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The Effect of Methylphenidate on Executive Functions in Children with Attention-Deficit Hyperactivity Disorder

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ÖZET:

Dikkat Eksikliği Hiperaktivite Bozukluğu olan çocuklarda metilfenidatın yürütücü işlevler üzerine etkisi

Amaç: Bu çalışmanın amacı Dikkat Eksikliği Hiperaktivite Bozukluğu (DEHB) olan çocuklarda yürütücü işlevler ve metilfenidatın (MPH) bu işlevler üzerine olan etkisini değerlendirmektir.

Yöntem: Çalışmaya 7-12 yaş arası DSM IV tanı ölçütlerine göre DEHB-Bileşik Tip (DEHB-B) tanısı alan 30 çocuk ile bilinen bir psikiyatrik veya tıbbi rahatsızlık öyküsü bulunmayan, yaş ve cinsiyet açısından hasta grubu ile eşleştirilmiş 30 sağlıklı çocuk dahil edilmiştir. Deneklerin hepsine ilk görüşmede Okul Çağı Çocukları için Duygulanım Bozuklukları ve Şizofreni Görüşme Çizelgesi- Şimdi ve Yaşam Boyu- Türkçe Uyarlaması (ÇDŞG-ŞY), Wisconsin Kart Eşleme Testi (WKET) ve Stroop testi TBAG formu (ST) uygulanmıştır. DEHB'li grupta ilk testlerin uygulamasından sonra hastalara MPH başlanmış ve 1 ay sonra testler ikinci kez uygulanmıştır. Testler 1 ay sonra kontrol grubunda da tekrarlanmıştır.

Bulgular: DEHB'li çocukların sağlıklı yaşıtlarına göre ilk uygulanan WKET'de daha fazla yanlış yanıt verdikleri (p=0,02), daha az kategori tamamladıkları (p=0,02), kavramsal düzeyde tepki yüzdesinin daha düşük olduğu (p=0,02) saptanmıştır. DEHB-B'li çocukların ilk uygulamada renk söyleme görevini kontrol grubundan daha uzun sürede tamamladıkları görülmüştür. MPH kullanımı ile DEHB-B'li çocukların sağlıklı yaşıtlarına göre ilk kategoriyi tamamlamak için kullanılan tepki sayısının (WKET) daha fazla olduğu (p=0,03), interferans skorunun (Stroop test) daha düşük (p=0,02) olduğu saptanmıştır.

Sonuç: Bu çalışmada DEHB-B'li çocuklarda WKET (perseverasyon) ve ST (renk adlandırma) performanslarının sağlıklı yaşıtlarına göre daha kötü olduğu ve MPH kullanımının renk söyleme becerisinde düzelmeye neden olduğu saptanmıştır. Bu çocuklarda MPH kullanımı ile perseverasyon, kavramsal irdeleme (WKET) ve interferans etkisinde de (ST) olumlu değişiklikler gözlenmiştir. Ancak benzer olumlu değişikliklerin sağlıklı çocuklarda da gözlenmesi bu alanlardaki performans artışlarının MPH etkisiyle birlikte, testlerin tekrarlanması ve öğrenme süreçleri ile ilgili olabileceğine işaret etmektedir.

Anahtar sözcükler: Dikkat Eksikliği Hiperaktivite Bozukluğu, yürütücü fonksiyon, metilfenidat

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ABSTRACT:

The effect of methylphenidate on executive functions in children with Attention-Deficit Hyperactivity Disorder

Objective: The aim of this study was to evaluate the effect of methylphenidate (MPH) on executive functions in children with Attention-Deficit Hyperactivity Disorder (ADHD).

Methods: The study included 30 children between the ages of 7 and 12 with the diagnosis of ADHD Combined subtype (ADHD-C) and 30 healthy children with no known history of psychiatric or medical conditions, who were age and sex-matched with the patient group. At the first interview, the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version-Turkish Version (K-SADS-PL), the Wisconsin Card Sorting Test (WCST) and the Stroop Test-TBAG form (ST) were administered to all subjects. MPH treatment was initiated after the first interview in the ADHD-C group. One month later the WCST and ST were repeated in both groups.

Results: It was found that children with ADHD-C gave more incorrect responses (p=0.02), completed fewer categories (p=0.02), and their percentage of conceptual level responses was lower than their healthy peers (p=0.02) in the first WCST. At the first ST administration, it was observed that children with ADHD-C took longer to complete the task of color naming (4th card) than the control group. After MPH treatment, children with ADHD-C had more responses to complete the first category (WCST) (p=0.03), and the interference score (ST) (p=0.02) was also lower than healthy children.

Conclusions: In this study, it was found that children with ADHD-C showed lower performances on the WCST (perseveration) and ST (color naming) than healthy children. In addition MPH treatment resulted in improvements on the WCST (perseveration and conceptualization/reasoning) and ST (color naming and interferences effect) performances in the ADHD-C group. However, we also observed similar positive changes in healthy children, indicating that improved performances in these areas could be related to the practice effect and learning processes, in addition to the potential effects of MPH in children with ADHD-C.

Key words: Attention-Deficit Hyperactivity Disorder, executive function, methylphenidate

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INTRODUCTION

Attention-Deficit Hyperactivity Disorder (ADHD) begins in early childhood and includes the major symptoms of inattention, impulsivity and hyperactivity. ADHD affects 3 to 7% of school age children (1). Debate about the underlying disturbances that cause ADHD has been ongoing for many years and remains unresolved. In the past, it has been suggested that hyperactivity was the primary problem but later it has been suggested that the main problem is attention deficit. Recently, some researchers have claimed that the main deficits involve executive functions (EF) located in the prefrontal lobe (2). The evidence for deficits of EF in ADHD is based on poor performances of ADHD patients in tests evaluating EF. Furthermore, differences have been observed between ADHD patients and healthy controls in the brain regions that are thought to be associated with ADHD.

The term executive function includes self-regulation, cognitive control, regulation and monitoring of behavior, selective inhibition of responses to instant stimuli, planning, and attention control. The prefrontal regions of the brain and the cortical and subcortical connections of these regions play an important role in EF (4). Although there are many studies about EF in ADHD, the findings are controversial due to poor control for the effects of other associated disorders, developmental differences, family history, and the concurrent use of psychostimulants in many studies (5). A variety of definitions and terms regarding the components of EF have also been used by different researchers. Inhibition, set shifting, working memory, planning, and fluency are the most emphasized components of EF. It is commonly suggested that inhibition dysfunction is the main EF deficit in ADHD (6). According to Barkley's model, poor behavioral inhibition is specified as the central deficiency in ADHD and ADHD symptoms can be best explained as deficits in inhibition (7). The Stroop Test (ST) and the Wisconsin Card Sorting Test (WCST) are the recognized tests for assessing the ability of response inhibition. Whereas the type of inhibition evaluated by the WCST is associated with the tendency for persisting on the same response, even when a feedback is given that the response is incorrect (perseveration), the type of inhibition measured by ST is associated with leaving familiar stimuli to create unfamiliar stimuli (interference effect) (8).

Methylphenidate (MPH) is the most commonly used pharmacological agent for the treatment of ADHD. In the clinical literature, it is frequently reported that MPH improves overall cognitive functioning in children with ADHD (9). When studies evaluating the effects of MPH treatment on cognitive functions in children with ADHD have been reviewed, it has been observed that, 63.5% demonstrated some improvement in cognitive functioning following methylphenidate treatment. High rates of positive response to MPH treatment have been observed on tasks of planning/cognitive flexibility (71.4%), attention/vigilance (70.6%), and inhibitory control (69.7%). High-dose effects were more consistently observed on attention/vigilance, memory, and working memory tasks, while both low and high dose effects were noted on tasks of planning/cognitive flexibility, inhibitory control, naming, and motor speed (10).

In this study, we aimed to evaluate the effects of MPH on EF in children with combined subtype ADHD. We also controlled some factors such as comorbidity, medication use, subtypes of ADHD, the use of non-standardized tests, and the effect of the repetition of tests (practice effect), because it has been suggested that these factors were related to contradictory findings in previous studies.

METHODS

Sampling and Procedure

Thirty children, aged between 7-12 years, admitted to the Department of Child and Adolescent Psychiatry outpatient clinic at Akdeniz University and diagnosed with ADHD-C according to the DSM IV criteria, were included in this study. Having an IQ score below 80 on the WISC-R, marked vision and hearing problems, psychotropic or antiepileptic drug use history other than MPH,

pervasive developmental disorders, receptive language disorder, determination of psychopathology other than ADHD-C in a semi-structured interview, head trauma or previous seizure history, or a history of a chronic medical disorder were defined as the exclusion criteria for this study. The control group was composed of 30 healthy children, aged between 7-12 years, with no prior admission history to a pediatric psychiatry clinic for any reason, no known psychiatric or medical disorder or mental retardation, age-and sex-matched with the patient group. The presence of psychiatric disorders was excluded by using semi-structured interviews. The control group consisted of children of individuals from the researchers' work and social environment, who agreed to participate in the study. The level of intelligence of the children in the control group was determined through clinical observation, developmental and school performance history and performances on the Bender-Gestalt Test of Visual Motor Perception, and the Good-Enough (Draw a human) test. All the participating children and their parents in the study were informed about the research and gave written informed consent.

A semi-structured clinical interview was performed with each participant (patients and controls) in order to confirm the ADHD-C diagnosis and to exclude other psychiatric disorders and then the children completed the neuropsychological tests. These tests were repeated one month later. The children, who were previously diagnosed with ADHD-C and on MPH treatment, stopped MPH at least 48 hours before the first administration of the neuropsychological tests. Drug therapy was started after the completion of the first testing session both in the previously or newly diagnosed group. The WCST and ST were administered one month later for the 2nd time (1 hour after taking the daily dose of MPH in the morning). The semi-structured clinical interview and neuropsychological tests were administered by the same investigator in all children.

Approval for the study was received from the Ethics Committee of the Faculty of Medicine, Akdeniz University.

Data Collection Tools

A sociodemographic information form was filled out during the first interview by all the parents.

The Schedule for Affective Disorders and Schizophrenia for School Age Children - Present and Lifetime Version-Turkish Version (K-SADS-PL) is a semi-structured diagnostic interview developed in order to assess the past and current psychopathology of children and adolescents according to DSM-III and DSM-IV criteria. The Turkish version of K-SADS was adapted by Gökler et al. and the validity and reliability study was carried out in Turkey (11). Mood disorders, psychotic disorders, anxiety disorders, elimination disorders, disruptive behavior disorders, substance abuse, eating disorders and tic disorders can be evaluated with K-SADS-PL. It was carried out during the interview with the parents and the child himself, and at the end an evaluation was made based on the information received from all sources. If there was a discrepancy between the information from different sources, the clinician made his own clinical judgment.

The Wisconsin Card Sorting Test (WCST) has been developed in order to evaluate the abilities of abstraction, cognitive flexibility, and set maintenance (12). The test consists of 128 response cards and four stimulus cards. The subject is asked to match each card with one of four stimulus cards. And after each response, the subject is provided feedback about whether his/her response was correct or not. The correct matching rule is changed by the administrator during the test, and insisting on the old rule despite provided feedback is considered to be perseveration. The following scores are utilized in the evaluation of the WCST: the total number of errors (TE) and the total number of correct responses (TC), the total number of responses (TNR), total number of categories achieved (TCA), the number of perseverative responses (PR), the number of perseverative errors (PE), the number of non- perseverative errors (NPE), the percentage of perseverative errors (PPE),

Table 1: Socio-Demographic features of the subjects

	ADHD group (n=30)	Control group (n=30)	p
Age (months)*	105.17±13.45[1]	106.73±13.23	0.65
Gender**			1
Male	27 (90%)[2]	26 (86.7%)	
Female	3 (10%)	4 (13.3%)	
Education (year)*	3.57±1.17	3.53±1.22	0.91
Hand Preference**			0.52
Right	25 (83.3%)	23 (76.7%)	
Left	5 (16.7%)	7 (23.3%)	

ADHD: Attention Deficite Hyperactivity Disorder, [1]: Mean±standard deviation, [2]: n (%), *: student t test, **: χ^2 test

number of responses to complete the first category (NRCFC), the number of conceptual level responses (NCLR), the percentage of conceptual level responses (PCLR), failure to maintain set (FMS), and learning to learn (LL).

The standardization studies were conducted in adults and among primary school children in Turkey (13). WCST scores in primary school children were distributed to two factors, the first factor was related to "perseveration" (TNR, TE, TCA, TNPR, TNPE, TNNPE, PCLR), and the second factor was related to "conceptualization/reasoning" (TC, NCLR, FMS) (14). In this study, the computer version of the WCST was used and the number of conceptual level responses was not calculated.

The Stroop test (ST) evaluates the ability to change perceptual configuration in the direction of changing demands while subjected to interference, and to repress a familiar behavioral pattern and perform an unusual behavior (15). The standardization study of the Stroop Test-TBAG form for 6-11 year-old healthy Turkish children was conducted by Kılıç et al. (16). In this study, we used the time to complete the 5th card as the interference score, which was proposed by the standardization study in Turkey. Reduced time to completion of the 5th card is interpreted as a decrease in the interference effect.

Statistics

The Student's t-test was used for comparison of differences between the two groups (The t-test was performed with and without assuming the presence of equal variance between the two groups). The significance of differences between the two dependent groups was analyzed with the 'paired t-test'. The associations between variables were analyzed by Pearson product-moment correlation coefficient. "R Foundation for Statistical Computing'' (R Development Core Team 2009) was used in all statistical analyses.

RESULTS

In our study, no significant differences were found between the two groups in terms of age, gender, education or hand preference (Table 1). Children with ADHD-C had mean IQ scores of 96.4±12.7 on verbal IQ, 99.7±13.3 on performance IQ and 97.93±12.28 on total IQ. In the ADHD-C group, 4 patients were treated with immediate release MPH (IR-MPH) and 26 patients were treated with osmotic controlled release MPH (OROS-MPH) (mean dose±sd: 0.54±0.17 mg/kg/day and 0.70±0.22 mg/kg/day respectively).

Wisconsin Card Sorting Test

The WCST performance scores at the 1st and 2nd administrations are presented in Table 2. Children with ADHD-C had more TE scores (p=0.02) and lower PCLR (p=0.02), TCA (p=0.02) and LL scores (p=0.01) than healthy peers on the 1st WCST administration. In the 2nd WCST administration after one month, the children with ADHD-C had significantly higher NRFFC scores than control children (p=0.03). Other WCST scores showed no significant differences between two groups at this point.

The first and second WCST performances were

Table 2: The performance scores of the 1st and 2nd WCST administrations

WCST Scores	Test no	ADHD group (n=30) Mean±SD	Control group (n=30) Mean±SD	p*
Total number of responses	1	128.00±0	124.80±9.56	0.08
	2	125.47±7.36	121.53±13.96	0.18
Total number of errors	1	57.43±16.79	47.47±16.43	**0.02**
	2	45.07±16.19	37.57±15.99	0.08
Total number of corrects	1	70.57±16.79	76.67±13.19	0.12
	2	81.07±15.40	83.97±12.12	0.42
Number of categories achieved	1	2.63±1.71	3.67±1.49	**0.02**
	2	3.43±1.87	4.13±1.36	0.10
Total number of perseverative responses	1	33.50±16.84	35.33±39.67	0.82
	2	26.97±15.22	20.40±13.97	0.09
Total number of perseverative errors	1	29.50±13.12	25.47±13.16	0.24
	2	24.30±11.98	18.43±11.31	0.06
Total number of non-perseverative errors	1	27.93±14.76	22.10±9.13	0.07
	2	20.83±8.37	19.13±7.02	0.40
Percentage of perseverative errors	1	23.05±10.25	20.01±9.92	0.25
	2	19.08±9.26	14.80±8.47	0.07
Number of responses to complete first category	1	22.69±16.37	27.38±23.24	0.40
	2	29.93±24.87	18.67±10.64	**0.03**
Percentage of conceptual level responses	1	40.05±18.80	51.21±16.12	**0.02**
	2	52.56±17.06	59.67±16.59	0.11
Failure to maintain set	1	2.00±1.41	2.30±1.53	0.44
	2	2.73±1.72	2.60±2.01	0.78
Learning to learning	1	-9.87±10.19	-2.64±8.55	**0.01**
	2	-4.02±10.94	-4.85±9.60	0.77

WCST: Wisconsin Card Sorting Test, ADHD: Attention Deficit Hyperactivity Disorder, Test no 1: 1st WCST administration, Test no 2: 2nd WCST
*: ADHD-C vs Control group comparisons (with student t test), Mean±SD: Mean±Standard deviation

Table 3: Scores of the first and second Stroop Test administrations

Stroop Test scores	Test no	ADHD group (n=30) Mean±SD	Control group (n=30) Mean±SD	p*
1. card (reading time)	1	13.24±6.71	12.04±3.04	0.38
	2	11.52±2.76	10.68±2.30	0.21
2. card (reading time)	1	15.05±5.99	15.69±5.20	0.35
	2	13.71±4.49	14.00±3.96	0.79
3. card (color naming time)	1	21.92±5.13	19.75±5.10	0.11
	2	19.62±4.67	18.50±7.12	0.48
4. card (color naming time)	1	36.43±9.41	31.03±10.32	0.04
	2	30.63±7.85	28.15±13.59	0.39
5. card (color naming time)	1	48.91±11.86	42.77±14.93	0.08
	2	43.59±12.03	35.32±14.95	**0.02**

ADHD: Attention Deficit Hyperactivity Disorder, Test no 1: 1st Stroop Test, Test no 2: 2nd Stroop test administraiton
*: ADHD-C vs Control group comparisons (with student t test), Mean±SD: Mean±Standard deviation

also investigated within the groups for better interpretation of the effect of MPH, and/or the effect of practice on performances. Accordingly, in healthy children, TC (p=0.01), TCA (p=0.03) and PCLR scores (p=0.01) significantly increased, while TE (p=0.00), PR (p=0.01), PE (p=0.00) and PPE (p=0.01) scores were significantly decreased in the second WCST, compared to the first implementation. In children with ADHD-C, MPH treatment statistically improved TC (p=0.00), TCA (p=0.00), and PCLR scores (p=0.00), and significantly decreased TE (p=0.00), PR (p=0.02), PE (p=0.02) and PPE scores (p=0.02) compared to baseline WCST performance. Additionally unlike the controls, after one month treatment period TNNPES (p=0.00), and FMS scores (p=0.04) decreased and LL scores (p=0.01) increased in ADHD-C in the second

WCST, compared to the first assessment.

The percentage performance difference (1st test -2nd test/1st test x100) was calculated in each group in order to compare these positive performance alterations between groups by using a Student's t-test. According to this analysis, no significant difference between the two groups in terms of the percentage performance changes from the first to the second WCST trial was found (p>0.05).

Stroop Test

Test performances on the 1st and 2nd trials of the ST are presented in Table 3. In the 1st ST trial, no significant difference was found in the interference scores (time to completion of the 5th card) between ADHD-C and control groups (p>0.05). Children with ADHD completed the task of color naming (4th card) in a significantly longer time than controls (p=0.04). In the second ST, interference scores of children with ADHD were found to be significantly worse than their healthy peers (p=0.02). There was no difference between the groups in terms of other ST parameters in the second administration.

As the first and the second ST performances were analyzed within the groups (1st test-2nd test), it was found that when the children with ADHD-C used MPH, they completed the 3rd and 4th cards more rapidly (p=0.00 and p=0.00, respectively) and the interference effect (5th card) was significantly lower (p=0.01), compared to the first trial. In the control group, the basic reading speed was increased (time to completion of the 1st card) and the interference effect was decreased (p=0.00) in the second ST, compared to the first trial.

The percentage performance alteration (1st test -2nd test/1st test x100) was calculated within each group in order to compare positive performance changes in ST between the groups. There was no difference in percentage of performance changes in the ST scores between two groups (p>0.05).

When the correlation between age and WCST performance was examined, there was no significant association between age and performance scores, with the exception of the number of completed categories growing with increasing age (r=0.38, p=0.04). In the control group, there was no correlation between age and any of WCST scores.

When the relationship between age and ST scores was examined, the length of time to color naming significantly shortened with the increase of age in children with ADHD-C (time to complete 3rd, card r=-0.38, p=0.04, time to complete 4th, card r=-0.42, p=0.02). There was no significant relationship between age and interference score in children with ADHD-C. In the control group, the time to color naming (3rd card, r=-0.38, p=0.04), and interference effect (5th card, r=-0.54, p=0.00) decreased with increasing age.

The relationship between gender and test performances were not analyzed because of the low number of girls.

When the correlations between MPH dose in children with ADHD-C and performances in the WCST and ST were examined, the only statistically significant relation was between the time to complete 5th card in the ST and the dose of MPH (r=0.38, p=0.04). In other words, the interference effect was reduced with increasing MPH dose. In the analysis of the WISC-R scores in children with ADHD-C, a significant positive correlation was found between the performance score and TD score in the WCST (r=0.41, p=0.03).

DISCUSSION

In this study, we found that children with ADHD-C, who were not on medication generally, had deficits in some types of EF in comparison to their healthy peers. In addition, the use of MPH in children with ADHD-C increased performance on tests assessing EF, although similar improvements were observed in healthy children. The increased performance was considered to be associated with practice effect and learning processes, in addition to the effect of MPH in ADHD-C.

The WCST is one of the most frequently used tests for assessing EF. It measures some cognitive features such as identifying a principle of classification based on given feedback, demonstrating an ability to pay selective attention to one aspect of the stimuli, using this principle as

long as it is valid, and ability to quit this principle, when it results in wrong behavior (set shifting). It also measures the tendency of persistence with the same response even when that response is incorrect (perseveration) (13).

In our study, children with ADHD who were not taking medication were found to have more problems related to perseveration in the WCST (1st test) than their healthy peers. In addition, considering that the perseveration is related to deficits in response inhibition, the results of this study support the hypothesis of response inhibition deficits existing in ADHD (13). Tripp et al. found that children with ADHD have less mental flexibility, poorer working memory, and more perseveration (WCST) than a control group (17).

The Stroop test is another widely used tool to evaluate inhibition, which is one of the executive functions. The Stroop interference score has been used in research on ADHD. The interference effect appears in a color-word condition, which consists color-words printed in incongruently colored ink (e.g. the word 'blue' printed in red). The subject is requested to name the ink color, thereby inhibiting the prepotent response of reading the word (18). In our study, children with ADHD who weree not on medication did not differ in terms of the interference effect in the first ST administration, compared to their healthy peers. In the literature, there are contradictory results regarding the interference effect in ADHD. In some studies it was reported that the response inhibition evaluated by the Stroop test (interference effect) is worse in children with ADHD than a control group (19,20). There are other studies indicating that interference scores cannot provide strong evidence for ADHD (18). The authors have reported that the different results might be due to differences in methodologies for calculating interference score, features of the samples (the presence of comorbid disorders, different subtypes of ADHD, gender, age, drug use, intelligence level, etc.) and sample size (18). We did not find a significant difference in interference score between groups, which could be due to characteristics of our samples and the method of calculating the interference scores. We used the time to complete 5th card (to name the color of the ink of the color-word) as suggested in the validity and reliability study of the ST in a Turkish population (16). Only children who had been diagnosed with ADHD-C were included in the study. In addition to this, unlike other studies, children with any comorbid psychiatric disorders including conduct disorder and oppositional disorder were excluded. In this way, the possible influence of disruptive behavior disorders accompanying ADHD and the other psychiatric disorders on the interference effect were excluded.

We also found that children with ADHD-C, who were off medication completed their tasks related to color naming (4th card) over a longer period of time than their healthy peers. In other words, these children had more problems in color naming. Similar to our findings another study has reported that these children were slower at color naming than the control group but hade no difference in the interference effect (21).

In this study the tests were repeated after 1 month in order to examine the effects of MPH on executive functions in children with ADHD-C. MPH treatment in children with ADHD-C, significantly improved the performance on almost all scores of the 2nd WCST compared to the first administration. However in the healthy control group, we also observed increased performances in the 2nd WCST compared to the first trial, but not in as many fields as in the ADHD-C group.

Jung et al. have reported that MPH reduces perseverative responses and has a positive effect on cognitive functions (22). When we consider that perseveration is a tendency to persist in the same response even when feedback is given that the response is incorrect, it can be said that MPH improves the ability to regulate responses by considering feedback and response inhibition in children with ADHD-C. The WCST has been used only in a small number of studies in order to observe the effects of MPH in ADHD. In a double-blind placebo-controlled study, MPH was given at 3 different doses to children with ADHD between the ages of 6-11, and the WCST test was repeated. At each of the 3 doses, similar to our findings, a reduction was reported in non-perseverative errors

(23). In another study, it was reported that perseverative errors decreased with MPH treatment (at the doses that caused improvement in clinical symptoms) in ADHD patient (24).

As a result, MPH treatment in children with ADHD-C positively affected their performance on the WCST. However, a similar improvement in performances was observed with repeated WCST in healthy children, and the percentage of performance changes in scores was not statistically different between the two groups. When these are taken together, these improvements are consequences of not only MPH usage but also the practice effect and learning process. When tasks that require complex strategies (WCST etc.) are evaluated after a treatment period, many different cognitive processes can be activated in the time after the initial evaluation (25). This also makes it difficult to define and to interpret the specific effects of stimulants on cognitive functions. One of the best ways to eliminate the effect of repeated testing (practice effect) is to administer the same testing protocol to the control group (10). In our study, the WCST was repeated in the control group after one month in order to control for the practice effect. These results point out that cognitive processes, such as learning of the test, are similar in children with ADHD-C and in healthy children.

In the second administration of the Stroop test, the ability in color naming increased (3rd and 4th card) and the interference effect decreased (5th card) with MPH treatment in the ADHD-C group; whereas in healthy children increased speed of basic reading (1st card), and reduced interference effect (5th card) were found. According to this study, MPH treatment in children with ADHD-C leads to improvement in the ability of color naming, and the observed difference in this skill between the groups at the first administration disappeared with MPH treatment. The control group had no significant difference in the ability for color naming between the two test administrations. Previously, it has been reported that color naming is less accurate in children with ADHD and MPH has beneficial effects on this ability (21). A comprehensive review has also indicated that MPH accelerates color naming and reading, but has no effect on the interference effect (18). In a study which was conducted in Turkey, the effects of MPH on attention and EF of 15 males between the ages of 9-13 with ADHD without any comorbid disorder were evaluated before and 6 months after the use of MPH. It was found that ST performances (increase in reading speed and reduction in interference effect) improved with MPH treatment (26). Despite these findings, it is difficult to determine the effect of MPH on ST performances in children with ADHD-C since significant improvement in the interference effect was observed in both groups in the second administration of ST. This finding suggests that the practice effect is as important as the MPH effect.

As a result of this study, performance on the WCST (perseveration), and the Stroop test (color naming) was found to be worse in children with ADHD-C than their healthy peers. MPH treatment in children with ADHD-C positively affects the performance on the WCST as well as the Stroop test. However, similar positive changes in the second administration of the test in the healthy children prevents us from concluding that MPH treatment alone is effective in increasing performance in these children. In other words, the use of MPH in children with ADHD-C results in positive changes in the perseveration and interference effect, but similar positive changes are also observed in healthy children, indicating that improved performances in these areas could be related to the practice effect and learning processes, in addition to the potential effects of MPH in children with ADHD-C.

There are some limitations of this study. We were unable to identify the relationship between level of intelligence and tests because the WISC-R was only applied to the ADHD-C group. We did not evaluate whether improvement in the test performances is correlated with clinical improvements. We also included only the subtype of ADHD-C in the study.

There are also strengths of the study. The study group of ADHD-C had no comorbid psychiatric disorders, and the tests were repeated after 1 month in both groups to examine whether there was improvement due to the effect of ADHD treatment. For future studies, the administration of the WISC-R to each group and examination of the relationship

between clinical improvement and performance changes in the neuropsychological tests and inclusion of all sub-types in the study will help provide a more robust interpretation of the results.

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