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FULL-LENGTH REPORT

Testing the transdiagnostic hypothesis of inhibitory control deficits in addictions: An experimental study on gambling disorder

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ABSTRACT

Background and aims: Many psychopathologies, including addictions, are characterized by inhibitory control deficits. In this regard, recent studies on substance-related disorders (SRD) have shown an impairment in the ability to inhibit potentially interfering memories, despite preserved motor inhibition. To investigate whether the same dissociation could also characterize gambling disorder (GD) in a transdiagnostic perspective, we tested both cognitive and motor inhibitory processes through dedicated tasks, for the first time in this behavioral addiction. *Methods:* 30 outpatients with GD and 30 healthy controls performed a go/no-go task addressing the integrity of motor inhibition, and the Retrieval Practice Paradigm, a task addressing the integrity of memory inhibition as indexed by the Retrieval-Induced Forgetting (RIF) effect. Self-report questionnaires assessing impulsivity were also administered. *Results:* Whereas RIF was similar across the two groups, patients showed more commission errors in the go/no-go task, and higher self-rated scores of impulsivity than controls. *Discussion:* The present findings suggest preserved memory inhibition and impaired motor response inhibition in GD, a pattern of inhibitory deficits opposite to that previously reported for SRD. Therefore, although both GD and SRD are characterized by altered inhibitory processing, a more fine-grained analysis revealed a specific inhibitory profile indicating vulnerability in different inhibitory components. *Conclusion:* The present study highlights the need to investigate the multifaceted construct of inhibition more thoroughly, using performance measures able to assess its various components. This approach would enable to both better characterize different psychopathologies and orient their treatment.

KEYWORDS

gambling, addictive disorders, substance-related disorders, response inhibition, retrieval-induced forgetting, transdiagnostic approach

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INTRODUCTION

Inhibitory control is essential to an adaptive and flexible goal-directed behavior, which requires the ability to override the automatic activation of irrelevant or inappropriate representations and responses. The most investigated part of inhibitory control is the ability to inhibit one's emotional responses and one's motor, overt behavior (i.e., self-control and discipline, both contributing to the so-called response inhibition). However, this

multicomponential executive function also includes interference control, which is assumed to exert its covert influence both on environmental stimuli (i.e., attentional inhibition), and thoughts or memories (i.e., cognitive inhibition; see Diamond, 2013).

Deficits in inhibitory control, found in a broad range of disorders, have been identified as a crucial transdiagnostic neuro-cognitive factor able to predict clinical problems (Goschke, 2014; Lozano, Soriano, Aznarte, Gómez-Ariza, & Bajo, 2016; Nelson, Strickland, Krueger, Arbisi, & Patrick, 2016; Schreiber, Odlaug, & Grant, 2013). This perspective is consistent with the emphasis on biologically meaningful dimensional constructs advocated by the NIMH Research Domain Criteria framework (RDoC, Insel et al., 2010). Inhibitory control in the clinical domain has primarily been addressed using subjective phenotypic indicators (i.e., clinical observations and self-report questionnaires) and motor response inhibition paradigms. Yet, an approach based on the simultaneous assessment of different inhibitory measures, also including interference control tasks, may represent a more fine-grained strategy to detect endophenotypic indicators of various psychopathologies (Gottesman & Gould, 2003). More specifically, the ability to inhibit competing or unwanted memories is relevant to achieve crucial adaptive functions, such as emotion regulation, and therefore is closely tied to both cognitive efficiency and psychological health (e.g., Nørby, 2015; Storm, 2011). The relatively few studies specifically addressing memory inhibition reported deficits in various phenotypically different disorders, which share a characterization in terms of scarce inhibitory control over different kinds of representations (e.g., ADHD, Storm & White, 2010; schizophrenia, Soriano, Jiménez, Román, & Bajo, 2009; obsessive–compulsive disorder, Demeter, Keresztes, Harsányi, Csigó, & Racsmány, 2014; clinical depression, Groome & Sterkaj, 2010; anorexia nervosa, Stramaccia, Penolazzi, Libardi, et al., 2018). In the above studies, an impaired suppression of competing/unwanted memories has mainly been investigated with the retrieval-practice paradigm (RPP; Anderson, Bjork, & Bjork, 1994), which probes incidental memory inhibition by means of Retrieval-Induced Forgetting (RIF). RIF is related to the observation that, under specific circumstances, the very act of retrieving information from memory can elicit forgetting of related information, temporarily inhibited to decrease recall interference from competing items (Anderson et al., 1994; Bajo, Gómez-Ariza, Fernandez, & Marful, 2006; Galfano, Penolazzi, Fardo, Dhooge, Angrilli, & Umiltà, 2011; Murayama, Miyatsu, Buchli, & Storm, 2014). Neurostimulation evidence has shown that the right lateral prefrontal cortex is causally involved in memory inhibition indexed by RIF (Penolazzi, Stramaccia, Braga, Mondini, & Galfano, 2014; Stramaccia, Penolazzi, Altoè, & Galfano, 2017a). This region is included in a specific neural network characterized by aberrant activation across psychiatric disorders and may represent a possible intermediate transdiagnostic phenotype of cognitive control impairment (McTeague, Huemer, Carreon, Jiang, Eickhoff, & Etkin, 2017). Consistent with the RDoC framework, this neurobiological evidence parallels cognitive evidence of a transdiagnostic inhibitory control impairment across psychopathologies.

In the case of addictive disorders, research has focused almost exclusively on inhibitory control of overt actions (e.g., Leeman & Potenza, 2012; Smith, Mattick, Jamadar, & Iredale, 2014), although the ability to inhibit interfering memories may be critical to suppress intrusive thoughts that can, in turn, trigger craving episodes (May, Andrade, Panabokke, & Kavanagh, 2004). In this regard, a recent study in the domain of substance-related disorders (SRD) has reported a selective deficit in inhibiting competing memories in two clinical samples diagnosed with alcohol and heroin addictions, despite preserved motor inhibition (Stramaccia, Penolazzi, Monego, Manzan, Castelli, & Galfano, 2017b). In addition to self-report measures, this study used cognitive tasks tapping different components of inhibitory control: i.e., a go/no-go task, to assess motor response inhibition, and the RPP, to measure incidental memory inhibition.

So far, similar to SRD, gambling disorder (GD) has been investigated almost exclusively with measures of motor inhibition. By adopting a transdiagnostic approach, the present study aimed to broaden our knowledge of this behavioral addiction, by using, along with subjective self-report questionnaires, also performance-based cognitive tasks. In addition to a go/no-go task commonly employed to measure response inhibition, the RPP was used to assess the integrity of incidental inhibitory control over interfering memories. Consistent with Stramaccia et al. (2017b), we expected patients with GD to exhibit higher scores of self-rated impulsivity than controls. Based on recent evidence showing impairments of different inhibitory components in GD (Kertzman, Vainder, Aizer, Kotler, & Dannon, 2017), and given the similarity of GD and SRD with respect to various inhibitory deficits indexed by response and choice impulsivity (Leeman & Potenza, 2012), we expected a cognitive inhibition impairment in our sample, similar to that reported for patients with SRD (e.g., Noël et al., 2009; Stramaccia et al., 2017b; Zou, Zhang, Huang, & Weng, 2011). Correlations between task performance and questionnaire scores were expected, with self-report gambling features being mainly associated to inhibitory deficits. The simultaneous investigation of different components of inhibitory control through different tasks, allowed us to perform an exploratory comparison of GD (investigated in the present study) and SRD (investigated in previous studies). This may be useful to address differences vs. commonalities between addictive disorders with respect to their inhibitory profile, aimed at improving their characterization and treatment.

METHOD

Participants

Sixty participants entered the study: 30 outpatients with a diagnosis of GD and 30 healthy control (HC) individuals

matched for the most relevant socio-demographic variables (see Table 1). Sample size was based on the study by Stramaccia et al. (2017b). Patients were recruited in two mental health services in Northern Italy and diagnosed by a board-certified attending research team of psychiatrists through the examination of past medical records and a semi-structured interview based on the *DSM-IV-TR* adapted to the *DSM 5*. HCs were recruited in the same geographical area. The only inclusion criterion for patients was having an ongoing GD diagnosis. Exclusion criteria were: for all participants, having neurological disorders or learning disabilities; for HCs, having a past history of addiction. At the time of data collection, 30% of the patients also reported SRD symptoms (20% alcohol-abusers; 10% poly-abusers: alcohol and opiates/cannabis) whereas 13.3% had a secondary diagnosis of a psychiatric disease (psychotic, bipolar, or personality disorder). All participants were native Italian speakers.

Procedures and measures

Participants were tested in two sessions carried out in different days in consecutive weeks to avoid fatigue effects. In one session, the integrity of motor response inhibition was tested by using the *Sustained Attention to Response Task* (SART, Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). All participants completed a self-report questionnaire on impulsivity (which is, supposedly, inversely related to inhibitory abilities), and a self-report questionnaire on depressive symptoms to control for possible detrimental effects of mood alterations on performance. Patients also completed a series of questionnaires related to different features of GD detailed below (see Table 2). In the other session, the integrity of inhibitory control over interfering memories was tested by using the RPP (Anderson et al., 1994).

Experimental tasks. Participants were placed in front of a 15-in. laptop monitor (1,024 × 768 pixels, 60 Hz), where stimuli appeared in black against a gray background. Motor inhibition was addressed by means of the *SART* (Robertson et al., 1997). Participants were presented with a rapid sequence of digits. They were instructed to press the spacebar to respond as quickly as possible to each digit except for the digit "3", for which they were asked to withhold the response. There were 225 single digits from "1" to "9", presented with various font size (48, 72, 94, 100, or 120 point, Symbol font). The digits appeared at the center of the screen for 250 ms, 25 times each. A mask (the "#" symbol), appeared after each digit for 900 ms. The SART is aimed to elicit slips of attention, as the task proceeds very quickly and repetitively but also includes highly infrequent trials associated to the instruction to inhibit a response.

Table 1. Sociodemographic, clinical, and task performance variables for control and clinical groups

Variable	Control group	GD group	Group comparisons $t(df)$ or $\chi^2(df)$
Gender	18 males 12 females	21 males 9 females	$\chi^2(1) = 0.66$
Age (years)	50.33 (13.52)	49.27 (13.65)	$t(58) = 0.30$
Education (years)	12.23 (4.91)	10.50 (3.30)	$t(58) = 1.60$
Employment (n)	Employed: 21 Unemployed: 1 Retired: 6 Housewife: 2	Employed: 19 Unemployed: 4 Retired: 5 Housewife: 1	$\chi^2(34) = 33.22$
BIS-11 – Total (score) [0.82]	59.57 (7.06)	67.39 (11.68)	$t(56) = -3.11^{**}$
BIS-11 – Attent. Imp. (score) [0.64]	15.87 (3.00)	17.00 (3.89)	$t(58) = -1.26$
BIS-11 – Motor Imp. (score) [0.64]	19.50 (2.94)	22.32 (4.93)	$t(56) = -2.67^{**}$
BIS-11 – Non planning Imp. (score) [0.63]	24.20 (3.63)	27.97 (4.69)	$t(58) = -3.48^{***}$
BDI-II – Total (score) [0.86]	5.40 (5.07)	15.65 (11.71)	$t(54) = -4.14^{***}$
RPP: FAC (%)	22.96 (16.22)	27.22 (17.53)	$t(58) = -0.98$
RPP: RIF (%)	5.8 (17.15)	7.78 (12.32)	$t(58) = -0.50$
SART: RTs (ms)	407.17 (98.08)	384.26 (93.34)	$t(58) = 0.93$
SART: PES (ms)	35.67 (87.22)	43.37 (79.17)	$t(57) = -0.35$
SART: total errors (%)	13.29 (8.81)	16.31 (10.50)	$t(58) = -1.21$
SART: commissions (%)	35.33 (20.23)	50.67 (26.35)	$t(58) = -2.53^{*}$

Note. For non-categorical variables, values are means with standard deviations in parentheses, unless otherwise noted. For questionnaires, Cronbach's alphas, collapsed across groups, are reported in square brackets below each total scale and subscale. BDI-II: Beck Depression Inventory–Second Edition. BIS-11: Barratt Impulsivity Scale; BIS-11 – Total: total score of BIS-11; BIS-11 – Attent-Imp.: Attentional Impulsivity subscale of BIS-11; BIS11 – Motor Imp.: Motor Impulsivity subscale of BIS-11; BIS-11 – Non planning Imp.: Non planning subscale of BIS-11. BIS-11 questionnaires were fully completed by 30 healthy controls and 28 patients; BDI-II questionnaires were completed by 30 healthy controls and 26 patients. RPP: Retrieval Practice Paradigm; FAC: facilitation effect (correct recall of RP+ minus correct recall of NRP+ items), RIF (correct recall of NRP− minus correct recall of RP− items): retrieval induced forgetting effect; SART: Sustained Attention to Response Task; PES: Post-Error Slowing (i.e., for every error E: difference between RT to trial E + 1 and RT to trial E − 1). As concerns PES, one healthy control did not commit any error and hence was excluded from the analysis.
$^{*}p \leq 0.05$ $^{**}p \leq 0.01$ $^{***}p \leq 0.001$

Table 2. Descriptive statistics of clinical group's gambling self-report measures

Questionnaire scales and sub-scales on gambling		Mean (SD)
SOGS [0.85]		9.94 (3.71)
GABS [0.90]		79.56 (15.51)
GFA [0.81]	**Sensory experience** [0.74]	10.28 (7.31)
	Escape [0.85]	9.76 (8.38)
	Social attention [0.25]	3.93 (3.94)
	Tangible rewards [0.44]	10.28 (9.99)
GRCS-I [0.91]	**Gambling expectancies** [0.70]	9.96 (4.92)
	Illusion of control [0.76]	6.68 (4.23)
	Predictive control [0.78]	12.08 (6.75)
	Inability to stop gambl. [0.71]	14.08 (6.37)
	Interpretative bias [0.73]	11.12 (6.22)
GBQ-I [0.93]		40.36 (31.67)

Note. Cronbach's alphas are reported in square brackets after each total scale and subscale. SOGS: South Oaks Gambling Screen; GABS: Gambling Attitudes and Beliefs Survey; GFA: Gambling Functional Assessment; GRCS- I: the Gambling Related Cognitions Scale-Italian; GBQ-I: Gamblers' Beliefs Questionnaire-Italian.

Commission errors (responses to the "no-go" digit) were taken as measures of motor inhibition failure (e.g., Leeman & Potenza, 2012; Smith et al., 2014).

Memory inhibition was addressed by means of the RPP (Anderson et al., 1994). The material was selected from the categorical production norms for Italian language (Boccardi & Cappa, 1997). The RPP included three phases, i.e., a Study phase, a Practice Phase, and a Test Phase. The stimulus material included 84 category-exemplar word pairs belonging to 12 semantic categories and was created following four criteria: (i) for each category, four exemplars had high and three had low taxonomic strength; (ii) within the same category, each exemplar always had a different initial letter; (iii) semantic associations between and within categories were kept to a minimum; (iv) all exemplars were between 5 and 10-letter long. Stimuli were presented in a randomized blocked order, with the constraint that exemplars from the same category could not appear on consecutive trials. Blocks included 12 items, with each item randomly drawn from one of the 12 semantic categories. During the *Study phase*, participants were instructed to study all the 84 category-exemplar word pairs (e.g. "fruit-prune"). Each trial begun with a 500-ms fixation cross, replaced by a 500-ms blank screen and followed by the onset of a category-exemplar word pair centered on the screen. This remained visible for 3,500 ms and was followed by a 500-ms blank screen intertrial interval. During the *Practice phase*, in order to maximize competition and the need to inhibit interference from strong exemplars, participants performed repeated practice only on the weak exemplars of half the semantic categories. On each trial, participants were shown (for a maximum of 8,000 ms) only the category and the first two letters of each exemplar (e.g. "fruit-pr___"). Participants were required to type the full name of the associated exemplar. Weak exemplars practiced during this phase were identified as RP+ items, while non-practiced strong items belonging to practiced categories were labelled RP-. Weak and strong items belonging to non-practiced categories were labelled NRP+ and NRP−, respectively, and served as baseline. Four counterbalanced lists were created, so that categories used in this phase were counterbalanced across participants and groups (i.e., every category contributed equally to all four types of items). After completing the practice phase, participants filled unrelated questionnaires which prevented them from rehearsing the studied material. In the final, *Test phase,* participants were administered all the stimuli of the study phase. On each trial, participants were shown the category plus the first letter of an exemplar (e.g. "fruit-p____") and were asked to type the full name of the associated exemplar. The same constraints used in the previous phases were adopted for stimulus presentation. Moreover, all RP− and NRP− items were shown before all the RP+ and NRP+ items, thus controlling for output interference (Murayama et al., 2014). Whereas the typical finding of a better recall accuracy for RP+ items over NRP+ items at test is thought to reflect a memory facilitation reflecting the beneficial effects of practice, poorer recall accuracy for RP- items (i.e., non-practiced exemplars from practiced categories) than for NRP− items (i.e., non-practiced exemplars from non-practiced categories with comparable taxonomic strength) is the behavioral signature of RIF, illustrating the detrimental effects of selective retrieval practice. RIF is assumed to reflect an adaptive form of memory inhibition, useful for reducing the activation of task-interfering memories (Anderson et al., 1994; Murayama et al., 2014).

Self-report questionnaires

The battery of paper-and-pencil self-report questionnaires included: (1) the *Barratt Impulsiveness Scale–11* (*BIS-11*; Fossati, Di Ceglie, Acquarini, & Barratt, 2001), a 30-item-item scale encompassing motor impulsiveness (tendency to act on impulse), non-planning impulsiveness (lack of future planning), and attentional impulsiveness (difficulty in maintaining attention), with higher scores indicating higher impulsivity; (2) the *Beck Depression Inventory* (*BDI-II*, Ghisi, Flebus, Montano, Sanavio, & Sica, 2006), a 21-items inventory used to assess the presence and severity of depressive symptoms, with higher scores indicating higher levels of depressive symptoms. For patients only, the battery also included: (1) the brief version of *South Oaks Gambling Screen* (*SOGS*, Capitanucci & Carlevaro, 2004), a 16-item questionnaire used to assess gambling symptoms, with a total score of 0 indicating no problem with gambling, a score in the range 1–4 indicating possible pathological gambling, a score higher than 5 indicating probable pathological gambling; (2) the *Gambling Attitudes and Beliefs Survey* (*GABS*, Capitanucci & Carlevaro, 2004), a 35-item questionnaire assessing gambling-related dysfunctional attitudes and beliefs, with higher scores indicating higher levels of gambling affinity; (3) the *Gambling Functional Assessment* (*GFA*, Dixon & Johnson, 2007), a 20-item questionnaire assessing the main contingencies maintaining gambling behaviors (i.e., sensory experience, tangible

rewards, escape, social attention), with higher scores indicating higher tendency for the corresponding contingency; (4) the *Gambling Related Cognitions Scale-Italian* (*GRCS-I*, Iliceto et al., 2015), a 23-item scale assessing gambling-related cognitive distortions (i.e., gambling expectancies, illusion of control, predictive control, inability to stop gambling, interpretative bias), with higher scores indicating greater distortions; (5) the *Gamblers' Beliefs Questionnaire-Italian* (*GBQ-I*, Marchetti et al., 2016), a 21-item questionnaire assessing gambling-related cognitive distortions, with higher scores indicating greater distortions.

Statistical analysis

Chi-squared tests and t-tests were used to compare the two groups for the most relevant socio-demographic variables and for their questionnaire scores (see Table 1). Descriptive statistics of questionnaires on gambling were computed to describe the clinical sample (see Table 2).

For the RPP, in line with previous research (e.g., Demeter et al., 2014; Stramaccia et al., 2017b), beneficial (facilitation) and detrimental (RIF) effects of selective retrieval practice were analyzed separately by examining percentage of correct recall in the test phase as a function of item type. Facilitation was analyzed by means of a mixed-design ANOVA with group (GD group vs. HC group) as a between-participant factor and item type (RP+ vs. NRP+ items) as a within-participant factor. Similarly, RIF was analyzed by conducting a mixed-design ANOVA with group as a between-participant factor and item type (i.e., NRP− vs. RP− items) as a within-participant factor. Independent sample t-tests were conducted to analyze SART performance in the two groups using RTs for correct responses, percentage of total errors, and percentage of commission errors as dependent measures. Post-error slowing (PES) in SART (computed for every error E as the difference between RT to trial E + 1 and RT to trial E − 1, see Dutilh, van Ravenzwaaij, Nieuwenhuis, van der Maas, Forstmann, & Wagenmakers, 2012) was also analyzed as a possible index of cognitive control (Ridderinkhof, 2002). For both RPP and SART, ANCOVAs controlling for a possible impact of the variables that significantly differed between groups (i.e., BIS-11 and BDI-II) were computed only in case of significant effects involving Group in the ANOVAs. Finally, Bonferroni-adjusted partial correlations, controlling for BIS-11 and BDI-II, were performed separately for each group, to highlight possible associations between self-report measures and cognitive processes underlying SART and RPP. For each participant, individual scores for both facilitation (correct recall of RP+ minus correct recall of NRP+ items) and RIF (correct recall of NRP− minus correct recall of RP- items) were computed. Higher values of facilitation indicate stronger beneficial effects of practice, whereas higher values of RIF indicate more efficient memory inhibition.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the ethical committee for psychological research of the University of Padova.

RESULTS

Table 1 shows between-group differences for the examined variables. Groups were equivalent for the most relevant socio-demographic variables and, as regards self-report questionnaires, they differed for depressive symptoms and impulsivity, with patients showing significantly higher values than controls. Table 2 shows means and standard deviations for the questionnaires on gambling (administered to GD patients only).

Retrieval Practice Paradigm

The ANOVA on the facilitation effect revealed a significant main effect of Item Type, $F(1,58) = 132.41$, $p < 0.001$, $\eta^2_p = 0.69$, reflecting a better recall of RP+ items ($M = 45.09$, *95%CI* = 40.33/49.86) than NRP+ items ($M = 20.00$, *95%CI* = 17.33/22.67). Neither the main effect of Group, $F(1,58) = 0.01$, $p = 0.93$, $\eta^2_p = 0.001$, nor the Group x Item Type interaction, $F(1,58) = 0.95$, $p = 0.33$, $\eta^2_p = 0.02$, were significant. Hence, all groups were able to learn from practice to a similar extent (see Table 1 for a direct comparison of facilitation between groups).

As regards the RIF effect, the ANOVA revealed a significant main effect of Item Type, $F(1,58) = 12.47$, $p = 0.001$, $\eta^2_p = 0.18$ reflecting a better recall of NRP− items ($M = 41.04$, *95%CI* = 38.25/43.83) than RP- items ($M = 34.24$, *95%CI* = 31.30/37.17). Neither the main effect of Group, $F(1,58) = 1.73$, $p = 0.19$, $\eta^2_p = 0.03$, nor the theoretically-relevant Group × Item Type interaction, $F(1,58) = 0.25$, $p = 0.62$, $\eta^2_p = 0.004$, were significant, thus suggesting a similar ability to inhibit interfering memories in the two groups (HC group: NRP−: $M = 41.94$, *95%CI* = 38.00/45.89, RP- items: $M = 36.11$, *95%CI* = 31.96/40.26; GD group: NRP−: $M = 40.14$, *95% CI* = 36.20/44.08, RP− items: $M = 32.36$, *95%CI* = 28.21/36.51; see Table 1 for a direct comparison of RIF between groups). Because a previous study (Stramaccia et al., 2017b) showed for SRD patients a specific impairment in memory inhibition, as indexed by RIF, and since our clinical sample included patients with this comorbidity (N = 9), further statistical analyses were conducted after removing these participants. This control analysis confirmed the pattern emerged in the analysis including all participants in that Item Type yielded a significant effect, $F(1,49) = 8.00$, $p=0.007$, $\eta^2_p = 0.14$, whereas neither the main effect of Group, $F(1,49) = 0.84$, $p = 0.36$, η^2_p 0.02, nor the Group × Item Type interaction were significant $F(1,49) = 0.01$, $p = 0.90$, $\eta^2_p=0.001$. The same pattern emerged also after removing patients with other comorbidities (Item type: $F(1,47) = 8.50$, $p=0.005$, $\eta^2_p = 0.15$; Group, $F(1,47) = 0.59$, $p=0.45$, $\eta^2_p = 0.01$; Group × Item Type interaction: $F(1,47) = 0.10$, $p=0.76$, $\eta^2_p = 0.002$).

SART

The t-tests showed no significant differences as a function of group in RTs for correct responses, percentage of total errors and post-error slowing (see Table 1). In contrast, groups significantly differed in the percentage of commission errors (i.e., a well-established marker of motor inhibition failure), as the GD group performed more commissions than the HC. Additional ANCOVAs controlling for the impact of self-reported depressive symptoms and impulsivity (which were significantly different in the two groups, see Table 1), confirmed that patients performed more commission errors than HCs, even when controlling for these variables (BDI-II as covariate: $F(1,55) = 5.22$, $p = 0.03$, $\eta^2_p = 0.090$, GD group: $M = 51.48$, *95%CI* = 41.94/61.02, HC group: $M = 35.65$, *95%CI* = 26.86/44.43; BIS-11-total score as covariate: $F(1,57) = 4.38$, $p = 0.04$, $\eta^2_p = 0.074$, GD group: $M = 49.13$, *95%CI* = 39.81/58.45, HC group: $M = 35.08$, *95%CI* = 26.10/44.06).

Partial correlations among measures

Partial correlation analyses (controlling for BDI-II) among RPP measures, SART measures, and BIS-11 scores revealed no significant association in both groups. For the clinical group, that completed additional self-report questionnaires assessing different gambling features, partial correlations (controlling for BIS-11 and BDI-II) showed no significant associations between gambling measures and behavioral task outcomes.

DISCUSSION AND CONCLUSIONS

The present study aimed to extend the investigation of inhibitory control in GD, by testing, for the first time in this disorder, the integrity of incidental inhibitory control over interfering episodic memories, along with the more frequently investigated motor response inhibition. Given the documented similarities between GD ad SRD as concerns inhibitory performance (Kertzman et al., 2017; Leeman & Potenza, 2012), we expected to observe an impairment of cognitive inhibition in GD patients, as earlier reported in SRD patients tested with the same experimental paradigms employed here (Stramaccia et al., 2017b). Unexpectedly, the RIF effect, indexing cognitive inhibition in the memory domain, was not statistically different across groups, thus suggesting a preserved ability to inhibit interfering episodic memories in GD patients. In contrast, they made more commission errors than controls in the SART, indicating the vulnerability in response inhibition as the most reliable marker of their altered inhibitory abilities. The lack of group differences in PES does not necessarily speak against an inhibitory deficit in GD, in that the link between such index and inhibitory processing is still debated (e.g., Notebaert, Houtman, Van Opstal, Gevers, Fias, & Verguts, 2009). Interestingly, consistent with previous evidence (Kertzman et al., 2017), correlational analyses between measures of inhibition and impulsivity (and between these measures and patients' self-reported gambling variables) showed scarce associations, suggesting that subjective and objective measures of similar constructs need to be considered as complementary rather than interchangeable. Nevertheless, some co-occurrences between our phenotypic and endophenotypic measures were detected: The higher values of self-reported motor impulsivity in GD patients (see Table 1) paralleled their response inhibition deficit, whereas values of self-reported attentional impulsivity, equivalent across groups, appeared in line with the lack of cognitive inhibition impairments suggested by the intact RIF in GD patients.

The present study suggests that GD does not entail deficits of high-level inhibitory control. At first glance, this may look inconsistent with previous data reporting deficits in many components of inhibitory control (i.e., response inhibition, reflective impulsivity, attentional inhibition) in GD patients (Kertzman et al., 2017). However, it is worth noting that covert cognitive inhibition over interfering memories has never been investigated before in GD. Therefore, its impairment in this behavioral addiction could not be a priori ruled out. Along with attentional inhibition, cognitive inhibition is likely to represent one of the highest levels of interference control (Diamond, 2013). The inconsistency found across different studies for this multidimensional function (e.g., impaired attentional inhibition in Kertzman et al., 2017 vs. preserved incidental memory inhibition in the present study) corroborates the view that inhibitory control is a multifactorial construct in need of further investigation (Bäuml, 2008; Friedman & Miyake, 2004; Nigg, 2000). One possibility is that the dissociation in performance observed in tasks tapping different components of inhibitory control depends on relevant features of the task set. In this regard, whereas cognitive inhibition over memory representations underlying the RIF effect is thought to be elicited *involuntarily*, other tasks assessing attentional inhibition (e.g., the Stroop task) may rely on more *voluntary* inhibitory processes.

The lack of a direct comparison between SRD and GD patients within the same experiment, along with the relatively small sample size, represents the main limitation of the present study. However, the use of the same experimental paradigms previously administered to SRD patients by Stramaccia et al. (2017b) enabled us to perform an exploratory comparison of the inhibitory profile in different addictive disorders. This suggests that both GD and SRD are characterized by impairments in inhibitory control, although each category of patients displayed a specific inhibitory profile with deficits involving different components. This pattern is in need of further investigation through experiments testing both GD and SRD patients within the same study.

In view of the multicomponential nature of inhibitory control, testing its integrity using different measures may be very useful to typify different psychopathologies, whose characterization or diagnostic classification is still debated. Moreover, determining an inhibitory profile for different categories of patients can be valuable also to orient their

treatment. In this respect, unlike the well-documented executive deficits of SRD patients (Leeman & Potenza, 2012), the integrity of incidental memory inhibition in GD patients is consistent with the lack of strong evidence for other executive function impairments in this clinical population. Thus, clinical interventions may capitalize on the preserved high-level control processes to increase the likelihood of good outcomes. This may be accomplished by promoting treatment motivation and compliance and the use of a broader range of sophisticated therapeutic strategies based on higher-level cognitive functions.

Given that specific patterns of inhibitory impairments have been found in a broad range of pathological conditions, and that cognitive control, along with decision-making, might be a transdiagnostic factor in psychopathology (Goschke, 2014; Lozano et al., 2016), a fine-grained analysis of inhibitory functions, through subjective and objective measures aimed at determining patients' specific inhibitory profiles, may represent a precious element in the diagnostic and rehabilitative process in clinical practice.

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