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Response Inhibition and Interference Control in Adult Attention Deficit Hyperactivity Disorder

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ABSTRACT

Introduction: Among the executive functions affected in attention deficit hyperactivity disorder (ADHD), inhibitory control is one of the primary areas of impairment, characterized by components that include response inhibition and interference control. Determining the impaired inhibitory control components will be useful in the differential diagnosis and treatment of ADHD. The present study aimed to investigate response inhibition and interference control abilities of adults with ADHD.

Methods: The study included 42 adults diagnosed with ADHD and 43 healthy controls. The stop-signal task (SST) and Stroop test were used for assessing the response inhibition and interference control, respectively. Multivariate analysis of covariance was used for comparing the ADHD and healthy control groups in terms of their SST and Stroop test scores, wherein the age and education level of the participants were taken as covariables. The relationship between SST and Stroop Test and Barratt Impulsiveness Scale-11 (BIS-11) was tested by Pearson correlation analysis. Mann-Whitney U test was used for comparing the test scores between those who were administered with psychostimulants among the adults with ADHD and those who were not.

Results: Response inhibition was observed to be impaired in adults with ADHD compared with the healthy controls, whereas no difference regarding interference control was observed. As per the Barratt Impulsiveness Scale-11 (BIS-11), a weak and moderately negative relationship was found between the stop signal delay and the attentional, motor, non-planning scores, and total scores and a weak positive relationship was found between the stop-signal reaction time and the attentional, motor, non-planning scores, and total scores. A significant improvement was observed in the response inhibition skills of the adults with ADHD who had received methylphenidate treatment compared to those who had not, and the former also showed lower impulsivity levels as measured by the BIS-11.

Conclusions: It should be noted that response inhibition and interference control, which are considered under the umbrella of inhibitory control, may exhibit different characteristics in adult individuals diagnosed with ADHD and this is important for differential diagnosis. An improvement was observed in the response inhibition of adults with ADHD caused by psychostimulant treatment, which was associated with positive outcomes that were also noticeable by the patients. Understanding the underlying neurophysiological mechanisms of the condition would further facilitate the development of appropriate treatments.

Keywords: Attention deficit hyperactivity disorder, inhibitory control, interference control, impulsivity, response inhibition

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is the most prevalent psychiatric disorder in children, characterized by neurocognitive impairment and impulsivity (1). Furthermore, approximately half of the children diagnosed with ADHD continue to meet the ADHD diagnosis criteria into their adulthood, with the prevalence of adult ADHD reported to be 4%–5% (2,3). The primary problem arising from ADHD is considered to be inhibitory control impairment (4). Inhibitory control is a component of both executive function and behavioral impulsivity (5,6). It has been suggested that inhibitory control is not a singular construct but comprises of "response inhibition," the stopping of a response to an ongoing stimuli, and "interference control," the ability to control the disruptive effect (7). Although there have been reports regarding the interrelation between these two concepts, relevant studies have shown them not to be the same entity.

The Stop-Signal Task (SST) is a popular method used for measuring the response inhibition in a laboratory environment (8). Numerous studies have utilized SST to demonstrate response inhibition impairment in adults with ADHD, which was improved by methylphenidate therapy (9–11). On the other hand, there have been studies that have not found any difference in terms of SST between adults with and without ADHD (12,13).

Highlights

- **Response inhibition was impaired in adults with ADHD compared to the healthy controls, but not interference control.**
- **Psychostimulant treatment improved the response inhibition in adults with ADHD.**
- **Response inhibition and interference control may manifest as different characteristics in adults with ADHD.**

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The Stroop test is used for assessing interference control, which is the ability to control the disruptive effect (14). In a meta-analysis, which evaluated individuals with ADHD based on their interference control, no difference between the individuals diagnosed with ADHD and healthy controls were found, and interference control did not show any change in terms of age (15). Contrarily, certain studies have suggested that interference control was impaired in individuals with ADHD compared to healthy individuals based on different methodologies used for measuring interference control (16).

Methylphenidate is a frequently used treatment for ADHD with proven efficacy (17). A number of studies have found it to be effective not only in childhood but also in adulthood for inhibitory control and the core symptoms of ADHD (11,18). To the best of our knowledge, no study has investigated the effect of methylphenidate treatment on response inhibition and interference control skills.

Although response inhibition and interference control have been typically investigated under the umbrella of inhibitory control, it may be beneficial to investigate those parameters separately to determine the conceptual difference between them. Distinguishing the type of inhibitory control impairment can be imperative for the differential diagnosis and treatment of ADHD. The primary aim of the present study was to investigate the response inhibition and interference control skills of adults with ADHD. The secondary objective was to investigate the effect of methylphenidate therapy on response inhibition and interference control.

METHOD

This is a cross-sectional and observational study. Individuals with ADHD diagnosis (n=42) who were followed up in Dokuz Eylül University, Faculty of Medicine, Department of Psychiatry between 2013–2015 or newly diagnosed were included in the study. Healthy controls (n=43) were selected from the individuals who applied to participate in the study by the flyers handed out in the psychiatric clinic. Written consents of all participants were obtained prior to the commencement of the study. The required approval for conducting the study was obtained from the Ethics Committee of the Faculty of Medicine, Dokuz Eylül University University (Date 24.07.2014/ Number 2014/25-35).

Participants

The participants were aged between 18–65 years and attended a structured clinical interview for DSM-IV axis I disorders conducted by the clinician and developed on the basis of DSM-IV-TR. Following this, all participants were asked in detail about the ADHD diagnostic criteria in the DSM-IV-TR for ADHD, and those who met the criteria were diagnosed with ADHD through clinical interview. The diagnosis of ADHD was supported by applying the Adult Attention Deficit Hyperactivity Disorder Self-Esteem Scale (ASRS), which includes the symptoms of ADHD in adulthood, and the Wender Utah Rating Scale (WURS), which questioned childhood symptoms, and taking into account the cutting scores (ASRS: 24 points, WURS: 36 points). The Hamilton Depression Rating Scale (HAMD-17) and Barratt Impulsiveness Scale-11 (BIS-11) were applied to all the participants. All participants scored ≤7 on HAMD-17. Following the administration of the scales, the participants were subjected to a computer-based SST and Stroop test.

Individuals with a history of degenerative neurological disorders, mental retardation (at a noticeable level during the interview), epilepsy, cerebral tumors, cerebrovascular diseases, loss of consciousness as a result of head trauma, and alcohol or substance abuse were excluded from the study. Furthermore, individuals who received electroconvulsive therapy within the last 6 months and who were administered with benzodiazepines or psychostimulants within the last 24 hours prior to the tests were not included in the study. The individuals in the ADHD group with additional diagnoses of schizophrenia, schizophreniform disorders, schizoaffective disorders, brief psychotic disorders, not otherwise specified psychotic disorders, and bipolar disorders pursuant to DSM-IV-TR, and the healthy controls with any axis I diagnosis under the DSM-IV-TR were excluded from the study.

Stop-Signal Task (SST)

The stop sign task comprises of a practice step, including 32 trials, and an experimental step, including 3 blocks of 64 trials. Each block begins with a white dot in the middle of a black screen on the computer and a square or circle stimulus that appears after 250 ms, signifying the "go signal." The participants were instructed to press the left direction key when a square was displayed and the right direction key when a circle was displayed. In each trial, the participant was prompted to press the direction key for the corresponding shape as quickly as possible after the shape appeared on the screen. Each shape remained on the screen until the participant responded or for a maximum duration of 1.250 ms, following which a new shape was displayed. In one-fourth of the attempts, a sound stimulus (stop signal) was heard immediately after the shapes were displayed, which signaled the participants to stop their response. The participants were instructed to not press any keys for that trial only when they heard that sound.

The time elapsed between the arrival of the stop signal following the go signal is called the "stop signal delay" (SSD). The SSD is initially 250 ms and is progressively prolonged on each subsequent, successful attempt of the participant in response inhibition, and shortened in cases of failure. The response inhibition is easier for shorter SSD and more difficult for longer SSD. The stop-signal response time (SSRT) is not directly observed but calculated by subtracting SSD from the average response time of the individuals participating in the trials with no stop signal. This parameter indicates the time required by the participants to inhibit their response. Longer SSRT is suggestive of difficulty in response inhibition, whereas shorter SSRT indicates successful response inhibition.

Stroop Test

The Stroop test measures the ability to control the disruptive effect (interference control) of an individual. The test comprises of three stages. In the first stage, the participant is asked to identify the colors of three differently colored squares to increase their compliance with the test and initiate the tendency of naming colors. In the second stage, the participant is asked to read the names of the colors written in the three different colors. In the final stage, the participant is asked to identify the color in which the three different colors names have been written. This final stage is related to interference (incongruous response tendency).

Barratt Impulsivity Scale-11 (BIS-11)

BIS-11 is a 30-item Likert-type self-report scale developed for measuring impulsivity. All items are rated over four points. A higher total score is indicative of high impulsivity. There are three separate subdomain scores in addition to the total score: attention, motor, and non-planning. The reliability and validity studies of the scale intended for Turkish speakers were conducted by Hidiroğlu et al. (19).

Statistical Analyses

The IBM SPSS Version 23.0 (Chicago IL, USA) was used for statistical analyses. Chi-Square test was used to compare the categorical variables. Kolmogorov–Smirnov test was used to confirm the normality hypothesis for the continuous data. Student t test was used in the binary group comparisons of the data that conformed to the normal distribution hypothesis. Multifactor analysis of covariance model (MANCOVA) was used for comparing the SST and Stroop test scores between the ADHD and healthy control groups, where age and education level were taken

as covariates, and the groups were compared by post-hoc Bonferroni test. Pearson correlation analysis was performed between the SST, Stroop test, and BIS-11 scores. Mann-Whitney U test was used to compare the SST, Stroop test, and BIS-11 scores between the individuals in the ADHD group who received psychostimulant treatment and those who did not. A p level of <0.05 was considered as statistically significant and the mean ± standard deviation values were provided for all the test results.

RESULTS

An intergroup comparison between the study groups regarding demographic and clinical characteristics is given in Table 1. No significant difference in terms of age, gender, level of education, and employment status between the groups were observed (p=0.81, p=0.740, p=0.399, and p=0.194, respectively). The rate of singlehood or divorce was significantly higher among the adults with ADHD compared to those without an ADHD diagnosis (p=0.034).

Adults with ADHD had significantly shorter SSD and prolonged SSRT compared with the healthy controls as demonstrated by the group comparison with MANCOVA, adjusted for age and level of education, and tested by post-hoc Bonferroni test (p=0.001, p=0.041, respectively). No intergroup difference regarding the Stroop test scores were observed. An intergroup comparison of the SST and Stroop test scores is given in Table 2 and Fig. 1.

On examining the relationship between the Stroop interference, SSD, SSRT and BIS-11 scores across all the groups, a weak and moderately negative correlation between SSD and the attentional, motor, non-planning scores, and total scores of the BIS-11 was found (p<0.001, r=-406; p<0.001, r=–0.418; p=0.002, r=-0.335; and p<0.001 r=-0.426, respectively) and a weak positive correlation was found between SSRT and the attentional, motor, non-planning scores, and total scores (p<0.001, r=0.345; p<0.001, r=0.349; p=0.010, r=278; and p<0.001, r=0.357, respectively).

In terms of age, there was no difference between individuals who used psychostimulants and those who did not (p=0.281 and p=0.516). Adults with ADHD who received psychostimulant treatment had a significantly longer SSD and shorter SSRT compared with those who did

Table 1. Comparison of the demographic and clinical characteristics of the ADHD and HC's

	ADHD (n=42) Mean (SD) / n (%)	HC (n=43) Mean (SD) / n (%)	Test statistic t/χ^2	p
Age	28.48 (8.43)	31.67 (8.28)	-1.764	0.81
Sex (n, %)			0.110	0.740
Male Female	19 (45.2) 23 (54.8)	21 (48.8) 22 (51.2)		
Years of education	13.24 (2.99)	13.81 (3.27)	-0.848	0.399
Employment status			1.690	0.194
Employed Unemployed	34 (81.0) 8 (19.0)	39 (90.7) 4 (9.3)		
Marital status			4.518	0.034
Married Single/Divorced	12 (28.6) 30 (71.4)	22 (51.2) 21 (48.8)		
HAMD-17	1.76 (0.30)	-	-	-
ADHD type				
Attention deficit Hyperactivity Mixed	17 (40.5) 3 (7.1) 22 (52.4)	-	-	-
Psychostimulant				
Yes No	13 (31.0) 29 (69.0)	-	-	-
BIS-11				
Attention Motor Non-planning Total score	23.24±4.15 26.36±4.51 30.29±4.78 79.88±10.74	14.81±3.13 17.93±4.00 22.14±4.44 54.88±9.30	11.482 10.570 9.124 8.146	<0.001 <0.001 <0.001 <0.001

ADHD: Attention deficit hyperactivity disorder; BIS-11: Barratt Impulsiveness Scale; HAMD-17: The Hamilton Depression Rating Scale-17; HC: healthy control ; n: number; SD: Standard deviation.

Table 2. Comparison of the Stop-Signal Task and Stroop test scores between ADHD and HC groups

	ADHD (n=42)	HC (n=43)	Test statistic F	p
Stop-Signal Task				
SSD SSRT	421.65±177.15 320.97±88.35	555.78±149.82 289.16±61,81	11.594 4.333	0.001 0.041
Stroop interference	43.74±20.28	38.79±19.27	1.905	0.171

ADHD: Attention deficit hyperactivity disorder; HC: healthy control; SSD: Stop signal delay; SSRT: Stop-signal response time.

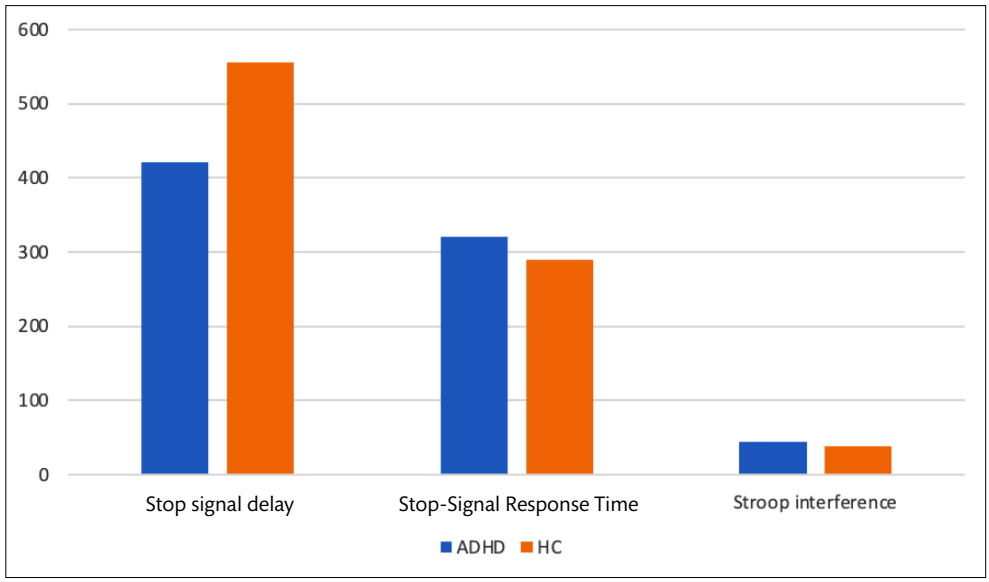

Figure 1. Comparison of Stop-signal task and Stroop test scores between ADHD and HC groups. ADHD: Attention deficit hyperactivity score; HC: Healthy control

Table 3. Comparison of the Stop-Signal Task, Stroop test, and BIS-11 scores of individuals diagnosed with ADHD in terms of psychostimulant treatment

	Patients with psychostimulant (n=13)	Patients without psychostimulant (n=29)	Test statistic Z	p
Stop-signal Task				
SSD	524.48±53.58	375.55±28.07	-2.353	0.019
SSRT	254.35±61.60	350.84±15.33	-3.251	0.001
Stroop interference	35.85±4.19	47.28±21.59	-1.934	0.053
BIS-11				
Attention	21.15±5.08	24.17±3.36	-1.467	0.143
Motor	24.00±3.19	27.41±4.66	-2.334	0.020
Non-planning	27.92±4.90	31.34±0.82	-2.048	0.041
Total score	73.08±10.62	82.93±9.46	-2.669	0.008

BIS-11: Barratt Impulsiveness Scale-11; SSD: Stop signal delay; SSRT: Stop-signal response time.

not receive psychostimulant treatment (p=0.019, p=0.001, respectively). No significant difference by Stroop interference time was observed between adults with ADHD who received psychostimulant treatment and those who did not (p=0.053). Furthermore, the BIS-11 motor, non-planning, and total scores were significantly lower in the adults with ADHD who received psychostimulant treatment compared with those who did not (p=0.020, p=0.41, and p=0.008, respectively), and no significant difference by the BIS-11 attention scores between both the groups was observed (p=0.143). A comparison of the SST, Stroop test, and BIS-11 scores of the adults with ADHD in terms of psychostimulant administration is given in Table 3.

DISCUSSION

The present study demonstrated impairment in response inhibition in adults with ADHD compared to healthy controls, whereas no difference in interference control was observed between the groups. A wealth of data has been presented in the relevant literature regarding impaired response inhibition in adults with ADHD (9,10). However, studies on interference control in adults with ADHD have reported inconsistent results (15,16). Regarding the response rate, there have been consistent findings concerning the lack of difference in interference control between adults with ADHD and healthy individuals (20,21). This suggests that the impaired interference control observed in adults with ADHD is potentially associated with a prolonged response time. In 2004, Lustig et al. (22) suggested that the Stroop test and SST served a similar inhibitory function, including suppressing strong but incongruous responses, and that the performances on the two tasks were interrelated and reflected a common basic structure. Conversely, there have been other studies, which have suggested that these two tests are unrelated and associated with independent characteristics in different patient groups and possessed different inhibition mechanisms (23,24). The primary difference between the tests is that the Stroop test involves occasionally ceasing a previously well-learned stimulus, whereas SST involves attempts in stopping a newly learned stimulus at each occasion (25). Response inhibition is the ability to stop a dominant and powerful or already initiated response, while interference control is the ability to control the distracter effect, and thus, these two tasks can be considered to reflect different structures. Despite the fact that those two components have been mostly investigated under the umbrella of inhibitory control, a separate examination may help in differential diagnosis because relevant studies suggested that the manifestation of the two components varied among adults with ADHD. The difference in response inhibition and interference control in individuals with ADHD may be indicative of their association with different neurobiological mechanisms. In ADHD, it was demonstrated that not only the frontostriatal circuits but also the frontoparietal, dorsal attention, motor, visual, and default connection networks were affected (26). Although it is known that impaired response inhibition and interference control in ADHD are associated with the abnormal functioning of the anterior cingulate cortex, dorsolateral prefrontal cortex, anterior prefrontal cortex, lateral cerebellum, anterior insula,

caudate, and inferior parietal lobe, the exact neural networks that differ in the impairment of response inhibition and interference control are yet to be uncovered (9,26).

In this study, the attentional, motor, non-planning scores, and total BIS-11 scores showed weak and moderately negative and weak positive correlations with SSD and SSRT, respectively. Relevant studies have suggested that the motor and total impulsivity scores as measured by the BIS-11 were associated with SSRT (27). Inhibitory control is considered as a parameter of executive function; however, it is also linked to impulsivity, defined as a predisposition to respond quickly and in an unplanned manner to stimuli without considering the long-term adverse consequences of one's actions or without adequate precognition (27). Furthermore, impulsivity was suggested to be a result of impaired executive functions paired with a strong impulse (28). The behavioral dimension of impulsivity is considered to be measured by SST (27). Relevant literature has demonstrated an impairment in SST in certain disorders characterized by behavioral impulsivity, including ADHD, substance abuse disorder, and compulsive gambling (29).

On the contrary, the present study found that adults with ADHD who received methylphenidate treatment showed better performance in response inhibition skills compared with untreated individuals, and their impulsivity levels, as measured by the BIS-11, were also lower. Methylphenidate treatment has been associated with improved inhibitory control (11,18). Functional magnetic resonance imaging studies involving inhibitory tasks have indicated that methylphenidate treatment normalized brain activation patterns by increasing activation in the frontostriatal circuits in children with ADHD (30). Furthermore, it was shown that the default mode network, which is not suppressed during inhibitory control in children with ADHD, could be adequately suppressed by methylphenidate treatment (31). A limited number of studies have been conducted on the effects of methylphenidate treatment on inhibitory control and associated brain circuits in adults diagnosed with ADHD (32). Although adults with ADHD who received methylphenidate therapy during the study did not take daily doses of methylphenidate prior to testing, regular methylphenidate use may be associated with improved inhibitory control with a cumulative effect. It is well-established that as the prolonged use of methylphenidate is associated with improved performance in a variety of fields, and especially education in individuals with ADHD (33).

The fact that the individuals in the ADHD group belonged to different subtypes (attention deficit predominant type, hyperactivity-impulsivity dominant type, mixed type) constituted one of the limitations of the present study. The inhibitory control results could not be compared between the ADHD subtypes because an adequate sample size could not be achieved. Various studies have emphasized the association of SST and Stroop test with different parameters of impulsivity (27). Hence, it is difficult to comment on the inhibitory control properties specific to the ADHD subtypes. Furthermore, although there was an improvement in the inhibitory control mechanisms due to psychostimulant use, it is necessary to report reproducible results in larger sample groups to reach a general consensus, given the limited sample size in the present study. Another limitation of the present study is that it was designed as a cross-sectional study, so further longitudinal studies would be able to clearly determine the effects of methylphenidate on response inhibition and interference control.

It is widely accepted that executive functions are adversely affected in ADHD. The results of the present study conclude that the ability to inhibit response was the most affected inhibitory control component in ADHD, showing significant improvement with methylphenidate treatment. The fact that response inhibition and interference control skills, which have been typically considered under the definition of inhibitory control despite different clinical manifestations, vary in adults with ADHD suggests that these two components should be used in the differential diagnosis. Accordingly, the results of the present study should be supported by future research of a similar nature. Further studies with larger samples and employing brain imaging methods would be useful in understanding the underlying neurobiological mechanisms of the condition and developing the appropriate treatments.

Ethics Committee Approval: The required approval for conducting the study was obtained from the Ethics Committee of the Faculty of Medicine, Dokuz Eylül University University (Date 24.07.2014/ Number 2014/25-35).

Informed Consent: Written consents of all participants were obtained prior to the commencement of the study.

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