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Executive Functions and Social Responsiveness in Children and Adolescents With Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder

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Abstract

Objective: To evaluate the executive functions and social reciprocity of children and adolescents diagnosed with autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) and compared them with healthy controls.

Material and Method: Patients aged 6-17 years diagnosed with ASD ($n=33$) and ADHD ($n=37$) and healthy controls in the same age range ($n=33$) were included in the study. Behavioral Rating Inventory of Executive Functions (BRIEF) sub-scales and Social Responsiveness Scale (SRS) were used for evaluating executive function areas and social responsiveness.

Results: Our results revealed that children and adolescents with ASD and ADHD were significantly impaired for all BRIEF sub-scales except emotional control and that the significant increase in sub-scale scores expressing deterioration continued after adjustment for SES, verbal IQ scores, and gender. ASD patients received significantly higher SRS scores compared to ADHD and control groups and ADHD patients also had significantly higher values compared to the controls.

Conclusion: Further studies with parent-report scales that allow easier and faster evaluation of executive functions and social reciprocity will contribute to better understanding of the personal needs of children with neurodevelopmental disorders and the finding of new treatments.

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INTRODUCTION

Autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD) are neurodevelopmental psychiatric conditions of childhood. Symptoms of ADHD (attention deficit, impulsivity, and hyperactivity) are observed in a significant number of ASD patients while cases with ADHD also have symptoms of ASD. In ASD cases, impairments in executive cognitive functions are frequently seen in addition to deterioration in social interaction, communication, and behavioral patterns, which are the main symptoms of the disease.[1]

The executive function term is used to express many cognitive tasks such as planning, initiation, set-shifting, monitoring, inhibition, emotional control, and working memory that regulate an individual's behaviors. Symptoms that severely disrupt academic achievement and social adjustment skills in children with ADHD are also thought to be due to disturbances in executive functions.[2] A supporting evidence came from a recent systematic review, stating that ADHD symptoms were reduced by the improvement of executive functions[3].

Several studies examining executive functions in these 2 particular disorders were frequently encountered in the literature. The common finding was that there were impairments in executive functions in both disorders, but in different areas.[4-7]

Although it is not included as a criterion in diagnostic classifications, most of the individuals with ADHD suffer from dysfunctions in social interaction skills. In previous studies, it has been discussed whether the difficulties in peer relations and social interaction in children with ADHD develop secondary to the manifestations of ADHD or a reflection of the psychopathology itself.[8] In recent years it has been emphasized that both symptoms of the disorder and executive dysfunctions per se play a role in the social impairment encountered in children with ADHD[9-11].

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Comparing the findings related to overlapping or separately occurring dysfunctions in both disorders and investigating their possible relationships may contribute to our understanding of the nature of these 2 neurodevelopmental disorders as well as it may confer an opportunity for personalized treatment options.[12-14] We undertook this study to evaluate the executive functions and social reciprocity of children and adolescents diagnosed with ASD and ADHD by using Behavioral Rating Inventory of Executive Functions (BRIEF) and Social Responsiveness Scale (SRS) parent forms and to compare them with healthy controls.

METHODS

Sample and Procedure

Consecutive patients between June 2017 and August 2017 admitted to our outpatient clinic aged between 6 and 17 years with diagnoses of ASD ($n=33$) and ADHD ($n=37$) were included in the patient groups. The ASD group consisted of children and adolescents with Asperger syndrome (AS) and high functioning autism (HFA). Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL) was used to determine psychiatric diagnoses of the participants. However, autism diagnosis criteria are not scanned with K-SADS. The AS and HFA diagnoses were established by the psychiatric interviews of the child and the parents based on DSM-IV criteria. Similar to autism, AS was also included under the category of Pervasive Developmental Disorders in DSM-IV. Although difficulties in social interaction are common in both disorders, ASD differs from typical autism by the lack of delayed language development. The term HFA, on the other hand, includes individuals with autism whose mental abilities are at or above the limit.[15] Autism Spectrum Screening Questionnaire (ASSQ) and Childhood Autism Rating Scale (CARS) were used to support the clinical diagnosis of autism. All patients included in our study were diagnosed with "mild autism" according to the CARS. The rates of ADHD subtypes were 62.1%, 27.02%, and 10.8% for combined type, predominantly inattentive type, and predominantly hyperactive type, respectively. Exclusion criteria were intelligence quotient below 70, history of using any psychotropic drug and significant neurological illness including history of head injury leading to loss of consciousness. The control group consisted of 39 children and adolescents within the same age range who were admitted to the pediatric outpatient clinic in the same hospital with no history of chronic disease and psychiatric admissions. Except for 4 children with enuresis, those without a psychiatric diagnosis according to K-SADS-PL were included in the control group. Three children with ASD with an IQ score below 70 and 1 child with ADHD who did not want to be involved in the study were excluded from the study. Sociodemographic information was collected by the researchers from all participants. This investigation was approved by the Ethical Committee of Marmara University (Date: April 07, 2017, Approval Number: 09.2017.318).

Instruments

Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL): K-SADS-PL is an assessment tool for psychiatric diagnosis of children and adolescents according to DSM-III-R and DSM-IV diagnostic criteria. K-SADS was developed by Kaufman et al. and validated and tested for reliability in 1997. K-SADS is a semi-structured interview, scanning for many psychiatric disorders except learning disorders, ASDs and schizophrenia with negative symptoms. The validity and reliability study in Turkey was carried out by Gökler et al.[16] in 2004. K-SADS was used to evaluate the psychopathology of the participants in our study.

Wechsler Intelligence Scale for Children-Revised (WISC-R): The Wechsler Intelligence Scale for Children (WISC) was developed by David Wechsler in 1949 for the evaluation of intelligence in children aged 6-16 years. With the standardization in 1974, the scale named as WISC-R (Revised Version) was adapted to Turkish culture.[17] In our study, intelligence quotient (IQ) assessments were made by using 3 subtests of the Wechsler Intelligence Scale for Children-Revised (Information, vocabulary, picture completion).

Behavioral Rating Inventory of Executive Functions (BRIEF): Behavioral Rating Inventory of Executive Functions (BRIEF) is a measurement tool that enables the assessment of executive functioning in the home and school environments of children and adolescents aged 5-18 years. The scale was developed by Gerard A. Gioia, Peter K. Isquith, Steven C. Guy, and Lauren Kenworthy in 2000. BRIEF consists of 2 forms: parent and teacher. In both forms, there are 86 expressions indicating a certain behavior. Items are evaluated with a 3-point Likert type scale. BRIEF consists of 8 sub-scales to measure different areas of the executive functions: inhibition, set-shifting, emotional control, initiation, working memory, planning/organization, organization of materials, and monitoring. The initiation (INI), working memory (WM), planning/organization (P/O), organization of materials (OofM) and monitoring (MON) scales are determined as Metacognitive Index (MCI). Inhibition, shift (SHIFT), and emotional control (EC) sub-scales are combined to form the Behavioral Regulation Index (BRI). A Global Composite Index (GCI) represents the sum of all sub-scale scores. High scores indicate the severity of deterioration in executive functions.[18] In our study, we used the parent form. Validity and reliability study of the BRIEF in the Turkish sample was carried out in 2011.[19]

Social Responsiveness Scale (SRS): The SRS scale used for evaluating social reciprocity was developed by Constantino in 2000. Validity and reliability were determined also by Constantino et al in 2003. It is useful for distinguishing the presence of autism from other child psychiatric conditions by identifying the type of social impairment that is characteristic of autism spectrum conditions in children as young as 4 years of age. It is a 65-item scale that describes a child's behavior in the last 6 months by giving a score on the Likert type scale between 0 (not true) and 3 (almost always true). Higher total scores are indicative of more severe social impairment. Although reliability and validity study of this scale has not been conducted in Turkey, it was used in a study on school-age children with and without ADHD by Ünal et al. In that study, the value of internal consistency was reported to be 0.86 for the clinical population that filled the SRS.[20]

Childhood Autism Rating Scale (CARS): CARS scale is widely used for diagnosing autism and for rating the severity. Validity and Reliability Analysis of Turkish Version of Childhood Autism Rating Scale was conducted.[21]

Autism Spectrum Screening Questionnaire (ASSQ): The ASSQ scale is a tool used to assess social interaction and communication problems, repetitive behaviors, and related problems such as motor stiffness and motor and/or vocal tics in individuals with ASD. The ASSQ was developed by Ehlers et al. in Sweden, in 1999. Reliability and validity study has been conducted in Turkey by Köse et al. They reported that the highest sensitivity in distinguishing children and adolescents with ASD from health controls was obtained when the cut-off score was 16.[22] In our study, the groups were compared based on the mean and standard deviation values of the scores obtained from the ASSQ scale.

Statistical Analyses

The data were evaluated by using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM SPSS Corp.; Armonk, NY, USA). Descriptive statistics were shown as mean–standard deviation or frequency (%). A 95% confidence interval was used to assess the data. The chi-square test was applied to categorical variables when comparing gender and psychiatric diagnosis. One-way analysis of variance (ANOVA) was used while evaluating socioeconomic status (SES), means of age, WISC-R, BRIEF, SRS, and ASSQ scores. Although the educational level and working status of the parents were ordinal variables, they were accepted as dummy variables and evaluated as continuous variables in our study. The sum of the scores was expressed as SES. SES, verbal IQ, and gender variables were adjusted by 1-way analysis of covariance. The variables that might influence SRS scores in ASD and ADHD samples were evaluated using hierarchical linear regression analysis. Hierarchical linear regression was used to examine the measure's unique contribution to social responsiveness. For all analyses, statistical significance was set at $P < .05$.

RESULTS

Table 1 shows the mean and standard deviation values of age, IQ, SES, and the percentage values for the male sex ratio. All groups were similar in terms of age, total IQ, and performance IQ. The ASD group scored significantly lower than the control group in terms of verbal IQ. In the control group, SES scores were significantly lower than the ASD group. The rate of male gender was 86.5% in the patients with ADHD; 78.8% in the ASD patients, and 42.4% in controls ($P < .001$). In the control group, the number of boys and girls were close to each other, while the male/female ratio was high in the ADHD and ASD groups. The average score of the children and adolescents in the ASD group from the CARS scale was 30.18.

The rates of psychiatric comorbidity (>1 psychiatric diagnosis) in ADHD and ASD groups were 70.3% and 68.8%, respectively. Oppositional defiant disorder (ODD) (37.8%), separation anxiety disorder (SAD) (18.9%), specific phobia (16.1%), and tic disorder (13.5%) were the most frequent comorbid disorders in the ADHD group. ADHD (58.1%), specific phobia (16.1%), generalized anxiety disorder (GAD) (16.1%), ODD (12.9%), and separation anxiety disorder (SAD) (12.9%) were the leading comorbid disorders in the ASD group. When the ADHD and ASD groups were compared in terms of comorbid psychiatric disorders, it

Table 1. Sociodemographic features, and WISC-R sub-scores of the sample

	ADHD Group ($n = 37$)	ASD Group ($n = 33$)	Control Group ($n = 33$)	F	P
Mean±SD					
Age	125.62±22.7	133.51±33.9	120.27±28.9	1.781	.174
SES	9,81±2.1	10.87±2.6	9,33±2.5	3.275	**.042**
WISC-R total	103.32±13.4	96.27±19.1	106.15±13.0	2.651	.077
WISC-R verbal	98.31±15.6	90.55±20.7	107.39±14.6	6.452	**.002**
WISC-R performance	109.05±16.3	103.05±17.9	104.03±16.1	1.108	.335
%					
Gender (boy)	86.5	78.8	42.4		**<.001**

ASD: Autism spectrum disorder; ADHD: Attention deficit hyperactivity disorder; SES: socio-economic status; WISC-R: Wechsler Intelligence Scale for Children-Revised.

was determined that the ODD was significantly higher in the ADHD group ($P=.028$,) and there was no statistically significant difference between the 2 groups in terms of rates of other comorbid disorders.

To test the hypothesis that the groups would differ on measures of INH, SHIFT, EC, INI, WM, and P/O, OofM and MON scales of the parent BRIEF were compared using 1-way ANOVA with post hoc Tukey tests. Post-hoc analyses revealed that the control group was rated better compared to both clinical groups for all sub-scales of BRIEF. All sub-scale scores except EC differed statistically significantly among the groups. The ADHD group and ASD group were rated worse compared to the control group for the INH, SHIFT, INI, WM, P/O, and MON sub-scales but the difference between ADHD and ASD groups was not statistically significant. For the OofM scale, the ADHD group was rated higher compared to the control group. There was no statistically significant difference between ASD-ADHD groups and ADHD-control groups. The INI, WM, P/O, OofM, and MON sub-scale scores were grouped to determine the MCI. INH, SHIFT, and EC sub-scale scores indicated as the BRI. GCI is a total score of all the clinical scales. Patients with ADHD and ASD had significantly higher scores in MCI, BRI, and GCI compared to the controls. After adjusting for SES, verbal IQ score and gender were still significantly higher in the ASD and ADHD groups than in controls. ADHD

Table 2. Mean Values of BRIEF, SRS, and ASSQ Sub-scales and Index Scores

	ADHD Group (mean ± SD)	ASD Group (mean ± SD)	Control Group (mean ± SD)	*P* Unadjusted	*P* Adjusted[a]	Contrasts
BRIEF						
INH	29.21 ± 7.5	28.30 ± 5.8	19.51 ± 3.7	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
SHIFT	21.51 ± 5.3	23.03 ± 5.4	17.24 ± 3.8	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
EC	20.05 ± 4.8	20.93 ± 5.6	18.18 ± 3.8	.069	.151	ASD=ADHD=C
INI	17.00 ± 3.3	17.60 ± 3.2	13.30 ± 2.6	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
WM	24.67 ± 5.3	22.73 ± 4.9	16.78 ± 3.0	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
P/O	30.83 ± 7.1	29.16 ± 6.4	12.33 ± 2.4	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
OofM	16.62 ± 4.5	14.83 ± 5.1	12.33 ± 2.4	**<.001**	**.002**	ADHD > C ADHD=ASD ASD=C
MON	18.43 ± 4.2	17.70 ± 3.6	12.42 ± 2.8	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
BRI	71.32 ± 15.1	72.26 ± 14.7	54.93 ± 10.0	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
MCI	107.56 ± 21.4	102.03 ± 20.3	75.45 ± 11.7	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
GCI	178.35 ± 35.4	174.30 ± 32.4	130.36 ± 18.8	**<.001**	**<.001**	ASD > C ADHD > C ASD=ADHD
SRS	67.69 ± 20.4	88.13 ± 24.3	25.09 ± 17.8	**<.001**	**<.001**	ASD > C ASD > ADHD ADHD > C
ASSQ	6.47 ± 4.4	25.73 ± 11.2	4.21 ± 4.5	**<.001**	**<.001**	ASD > ADHD ASD > C ADHD=C

SRS, Social Responsiveness Scale; ASSQ, Autism Spectrum Screening Questionnaire; INH, Inhibition; SHIFT, shifting; EC, emotional control; INI, initiation; WM, working memory; P/O, planning/organization; OofM, organization of materials; MON, monitoring; MCI, Metacognitive Index; BRI, Behavioral Regulation Index; GCI, A Global Composite Index.
[a]Adjusted for SES, Verbal IQ, and gender.

and ASD groups were not statistically different regarding index scores (Table 2).

Mean SRS scores of the groups are shown in Table 2. According to the post hoc analyses, ASD patients received significantly higher scores compared to ADHD and control groups and ADHD patients also had significantly higher values compared to the controls (P < .001). These differences remained stable after controlling for SES, verbal IQ scores, and gender. A total score in the range 60-75 indicates clinically significant deficits in social reciprocal interaction, and a mild to moderate interference in everyday interactions. According to our results, in 61.1% (22) of the ADHD group, in 89.7% (26) of the ASD group, and in 12.8% (5) of the control group, SRS scores were ≥60.

Mean ASSQ scores of the groups are shown in Table 2. In ASD patients, ASSQ scores were statistically higher compared to the ADHD group and controls (P < .001), and this significant difference also remained after adjusting for SES, verbal IQ scores, and gender. There was no significant difference between ADHD and control groups in terms of ASSQ scores.

The variables that might influence SRS scores were evaluated in the ADHD and ASD groups by using hierarchical linear regression analysis. For the ASD group, gender and verbal IQ scores were entered as the first block when examining predictors of SRS scores, and the results indicated that gender and verbal IQ did not significantly predict SRS (explaining 22.3 % of the variance in SRS scores) (F=1.860, P=.195). After entry of the BRI and MCI variables at the second block, the total variance explained by the model as a whole was 89.7% (F=24.049, P < .001, R squared change=0.674.). In the final model, only the BRI value was statistically significant (P < .001) (Table 3).

For the ADHD group, gender and verbal IQ scores were entered as the first block, and these variables were not significant for predicting SRS (explaining 7.9% of the variance in SRS scores) (F=1.324, P=.281). The presence of ODD comorbidity was entered as the second block and the model was still not significant (explaining 12.6% of the variance in SRS scores) (F=1.447, P=.249). After entry of the BRI and MCI variables at the third block, the total variance explained by the model as a whole was 52.6 % (F=6.219, P < .001, R squared change=0.40). In the final model, only the BRI value was statistically significant (P=.003) (Table 3).

Table 3. Hierarchical Linear Regression Analysis for Variables Predicting Social Responsiveness in the ASD and ADHD Samples

	B	Std. Error	Beta	*P*	*R* square
ADHD					
Model 1					**0.079**
Gender	−14.844	10.31	−0.252	.160	
Verbal IQ score	0.116	0.22	0.089	.614	
Model 2					**0.126**
Gender	−11.070	10.62	−0.188	.306	
Verbal IQ score	0.084	0.22	0.064	.715	
ODD comorbidity	5.144	4.02	0.230	.211	
Model 3					**0.526**
Gender	−5.553	8.19	−0.094	.503	
Verbal IQ score	0.068	0.173	0.052	.696	
ODD comorbidity	−0.267	3.27	−0.012	.936	
BRI	1.090	0.333	0.808	*.003*	
MCI	−0.137	0.22	−0.143	.547	
ASD					
Model 1					**0.223**
Gender	28.429	14.99	0.490	0.080	
Verbal IQ score	−0.326	0.341	−0.247	0.357	
Model 2					**0.897**
Gender	21.346	6.54	0.368	.008	
Verbal IQ score	−0.201	0.13	−0.152	.167	
BRI	1.500	0.24	0.890	*<.001*	
MCI	−0.110	0.20	−0.083	.609	

B, unstandardized B; ODD, Oppositional Defiant Disorder; BRI, Behavioral Regulation Index; MCI, Metacognitive Index.

DISCUSSION

In the present study, children and adolescents aged 6-17 years who were recently diagnosed with ASD or ADHD and healthy controls were compared in terms of executive functions and social reciprocity by using BRIEF and SRS.

Our results demonstrated that ASD and ADHD groups were significantly impaired for all BRIEF sub-scales except emotional control and that the significant increase in sub-scale scores expressing deterioration continued after adjustment for SES, verbal IQ scores, and gender. Executive dysfunction is a common finding of ADHD and ASD. However, if an executive function profile that distinguishes the 2 disorders is identified, it may be regarded as a possible endophenotypic marker for the diagnosis.[23] The results of previous studies, examining the executive functions of individuals with different neurodevelopmental psychiatric disorders including ASD and ADHD, revealed a more general and severe deterioration in executive function domains in individuals with ASD[6,7] and that executive dysfunction profiles differ between disease groups. Patients with autism frequently demonstrated pronounced impairment in flexibility and planning while ADHD patients had significant difficulties with inhibitory function.[6,24] On the other hand, in a study conducted by Clikeman et al. in 2010, no significant difference was found between children and adolescents with ADHD and AS, either in terms of the inhibition subtest of BRIEF or planning and working memory functions.[25] In the study of Corbett et al., which examined executive functions in individuals with ASD, ADHD, and

healthy control group, it was revealed that ASD patients showed more deterioration in many areas. Similar to our study, the majority of individuals with ASD were more impaired than other groups in all domains, including the area of inhibition that has been shown to be associated with ADHD.[7] The fact that the BRIEF scores of children and adolescents with ASD and ADHD did not show a statistically significant difference from each other according to our results may be due to the mild severity of ASD cases in our study. Executive function problems in mildly severe autism may not be different from children with ADHD and that executive functions may be related to ADHD symptoms rather than autism symptoms.

Another finding of our study was that ASD patients showed more pronounced impairment in social reciprocity compared to both the ADHD group and controls. Meanwhile, ADHD patients were statistically more impaired in social reciprocity compared to the controls. In order to better understand the underlying mechanism in both disorders, it is important to examine autistic features in children with ADHD.[26] In several previous studies which were conducted using SRS and the Autism Criteria Checklist, the results revealed that a significant number of children with ADHD showed social difficulties that might qualitatively resemble autistic traits.[26,27] Additionally, when interventions targeting executive dysfunction were implemented, improvements in social skills have been shown[28]. Several studies indicated that children with ADHD, especially those with impaired social skills, were more likely to have oppositional behaviors and experience conflict with family members and peers. The results of a study using SRS revealed that in a subgroup of ADHD with autistic symptoms, oppositional behaviors were significantly higher.[26] Similarly, in our study, ODD was significantly more frequent in the ADHD group compared to other groups. However, according to the results of the regression analysis, it was revealed that ODD comorbidity did not predict social reciprocity in the ADHD sample.

The relationship between executive dysfunction and social skills has been discussed in recent years. Baez et al. compared children with typical development and children with ASD in terms of executive functions, and they found that social skills were also impaired in children with impaired executive functions from different diagnoses[29]. In a study evaluating the relationship between theory of mind skills, which is an indicator related to social cognition, and executive functions using BRIEF, it was found that children with HFA had impairments related to metacognitive processes (initiation, planning) while children with ADHD had more problems with behavioral regulation skills (inhibition, emotional control).[30] In another study conducted with children with ASD, the cognitive flexibility sub-score explained 11.5% of the variance in communication skills of the sample and it remained significant even after controlling for the ADHD symptoms.[9] Our results also share similarities with Bednarz et al.'s findings that behavioral regulation function contributed to social impairment in children with ASD.[11] Hutchisson et al., in their study where executive functions and communication skills were evaluated by a questionnaire, reported that the BRIEF metacognition subscale was a strong predictor of communication skills while the behavioral regulation subscale was related to verbal conversation[10]. On the other hand, the results of 2 adult studies, in which executive functions associated with social skills were evaluated with cognitive tests, showed that the cause of the social impairment was independent of executive functions; rather it was associated with comorbid conditions.[31,32] However, they must be interpreted with caution since such contradictory findings might be related to the improvement of deficiencies during normal developmental trajectory into adulthood.

There were several limitations of the present study. The relatively small sample size, the absence of the full scale of WISC-R, and the lack of assessment of the severity of ADHD cases were among the limitations of our study. Another limitation was the heterogeneity of patients in the ASD group. Although the majority of the ASD group consisted of patients with AS, high-functioning autism patients were also included. The evaluation of executive functions and social responsiveness by using parental report scales instead of cognitive tests could be regarded as a limitation since it was an indirect measure; on the other hand, administration of the scales was easier and provided a practical evaluation. Besides these limitations, we should emphasize that the strength of the present study was that the participants in the ADHD group were drug-naive individuals; therefore we could control the medication effect on the social skills, an improvement could be expected by treatment since it has been stated that social skills improve after medication.[33]

Elucidating the impairments in executive functions and social skills will enable clinicians to implement new interventions and eventually may provide an improvement in the daily life functioning of the patients. Therefore, further studies, with larger sample sizes, using standardized cognitive tests besides parental report scales should be undertaken.

Ethics Committee Approval: Ethical committee approval was received from the Marmara University School of Medicine (Date: April 07/2017; Number: 09.2017.318).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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