Gender and gambling disorder: differences in compulsivity-related neurocognitive domains

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ABSTRACT

Background and aims: It has been suggested that compulsivity has an essential role in gambling disorder (GD), yet there is a lack of literature exploring the link between GD, compulsivity and gender. Our main aim was to explore gender differences between two of the neurocognitive domains of compulsivity (attentional set-shifting and attentional bias and disengagement) in patients with GD and compare them with healthy controls (HCs). **Methods:** The sample included 57 treatment-seeking adults with GD and 60 HCs recruited from the general population. **Results:** The pairwise comparisons showed a worse attentional set-shifting performance in women with GD than in men (total trials (p= 0.042, |d|= 0.56), perseverative responses (p= 0.001, |d|= 0.89), trails to complete the first category (p= 0.001, |d|= 0.78) and categories completed (p= 0.001, |d|= 0.98. Also, men with GD presented higher difficulties than HC men in the two assessed compulsivity domains (attentional bias and disengagement and attentional set-shifting; Stroop interference (p= 0.015, |d|= 0.11), TMT-B (p= 0.041, |d|= 1.96) and lower scores for the WCST perseverative responses (p= 0.007, |d|= 0.78), whereas the differences observed in women with GD and HCs were most significantly in attentional set-shifting. **Conclusions:** This study provides the first evidence of gender compulsivity differences in GD. The results are relevant for improving current treatments by targeting specific compulsivity domains that can lead to more successful treatment options.

Keywords: gambling disorder; gender; compulsivity; attentional set-shifting; attentional bias/disengagement; neurocognition.

1. INTRODUCTION

In recent years, there has been growing interest in the study of compulsivity from a clinical and neurophysiological perspective, just as it has shown to be related to numerous clinical conditions such as gambling disorder (GD) (Figee et al., 2016; Yücel & Fontenelle, 2012). Compulsivity is a complex construct that can be described as "the performance of repetitive and functionally impairing overt or covert behavior without adaptive function, performed in a habitual or stereotyped fashion, either according to rigid rules or as a means of avoiding perceived negative consequences" (Berlin & Hollander, 2014; Fineberg et al., 2014; Robbins et al., 2012). Therefore, it represents a lack of control over one's own behavior (Denys, 2014).

Due to the multifactorial nature of compulsivity, different neurocognitive dimensions have been proposed for its characterization and assessment; yet two of the most outstanding ones are attentional set-shifting and attentional disengagement (van Timmeren et al., 2018).

Attentional set-shifting refers to the ability to frequently switch attention between a set of stimuli (van Timmeren et al., 2018). It is possible to evaluate it using laboratory tools, such as the Wisconsin Card Sorting Task (WCST) (Lezak & Howieson, 2012). In the specific case of GD, previous literature reported significantly worse performance in one or more of the parameters of the WCST when comparing individuals with GD to healthy controls (HCs), suggesting attentional set-shifting impairments in GD patients (Álvarez-Moya et al., 2010; Álvarez-Moya et al., 2009; Black et al., 2013; Ledgerwood et al., 2012; van Timmeren et al., 2018). Some other authors highlight that individuals with GD show difficulties when they have to alter a response that has been previously rewarded but no longer is (Boog et al., 2014; Brand et al., 2005; Cavedini et al., 2002).

Attentional bias and disengagement involve the capacity to inhibit an automatic response. In other words, the ability to respond to certain environmental stimuli while others are ignored (van Timmeren et al., 2018). Not achieving to inhibit the dominant response, can lead to inflexible behavior. It can be assessed with behavioral measures of cognitive control such as the Stroop Color and Word Test (SCWT) (Golden, 1978, 1999) and the part B of the Trail Making Test (TMT) (Bowie & Harvey, 2006). It is also worth noting that these domains can depend on other executive functions thus present an indirect link to compulsivity (van Timmeren et al., 2018). Regarding GD, findings about this compulsivity dimension seem to be disparate. While some studies highlight worse performance in individuals with GD (using SCWT or TMT), meaning attentional disengagement difficulties (Albein-Urios et al., 2012; De Wilde et al., 2013); others do not observe differences with HCs (Hur et al., 2012; Lai et al., 2011). In this line, GD has been related with relatively diminished activation of the ventromedial prefrontal cortex during the SCWT (Potenza et al., 2003, 2013).

When analyzing gender differences within these domains, results are still inconsistent. Some authors suggest that gender differences in inhibitory capacities are domain specific and that more studies are needed in this area (Bjorklund & Kipp, 1996; Colin M. Macleod, 1991; Kertzman et al., 2018). Furthermore, in general terms, GD has been understudied in the case of women, and there is a male bias in the research field (McCarthy et al., 2019). Nevertheless, there seem to be numerous gender differences in this disorder, such as differences in lifetime prevalence rate of GD (Blanco et al., 2006), emotion regulation (Sancho et al., 2019), gambling urges (Dunsmuir et al., 2018), and shame and guilt (Kushnir et al., 2016). Further studies are therefore needed to precisely define possible gender differences in phenotypes related with GD.

Even though data concerning the link between GD, compulsivity and gender are scarce, it has been suggested that compulsivity plays a crucial role in understanding this pathology (Leeman & Potenza, 2012; van Timmeren et al., 2018). As such, the primary aim of the present study was to explore possible gender differences between two of the compulsivity neurocognitive domains (attentional set-shifting and attentional bias and disengagement) in patients with GD. A secondary aim of this study was to compare this neuropsychological performance between clinical samples with GD and HCs while also considering gender. We hypothesize a possible alteration of both neurocognitive domains in the clinical samples in comparison with the performance obtained by HCs in the administered compulsivity behavioral measures.

2. METHODS

2.1 Sample and procedure

The total sample consisted of 117 participants. They were divided into four groups: two clinical groups that included women (n=27) and men (n=30) with a GD diagnosis and two HC groups that comprised women (n=30) and men (n=30) without psychopathology.

The clinical group included patients with a diagnosis of GD who sought treatment at the Gambling Disorder Unit within the Department of Psychiatry at Bellvitge University Hospital (Barcelona, Spain). All the participants individually completed the neuropsychological assessment required for this study before initiating outpatient treatment. Apart from the behavioral measures listed below, additional sociodemographic and clinical information was taken. Exclusion criteria for being part of the treatment protocol were: (1) brain trauma, a learning disability or intellectual disabilities; (2) history of chronic medical illness or neurological condition that might affect cognitive function; and (3) age under 18 or over 65. Our study sample also incorporated HC participants', which were recruited using word of mouth from the surrounding community. The exclusion criteria for these two HC groups included the above mentioned for the clinical group and a lifetime history of GD. The neuropsychological protocol was identical to that of the clinical groups.

The mean age was 45.7 yrs-old (SD=10.1) in the GD group and 37.7 yrs-old (SD=11.6) in the HC ($p<.001$). The mean years of schooling was 10.5 (SD=3.4) within GD patients and 14.3 (SD=3.9) within HC ($p<.001$). Regarding the gambling profile within the clinical sample, mean age onset was 33.9 yrs-old (SD=12.4) and mean duration of the gambling activity 6.6 yrs (SD=6.5). The frequency distribution of GD severity (according to the number of positive DSM-5 criteria) was: n=18 (31.6%) in the moderate group (between 4-5 criteria), n=10 (17.5%) in the severe group (6-7 criteria), and n=29 (50.9%) in the extreme group (8-9 criteria). Most GD patients reported preference for non-strategic gambling (slot-machines, bingo and/or lotteries; n=46, 80.7%), while n=11 (19.3%) reported preference for strategic gambling (casino, cards or sport betting).

2.2 Instruments

2.2.1 GD diagnosis and severity

Patients were assessed using the DSM-5 criteria (American Psychiatric Association, 2013) through a clinical face-to-face interview. Sociodemographic variables related to the gambling behavior were also measured.

2.2.2 Attentional set-shifting

The WCST (Lezak & Howieson, 2012) is a computerized set-shifting task for measuring cognitive flexibility. It consists of 128 cards that differ on three characteristics: number, color and shape. The participant has to pile the cards under four reference cards that also differ on these same dimensions and, in order to succeed they have to settle upon a predetermined sorting rule. The only feedback given to the participant is the word “right” or “wrong” after each sorting. After 10 consecutive correct sorts the rule changes. Thus, the positive feedback is only given when the sorting matches the new category. By trial and error, the participant must learn to change the sorting categories according to the given feedback. The test is completed when six full categories are accomplished or all 128 cards are sorted. Participants are not informed of the correct sorting principle and that the sorting principal shifts during the test. In our study, five main types of WCST were used for analysis: completed categories (i.e.: the number of runs of 10 correct responses), trials to complete the first category (i.e.: the total number of trials needed to achieve the first 10 consecutive correct responses), perseverative errors (i.e.: the number of errors where the participant has used the same rule for their choice as the previous choice; hence, the failure to change sorting strategy after negative feedback), perseverative responses (i.e.: the number of incorrect responses that would have been correct for the preceding category / rule) and the total trials (i.e.: the total number of cards matched minus the number of the last trial).

2.2.3 Attentional bias and disengagement

The TMT (Bowie & Harvey, 2006) consists of 25 circles spread out over two parts (parts A and B). Part A (TMT-A), participants are requested to connect by drawing a line consecutive numbers (1-2-3-…) in ascending order. In part B (TMT-B), participants have to link consecutive numbers and letters in an alternating numeric and alphabetic sequence (1-A, 2-B, 3-C-…). Each part is scored according to the time spent (seconds) to complete the task (the lower the score the better the performance). The task is frequently used to evaluate executive function. The present study specially targets TMT-B as it can indicate impaired shifting of mental sets away from stimuli (attentional bias and disengagement deficits). Lower scores suggest a better performance in this task.

The SCWT (Golden, 1978, 2001) is a test to assess the cognitive ability to overtake the foremost behavioral response to a stimuli, namely inhibitory control. It consists of three different lists: a word list containing the names of colors printed in black ink, a color list that comprises letter Xs printed in color, and a color-word list constituted of names of colors in a color ink that does not match the written name. Three final scores are obtained based on the number of items that the participant is able to read on each of the three lists in a time window of 45s. There is also an interference score that is computed with all three lists that enables the assessment of individual's cognitive flexibility and the ability to inhibit cognitive interference. Thus, the present study specially focuses on the interference score as an adequate measure for assessing impaired shifting of mental sets away from stimuli (attentional bias and disengagement). Higher scores in this index suggest better inhibitory control.

2.2.4 Depression state

The Symptom Checklist-Revised (SCL-90-R; (Derogatis, 1994) is a self-reported questionnaire that evaluates psychopathological symptoms. This questionnaire contains 90 items and measures nine primary symptom dimensions and it has been validated in Spanish population with good internal consistency (Derogatis, 2002). For the aims of the present study, we special focused on the depression scale, which in our studied sample presented an excellent consistency (α = .923).

2.3 Statistical analyses

Statistical analysis was carried out with Stata16 for Windows. Comparisons between neuropsychological profile between the groups of the study was based on analysis of variance (ANOVA), adjusted by the participants' age, education level, depression state and abuse of alcohol or illegal drugs. In this study, the ANOVA were executed defining a single between-subject factor based on the classification of the participants within four groups: HC-men, HC-women, GD-men and GD-women. This approach correspond to one-factor ANOVA comparing a grouping factor with k=4 levels, with the aim to contrast the mean differences across the different categories of the factor implied in the empirical hypothesis of the study [see the pairwise comparisons (contrasts) reported in Table 1]. The alternative to this method, two-factor ANOVA defining the between-subjects factors group (HC *versus* GD) and sex (men *versus* women), was not considered because the relatively low sample size did not provide power enough to identify the interaction parameter group-by-sex. Therefore, the analytical procedure in this study is a simpler approach which allowed provided the specific contrasts to assess the objectives of the study and allowed controlling the set of covariates.

Effect size for the mean comparison was based on Cohen's-d coefficients (poor-low effect size was considered for $|d|>0.20$, mild-moderate for $|d|>0.50$ and large-high for $|d|>0.80$) (Kelley & Preacher, 2012). Finner's correction (a method classified into the Familywise error rate stepwise procedures which offers more powerful results than the classical Bonferroni correction) (Finner, 1993) controlled increase in Type-I error due to the multiple statistical comparisons. In this study, and due the relatively low sample size for the groups of the study, it was considered as clinically relevant any comparison which achieved statistical significance and/or was at least into the moderate high effect size ($|d|>0.50$).

2.4 Ethics

The study procedures were carried out in accordance with the Declaration of Helsinki. The University Hospital of Bellvitge Ethics Committee of Clinical Research approved the study. All subjects were informed about the study and all provided informed consent for participation.

3. RESULTS

Table 1 contains the results of the ANOVA (adjusted by age, education level, depressive symptoms and abuse of substances) comparing the neuropsychological profiles between the four groups of the study defined by the diagnostic subtype and the participants' gender.

The most relevant differences were found for the pairwise comparisons between men with GD versus women with GD in the WCST, with women obtaining a worse performance in: total trials, perseverative responses, trails to complete the first category and categories completed. Additionally, men with GD obtained a lower mean score than women in the TMT-A, and a higher mean score in the TMT-B (for this last measure, there was no significant result but there was a relevant effect size).

We also compared the clinical and control groups according to gender. Regarding the comparisons of men with GD and HC, the clinical group obtained higher scores (significant results and/or relevant effect sizes) in Stroop interference, TMT-B and WCST completed categories, and lower scores for the WCST perseverative responses. Concerning the comparisons of women with GD and HCs, significant and/or relevant effect sizes were found for all the WCST scales, with higher mean scores among GD for all the scales except for the trials to complete the first category. Additionally, non-significant results but relevant effect sizes were also observed comparing women with GD versus women from the HCs: lower mean score in the clinical group for the Stroop-word and higher mean in the TMT-B.

The comparison between HC-men versus HC-women obtained no significant differences but a moderate effect size in the Stroop-interference and TMT-B measures, showing a tendency to present a better task performance in men.

Figure 1 contains the radar-chart which summarizes the neuropsychological profile of each group. Z-standardized scores has been plotted to allow easy interpretation (since variables have been measured with different measurement scale).

4. DISCUSSION

This study examined gender differences in compulsivity related variables (i.e.: attentional set-shifting and attentional bias/disengagement) in a sample of patients with GD and compared them with a sample of HCs. Results showed a worse attentional set-shifting performance in women with GD than in men with GD and revealed that these results were not found when comparing men and women in HC groups. Results also displayed two different gender profiles when comparing the two clinical groups with their HC counterparts: men with GD presented higher difficulties than HC men in the two assessed compulsivity domains (attentional bias/disengagement and attentional set-shifting), whereas the differences observed in women with GD and HCs were mainly in attentional set-shifting.

Few studies have explored compulsivity related variables in GD with mixed results. It has been noted that the extent to which the individuals with GD may present compulsivity impairments can be linked to the specific domains which are assessed. The available studies testing attentional set-shifting with WCST, provide substantial evidence for task performance deficits in individuals with GD when compared to HCs (van Timmeren et al., 2018). Thus, the current findings reinforce previous knowledge regarding attentional set-shifting impairments in GD and add evidence of higher impairments in women than men. The tasks included within the attentional bias/disengagement domain (i.e.: SWCT-Interference and TMT-B) have previously demonstrated less consistent results; with some studies reporting significant impairments in patient with GD (Albein-Urios et al., 2012; Álvarez-Moya et al., 2010) and others not (Black et al., 2013; Choi et al., 2014; Ledgerwood et al., 2012). It is of special interest that our results point towards a significantly worse attentional bias/disengagement performance in GD when compared to a HC group but only in the group of men.

Therefore, our results support the idea that compulsivity should be understood as a construct integrated for different domains (van Timmeren et al., 2018) and that GD patients exhibit gender differences in compulsivity depending on the specific domain evaluated (Bjorklund & Kipp, 1996). Different studies have reported gender substantial differences in addictive disorders and in GD in particular (Fattore et al., 2014). Yet, to our knowledge, no previous studies have compared compulsivity variables between men and women with GD. The present findings show that gender may provide a useful window on the heterogeneity so far described for compulsivity-related measures in GD. This has important clinical implications as, like some authors have suggested, the evaluation of these neurocognitive dimensions may be particularly relevant to understanding the mechanisms of some approaches to GD, especially those involving the promotion of self-control skills toward gambling behaviors (Potenza et al., 2013). Going one step further while thinking about the integration of the present results with previous clinical knowledge, current findings could be indirectly related to emotion regulation difficulties and distress which are in fact found to be more present in women than in men (Venne et al., 2019). Thus, women could experiment bigger difficulties than men for changing their attention towards more adaptive behaviors other than gambling. In its turn, men could present higher difficulties for inhibiting the automatic response (gambling) while ignoring other stimulus (monetary losses, negative consequences). With this in mind, future studies should further test this initial hypothesis so that the present results can be further linked to other clinical measures (e.g.: emotional regulation, distress, anxiety, among others).

The findings of our study may be considered with certain caveats in mind. First, although the use of neurocognitive laboratory tasks have clear benefits, such as the fact that they are objective and more engaging than other evaluation tools, they assess a transitory state associated only with a specific context or situation (Ellingson et al., 2018), which must be taken into account when interpreting the present results. Second, the present study has only focused on two of the neurocognitive domains of compulsivity. However, it has been suggested that other domains, such as habit learning and contingency-related cognitive flexibility, may also be part of the compulsivity construct (van Timmeren et al., 2018). Third, the cross-sectional nature of this study does not allow obtaining conclusions regarding causality and the direction of the effects examined and, despite controlling for different confounding factors including educational level, future studies should also explore if intelligence quotient could be having a role in the reported associations. Fourth, our clinical sample was only made up of patients who sought treatment for GD. The inclusion of gamblers from the general population would allow obtaining a more exhaustive perspective of the link between compulsivity and this disorder. And finally, the sample size is relatively low in the study, with the consequence of potential underpowered for the ANOVA. It must be considered, however, that this study included both statistical significance tests (p-values are strongly related to the sample sizes) and the estimation of the effect sizes through a standardized coefficient (which is not dependent of the sample size).

5. CONCLUSIONS

We provide the first evidence of gender compulsivity differences in GD. The results are highly relevant for improving current treatments by targeting specific compulsivity domains that can lead to a more successful treatment option.

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Table 1. Comparison of the neuropsychological profiles between the groups of the study: ANOVA adjusted by the participants' age, education, depressive symptoms and substances

	HC-men		HC-women		GD-men		GD-women		HC-men				GD-men				HC-men				HC-women			
	n=30		*n=30*		*n=30*		*n=27*		vs HC-women				vs GD-women				vs GD-men				vs GD-women			
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*p*	|*d*|	*95% CI MD*		*p*	|*d*|	*95% CI MD*		*p*	|*d*|	*95% CI MD*		*p*	|*d*|	*95% CI MD*	
SCWT																								
Word reading	103.4	13.5	103.5	6.4	101.8	14.0	97.1	18.2	.981	0.01	-8.6	8.4	.311	0.29	-4.5	13.9	.730	0.11	-7.4	10.6	.254	**0.51†**	-4.7	17.4
Color naming	72.0	33.4	69.5	10.8	68.3	78.1	68.2	39.6	.438	0.10	-3.8	8.8	.980	0.00	-6.7	6.9	.277	0.06	-3.0	10.3	.756	0.04	-6.9	9.4
Interference	-1.7	4.7	1.1	4.5	3.8	68.1	4.3	40.7	.185	**0.60†**	-6.9	1.4	.811	0.01	-5.0	3.9	**.015***	0.11	-9.8	-1.1	.237	0.11	-8.6	2.1
TMT																								
TMT-A (seconds)	31.5	17.5	37.3	16.6	29.0	14.3	36.9	18.5	.078	0.34	-12.3	0.7	**.027***	**0.54†**	-14.9	-0.9	.471	0.16	-4.3	9.3	.924	0.02	-8.0	8.8
TMT-B (seconds)	78.5	15.5	88.8	13.2	103.0	8.4	96.8	13.7	.362	**0.71†**	-32.4	11.9	.612	**0.54†**	-17.8	30.1	**.041***	**1.96†**	-47.9	-1.0	.581	**0.60†**	-36.9	20.8
WCST																								
Total trials	104.6	22.1	100.6	19.0	100.6	21.7	111.2	15.6	.398	0.20	-5.4	13.5	**.042***	**0.56†**	-20.8	-0.4	.424	0.19	-6.0	14.1	.090	**0.61†**	-22.9	1.7
Persevera.respon.	23.2	20.3	16.2	9.7	10.1	12.2	26.8	23.6	.123	0.44	-1.9	15.9	**.001***	**0.89†**	-26.3	-7.0	**.007***	**0.78†**	3.6	22.5	.073	**0.59†**	-22.2	1.0
Persevera.errors	19.3	16.7	14.2	8.3	15.3	14.7	21.7	16.9	.172	0.39	-2.3	12.5	.116	0.40	-14.3	1.6	.312	0.25	-3.8	11.8	.124	**0.56†**	-17.1	2.1
Completed categ.	4.9	1.9	5.2	1.1	5.7	1.2	3.7	2.5	.449	0.22	-1.2	0.6	**.001***	**0.98†**	1.0	2.9	.105	**0.51†**	-1.7	0.2	**.010***	**0.78†**	0.4	2.7
Trials-firs- categ.	17.8	23.3	15.6	4.1	18.8	15.1	44.7	44.5	.748	0.13	-11.4	15.8	**.001***	**0.78†**	-40.6	-11.3	.894	0.05	-15.3	13.4	**.001***	**0.92†**	-46.8	-11.5

Note. SCWT: Stroop Color and Word Test. TMT: Trait Making Test. WCST: Wisconsin Card Sorting Test.

SD: standard deviation. 95%CI MD: 95% confidence interval for mean difference.

p-value includes Finner's correction for multiple statistical comparisons.

*Bold: significant comparison (.05 level).

†Bold: effect size into the moderate (|*d*|>0.50) to high range (|*d*|>0.80).

Figure 1. Radar-chart: z-mean scores for the neuropsychological profile of compulsivity related variables