flow of participants in the study

Table 2: Frequency of symptoms before and after adenotonsillectomy

Symptom	Baseline (n=33) 3 months postsurgery (n=31) 6 months postsurgery (n=31)			P		
	A	B	C	A versus B	B versus C	A versus C
Snoring	28 (84.8)	4 (12.9)	5 (16.1)	<0.001	1.000	<0.001
Witnessed choking while asleep	19 (57.6)	3 (9.7)	3 (9.7)	<0.001	1.000	<0.001
Nocturnal drooling of saliva	11 (33.3)	5 (16.1)	5 (16.1)	0.063	1.000	0.063
Daytime sleepiness	11 (33.3)	2 (6.5)	2 (6.5)	0.004	1.000	0.004
Fatigue	10 (31.3)	3 (9.7)	2 (6.5)	0.016	1.000	0.008
Night terrors	5 (15.2)	2 (6.5)	2 (6.5)	0.250	1.000	0.250
Night mare	3 (9.1)	2 (6.5)	2 (6.5)	1.000	1.000	1.000
Sleep walking	2 (6.1)	2 (6.5)	2 (6.5)	1.000	1.000	1.000
Difficulty in morning awakening	16 (48.5)	11 (35.5)	8 (25.8)	0.063	0.250	0.008
Nocturnal enuresis	11 (33.3)	4 (12.9)	4 (12.9)	0.063	1.000	0.063

Data expressed as n (%). P<0.05 was considered significant (shown in bold)

Table 3: Correlation of the baseline neurocognitive assessment with the sleep parameters

	Total group score (n=33)	Number (%) with abnormal score (n=33)	Correlation with PDSS	P	Correlation with AHI	P	Correlation with ODI	P	Correlation with lowest O ₂ saturation	P
Malin's intelligence scale										
Information	87.64±7.31	11 (33.3)	-0.186	0.300	-0.098	0.588	-0.177	0.325	-0.109	0.544
Comprehension	102.12±19.23	3 (9.1)	-0.218	0.222	-0.239	0.181	-0.409	0.018	0.012	0.947
Arithmetic	95.30±16.68	3 (9.1)	0.188	0.296	0.074	0.682	-0.053	0.772	-0.099	0.585
Similarities	95.24±12.49	4 (12.1)	-0.185	0.302	-0.053	0.772	-0.039	0.830	-0.015	0.932
Vocabulary	86.82±14.52	9 (27.3)	-0.017	0.927	-0.192	0.284	-0.161	0.371	-0.111	0.538
Digit span	90.15±11.86	5 (15.2)	-0.202	0.259	-0.109	0.545	-0.102	0.573	-0.007	0.970
Picture completion	99.52±16.38	4 (12.1)	-0.157	0.383	0.018	0.922	-0.162	0.369	-0.093	0.607
Block design	96.58±18.41	4 (12.1)	0.137	0.445	-0.092	0.0611	0.011	0.950	0.072	0.689
Object assembly	84.76±14.64	16 (48.5)	-0.089	0.624	0.031	0.866	0.032	0.858	0.050	0.783
Coding	99.97±16.29	4 (12.1)	0.002	0.990	-0.009	0.959	-0.096	0.596	-0.069	0.705
Mazes	109.85±20.34	2 (6.1)	-0.042	0.815	0.150	0.406	-0.023	0.901	-0.219	0.221
Verbal IQ	92.84±12.86	3 (9.1)	-0.201	0.262	-0.127	0.481	-0.206	0.249	-0.065	0.719
Performance IQ	98.12±13.16	2 (6.1)	-0.031	0.863	0.030	0.866	-0.059	0.744	-0.077	0.672
Total IQ	95.48±12.06	2 (6.1)	-0.124	0.491	-0.051	0.777	-0.142	0.430	-0.076	0.673
Modified Wisconsin Card Sorting Test										
Categories completed	51.87±12.33	4 (12.1)	-0.200	0.265	0.142	0.431	-0.054	0.764	-0.379	0.029
Total errors	46.30±8.96	1 (3.0)	0.211	0.238	0.017	0.924	0.192	0.285	0.159	0.376
Perseverative errors	56.99±12.14	7 (21.2)	0.459	0.007	0.007	0.969	0.306	0.083	0.189	0.292
Percentage of perseverative errors	66.38±9.47	-	0.451	0.008	0.111	0.539	0.210	0.240	-0.040	0.823
Nonperseverative errors	40.31±5.45	0 (0.0)	0.033	0.855	0.100	0.582	0.244	0.171	-0.049	0.787
Percentage of nonperseverative errors	34.54±8.36	-	-0.408	0.018	-0.123	0.495	-0.176	0.328	0.094	0.604
Categorizing efficiency	52.27±12.30	3 (9.1)	-0.214	0.232	0.109	0.545	-0.091	0.614	-0.310	0.079
Failure to maintain sets	55.13±14.58	12 (36.4)	0.152	0.397	-0.248	0.164	-0.030	0.868	0.386	0.026
Conners' scale										
Inattention	62.06±17.53	15 (45.5)	0.175	0.330	0.043	0.814	-0.094	0.602	-0.029	0.874
Hyperactivity	65.00±18.64	15 (45.5)	0.190	0.290	-0.040	0.825	-0.210	0.241	0.091	0.615
Learning problems	63.79±18.47	14 (42.4)	0.293	0.099	0.144	0.424	-0.031	0.862	0.085	0.637
Executive dysfunction	52.85±9.71	5 (15.2)	0.284	0.110	0.034	0.851	0.003	0.988	-0.119	0.509
Aggression	64.42±21.07	15 (45.5)	0.163	0.364	-0.059	0.745	0.071	0.695	-0.083	0.647
Peer relations	54.21±14.46	7 (21.2)	0.011	0.952	-0.013	0.943	-0.107	0.552	-0.096	0.594
Inattention DSM IV	59.12±15.48	8 (24.2)	0.231	0.196	0.125	0.488	-0.061	0.735	0.036	0.845
Hyperactivity DSM IV	64.76±19.02	13 (39.4)	0.245	0.196	-0.007	0.967	-0.176	0.328	0.035	0.848
Conduct disorder DSM IV	64.67±20.63	11 (33.3)	0.196	0.275	-0.041	0.822	-0.089	0.622	-0.101	0.574
Oppositional defiance disorder DSM IV	59.52±17.40	8 (24.2)	0.089	0.623	-0.121	0.503	-0.131	0.466	-0.065	0.718
ADHD index	51.55±30.36	11 (33.3)	0.170	0.345	0.017	0.927	-0.162	0.369	0.098	0.588
CBCL										
Activity score	36.27±12.94	16 (48.5)	-0.108	0.549	0.076	0.674	0.123	0.496	-0.090	0.618
Social score	40.39±11.71	5 (15.2)	-0.032	0.860	0.208	0.246	0.18	0.295	-0.129	0.473
School score	42.27±12.46	7 (21.2)	-0.148	0.410	0.092	0.612	0.149	0.408	-0.252	0.157
Total score	33.58±11.85	25 (75.8)	-0.109	0.545	0.219	0.220	0.238	0.182	-0.250	0.160
Affective problems	58.52±6.52	6 (18.2)	-0.136	0.449	-0.107	0.554	-0.124	0.492	0.190	0.288
Anxiety problems	51.70±3.65	0	0.168	0.350	-0.109	0.545	-0.051	0.778	0.192	0.283
Somatic problems	51.42±2.95	0	-0.070	0.700	-0.022	0.905	-0.071	0.694	0.230	0.197
AD/HA problems	61.94±9.76	13 (39.4)	0.183	0.309	-0.126	0.484	-0.212	0.236	0.147	0.413
Oppositional defiance problems	54.70±6.87	3 (9.1)	-0.083	0.646	-0.271	0.127	-0.194	0.280	0.098	0.588
Conduct problems	54.30±6.64	4 (12.1)	0.032	0.494	-0.258	0.147	-0.192	0.248	-0.026	0.884

P<0.05 was considered significant (shown in bold). DSM: Diagnostic and Statistical Manual, ADHD: Attention-deficit hyperactivity disorder, PDSS: Pediatric Daytime Sleepiness Scale, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, IQ: Intelligence quotient, CBCL: Childhood Behavior Checklist, AD/HA: Attention-deficit/hyperactivity

36.4% of children failed to maintain sets and 21.2% made perseverative errors [Table 3].

In the Parent Conners' scale, almost half of the children were in clinical range for inattention (45.5%), HA (45.5%), aggression (45.5%), and learning problems (42.4%). About

one-third had problems related to conduct (33.33%) and oppositional defiance (24.2%) when scored on the basis of DSM IV criteria. In the Childhood Behavior Checklist (CBCL/6-18), almost half (51.60%) of the subjects showed abnormal activity score. High frequencies of attention-deficit/hyperactivity (AD/HA) problems (39.4%),

affective problems (18.2%), conduct problems (12.1%), and oppositional defiance disorder (9.1%) were also seen in many children [Table 3].

The children with a higher PDSS (excessive daytime sleepiness) made more perseverative errors during assessment using the MWCST ($r = 0.459$; $P = 0.007$). Furthermore, with increasing frequency of oxygen desaturation (increase in ODI), decrement was observed in comprehension scores of MIS ($r = -0.409$; $P = 0.018$). The lowest O_2 saturation during sleep showed negative correlation with categories completed ($r = -0.379$; $P = 0.029$) and positive correlation with failure to maintain sets ($r = 0.386$; $P = 0.026$) [Table 3].

Neurocognitive assessment: Before and after surgery

In the MIS, statistically significant improvement was seen in all scores at 3 months and further improvement at the 6 month assessment [Figure 2]. In the MWCST, statistically significant drop in mean values of almost all MWCST parameters was seen; improvement was evident at 6 months [Figure 3]. In the Parent Connors' Scale, decrease in mean scores of inattention, HA, and learning problems was seen [Figure 4]. The mean scores of conduct disorder and oppositional defiance disorder when assessed using DSM IV criteria also decreased after surgery. Attention-deficit hyperactivity disorder (ADHD) index, a combined score of problems related to inattention and HA, decreased substantially with significant improvement within 3 months of surgery. In the CBCL, significant improvement occurred in mean scores of affective problems, AD/HA problems, and conduct problems after 6 months of surgery [Figure 5]. Although improvements in these domains are statistically significant, the clinical relevance may be questionable. In spite of improvement in scores, children who were impaired initially continued to remain in abnormal range even after 6 months of treatment.

The study population was categorized based on severity of pre-operative AHI (AHI <5/h and AHI ≥5/h). The improvement over 6 months in various scales in each group was compared [Supplementary Table S2]. Most domains of various scales improved in both groups. Statistically significant improvement was seen amongst those with a higher AHI, in the perseverative errors and failure to maintain sets (in the MWCST); inattention and HA domains (in the Parent Connors' scale); and in school score and AD/HA problems (in the CBCL/6–18 scores), while there was no significant improvement in these domains in the group with AHI <5/h. Statistically significant improvement was also seen in mild SDB group in oppositional defiance disorder scale (in the Parent Connors' scale) and activity score (in the CBCL/6–18 scores); however, such an improvement was lacking in the group with severe SDB. However, when we compared the improvement in various subscales in the two groups, the difference was not statistically significant.

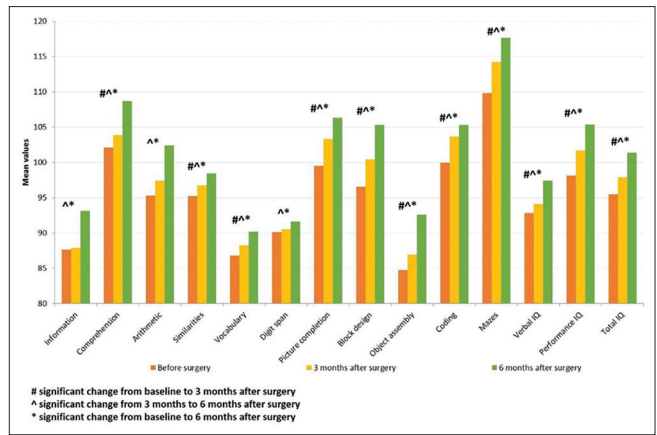


Figure 2: Mean scores of Malin's intelligence scale in children before and after surgery

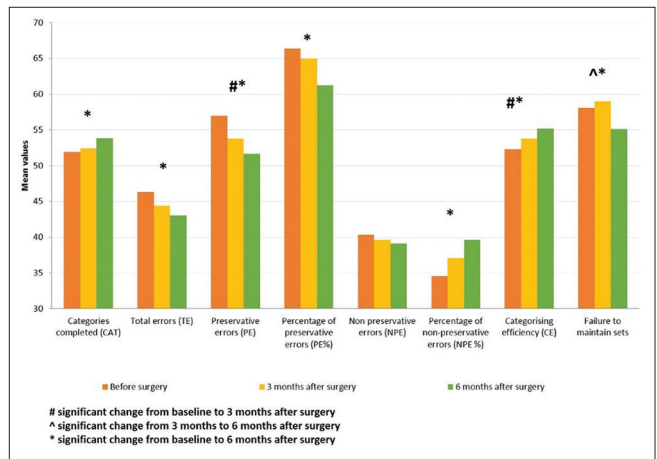


Figure 3: Modified Wisconsin Card Sorting Test scores, before and after surgery

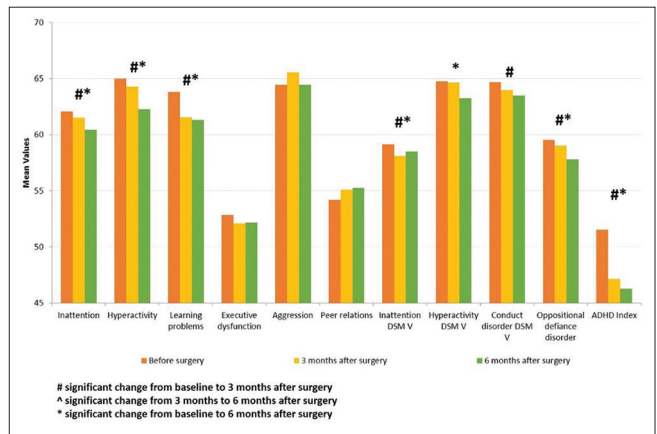


Figure 4: Mean scores of Parent Connors' Scale before and after surgery

The improvement after 6 months was compared between patients in whom SDB was completely cured and those with residual SDB [Supplementary Table S3]. Here also, most domains of various scales improved in both groups. Statistically significant improvement was seen in whom

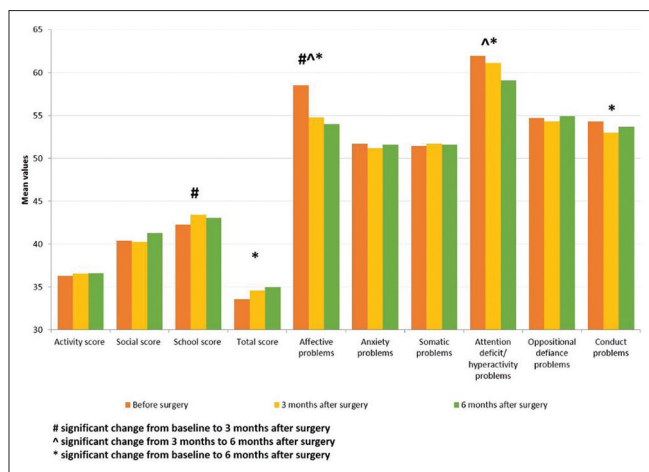


Figure 5: Mean scores of Childhood Behavior Checklist in children before and after surgery

SDB was cured in the similarities, coding, and mazes subscales (in the MIS); categories completed and total errors (in the MWCST); inattention and HA domains and the oppositional defiance disorder scale and ADHD index (in the Parent Connors' scale); and in the activity and total score (in the CBCL/6–18 scores); however, there was no significant improvement in these domains in those with persisting SDB. When improvement between groups was compared, the mazes subscale in the MIS showed significant improvement in patients in whom SDB was completely cured ($P = 0.028$).

DISCUSSION

This is one of the few prospective studies to have used attended PSG, both for diagnosing SDB before AT and for evaluating residual disease after surgery, along with extensive and objective assessment of neurocognitive and behavioral functions in affected children using validated instruments. We observed that neurocognitive impairment was common in these children, and though there was significant improvement after AT, residual abnormalities persisted in patients.

Most studies in children with SDB have reported lower intelligence scores than normal controls. Although we did not have a control group, a significant proportion of children showed a clinically abnormal score. Studies conducted so far have not found a strong association between severity of SDB (assessed using AHI) and baseline neurocognitive impairment in children with SDB.^[10,11,21,22] We observed that children with excessive daytime sleepiness made more perseverative errors. The present study also found a negative correlation between comprehension scores (a domain of verbal intelligence) and ODI and between the lowest oxygen saturation and the categories completed in the MWCST – these correlations are scientifically plausible given the expected effect of sleep disruption due to oxygen desaturation on the neurocognitive development in these children. This

could reflect that probably oxygen desaturation rather than apneas may be the important mediators of neurocognitive deficits in these patients; similar results have been reported in adult SDB patients.^[38] In studies done in chronic obstructive pulmonary disease, patient's oxygen saturation has been found to be related to increased risk of cognitive impairment and the regular use of supplemental oxygen therapy decreased the risk for cognitive impairment in them.^[39] It is possible that in children with SDB also, the goal of therapy should be to abolish oxygen desaturation.

AT in our study group led to a sharp decrease in almost all PSG abnormalities. This is similar to the earlier studies.^[40,41] However, complete cure of SDB defined as AHI ≤ 1 h was seen in 53.1% of the subjects. This is also commensurate with previous studies.^[5,40,41] A multicenter retrospective study has reported complete resolution of the SDB in about a quarter of the children undergoing AT.^[42] This suggests that though AT improves SDB, it completely resolve SDB only in a minority of children.

Significant improvement in mean scores was seen in most of the tested neurocognitive and behavioral domains. The first postoperative assessment at 3 months showed gradual improvement. Further improvement was seen at the 6 months assessment. The change in mean scores of MWCST was significant only at 6 months and not 3 months after surgery in most parameters. This indicates that improvement after surgery in these domains is gradual and may take some time before becoming evident clinically.

Despite improvement, residual neurocognitive deficits persisted in children even 6 months after surgery. This is in agreement with previous studies which have shown improvement in some aspects as well as residual disabilities.^[10,11,14,15] We observed that aggression (assessed using the Parent Connors' scale) and oppositional defiance (assessed using the CBCL/6–18) persisted after the surgery. The persistence of neurocognitive problems in these children could be due to the incomplete resolution of SDB or to other nonsleep-related factors. It is also conceivable that 6 months duration may not be enough for resolution of neurocognitive problems even in children in whom SDB is cured by AT. Another possible reason could be that the cognitive and behavioral impairment may be irreversible.

Previous studies have reported that baseline PSG assessment and its subsequent amelioration did not predict the improvement in neurocognitive and behavioral morbidity.^[11,43] However, we saw that patients with a baseline AHI >5 /h and those who have complete resolution of the SDB (postoperative AHI <1 /h) had shown improvement in more subscales than patients with baseline AHI <5 /h and patients who had incomplete resolution of the SDB. However, when we compared the degree of improvement, only the maze subscale (a measure of performance IQ in the MIS) showed significant improvement in the patients in whom the SDB was completely cured. The lack of

significant difference in the improvement in the various subscales of neurobehavioral morbidity could be attributed to the small sample size.

As AT may not lead to complete cure of PSG abnormalities and neurocognitive impairment, the use of repeat PSG after surgery may be warranted to evaluate for residual disease and plan further treatment in these patients.^[23,44]

The strength of this study is the use of high-quality attended diagnostic overnight PSGs both before and after surgery and application of objective, well-validated instruments for neurocognitive and behavioral assessment in these children. Furthermore, after surgery, reassessment was done at 3 and 6 months interval to look for short- and intermediate-term improvement. The shortcomings in this study are a fairly small number of patients. It can be argued that the improvement in the score could be due to a learning effect; by the inclusion of a control group in further studies, this can be negated. A longer follow-up period may be required to assess the long-term impact of residual SDB. In addition, the use of other adjunctive techniques in addition to AT (e.g., lingual tonsillectomy), with the aim of completely ameliorating sleep fragmentation and nocturnal hypoxia, needs to be assessed.

CONCLUSION

We conclude that children suffering from SDB have impaired neurocognitive and behavioral functions. The decrements in neurocognitive performance related to SDB appear to be predominantly a result of hypoxemia, rather than the frequency of SDB events. AT significantly reduced the apneas, and there was substantial improvement in neurocognitive and behavioral parameters; a greater resolution being observed patients with AHI >5/h and in those with complete resolution of the SDB. However, despite treatment, residual disease is common and such patients may require further treatment.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table S1: Sleep parameters - Baseline and after surgery

	Total group		
	Baseline (n=33)	Postsurgery (n=32)	P
PDSS	5.58±3.96	3.06±2.28*	< 0.001
AHI	7.88±7.78	2.03±3.10	< 0.001
ODI	6.82±4.95	1.87±2.10	< 0.001
Lowest O ₂ saturation	89.76±4.21	93.41±3.23	< 0.001

*Postsurgery PDSS at 6 months Data expressed as mean±SD. $P < 0.05$ was considered significant (shown in bold). PDSS: Pediatric Daytime Sleepiness Scale, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, SD: Standard deviation

Supplementary Table S2: Neurocognitive and behavioral improvement after surgery in the groups based on severity of sleep-disordered breathing

	AHI <5				AHI ≥5			
	Baseline (n=15)	6 months (n=14)	P [#]	Improvement	Baseline (n=18)	6 months (n=17)	P [#]	Improvement
Malin's intelligence scale								
Information	87.87±19.56	92.29±19.20	0.010	6.36±7.94	87.44±15.78	93.82±15.29	<0.001	6.24±5.49
Comprehension	103.27±19.37	108.57±19.26	0.008	6.43±7.67	101.17±19.62	108.76±20.06	0.002	7.12±7.83
Arithmetic	91.07±13.92	99.14±18.49	0.016	9.07±12.24	98.83±18.31	105.12±18.58	0.003	5.18±6.21
Similarities	96.13±12.36	97.86±10.80	0.005	2.86±3.16	94.50±12.91	98.94±11.63	0.009	3.29±4.55
Vocabulary	87.07±16.18	88.14±15.12	0.001	3.07±2.81	86.61±13.46	91.81±12.90	0.010	4.34±6.10
Digit span	88.00±10.47	88.29±9.79	0.165	1.14±2.91	91.94±12.92	94.35±13.67	0.098	2.47±5.79
Picture completion	98.33±16.28	103.14±16.42	0.001	6.29±5.30	100.50±16.87	108.94±16.88	<0.001	7.76±6.99
Block design	96.60±22.22	105.14±29.10	0.026	9.64±14.31	96.56±15.24	105.47±16.69	0.015	8.88±13.40
Object assembly	83.87±14.93	89.36±15.78	0.001	7.50±6.80	85.50±14.78	95.24±13.91	0.004	9.12±11.02
Coding	102.67±17.55	106.07±18.61	0.006	4.29±4.87	97.72±15.30	104.65±13.28	0.029	5.76±9.89
Mazes	108.00±22.88	113.93±23.66	0.035	7.21±11.46	111.39±18.49	120.76±16.26	0.009	8.94±12.43
Verbal IQ	92.23±13.24	95.71±12.71	<0.001	4.82±3.66	93.35±12.89	98.80±12.46	<0.001	4.84±3.66
Performance IQ	97.85±15.17	103.53±16.62	<0.001	7.03±5.40	98.33±11.68	106.90±11.30	<0.001	7.98±6.19
Total IQ	95.04±13.59	99.65±13.81	<0.001	5.96±4.40	95.84±11.03	102.88±10.23	<0.001	6.44±4.55
Modified Wisconsin Card								
Sorting Test								
Categories completed	51.34±10.63	54.06±11.39	0.047	2.36±4.03	52.32±13.87	53.68±11.87	0.078	1.95±4.28
Total errors	47.42±9.53	43.33±8.15	0.041	2.81±4.63	45.38±8.63	42.83±8.32	0.007	2.44±3.27
Perseverative errors	57.64±13.30	53.37±13.93	0.070	4.32±8.19	56.45±11.45	50.25±7.93	0.012	6.29±9.15
Perseverative errors percentage	64.22±10.64	62.08±12.12	0.271	2.26±7.35	68.17±8.24	60.56±9.47	0.052	7.94±15.60
Nonperseverative errors	40.24±3.40	38.32±2.96	0.139	2.14±5.08	40.36±6.82	39.73±5.93	0.715	0.53±5.92
Nonperseverative errors percentage	36.68±9.13	39.26±11.32	0.237	-2.37±7.16	32.76±7.46	39.89±9.17	0.053	-7.42±14.66
Categorization efficiency	51.29±10.30	54.72±11.94	0.006	3.56±4.04	53.09±13.99	55.53±13.80	0.018	3.44±5.40
Failure to maintain sets	61.66±15.45	59.42±17.81	0.401	2.22±9.57	55.05±12.38	51.59±10.56	0.033	4.29±7.58
Parent Conners' Scale								
Inattention	62.33±19.50	62.29±19.63	0.231	1.64±4.89	61.83±16.29	58.94±16.14	0.017	3.24±5.03
Hyperactivity	66.47±19.15	66.00±19.29	0.109	2.36±5.12	63.78±18.66	59.18±17.86	0.043	4.59±8.59
Learning problems	67.07±19.05	64.43±18.58	0.077	4.00±7.79	61.06±18.06	58.76±17.09	0.078	2.71±5.93
Executive dysfunction	52.60±11.38	51.79±9.24	0.400	1.14±4.91	53.06±8.41	52.47±8.75	0.961	-0.06±0.24
Aggression	69.00±21.33	69.43±22.18	0.250	1.64±5.11	60.61±20.67	60.29±19.82	0.286	0.88±3.30
Peer relations	55.53±16.31	56.79±18.38	0.812	-0.36±5.51	53.11±13.12	54.00±13.54	0.772	-0.53±7.40
Inattention DSM IV	61.00±17.31	61.43±16.70	0.300	1.07±3.71	57.56±14.09	56.12±13.25	0.018	2.06±3.23
Hyperactivity DSM IV	65.80±19.79	64.93±20.40	0.129	2.50±5.77	63.89±18.89	61.82±19.59	0.043	2.53±4.74
Conduct disorder DSM IV	69.73±19.94	67.86±21.22	0.150	3.79±9.25	60.44±20.79	59.88±18.74	0.196	1.59±4.85
Oppositional defiance disorder DSM IV	63.67±18.25	62.14±18.39	0.007	3.21±3.75	56.06±16.37	54.24±16.05	0.105	2.12±5.07
ADHD index	55.47±32.14	51.43±33.94	0.149	7.21±17.59	48.28±29.32	42.00±26.32	0.012	7.12±10.36
ASEBA CBCL scores								
Activity score	34.47±11.14	35.36±11.77	0.031	0.93±1.44	37.78±14.40	37.59±14.64	0.835	-0.06±1.14
Social score	37.93±11.22	38.71±11.73	0.336	0.93±3.47	42.44±12.04	43.41±11.69	0.169	1.12±3.20
School score	39.87±11.49	39.21±11.46	0.657	-0.64±5.30	44.28±13.20	46.18±11.76	0.041	1.88±3.50
Total score	30.60±8.44	30.57±8.70	0.108	0.64±1.39	36.06±13.83	38.65±13.82	0.085	2.35±5.28
Affective problems	60.20±6.77	55.71±6.29	0.003	4.86±5.10	57.11±6.13	52.59±4.21	0.004	4.35±5.27
Anxiety problems	52.87±4.24	53.07±4.80	1.000	0.00±1.57	50.72±2.85	50.41±2.79	0.332	0.24±0.97
Somatic problems	51.27±3.13	51.50±3.82	0.336	-0.29±1.07	51.56±2.87	51.71±2.91	0.332	-0.06±0.24
AD/HA problems	64.93±9.15	63.14±10.55	0.074	2.14±4.13	59.44±9.79	55.76±7.95	0.002	3.47±3.91
Oppositional defiance problems	57.13±7.89	57.50±8.33	0.869	0.07±1.59	52.67±5.29	52.76±5.48	0.579	-0.18±1.29
Conduct problems	56.40±6.90	55.79±6.41	0.114	1.07±2.37	52.56±6.07	51.94±5.48	0.104	0.71±1.69

[#] P value: Comparing the baseline with the 6 months. Data expressed as mean±SD. P<0.05 was considered significant (shown in bold). DSM: Diagnostic and Statistical Manual, ADHD: Attention-deficit hyperactivity disorder, AHI: Apnea-hypopnea index, IQ: Intelligence quotient, CBCL: Childhood Behavior Checklist, ASEBA: Achenbach System of Empirically Based Assessment, AD/HA: Attention-deficit/hyperactivity, SD: Standard deviation

Supplementary Table S3: Neurocognitive and behavioral improvement after surgery in the groups based on complete cure of sleep-disordered breathing

	SDB cured				SDB not cured			
	Baseline	6 months (n=17)	P [#]	Improvement	Baseline (n=15)	6 months (n=14)	P [#]	Improvement
Malin's intelligence scale								
Information	78.94±9.93	86.88±13.62	0.001	7.94±7.55	97.67±19.28	100.71±17.80	0.005	4.29±4.71
Comprehension	95.24±17.78	103.88±20.04	0.001	8.65±8.32	110.53±18.56	114.50±17.47	0.018	4.57±6.30
Arithmetic	92.18±17.18	99.24±18.94	0.001	7.06±8.05	99.87±15.74	106.29±17.80	0.042	6.79±11.24
Similarities	90.76±11.57	94.59±10.55	<0.001	3.82±2.72	101.67±10.29	103.14±10.19	0.121	2.21±4.99
Vocabulary	85.94±9.05	89.65±9.92	0.001	3.71±3.84	88.80±19.17	90.77±17.88	0.033	3.84±6.04
Digit span	86.59±10.64	89.24±11.45	0.084	2.65±5.92	94.00±12.66	94.50±13.04	0.177	0.93±2.43
Picture completion	98.06±16.28	104.94±17.42	<0.001	6.88±5.85	101.87±17.14	108.00±16.16	0.002	7.36±6.88
Block design	97.18±22.30	104.35±27.88	0.039	7.18±13.13	95.93±14.38	106.50±15.18	0.009	11.71±14.21
Object assembly	83.18±14.81	89.24±15.84	<0.001	6.06±5.57	87.20±14.93	96.64±12.89	0.004	11.21±11.97
Coding	98.06±16.87	104.71±16.87	0.009	6.65±9.27	103.60±15.10	106.00±14.60	0.056	3.21±5.73
Mazes	102.77±21.49	115.24±23.60	0.001	12.47±12.25	118.27±16.68	120.64±14.49	0.255	2.93±9.20
Verbal IQ	88.27±10.22	93.91±11.56	<0.001	5.64±3.93	98.68±13.77	101.65±12.59	<0.001	3.85±2.99
Performance IQ	95.81±14.82	103.58±16.15	<0.001	7.77±6.34	101.37±10.97	107.56±10.46	<0.001	7.29±5.21
Total IQ	92.04±11.50	98.74±12.73	<0.001	6.70±4.96	100.03±11.76	104.67±10.27	<0.001	5.63±3.74
Modified Wisconsin Card								
Sorting Test								
Categories completed	55.02±9.97	57.43±10.02	0.021	-2.41±3.89	47.61±13.94	49.51±11.95	0.155	-1.80±4.47
Total errors	44.68±8.90	41.44±8.11	0.007	3.24±4.30	48.08±9.30	45.02±7.95	0.057	1.83±3.28
Perseverative errors	56.94±12.81	51.65±13.03	0.018	5.29±8.25	57.17±12.21	51.67±8.26	0.047	5.53±9.41
Perseverative errors percentage	67.84±8.69	63.15±10.88	0.187	4.69±14.02	64.98±10.62	58.95±10.12	0.062	6.21±11.38
Nonperseverative errors	39.44±5.42	37.59±4.47	0.138	1.85±4.88	41.17±5.70	40.90±4.70	0.753	0.55±6.34
Nonperseverative errors percentage	33.72±6.95	38.31±10.17	0.157	-4.59±12.75	35.27±10.13	41.18±9.98	0.079	-5.80±11.39
Categorization efficiency	54.89±10.41	59.17±12.08	0.004	4.28±5.23	48.12±13.13	50.31±12.31	0.037	2.55±4.10
Failure to maintain sets	57.50±15.32	55.26±16.46	0.304	2.25±8.72	59.83±12.57	54.97±12.54	0.052	4.70±8.22
Parent Connors' Scale								
Inattention	62.12±17.73	58.88±18.10	0.042	3.24±6.05	62.40±18.46	62.36±17.38	0.075	1.64±3.18
Hyperactivity	67.59±18.97	63.18±19.13	0.048	4.41±8.51	62.13±19.12	61.14±18.43	0.097	2.57±5.37
Learning problems	66.47±18.54	61.76±17.70	0.040	4.71±8.70	61.40±19.12	60.79±18.36	0.032	1.57±2.44
Executive dysfunction	53.06±10.50	51.82±8.99	0.266	1.24±4.42	52.00±9.10	52.57±8.95	0.843	-0.07±0.27
Aggression	65.65±21.43	63.53±22.03	0.115	2.12±5.23	63.93±21.81	65.50±20.62	0.789	0.14±1.96
Peer relations	51.24±12.54	51.76±14.88	0.807	-0.53±8.79	58.07±16.38	59.50±16.14	0.431	-0.36±1.65
Inattention DSM IV	60.29±15.68	59.12±16.27	0.206	1.18±3.68	58.60±15.95	57.79±13.59	0.025	2.14±3.16
Hyperactivity DSM IV	66.41±20.20	63.82±21.47	0.080	2.59±5.70	63.47±18.71	62.50±18.05	0.069	2.43±4.59
Conduct disorder DSM IV	65.47±20.38	61.94±20.27	0.129	3.53±9.09	65.20±21.54	65.36±20.19	0.163	-1.43±3.61
Oppositional defiance disorder DSM IV	59.18±18.42	56.12±18.61	0.020	3.06±4.87	60.47±17.27	59.86±16.05	0.080	2.07±4.08
ADHD index	53.06±32.42	43.88±31.92	0.036	9.18±16.49	51.00±29.68	49.14±28.05	0.094	4.71±9.76
Comparison of postoperative ASEBA CBCL scores								
Activity score	35.47±13.22	36.18±13.00	0.035	0.71±1.26	36.93±13.44	37.07±14.03	1.000	0.00±1.41
Social score	39.06±10.33	40.47±9.88	0.165	1.41±4.00	41.60±13.65	42.29±14.03	0.336	0.57±2.14
School score	41.65±11.20	42.94±10.53	0.347	1.29±5.51	42.87±14.52	43.14±13.92	0.929	0.07±2.95
Total score	31.53±10.03	32.65±9.70	0.005	1.12±1.41	36.00±13.94	37.86±14.74	0.198	2.14±5.91
Affective problems	59.00±6.35	53.88±5.59	0.001	5.12±5.44	57.87±7.08	54.14±5.36	0.009	3.93±4.80
Anxiety problems	51.53±3.54	51.29±3.50	0.332	-0.24±0.97	51.87±4.02	52.00±4.62	1.000	0.00±1.57
Somatic problems	51.12±3.06	51.12±3.06	NP	0.00±0.00	51.87±2.95	52.21±3.58	0.239	0.36±1.08
AD/HA problems	61.76±9.56	58.53±9.67	0.007	3.24±4.34	62.07±10.64	59.79±10.26	0.027	2.43±3.65
Oppositional defiance problems	54.88±6.66	55.29±6.81	0.300	-0.41±1.58	54.53±7.56	54.43±7.88	0.239	0.36±1.08
Conduct problems	54.65±5.85	53.88±5.64	0.097	0.76±1.79	54.13±7.80	53.43±6.89	0.126	1.00±2.29

P: Comparing the baseline with the 6 months result. Data expressed as mean±SD. P<0.05 was considered significant (shown in bold). DSM: Diagnostic and Statistical Manual, ADHD: Attention-deficit hyperactivity disorder, SDB: Sleep-disordered breathing, IQ: Intelligence quotient, CBCL: Childhood Behavior Checklist, ASEBA: Achenbach System of Empirically Based Assessment, AD/HA: Attention-deficit/hyperactivity, SD: Standard deviation, NP: Not performed