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The cognitive impairments and psychological wellbeing of methamphetamine dependent patients compared with health controls

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ABSTRACT

Background and aims: Chronic methamphetamine (MA) use is associated with cognitive impairment and psychopathological symptoms. This longitudinal study aims to examine the cognitive function of MA addicts during periods of abstinence.
Methods: Fifty-four MA dependent individuals and 58 healthy controls (HC) completed the psychological wellbeing scales and the CogState Battery that evaluated seven cognitive domains. During approximately 6-month abstinence, the subjects completed the CogState battery twice at the interval of 3 months.
Results: In the tasks of verbal memory, social emotional cognition, and spatial working memory, working memory, and problem solving the MA group performed worse than the HC group ($P < 0.05$). After 6-month abstinence, impaired verbal memory, social emotion, and problem solving were improved in the MA group ($P < 0.01$). Furthermore, the MA group showed lower scores in batteries of social adaptation ($t = 3.13$, $P = 0.002$) and quality of life ($t = 3.70$, $P < 0.001$) than the HC group, and 83.3% MA addicts displayed various psychiatric symptoms before study entry.
Conclusions: Chronic MA addicts exhibited impairment of some CogState battery domains and poor psychological wellbeing, and that some of these subdomains were recoverable on abstinence. Therefore, improved cognitive function should be considered an important component in the treatment of MA dependence.

1. Introduction

Methamphetamine (MA) dominates the global market for synthetic drugs, especially increasingly expanding in East and South-East Asia, and parts of North America and Europe (United Nations Office on Drugs and Crime, 2015). The proportion of individuals using synthetic drugs increased from 19.0% of total drug users in 2008 to 49.4% of total drug users in 2014 in China (The office of National Narcotics Control Commission, 2015). Many chronic MA users endure negative consequences, such as physical illness, poor psychological wellbeing, cognitive impairments, bad social adaptation or various psychiatric symptoms (Iudicello et al., 2010; Scott et al., 2007). There is a high demand for treatment of Amphetamine (ATS) use disorder, but the expertise in treating is not at the same level.

Majority of previous studies demonstrated that MA addicts showed lower scores than healthy controls on some cognitive tests (Dean et al., 2013), including the cognitive domains of verbal memory (Hoffman et al., 2006; Iudicello et al., 2010), visual spatial memory (Hoffman et al., 2006; Iudicello et al., 2010; Moon et al., 2007), prospective memory (Rendell et al., 2009), working memory (Hoffman et al., 2006; Iudicello et al., 2010; van der Plas et al., 2009; Weber et al., 2012), cognitive inhibition (Hoffman et al., 2006; Iudicello et al., 2010; Salo et al., 2009; van der Plas et al., 2009), attention network (Salo et al., 2011), decision-making (Hoffman et al., 2006; van der Plas et al., 2009). Cognitive impairments could influence the daily function of the MA users. For example, MA dependent individuals who exhibited poor cognitive control and maladaptive decision-making tend to pursue immediate reward from drugs or show bad social adaptation (London et al., 2014; Kim et al., 2011). However, most of these studies used single cognitive assessment scales and few focused on the overall cognitive function and social cognition of MA addicts.

Some studies found that cognitive impairment in MA addicts was associated with some factors, such as years of usage (van der Plas et al., 2009), abstinence (Iudicello et al., 2010; Salo et al., 2009), daily functioning (Weber et al., 2012), education, gender (van der Plas et al.,

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2009), and impulsivity (Hoffman et al., 2006). Most of the evidence comes from the cross-sectional studies. Despite short periods of abstinence (3 months) chronic MA users endure continued cognitive impairment (Scott et al., 2007; Simon et al., 2010). A longitudinal study showed some cognitive improvement after one year of abstinence (Iudicello et al., 2010). The partial recovery from cognitive impairments of the MA users might be related to neuroplasticity (Fleckenstein et al., 2007). Identifying factors related to cognitive impairment in MA addicts, and after the effect of abstinence, might provide important information for MA dependence treatment.

Previous studies showed that repeated MA use caused prolonged psychiatric symptoms (e.g. visual and auditory hallucinations, paranoid ideation, persecutory delusions, depression, or suicidal behavior) (Scott et al., 2007), as well as MA psychosis that mimic the symptoms of schizophrenia (Fasihpour et al., 2013). Some studies demonstrated that MA dependent individuals exhibited impairments on everyday functional ability, such as finance, transportation, comprehension, communication, and medication management compared with drug-free comparison subjects (Henry et al., 2010). Chronic MA users who exhibited poor psychological wellbeing might show more cognitive impairments and harder to rehab, so identifying the psychological wellbeing of MA users may attribute to find the treatment target for MA dependent rehabilitation.

The current study aims to understand the psychological wellbeing and cognitive function and its changes, after six months of abstinence in MA addicts. We hypothesize that MA dependent patients have broad cognitive impairments, and that these impairments are partially recovered after abstinence.

2. Methods

2.1. Subjects

Two groups were recruited: 54 MA addicts (abstinent from MA for less than 3 months) from Shanghai Compulsory Rehabilitation Center, who met the diagnosis of MA dependence according to Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV) (First et al., 1995); 58 healthy controls (HC) from local community. The inclusion criteria were: (1) more than 9 years of education; (2) aged between 18 and 45 years old; (3) Han nationality and proficient at Chinese; and (4) normal or corrected-to-normal vision and audition. The exclusion criteria were: (1) physical or neurological illness affecting cognitive function (e.g., stroke, seizure, or severe head injury); (2) other Axis I disorder of DSM-IV criteria; (3) use of cognitive enhancing drugs within 6 months of study enrollment; and (4) substance dependence other than nicotine, within the past 5 years. Throughout the study period, the MA dependent subjects lived in Shanghai Compulsory Rehabilitation Center, where they were involved in a usual rehabilitation plan (including education, working, and excise) without any medicine for MA dependent rehabilitation.

The study was approved by the Institutional Review Board (permission number: 2011-37R) of Shanghai Mental Health Center, to ensure the highest standards of ethical consideration. It was made clear to all subjects that participation in the study was voluntary, and that their decision would not impact future treatment or rehabilitation. All subjects gave written informed consent, after a full explanation of study procedures. The study was performed in accordance with the Declaration of Helsinki II.

2.2. Measurements

The *Chinese version of the CogState Battery* is a repeatable and sensitive computerized cognitive test with good validity and reliability, and largely free of practice effects on repeated applications (Cairney et al., 2007; Yoshida et al., 2011; Zhong et al., 2013). The eight tasks listed below were examined, with participants requiring approximately 40 min to complete the battery as quickly and accurately as they could. *International shopping list task* (*ISLT, verbal learning and memory*) (Rahimi-Golkhandan et al., 2012) is a 12-word, 3-trial verbal memory test. The subjects are required to recall the words within 60 s in each trial. The score is defined as the total number of correct responses. *Detection task* (*DET, processing speed*) requires the subjects to press a "Yes" key to a red card. *Identification task* (*IDN, attention/vigilance*) asks the subjects to press a "Yes" key to a red card or a "No" key to a black card. The scores of DET and IDN are the mean of reaction times for correct responses. *One card learning task* (*OCL, visual learning and memory*) asks the subjects to decide whether a poker card has been shown before. *Two back task* (*TWOB, working memory*) requires subjects to decide whether a card is identical to the one shown just before. *Social emotional cognition task* (*SEC, social cognition*) asks the subjects to pick out the different facial expressions, from a choice of four human facial expressions. The scores of OCL, TWOB and SEC tasks are the proportion of correct responses, denoting the accuracy of performance. *Continuous paired association learning task* (*CPAL*) taps spatial working memory. Subjects first learn and remember 8 different pictures hidden beneath 10 different locations on the screen, and then tap on the location where the pictures previously appeared. The *Groton maze learning task* (*GML*) taps problem solving/error monitoring. Subjects follow a 28-step pathway for 5 times with same pathway hidden among the 100 possible locations. The scores of CPAL and GML tasks are the total number of errors. These tasks are displayed on a green screen, along with standardized instructions given by trained researchers before the commencement of each task. The results of the CogState Battery are uploaded to a secure account on the CogState server site (http://www.Cogstate.com), where data were calculated and normalization was transformed (logarithmic transformation for reaction time, arcsine transformation for accuracy).

WHO-quality of life instrument (*WHOQOL-BREF*) is 26-item, self-administered, widely validated questionnaire which is a short version of WHOQOL-100 scale (Xia et al., 2012). It measures following four domains, namely physical health and wellbeing, psychological health and wellbeing, social relationship, and environment, with higher scores representing a better quality of life (Saxena et al., 2001).

Social Adaptation Self-evaluation Scale (*SASS*) is 21-item, self-report scale used to evaluate broad areas of social functioning. The score for each item ranges from 0 to 3, with higher scores representing better social adjustment (Bosc et al., 1997). The Chinese version of SASS shows good validity (Tse and Bond, 2007).

2.3. Procedure

Fifty-four MA addicts and 58 healthy controls were recruited during February to October of 2012, and all provided informed consent. The subjects underwent a semi-structured interview to document their demographic data and clinical histories. They were then required to complete the psychological wellbeing scales (WHOQOL-BREF, SASS), and lastly complete the Cogstate battery, in a separate quiet room. Short breaks of approximately 5 min or smoking breaks were allowed to avoid any impact from fatigue or nicotine abstinence on cognition. Three months later after enrollment, 44 MA addicts and 29 healthy controls were re-tested on the CogState Battery. And six months later after enrollment, 35 MA addicts and 25 healthy controls were re-tested on the CogState Battery. (Fig. 1).

2.4. Data analysis

Statistical product and service solutions (SPSS) were used to analyze. Continuous variables were analyzed by *t*-tests and dichotomous variables were examined with Chi-square tests for group comparisons. Considering 8 cognitive tests performed, Omnibus results (Wilk's lambda) produced by multivariate analyses of variance (MANOVAs) are reported to evaluate overall statistical significance, followed by individual *t*-tests