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## Executive functions in adolescents with gender dysphoria

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### ABSTRACT

**Aim:** Aim of this study is evaluating EF by performing neurocognitive tests, and to identify gender-related differences in EF between adolescents with and without GD.

**Methods:** 8 Female-to-Male transgender adolescents (FtMs), and 14 Male-to-Female transsexual adolescents (MtFs) (Gender Dysphoria Group, GDG) and 29 boys, 21 girls (Control Group, CG), were tested in a cross-sectional study, using the Wisconsin Card Sorting Test (WCST), Controlled Oral Word Association Test (COWAT), and Stroop Color and Word Test (SCWT). The psychiatric diagnoses were established by using the KD-SADS.

**Results:** Among GDG 72.7%, had at least one psychopathology. There weren't any significant differences in, estimated IQ scores, or WCST subtest scores between the 2 groups. COWAT total word count and SCWT-5 total duration test scores were better in the CG.

**Conclusion:** CG had better performance on verbal fluency and response inhibition whereas no differences found on set shifting abilities. In consideration of the existence of EF-related impairment in adolescents with GD, appropriate support and interventions are expected to improve their adaptation skills and comorbid psychopathologies. These results should be interpreted cautiously and additional larger scale studies are needed to obtain more comprehensive data related to gender differences in EF of adolescents with GD.

### KEYWORDS

Adolescents; executive functions; gender dysphoria; neurocognition

### HIGHLIGHTS

1. Adolescents with Gender Dysphoria had high rates of co-morbid psychopathology.
2. The control group had significantly better response inhibition and verbal fluency scores than the GD group.
3. There were no significant difference in set shifting abilities between two groups.

## Introduction

Referrals to clinics that specialize in gender dysphoria (GD) have been increasing significantly (Zucker, 2019) and in response standardized manuals for the management of GD in adolescents have been published worldwide (Coleman et al., 2012; Janssen & Leibowitz, 2018). While the individual etiological effects of biological, psychological, and social factors were highlighted in the past, current studies emphasize an integrative biopsychosocial model for GD (Fausto-Sterling et al., 2015; Kaltiala-Heino et al., 2018; Steensma et al., 2013).

Executive function (EF) refers to a family of top-down mental processes associated with goal-directed behaviors (Diamond, 2013). There are 3 fundamental EFs: inhibition; working memory; cognitive flexibility. In addition, reasoning, problem solving, and planning are higher level EFs that develop from these 3 core skills (Diamond, 2013). Some EFs may exhibit gender-specific variation. For example, females tend to have slightly better verbal fluency, information processing, and spatial organization scores (Anderson et al., 2001; Scheuringer & Pletzer, 2017), whereas males may

perform better on spatial working memory tasks (Gaillard et al., 2021). To the best of our knowledge there are only a limited number of studies on EF and neurocognition in GD/transgender individuals. Soleman et al. reported that male to female transgender adolescents tend to outperform birth assigned males, female to male transgenders, and even birth-assigned females on such female-favoring tasks as verbal fluency (Soleman et al., 2013). Moreover, Schöning et al. (2010) observed that spatial abilities in birth-assigned males were better than in male-to-female transgenders.

The most common comorbid psychiatric disorders in adolescents with GD are anxiety and depression (10–60%) (Chen et al., 2021; Connolly et al., 2016) also adolescents with GD have, on average, higher rates of autism spectrum disorders and other neurodevelopmental disorders (Warrier et al., 2020). Clinical exacerbation of anxiety and depression shows that they can negatively affect such EF resources as concentration, planning, inhibition, working memory, and cognitive flexibility (Park & Moghaddam, 2017). Moreover, the characteristics of autism spectrum disorder (ASD)-related neurodiversity can interact with gender diversity-

related needs, posing a difficult puzzle to solve on EF (Strang et al., 2018). Also of note, the relationship between mental health and EF is bidirectional; whereas emotional, social, or physical stress and chronic psychiatric disorders can negatively affect EF skills (Diamond, 2013), EF dysfunction can exacerbate psychiatric disorders (Zainal & Newman, 2018).

EF in adolescents with GD are affected by experiencing a gender different than that assigned at birth, as well as the associated emotional and social challenges. Depletion of available EF resources might occur as a result of comorbid psychiatric conditions, as well as excessive EF demands that are primarily related to navigating interpersonal interactions, self-advocating for gender-related needs, and affirming a gender different than that assigned at birth (Strang et al., 2022). Accordingly, the present study aimed to evaluate EF skills by performing neurocognitive tests, and to identify gender-related differences in EF between adolescents with and without GD.

## Methods

### Study design and participants

This cross-sectional study (Gender Dysphoria Group-GDG) included 22 adolescents aged 10–17 years that met the DSM-V diagnostic criteria for GD and their parents, and 50 age- and natal sex-matched adolescent controls (control group-CG). All of the adolescents were being followed-up by the Marmara University, School of Medicine, Child and Adolescent Psychiatry Clinic. None of the participants had ever received any type of gender-affirming hormonal treatment.

All the participants were administered the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version-Turkish Version (K-SADS-PL-T) to screen for psychiatric disorders. Exclusion criteria included the following: mental retardation (Wechsler Intelligence Scale for Children-Revised [WISC-R] verbal, performance, and/or total score <70), chronic or severe medical conditions, and such neurological diseases as seizure, and psychosis. Due to the limited number of cases in the GD group, comorbid psychiatric disorders other than those mentioned above were not considered exclusionary. In all, 2 adolescents were excluded from the GD group after being diagnosed with mild mental retardation. The study protocol was approved by the local ethics committee (protocol number 09.2017.436), and the adolescents and/or their parents provided written informed consent.

### Clinical measures, psychopathology

Sociodemographic data for the adolescents were collected using a sociodemographic information form developed by the researchers. DSM-IV Axis I diagnoses were made via administration of K-SADS-PL-T (Gökler et al., 2004) to all the adolescents and their parents. Psychiatric disorders that

could not be diagnosed based on K-SADS-PL-T were diagnosed with DSM-5 based clinical evaluation.

### EF assessment

WISC-R and the Wechsler Adult Intelligence Scale (WAIS) were administered in both groups to calculate estimated full-scale IQ scores. Estimated IQ was derived using the Booker and Cyr Formula (Booker & Cry, 1986), and the Vocabulary and Block Design subtests. The WISC-R Turkish version was reported to be valid and reliable (Savaşır & Şahin, 1994). EF, including cognitive flexibility, verbal fluency, and response inhibition, were evaluated using the Wisconsin Card Sorting Test (WCST), Controlled Oral Word Association Test (COWAT), and Stroop Color and Word Test (SCWT).

The WCST computer version was used to evaluate cognitive flexibility (Heaton & Staff, 1993), and WCST-3 total correct number score and WCST-4 categories completed score were used. COWAT was used to evaluate verbal fluency (Benton, 1968) based on the total word score. The COWAT Turkish version was reported to be valid and reliable (Sahin-Aközel et al., 2006). Response inhibition was evaluated based on SCWT-5 completion period scores (Golden & Freshwater, 1978; Stroop, 1935). The SCWT Turkish version was reported to be valid and reliable (Karakaş et al., 1999).

### Statistical analysis

IBM SPSS Statistics for Windows v.21.0 (IBM Corp., Armonk, NY) was used for statistical analysis. The chi-square ( $\chi^2$ ) test and Fisher's exact test were used to analyze categorical data, and Student's *t*-test was used to analyze continuous data. The Mann-Whitney U Test was used to compare 2 non-parametric groups and Kruskal-Wallis variance analysis (KW) was used to compare multiple non-parametric groups. Analysis of covariance was used to test the main and interaction effects of categorical variables on a continuous dependent variable. The level of statistical significance was set at  $p \leq 0.05$ .

## Results

### Demographic and clinical characteristics

There wasn't a significant difference in mean age between the GD group and control group. The GD group included 8 birth assigned female to males (FtMs) and 14 birth assigned male to female adolescents (MtFs), and the control group included cisgender 21 birth assigned female and 29 birth assigned male adolescents. Maternal age was significantly higher in the GD group than in the control group ( $p = 0.047$ ). There weren't any significant differences in paternal age, number of family members, number of siblings, or monthly income per person between the 2 groups. Parental level of education did not differ significantly between the 2 groups (Table 1).

**Table 1.** Sociodemographic variables in the GD and control groups.

	GD group (n = 22)	Control group (n = 50)	Statistical analysis
	n (%)	n (%)	
Sex (female)	8 (34.4%)	21 (42%)	$\chi^2 = 0.202, p = 0.653$
Mother's level of education			
Illiterate	1 (4.5%)	2 (4%)	$\chi^2 = 6.188, p = 0.186$
Primary school	10 (45.5%)	22 (44%)	
Secondary school	1 (4.5%)	12 (24%)	
High school	8 (36.4%)	8 (16%)	
University	2 (9.1%)	6 (12%)	
Father's level of education			$\chi^2 = 1.151, p = 0.765$
Primary school	9 (40.9%)	15 (30%)	
Secondary school	3 (13.6%)	8 (16%)	
High school	6 (27.3%)	19 (38%)	
University	4 (18.2%)	8 (16%)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Age	14.10 $\pm$ 2.37	14.41 $\pm$ 2.28	$Z = -0.619, p = 0.536^b$
Age of mother at birth, years	30.07 $\pm$ 6.03	26.03 $\pm$ 5.80	<b><math>t = 2.692, p = 0.009^a</math></b>
Age of father at birth, years	33.66 $\pm$ 6.52	30.59 $\pm$ 5.75	<b><math>t = 2.006, p = 0.049^a</math></b>
Number of siblings	2.82 $\pm$ 1.56	2.48 $\pm$ 1.49	$Z = -1.046, p = 0.295^b$
Monthly income per person (TL)	859.09 $\pm$ 423.32	920.60 $\pm$ 414.99	$Z = -0.518, p = 0.605^b$

<sup>a</sup>Student's *t*-test. <sup>b</sup>Mann-Whitney U test. GDG: Gender dysphoria group; CG: control group; TL: Turkish Lira. Bold represents statistically significant differences.

**Table 2.** Assessment of EF in the GD and control groups.

	GD group (n = 22) Mean $\pm$ SD	Control group (n = 50) Mean $\pm$ SD	Statistical analysis
Vocabulary test score	10.68 $\pm$ 3.82	11.48 $\pm$ 2.33	$t = -1.090, p = 0.372, \text{Eta}^2 = 0.253^a$
Block design test score	10.31 $\pm$ 2.99	11.32 $\pm$ 2.81	$t = -1.363, p = 0.177, \text{Eta}^2 = 0.348^a$
Estimated IQ score	103.22 $\pm$ 17.98	110.06 $\pm$ 15.94	$t = -1.611, p = 0.112, \text{Eta}^2 = 0.036^a$
WCST3: Total number correct	90.57 $\pm$ 16.95	95.24 $\pm$ 14.13	$Z = -1.028, p = 0.304, \text{Eta}^2 = 0.121^b$
WCST4: Categories completed	5.57 $\pm$ 2.56	6.26 $\pm$ 2.34	$Z = -0.949, p = 0.343, \text{Eta}^2 = 0.112^b$
COWAT-Total word count	33.00 $\pm$ 12.79	39.96 $\pm$ 10.58	<b><math>Z = -2.587, p = 0.010, \text{Eta}^2 = 0.305^b</math></b>
SCWT-5 Total duration	29.34 $\pm$ 9.83	23.82 $\pm$ 7.09	<b><math>Z = -2.287, p = 0.022, \text{Eta}^2 = 0.269^b</math></b>

<sup>a</sup>Student's *t*-test. <sup>b</sup>Mann-Whitney U test. GDG: Gender dysphoria group; CG: control group; WCST: Wisconsin Card Sorting Test; COWAT: Controlled Oral Word Association Test; SCWT: Stroop Color and Word Test. Bold represents statistically significant differences.

In the GD group 72.2% had psychopathologies, including depression (72.7%,  $n = 16$ ), oppositional defiant disorder (ODD) (45.5%,  $n = 10$ ), specific phobia (22.7%,  $n = 5$ ), attention deficit hyperactivity disorder (ADHD) (18.2%,  $n = 4$ ), separation anxiety disorder (18.2%,  $n = 4$ ), conduct disorder (9.1%,  $n = 2$ ), and social anxiety disorder (4.5%,  $n = 1$ ). In the control group 2 adolescents were diagnosed as anxiety disorder, 2 as ADHD, and 1 as depression.

### Assessment of EF

EF assessment results are shown in Table 2. Although there weren't any significant differences in Vocabulary test scores, Block Design scores, estimated IQ scores, or WCST subtest scores between the 2 groups, COWAT total word count and SCWT-5 total duration test scores were better in the control group. After adjusting for age, the control group still had higher COWAT total word count scores ( $F(1, 69) = 5.439, p = 0.023, \text{partial eta squared} = 0.073$ ) and lower SCWT-5 total duration test scores ( $F(1, 69) = 7.110, p = 0.010, \text{partial eta squared} = 0.093$ ).

After dividing the GD and control groups into subgroups (GD group-assigned female at birth [GDG-F], GD group-assigned male at birth [GDG-M], control group-assigned female at birth [CG-F], and control group-assigned male at birth [CG-M]), there were significant differences in COWAT total word count scores (Table 3). Pair-wise comparisons between the subgroups (using Bonferroni

correction) showed that the GDG-M subgroup had significantly lower CWFT total word count scores than the CG-F subgroup ( $Z = -2.830, p = 0.004$ ); after controlling for the effect of age there was still a significant difference between these 2 subgroups ( $F(3, 67) = 2.894, p = 0.042, \text{partial eta squared} = 0.115$ ).

### Discussion

The present study compared psychopathology and EF in adolescents with GD, and in age- and sex-matched controls. Parental level of education, family profiles, and level of income did not differ significantly between the GD and control groups; however, adolescents with GD had higher maternal and paternal age at birth; considering the biological basis of GD, this could prove to be an interesting avenue for further investigation. It is known that advanced maternal and paternal age constitute a risk for some disorders related to psychopathology (Sandin et al., 2012). Although to the best of our knowledge only a limited number of studies examined parental age in individuals with GD, accumulated genetic mutations or exposure to toxic substances that affect gene expression might predispose to GD and although speculative, it constitutes an area worthy of closer examination.

Similar to earlier reports, 75% of the present study's GD group had  $\geq 1$  psychopathology (Connolly et al., 2016; Dawson et al., 2017; Yazkan Akgül et al., 2020). The most

**Table 3.** Neurocognitive abilities in the four subgroups.

	GDG-F ( <i>n</i> = 8) Mean ± SD	GDG-M ( <i>n</i> = 14) Mean ± SD	CG-F ( <i>n</i> = 21) Mean ± SD	CG-M ( <i>n</i> = 29) Mean ± SD	Statistical analysis
Vocabulary Test Score	10.62 ± 4.17	10.71 ± 3.77	11.33 ± 2.12	11.58 ± 2.50	<i>F</i> = 0.418, <i>p</i> = 0.741, Eta <sup>2</sup> = 0.018 <sup>a</sup>
Block Design Score	9.37 ± 2.72	10.85 ± 3.10	12.04 ± 2.85	10.79 ± 2.71	<i>F</i> = 1.892, <i>p</i> = 0.139, Eta <sup>2</sup> = 0.077 <sup>a</sup>
Estimated IQ Score	98.62 ± 10.59	105.85 ± 21.01	112.23 ± 15.54	108.48 ± 16.30	<i>F</i> = 1.388, <i>p</i> = 0.254, Eta <sup>2</sup> = 0.058a
WCST3: Total number correct	98.00 ± 14.44	86.00 ± 17.26	94.80 ± 14.54	95.55 ± 14.08	KW = 5.039, <i>p</i> = 0.169 Eta <sup>2</sup> = 0.071 <sup>b</sup>
WCST4: Categories completed	6.37 ± 2.87	5.07 ± 2.32	6.23 ± 2.18	6.27 ± 2.49	KW = 2.700, <i>p</i> = 0.440 Eta <sup>2</sup> = 0.038 <sup>b</sup>
COWAT-Total word count	35.37 ± 14.59	31.64 ± 12.00	42.71 ± 9.85	37.96 ± 10.81	<b>KW = 9.717, <i>p</i> = 0.021</b> <b>Eta<sup>2</sup> = 0.136<sup>b</sup></b>
SCWT-5 Total duration	29.59 ± 10.94	29.20 ± 9.56	23.16 ± 5.84	24.29 ± 7.94	KW = 5.384, <i>p</i> = 0.146 Eta <sup>2</sup> = 0.075 <sup>b</sup>

<sup>a</sup>ANOVA. <sup>b</sup>Kruskal–Wallis test. GDG-F: Gender dysphoria group-assigned female at birth; GDG-M: gender dysphoria group-assigned male at birth; CG-F: control group-assigned female at birth, CG-M: control group assigned male at birth; WCST: Wisconsin Card Sorting Test; COWAT: Controlled Oral Word Association Test; SCWT: Stroop Color and Word Test. Bold represents statistically significant differences.

common psychopathologies noted in the GD group were anxiety and depression (internalization problems), and ODD and ADHD (externalization problems). A recent study reported that compared to cisgender individuals, transgender individuals had higher rates of ADHD, bipolar disorder, depression, learning disorder, obsessive compulsive disorder, and schizophrenia, even after accounting for level of education and age (Warrier et al., 2020). Considering that psychopathology can negatively affect EF, including inhibition, flexibility, and working memory, it is possible to detect high rates of psychopathology and EF impairment in clinical samples. Moreover, in the present study the ADHD rate was higher in the GD group. ADHD prevalence studies report that the disorder is more common in males (Polanczyk et al., 2014). The higher incidence of ADHD in the present study's GD group highlights the inadequacy of explaining the etiology of GD based on social, psychodynamic, and environmental factors only, which is supported by the high rates of ASD in individuals with GD that were recently reported (Øien et al., 2018; VanderLaan et al., 2015). Based on these findings, it should be kept in mind that executive dysfunction in individuals with GD might be indirectly due to ADHD or autism spectrum disorder-related symptoms. In essence, gendered behaviors are most probably the result of genes related to gender identification, gonadal hormones, socialization, and cognitive functions (Hines, 2011). Furthermore, in the present study comorbid diagnoses were not investigated comprehensively, and disorders that can impair cognitive processes, such as mental retardation, and psychosis, were exclusionary. The specialized effect of comorbid psychopathologies on cognitive processes in transgender individuals is worthy of further research.

Among the most striking of the present study's findings is that the control group had significantly better response inhibition and verbal fluency scores than the GD group. Problems with inhibition, which is a primary component of EF dysfunction, is also seen in patients with various psychiatric disorders, such as ADHD, conduct disorder, autism, depression, and anxiety disorders (Diamond, 2013). Whereas symptoms of ASD are associated with low-level inhibition and flexibility in GD adolescents, symptoms of anxiety are

associated with low-level inhibition, flexibility, and working memory (Strang et al., 2022). An earlier study on GD in adolescents used the Behavior Rating Inventory of Executive Function (BRIEF) scale to evaluate EF and reported that the GD group had widespread EF dysfunction (Akgül et al., 2018). As seen in the present study, impaired response inhibition in individuals with GD might be due to the high rate of comorbid psychopathologies, especially ADHD. On the other hand, impulsive behavior patterns, including discovery of new gender identities, in the adolescents with GD might have resulted from their impaired inhibition. Interestingly, though, the present findings show that set shifting, which may be related to flexibility in daily life, was unaffected in the GD group. The set shifting task in most earlier studies was assessed using various scales (Strang et al., 2022; Yazkan Akgül et al., 2020), whereas in the present study it was assessed via one-to-one tests, which suggests that EF impairment might not be as pervasive in adolescents with GD as hypothesized.

The verbal fluency test scores in the present study are another notable finding. The control and GD groups were divided into four subgroups according gender assigned at birth. The only significant difference observed between the four subgroups was verbal fluency—a gender-biased skill that is known to be superior in females (Cohen-Kettenis et al., 1998; Soleman et al., 2013). Accordingly, verbal fluency scores in the present study were highest in the CG-F subgroup, followed by CG-M, GDG-F, and GDG-M subgroups, even after controlling for age. Although the GD group had lower verbal fluency scores than the control group, the GDG-F subgroup scored better than the GDG-M subgroup.

Some earlier previous studies reported that certain neurocognitive functions and EF in transgender individuals correlated with their gender identity (Berglund et al., 2008; Cohen-Kettenis et al., 1998; Lin et al., 2014; Luders et al., 2012; Soleman et al., 2013), whereas others reported they were not (Haraldsen et al., 2003; Hoekzema et al., 2015; Luders et al., 2009). The inconsistency in these findings might be due to differences in methodology and the limited number of cases studied (Nguyen et al., 2019) Numerous

cross-sectional studies show a substantial correlation between having an autism spectrum disorder and being transgender or gender nonconforming (Warrier et al., 2020), this comorbidity might have had an effect on verbal skills. Longer term research that follows up these changes over time might yield more useful data. Lastly, response inhibition and set shifting skills did not differ significantly between the present study's four subgroups. The difference in response inhibition between the GD and control groups disappeared when they were divided into four subgroups according to gender assigned at birth. These findings indicate that larger scale studies are required.

### Strengths and limitations

The present study evaluated biased gender differences in EF between adolescents with and without GD. The Marmara University, School of Medicine, Child and Adolescent Psychiatry Clinic is among the limited number of specialized centers where adolescents with GD are followed-up. Nevertheless, because of social prejudices adolescents may avoid referral for GD and GD in adolescents may be under reported; this might have limited the representativeness of the present study's GD group, which is a limitation. Another limitation is the small sample size. In particular, the small size of the GDG-M subgroup made it difficult for the statistical analyses to provide unambiguous and significant data. Additional larger scale studies are needed to obtain more comprehensive data related to gender differences in adolescents with GD. Moreover, psychiatric disorders, such as anxiety, depression, autism, and ADHD, might impair EF in adolescents. In order to identify EF impairment, it is important to screen for comorbid psychopathologies, so as to achieve elimination or covariation of their possible effects. Accordingly, examination of EF in a clinical sample with psychopathologies as a third study group might improve the reliability of the present findings.

To the best of our knowledge the present study is the first from Turkey to examine GD in adolescents based on a neurocognitive perspective. As such, we think the clinical relevance of this study, that there might be a neurocognitive basis of GD is twofold, but there remains much to work to do. Further investigations should aim to include the effects of hormonal treatments on EF in transgender individuals in an effort to promote the most effective treatment methods possible.

### Acknowledgements

The authors thank all the participants and their families whose participation made this study possible. The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Ethical approval

All study procedures were performed in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

### Informed consent

All the participants, both patients and parents, provided written informed consent for inclusion in the study.

### Disclosure statement

The authors declare there are no conflicts of interest—financial or otherwise—related to the material presented herein.

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