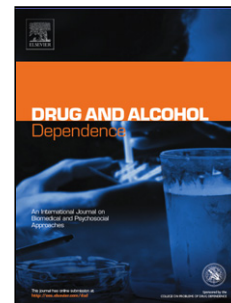


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Working memory and affective decision-making in addiction: A neurocognitive comparison between heroin addicts, pathological gamblers and healthy controls

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ABSTRACT

Background: Cognitive deficits are observed both in heroin dependence and in pathological gambling (PG) on various tasks. PG, as a non-substance addiction, is free of toxic consequences of drug use. Therefore a direct neurocognitive comparison of heroin addicts and pathological gamblers helps dissociate the consequences of chronic heroin use on cognitive function from the cognitive vulnerabilities that predispose addiction. **Methods:** A case-control design was used, comparing 58 abstinent heroin addicts, 58 pathological gamblers, and 60 healthy controls on working memory and affective decision-making functions. Working memory was assessed using the Self-ordered Pointing Test (SOPT). Affective decision-making was measured by the Iowa Gambling Task (IGT). **Results:** Heroin addicts performed significantly worse both on the IGT and on the SOPT, compared to healthy controls. Pathological gamblers performed worse on the IGT than healthy controls, but did not differ from controls on the SOPT. Years of heroin use were negatively correlated with working memory and affective decision-making performance in heroin addicts, while severity of gambling was not significantly correlated with any task performance in pathological gamblers. **Conclusions:** Our findings indicate that deficits in affective decision-making shared by heroin dependence and PG putatively represent vulnerabilities to addiction and that working memory deficits detected only in heroin addicts may be identified as heroin-specific harmful effects.

KEYWORDS: Heroin dependence; pathological gambling; working memory; affective decision-making

1. INTRODUCTION

Heroin abuse is a major public health issue both in Europe and North America (Anton et al., 2009; Fischer et al., 2007) and in China (Tang et al., 2006; Tang and Hao, 2007). Heroin addicts have extensive impairments in neurocognitive functioning, including inhibitory control (Brand et al., 2008; Pau et al., 2002; Prosser et al., 2006), cognitive flexibility (Brand et al., 2008; Mintzer et al., 2005), working memory (Ersche et al., 2006; Fernández-Serrano et al., 2010; Ornstein et al., 2000), delay discounting (Cheng et al., 2012; Kirby et al., 1999; Kirby and Petry, 2004), and decision making (Barry and Petry, 2008; Brand et al., 2008; Fishbein et al., 2007; Verdejo-García and Pérez-García, 2007). These deficits may affect the addicts' daily life, family relations, and occupational status (Bechara et al., 2001), and are essential in the treatment and relapse of drug addiction (Teichner et al., 2002). However, it is quite controversial whether the cognitive dysfunction in heroin-dependent individuals is the consequence or the predisposing factor of persistent heroin use.

Cognitive impairments have also been observed in pathological gambling (PG) (see review in van Holst et al., 2010). PG is regarded as a non-substance induced behavioral addiction (Holden, 2001; Petry, 2006; Potenza, 2006), sharing many similarities with drug addiction, such as on neurobiological underpinnings (Potenza et al., 2003; Potenza, 2008; Slutske et al., 2000) and treatment approaches (Hodgins et al., 2001; Kim et al., 2001; Petry et al., 2008). Because PG does not necessarily involve the neurotoxicity associated with concomitant drug use, a comparison of PG and drug addiction may help dissociate the specific effects of chronic drug use on cognitive function from the cognitive vulnerabilities that predispose addiction (Verdejo-García et al., 2008). It is assumed that predisposing factors associated with the vulnerability to addiction should be present in both drug addicts and pathological gamblers, while impairments associated with the long-term effects of drug use would be present in drug addicts but absent in pathological gamblers (Lawrence et al., 2009a).

Previous studies have compared impulsivity, response inhibition, working memory and risky decision-making

between alcohol-dependent and PG patients (Lawrence et al., 2009a, 2009b) and between cocaine-dependent and PG individuals (Albein-Urios et al., 2012). Indeed, some specific deficits of cocaine/alcohol use (e.g., on working memory) and some common deficits (e.g., on response inhibition) have been found. Nevertheless, little work has directly compared heroin addicts and pathological gamblers. Amassing evidence has suggested that cognitive deficits caused by cocaine, alcohol and heroin abuse are somewhat different (Badiani et al., 2011; Fernández-Serrano et al., 2010). Specifically, chronic psycho-stimulants and alcohol use seems to cause relatively more pronounced deficits in impulse control and cognitive flexibility, while there are persistent heroin-related effects on updating and decision-making (Fernández-Serrano et al., 2011). From a neurochemical point of view, opioids (e.g., heroin, morphine) produce their effects by binding to opioid receptors (μ , κ and δ) located principally in the central and peripheral nervous system and the gastrointestinal tract, and the neurotoxic effects of opioids abuse are often associated with oxidative stress and apoptosis (e.g., in prefrontal cortex and basal ganglia) and inhibition of neurogenesis (e.g., in hippocampus), leading to various neurological impairments (Cunha-Oliveira et al., 2008). PG is free of the toxic consequences that are closely associated with heroin abuse, whereas it shares some notable similarities with heroin dependence. For example, these two disorders have similar clinical features characterized by craving, tolerance (i.e., needs to gamble more or increase doses of heroin), withdrawal (e.g., restless, irritable), and frequent relapses. A direct comparison of PG and heroin dependence may thus help search for neurobiological vulnerabilities to these disorders, and meanwhile, benefit further understanding of heroin-induced neurotoxicity.

Prefrontal cortex (PFC)-dependent neurocognitive functions have been of particular interests in addiction research (Goldstein and Volkow, 2011). Although the function of the PFC is highly integrated, two partially distinct PFC networks have been implicated in different aspects of neurocognitive function. The dorsolateral sectors and the anterior cingulate cortex have been linked to so-called “cold” cognitive processes, including working memory, response inhibition, task switching, and conflict monitoring (Badre and D'Esposito, 2009;

Gläscher et al., 2012; Koechlin et al., 2003), and the ventral and medial sectors have been more involved in reward/emotion-related functions, including valuation, emotion regulation, and decision making (Bechara and Van der Linden, 2005; Gläscher et al., 2012; O' Doherty, 2004; Peters and Buchel, 2010; Rangel et al., 2008).

Affective or value-based decision-making ability, as typically measured by the Iowa Gambling Task (IGT; Bechara et al., 1994, 1999) and other analogous tasks such as the Cambridge Gamble Task (CGT; Rogers et al., 1999), is essential for making choices in complex situations involving positive and negative affective consequences and has been ascribed to the function of the ventromedial/orbital frontal cortex (Bechara et al., 1999, 2000). Affective decision-making deficits have been reported among individuals with different forms of substance use disorder (e.g., alcohol, marijuana and cocaine; Barry and Petry, 2008; Bechara et al., 2001; Bechara and Damasio, 2002; Bechara and Martin, 2004; Fernández-Serrano et al., 2010; Noël et al., 2007; Verdejo-García et al., 2007). Heroin addicts have also been found to reveal severe affective decision-making impairments (Fishbein et al., 2007; Vassileva et al., 2007; Zhang et al., 2011). Interestingly, pathological gamblers have shown impaired performance on decision-making tasks as well (Cavedini et al., 2002; Goudriaan et al., 2005, 2006; Lawrence et al., 2009b). Working memory, by contrast, is one well-known cognitive process linked to the function of dorsolateral sectors of the PFC, mainly involved in processing competing considerations and interference of various demands on cognitive resources (Johnson et al., 2008). Cocaine and amphetamine abusers have notable working memory deficits compared to controls (Albein-Urios et al., 2012; Fernández- Serrano et al., 2010). Heroin abusers also reveal significant deficits on different tasks of working memory (Ersche et al., 2006; Ornstein et al., 2000). Comparatively, pathological gamblers show intact working memory on the Self-Ordered Pointing Task (SOPT) and N-back tasks (Albein-Urios et al., 2012; Leiserson and Pihl, 2007), and there is still lack of strong evidence that working memory is compromised in PG (Leeman and Potenza, 2012).

We hypothesized that deficits in affective decision-making might represent a potential vulnerability to

addiction, while deficits in working memory could be associated with the specific effects of chronic drug use. The present study directly compared affective decision-making (measured by the IGT) and working memory (measured by the SOPT) functions in heroin addicts (HAs), pathological gamblers (PGs), and healthy controls with a large sample size. We expected that both PGs and HAs would show deficits in affective decision-making, while only HAs would show deficits in working memory.

2. METHODS

2.1. Participants

A total of 176 adult subjects participated in the study. Fifty-eight abstinent heroin addicts (HAs) aged 23-48 years were voluntarily enrolled in the Beijing Tian-Tang-He Compulsory Addiction Rehabilitation Center. Because most heroin addicts are men in China and all patients are male in the center, only male participants were included in the study. All of the patients met the diagnostic criteria for a lifetime history of heroin dependence, but without abuse or dependence to any other drug (e.g., cocaine, methamphetamine, marijuana) except nicotine, assessed with the Structured Clinical Interview for DSM-IV disorders (SCID; First et al., 1995). All of them were reported “pure” heroin users and those who had poly-drug use were excluded. The average duration of heroin use was 8.0 ± 6.5 years, ranging from half a year to 20 years. The average abstinence from last drug use was 12.6 ± 5.9 months by self-report. The exclusion criteria for the patients included a history of major psychiatric disorders (schizophrenia, psychotic episodes, major depressive disorder or bipolar disorder), a history of brain injury/trauma, physical conditions known to influence cognitive performance, current/past neurological diseases or mental disorders, and use of psychotropic medication within two weeks of the study enrollment.

Fifty-eight pathological gamblers (PGs) aged 20-50 years were enrolled, only male included. The gamblers were recruited from the Beijing Xin-An Reeducation-Through-Labor Center, a local compulsory rehabilitation center for individuals suffering from gambling problems and other maladaptive or illegal behaviors. They were

preliminarily screened and advised to participate in the study by their psychology therapist. The gamblers have not been under any psychotherapy or medicinal treatments for PG before this study. All of them were formally screened with a scheduled assessment for PG. The main inclusion criterion for PGs was a score ≥ 5 on the South Oaks Gambling Screen (SOGS; Lesieur and Blume, 1987), indicating probable PG in the past 12 months. Moreover, the gamblers were evaluated using the Structured Clinical Interview for Pathological Gambling (SCI-PG; Grant et al., 2004), a 10-question diagnostic instrument for DSM-IV pathological gambling, with a score of 5+ indicating current PG. Most of the forms of gambling among the gamblers are mahjong, poker cards, and lottery, because casino games are legally prohibited in whole Mainland China. Gamblers who had a history of drug abuse or alcohol dependence, except for smoking, were excluded. Further exclusion criteria were major medical illness, brain injury/trauma, current/past neurological diseases, psychosis or mental disorders, current use of psychoactive medication within the past two weeks, and an inability to complete the tasks.

Sixty healthy controls were recruited in local community, matched with gender, age, and education with PGs and HAs. The inclusion criteria for controls comprised no history of drug abuse (with the exception of smoking), non-alcoholic, non-problem or pathological gambler ($\text{SOGS} \leq 2$). The exclusion criteria for healthy controls were the same as that for PGs. All subjects gave written informed consent and were compensated for their time. This study was approved by the Institutional Review Board at Institute of Psychology, Chinese Academy of Sciences.

2.2. Measures

2.2.1. The Self-ordered Pointing Test (SOPT)

The SOPT (Peterson et al., 2002) is a well-constructed visual working memory task, which was based upon an original task developed by Petrides and Milner (1982). The task consists of both verbal (concrete) and non-verbal (abstract) components, each with three trials. In the verbal component, pictures of concrete and nameable objects are presented, whereas in the non-verbal component, abstract designs difficult to name verbally

are presented. In each trial, 12 pages are presented sequentially on the computer with the same 12 pictures, but in a different spatial arrangement. Subjects have to point to a different picture on each presentation until the 12 pages are fully pointed. The total number of correct selections represents the working memory score. Higher scores reflect better working memory capacity. There is a possible maximum score of 12 on each trial and 72 for all trials in this task.

2.2.2. *The Iowa Gambling Task (IGT)*

We employed the original Iowa Gambling Task (Bechara et al., 1994; Bechara et al., 1999) to assess affective decision-making ability. In the task, participants were required to select one card at a time from one of the four card decks labeled A, B, C, and D, with the goal of maximizing their net profit over 100 card choices. Unbeknownst to participants, decks A and B yield high immediate gain but a greater loss, while decks C and D result in lower immediate gain but a smaller loss. Total gain is \$1,000 in every 10 cards in decks A and B, compared to \$500 in decks C and D. Total losses amount to \$1,250 in every 10 cards in decks A and B, compared to \$250 in decks C and D. Therefore, decks A and B are disadvantageous and decks C and D are advantageous in the long run. In the IGT, net score was calculated and analyzed, that is, total number of selections from advantageous decks (C+D) minus that from disadvantageous decks (A+B). Thus, positive numbers of net score reflect advantageous or non-impaired decision-making ability, while negative numbers of net score reflect disadvantageous or impaired decision-making ability. In addition, the 100 card choices could be divided into five blocks with 20 cards each according to the time sequence, so as to test the change of decision-making strategy.

2.3. *Data analysis*

The data were analyzed with the Statistical Package for the Social Sciences for Windows, Version 15.0 (SPSS Inc., Chicago, IL, USA). Categorical data (i.e., marital status) were analyzed with chi-square tests. Task scores on SOPT and IGT were compared between the groups by analysis of variance tests (ANOVAs). To analyze the IGT

performance across blocks, between-within ANOVAs were used, with block as the within-group factor and group as the between-group factor. Post-hoc comparisons were investigated using Fisher's least significant differences protected t-test. The relationships between years of heroin use and task scores in HAs, and between severity of gambling (years of regular gambling, SOGS score) and task scores in PGs were tested using partial correlations, controlling for age, education, marital status, and smoking. The threshold for statistical significance was set at $p < 0.05$, two-tailed.

3. RESULTS

3.1. Demographic characteristics

A description of demographics, drug use and smoking variables, and scores on the SOGS is presented in Table 1. No between-group differences were present in the distribution of age, education, or marital status. However, one-way ANOVAs revealed that HAs consumed more cigarettes per day than PGs and healthy controls ($p < 0.001$), thus in further analyses, smoking was controlled for as a covariate. The mean SOGS score for PGs was 9.9 (standard deviation 3.5), consistent with that in previous studies (e.g., Lawrence et al., 2009a).

3.2. Performance on the SOPT

SOPT scores are presented in Figure 1. One-way ANOVAs showed significant between-group differences on total score ($F_{(2,173)} = 19.971$, $p < 0.001$). Post-hoc tests indicated that HAs performed significantly worse than both healthy controls and PGs ($ps < 0.001$), but there was no difference between PGs and healthy controls ($p = 0.872$). A 2 (task difficulty: verbal, non-verbal) \times 3 (group) between-within ANOVA test, with smoking as the covariate, revealed significant effects of task difficulty ($F_{(1,172)} = 41.540$, $p < 0.001$, $\eta_p^2 = 0.195$) and group ($F_{(2,172)} = 11.880$, $p < 0.001$, $\eta_p^2 = 0.121$), but without a significant interaction effect between task difficulty and group ($F_{(2,172)} = 0.905$, $p = 0.406$). Post-hoc tests revealed that HAs were significantly impaired in both verbal and non-verbal components of working memory, compared to healthy controls and PGs ($ps < 0.001$). PGs did not differ from healthy controls

neither on verbal ($p=0.501$) or non-verbal ($p=0.392$) components.

3.3. Performance on the IGT

Net scores on the IGT are presented in Figure 2 (a). One-way ANOVAs revealed significant between-group differences on total net score ($F_{(2,173)}=4.886$, $p=0.009$). Post-hoc tests revealed that HAs had worse performance in decision making when compared with healthy controls ($p=0.003$, Cohen's $d = 0.58$). PGs also showed worse decision-making performance than healthy controls ($p= 0.029$, Cohen's $d = 0.43$), but did not differ from HAs ($p=0.423$). In order to analyze the temporal changes of decision-making strategy across five blocks of 20 cards, we used a 3 (group) \times 5 (block) between-within ANOVA test, with smoking as the covariate. Figure 2 (b) clearly shows the condition effects between healthy controls and the other two groups. There is a significant main effect of group ($F_{(2, 172)} = 3.304$, $p=0.039$, $\eta_p^2 = 0.037$), but without a significant effect of block ($F_{(4, 688)} = 1.787$, $p=0.130$) or an interaction effect between group and block ($F_{(8, 688)} = 1.522$, $p=0.146$). An analysis within each group reveals that the block effect is significant in controls and PGs, but not in HAs. This suggests that although PGs show decision-making deficits, they still have the capability to learn, whereas HAs not only show decision-making deficits, but also the inability to learn. HAs are more like patients with prefrontal cortex damage.

3.4. Correlations between severity of heroin use or gambling and cognitive performance

Results of partial correlations are presented in Table 2. In HAs, there was a negative association between working memory score (concrete/verbal component) and years of heroin use ($r_{(52)} = -0.327$, $p = 0.016$), such that longer heroin use was associated with worse concrete memory deficits (see also Figure 3). There was also a negative association between years of heroin use and IGT net score ($r_{(52)} = -0.299$, $p = 0.028$), see Table 2 and Figure 3. Age of onset did not correlate significantly with working memory, but there was a significant association between IGT net score and age of onset ($r_{(52)} = 0.309$, $p = 0.023$). Duration of abstinence was not significantly related to working memory or decision-making performance.

In PGs, no significant associations between SOGS score and working memory or IGT net score were found. Nor significant associations were detected between duration of gambling and working memory or IGT net score (see Table 2). Total money loss did not correlate significantly with any task performance. We also tested the associations between smoking and cognitive performance in healthy controls. Numbers of cigarettes per day were not significantly correlated with IGT net score or working memory score.

4. DISCUSSION

In this study, we contrasted working memory and affective decision-making functions in individuals with PG and heroin dependence compared with a group of healthy controls. Our data revealed significant decision-making impairments in both PGs and HAs and impaired working memory in only HAs. Years of heroin use were significantly associated with working memory and decision-making deficits in HAs, while severity of gambling was not related to any task performance in PGs. These results support our hypotheses that heroin toxicity might be more related to working memory deficits, whereas impaired affective decision-making leading to addiction is a common deficit among PGs and HAs, and independent of any potential toxic effects of drugs.

Working memory is one of the specific and well-researched “cold” executive function that keeps competing considerations “online” (Kane and Engle, 2002). The working memory deficit we found in heroin addicts is in keeping with the present literature consistently demonstrating significant deficits of working memory in heroin abusers (Ersche et al., 2006; Fernández-Serrano et al., 2010; Fishbein et al., 2007; Ornstein et al., 2000; Verdejo-García and Pérez-García, 2007). More interestingly, we found that longer duration of prior heroin use correlated significantly with worse working memory (concrete/verbal component) in HAs, and that this deficit was not alleviated by abstinence. Conversely, we did not find working memory deficits in PGs who are in a condition of drug-free addiction, in agreement with previous observations (Albein-Urios et al., 2012; Leiserson and Pihl, 2007). These results implied that working memory deficits in HAs could be a direct effect of long-term heroin use. Our

findings, together with other reports of impaired working memory in alcohol and cocaine dependence (Albein-Urios et al., 2012; Lawrence et al., 2009a, 2009b), support the notion that repeated exposure to addictive drugs causes abnormalities in frontal cortex functions (Kalivas et al., 2005), especially the dorsolateral part. Indeed, a dysfunction of the dorsolateral prefrontal cortex (dlPFC), as a result of neurotoxicity in chronic heroin abuse, may account for working memory deficits in HAs (Goldstein and Volkow, 2011). We also suggest that the development of this working memory deficit, as a result of chronic drug use, exacerbates the poor decision-making capacity that predated the drug use and probably served as a predisposing factor in the decision to use drugs in the first place (e.g., Bechara, 2005). This is corroborated by the fact that correlation analyses further indicated that duration of heroin use was negatively associated with affective decision-making in HAs.

In terms of affective decision-making, the IGT has been shown to tax aspects of decision-making that are guided by affect and emotions (Bechara et al., 1996; Bechara, 2003; Turnbull et al., 2005). Individuals who display a tendency toward instant gratification or myopia for the future continue to choose from the disadvantageous decks in despite of a greater long-term loss on the IGT, indicating impaired decision-making (Bechara and Van der Linden, 2005). In our study, HAs showed significant decision-making deficits on the IGT compared to healthy controls, consistent with previous reports (Vassileva et al., 2007; Zhang et al., 2011). More importantly, the PGs who are free of toxic consequences of chronic drug use also revealed severe decision-making deficits relative to healthy controls, which were similar to HAs. Although previous evidence suggested that individuals with both PG and substance abuse/dependence problems may show poor decision-making capacity as measured by the IGT (Leeman and Potenza, 2012), our findings add a further evidence and directly show that this poor decision-making capacity also exists in PGs who have not abused drugs, and that it is similar to those who used heroin (i.e., HAs). These results suggest that poor decision-making is a condition that predates any toxic effects of drugs. This hypothesis is consistent with prior evidence showing that impaired performance on the IGT significantly predicted

smoking and binge-drinking behaviors in adolescents who have not yet been chronically exposed to substances and were followed up in a longitudinal study (Johnson et al., 2008; Xiao et al., 2008), and conversely, that improved affective decision capacity predicted less binge-drinking in these adolescents (Xiao et al., 2011). Taken together, these findings suggest that affective decision-making may serve as a neurocognitive vulnerability marker for the development of different forms of addiction.

Several limitations should be noted in this study. Firstly, we did not include female participants simply because they were not available. Therefore, the findings could not be generalized to the entire population of HAs and PGs, and future similar studies in females are warranted. Secondly, as the practice in most studies on addiction, we did not exclude the confounder of cigarettes smoking in HAs and PGs, albeit that smoking is considered in some circles as an addiction. We then controlled for smoking in main statistical analyses and the relationships of smoking with cognitive performance were analyzed. However, no significant correlations between smoking and any task performance were found, so that any difference in smoking status between healthy controls, PGs and HAs could not change the results of this study in a significant manner. Third, while the neuropsychological tasks are valid tasks that have been perfected over the year to evaluate the relationships between a certain brain damage or dysfunction and behavior, a more direct neural test of whether different sectors of the prefrontal cortex were differentially affected in PGs or HAs would require the use of neuroimaging approaches. In addition, the sample size within each group was reasonably large, while the effect sizes for group differences were moderate to small (mainly on the IGT). This raises concerns about the effects of some confounding factors on group difference, for instance, the motivation and effort put on the task by the addicted subjects (i.e. HAs or PGs). Though we had made detailed instruction to guide every participant to make their efforts in the task and try to win more money, as well as a motivation-effort check to exclude inercious response in the end of the task, these contextual/ motivational factors should be better controlled for in further research.

In addition to these limitations, one interesting and notable topic should be further raised that although the addicts performed more poorly than controls on the cognitive tasks (i.e., SOPT and IGT), it is unclear whether the poorer cognitive performance of the addicts (e.g. heroin abusers) compared to controls was really defective or within the “normal range.” We then compared our findings to some available normative data (mainly for the IGT). We found that our heroin addicts had a significant negative average of total net score on the IGT (Mean= -10.69) compared to our controls (Mean=3.17) and a large converged sample of healthy participants (N=479), of whom the weighted mean of total IGT net score was about 6 (Steingroever et al., 2013). Moreover, we further found that the proportion of subjects with impaired IGT performance (i.e. total net score below zero) in our heroin group was 72.41% (42/58), markedly higher than that of 26.67% (16/60) in our control group and 7.5-32.5% in control group in previous studies (Adinoff et al., 2003; Bechara et al., 1999, 2001; Bowman and Turnbull, 2003; Lehto and Elorinne, 2003). Overall, these findings suggested that heroin addicts performed more impaired on the IGT than controls, putatively representing impairments in daily-life decision making. Nevertheless, the paradox that at least some heroin addicts’ decision-making performance measured by the IGT was advantageous or non-impaired, while their decision-making about drug use in reality seems not so advantageous, still warrants further explanation.

In conclusion, our findings indicate that impaired affective decision-making shared by heroin dependence and PG putatively represents vulnerability traits for addiction and that working memory deficits merely detected in HAs may be identified as heroin-specific harmful effects.

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FIGURE LEGENDS

Figure 1. Total, verbal, and non-verbal scores on the Self-ordered Pointing Test (SOPT) for healthy controls, pathological gamblers, and heroin addicts. Data are presented as $M \pm S.E.$

Figure 2. Net scores on the Iowa Gambling Task (IGT): (a) total net score by group, and (b) net score across five blocks of 20 cards by group. Positive net scores reflect advantageous or non-impaired performance while negative net scores reflect disadvantageous or impaired performance. Data are presented as $M \pm S.E.$

Figure 3. Correlations between (a) years of heroin use and working memory performance (concrete/verbal), and

(b) years of heroin use and IGT net score. R values are presented as zero-order correlations.

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Table 1

Demographic characteristics of healthy controls, pathological gamblers (PGs), and heroin addicts (HAs).

| Variables | Healthy controls (n=60) | PGs (n=58) | HAs (n=58) | <i>p</i> |
|---|----------------------------|---------------|---------------|----------|
| Mean age, years (SD) | 34.3 (8.5) | 35.6 (7.1) | 35.7 (6.4) | 0.504 |
| Years of education (SD) | 9.5 (2.6) | 8.9 (3.2) | 8.4 (2.0) | 0.072 |
| Marital status, n (%) | | | | 0.458 |
| Never married | 18 (30.0) | 16 (27.6) | 14 (24.1) | |
| Married | 40 (66.7) | 36 (62.1) | 37 (63.8) | |
| Divorced/widowed | 2 (3.3) | 6 (10.3) | 7 (12.1) | |
| Drug use variables | | | | |
| Years of heroin use (SD) | NA | NA | 7.5 (5.4) | |
| Age of first use (SD) | NA | NA | 26.7 (5.8) | |
| Dosage per day, gram (SD) | NA | NA | 0.51 (0.56) | |
| Months of abstinence (SD) | NA | NA | 13.1 (5.9) | |
| Gambling-related variables | | | | |
| Years of regular gambling (SD) | NA | 7.2 (4.9) | NA | |
| Money lost, RMB ¥ (Median) ^a | NA | 120,000.00 | NA | |
| SOGS score, Mean (SD) | 0.9 (0.9) | 9.9 (3.5) | NA | |
| Cigarettes per day (SD) | 8.1 (9.4) | 12.2 (10.9) | 20.1 (9.4) | < 0.001 |

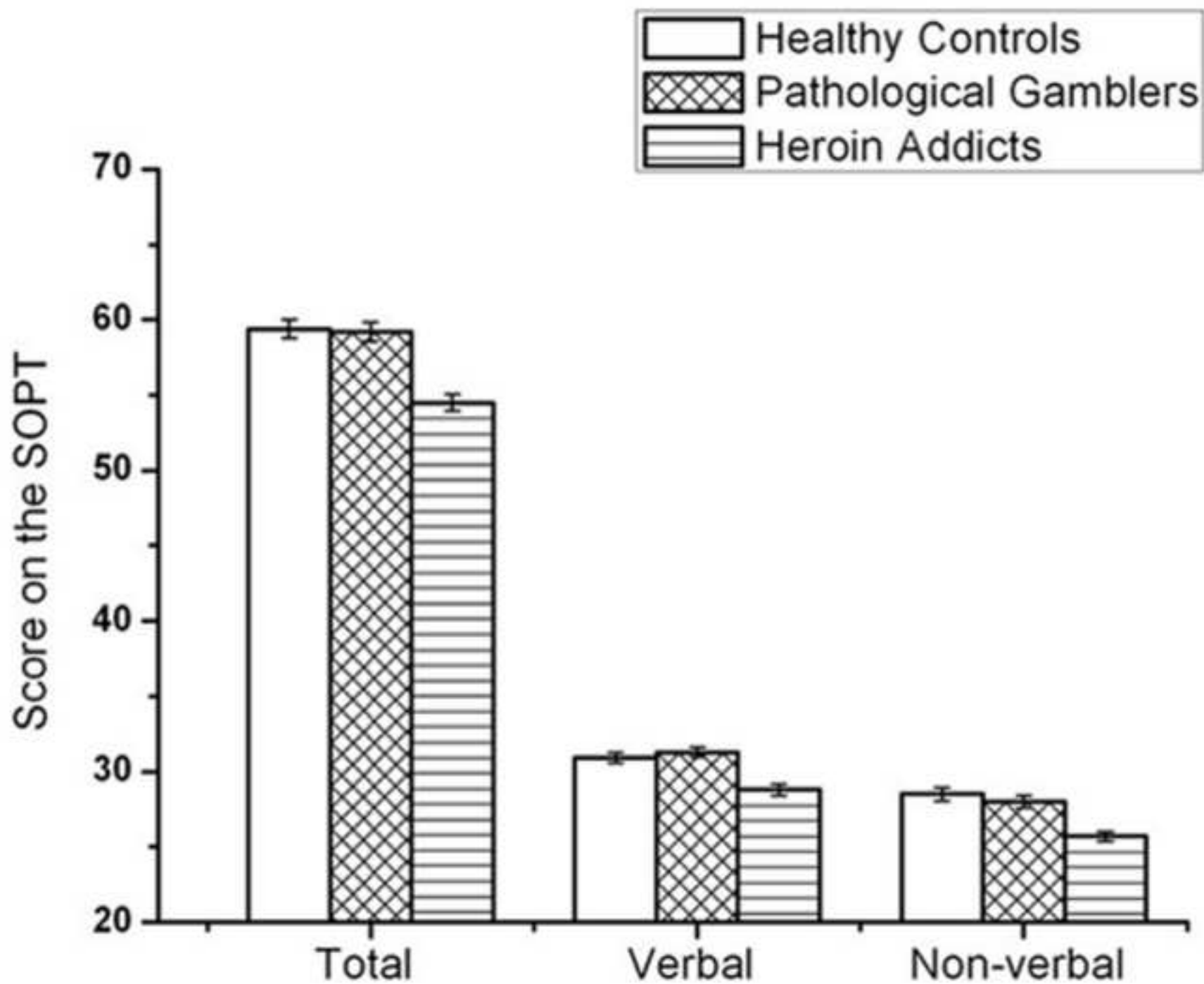
Note. All participants are male. SOGS=South Oaks Gambling Screen. SD= standard deviation. ^aEstimated total money lost in gambling for pathological gamblers, with two data missing. RMB ¥1≈ US \$ 0.161 (Jan, 2013).

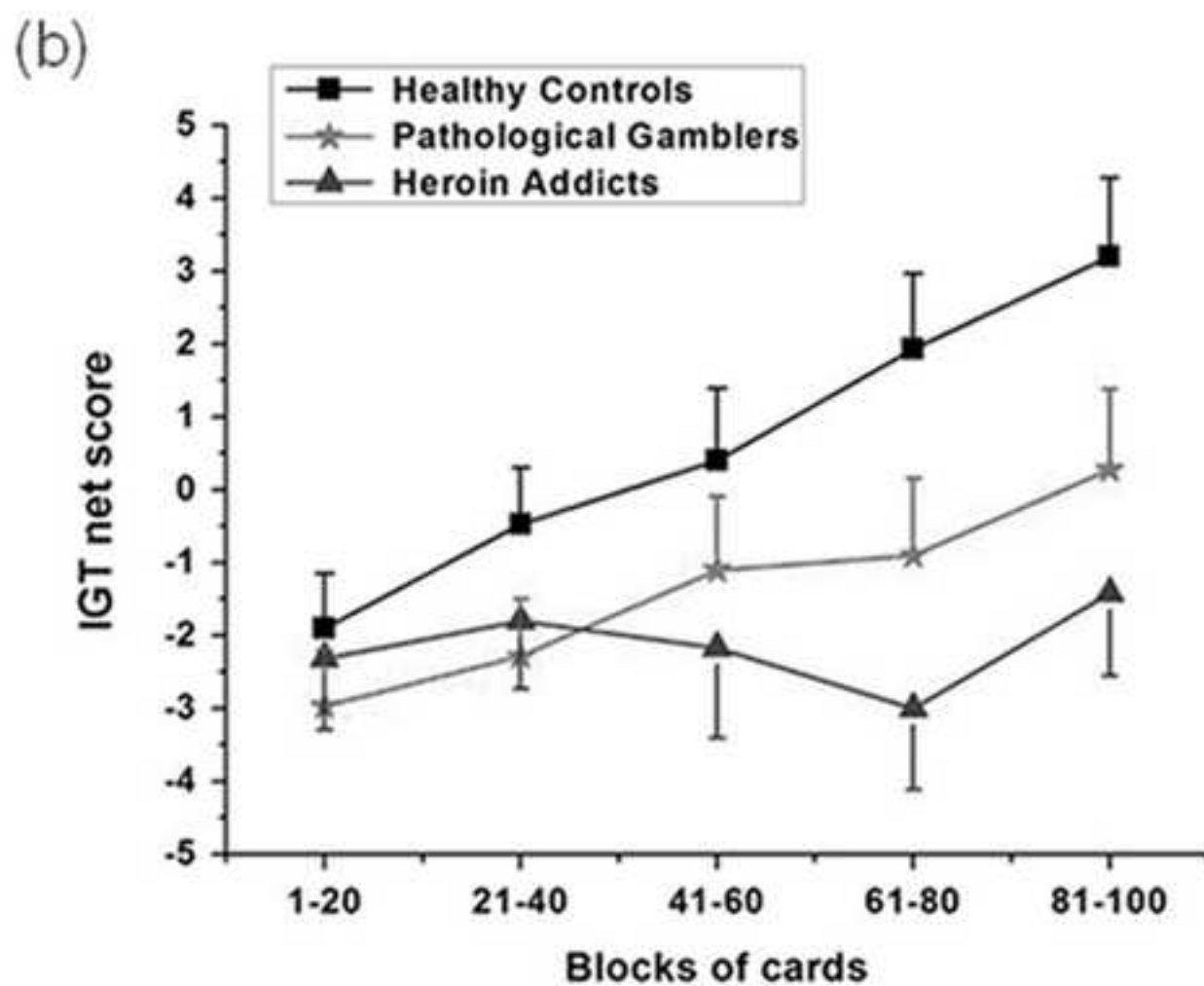
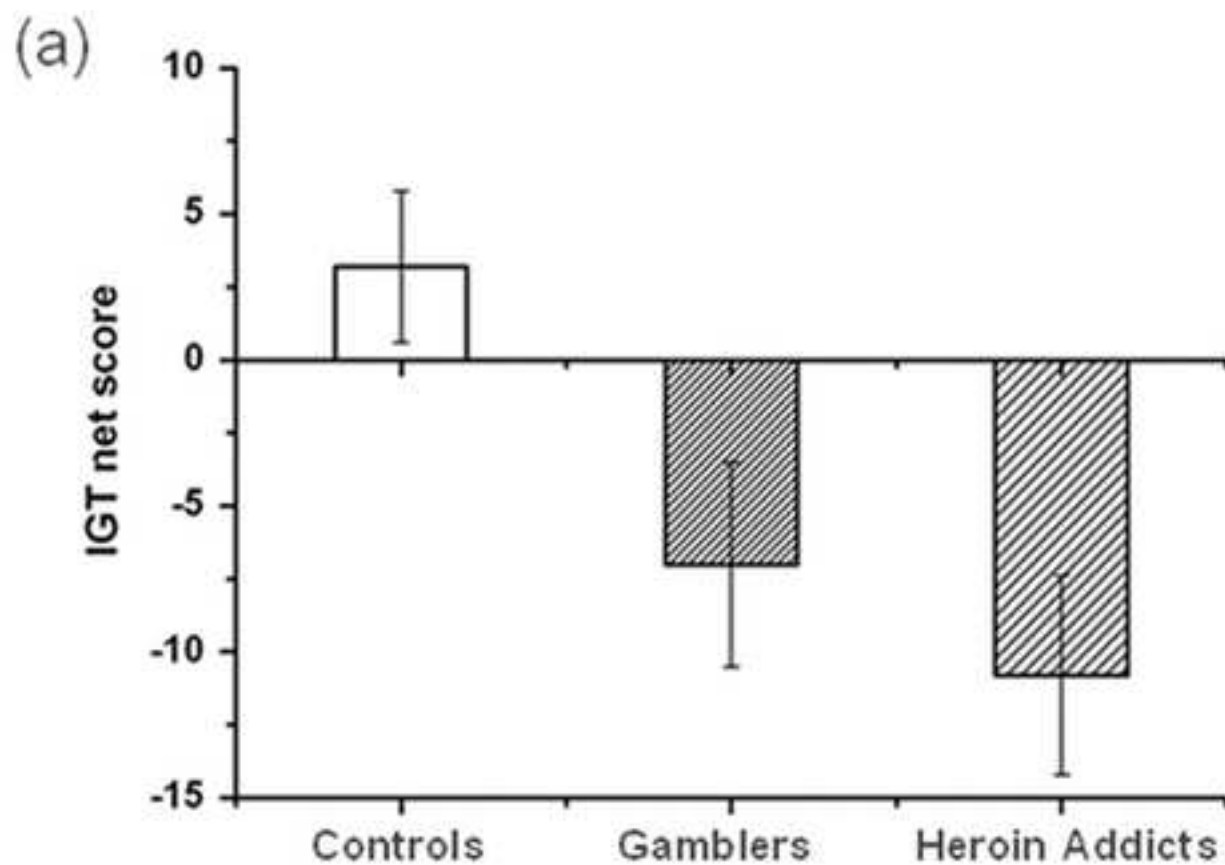
Table 2Partial correlations (r_p) between severity of heroin use or gambling and cognitive performance.

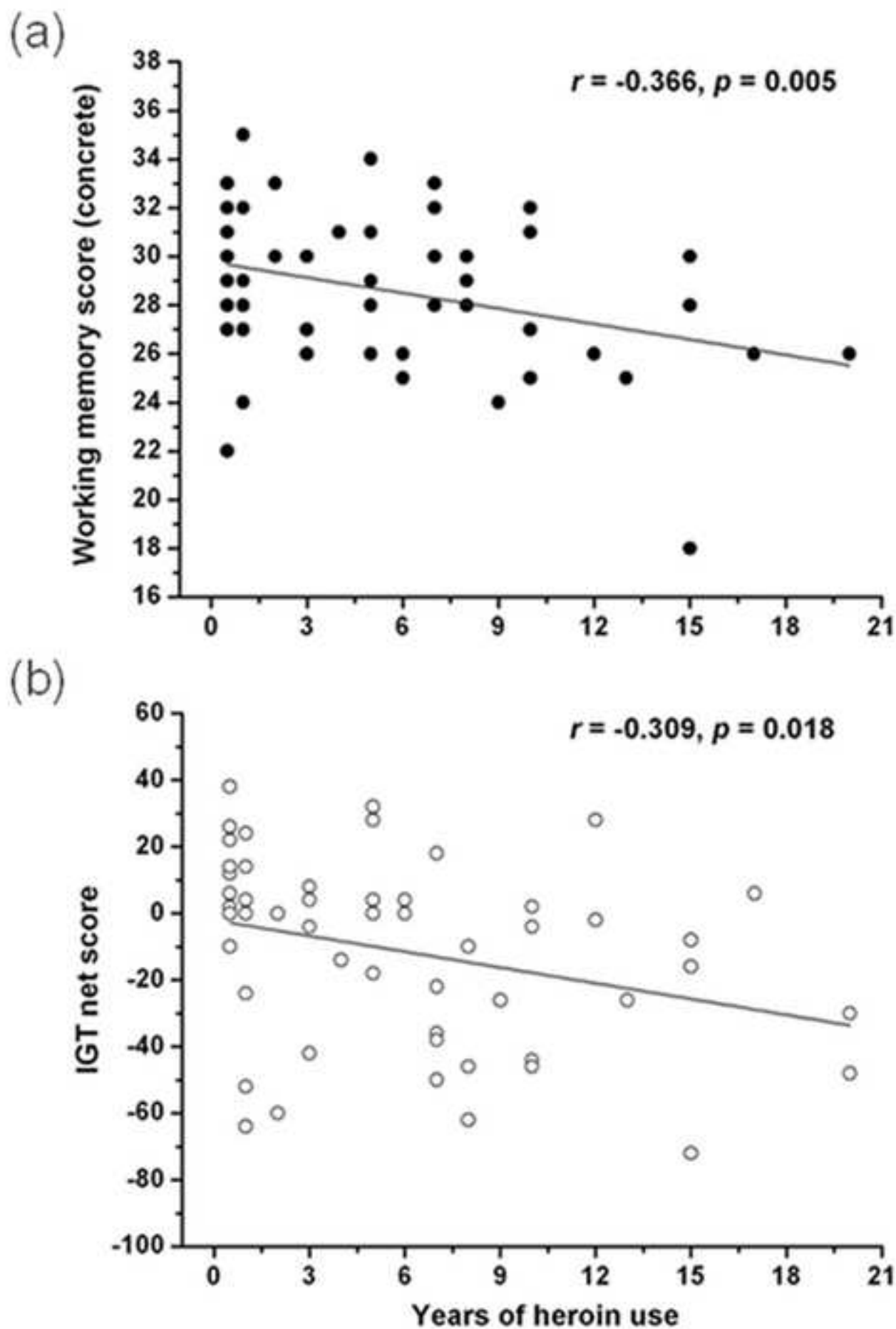
| Variables | SOPT score | | | IGT net score |
|--|-------------|----------------------------|------------|----------------------------|
| | Total score | Verbal | Non-verbal | |
| In Heroin Addicts (<i>n</i> =58) | | | | |
| Years of heroin use | -0.184 | -0.327* (<i>p</i> =0.016) | 0.084 | -0.299* (<i>p</i> =0.028) |
| Age of first use | 0.076 | 0.039 | 0.078 | 0.309* (<i>p</i> =0.023) |
| Dosage per day | -0.168 | -0.229 | 0.004 | -0.132 |
| Months of abstinence | -0.090 | -0.205 | 0.093 | 0.217 |
| In Pathological Gamblers (<i>n</i> =58) | | | | |
| Years of regular gambling | 0.172 | 0.221 | 0.095 | -0.003 |
| SOGS score | -0.092 | 0.020 | -0.151 | 0.000 |
| Total money loss | 0.112 | 0.174 | 0.039 | -0.068 |

Note. SOPT = the Self-ordered Pointing Test. IGT = the Iowa Gambling Task. SOGS = South Oaks Gambling Screen. Control variables: age, education, marriage status, and smoking. * $p < 0.05$.

Figure 1







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Nothing declared.

Contributors

The first two authors, W.S. Yan and Y.H. Li, contributed equally to this study. N. Sui, W.S. Yan and Y.H. Li designed the study. W.S. Yan and Y.H. Li performed clinical and neuropsychological assessments. W.S. Yan wrote a first draft of the manuscript. All authors contributed to the final version of the manuscript.

Conflict of Interest

No conflict declared.

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