Does the coexistence of attention deficit hyperactivity disorder and sluggish cognitive tempo affect the treatment response in children?

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SUMMARY

Objective: We aimed to evaluate treatment response in children with sluggish cognitive tempo and attention deficit/ hyperactivity disorder.

Method: Child Behavior Checklist and Barkley Child Attention Scale were used to define SCT symptoms. Parents and teachers completed Turgay DSM-IV-Based Screening Scale for Disruptive Behavior disorders, severity and improvement were eva-luated via Clinical Global Impressions Scale- Severity and CGI- Improvement. Methylphenidate responses were evaluated retrospectively by patient charts.

Results: SCT + ADHD group was rated as more inattentive by their parents while teachers rated children with ADHD as more hyperactive/ impulsive ($p<0,01$; $p<0,01$, respectively). Symptom reduction was significantly greater for teacher rated hyperactivity/ impulsivity in the ADHD group and children with SCT+ ADHD were still rated as more inattentive by their parents after treatment. The sole predictor of treatment response in the SCT+ ADHD group was treatment duration ($p=0.012$).

Discussion: Longer treatment duration seemed to be more effective in the SCT group.

Key Words: Sluggish cognitive tempo, methylphenidate, attention deficit hyperactivity disorder, treatment response, treatment duration

INTRODUCTION

Attention Deficit/ Hyperactivity Disorder (ADHD) is among the most common neurodevelopmental disorders of childhood characterized by developmentally inappropriate and impairing symptoms of inattention, hyperactivity and/ or impulsivity (1). Impairing symptoms of ADHD may persist in up to of adults diagnosed in childhood (1). Currently accepted subtypes of ADHD include inattentive (IA), hyperactive/ impulsive (HIP) and combined (C) presentations which are classified according to dominant symptoms (1,2).

A subgroup of children among those with ADHD may present with mental confusion (i.e., "fogginess"), slow behavior and thinking and excessive daydreaming and they were classified as having "Sluggish Cognitive Tempo" (SCT) (3). Although initially thought to be a subgroup within the ADHD- inattentive type, a series of studies and meta-analyses have established the SCT as a clinical entity partially overlapping with ADHD (3–7). In addition to ADHD, it may accompany other neurodevelopmental disorders and lead to further impairment especially by increasing social problems and internalizing symptoms (7,8). According to population-based studies, up to a third of child-

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ren with ADHD may also have SCT (9).

Recent studies have advanced our knowledge on the psychiatric, neuropsychological, neurophysiological, and neurobiological correlates of SCT. Children with ADHD and comorbid SCT symptoms may display elevated levels of autistic traits, mind-wandering/ rumination, emotional dysregulation, symptoms of anxiety and depression and eveningness chronotype (8,10-14). Also, there are recent findings that children with SCT may be impaired in orienting attention and memory (15,16). SCT accompanying ADHD may further impair executive functions (17). SCT may also be associated with greater behavioral inhibition and pronounced autonomic system reactivity in social situations and slower processing speed especially with elevated motor demands (10, 18-19). A specific allele of the DRD4 gene (i.e., 7R) may be associated with SCT and children with SCT may also display changes in internal capsules, cerebral peduncles and fornices bilaterally (20,21).

Despite better characterization of SCT symptoms and comorbidity, the effects of SCT comorbidity in ADHD on treatment response is relatively less studied (22,23). Froehlich and colleagues (22) reported that increased SCT- sluggish/ sleepy symptom scores were associated with methylphenidate (MPH) non-response/ placebo response and with lower MPH responses to parent and teacher –rated IA symptoms. Fırat and colleagues (23) reported that MPH treatment improved SCT-total and SCT-daydreaming scores at home and school while SCT-sluggish scores were improved only at school. In this study, older age predicted treatment response in SCT symptoms while pretreatment SCT and ODD symptoms predicted lower MPH treatment response. McBurnett and colleagues (24) found that treatment with atomoxetine (ATX) may improve SCT symptoms among children with ADHD and dyslexia and that this effect was independent of inattentive symptoms. In a recent case report, Tahillioglu and Ercan (25) suggested that ATX may be more beneficial for SCT, and subthreshold ADHD compared to MPH. Additional preliminary evidence suggests that children with SCT may also respond less to behavioral interventions which was posited to be related to memory problems (26).

Therefore, the aims of this study were;

a. To evaluate the difference in treatment response among Turkish children with ADHD with (ADHD + SCT) or without SCT (ADHD) symptoms under naturalistic treatment;

b. To determine the predictors of MPH treatment response (according to clinician evaluations) in ADHD+SCT group.

METHODS

Study center, sampling, and ethics

This naturalistic study was conducted at Duzce University Medical Faculty Department between February 2016 and December 2019. Children who applied to the department of Child and Adolescent Psychiatry and were diagnosed with ADHD according to DSM-5 based clinical interviews were eligible for enrollment. Children diagnosed with ADHD were screened for SCT symptoms at baseline with Child Behavior Checklist (CBCL) and those scoring 1.5 standard deviations above the mean of the ADHD group in the SCT index of CBCL (8th, 17th, 80th, 102nd items) were further evaluated with parent-completed Barkley Child Attention Scale (BCAS). Inclusion criteria for patients with ADHD were being diagnosed with ADHD according to DSM-5 based clinical interviews and receiving at least two months of treatment with MPH. Intellectual disability (ID, as evaluated by Wechsler Intelligence scale for Children-Revised Turkish version), a history of head trauma causing loss of consciousness, presence of chronic neurological/ medical disorders requiring treatment, comorbid bipolar disorder, autism spectrum disorder (ASD), psychosis and substance use disorders were criteria for exclusion.

Briefly; 434 patients were eligible for potential enrollment while 25, 30 and 62 Patients were excluded due to ID, history of head trauma and chronic neurological/ medical disorders requiring treatment; respectively. Thirteen patients had comorbid ASD while 38 had comorbid specific learning disability.

Two of the patients were excluded due to comorbid bipolar disorder while none were excluded due to comorbid psychosis. Among patients with ADHD fifteen were initiated ATX and were excluded from the present sample. Ten patients did not attend follow-up interviews and were excluded leading to a final sample of 241 patients with ADHD.

Parents and teachers completed Turgay DSM-IV-Based Screening Scale for Disruptive Behavior disorders at baseline and after at least two months of treatment, disorder severity and improvement were evaluated by clinicians via Clinical Global Impressions Scale- Severity (CGI-S) and CGI-Improvement (CGI-I). Methylphenidate responses were evaluated retrospectively by patient charts. The daily equivalent dose was calculated according to clinician toolkits of Utah Academy of Child and Adolescent Psychiatry (https://www.uacap.org/_files/ugd/1da6d0_55267f5b04204cb58bcc848398c0286f.pdf) as well as product sheets. IRB approval for study was granted by Duzce University Medical Faculty Ethics Committee (No: 2019/ 259). Written informed consent of parents/ guardians were procured as well as verbal assent of children prior to participation. All the study procedures were in accordance with the Declaration of Helsinki as well as local laws and regulations.

Measures

Sociodemographic Data Form: The form was prepared to collect information about sociodemographic characteristics of children and parents. It consisted of questions examining child's age, gender, grade, family structure, parent's age, marital status, family history of medical and psychiatric illnesses and it was completed by the clinician.

Turgay DSM-IV- Based Screening Scale for Disruptive Behavior Disorders (T-DSM-IV-S): This Scale was used to evaluate severity of symptoms of ADHD, ODD and Conduct Disorder (27. The items in the scale are identical to the list of symptoms described in the DSM-IV criteria for ADHD, ODD and CD and are scored by assigning a severity estimate for each symptom on a 4-point Likert-type scale. The T-DSM-IV-S was developed by Turgay (1994) and translated and adapted to Turkish by Ercan and colleagues (28).

Child Behavior Checklist (CBCL/ 6-18): The CBCL is a broad-band scale to evaluate problematic behaviors in children and adolescents from 6 to 18 years old according to parent or teacher reports. The problematic behaviors are evaluated in 113 3-point Likert type items (0 to 2) according to their frequency in the past six months. Apart from a total problem score, the CBCL provides internalizing (anxious/ depressed, withdrawn/ depressed, somatic complaints), externalizing (rule breaking and aggressive behavior), attention and thought problem scores29. The Turkish translation, validity and reliability was established previously (30,31). In this study the SCT index (8th, 17th, 80th, 102nd) of the parent version of the Child Behavior Checklist (CBCL) was used to differentiate probable SCT comorbidity (i.e., those with a score above 1.5 standard deviations above the ADHD group (17, 21, 32). The mean SCT index score in our patients with ADHD was 2.0 (S. D=1.3) which led to a cut-off score of 4.0 similar to previous studies (17,21).

Barkley Child Attention Scale (BCAS): The BCAS consists of 12- item four point-likert type scale evaluating two dimensions of SCT (i.e., sluggishness and daydreaming (33). The reliability and validity of the Turkish version was established by Fırat and colleagues (34). We used BCAS completed by the parents to evaluate SCT symptom severity in children above cut-off in the CBCL-SCT index.

Clinical Global Impressions Scale (CGI): The Clinical Global Impressions Scale (CGI) is a clinician rated scale developed by the National Institute of Mental Health to evaluate patients according to symptom severity and change with treatment (35). It consists of three sections in which disease severity, improvement and side effect severity are evaluated. We used the severity section before treatment, and the recovery section in the period after treatment.

Statistical analysis

The data were entered into a database prepared with Statistical Program for Social Sciences (IBM

Inc., Armonk, NY) Version 23.0. Qualitative variables were summarized in counts and frequencies while quantitative variables were summarized either as means and standard deviations or medians and inter-quartile ranges depending on assumptions of normality. Assumptions of normality were evaluated with Kolmogorov Smirnov test. Bivariate comparisons of nominal variables were conducted with chi square test (with Yates', Fisher's and Likelihood Ratio corrections as needed). Bivariate comparisons of quantitative variables were conducted with Mann-Whitney or Student's t tests. Logistic regression was used in evaluating the predictive value of SCT symptoms for ADHD treatment. Multivariate analyses of variance (MANOVA) were conducted to evaluate the effects group on baseline and end-visit ADHD symptoms. P was set at 0.05 (two-tailed).

RESULTS

Within the specified time period 241 patients (ADHD, n= 141, 58.5 %, ADHD + SCT, n= 100, 41.5 %) were enrolled in the study. Clinical and sociodemographic variables according to patient groups are illustrated in Table 1.

The groups were similar in terms of age, gender and clinician evaluated severity of symptoms at baseline while ADHD- IA type was significantly more common among children with SCT comorbidity.

Most common comorbid disorders in the SCT group were Oppositional Defiant Disorder (ODD, n= 20, 20.0 %), Learning Disorders (n= 18, 18.0 %), Conduct Disorder (CD, n= 10, 10.0%) and Anxiety Disorders (n= 7, 7.0 %). Most common comorbid disorders in the ADHD group were Learning Disorders (n= 32, 22.7 %), ODD (n= 28, 19.9 %), CD (n= 21, 14.9 %) and Anxiety Disorders (n=5, 3.5 %). The groups did not differ significantly in terms of comorbid disorders (Table 2).

Long-acting MPH formulations were the most common choice of treatment in both groups (ADHD, n= 73, 51.8 % vs. SCT, n= 49, 49.0 %) and the groups did not differ significantly in terms of MPH formulations selected for treatment (x^2= 0.36, dF= 2, p= 0.837, Likelihood ratio). Daily mean equivalent dose of MPH for SCT and ADHD groups were 26.0 (S.D.= 12.3) and 24.3 (S.D.= 12.4) milligrams, respectively. The groups did not differ significantly in terms of mean daily equivalent dose of MPH (t (239) = 1.1, p= 0.291, 95 % Confidence Interval= - 1.5- 4.9). Five patients in both groups received additional treatment with SSRIs while four patients in the SCT and nine in ADHD groups received atypical antipsychotics

Table 1. Clinical and sociodemographic variables of children with Attention Deficit/ Hyperactivity Disorder (ADHD) with or without accompanying SCT symptoms.

N, % or Median, IQR		SCT+ADHD (n= 100)	ADHD (n= 141)	x^2/ Z*	P**
Gender (male)		75 (%75.0)	113 (%80.1)	0.63	0.429
ADHD Type	IA	51 (%51.0)	40 (%28.4)	13.7	***0.001***
	HIP	4 (%4.0)	14 (%9.9)		
	C	45 (%45.0)	87 (%61.7)		
Age		9.0 (%4.0)	8.1 (%2.9)	- 0.89	0.372
CGI-S		4.0 (%1.0)	4.0 (%1.0)	-0.49	0.627

*: Mann-Whitney U test, **: Chi Square, IQR: Inter-quartile range, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity Disorder, E.S: Effect Size (Cramer s V), IA: Inattentive, HIP: Hyperactive/ Impulsive, C: Combined, CGI-S: Clinical Global Impression- Severity

Table 2. Comorbid disorders in children with Attention Deficit/ Hyperactivity Disorder with or without accompanying SCT

N, %	SCT+ADHD (n= 100)	ADHD (n= 141)	x^2	P*	O.R.
Learning Disorders	18 (%18.0)	32 (%22.7)	0.53	0.469	1.3 (0.7- 2.6)
Oppositional Defiant Disorder	20 (%20.0)	28 (%19.9)	0.00	1.000	1.0 (0.5- 1.9)
Conduct Disorder	10 (%10.0)	21 (%14.9)	0.85	0.356	1.6 (0.7- 3.5)
Anxiety Disorders	7 (%7.0)	5 (%3.5)	1.48	0.244	0.5 (0.2- 1.6)

*Chi Square Test (with Fisher and Yates corrections as needed), SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity Disorder, O.R.: Odds Ratio (with 95 % Confidence Interval), E.S.: Effect Size

Table 3. Baseline symptom severity reported by parents and teachers in children with Attention Deficit/ Hyperactivity Disorder with or without accompanying SCT

Mean, S.D.	SCT (n= 100)	ADHD (n= 141)	F	P*	Partial n^2
T-DSM-IV-S- IA- P	19.2 (5.2)	16.4 (5.6)	*16.9*	***0.000***	*0.07*
T-DSM-IV-S- HIP- P	13.0 (8.3)	14.3 (7.3)	1.8	0.187	0.01
T-DSM-IV-S- ODD- P	10.2 (7.2)	9.7 (6.7)	0.3	0.585	0.00
T-DSM-IV-S- CD-P	3.6 (5.6)	3.8 (5.4)	0.1	0.780	0.00
T-DSM-IV-S- IA- T	17.9 (5.1)	17.0 (5.6)	1.9	0.174	0.01
T-DSM-IV-S- HIP- T	10.5 (8.3)	13.9 (7.8)	*10.7*	***0.001***	*0.04*
T-DSM-IV- S- ODD- T	8.2 (6.7)	9.0 (7.0)	0.9	0.357	0.00
T-DSM-IV-S- CD- T	2.7 (4.6)	3.7 (5.4)	2.2	0.141	0.01

*Univariate ANOVAs, S.D.: Standard Deviation, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity disorder, dF: degrees of freedom, CI: Confidence Interval, T-DSM-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, IA: Inattention, HIP: Hyperactivity/ Impulsivity, ODD: Oppositional Defiant Disorder CD: Conduct Disorder, P: Parent, T: Teacher

Table 4. Parent and teacher reported symptoms at baseline and end point among children with ADHD + SCT (SCT) and those with ADHD only

Mean (SD)	SCT (n= 100)		ADHD (n= 141)	
	Baseline	End point	Baseline	End point
T-DSM-IV-S- IA- P	19.2 (5.2)	8.5 (4.5)	16.4 (5.6)	6.7 (3.6)
T-DSM-IV-S- HIP- P	13.0 (8.3)	4.3 (4.2)	14.3 (7.3)	5.2 (4.3)
T-DSM-IV-S- ODD-P	10.2 (7.2)	3.6 (4.2)	9.7 (6.7)	3.4 (4.0)
T-DSM-IV-S- CD-P	3.6 (5.6)	1.1 (2.5)	3.8 (5.4)	1.2 (2.6)
T-DSM-IV-S- IA- T	17.9 (5.1)	7.5 (4.1)	17.0 (5.6)	6.8 (4.2)
T-DSM-IV-S- HIP- T	10.5 (8.3)	4.0 (4.1)	13.9 (7.8)	4.8 (4.1)
T-DSM-IV- S- ODD-T	8.2 (6.7)	2.8 (3.5)	9.0 (7.0)	2.8 (3.5)
T-DSM-IV-S- CD- T	2.7 (4.6)	1.1 (2.3)	3.7 (5.4)	1.1 (2.1)

S.D.: Standard Deviation, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity disorder, T-DSM-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, IA: Inattention, HIP: Hyperactivity/ Impulsivity, ODD: Oppositional Defiant Disorder, CD: Conduct Disorder, P: Parent, T: Teacher

(AAP) The groups did not differ significantly in terms of receiving additional treatment with SSRIs or AAPs (x^2=0.31, p=0.745 and x^2=0.65, p=0.566, both with Fisher's corrections).

Baseline symptom severity reported by parents and teachers were compared between groups with MANOVA. Covariance matrices were not equal (Box's M= 54.0, p=0.041) while error variances were equal for all subtests of T-DSM-IV-S (p> 0.05, Levene test); therefore Pillai's trace was used in analyses. Children with ADHD with and without SCT differed significantly in terms of baseline symptoms reported by parents and teachers (F (8.0, 232.0)= 5.1, p< 0.001, partial η^2=0.15). Follow-up univariate analyses are illustrated in Table 3.

SCT group were rated as significantly more inattentive by their parents at baseline (p=0.000, 95 % CI= 1.5- 4.3) while the ADHD group were rated as significantly more hyperactive and impulsive (p=0.000, 95 % CI= 1.4- 5.5) by their teachers.

Median duration of treatment for SCT and ADHD groups were 5.0 (IQR= 7.0) and 6.0 (IQR= 10.0) months; respectively with no significant difference across groups (Z= - 1.3, p= 0.183, Mann-Whitney U test).

After treatment most of the patients in both groups were rated by clinicians as "much" (SCT, n= 38, 38.0 % vs. ADHD, n= 67, 47.5 %) or "very much" improved (SCT, n= 30, 30.0 % vs. ADHD, n= 44, 31.2 %). Median CGI-I scores in SCT+ADHD and ADHD groups were 2.0 (IQR= 2.0) and 2.0 (IQR= 1.0); respectively with no significant difference (Z= -1.1, p=0.256, Mann-Whitney U test). MANOVA was used to evaluate the effects of group on treatment related change in parent and teacher reports (Table 4) .

Covariance matrices (Box's M= 61.4, p=0.009) were not equal while error variances except for parent reported change hyperactive/ impulsive symptoms (p=0.007, Levene test) were equal. The groups differed significantly in terms of parent and teacher reported change in ADHD symptoms (F (8.0, 232.0) = 3.0, p=0.004, partial η^2= 0.09, Pillai's trace). Follow-up univariate ANOVAs revealed that teachers rated hyperactive/impulsive symptoms of children with ADHD + SCT as less responsive to treatment (F= 9.2, p=0.003, partial η^2=0.04). Change in other symptom domains reported by parents and teachers did not differ across groups.

Afterwards, patients with CGI-I scores of "much" or "very much improved" were classified as treatment responders and logistic regression analysis was used to evaluate predictors of treatment response in children with SCT+ADHD. Gender, ADHD type, presence of any comorbidity, mean equivalent daily dose of MPH, duration of treatment, parent ratings of inattention and oppositionality, teacher ratings of hyperactivity/ impulsivity and BCAS sluggishness and daydreaming scores (dummy-coded according to median as significant/ not significant) were entered as predictors. The

Table 5. Predictors of treatment response in children with Attention Deficit/ Hyperactivity Disorder and Sluggish Cognitive Tempo according to logistic regression

Variable	O.R.	95 % Confidence Interval	p
Gender (Male)	0.6	0.2- 2.0	0.404
ADHD-IA	2.2	0.4-11.1	0.359
Comorbid diagnosis	0.4	0.1- 1.2	0.115
Mean daily equivalent dose of MPH	1.0	1.0- 1.1	0.598
Treatment duration (month)	1.1	1.0- 1.3	*0.012*
BCAS- daydreaming	0.5	0.2- 1.3	0.167
BCAS- sluggishness	1.3	0.5- 3.7	0.621
T-DSM-IV-S-P-IA	1.0	0.9- 1.1	0.718
T-DSM-IV-S-P- ODD	0.9	0.8- 1.0	0.149
T-DSM-IV-S-T-HIP	1.0	0.9- 1.1	0.911

O.R.: Odds Ratio, ADHD: Attention Deficit/ Hyperactivity Disorder, IA: Inattention, MPH: methylphenidate, BCAS: Barkley Child Attention Scale, T-DSM-IV-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, ODD: Oppositional Defiant disorder.

model was significant (Hosmer- Lemeshow x^2 (8) = 6.6, p=0.582) and could explain 22.7 % of the variance in treatment response (Nagelkerke R2=0.227). The predictors could classify 86.8 % of treatment responders and 40.6 % of treatment non-responders in the SCT group for an overall accuracy of 72.0 % (Table 5). The sole predictor of treatment response was its duration.

DISCUSSION

This study aimed to evaluate the difference in treatment response in children with ADHD with or without SCT symptoms and to evaluate the predictors of MPH treatment response in ADHD+SCT group. We found that SCT was more frequently associated with ADHD- inattentive type. Parents rated children with SCT + ADHD as more inattentive by their parents while teachers rated children with ADHD as more hyperactive/ impulsive. Parent and teacher reported symptoms reduced significantly with treatment in both groups. However, reduction was significantly greater for teacher rated hyperactivity/ impulsivity in the ADHD group. The sole predictor of treatment response in the SCT+ ADHD group was treatment duration.

In our study, the ADHD-I subtype ratio was higher in the SCT+ADHD group than the ADHD group. Although SCT symptoms are found to be distinct from the ADHD symptom dimensions and can be seen in both ADHD-combined (ADHD-C) and ADHD-inattentive types (ADHD-I), they display greater correlations with inattentive symptoms than hyperactive-impulsive symptoms (33). In a clinical sample study, Garner and colleagues found that SCT symptoms were higher in children with diagnosis of ADHD-I (36). In a randomized controlled trial to examine the association between SCT symptomatology and response to methylphenidate, Froehlich and colleagues (22) also found that children with SCT formed a greater proportion of cases with ADHD-I than ADHD-C subtype. Cevher, Binici and Kutlu (37) also reported that children with SCT symptoms were predominantly diagnosed with ADHD- IA. Therefore, our finding is consistent with studies reporting a partial overlap between inattention and SCT symptoms which may pose difficulties in accurate diagnosis. In the baseline symptom assessment, SCT+ADHD group in our sample were rated as significantly more inattentive by their parents but not by their teachers, while the ADHD group were rated as significantly more hyperactive and impulsive by their teachers. Various studies suggest that parent and teacher reported SCT symptom scores did not display significant correlations among children diagnosed with ADHD (22, 36). In contrast to our study, Garner and colleagues' study indicated that teacher ratings of SCT showed a clearer distinction between ADHD subtypes than parent ratings as the classroom could be a structured setting when compared to home. Cevher Binici and Kutlu (37 found that both parents and teachers rated children with SCT + ADHD as less aggressive and more withdrawn/ anxious while they rated children with ADHD as more aggressive and displaying greater behavioral problems. The difference in our results could be due to closer observations and greater academic expectations of parents or preferences of teachers for calm but inattentive pupils compared to hyperactive/ impulsive ones in the classroom. The manifestations and validity of SCT symptoms across the school and home settings and in differing cultures may be an important area for further research.

The clinicians rated symptom severities and improvement as similar across groups and parent and teacher reported symptom scores in both groups reduced significantly with treatment. Similar to our study, a retrospective naturalistic follow up study which evaluated the prognostic validity of SCT symptoms in MPH treatment response by comparing patients with inattentive ADHD (with and without SCT symptoms) also found no significant difference in ADHD total scores after a month of treatment (36). However, reductions in teacher-rated hyperactivity/ impulsivity symptoms were greater in the ADHD group among our sample. This may indicate a reduced response to MPH treatment among children with SCT and/ or IA symptoms. Supporting this position prior studies have suggested that children with the inattentive subtype of ADHD may show a less robust response to methylphenidate (38). Froehlich and colleagues (22) also reported that hyperactive-impulsive symptoms were more responsive to MPH treatment compared to inattentive/ SCT symptoms and

children with ADHD + SCT may respond to MPH treatment less. A recent study from Turkey also supports that SCT symptoms accompanying ADHD may signify reduced response to stimulant treatment (23. Although some studies suggest that children with ADHD + SCT may not differ in treatment response to those with ADHD alone, this difference may be due to dependence on parental reports alone (39. The reduction in sluggishness symptoms at school with treatment in our sample with ADHD + SCT may be interpreted as hyperactivity/ impulsivity by their teachers. We could not test this hypothesis due to our dependence on parent forms of BCAS completed at baseline. Further studies on treatment response among children with ADHD+ SCT may use repeated evaluations by BCAS completed by multiple informants to test this hypothesis. Also, as suggested by some recent studies, SCT symptoms accompanying ADHD may be more responsive to treatment with ATX (24,25). Future studies on treatment response among children with ADHD+ SCT may also evaluate the effects of non-stimulant treatments.

When we analyzed predictors of treatment response in children with the SCT+ADHD group, we found no relationship between SCT sluggish or daydreaming factors and treatment response with the sole predictor being treatment duration. This finding may suggest the relative resistance of SCT symptoms to MPH treatment and/ or the importance of cumulative dose of MPH received/ maturation in addressing symptoms of SCT. Partially supporting the importance of cognitive maturation in addressing SCT symptoms, Fırat and colleagues reported that MPH treatment may improve SCT symptoms especially among older children (23). Because of the preponderance of prepubertal children in our sample we could not evaluate the effects of cognitive maturation on MPH treatment for SCT symptoms accompanying ADHD. Further studies may enroll patients from varied age groups (i.e., prepubertal, early-mid-late adolescent) to determine the effects of cognitive maturation.

Limitations

Our results should be evaluated within their limitations. Firstly, the retrospective, single-center design of the study may affect our results and limit external validity. Secondly, we used a two-stage screening design to evaluate probable SCT (i.e CBCL-SCT index and BCAS) and this may have led to false negatives/ positives. Supporting this position, Wu and colleagues (17)reported that 10.8 % of their sample with ADHD were classified as having SCT symptoms while this increased to 30.0-60.0 % with BCAS. Third, addition of a placebo or atomoxetine arm could have enriched our results. Fourth we could not control for the effect of maturation on SCT symptoms. Fifth, we did not evaluate for the effects of autism spectrum disorder symptoms, anxiety and depression on treatment response among children with ADHD +/ - SCT.

Despite those limitations this naturalistic study may support the differing nature of inattentive symptoms in SCT and ADHD-IA. Also, longer treatment duration seemed to be more effective in the SCT group so randomized controlled studies with longer treatment duration with different dose regimes should be conducted to investigate validity of SCT symptoms across the school and home settings and the effect of different dimensions of SCT on MPH response.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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