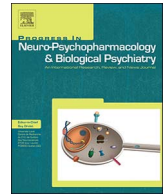




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## Diversities of behavioral traits and neuropsychological function in different substance addiction

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### ABSTRACT

**Objective:** There are various temperaments and personality characters that modulate the development of substance addiction. The pharmacological properties of substances would alter the homeostasis of brain function and influence the neuropsychological performance through different neurotransmissions which then facilitate diverse emotional and behavioral responses. Our goal is to assess the interaction between personality characteristics, neuropsychological performances and Stroop interference in alcoholics, heroin and amphetamine dependent persons.

**Methods:** Subjects with alcohol ( $N = 95$ ), heroin ( $N = 82$ ) and amphetamine ( $N = 57$ ) dependence were recruited. Diagnostic interview and questionnaires evaluating the psychiatric symptoms were done, followed by neuropsychological assessments of Stroop and Wisconsin card sorting tests (WCST). Differences between the study groups were analyzed by one-way ANOVA with Scheffe's test.

**Results:** The individuals with alcohol dependence had significantly higher scores of neurotic, dysphoric and impulsive traits ( $P < 0.001$ ) than heroin and amphetamine dependent groups. In Stroop tests, the alcohol dependent subjects also showed delayed response on incongruent naming interferences compared to both of heroin and amphetamine groups ( $P < 0.001$ ). Perseverative errors and responses of WCST were significantly higher in heroin than in alcoholic dependent persons ( $P < 0.01$ ).

**Conclusions:** Individuals with different substance dependence have distinct behavioral traits for developing addicted behaviors and had variant deficits of neuropsychological function.

### 1. Introduction

Substance addiction is a complex process starting from primary reward to sensitization and addiction, which then incentive salience, learning, and novelty seeking induces compulsive drive for secondary reward. However, it is impulsivity and lack of behavioral inhibition that may further accelerated relapse (Adinoff, 2004; Wilcox et al., 2016). The critical brain area responsible involves orbitofrontal cortex (OFC) and anterior cingulate of mesocorticolimbic pathway in which its activity correlated with decreased striatal D2 receptor activity in methamphetamine- and cocaine- dependent patients (Volkow et al., 1997). There were also functional imaging focusing on OFC of cocaine (Adinoff et al., 2001), alcohol (Volkow et al., 1992), methamphetamine (Volkow et al., 1997) and heroin (Li et al., 2012) dependent subjects where decreased activities were found. These results also suggested that they are hyper-responsive to drug related cues but appropriately engaged in non-drug related stimuli. These could also be demonstrated by neuropsychological testing assessing response inhibition. Stroop test

is a task to assess interference in the reaction time to name a color or to read a word under congruent or incongruent color or word stimuli. It could be used to test person's ability to inhibit a prepotent response (word reading). Longer reaction time or higher error rates reflect inefficient inhibition of task-irrelevant responses. The relationship between Stroop task performance and OFC activation is disrupted in substance dependent persons (Preti, 2000). Using Wisconsin card sorting test (WCST), a relatively complex task that involves in a variety of executive functions, it had been found that the underlying cause of poor performances in substance dependent persons were more likely related to its set-shifting component, or inhibition needed, as opposed to its concept formation or working memory components. This ability may be dependent more on the integrity of the lateral orbitofrontal and inferior frontal gyrus sector of the prefrontal cortex (PFC) (Bechara, 2005).

Yet alcohol, heroin and amphetamine have some different pharmacological effects on central nervous system. Long-term substance addiction can affect neural plasticity and cause different kinds of neural

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degradation based on pharmacological mechanisms of substances. Specifically, amphetamine triggers dopamine release (Ventura et al., 2004), heroin alters opiate neurotransmission (Hu et al., 2003) and chronic alcohol ingestion induces glutamatergic hyperexcitability (Hu et al., 2004). Researchers have noted that there were several specific domains of cognitive function impairment in different substance users also. Chronic alcohol dependent subjects revealed cognitive dysfunction especially related to tasks which involve prefrontal function such as learning, memory, problem solving, abstraction, visual perception and attention (Beatty et al., 1995; Ratti et al., 2002; Tedstone and Coyle, 2004), which is not merely a risk factor, but a consequence of addicted behavior (Tapert et al., 1999). Some cognitive abilities, particularly executive function for instance, in alcohol addicts might be more resistant to recovery (Munro et al., 2000). While drinking-related variables like the frequency and duration of alcohol consumption had been claimed to relate to a decline of frontal lobe function (Fein et al., 1990) where down regulation of NMDA receptor and glutamate hyperexcitability after chronic alcohol exposure mostly occurred (Krill et al., 1997) as a result of decreases GABA receptor activation, it is still no definite contributed factors of cognitive decline, or even factors that affected its recovery. Central nervous system stimulant abusers, such as amphetamine, methamphetamine and cocaine, showed impairment in memory, learning, inhibition, psychomotor speed and attention (Kalechstein et al., 2003; Salo et al., 2002; Simon et al., 2000). These impairments, especially in fields of selected attention, or chronically in attention slowness, could be observed and probably related to frontostriatal damage in dopaminergic system (Salo et al., 2002). This is suggested also by the correlation of poorer performance score when testing for abstracting ability in WCST or non-verbal short term memory with life-time cocaine abuse (Rosselli and Ardila, 1996). However, verbal fluency and long-term memory were relatively preserved, especially when O'Malley et al. (1992) noted that cocaine abusers performed poorly on the Category Test, but surprisingly were superior in verbal fluency tests. Similar test results could also be found (Parsons and Farr, 1981; Washon and Gold, 1984). Comparing with CNS stimulants, heroin showed more negative effects on spatial planning, updating, shifting and decision-making abilities (Ersche and Sahakian, 2007; Verdejo-García and Pérez-García, 2007). Especially on the aspects of impulsivity (risk taking) and cognitive flexibility were the long term declined ability noted in one meta-analysis (Baldacchino et al., 2012). But previous results have couldn't differentiate opiate users from controls in aspect of abstract thinking and verbal fluency (Rounsaville et al., 1982), which thought to correlate more with frontal lobe damage.

Impulse is a behavioral trait to reduce internal desire. Lacking of responsible consideration had created unexpected behavioral consequences (Chambers et al., 2003; Marinelli et al., 2003). It involves self-harm, aggression and violence, pathological gambling, certain compulsive behavior of psychiatric patients and substance addiction (Poulos et al., 1995). Several models demonstrated impulsivity and the associated drug cues of substance addiction. The concept of reward deficit and rash, spontaneous act has also been proposed as possible contributing factors of substance misuse disorder (Dawe et al., 2004). Additionally, the drug cue, or the obsessive thought of drug use following traumatic events can be ignited by a robust inhibitory dyscontrol, which provide a window for drive to express (Adinoff, 2004). Besides neurocognitive measures stated above which reveal deficits in the ability to inhibit innate (or powerfully habituated) response and to choose greater delayed rewards over lesser immediate ones (Bechara et al., 1994, 2001), Cloninger's personality taxonomy, which discriminated impulsivity to three dimensions of Novelty Seeking, Harm Avoidance and Reward Dependence (Cloninger, 1986), has also been severed as clinical tools to evaluate the substance addicts. There were numerous studies focusing on the issue of the association between personality traits and substance abuse behavior, but the results were inconsistent. A systemic review in 1997 revealed that only novelty

seeking trait was associated with early onset of alcohol abuse and criminal behaviors (Howard et al., 1997). As for illicit drugs, low scores of harm avoidance and high trait of reward sensitivity were associated with the activation effect of amphetamine and indicating the vulnerability to psychostimulant addiction (White et al., 2006). However, little has been done to determine the association between particular personality trait and misusing different kinds of substances.

Looking into the interaction between behavioral pattern, personality trait and neuropsychological functioning involving particularly in impulse-reward system focusing on people addicted to various substance, we hypothesized that long term use of different psychoactive substance will cause different domains of cognitive deficit, especially in inhibition and shifting. In addition, little is known about different dimensions of personality trait and the association with preferences of different substances. The aim of our study is therefore to compare the level of impulsivity in persons dependent to alcohol, heroin and amphetamine by performing personality trait questionnaire, Stroop task and WCST with which the degree of impulsivity could be measured subjectively and objectively.

## 2. Methods

### 2.1. Subjects

The subjects who met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) for substance dependence were recruited for the study. The experimental procedures were approved by the Institutional Review Board for Human Studies to ensure the rights and welfare of the subjects who participate the study. Informed content was obtained from each subject. The participants with histories of head injury or major systemic disease influencing the neurocognitive function were excluded in the study. We recruited alcohol dependent subjects ( $N = 95$ ) from the hospitals' inpatient as well as outpatient departments, heroin ( $N = 82$ ) and amphetamine group ( $N = 57$ ) from jail units and the outpatient departments of hospitals.

### 2.2. Materials and procedures

To ensure there were no remarkable medical illnesses or active psychotic disorders, the participants received diagnostic interview and psychological testing after acute intoxicated and withdrawal symptoms subsided. The use of psychotropic or medications known to affect the attention lasting and arousal level would be excluded in the study. In this study, Chinese version of Mini International Neuropsychiatric Interview (MINI) and Brief Psychiatric Rating Scale (BPRS) were performed to screen the general psychopathology and psychiatric comorbidity. The Beck Anxiety and Depression Inventory and Barratt Impulsiveness Scale were adapted to assess the personality traits and the states of impulse inhibition. The computer-based Wisconsin card sorting test (WCST-CV4; Psychological Assessment Resources, Inc. U.S.) and Stroop interference test (release 23.00; Schuhfried, Mödling, Austria) were used to evaluate the neurocognitive functions, attention interference and impulse inhibition, respectively. Following psychiatric interview, the subjects were seated in a quiet situation and then instructed to perform Stroop test and WCST. Stroop interference test consists of neutral, congruent and incongruent stimuli presented in two runs. The WCST consists of four stimuli cards and 128 response cards that depict figures of varying colors and forms.

### 2.3. Statistical analysis

Factor analysis was applied to cluster and classify psychiatric symptoms and personality traits. Based on the regression factor scores from the anxiety, depression and impulsiveness questionnaires, the differences of mean value of each factor between groups were evaluated by analysis of variance (ANOVA) with the Scheffe's post-hoc test.

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