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Neurocognitive functions in pathological gambling: a comparison with alcohol dependence, Tourette syndrome and normal controls

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ABSTRACT

Aims Neurocognitive functions in pathological gambling have relevance for the aetiology and treatment of this disorder, yet are poorly understood. This study therefore investigated neurocognitive impairments of executive functions in a group of carefully screened *Diagnostic and Statistical Manual* version IV (DSM-IV-TR) pathological gamblers. Performance was compared to a group of normal control participants. To study the specificity of these neurocognitive deficits, a substance dependence group (alcohol dependence) and an impulse control disorder group (Tourette syndrome) were included. **Design** Cross-sectional study. **Setting** Addiction and general mental health treatment centres. **Participants** Forty-nine pathological gamblers, 48 abstinent alcohol-dependent patients, 46 participants with Tourette syndrome and 49 normal control participants. **Measurements** A comprehensive neuropsychological battery measuring executive functions as well as basic cognitive functions. **Findings** Both the pathological gambling and the alcohol dependent groups were characterized by diminished performance on inhibition, time estimation, cognitive flexibility and planning tasks. The Tourette syndrome group showed deficits only on inhibition tasks. Basic cognitive functions were intact in all clinical groups. Comorbid attention deficit hyperactivity disorder, antisocial personality disorder and nicotine dependence influenced the impaired functions of the clinical groups only minimally. **Conclusions** Carefully screened groups of pathological gamblers and alcohol dependents were characterized by diminished executive functioning, suggesting a dysfunction of frontal lobe circuitry in these disorders. The resemblance between the pathological gambling group and the alcohol dependence group suggests a common neurocognitive aetiology for these disorders. Psychosocial treatment of these disorders could benefit from assessing and targeting deficits in executive functions, as they probably influence the course of these disorders negatively.

Keywords Executive function, impulse control disorder, neuropsychology, substance dependence.

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INTRODUCTION

Pathological gambling (PG) is characterized by persistent, non-adaptive gambling and is classified in the *Diagnostic and Statistical Manual of Mental Disorders* version IV (DSM-IV-TR) as an impulse control disorder [1]. PG is a serious public health problem, because it poses psychosocial problems to the person involved and often causes severe financial problems [2,3]. Estimated 1-year prevalence of PG is 1.4% in the United States, and with growing availability of gambling opportunities, the prevalence of PG is increasing [4,5].

Although classified as an impulse control disorder, PG is regarded as a 'behavioural addiction' by some researchers [6,7]. Several DSM-IV-TR criteria for PG resemble those of substance dependence, such as loss of control, tolerance, withdrawal and the experience of negative consequences due to the gambling-related behaviour (for reasons of conciseness, substance dependence also refers to alcohol dependence in this paper). Apart from the diagnostic similarities that PG shares with substance dependence and impulse control disorders, these disorders are all characterized by behavioural deficits in self-regulation, as manifested in an impaired ability to inhibit the

urge for the desired behaviour or drug. In the neurocognitive literature, self-regulatory functions are usually defined as executive functions (EFs), and besides inhibition also include functions such as planning, working memory, cognitive flexibility and sense of time [8]. EFs rely on an intact functioning of the prefrontal cortex and subcortico–cortical networks projecting to the prefrontal cortex, such as basal ganglia–thalamic and parietal networks [9–11].

In substance dependence diminished EFs have been found [12–14], as well as abnormalities in brain structures and functions of the prefrontal cortices and connecting circuits [15–19]. In impulse control disorders with a childhood onset, such as attention deficit hyperactivity disorder (ADHD) and Tourette syndrome (TS), studies indicate that diminished EFs are present [20–23], and abnormalities in brain structures and functions involved in EFs are present [21,24,25]. In contrast, research into EFs in PG is scarce, and findings are inconsistent (for a review see [26]). The most important reason for these inconsistencies concerns methodological limitations: some studies targeted only a single EF, most studies were restricted to small groups and studies often failed to assess and control for comorbid disorders and medication use. In addition, most studies did not investigate whether deficits in EFs were independent of deficits in basic cognitive functions. Finally, the specificity of EF deficits in PG is not known, because clinical comparison groups were not included in most of these studies. The present study was aimed at remedying these limitations.

Three research questions were addressed. First, we investigated whether EFs were impaired in pathological gamblers, compared to normal controls. Tests assessing five important EF domains were included: (1) inhibition, (2) time estimation and reproduction, (3) cognitive flexibility, (4) working memory and (5) planning. As EFs are related strongly to the intact functioning of the frontal lobe and its (sub)cortical interconnections [27], EF tests were selected that have been shown to rely heavily on these brain structures, supporting their validity [28–33]. Several basic cognitive tasks, such as measures of response speed and short-term memory, were also administered. In this way, it could be ruled out that deficits in EFs would be present due to impairments in basic cognitive functions upon which EFs rely. Given the similarities in diagnostic criteria between PG, impulse control disorders and substance dependence, the evidence for diminished behavioural self-regulation in PG and neurocognitive deficits in EFs in related disorders, it was expected that pathological gamblers would show diminished EFs, compared to normal controls.

The second research question referred to the *specificity* of EF deficits for PG. In addition to a normal control (NC) group, the performance of the PG group was compared to the performance of an abstinent substance dependence group (alcohol dependence: AD) and an impulse control disorder group (Tourette syndrome: TS). Inclusion of these clinical control groups allowed for a better understanding of whether EF deficits in PG are comparable to EF deficits in AD and TS. Comparing the EF profiles of the PG, AD and TS groups will render a neurocognitive endophenotype of these disorders. By comparing the profile of the PG group to the other groups it could be clarified whether a neurocognitive profile of PG should have a role in future diagnostic classification systems.

The third question addressed the role of comorbid psychopathological conditions in the performance of EF tasks. ADHD, antisocial personality disorder, nicotine dependence, depression and anxiety disorders co-occur frequently with PG [34–36]. Some of these conditions are also associated with EF deficits [37–39]. Therefore, the third research question addressed whether comorbid conditions influenced performance on EF tasks and whether comorbid disorders could account for EF deficits in PG, AD and TS.

METHODS

Recruitment

Pathological gamblers were recruited from a consecutive sample of out-patients of a local addiction treatment centre. The PG patients were recruited through information leaflets attached to the treatment information sent by mail, and through follow-up telephone calls. The AD, TS and NC groups were matched as closely as possible to the PG group in terms of age, gender and intelligence. The AD patients were recruited from the same treatment centre as the PG group, through information leaflets. TS participants were recruited from an out-patient treatment centre for general mental health care through information sent by the out-patient treatment centre, by advertisements in the newsletter of the Dutch patient organization for TS and by flyers distributed during an information day of this organization. NC subjects were recruited through advertisements in local newspapers and in a local hospital newsletter.

Selection criteria and screening

The PG participants were diagnosed according to DSM-IV-TR PG criteria, using the Dutch version of section T of the Diagnostic Interview Schedule (DIS) [40]. This interview schedule contains questions referring to all DSM-IV-TR diagnostic criteria for PG, on a dichotomous scale (yes/no). In order to be included in the study as a pathological gambler, at least five of the defining criteria had to be present currently or recently, i.e. up to 4 weeks prior to the assessment. Furthermore, the Dutch version of the

South Oaks Gambling Screen (SOGS [41]) was administered to obtain a sensitive measure of gambling severity [42].

AD participants were diagnosed according to DSM-IV-TR AD criteria with section J of the Dutch version of the Clinical International Diagnostic Inventory (CIDI [43]). This structured interview schedule contains questions referring to all DSM-IV-TR diagnostic criteria for AD on a dichotomous scale (yes/no). A minimum Mini-Mental State Examination (MMSE) score of 25 was required in order to exclude AD patients with severe cognitive impairment, such as alcohol-related dementia [44]. The MMSE examines mental status and contains 20 items, of which half are designed to assess orientation and half are designed to assess basic cognitive skills such as language comprehension, memory and attention.

All subjects who were included in the TS group were diagnosed previously with TS by a psychiatrist or neurologist. Severity of current and past verbal and motor tics was assessed with the Dutch version of the Yale Global Tic Severity Scale (YGTSS) [45].

Exclusion criteria for all groups were: (1) (a history of) substance abuse or dependence (section L of the Dutch CIDI)—except for alcohol abuse and dependence in the AD group; (2) (a history of) major psychiatric disorders such as schizophrenia, psychotic episodes or hospitalization for psychiatric disorders; (3) current treatment for mental disorders other than those under study in this investigation; (4) physical conditions known to influence cognition or motor performance (e.g. multiple sclerosis, rheumatic disease); (5) the use of psychotropic medication which could not be discontinued; (6) having another language than Dutch as first language; (7) age over 60 or under 18 years; (8) positive urine screen for alcohol, cannabis or benzodiazepines. The groups were mutually exclusive with regard to the psychiatric disorder under study. For example, pathological gamblers had no history of AD and were not suffering from TS.

Further comorbidity screening, not used as exclusionary criteria, focused on occurrence of manic episodes (CIDI-F [43]), obsessive compulsive disorder (CIDI-K [43]), ADHD (DIS-L [40]) and ADHD questionnaire [46] and antisocial personality disorder (DIS-P [40]). Current nicotine dependence was assessed with the Fagerström Test for Nicotine Dependence on a scale of 0–10 [47]. Level of trait anxiety was assessed with the State–Trait Anxiety Inventory on a scale of 20–80 [48,49]. Depressive symptoms were assessed with the Beck Depression Inventory on a scale of 0–63 [50,51]. No participants had experienced manic episodes. The numbers of participants fulfilling the other comorbid disorders and the mean scores and standard deviations on the ADHD, nicotine dependence, anxiety and depression questionnaires are presented in Table 1.

Final sample

From 133 PG referrals, 49 pathological gamblers were included in the study. Reasons for dropout or exclusion were: refusal to participate ($n = 18$), not traceable after first contact with treatment centre ($n = 17$), insufficient knowledge of the Dutch language or Dutch as secondary language ($n = 17$), alcohol/substance abuse or dependence or a positive urine test for opiates and/or benzodiazepine ($n = 11$), presence of other psychiatric disorders ($n = 5$), use of psychotropic medication ($n = 6$), no recent PG diagnosis ($n = 4$), no show after appointment ($n = 3$), over age limit of 60 years ($n = 3$).

The final sample contained 49 pathological gamblers, 48 alcohol dependants, abstinent for a period of 3–12 months, 46 TS patients and 50 normal controls. Gender and age for the four groups are presented in Table 1. This study was part of a larger study on pathological gambling and self-regulation. A paper regarding decision-making skills under reward and loss conditions in PG and subgroups of pathological gamblers is described elsewhere [52]. The current study, however, focused on different research questions regarding a broad range of neurocognitive functions in PG compared to AD, TS and normal controls.

Procedure

Participants were tested individually during two sessions, on separate days. Each session lasted 3–4 hours. The tests were administered in a quiet room, located at the university or at the addiction treatment centre. Participants received €50 for their participation. Tests were administered in two different fixed orders. Frequent breaks were introduced to avoid fatigue. This study was approved by the Amsterdam Medical Centre Local Ethical Committee and written informed consent was given by all participants before testing.

Executive function tasks

Inhibition

Stop Signal Task [53]. This task measures inhibition of a pre-potent response. A total of six blocks of 64 trials was administered: the first block consisted of only Go trials; subsequent blocks were comprised of both Go trials (75%) and Stop trials (25%). Go trials required the subjects to perform a two-choice reaction time task in which subjects had to react as quickly as possible to an airplane appearing on the screen by a right button press (airplane flying to the right) or a left button press (airplane to the left). Stop trials were identical to Go trials but in addition an auditory stop signal was presented, requiring subjects to inhibit their response. Stop signals were presented using a tracking algorithm which accomplished 50% successful inhibition

Table 1 Demographical data and standard deviations for pathological gambling (PG), alcohol dependence (AD), Tourette syndrome (TS) and normal control (NC) groups.

	Pathological gambling	*Alcohol dependence*	*Tourette syndrome*	*Normal control*	*Test statistics*	*Bonferroni-corrected pairwise comparisons*
n	49	48	46	50		
Age (SD)	37.3 (9.5)	47.2 (8.3)	36.8 (12.1)	35.6 (11.4)	$F_{3,193} = 12.7$, $P < 0.001$	NS
Male/Female	40/9	37/11	32/14	35/15	$\chi^2_{193} = 2.61$, $P = 0.46$	NS
Estimated IQ	118.3 (14.2)	119.0 (18.4)	122.5 (16.4)	120.6 (15.5)	$F_{3,192} = 0.73$, $P = 0.53$	NS
ADHD questionnaire	24.2 (10.4)	24.6 (10.1)	34.3 (11.2)	16.6 (9.1)	$F_{3,190} = 24.2$, $P < 0.001$	PG, AD, TS > NC; PG < TS
Nicotine dependence (FTND)	4.0 (3.1)	5.1 (3.3)	2.1 (2.7)	1.4 (2.4)	$F_{3,192} = 16.2$, $P < 0.001$	PG, AD > NC, TS
Trait anxiety (STAI)	43.8 (8.6)	43.7 (8.6)	47.9 (11.3)	33.0 (6.5)	$F_{3,186} = 25.1$, $P < 0.001$	PG, AD, TS > NC
Beck Depression Inventory	12.5 (8.3)	11.4 (7.6)	9.7 (7.2)	3.0 (3.2)	$F_{3,185} = 18.9$, $P < 0.001$	PG, AD, TS > NC
South Oaks Gambling Screen	11.6 (0.58)	–	–	–		
Number of DSM-IV-TR criteria AD	–	4.8 (1.2)	–	–		
Age of onset AD	–	35.5 (9.7)	–	–		
Total AD years	–	11.2 (9.2)	–	–		
YGTSS	–	–	20.9 (10.2)	–		
ADHD diagnosis (*n*)	4	2	2	0		
APD diagnosis (*n*)	2	1	0	0		
OCD diagnosis (*n*)	0	0	10	0		

Means are displayed with standard deviations in parentheses. The South Oaks Gambling Screen was administered only in the PG group. The YGTSS was administered only in the TS group. Degrees of freedom differ due to missing data and exclusion of subjects. STAI = State-trait anxiety inventory; FTND = Fagerström Test for Nicotine Dependence; ADHD = attention deficit hyperactivity disorder; IQ = intelligence quotient; YGTSS = Yale Global Tic Severity Scale; APD = antisocial personality disorder; OCD = obsessive compulsive disorder.

for each subject by varying the delay between presentation of the airplane and the stop signal. A full description of the specifications used in this task is provided in Scheres, Oosterlaan & Sergeant [54]. The dependent measure was the Stop Signal Reaction Time (SSRT), with higher SSRTs reflecting lower levels of inhibition.

Circle Tracing Task [55,56]. This task measures inhibition of an ongoing response. In this task, a circle had to be traced continuously with the dominant pointer finger. The circle had to be traced once with neutral tracing instructions, and three times with the instructions to trace the circle as slowly as possible. The circle was 20 cm wide, printed on A4 paper, plastified and attached to a larger plastic board. The dependent measure was the summed time of the three slow conditions.

Stroop Colour–Word Test [57,58]. The Stroop was administered as a measure of interference control. In this task an automated response (reading) has to be inhibited actively, and a controlled process (naming colours) has to be executed. This test consists of three cards which are presented consecutively. On the first card, colour words are printed in black. The subject has to name the words as quickly as possible. The second card consists of coloured rectangles, and the colours have to be named. The last card consists of colour words which are printed in an ink colour differing from the colour name of the word. In this last condition the automatic process of reading has to be suppressed, and the ink colour in which the words are printed has to be named. The dependent variable of this task was the interference score: time in seconds needed to read the third card minus the time needed to read the second card.

Time estimation and reproduction

Time estimation and reproduction tests [59]. These tests measure sense of time. In the time estimation task, subjects had to estimate the duration of periods of 2, 4, 8, 12 and 20 seconds, measured by the research assistant on a stopwatch. In the time reproduction task attention had to be paid to the same time periods, presented as a tone, following which the tone length had to be reproduced by a button press, while keeping the specific time-period in memory. Thus, time reproduction is more demanding than time estimation, and also relies on working memory. An absolute discrepancy score was calculated for both tasks: estimated or reproduced time in seconds minus the actual time duration in seconds.

Cognitive flexibility

Wisconsin Card Sorting Test (WCST) [60,61]. This task measures concept generation, cognitive flexibility and the lack thereof: perseveration. The purpose of this task is to sort test cards so that they match one of four stimulus cards, according to a concept which is not known to the subject (form, colour or number). Feedback is given regarding correctness of the response. After 10 consecutive correct responses the concept shifts, and the subject has to shift strategy and learn to sort the cards according to a new sorting concept. The standardized paper-and-pencil WCST administration with cards as used by Grant & Berg [60] was employed (see [62]). The dependent variables included in the analyses were: total categories completed (as a measure of concept generation) and percentage of perseverative responses (as a measure of perseveration).

Fluency: Controlled Oral Word Association Test (COWAT) [63]. The COWAT is a measure of phonological and semantic verbal fluency. A revised version of this task was administered. In the phonological condition subjects were asked to name as many words as possible in 1 minute starting with the letters N, A or K, and were not allowed to give proper names or to repeat words starting with the same word stem (e.g. table, tablecloth). In the semantic condition, subjects had to name as many animals or professions as possible in 1 minute. The dependent variables were (1) the summed number of correct words named in the semantic and phonological condition, and (2) the total number of perseverative errors; i.e. words named twice or more within each letter or category.

Working memory

Self-Ordered Pointing Task—abstract designs (SOP) [64]. This task measures visual working memory. The task consists of four series of cards with 6, 8, 10 or 12 abstract designs on each card. On each card within a series, the same designs are presented but the position of the designs differs. Each series consists of different designs. The subject had to point to a different design on each card. The task was self-paced, and subjects were instructed to perform as accurately as possible. In this task, active maintenance and monitoring of one's actions is required. Because a linear increase in the number of errors in the consecutive series was anticipated, regression coefficients (standardized beta scores) were determined for each participant. Difficulty (four levels) was entered as the predictor and number of errors was entered as the dependent variable. The dependent measure of this task was the beta weight of the error score. Higher beta scores reflect a steeper increase in amount of errors, and thus a worse performance. For the time measure of the SOP, a beta score was calculated in the same way; A higher SOP beta time score indicated a steeper increase in time on task in the consecutive levels of the SOP.

WAIS Digit Span Forward and Backward [65]. In the Digit Span Forward, an increasing list of numbers has to be remembered and reproduced immediately after verbal presentation. The dependent measure of this task is the total number of correct digit spans reproduced. In the Digit Span Backward, a list of numbers has to be reproduced in reverse order. The dependent variable of this task is the total number of correctly reproduced backward spans. The verbal working memory measure used as a dependent variable was the correct score on the Digit Span Backward divided by the correct score on the Digit Span Backward score.

Planning

Tower of London (ToL) [66]. This test measures planning ability. The subject has to move coloured balls on pegs from a fixed starting configuration to a goal configuration in a limited number of steps. In the version applied in this study two, three, four and five move problems were presented to the subjects, and the required number of steps was indicated (see [66]). When subjects failed an item, they would have up to two extra trials to attain the goal configuration. The correct score of each item ranged from 1 to 3 points, with a reduction of 1 point for each extra trial that was needed. A linear decrease was expected in the number of correct trials. Therefore, regression coefficients (standardized beta scores) were determined for each participant and beta weights were calculated, with the number of correct trials as the dependent variable and difficulty level (four levels) as the predictor. A lower beta score indicated a steeper decrease on correct trials and thus indicated a worse performance. The dependent measure of this task was the beta weight of the correct score.

Basic cognitive function tasks

Stop Signal Task Mean Reaction Time [53]. Mean Reaction Time (MRT) on Go trials from the Stop Task was used as a control measure for psychomotoric response speed.

WAIS Digit Span Forwards [65]. The Digit Span Forwards was taken as a control measure for immediate short-term memory. The dependent measure was the total number of correct digit spans reproduced.

Benton Visual Retention Test (BVRT) [67]. This test was included to control for immediate visual short-term memory abilities, necessary for performance on the SOP. Form C was administered consisting of 10 abstract designs, which are presented for 10 seconds. After each presentation, subjects have to draw the design by heart. The number of correctly reproduced designs was included as the dependent measure.

Sorting Task of the Groningen Intelligence Test (GIT) [68]. This subtest of the GIT was included to control for categorization skills, a requirement for performance of the WCST. In this task, 10 series of eight cards consisting of abstract designs are presented to the subject and have to be divided into two groups of four cards, according to two different sorting principles. Three practice series preceded the 10 series of cards. The dependent variable was the number of series categorized correctly.

Intelligence estimation

WAIS block design and vocabulary [65]. Two subtests of the WAIS, block design and vocabulary, were administered to obtain an estimation of the full-scale IQ. This short form of the WAIS correlates with the full scale WAIS IQ in the 0.90 range [69].

Statistical analysis

Missing data due to technical difficulties, not attending the second testing session or refusal to perform the task resulted in a smaller *n* for some tasks. Furthermore, data were excluded from the analyses when *Z* scores were higher than five or when observational measures indicated poor motivation or understanding of the task. The number of excluded and missing data ranged from zero to five in each group, resulting in zero to nine missing cases for each analysis.

MANOVAs were performed at the domain levels (inhibition, time estimation and reproduction, cognitive flexibility, working memory, planning and non-EF basic cognitive tasks). Pairwise Bonferroni corrected group comparisons (PG–NC, PG–AD, PG–TS, AD–NC and TS–NC) were performed only when main effects of group or group × factor interactions were significant at the $P < 0.05$ level. Because the AD group differed significantly in terms of age from the other groups, age was entered as a covariate in all analyses. Adding administration order as a factor in the MANOVAs affected only performance on the Digit Span Backwards task ($P < 0.01$). Administration order was therefore entered as a covariate in the working memory analyses. No significant correlations between administration order and performance were present ($r < 0.10$ on all dependent measures).

RESULTS

Demographics

Mean age, gender distributions, estimated IQ, scores on the Fagerström Test for Nicotine Dependence, the ADHD questionnaire, the Trait version of the State–Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI) and the numbers of participants with comorbid disorders are presented in Table 1. Compared to the NC group, the

PG group, the AD group and the TS group reported higher levels of ADHD symptoms (ADHD questionnaire), anxiety (STAI) and depression (BDI). The PG and AD group scored higher on the Fagerström Test for Nicotine Dependence (FTND) than the TS and the NC group.

EF measures

In Table 2, means, standard deviations and results of statistical analyses are presented for all EF and non-EF basic cognitive tasks for the PG, AD, TS and NC groups (see also Fig. 1).

Inhibition

A MANCOVA on the inhibition measures indicated a significant main effect of group. Pairwise group comparisons revealed slower SSRTs for the PG group, the AD group and the TS group compared to the NC group. This indicated poor inhibition of a discrete response in the clinical groups compared to the NC group. On the circle tracing task, the PG group and the TS group traced the circle faster than the NC group, showing poor inhibition of an ongoing response. On the Stroop Colour–Word Test, the clinical groups experienced more interference, and had more difficulty with the inhibition of interfering stimuli than the NC group.

Time estimation and reproduction

A repeated-measures analysis on absolute time discrepancies, with group as a between-subject factor and time length (2, 4, 8, 12, 20 seconds) and task (estimation and reproduction) as repeated-measures factors, showed a group effect (see Table 2) and a group × task interaction ($F_{3,165} = 4.27$, $P < 0.01$, $\eta^2 = 0.07$). Pairwise comparisons on the time estimation task revealed that both the PG and the AD group had higher absolute discrepancy scores, and thus showed less accurate time estimations compared to the NC group. The group × time length interaction indicated a less accurate time estimation during the longer time durations in the PG and the AD group, compared to the NC group. On the Time Reproduction Task, no main effects of group or group by time length interactions were found.

Cognitive flexibility

A MANCOVA on the cognitive flexibility measures indicated a significant group effect. The PG group completed less WCST categories than the NC group. On the WCST, no group differences existed for the percentage of perseverative errors. The PG group named fewer correct words than the NC group, the AD group and the TS group. There was a group effect for the number of perseverations on the fluency task. The AD group made more perseverations compared to the NC group.

Working memory

The MANCOVA on the working memory measures indicated no significant differences between the groups.

Planning

The MANCOVA on the Tower of London task indicated a significant group effect. In the PG group, lower beta value correct scores were found than in the NC group and the TS group, indicating a stronger decrease of scores with increasing difficulty level in the PG group than in the NC group and the TS group. A similar difference was found when comparing the AD group to the NC group.

Non-EF basic cognitive measures

Neither MANCOVA nor pairwise group comparisons on the non-EF basic cognitive measures yielded group differences. Thus, differences in basic cognitive functions required for adequate performance on the EF tasks could not account for group differences found on the EF measures.

Co-morbidity analyses

Eight participants were diagnosed with either ADHD inattentive subtype and/or ADHD hyperactive–impulsive subtype (see Table 1). Only three participants were diagnosed with antisocial personality disorder, using the DIS-P. Therefore, separate analyses comparing subjects with and without a diagnosis of ADHD or antisocial personality disorder were not feasible. Data were re-analysed excluding participants with ADHD and/or antisocial personality disorder diagnoses. Results for all omnibus tests and pairwise group comparisons remained the same. However, two exceptions should be noted. For one of the three inhibition measures, the significant group difference between the PG and NC group became marginally significant (SSRT, $P = 0.05$). This was due mainly to a loss of power, because the effect size remained the same. Furthermore, the difference between the TS group and the NC group on the circle tracing task disappeared. A lower power was the main reason for this, as the effect size did not change. Covarying for nicotine dependence, measured by the Fagerström Test for Nicotine Dependence, did not alter the results of the analyses.

No analyses with anxiety and depression as covariate were employed as the SOGS scores correlated strongly with anxiety and depression ($r = 0.42$ and $r = 0.43$, respectively, $P < 0.01$), and covarying thus would result in the elimination of variance associated with PG [70]. Furthermore, anxiety and depression scores did not correlate with performance on the EF measures (all correlations: $r < 0.15$).

Table 2 Marginal group means corrected for age, standard deviations (SD), MANOVA results and planned pairwise group comparisons for EF and non-EF basic cognitive measures.

	PG		*AD*		*TS*		*NC*					
	M	*SD*	*M*	*SD*	*M*	*SD*	M	SD	*F (d,f)*	η^2	*P-value*	*Bonferroni-corrected planned group comparisons*
Inhibition									$2.90_{(9528)}$	0.05	< 0.01	
Stop Signal Reaction Time	143.5	58.7	149.8	60.2	146.2	61.2	114.0	28.4				PG, AD, TS < NC; PG = AD, TS
Circle tracing time	260.1	181.0	341.4	240.4	308.4	186.6	428.6	302.8				PG, TS < NC; PG = AD, TS
SCWT† interference score	33.8	14.6	35.3	12.9	32.2	11.6	27.0	7.6				PG, AD, TS < NC; PG = AD, TS
Time estimation and reproduction									$3.58_{(3165)}$	0.05	< 0.05	
Time estimation‡	3.26	2.95	2.60	2.28	2.12	1.55	1.65	1.06				PG, AD > NC; PG = AD PG > TS (trend)
Time reproduction§	0.96	0.11	0.98	0.11	0.92	0.11	1.07	0.10	NS			NS
Cognitive flexibility									$2.25_{(12,522)}$	0.05	< 0.01	
WCST percentage perseveration¶	15.1	8.4	15.1	9.6	13.9	8.3	11.9	6.0				NS
WCST *n* correct categories††	4.6	1.8	5.0	1.7	5.1	1.4	5.5	1.0				PG < NC; PG = AD, TS
Fluency *n* correct	71.6	18.2	82.0	16.2	82.1	15.8	83.7	16.4				PG < NC, AD, TS
Fluency *n* perseverations	1.49	1.53	2.25	1.81	1.69	1.51	1.25	1.28				AD > NC
Working memory									$0.75_{(9483)}$	0.01	0.67	
SOP beta errors‡‡	0.53	0.47	0.45	0.43	0.43	0.45	0.53	0.47				
SOP beta time§§	0.95	0.04	0.94	0.08	0.93	0.10	0.95	0.06				
Digit Span Backwards	–0.08	2.34	0.10	1.84	0.48	1.91	0.26	2.08				
Planning: Tower of London task									$6.35_{(3187)}$	0.08	< 0.001	
Correct score	–0.61	0.40	–0.66	0.37	–0.31	0.64	–0.38	0.51				PG, AD < NC; PG = AD; PG < TS
Basic cognitive tasks									$0.68_{(12,540)}$	< 0.01	0.76	
Two choice MRT¶¶	398.3	74.6	388.8	49.6	392.6	43.5	396.9	51.3				NS
Digit Span Forwards	7.19	2.1	7.00	2.3	7.44	2.6	7.38	2.2				NS
BVRT *n* correct†††	7.23	1.6	7.38	1.8	7.59	1.5	7.54	1.3				NS
Sorting task *n* correct	4.85	1.7	5.18	1.9	5.20	1.7	5.25	1.7				NS

†SCWT = Stroop Colour Word Test; ‡time estimation = time estimation absolute discrepancy score; §time reproduction = time reproduction absolute discrepancy score; ¶WCST percentage perseveration = Wisconsin Card Sorting Test percentage perseverative errors; ††WCST *n* categories = Wisconsin Card Sorting Test number of categories completed; ‡‡SOP beta errors = Self-Ordered Pointing Task beta value of error scores; §§SOP beta time = Self-Ordered Pointing Task beta time score; ¶¶two choice MRT = two choice mean reaction time Stop Signal Task; †††BVRT = Benton Visual Retention Test.

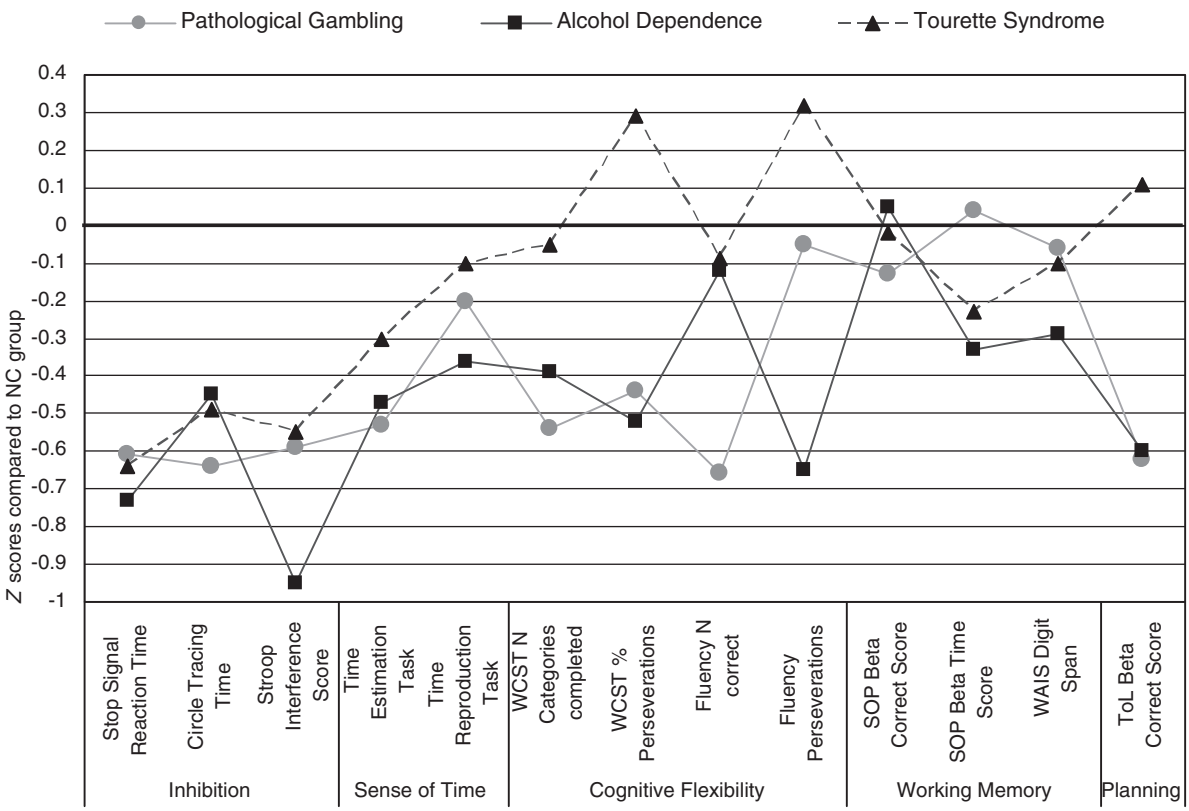

Figure 1 Executive function *Z*-profile of pathological gambling, alcohol dependence and Tourette syndrome participants, with the normal control group as the reference group ($Z = 0$)

DISCUSSION

With regard to our first research question on the presence of EF deficits in PG, it can be concluded that comprehensive EF deficits were present in the PG group compared to the NC group. The deficits found in EFs in the PG group could not be explained by deficits in basic cognitive functions, which are proposed as a prerequisite for performance of EF tasks [71,72]. These results are consistent with the only existing study in a PG group without comorbid psychopathological conditions or medication use, which also found that complex functions such as planning were diminished in pathological gamblers, but that more simple cognitive functions, such as attention, were intact [73]. The only study which indicated that basic cognitive functions, such as memory functions, were impaired in PG was a study which included pathological gamblers who had a history of traumatic brain injury and/or were using psychotropic drugs [74]. The results of this last study are therefore likely to be associated with these comorbid conditions [75–77]. Because only a preliminary study showing diminished inhibition in a subgroup of 12 former pathological gamblers exists [78], this study substantiates these preliminary findings, and was the first to indicate that a pervasive deficit in inhibition was present in a PG group. This study was the first to investigate time estimation in PG, and the finding of diminished time estimation in PG is consistent with studies that report on deficiencies in time estimation in ADHD compared to normal controls [79]. The findings of diminished cognitive flexibility functions in PG compared to normal controls in our study are consistent with findings of two studies in PG, one employing the WCST [73] and one using a Verbal Fluency Task [74], but are inconsistent with a study that reported no impairments on the WCST in a smaller PG group [80].

With regard to the second research question regarding the specificity of EF deficits in PG, our results indicate that the PG group resembled the AD group more than the TS group. The PG group did not differ from either the AD group or the TS group in the larger part of the comparisons. Despite this, the PG group shared a broader range of EF deficits with the AD group than with the TS group. The finding that inhibition deficits were present in PG, AD and TS is in keeping with an abundance of experimental studies indicating that inhibition deficits are present in other disorders of behavioural disinhibition, e.g. ADHD [81], psychopathic and antisocial conditions [82,83], alcohol dependence, [84], cocaine dependence [85] and bulimic eating disorder [86].

As discussed in the Introduction, the DSM-IV-TR diagnostic criteria for PG resemble both substance dependence criteria as well as impulse control disorder criteria. The classification of PG in the DSM-III and DSM-IV-TR has been subject to scientific debate. PG, although classified as an impulse control disorder, is also regarded as a behavioural addiction or as an obsessive compulsive spectrum disorder [6,87]. Our findings may contribute to this debate: the deficits in more complex goal-directed EFs in PG and AD compared to the NC group point to a common, broader neurocognitive deficit underlying PG and AD, whereas the diminished inhibition as present in the three clinical groups compared to the NC group seems to be common to both impulse control disorders and substance dependence [24,88,89]. However, the present findings need to be replicated before firm conclusions regarding the neurocognitive aetiology of PG can be drawn. Therefore, the role of neurocognitive impairments should be investigated in studies including pathological gamblers, other impulse control disorders and substance-dependent groups.

With regard to the third research question, our findings indicate that comorbid symptoms had limited influence on EF performance. The neurocognitive deficits found in our study can therefore be ascribed to the disorders under study. Due to the stringent exclusion criteria, our sample excluded people with serious psychopathological conditions, which are in itself associated with neurocognitive dysfunctions [75–77]. It is therefore likely that when PG, AD or TS are accompanied by comorbid conditions, such as substance dependence or major depressive disorder, more severe neurocognitive deficits or a broader range of deficits will emerge.

Some limitations to this study should be noted. Our sample consisted of an adult sample of predominantly male pathological gamblers. The results can therefore not be generalized to female pathological gamblers, or to adolescent pathological gamblers. Due to the low numbers of pathological gamblers with ADHD or ASP included in our study, it was not possible to investigate whether pathological gamblers with other comorbid disorders would have more serious EF deficits. The inclusion of female and adolescent participants and PG groups with and without comorbid psychopathological disorders in future studies would therefore be advisable. Because the AD and TS group were matched to the PG group, a selection bias could have been present, and this limits the generalization of the findings to AD and TS groups in general. The inclusion of PG subjects who already presented for treatment limits generalization of the study findings to pathological gamblers who seek treatment. However, the severity of PG in our study was comparable to the severity of PG as reported in a study including pathological gamblers who did not seek treatment, as the SOGS scores in our study were similar to the SOGS scores reported in that study [90].

Diminished neurocognitive functions are proposed both as vulnerability factors for developing substance dependence and as the result of extraneous drugs on brain functions [12,91]. Several studies suggest that mild dysfunctions in EFs mediate the enhanced risk for later development of substance and alcohol dependence in children with a familial risk for developing substance dependence [92–94]. In gambling research, only one longitudinal study exists on this topic. This study reports that adolescents with a diminished performance on an inhibition task had a higher chance of developing problem gambling later in life [95]. Although our study was limited to a cross-sectional study of neurocognitive functions, our findings give indirect evidence that diminished EFs may be a vulnerability factor for developing PG, because our sample consisted of pathological gamblers without a history of substance dependence. Future studies on the role of EFs in the development of PG, AD or other addictive behaviours could shed light on the aetiology of neurocognitive impairment.

The first neuroimaging studies in PG indicate that abnormalities exist in the ventromedial prefrontal cortex and cortico–basal ganglionic–thalamic circuits [90,96]. Studies also indicate dysfunctions in frontal and fronto–striatal circuits in substance dependence [15,97]. Neuroimaging studies have shown that EF tasks similar to those used in our study activate a variety of areas within the prefrontal cortex [28,31,98] and in addition to this, activate areas with important connections to the prefrontal cortex, such as the caudate nucleus, the putamen, thalamic areas [30], cingulate and parietal cortex [29,99]. The deficits in EFs as found in our PG and AD group are therefore likely to be associated with dysfunctions of these brain structures and brain circuits. Therefore, in future studies it seems critical to test the hypothesis of abnormal brain functioning in PG more thoroughly, using EF tasks in a neuroimaging setting.

Deficits in EFs are proposed as important mediators in drug bingeing [15], and several studies suggest that impairments in EFs have a negative impact on treatment success and relapse in substance dependence [100–103]. The EF deficits as found in PG as well as AD in this study may therefore foster the continuation of these disorders, limit the impact of psychosocial treatment and promote relapse after discontinuation of PG or AD. Therefore, it would be advisable to assess EFs both in AD and PG, and provide those clients with diminished EFs with extra interventions during psychosocial treatment. For example, by providing treatment goals in a structured format and helping clients to apply abstract treatment information to their personal situation, clients with diminished EFs may benefit more from the treatment provided [12].

Research into the effects of psychopharmacological treatment on diminished EFs in PG, as applied in ADHD, is indicated [20]. More general, longitudinal studies are warranted, investigating whether in PG diminished EFs negatively influence treatment effects, relapse and chronicity.

In conclusion, a broad range of EF deficits was found in a carefully screened PG and AD group, whereas in a TS group only inhibition deficits were present. These results substantiate the literature on neurocognitive deficits in PG and indicate that a similar neurocognitive aetiology may underlie PG and AD. Treatment of PG and AD may benefit from interventions targeting these EF dysfunctions. Future studies, applying neuroimaging techniques to neurocognitive paradigms and investigating the effects of diminished EFs on the course of PG, are warranted.

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