

Regular article

Drug abstinence and cognitive control in methamphetamine-dependent individuals

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Abstract

Chronic methamphetamine (MA) abuse is associated with disruption of frontostriatal function as well as deficits in cognitive control. To examine the relationship between drug use patterns and cognitive deficits, we pooled previously published behavioral data with new data collected using the Stroop Attention Test. Subject groups are composed of 38 MA-abusing individuals who recently initiated abstinence (36.1 ± 8.8 years of age), 27 MA-abusing individuals who had initiated abstinence more than 1 year prior to study (38.7 ± 7.7 years of age), and 33 non-substance-abusing controls (33.9 ± 8.5 years of age). The recently abstinent MA-abusing individuals exhibited greater Stroop reaction time (RT) interference compared with both the control group ($p = .001$) and the long-term abstinent MA-abusing individuals ($p = .01$). No difference was seen between long-term abstinent MA-abusing individuals and controls ($p = .87$). Stroop RT interference correlated positively with both duration of drug use ($p = .003$) and drug abstinence ($p = .05$). The data in the current study provide evidence that cognitive function may improve with protracted drug abstinence. © 2009 Elsevier Inc. All rights reserved.

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1. Introduction

In the past decade, the use of the stimulant methamphetamine (MA) has increased in the general population with more than 35 million people estimated to use amphetamine-like drugs throughout the world (Office of Applied Studies, 2004, 2006). The statistics on the growing pandemic of MA abuse are overwhelming and include the following: (a) admissions to substance abuse treatment programs with MA as the primary substance increased 182% from 1994 to 2004, with 44 of 45 states reporting increases (Office of Applied Studies, 2006); (b) emergency room admissions

related to MA use have doubled during the period of 1994 to 2002 (National Drug Intelligence Center, 2006); and (c) several acts of national legislation, such as the Comprehensive Methamphetamine Control Act of 1996 and the Methamphetamine and Club Drug Anti-Proliferation Act of 2000, have focused specifically on the growing problem of MA abuse throughout the United States (Community Epidemiology Work Group, 2004; Gibson, Leamon, & Flynn, 2002; National Drug Intelligence Center, 2006). Compounding the problem is evidence that psychostimulants, such as MA, are neurotoxic to dopaminergic frontostriatal brain regions with corresponding deficits in selective attention and cognitive control (Nordahl, Salo, & Leamon, 2003; Quinton & Yamamoto, 2006; Simon et al., 2000).

Cognitive impairments exhibited by MA-dependent individuals may be a result of neurotoxic effects to multiple neurotransmitter systems distributed throughout the cortex

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(Nordahl et al., 2003; Quinton & Yamamoto, 2006). Damage following MA abuse to frontostriatal brain regions such as the striatum, prefrontal cortex, anterior cingulate cortex, and amygdala may contribute to the wide range of cognitive deficits observed in MA-dependent human subjects. Cognitive deficits have been observed in MA-dependent individuals with increased performance deficits appearing on tasks that require the suppression of task irrelevant information (Kalechstein, Newton, & Green, 2003; Monterosso, Aron, Cordova, Xu, & London, 2005; Salo et al., 2008; Salo et al., 2007), decision making (Paulus, Hozack, Frank, Brown, & Schuckit, 2003; Paulus, Tapert, & Schuckit, 2005), and working memory (Chang et al., 2002; McKetin & Mattick, 1997, 1998). Although numerous studies have documented cognitive deficits in MA-abusing individuals, few have examined the role of abstinence on cognitive processes (Simon, Dacey, Glynn, Rawson, & Ling, 2004; Volkow et al., 2001). One longitudinal study followed three groups of MA-abusing individuals for 6 months and reported that the MA-abusing individuals who remained abstinent performed worse on a subset of the neuropsychological tasks compared with those who used continuously or who relapsed (Simon et al., 2004). Another imaging study that retested five MA-abusing individuals at a 12- to 17-month period of abstinence showed significant improvement on a subset of cognitive tasks that assessed motor and memory function (Volkow et al., 2001).

1.1. Study rationale

The goal of this study was to examine the relationship between drug usage status (i.e., years of use and time since last use) and performance on the single-trial version of the Stroop attention task. The Stroop task is a widely validated measure of response inhibition and cognitive control in clinical populations (Carter, Robertson, & Nordahl, 1992; Ochsner et al., 2001; Swick & Jovanovic, 2002) and is therefore a powerful tool to assess cognitive control and attention in MA-abusing subjects. Cognitive control is defined as the ability to flexibly adapt behavior to current demands by promoting task-relevant information and behaviors over temporally extended periods in the face of attentional interference (Botvinick, Braver, Barch, Carter, & Cohen, 2001). In the context of addiction, cognitive control is interpreted as the inhibition of a prepotent response (e.g., compulsive drug use) to carry out behaviors associated with long-term rewards and positive outcomes (e.g., abstaining from drug use). The ability to engage cognitive control and overcome the impulse to engage in drug-seeking behavior may be a key component of remaining abstinent. If the two processes are related (i.e., refraining from drug seeking and cognitive control), then one might predict that performance on a task that measures cognitive control (i.e., Stroop task) and length of drug abstinence might be linked.

To examine the relation between MA abstinence and cognitive control, we pooled new, unpublished behavioral data from 21 MA-dependent subjects with data from 44

subjects previously reported in two published studies (Salo et al., 2002; Salo et al., 2007). All data reported in this study were generated using the same version of the single-trial Stroop attention task. Although different versions of the Stroop task are available (MacLeod, 1991; Salo, Henick, & Robertson, 2001), the computerized single-trial version has advantages over the paper version in that (a) more precise reaction times (RTs) can be recorded in milliseconds, (b) RTs are not summed across a large stimulus set thus controlling for outliers, (c) errors can be recorded for individual stimuli, and (d) single-word stimuli can be presented without the presence of distractors that may impact attentional performance in clinical populations (Boucarter, Mobarek, Cuervo, & Danion, 1999; Salo et al., 2001). Given the powerful neurotoxic profile of MA, we predicted that longer duration of MA use would correlate with greater deficits on the Stroop attention task as measured by increased RT Stroop interference. In addition, given the evidence from the neuroimaging literature on the normalization of brain function over periods of protracted MA abstinence (Nordahl et al., 2005; Volkow et al., 2001), we also predicted an inverse correlation between RT Stroop interference and time drug abstinent. Specifically, we predicted that those MA-dependent individuals with longer periods of MA abstinence would exhibit the lowest RT Stroop interference scores.

2. Materials and methods

2.1. Subjects

Sixty-five MA-dependent subjects (28 males and 37 females) were recruited through outpatient substance abuse treatment centers. Thirty-eight MA-abusing individuals had recently initiated abstinence (3 weeks to 6 months), and 27 MA-abusing individuals had initiated abstinence more than 1 year prior to study. The recent and distant abstinent MA-abusing individuals did not differ from each other in age, $F(1, 63) = 1.46, p = .23$, years MA use ($F < 1$), education ($F < 1$), or scores on a measure of premorbid IQ as determined by the National Adult Reading Test (NART; $F < 1$). All MA-abusing subjects had been diagnosed with MA dependence as determined by the Structured Clinical Interview for DSM Disorders (SCID) and had been drug abstinent a minimum of 3 weeks (First, Spitzer, Gibbon, Williams, 1995). Random urine screens were performed at the referring sites to verify drug abstinence, and none of the screens yielded positive results.

Exclusionary criteria included the following: (a) history of significant head trauma or neurological injury, (b) co-occurring non-substance-related Axis I disorder, and (c) substance dependence other than MA (except nicotine) within the past year and no alcohol abuse in 5 years. All subjects reported normal color vision and normal or corrected to normal visual acuity. The 65 MA-dependent subjects had been drug abstinent for a minimum of 3 weeks and a maximum of 10 years. Median length of MA abuse

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