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Abstract

Like drug addiction, pathological gambling (PG) has been associated with impairments in executive functions and alterations in dopaminergic functioning; however, the role of dopamine (DA) in the executive profile of PG remains unclear. The aim of this study was to identify whether the DRD2/ANKK1 Taq1A-rs1800497 and the DAT1-40 bp VNTR polymorphisms are associated with cognitive flexibility (measured by Wisconsin Card Sorting Test (WCST) and Trail Making Test (TMT)) and inhibition response (measured by Stroop Color and Word Test (SCWT)), in a clinical sample of 69 PG patients. Our results showed an association between DA functioning and cognitive flexibility performance. The Taq1A A1+ (A1A2/A1A1) genotype was associated with poorer TMT performance ($p < 0.05$), while DAT1 9-repeat homozygotes displayed better WCST performance ($p < 0.05$) than either 10-repeat homozygotes or heterozygotes. We did not find any association between the DRD2 or DAT1 polymorphisms and the inhibition response. These results suggested that pathological gamblers with genetic predispositions toward lower availability of DA and D2 receptor density are at a higher risk of cognitive flexibility difficulties. Future studies should aim to shed more light on the genetic mechanisms underlying the executive profile in PG.

Keywords

Addiction, cognition, cognitive flexibility, dopamine, dopamine receptor, dopamine transport, executive functions, gambling, genetics, inhibition response, pathological gambling, polymorphism

Introduction

Pathological gambling (PG) is the diagnostic term used to describe excessive and interfering patterns of gambling (American Psychological Association, 2000). PG is considered a behavioral or non-substance-related addiction, since pathological gamblers share certain common features with drug users, includ- ing tolerance, withdrawal and repeated unsuccessful attempts to restrain or stop their habit (Prakash et al., 2012). Like drug addic- tion, PG is also associated with executive function impairments. Executive functions (EF) are higher-order, cognitive capacities that allow persons to orient toward the future, display self-control

and effectively have goal-oriented behavior (Stuss and Alexander, 2000). In this regard, pathological gamblers show a dysfunc- tional executive profile characterized by deficits in cognitive flexibility, inhibition response, planning and decision-making (Goudriaan et al., 2006; Lawrence et al., 2009).

Of all the signals involved in EF, dopamine (DA) has been the most thoroughly investigated (Savitz et al., 2006). The anatomical distribution of DA projections, which originate in the ventral teg- mental area of the midbrain and project to the prefrontal cortex (PFC), anterior cingulate cortex and basal forebrain (Bannon and Roth, 1983), offers a reasonable basis for suggesting a role for DA in EF (Floresco and Magyar, 2006). In addition, psychopharmaco- logical studies show that administration of dopaminergic drugs might result in opposite effects on cognitive performance (Cools and D'Esposito, 2011), mainly on executive tasks (Mattay et al., 2003; Mehta et al., 2004). In fact, administration of DA drugs is associated with a positive or negative effect on executive func- tions, depending on if the baseline executive efficiency level is low or high. These findings led to a proposed model in which the association between cognition and DA follows an 'inverted-U- shaped' function, defining an optimal DA level depending on the cognitive task (Cools and D'Esposito, 2011). In humans, evidence supporting this theory comes from studies allowing for genetic differences between individuals (Frank and Fossella, 2011).

Genes regulating DA transmission are of obvious interest in pathological gambling, due to the compelling evidence that the mesocorticolimbic DA system is a core component of the natural reward system, and is directly or indirectly activated by all abused drugs and behavioral addictions (Hyman et al., 2006; Zack and Poulos, 2009). Specifically, genetic differences in DA are associ- ated with drug addiction, including amphetamine (Mattay et al., 2003) or alcohol use (Noble, 2000). As for PG, alterations in DA functioning have been proposed as underlying the reward capacity of gambling, by activating the release of DA both in healthy con- trols and in pathological gamblers (Zack and Poulos, 2009). There is also evidence of an association between the DA response and unpredictable reward in PG patients, whom display an appreciably higher heart rate response and increased plasma levels of DA while gambling (Meyer et al., 2004; Joutsa et al., 2012).

Typically, the executive-related effects of DA are attributed to modulation of the prefrontal cortex (PFC); however, recent stud- ies highlight a complementary role for DA in the striatum, in executive functioning (Leber et al., 2008). Dopaminergic func- tioning in the striatum depends on both the level of DA available (which in turn depends on DA reuptake via the dopamine trans- porter [DAT]), and on DA receptor binding and activity, mainly D2 receptors (Cropley et al., 2006). The DA receptor D2 (DRD2) is a G protein-coupled receptor located on postsynaptic dopamin- ergic neurons and is associated with a protective effect on cogni- tion (Kemppainen et al., 2003). The *DRD2* gene encoding this receptor is located on chromosome 11q23, and most studies have focused on the Taq1A (rs1800497) polymorphism (Neville et al., 2004; Noble, 2003), which was recently shown to map in the neighboring ankyrin repeat and 'kinase domain containing 1' (*ANKK1*) gene (Neville et al., 2004). The prevalence of the mutated A1 allele (amino acid: K, nucleotide base: T) is 28%, and A1 carriers show a 30–40% reduction in D2 receptor density (Ritchie and Noble, 2003). The A1 allele has been associated with EF, with A1 carriers showing both higher and lower perfor- mance in impulsivity (Eisenberg et al., 2007; White et al., 2008), inhibition response (Markett et al., 2011; Reuter et al., 2005) and cognitive flexibility (Markett et al., 2011; Stelzel et al., 2010).

The DAT is a protein that plays a decisive role in DA func- tioning, while removing DA from the extracellular space (Bannon et al., 2001). A variable number tandem repeat (VNTR) polymor- phism of the *DAT1* gene (SLC6A3), resulting in variants that range from 3–13 repeats (with the 9- and 10-repeats occurring most commonly (Bannon et al., 2001). It was studied in depth and its length related to DAT expression and DA availability (Mill et al., 2002). The 9-repeat allele is associated with lower

DAT expression and, as a result, with higher levels of DA in the synaptic cleft (Mill et al., 2002). It has been demonstrated that 9-repeat carriers have better EF performance, including working memory, attention processes and impulsivity (Loo et al., 2003; Brehmer et al., 2009; Simon et al., 2011). Neuroimaging studies also suggest that 10-repeat allele homozygotes show increased activation in brain areas underlying executive tasks, indicating that executive functioning requires greater effort in this group (Braet et al., 2011; Gordon et al., 2013).

Despite evidence of the involvement of the dopaminergic sys- tem in EF, there appear to be no genetic studies linking EF per- formance with DRD2 and DAT functioning in pathological gamblers. We aimed to investigate the association between cog- nitive flexibility (measured by Wisconsin Card Sorting Test (WCST) and Trail Making Test (TMT)) and inhibition response (measured by Stroop Color and Word Test (SCWT)), and poly- morphisms in genes encoding DRD2/ANKK1 (Taq1A-rs1800497) and DAT (DAT1 VNTR) in a PG sample.

Methods and materials

Study sample

Our initial sample comprised 69 consecutive Caucasian patients seeking treatment at the PG Unit within the Department of Psychiatry, University Hospital of Bellvitge in Barcelona, Spain. Results for the DAT1 phenotype were not obtained for three of the participants, because of analytical reasons (total study sample $n = 66$). PG was diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders*, Version 4 (*DSM-IV-TR*) criteria (American Psychiatric Association, 2000); we also assessed patients with the South Oaks Gambling Screen (SOGS) (Lesieur and Blume, 1987). All participants were males aged between 18–65 years, whom spoke Spanish as their first lan- guage. We enrolled participants between November 2005 and September 2007.

Exclusion criteria were:

- History of chronic medical illness or neurological condition that might affect cognitive function;
- Head trauma, learning disability or mental retardation;
- Lifetime history of an Axis I mental disorder, according to the *DSM-IV-TR* (American Psychiatric Association, 2000);
- History of substance abuse in the previous 3 months;
- Age under 18 or over 65 (to preclude neuropsychological deficits associated with age).

Our research procedures were explained in full to the partici- pants, and all subjects gave written informed consent, prior to enrollment. The procedures were approved by the Ethical Committee of the University Hospital of Bellvitge.

Neuropsychological assessment

As described in a previous study (Alvarez-Moya et al., 2011), we determined verbal intelligent quotient (IQ) using the vocabulary subtest of the Wechsler Adult Intelligence Scale-III (WAIS-III) (Wechsler, 1997). For the purpose of this study, we included the following tests (for further information on these tests, see the Supplementary material):

1. Stroop Color and Word Test, or SCWT (Golden, 1978): It measures interference control, flexibility and atten- tion. The main outcome variable is the 'interference score'. Higher scores on this variable indicate better capacity for response inhibition.

2. Wisconsin Card Sorting Test or WCST (Heaton 1981): It measures planning capacity, cognitive flexibility and capacity of shifting among stimuli. The main outcome is the number of categories completed: Higher scores indi- cate better cognitive flexibility and conceptualization. We also considered the number of errors and the number of cards used until the first category was successfully completed (initial conceptualization), as both these vari- ables are considered predictors of WCST results and mental set flexibility (Gligorovic and Buha, 2013).

3. The Trail-Making Test or TMT (Reitan, 1958): It meas- ures motor speed, attention and cognitive flexibility. The test consists of two parts ((a) and (b)). Higher scores on Part (a) suggest deficits in motor speed and attention; while higher scores on Part (b) suggest set-shifting dif- ficulties. In order to control for individual differences in speed of processing and attention, we generated a score based on the subtraction of time to complete Part (a) from the time to complete Part (b): TMT (a)–(b) Higher scores suggested difficulties with cognitive flexibility.

Genotyping and analysis methods

DNA was extracted from the blood sample and used as a template for the polymerase chain reaction (PCR). We performed genotyp- ing of the Taq1A (rs1800497) DRD2 single nucleotide polymor- phism (SNP) by real time PCR (n = 69), as follows: We used primers 5'-CCG TCG ACC CTT CCT GAG TGT CAT CA-3' and 5'-CCG TCG ACG GCT GGC CAA GTT GTC TA-3' to amplify a 310 base pair (bp) polymorphic fragment site of the *ANKK1* gene. PCR product was digested with five units of TaqI for 22 h at 65°C, to reveal three genotypes:

- Predominant homozygote (CC), indicated by two frag- ments (130 and 180 bp);
- Heterozygote (CT), indicated by three fragments (130, 180 and 310 bp); and
- Rare homozygote (TT), indicated by the uncleaved (310 bp) fragment.

The VNTR region of the *DAT1* gene was amplified from the genomic DNA using PCR. Results were not obtained for three of the participants (n = 66). In research on genetic polymorphisms, a non-amplified locus is not something exceptional and could be due to different causes; however, according to our rigorous quality con- trol in the application of the methods, the most likely hypothesis is that the PCR product was not amplified by the presence of muta- tions in the region of the primers' hybridization. To demonstrate this, it would be necessary to sequence the region, which goes

further than the objectives of the present study. Primers were used as follows: forward, 5-TGTGGT GTA GGG AAC GGC CTG AG-3 and reverse, 5-CTT CCT GGA GGT CAC GGC TCA AGG- 3. The PCR amplifications (25 l) were performed in a top-heated thermal cycler (Model GeneAmp System 9700, Applied Biosystems, Foster City, CA) for 35 cycles, and contained 1.5 µL MgCl2, 200 microM each of dNTP, 1.5µL each of the primer, and 0.25 units of AmpliTaq DNA polymerase. PCR cycles were: 95°C for 30 sec, 65°C for 30 sec and 72 °C for 30 sec. There was a 15-min pre-incubation at 95°C before starting

the cycles, and 5 min at 72°C after the completion of the cycles. The PCR products were separated on a 2.5% agarose gel and stained with ethidium bromide.

Statistical analysis

Analyses were carried out with SPSS20 for Windows. We explored the association between genetic indicators and cogni- tive outcomes with analysis of variance (ANOVA) procedures, adjusted for patient age and academic level. When significant effects emerged in the ANOVA, pair-wise comparisons of DRD2/ ANKK1 Taq1A and DAT1 VNTR polymorphism means were estimated through post-hoc comparisons, including Bonferroni's correction for multiple tests (with the level of significance fixed at .05), and Cohen's-d coefficient were used to measure the effect size of mean differences (moderate effect size was considered for |d>0.5| and good effect size for |d>0.8|). We used radar charts to represent group performance across the main cognitive domains (cognitive measures were plotted through z-scores).

Results

Our study patients' sociodemographic characteristics and gam- bling-related variables are presented in Table 1. No statistical differ- ences for the DRD2/ANKK1 Taq1A and DAT1 VNTR polymorphisms were obtained, except for level of education (p = 0.021 for the DRD2/ANKK1) and age (p = 0.001 for DAT1 VNTR). These two variables were included as covariates in the ANOVA comparisons. The outcomes of this study did not achieve significant associations with the gambling severity (measured by the SOGS-total score): correlation coefficients with $|r|$ lower than 0.14, rang- ing between r = 0.03 for WCST-total errors to r = 0.13 for TMT-B.

Role of DRD2/ANKK1 Taq1A (rs1800497) The genotype frequency for the *DRD2/ANKK1* Taq1A polymorphism was as follows: A1/A1, n = 7; A1/A2, n = 25 and A2/A2, n = 37. Homozygotes for the minor allele were grouped together with heterozygotes, i.e. the *DRD2/ANKK1* Taq1A A1+ group consisted of A1/A1 (TT) and A1/A2 (CT) genotypes. This analysis is consist- ent with the literature and a dominant model of inheritance (Noble, 2003). The genotype data were in Hardy-Weinberg equilibrium ($X2$= 0.78; p = 0.38).

DRD2/ANKK1 Taq1A (rs1800497) polymorphism was associ- ated with verbal IQ and cognitive flexibility performance (Table 2). Evaluation of mean scores indicated that the A1+ genotype was associated with higher vocabulary scores (p < 0.05), considered a measure of IQ, but also with higher scores on the TMT (Part (b); p < 0.05), suggesting difficulties with cognitive flexibility. No significant association was found between inhibition response perfor- mance (SCWT) and the *DRD2/ANKK1* polymorphism (Table 2).

Role of DAT1 VNTR

The genotype frequency for the *DAT1 VNTR* 40 bp was as fol- lows: 9/9, n = 7; 9/10, n = 27; 10/10, n = 32. The genotype data were in Hardy-Weinberg equilibrium ($X2$= 0.13; p = 0.71).

The DAT1 polymorphism was also associated with cognitive flexibility performance. Nine-repeat homozygotes displayed more WCST total correct responses (p = 0.02), and made fewer perseverative errors (p = 0.03) than heterozygotes and subjects with two copies of the 10-repeat allele, suggesting better cogni- tive flexibility performance. We found no significant association between inhibition response performance (SCWT) and the *DAT1* polymorphism (Table 2).

Discussion

This study set out to examine the association between DA poly- morphisms and executive functions in PG patients. A significant association was observed between DA-related genes (i.e. *DRD2/ ANKK1* and *DAT1*) and cognitive flexibility. Our results showed that greater availability of DA content and D2 receptor density were related to higher cognitive flexibility in PG patients. Interestingly, we did not observe genetic effects on response inhi- bition. Although DA modulation was previously related to cogni- tive performance in humans (Markett et al., 2011; Stelzel et al., 2010), this is, to the best of our knowledge, the first time that the dopaminergic system has been associated with executive func- tioning in a PG sample.

Our results suggest that *DAT* and *DRD2* have similar effects on cognitive flexibility in PG patients. Our finding of individual differences in DA associated with cognitive flexibility corrobo- rates those of both animal (Floresco et al., 2006) and human stud- ies (Jocham et al., 2009; Klein et al., 2007), suggesting that A1 carriers are less able to adjust their behavior, based on feedback obtained from the preceding trials. These data also support the pharmacological evidence that a *DRD2* agonist decreases task- switching performance and impairs cognitive flexibility (Mehta et al., 2004).

Interestingly, although both WCST and TMT are classical neuropsychological tests for measuring cognitive flexibility, a different association with the DRD2 and DAT polymorphisms was observed. These differences might be partially explained by dissimilarities in task complexity and the cognitive functions required for their performance: Whereas optimal performance on the TMT is based on preservation of the capacity of set shifting, attention processing and processing speed; the WCST also reflects strategic planning, organized searching, the ability to use environmental feedback to adjust cognitive sets and goal- ori- ented behavior (Nyhus and Barceló, 2009).

We failed to find an association between DA genes and the inhi- bition response. A number of studies associate DA functioning with behavioral inhibition (Congdon and Canli, 2008; Enoch and Goldman 2001), although some studies suggest that DA does not reach the extent and effect size originally hypothesized (Hack et al., 2011). Studies using the Stroop test found contradictory results, suggesting there is a positive association between haplotypes of

COMT and DRD2 (Reuter et al., 2005), while no role of DRD2 and DAT polymorphisms in the inhibition performance (Wohl et al., 2008). Interestingly, positive associations have been found between dopaminergic polymorphisms (DRD2, DAT and COMT) and other inhibition-based tasks, such as prepulse inhibition (Montag et al., 2011) and the stop signal task (Enoch and Goldman, 2001). These discrepant results highlight the importance of conducting further studies evaluating both the DA-related catabolic enzyme activity and receptor density, and conducting a more comprehensive assess- ment of the inhibition response.

Finally, we found an association between DA receptor density and verbal IQ. Patients with lower D2 binding potential had higher general verbal abilities. These results are in agreement with those showing a significant association between the Taq1A poly- morphism and general cognitive ability (Bolton et al., 2010); however, the results of studies investigating the role of DA in gen- eral IQ are inconsistent: Taq1A has not been associated with intel- ligence capacity in middle-aged adults (Moises et al., 2001), but it was associated with increased IQ in young women (Tsai et al., 2002). It should be borne in mind that we used only one subtest (vocabulary) as an estimating measure of verbal IQ, as the main focus of our study was executive functioning. Therefore, these findings should be confirmed by studies conducting thorough general cognitive assessments in PG.

Although we did not find an association between severity of gambling behavior (measured by means of SOGS) and the stud- ied polymorphisms, this finding should be interpreted with cau- tion. The lack of a

positive result does not necessarily mean that perhaps, if taking other more accurate clinical/psychometric measures of gambling severity, different results might be reached. The implications of these negative findings warrant additional attention and need further research.

This study has several important strengths, including the spe- cific characteristics of the selected sample and its genetic approach. We comprehensively assessed clinical and psycho- pathological profiles in a group of PG individuals attended con- secutively at a specialized PG unit. Molecular genetics, as applied in the present study, is an additional level of analysis above neu- ropsychological assessment, and it provides a practicable tool for the study of executive processes. Additionally, our study was specifically designed to comprehensively test executive dysfunc- tion in PG, by using three well-validated executive tests; how- ever, certain limitations of the study should also be borne in mind. First, no control group was included; however, the associa- tions observed between DA functioning and executive profile were the opposite of those found in healthy control studies, sug- gesting a specific pattern of associations in PG patients. Specifically, the availability of DAT has been negatively corre- lated with cognitive flexibility performance in healthy volunteers (Hsieh et al., 2010) and the group with the A1 genotype of the DRD2/ANKK1 scores significantly higher in both executive and memory tasks (Bartres-Faz et al., 2002; Tsai et al., 2002). Second, our data do not in any way demonstrate causality: Studies with a longitudinal design are required, in order to confirm the cause- effect relationship between DA functioning and executive func- tion in PG. Third, our study sample size was small; thus, further studies using a bigger sample are desirable. Finally, given that cognitive flexibility and the inhibition response are polygenetic EFs, future studies including serotonin, acetylcholine and brain- derived neurotrophic factor-related genes should be conducted in order to shed more light on the genetic mechanisms underlying the EF profile in pathological gamblers.

In summary, our results provide novel information regarding the influence of DA-related genes on EF in PG. Pathological gamblers with genetic predispositions associated with poorer DA efficacy are at a higher risk of presenting difficulties with cogni- tive flexibility. This study is particularly timely, given the impor- tant public health impact of PG and the potential significance of accurately-defined endophenotypes and genotypes associated with this disorder. Identifying gene-environment interactions is an essential element in the study of PG as an addiction, which, by definition, relies on the exposure to an addictive agent and is therefore powerfully modulated by genetics and environmental features. Thus, our understanding of PG will be improved by the detection of genes that have a role in altered gambling-specific vulnerabilities, such as personality traits, cognitive functioning

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Table 1. Sociodemographics and clinical variables.

	Total	*Taq1A (rs1800497)*			*DAT1 VNTR*			
	(*n* = 69)	A1+ (*n* = 32)	A1− (*n* = 37)	*p*	9R-9R (*n* = 7)	9R-10R (*n* = 27)	10R-10R (*n* = 32)	*p*
Age (yrs); mean (SD)	35.84 (10.69)	37.63 (11.99)	34.30 (9.32)	.199	41.43 (13.43)	40.33 (10.50)	31.34 (8.46)	**.001**
Duration gambling disease (yrs); mean (SD)	5.18 (6.01)	6.21 (7.71)	4.32 (4.05)	.212	13.67 (13.66)	4.92 (4.38)	3.88 (3.65)	.120
Education (yrs); mean (SD)	10.78 (3.15)	10.47 (3.08)	11.05 (3.22)	.445	10.00 (2.38)	10.70 (3.21)	11.00 (3.35)	.799
Education level (%)	72.1%	87.10%	59.46%	**.026**	100%	74.07%	67.74%	.515
Primary								
Secondary	22.1%	12.90%	29.73%		0%	18.52%	25.81%	
University	5.9%	0%	10.81%		0%	7.41%	6.45%	
Socioeconomic level (%)	3.2%	0%	5.71%	.089	0%	3.85%	3.57%	.596
High								
Mean-high	4.8%	0%	8.57%		0%	7.69%	3.57%	
Mean	11.1%	14.29%	8.57%		0%	7.69%	17.86%	
Mean-low	60.3%	53.57%	65.71%		66.67%	50.00%	64.29%	
Low	20.6%	32.14%	11.43%		33.33%	30.77%	10.71%	
Civil status (%)	38.2%	25.81%	48.65%	.127	14.29%	25.93%	54.84%	.097
Single								
Married/couple	52.9%	61.29%	45.95%		71.43%	66.67%	35.48%	
Divorced/separated	8.8%	12.90%	5.41%		14.29%	7.41%	9.68%	
Employment status (% employed)	86.8%	87.10%	86.49%	.941	85.71%	92.59%	80.65%	.421
Total number of problematic games	1.58 (1.12)	1.47 (1.14)	1.68 (1.11)	.447	2.29 (1.98)	1.26 (0.81)	1.75 (1.08)	.117
Smoker (% yes)	76.2%	72.41%	79.41%	.516	71.43%	60.87%	87.10%	.084
Gambling variables								
Maximum bets (Euros); mean (SD)	1.36 (0.97)	690.0 (1107)	891.8 (1672)	.577	901.4 (1218)	1082.5 (2086)	574.3 (734)	.785
Mean bets (Euros); mean (SD)	797.2 (1428)	168.8 (287)	247.9 (564)	.510	80.0 (70)	301.6 (683)	165.6 (201)	.403
Cumulative debt (Euros); mean (SD)	209.0 (448)	14,546.0 (24,789)	8534.8 (12,723)	.302	10,741.7 (18,825)	19,640.0 (26,759)	7380.8 (14,835)	0.69
SOGS total score; mean (SD)	10.94 (2.64)	11.29 (2.69)	10.65 (2.60)	.321	10.00 (3.92)	11.19 (2.17)	10.97 (2.73)	.795

Table 2. Association between the *DRD2/ANKK1 Taq1A (rs1800497)* and *DAT1 VNTR* polymorphisms and cognitive variables, after ANOVA adjusted by age, years of education and substance use.

	Taq1A (rs1800497)					***DAT1 VNTR***					
	A1+ (n = 32)	A1− (n = 37)	F (df = 1; 65)	p^a	Cohen | d |	9R-9R (n = 7)	9R-10R (n = 27)	10R-10R (n = 32)	F (df = 2; 61)	p^a	Post-hoc analysis
Vocabulary	37.03 (7.08)	34.54 (7.90)	4.27	**.043**	**0.54**[b]	32.86 (7.78)	34.96 (7.87)	36.66 (7.44)	0.95	.392	
SCWT											
Interference	−1.20 (10.05)	2.08 (9.94)	1.29	.261	0.29	−1.79 (6.73)	0.51 (10.28)	0.51 (10.63)	0.27	.762	
WCST											
Total correct	71.42 (13.30)	68.84 (10.74)	0.77	.383	0.23	82.00 (10.32)	67.48 (12.36)	68.71 (10.55)	4.42	**.017**	9–9 > 9–10; ϕ = 14.28; p = 0.024 9–9 > 10–10; ϕ = 14.14; p = .022
Total errors	42.15 (24.02)	39.38 (24.39)	0.01	.934	0.02	27.83 (15.09)	51.38 (22.52)	37.21 (24.85)	2.90	.065	
Pers errors	22.55 (15.82)	21.36 (14.44)	0.23	.637	0.11	12.67 (8.12)	31.67 (20.15)	19.50 (13.78)	3.79	**.030**	9–9 < 9–10; ϕ = 18.72; p = .029
Non-pers errors	13.09 (7.96)	19.94 (14.10)	0.84	.362	0.24	15.17 (8.61)	19.71 (11.92)	17.04 (14.49)	0.47	.624	
TMT											
TMT-A	31.35 (13.30)	24.86 (7.18)	2.70	.106	0.40	25.97 (11.92)	30.82 (9.99)	26.56 (11.27)	0.64	.532	
TMT-B	104.2 (76.75)	66.09 (24.97)	4.50	**.038**	**0.54**	74.09 (29.46)	94.08 (58.92)	72.63 (51.80)	0.38	.685	