BRIEF REPORT

A Dissociation in Attentional Control: Evidence from Methamphetamine Dependence

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Background: *Selective attention comprises multiple, dissociable component processes, including task shifting and selective inhibition. The goal of this study was to test whether task-shifting, selective inhibition, or both processes were impaired in long-term but currently abstinent methamphetamine-dependent individuals.*

Methods: *Participants were 34 methamphetamine-dependent subjects and 20 nonsubstance abusing controls who were tested on an alternating-runs switch task with conflict sequences that required subjects to switch tasks on every second trial (AABBAABB).*

Results: *Methamphetamine-dependent individuals committed more errors on trials that required inhibition of distracting information compared with controls (methamphetamine = 17%; controls = 13%; p = .02). By contrast, error rates did not differ between the groups on switch trials (methamphetamine = 7%; controls = 6%; p = .68).*

Conclusions: *These results indicate that selective inhibition, but not task switching, is selectively compromised by methamphetamine.*

Key Words: Methamphetamine, selective attention, task switching, frontostriatal, stimulant abuse, cognition

The dopaminergic system plays a key role in the neural mechanisms of selective attention, implicating dopamine-sensitive stimulants, such as methamphetamine, as agents capable of modulating attentional mechanisms (Clark and Geffen 1986; Davidson et al 2001; Nieoullon 2002; Servan-Schreiber et al 1998). Brain imaging studies of long-term methamphetamine users report significant changes to frontostriatal regions, areas involved in attentional regulation and executive control (Ernst et al 2000; London et al 2004; Nordahl et al 2002; Volkow et al 2001). A range of attention deficits have been reported in clinical populations with abnormal frontostriatal function including selective attention deficits (Ford 1999; Gehring and Knight, 2002; Henik et al 1993; Salo et al 2002; Simon et al 2000) and task-switching impairments (Brown and Marsden 1988; Harrington and Haaland 1991; Rogers et al 1998; Sullivan et al 1989). Performance deficits on selective attention or task switching tasks can result in slowed reaction times and/or increased error rates (Allport et al 1994; Jersild 1927; Meiran 1996).

Study Rationale

We tested the hypothesis that methamphetamine-dependent subjects would exhibit performance deficits on set-shifting and tasks of selective inhibition, functions subserved by frontostriatal brain regions.

Methods and Materials

Participants

The methamphetamine-dependent group comprised 15 men and 19 women meeting DSM-IV criteria for lifetime methamphetamine dependence. Random urine screens were performed at referring sites and all subjects had been methamphetamine abstinent for a minimum period of four weeks (range 4 weeks to 5 years). Exclusionary criteria were 1) history of neurological injury; 2) co-existing axis I disorder; 3) substance dependence other than methamphetamine within the past year; 4) reported history of a seropositive test for Human Immunodeficiency Virus (HIV).

The control group comprised 11 men and 9 women. Exclusionary criteria were the same as for the methamphetamine subjects with the exception of history of drug abuse or dependence. The two groups were matched on age [$F(1,52) = 1.09$; ns] and years of parental education [$F(1,52) = 1.22$; ns], but differed on years of education [$F(1,52) = 8.46$; $p < .01$]. Demographic characteristics are reported in Table 1. All subjects signed informed consent approved by the University of California Davis Institutional Review Board and were paid a modest stipend for study participation.

We employed an alternating-runs, switch task with conflict and nonconflict sequences (adapted from Rogers and Monsell [1995]). This design includes switch and repeat sequences within the same block and requires subjects to switch tasks on every second trial (AABBAABB). The repeat sequences are used as the baseline for comparison with switch trials to derive a residual cost. Performance measures are response time (RT) and error rate.

Stimuli

The tasks used were letter and number naming. Using the design of Rogers and Monsell (1995), each screen presentation consisted of a pair of stimuli displayed side by side. The stimuli consisted of 4 letters (M, C, D, K) and 4 numbers (2, 4, 5, 7) sampled randomly. Four symbols (#, @, *, &) were employed as the neutral stimuli.

Above the display was a cue, either the word 'letter' or 'number' (Figure 1), which directed the subject to name either the letter or the number that appeared. In the nonconflict condition, the nontarget stimulus would always be one of the nonalphanumeric symbols, which were never mapped to a target response. In the conflict condition, each stimulus display would contain both a number and a letter. Because both numbers and letters were possible targets, the pairing of these two stimuli types created a response mapping conflict.

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Table 1. Demographic Factors

Age (years)	Education (years)	Duration of Steady Methamphetamine Use	Methamphetamine Abstinence Prior to Testing
39	12	12 years	3 months
27	12	10 years	3 months
29	12	19 years	3 months
33	11	20 years	4 months
28	7	12 years	2 months
43	14	30 years	4 months
42	11	28 years	4 months
23	12	7 years	2 months
42	12	11 years	5 years
38	13	16 years	4 years
46	14	8 years	6 months
51	12	5 years	3 months
42	12	23 years	18 months
37	17	15 years	1 month
44	12	20 years	3 months
24	12	4 years	1 month
48	12	5 years	2 years
44	12	12 years	6 months
51	14	10 years	1 month
31	13	9 years	1 month
46	14	27 years	2 years
21	14	3 years	3 years
31	14	11 years	1 month
29	13	5 years	1 month
33	13	13 years	2 years
38	14	18 years	1 month
32	14	13 years	3 months
50	14	10 years	2 months
34	12	18 years	2 months
37	15	10 years	1 month
43	14	2 years	3 months
32	17	6 years	5 years
40	15	10 years	3 months
50	14	16 years	4 months
Mean Age = 37.6 (8.4)	Mean Education = 13.1 (1.8)	Mean Use = 12.9 yrs (7.2)	Mean Abstinence = 10.6 mos (16.7)

Procedure

Subjects were instructed to say aloud the target-cued name of the letter or number that appeared while ignoring the distracting stimulus. Voice responses were recorded via a voice-operated relay interfaced to the microcomputer. The response stimulus interval (RSI) was 600 msec.

Results

Median RTs for correct responses for every condition were computed for each subject and submitted to repeated measures analysis of variance (ANOVA).

Error Analyses

Error analyses revealed a main effect of switching [$F(1,52) = 69.84$, MSe = .001; $p < .001$] and response conflict [$F(1,52) = 169.80$, MSe =. 006; $p < .0001$]. There were significant interactions between group and response conflict [$F(1,52) = 5.66$; MSe = .006, $p = .02$] and between response conflict and switching [$F(1,52) = 175.64$, MSe = .001, $p < .0001$]. Methamphetamine-dependent subjects made significantly more errors on trials with response conflict than did control subjects collapsed across conditions [$F(1,52) = 5.7$, MSe = .005, $p = .02$]. In contrast, error rates did not differ between groups on switch trials [$F < 1$]. There was no evidence of a speed-accuracy trade-off in either group (methamphetamine-dependent $r = .232$; controls, $r = .267$). The group differences endured when education was included as a covariate analysis of covariance (ANCOVA) ($p < .05$).

Reaction Time Analyses

Analyses revealed main effects of switching [$F(1,52) = 10.33$, MSe = 3,540, $p < .005$] and response conflict [$F(1,52) = 150.9$, MSe = 9,457, $p <. 001$]. All subjects exhibited longer RTs on switch and response conflict trials than on nonswitch and nonresponse conflict trials. No interactions were significant, suggesting that the two operations operate independently.

Additional Analyses

To separate the effect of each function we subtracted the baseline (repeated nonconflict trials) from each condition. (Figure 2). Task switching and conflict suppression errors were not correlated in either group (methamphetamine-dependent: $r = .17$; Control: $r = .263$). Task switching and conflict suppression latencies were correlated in the control group ($r = .628$, $p = .003$) but not in the methamphetamine-dependent group ($r = .246$; $p = .16$). Although the pattern of correlations differed between groups, differences between correlations were not significant ($p = .10$). No correlations emerged between drug use variables (i.e. length of use, length of drug abstinence) and any experimental factor measured.

Discussion

The goal of this study was to examine the ability of methamphetamine-dependent individuals to perform a task requiring both conflict suppression and switching of attentional set. The results revealed a dissociation, with methamphetamine-dependent individuals committing more errors on conflict trials compared to controls but not on task switching trials. Similar dissociations in task performance have been reported in patients with schizophrenia (Manoach et al 2002) and in patients with frontal lobe lesions (Gehring and Knight 2002; Rogers et al 1998). Similar to our data, Gehring and Knight found an additive effect of distractor compatibility and switching on RT, suggesting that these two functions may be temporally and functionally distinct.

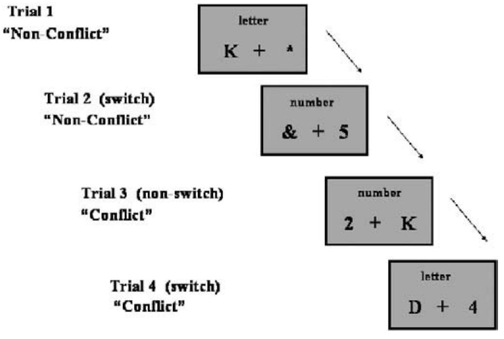

Figure 1. Experimental stimuli. The stimuli consisted of 4 letters (M, C, D, K) and 4 numbers (2, 4, 5, 7) sampled randomly. Four symbols (#, @, *, &) were employed as the neutral stimuli.

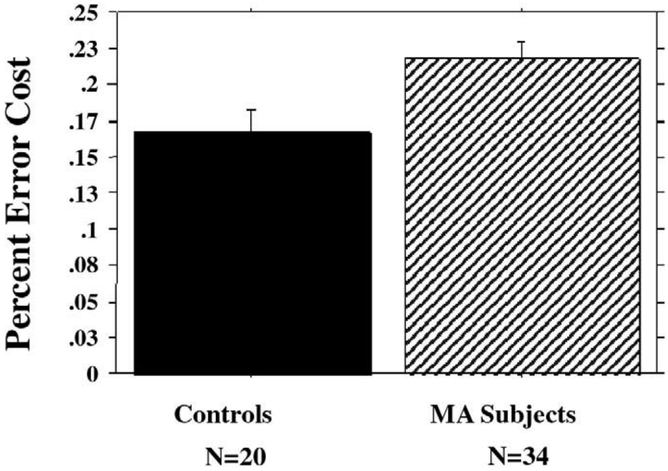

Figure 2. Conflict error cost. Response conflict trials minus baseline (repeated nonconflict trials). MA, methamphetamine. $p < .05$.

Limitations

It is possible that we were unable to detect group differences in switching costs between methamphetamine-dependent subjects and controls because our task design minimized the working memory load, which may be a contributing factor in many studies of task switching (Mayr and Kliegl 2000; Ravizza and Ciranni 2002; Rubinstein et al 2001). The potential involvement of working memory warrants further investigation given the evidence of switching deficits in other clinical populations with damage to frontostriatal regions (Harrington and Haaland 1991; Sullivan et al 1989). Nonetheless, our paradigm was adequately sensitive to observe significant switching effects and consequent switching costs.

Conclusion

Damage to frontostriatal regions following long-term methamphetamine use may underlie the selective attention deficits observed in the current study (Ernst et al 2000; Nordahl et al 2003). Excessive numbers of conflict errors observed in the methamphetamine-dependent group may result from the failure of frontal cortical function to sustain goal-directed behavior during the process of attending to the target stimulus (Miller and Cohen 2001). Failure to sustain long-term goals and suppress impulsive patterns of behavior, marks and may promote maintenance of the maladaptive actions associated with drug-seeking behavior (Porrino and Lyons 2000; Robbins and Everitt 1999).

Maladaptive drug seeking behavior and impulsive decision making in stimulant abusers are "consistent with an altered top-down modulation from outcome-related to stimulus-related response selection" (Paulus et al 2003). Altered function within the ventral striatum has been observed after repeated exposure to psychostimulants, with the nucleus accumbens exhibiting increased dopamine release following methamphetamine intake (Koob and Le Moal, 2001). Although regions of the ventral striatum and amygdala may lead to an increase in the impulse to seek drugs, the anterior cingulate and prefrontal cortices may serve to inhibit those pre-potent impulses (Chambers et al 2001; Jentsch and Taylor 1999). Damage to any of these regions could contribute to increased impulsiveness and dysregulation of attentional processes. Careful characterization of cognitive functioning is relevant to the treatment of substance abuse as many treatment programs rely on cognitive behavioral therapy as part of their intervention approach (Aharonovich et al 2003). Given that attention is the fundamental building block of many cognitive operations, deficits in the ability to pay attention are likely to undermine effective engagement in treatment.

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