

Autistic Traits and Factors Related to a Clinical Decision to Use Risperidone in Children with Attention Deficit Hyperactivity Disorder

Aysegül Selcen Guler¹, Yanki Yazgan², Ayca Uslu Pelin¹

ÖZET:

Dikkat eksikliği hiperaktivite bozukluğu olan çocuklarda otizm spektrumuna özgü özellikler ve risperidon kullanım kararını belirleyen faktörler

Amaç: Çalışmanın amacı, ana tanısı dikkat eksikliği hiperaktivite bozukluğu (DEHB) olan çocuk ve ergenlerde risperidon kullanma kararını belirleyen faktörleri, DEHB'de otizme özgü özellikleri (OO) ve bu özelliklerin tedavi tercihi üzerindeki etkilerini araştırmaktır.

Yöntem: Özel bir çocuk-ergen psikiyatrisi kliniğinde takip edilmekte olan, aldıkları tedaviye göre dört gruba ayrılan DEHB tanılı çocuklar geriye dönük olarak karşılaştırıldı (ilaçsız tedavi, İT (n=73, ortalama yaş=9.22±2.94 yıl), sadece stimulan, S (n=184, ortalama yaş=10.52±2.98 yıl), sadece risperidon R (n=51, ortalama yaş=10.18±3.52 yıl), ve stimulan ve risperidon, SR (n=30, ortalama yaş=9.37±2.71 yıl)). Yarı yapılandırılmış klinik görüşmeye ek olarak, ilk değerlendirmede, ebeveyn tarafından bir sosyodemografik form, Çocuklar için Davranış Değerlendirme Ölçeği-6-18 (ÇDDÖ-6-18) ve SNAP-IV (Swanson, Nolan and Pelham), öğretmen tarafından ise SNAP-IV ölçeklerinin doldurulması istendi.

Bulgular: ÇDDÖ toplam puanı, dışallaştırıcı problemler, sosyal problemler, düşünce problemleri, dikkat problemleri ve agresyon ölçekleri T skorlarında (bütün p'ler < 0.05) ve ebeveyn tarafından doldurulan SNAP dikkat eksikliği ve toplam puanlarında gruplar arası anlamlı fark bulundu (tek yönlü ANOVA analizi). SR grubunun (i) CBCL'in sözü geçen alt ölçeklerinin puanı, İT ve S gruplarından yüksekti, (ii) CBCL sosyal problemler alt ölçeği puanları R grubundan yüksekti, (iii) ebeveyn tarafından doldurulan SNAP dikkat eksikliği alt ölçeği puanları İT ve R gruplarından yüksekti (iv) ebeveyn tarafından doldurulan SNAP toplam puanı diğer üç gruptan yüksekti (Tukey post hoc testi). CBCL-OÖ eşliğinin üzerindeki 64 çocuğun ebeveyn ve öğretmen tarafından derecelendirilen DEHB belirti şiddetleri, CBCL-OÖ eşliğinin altında olanlardan daha yüksekti. Lojistik regresyon analizinde hekimin risperidon içeren bir tedaviyi (tek başına veya stimulanla birlikte) tercih etmesi CBCL sosyal problemler (p=0.025) ve düşünce problemleri (p=0.039) alt ölçekleri ile ilişkili bulundu. Kategorik olarak otistik özelliklerin bulunması tedavi tercihiyle ilişkilendirilemedi.

Sonuç: Bu klinik örnekte, ÇDDÖ ebeveyn bildirimindeki sosyal problemler ve düşünce problemlerinin, DEHB tanısı olan çocuklarda, hekimin tedavi için risperidon kullanma kararıyla ilişkili olduğu görülmektedir. Çalışmamızın sınırları içinde, otistik özellikleri olan çocuklarda DEHB belirtilerinin daha şiddetli olduğu ve bu çocuklarda daha fazla öğrenme güçlüğü olduğu, ancak otistik özelliklerin, bir kategori olarak alındığında, risperidon kullanımı ile ilişkili olmadığı anlaşılmaktadır. DEHB'li çocuklarda DEHB dışı belirtilerin ayrıntısıyla tanımlanması (sosyal ya da emosyonel belirtiler vb.), sosyal gelişimi destekleme yaklaşımları gibi, bireyselleştirilmiş klinik müdahalelerin geliştirilmesini sağlayarak, aynı belirtileri düzeltme amaçlı, doğrudan DEHB'ye dönük olmayan, ilaçlara daha az başvurulmasını sağlayabilir.

Anahtar sözcükler: Dikkat eksikliği hiperaktivite bozukluğu, risperidon, otistik özellikler, çocuklar

ABSTRACT:

Autistic traits and factors related to a clinical decision to use risperidone in children with attention deficit hyperactivity disorder

Objective: Our aim was to investigate the factors associated with a clinical decision to use risperidone in children and adolescents with a primary diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) and to investigate autistic traits (ATs) and their influence on treatment decisions in this population

Methods: We retrospectively compared four treatment groups of children with a primary diagnosis of ADHD [no psychotropics group, NPG (n=73, mean age (in years)= 9.22±2.94); stimulant-only, S (n=184, mean age (in years)= 10.52±2.98); risperidone-only, R (n=51, mean age (in years)= 10.18±3.52); and stimulant plus risperidone, SR (n=30, mean age (in years)= 9.37±2.71)] from a private child and adolescent psychiatry clinic. Baseline assessments, in addition to a semistructured interview, included a sociodemographic information form, the parent-rated Child Behavior Checklist for ages 6 to 18 (CBCL-6-18) and the parent and teacher-rated SNAP-IV scale (Swanson, Nolan and Pelham).

Results: There were significant between-group differences on CBCL T scores for total problems, externalizing problems, social problems, thought problems, attention problems, and aggression (all p<0.05) and on the parent SNAP inattention and combined scores (one-way ANOVA). The SR group had significantly higher scores (i) on the mentioned subscales of the CBCL when compared with the NPG and S groups, (ii) on the CBCL social problems subscale when compared with the R group, (iii) on the parent SNAP inattention scale when compared with the NPG and R groups and (iv) on the parent-rated SNAP total score when compared with the other 3 groups (Tukey post hoc test). Sixty-four children above the CBCL-AT cutoff had higher scores than those of children below the cutoff on parent and teacher-rated individual ADHD symptoms. In the logistic regression analysis, the clinician's decision to use risperidone (either alone or in combination with stimulants) was significantly related to higher scores on the CBCL social problems (p=0.025) and thought problems (p=0.039) subscales. The presence of AT as a category, however, did not predict treatment assignment.

Conclusion: In this clinical sample, parent-rated social problems and thought problems were associated with the clinician's decision to use risperidone in the treatment of ADHD cases (alone or in combination with stimulants). ADHD children with AT had more severe symptoms of ADHD and displayed more learning disability. However, AT profile as a category was not significantly associated with the use of risperidone. The better characterization of non-ADHD symptoms of ADHD children (social and emotional symptoms) may help to develop more individualized clinical interventions, such as nonpharmacological interventions for social development, which may result in a reduction in the use of medications targeting these symptoms in this group of children.

Keywords: Attention deficit hyperactivity disorder, risperidone, autistic traits, children



Poster presentation of the findings of this study received the best poster award at the 2nd Asian Congress on ADHD held in March 8-9, 2014, in Tokyo, Japan

¹M.D., ²M.D., Professor, Güzel Günlü Health Services, Istanbul - Turkey

Corresponding author:

Aysegül Selcen Güler,
Murat Reis Mah., Murat Reis Sok.,
Soyak Sitesi B-15/3, 34664, Üsküdar,
Istanbul - Türkiye

E-mail address:

selcenguler@yahoo.com

Date of submission:

March 05, 2014

Date of acceptance:

June 16, 2014

Declaration of interest:

A.S.G., Y.Y., A.U.P.: The authors reported no conflict of interest related to this article.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder with childhood onset that is associated with short- and long-term disability¹. Compared to the general population, children with ADHD are at higher risk for academic difficulties, substance abuse, head injury, arrest and occupational problems, and are more likely to have other psychiatric problems^{2,3,4}.

The efficacy of risperidone is well established in psychotic illness, both in adults and children^{5,6}. It has been reported to be effective in various non-psychotic conditions in children, such as mood and behavioral problems⁷, autism⁸, Tourette's syndrome⁹ and conduct disorder¹⁰. Risperidone use in a case series of bipolar disorder patients resulted in improvement in attention deficit hyperactivity disorder (ADHD) symptoms in patients with comorbid ADHD¹¹. Stimulants are the treatment of first choice for a primary diagnosis of ADHD, but risperidone has a place in the management of children with ADHD, particularly when there are comorbid disruptive behavior disorders and when children have subaverage IQ^{12,13}. The first favorable results with risperidone were from its augmentative effect in addition to stimulants in ADHD¹⁴. Several studies have shown that risperidone is associated with significant behavioral improvements in this population, both as a sole agent and in addition to other drugs¹⁴. Apart from the presence of comorbid disruptive behavior, the factors influencing the clinical decision to use risperidone in children with ADHD are not well studied.

Recent studies have identified that autistic traits (ATs) appeared in 20 % to 30 % of children with ADHD^{15,16,17}, which has been shown to share rare copy number variants with autism spectrum disorders (ASD)¹⁸. These children are generally more impaired than other children with ADHD, particularly in the domains of social functioning and communication. In a recent study, autistic traits have been found to be more prevalent in children with ADHD compared to those without

ADHD and ADHD children with autistic traits have been found to be more impaired in psychopathology, social relatedness, school and family functioning¹⁸. Risperidone was effective for symptoms of irritability in ASD¹⁹, and social disability in ASD was reported to benefit from risperidone²⁰.

However, there are also reports of and concern about the increased use of risperidone and other second-generation antipsychotics in children and adolescents. As a step in addressing these concerns, we aimed to document naturalistically in a 'treatment as usual' modality, the factors associated with use of risperidone in a common childhood psychiatric problem such as ADHD. The answer to this question may also guide us in identifying the symptoms that may be targeted by non-pharmacological methods such as parent management training or approaches to enhance social-emotional or cognitive competence.

The primary purpose of this study was to investigate the factors associated with a clinical decision to use risperidone in children and adolescents with a primary diagnosis of ADHD, in a clinical sample, in Istanbul, Turkey. The secondary aim was to examine the "autistic trait" profile in this clinical sample without an ASD diagnosis and its association with the treatment choice of risperidone.

METHODS

Participants

Four treatment groups of children with a primary diagnosis of ADHD [no psychotropics group, NPG; stimulant-only, S; risperidone-only R and stimulant plus risperidone, SR] from a private child and adolescent psychiatry clinic, who were in clinical follow-up, were compared. This private clinic serves a population with medium to high parental education and socioeconomic status. The most common reasons for referral were neurodevelopmental and neuropsychiatric disorders, such as ADHD, autism spectrum disorders (ASDs), learning disorders (LD), tic

disorders, obsessive compulsive disorder (OCD), depression and various anxiety disorders.

The study design was retrospective. The children received “treatment as usual”. Assessment forms and rating scales were completed at the time of the first visit, before this study was planned. The dataset used in statistical analysis did not contain any identifiers (name, date of birth etc.) about the subjects. Since autistic traits in ADHD were sought, children with co-occurring ASD (having autistic symptoms enough to fulfill a diagnosis of ASD) were excluded from the study sample. As stated in the introduction section above, risperidone use has been usually preferred in ADHD children with co-occurring disruptive behavior disorders (conduct disorder, oppositional defiant disorder) and mental retardation. None of the children in this sample had comorbid conduct disorder, mood disorder or mental retardation, allowing evaluation of other reasons underlying the treatment decision. Among 338 children with a primary diagnosis of ADHD, 184 children received only a stimulant medication, 51 only risperidone, 30 stimulant-plus-risperidone and 73 children received no psychopharmacologic intervention.

Measures

Baseline assessments in addition to a semi-structured interview included;

Sociodemographic Form: This parent-rated form was developed by the clinician and included the child’s birthdate, gender, handedness, number of siblings and birth order, and the parents’ current ages, level of education, current occupation and marital status. The form also asked about the child’s medical history, developmental history and past mental health interventions.

Child Behavior Checklist for ages 6-18 (CBCL 6-18)²¹: This parent-rated instrument measures competencies and behaviors of children and adolescents aged 6 to 18. Behaviors in the past 6

months are rated on a scale from 0 (never true) to 2 (almost always true) and items are grouped under several subscales. Two behavior scores are obtained from the scale: Internalizing and Externalizing behavior scores. Withdrawal, somatic complaints and anxiety/depression scores form the internalizing behavior scale and conduct behavior and aggression subscales form the externalizing behavior scale. There are other subscales assessing social problems, attention problems and thought problems. Scores of the entire subscales are summed up to form “total problem” score. Measurement structure of the Turkish version of the CBCL-6-18 has been reported by Dümenci et al.²²

SNAP IV²³: The SNAP is an 18-item scale derived from DSM-IV criteria for ADHD that may be completed by parents or teachers. Each item is rated from 0 to 3, where 0= not at all; 1= just a little, 2= quite a bit, 3= very much. There are nine items for inattention and nine items for hyperactivity/impulsivity. The SNAP has been used as an outcome measure in clinical trials²⁴ and in community surveys to identify children with probable ADHD²³. It has solid psychometric properties with coefficient alpha values on parent ratings of 0.94 for the total score, 0.90 and 0.79 for inattention and hyperactivity scores, respectively; the alpha coefficients for teacher ratings are 0.97, 0.96, and 0.92 for total, inattention and hyperactivity scales, respectively²³. DSM-IV-based ADHD rating scales, like SNAP-IV, are widely used in child and adolescent psychiatry practice in Turkey. A Turkish validation study has not yet been published; however, the scale has been used in a recently published large community survey from Turkey²⁵ in which per item mean thresholds for 1.5 SD were similar to those obtained in the US survey²³. In the current study, the SNAP was completed by parents and teachers.

Statistical Analysis

Statistical analyses of the data were conducted by SPSS 16.0. For comparison of categorical

variables Pearson's χ^2 test and for continuous variables the Student-t test and one-way ANOVA were used. The Tukey test was used for post hoc analysis. To define autistic traits (AT), an empirically derived profile from the Child Behavior Checklist (CBCL), using a cutoff of 195 from the combined T scores of the withdrawal, social problems and the thought problems subscales, was used. This profile was reported to correctly classify 78% of all subjects with ASD from a psychiatrically referred sample with and without ASD²⁶ and has been used in a recent study by Kotte and colleagues¹⁸.

Multivariate logistic regression analysis was conducted by taking risperidone-including treatments versus other treatments as dependent variable and sex, age, CBCL subscales, parent and teacher-rated SNAP scores and CBCL-AT as predictor variables. All tests were two tailed and significance was set at 0.05.

RESULTS

This clinical sample had a total ADHD population of 338 children, after exclusion of cases with comorbid ASD. Table 1 shows the demographic characteristics of the sample.

There were no differences between treatment groups in terms of co-occurring tic disorders, anxiety disorders and oppositional defiant disorder (in the total sample; 34 children had tics, 5 had ODD, 93 had an anxiety disorder). Children receiving risperidone as a sole agent had more comorbid obsessive compulsive disorder (OCD) than those in other treatment groups (31.4% of children in risperidone-only group versus 16.7% of children in stimulant plus risperidone versus 15.2% of children in stimulant-only versus 9.6% of children without pharmacotherapy; $p=0.012$). Children receiving a risperidone-including treatment (as a sole agent or as augmentation) had more developmental coordination disorder (DCD) than those in other groups (19.8% of children in risperidone-including treatments versus 6% of children in stimulant-only group versus 15% of children

Table 1: Characteristics of 338 children (mean age= 10.08±3.07; range 6 -18 yr) from a private clinic in Istanbul, Turkey

	n (%)
Gender	
Male	268 (79.3%)
Female	70 (20.7%)
Age (years)	
6 – 8	138 (40.8%)
9 – 11	102 (30.2%)
12 – 14	59 (17.5%)
15 – 18	39 (11.5%)
Language development^a (parent-rated)	
Poor	33 (9.8%)
Fair	61 (18%)
Very well	171 (50.6%)
Fine motor development^b (parent-rated)	
Poor	62 (18.3%)
Fair	105 (31.1%)
Very well	99 (29.3%)
Parent's Marital status^c	
Living together	236 (69.8%)
Separated	18 (5.3%)
Treatment	
No psychotropics group	73 (21.6%)
Stimulant-only	184 (54.4%)
Risperidone-only	51 (15.1%)
Stimulant + Risperidone	30 (8.9%)

^adue to missing data n=265, ^bn=266, ^cn=254

without pharmacotherapy; $p=0.002$).

Table 2 presents the distribution of parent CBCL and SNAP as well as teacher SNAP scores by treatment group. A one-way ANOVA indicated significant between-group differences on CBCL T scores for total problems, externalizing problems, social problems, thought problems, attention problems and aggression (all $p<0.05$) and on parent SNAP, inattention and combined scores. The SR group had significantly higher scores (i) on the mentioned subscales of the CBCL compared with the NPG and S groups, (ii) on the CBCL social problems subscale compared with the R group, (iii) on the parent SNAP inattention scale compared with the NPG and R groups and (iv) on the parent-rated SNAP total score compared with the other 3 groups (Tukey post hoc test).

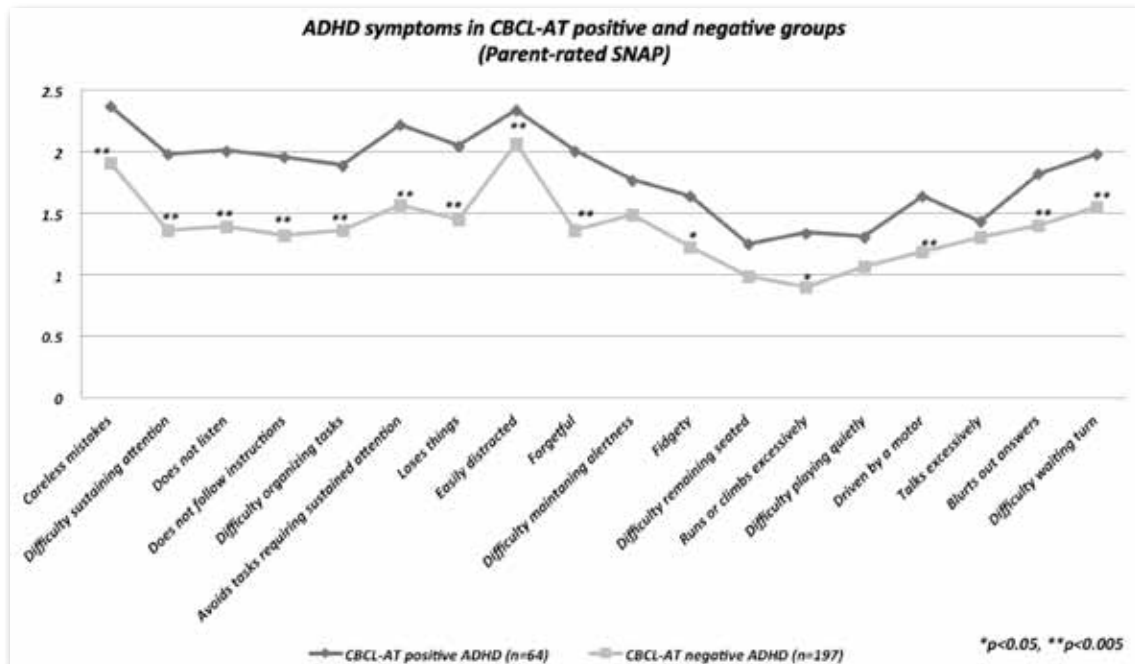
Figures 1 and 2 represent the distribution of ADHD symptoms in CBCL-AT positive and negative ADHD subjects, respectively.

As seen in the figures, scores on individual

Table 2: Comparison of parent CBCL and SNAP IV and teacher SNAP-IV scores for children age 6 to 18 years by treatment group (n=338)

	TREATMENT GROUPS				p*
	No psychotropics group	Stimulant-only	Risperidone-only	Stimulant + Risperidone	
	(n=73)	(n=184)	(n=51)	(n=30)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
CBCL					
total score	58.24±11.52	60.85±10.30	63.57±8.15	66.88±8.27	0.002
internalizing	55.75±11.24	58.23±11.23	58.90±12.10	60.16±9.24	0.318
externalizing	56.28±10.68	56.79±12.35	60.75±11.43	64.64±9.20	0.005
withdrawal	57.21±8.79	59.05±9.62	57.72±8.50	58.76±8.95	0.596
somatic	55.64±7.45	56.71±7.84	57.35±7.20	54.28±6.34	0.335
anxious	57.75±8.55	59.72±9.23	61.72±9.05	62.16±9.50	0.098
social problems	56.94±8.00	59.05±10.42	59.00±7.60	66.16±12.13	0.002
thought problems	59.42±9.23	60.83±9.22	62.50±9.48	66.32±8.98	0.014
attention problems	60.26±8.68	65.42±8.89	64.25±8.66	70.64±10.03	<0.001
delinquency	57.80±8.19	57.78±7.95	61.42±9.15	62.00±9.56	0.016
aggression	58.22±7.69	59.69±9.31	63.60±11.46	66.04±9.92	0.001
sexual problems	55.92±9.32	57.09±9.56	58.79±9.27	54.84±7.42	0.494
P-SNAP-inattention	12.17±5.19	16.09±5.91	13.48±5.87	18.85±6.35	<0.001
P-SNAP-HA	11.26±6.21	11.15±6.98	12.19±7.50	15.73±7.13	0.058
P-SNAP-total	23.55±9.74	27.30±11.17	26.13±11.02	34.73±12.72	0.003
T-SNAP-inattention	18.85±6.64	21.00±5.43	17.88±5.27	20.80±5.40	0.466
T-SNAP-HA	22.71±5.28	13.89±10.46	14.00±5.49	19.66±5.71	0.074
T-SNAP-total	41.57±10.78	34.77±13.39	33.00±7.79	39.60±8.67	0.419

*One-way ANOVA, Abbreviations: CBCL: Child Behavior Checklist (T scores were used), P-SNAP: Parent-rated SNAP, T-SNAP: Teacher-rated SNAP

**Figure 1: Parent-rated ADHD symptoms in the ADHD and ADHD + CBCL-AT groups**

ADHD symptoms rated on the SNAP-IV are higher for CBCL-AT positive ADHD subjects for both parents and teachers. Differences were significant for 14 out of 18 symptoms on the

parent-rated SNAP and 2 out of 18 on the teacher-rated SNAP.

There was no significant difference between treatment groups according to AT profile.

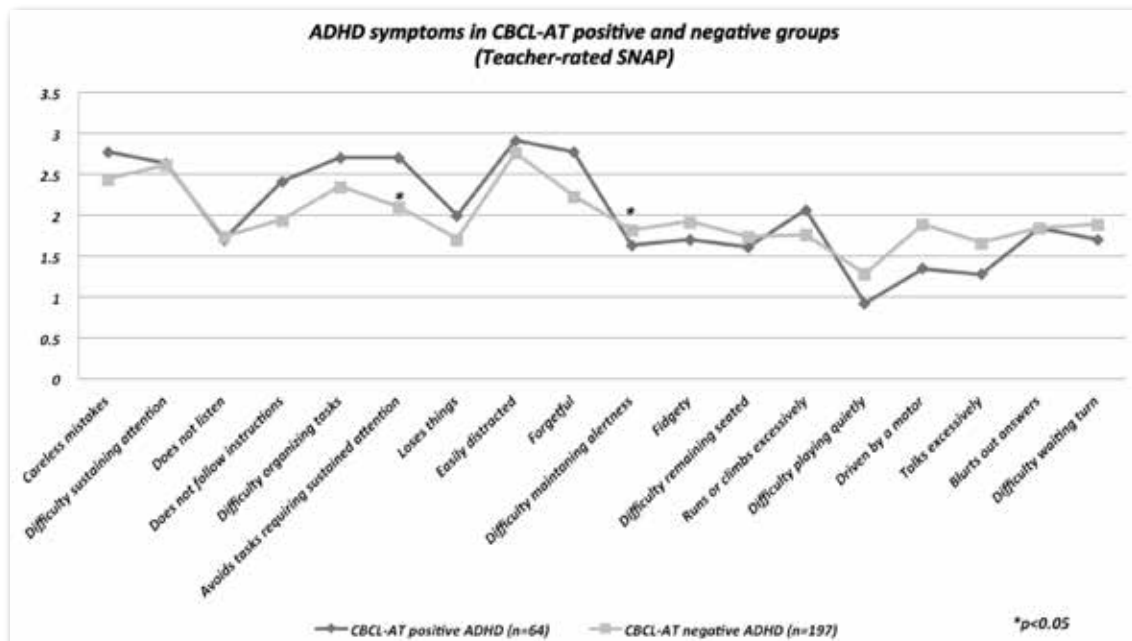


Figure 2: Teacher-rated ADHD symptoms in the ADHD and ADHD + CBCL-AT groups

Table 3: Predictors of the use of risperidone in the treatment plan of children with ADHD (multivariate logistic regression analysis)

Predictors	Exp(B)	95% CI	p
sex	0.406	[0.10-1.56]	0.19
age	1.035	[0.82-1.30]	0.76
CBCL total	0.903	[0.71-1.13]	0.38
CBCL internalizing	1.142	[0.93-1.39]	0.18
CBCL externalizing	1.096	[0.87-1.37]	0.42
CBCL withdrawal	0.937	[0.84-1.03]	0.21
CBCL somatic	0.944	[0.86-1.03]	0.22
CBCL anxious	0.919	[0.79-1.06]	0.25
CBCL social problems	1.120	[1.01-1.23]	0.025*
CBCL thought problems	1.095	[1.0-1.19]	0.039*
CBCL attention problems	0.943	[0.84-1.05]	0.29
CBCL delinquency	0.969	[0.88-1.06]	0.50
CBCL aggression	0.999	[0.85-1.16]	0.99
CBCL sexual problems	1.019	[0.96-1.08]	0.52
P-SNAP inattention	0.957	[0.85-1.06]	0.43
P-SNAP hyperactivity	1.030	[0.92-1.14]	0.57
CBCL-AT	1.322	[0.24-7.19]	0.74
Constant	0.013		0.36

*p<0.05 for CBCL social and thought problems. Dependent variable: Treatment plan including risperidone (alone or in combination with stimulants)= 1, treatment plan not including risperidone (no psychotropics or stimulants alone)= 0

Compared with ADHD participants, ADHD + CBCL-AT participants had a significantly higher prevalence of learning disorder (OR:3.4, 95% CI [1,90-6,16]). ADHD participants with ATs had significantly more impaired scores on each of the CBCL clinical and composite scales, including scales that were not used to define ATs, compared

with ADHD children without ATs (all $p<0.001$).

In the logistic regression analysis, the clinician's decision to use risperidone (either alone or in combination with stimulants) was significantly related to the CBCL social problems ($p=0.025$) and thought problems ($p=0.039$) subscales (Table 3).

DISCUSSION

In this retrospective clinical chart review, we found that the use of risperidone in ADHD children was not uncommon in a 'treatment as usual' setting, and that the children who were placed on risperidone, especially as an add-on to stimulants, had more severe ADHD symptoms (higher scores on the SNAP) and higher scores on several subscales of the CBCL. This finding is consistent with previous findings reporting administration of risperidone to ADHD subjects with more severe symptoms¹⁴.

In this clinical sample of children with ADHD, parent-rated scores of social and thought problems on the CBCL seem to predict the clinician's decision to use risperidone (alone or in combination with stimulants). The social problems scale of the CBCL is a broad-based behavioral measure and includes acting young, being clingy, not getting along with peers, clumsiness and preferring to play with younger children. Clumsiness and problems in peer relations are commonly reported in children with ADHD as well as ASD²⁷. In a recent study of ADHD children without an ASD diagnosis, two latent factors were created by factor analysis of the CBCL social problems subscale: peer rejection factor and the social immaturity factor. Both factors were found to be associated with the ASD risk, but social immaturity factor (formed by the items: clumsiness, being clingy, acting young, preferring to play with younger children) had a stronger association²⁷. Since there were children with DCD in our sample who were more likely to receive a risperidone-including pharmacotherapy and since 'ADHD- plus-DCD' has been reported to be associated with autistic features²⁸, a question emerged as to whether DCD might better account for the CBCL-ATs. The CBCL social problems subscale with its social immaturity factor, including clumsiness, could be related to DCD. However, ADHD children with an AT profile did not have significantly more comorbid diagnosis of DCD.

Thought problems, as rated on the CBCL, include seeing or hearing things, repeating acts

and strange ideas and behavior and have been associated with OCD²⁹, multiple complex developmental disorder³⁰ and fragile X syndrome³¹. Since there were significantly more children with OCD in the risperidone-only group and more children with DCD in the risperidone-including groups, the CBCL thought problems scores as a predictor of risperidone use might also be explained by the presence of categorical diagnoses of OCD and DCD. In a recent twin study of 7 year-olds investigating genetic influences on thought problems, CBCL thought problems were found to have a skewed distribution (the majority of subjects have few or no symptoms) with a strong heritability, which suggests that this scale measures a true syndrome³².

Sixty-four children with ADHD were above the CBCL-AT cutoff. These children were not diagnosable with ASD. All of the parent-rated and most of the teacher-rated individual ADHD symptom scores of children with ATs were higher than the children without an AT profile. The finding of more severe ADHD symptoms in children with ATs is consistent with a recent study investigating autistic traits in children with and without ADHD and comparing ADHD children with and without ATs¹⁸. Although the presence of a 'positive' CBCL-AT profile does not seem to predict risperidone-including pharmacotherapy use, two of the three components of the CBCL-AT profile (CBCL thought and social problems) seem to be associated with the clinical decision to use risperidone.

In our sample, ADHD children with ATs had significantly more learning disability, which is also consistent with previous findings reporting that children with both ADHD and a learning disability have greater difficulties in peer relations than children with only a learning disability³³.

Our findings need to be viewed in light of some limitations. Firstly, this study is based on retrospective data collected from a clinical sample. As such, the data reflect treatment as usual and cannot be generalized to draw any conclusions as to whether this practice is appropriate or would reflect practice in other settings. Since the study design was retrospective, our results should be

interpreted in caution. Further studies with a prospective design are needed. Secondly, our sample did not contain a comparison group of children with a diagnosis of ASD. Such a group would be useful to determine the degree to which our ADHD + CBCL-AT group exhibits features that are similar to or different from ASD. However, because our primary diagnosis of interest was ADHD, the absence of an ASD control group does not preclude the finding that ADHD children with ATs exhibit more severe symptoms than those with ADHD-only. Thirdly, although autism was excluded, it was done by using subject history as opposed to validated measures such as the Autism Diagnostic Observation Schedule or Autism Diagnostic Interview, thus allowing for the possibility that some children with undiagnosed ASD could have been included in our sample. However, considering that the mean age of our sample at baseline was 10 years, it is not likely that children with a clear diagnosis of ASD would have remained undiagnosed. Finally, because our sample was a set of referred patients of a private clinic, our findings may not be generalized to community samples or other clinical samples.

References:

1. Thapar A, Cooper M, Eyre O, Langley K. Practitioner review: what have we learnt about the causes of ADHD. *J Child Psychol Psychiatry* 2013;54(1):3-16. [\[CrossRef\]](#)
2. Wilens T, Biederman J, Spencer TJ. Attention deficit hyperactivity disorder across the lifespan. *Annu Rev Med* 2002;53:113-31. [\[CrossRef\]](#)
3. Barkley RA, Fischer M, Smallish L, Fletcher K. The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *J Abnorm Child Psychol* 2002;111(2):279-89. [\[CrossRef\]](#)
4. Mannuzza S, Klein RG. Long-term prognosis in attention deficit hyperactivity disorder. *Child Adolesc Psychiatr Clin N Am* 2000;9(3):711-26.
5. Armenteros JL, Whitaker AH, Welikson M, Stedje DJ, Gorman J. Risperidone in adolescents with schizophrenia: an open pilot study. *J Am Acad Child Adolesc Psychiatry* 1997;36(5):694-700. [\[CrossRef\]](#)
6. Leucht S, Pitschel-Walz G, Abraham D, Kissling W. Efficacy and extrapyramidal side-effects of the new antipsychotics olanzapine, quetiapine, risperidone and sertindole compared to conventional antipsychotics and placebo. A meta-analysis of randomized controlled trials. *Schizophr Res* 1999;35(1):51-68. [\[CrossRef\]](#)
7. Schreier HA. Risperidone for young children with mood disorders and aggressive behaviour. *J Child Adolesc Psychopharmacol* 1998;8(1):49-59. [\[CrossRef\]](#)
8. McDougle CJ, Holmes JP, Bronson MR, Anderson GM, Volkmar FR, Price LH, et al. Risperidone treatment of children with pervasive developmental disorders: A prospective open-label study. *J Am Acad Child Adolesc Psychiatry* 1997;36(5):685-93. [\[CrossRef\]](#)
9. Lombroso PJ, Scahill L, King RA, Lynch KA, Chappell PB, Peterson BS, et al. Risperidone treatment of children and adults with chronic tic disorders: A preliminary report. *J Am Acad Child Adolesc Psychiatry* 1995;34(9):1147-52. [\[CrossRef\]](#)
10. Findling R, McNamara N, Branicky L, Schluchter MD, Lemon E, Blumer JL. A double-blind pilot study of risperidone in the treatment of conduct disorder. *J Am Acad Child Adolesc Psychiatry* 2000;39(4):509-16. [\[CrossRef\]](#)
11. Frazier J, Meyer M, Biederman J, Wozniak J, Wilens TE, Spencer TJ, et al. Risperidone treatment for juvenile bipolar disorder: A retrospective chart review. *J Am Acad Child Adolesc Psychiatry* 1999;38(8):960-5. [\[CrossRef\]](#)
12. Kewley GD. Risperidone in comorbid ADHD and ODD/CD. *J Am Acad Child Adolesc Psychiatry* 1999;38(11):1327-8. [\[CrossRef\]](#)

CONCLUSION

Despite significant limitations, this study shows that in this ADHD sample without comorbid ASD and ODD, risperidone was chosen as an initial treatment when there was comorbid OCD and as an augmentative agent when there was comorbid DCD. The CBCL social problems and thought problems subscales, regardless of the comorbid diagnosis, predicted use of risperidone. DCD might have an association with a factor of the social problems scale and thought problems scale and OCD might have a relation with the thought problems scale of the CBCL.

ADHD children with a CBCL-AT profile displayed more severe symptoms and had increased diagnoses of learning disability. The possibility of identifying subgroups of ADHD children based on their non-ADHD symptom characteristics that may not prompt an independent diagnosis, may help to develop more individualized clinical interventions, avoiding possibly unnecessary use of pharmacotherapy for problems that can be addressed by psychosocial and educational strategies.

13. Pandina GJ, Aman MG, Findling RL. Risperidone in the management of disruptive behavior disorders. *J Child Adolesc Psychopharmacol* 2006;16(4):379-92. [\[CrossRef\]](#)
14. Bramble DJ, Cosgrove PVF. Parental assessments of the efficacy of risperidone in attention deficit hyperactivity disorder. *Clin Child Psychol Psychiatry* 2002;7(2):225-33. [\[CrossRef\]](#)
15. Mulligan A, Anney RJ, O'Regan M, Chen W, Butler L, Fitzgerald M, et al. Autism symptoms in attention-deficit/hyperactivity disorder: a familial trait which correlates with conduct, oppositional defiant, language and motor disorders. *J Autism Dev Disord* 2009;39(2):197-209. [\[CrossRef\]](#)
16. Grzadzinski R, Di Martino A, Brady E, Mairena MA, O'Neale M, Petkova E, et al. Examining autistic traits in children with ADHD: does the autism spectrum extend to ADHD? *J Autism Dev Disord* 2011;41(9):1178-91. [\[CrossRef\]](#)
17. Kochhar P, Batty MJ, Liddle EB, Groom MJ, Scerif G, Liddle PF, et al. Autistic spectrum disorder traits in children with attention deficit hyperactivity disorder. *Child Care Health Dev* 2011;37(1):103-10. [\[CrossRef\]](#)
18. Kotte A, Joshi G, Fried R, Uchida M, Spencer A, Woodworth KY, et al. Autistic traits in children with and without ADHD. *Pediatrics* 2013;132(3): e612-e622. [\[CrossRef\]](#)
19. McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, et al. Risperidone in children with autism and serious behavioral problems. *N Engl J Med* 2002;347(5):314-21. [\[CrossRef\]](#)
20. Scahill L, Hallett V, Aman MG, McDougle CJ, Arnold LE, McCracken JT, et al. Brief report: social disability in autism spectrum disorder: results from Research Units on Pediatric Psychopharmacology (RUPP) Autism Network Trials. *J Autism Dev Disord* 2013;43(3):739-46. [\[CrossRef\]](#)
21. Achenbach TM, Rescorla LA. Manual for the ASEBA School-Age Forms & Profiles. Burlington: University of Vermont, Research Center for Children, Youth, & Families; 2001.
22. Dümenci L, Erol N, Achenbach TM, Simsek Z. Measurement Structure of the Turkish Translation of the Child Behavior Checklist Using Confirmatory Factor Analytic Approaches to Validation of Syndromal Constructs. *J Abnorm Child Psychol* 2004;32(3):335-40. [\[CrossRef\]](#)
23. Bussing R, Fernandez M, Harwood M, Hou W, Wilson Garvan C, Eyberg S, et al. Parent and teacher SNAP-IV ratings of attention deficit hyperactivity disorder symptoms: Psychometric properties and normative ratings from a school district sample. *Assessment* 2008;15(3):317-28. [\[CrossRef\]](#)
24. The MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention deficit/hyperactivity disorder: The multimodal treatment study of children with ADHD. *Arch Gen Psychiatry* 1999;56(12):1073-86. [\[CrossRef\]](#)
25. Güler, AS, Scahill L, Jeon S, Taşkın B, Dedeoğlu C, Ünal S, Yazgan Y. Use of Multiple Informants to Identify Children at High Risk for ADHD in Turkish School-Age Children. *J Atten Disord* 2014; published online. DOI: 10.1177/1087054714530556. [\[CrossRef\]](#)
26. Biederman J, Petty CR, Fried R, Wozniak J, Micco JA, Henin A, et al. Child behavior checklist clinical scales discriminate referred youth with autism spectrum disorder: a preliminary study. *J Dev Behav Pediatr* 2010;31(6):485-90.
27. Carpenter Rich E, Loo SK, Yang M, Dang J, Smalley SL. Social functioning difficulties in ADHD: association with PDD risk. *Clin Child Psychol Psychiatry* 2009;14(3):329-44. [\[CrossRef\]](#)
28. Gillberg C. Deficits in attention, motor control, and perception: a brief review. *Arch Dis Child* 2003;88(10):904-10. [\[CrossRef\]](#)
29. Geller DA, Biederman J, Faraone S, Spencer T, Doyle R, Mullin B, et al. Re-examining comorbidity of obsessive compulsive and attention-deficit hyperactivity disorder using an empirically derived taxonomy. *Eur Child Adolesc Psychiatry* 2004;13(2):83-91. [\[CrossRef\]](#)
30. de Bruin EI, de Nijs PF, Verheij F, Hartman CA, Ferdinand RF. Multiple complex developmental disorder delineated from PDD-NOS. *J Autism Dev Disord* 2006;37(6):1181-91. [\[CrossRef\]](#)
31. Hessel D, Dyer-Friedman JD, Glaser B, Wisbeck J, Barajas RG, Taylor A, et al. The influence of environmental and genetic factors on behavior problems and autistic symptoms in boys and girls with fragile X syndrome. *Pediatrics* 2006;108(5):1-9.
32. Abdellaoui A, Bartels M, Hudziak JJ, Rizzu P, van Beijsterveldt TC, Boomsma DI. Genetic Influences on Thought Problems in 7-Year-Olds: A Twin-Study of Genetic, Environmental and Rater Effects. *Twin Res Hum Genet* 2008;11(6):571-8. [\[CrossRef\]](#)
33. Flicek M, Landau S. Social status problems of learning disabled and hyperactive/learning disabled boys. *J Clin Child Psychol* 1985;14(4):340-4. [\[CrossRef\]](#)