Psychiatry Research 220 (2014) 527–534

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Elevated intraindividual variability in methamphetamine dependence is associated with poorer everyday functioning

Erin E. Morgan [a,*], Katie L. Doyle [a,b], Arpi Minassian [a], Brook L. Henry [a], William Perry [a], Thomas D. Marcotte [a], Steven Paul Woods [a], Igor Grant [a], the Translational Methamphetamine AIDS Research (TMARC) Group

[a] Department of Psychiatry, University of California-San Diego, La Jolla, CA, USA
[b] SDSU/UCSD Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA

ARTICLE INFO

Article history:
Received 27 September 2013
Received in revised form
15 March 2014
Accepted 5 July 2014
Available online 14 July 2014

Keywords:
Substance dependence
Within-person variability
Cognitive control
Activities of daily living
Neuropsychological assessment

ABSTRACT

Methamphetamine (MA) dependence is associated with executive dysfunction, but no studies have evaluated MA-related elevations in neurocognitive intraindividual variability (IIV), an expression of cognitive dyscontrol linked to poor daily functioning in populations with frontal systems injury. We examined IIV during a vigilance task in a well-characterized sample of 35 MA-dependent (MA+) and 55 non-MA using comparison participants (MA-) as part of a larger neuropsychological battery that included self-report and performance-based measures of everyday functioning. A mixed model ANOVA was conducted while controlling for covariates, including factors that differed between the groups (e.g., education) and those with conceptual relevance to IIV: mean reaction time, global cognitive performance, and HIV-infection (which was comparable across groups; $p=0.32$). This analysis revealed significantly elevated IIV among MA+ relative to MA- individuals that was comparable in magnitude across all trial blocks of the vigilance task. Within the MA group, elevated IIV was associated with executive dysfunction, psychomotor slowing, and recency of MA use, as well as poorer automobile driving simulator performance, worse laboratory-based functional skills, and more cognitive complaints. MA-users are vulnerable to IIV elevation, likely due to cognitive dyscontrol, which may increase their risk of real-world problems.

1. Introduction

Chronic use of methamphetamine (MA) can substantially disrupt an individual's biopsychosocial functioning at multiple levels, ranging from alterations in central nervous system (CNS) structure to declines in cognitive performance and even failures in real-world activities. In the CNS, MA induces neurotoxicity that preferentially impacts the structure, function, and metabolism of the prefronto-striato-thalamocortical loops (Panenka et al., 2013). Likely as a combination of premorbid vulnerabilities and downstream effects, MA-dependent individuals are more likely to be neurocognitively impaired than non-MA users (Rippeth et al., 2004), particularly in domains subserved by frontal systems, including executive functions, the strategic aspects of memory, information processing speed, and attention (Scott et al., 2007). Importantly, among those with MA-dependence, deficient executive abilities appear to increase risk of poor everyday functioning status (Weber et al., 2012), including mismanagement of daily tasks, unemployment, and unsafe driving (Scott et al., 2007).

One aspect of neuropsychological functioning that has received very little study in MA users is intrainvidual variability in cognitive performance, or IIV. In contrast to the standard method for summarizing performance whereby measures of central tendency (such as mean performance) are emphasized, measures of IIV describe within-person fluctuations in an individual's cognitive performance across time. Under its broad definition, IIV can be measured in a number of ways, but many studies operationalize it as fluctuations in reaction time (RT), which is summarized as standard deviation of RT across trials, usually in the context of a sustained attention task. Although neurologically healthy individuals do show some degree of normal IIV (Schretlen et al., 2003), elevated levels of IIV are strongly associated with frontal systems dysfunction (see MacDonald et al., 2009, for a review). Accordingly, IIV is purported to be an expression of cognitive dyscontrol (West et al., 2002), or a behavioral manifestation of a breakdown in top-down processes that regulate and allocate cognitive resources (e.g., attention) across trials of a task. IIV may appear in the early stages of CNS dysregulation due to insult, thus having

* Corresponding author. Tel.: +1 619 543 5076; fax: +1 619 543 1235.
E-mail address: eemorgan@ucsd.edu (E.E. Morgan).

http://dx.doi.org/10.1016/j.psychres.2014.07.008
0165-1781/

the potential to identify those at risk for worse clinical outcomes in the future (MacDonald et al., 2009).

MA users can evidence a moderate deficit in sustained attention (Scott et al., 2007), which may be characterized by inconsistent performance across time. Specifically, one study reported elevated variability in response RT and a higher rate of omission errors over the course of a sustained attention task in a sample of mixed stimulant users (i.e., cocaine and/or MA) who were infected with HIV (HIV+; Levine et al., 2006). Interestingly, these findings were observed in the context of normal mean hit RT speed and signal detection (i.e., ability to discriminate between targets and non-targets), suggesting that the instability in response RT over time among the stimulant group was not simply due to overall poor performance. In fact, the typical effects of psychostimulants on task performance can include a decrease in response time, resulting in "better" performance as measured by RT speed, especially with more recent use (Toomey et al., 2003). Therefore the shift in perspective from mean level of performance to IIV could be particularly useful in characterizing the negative effect of MA use on sustained attention among MA users. Nevertheless, no study to date has conducted a targeted examination of the effect of MA on RT IIV.

From a clinical perspective, elevations in IIV may confer increased risk of difficulties with real world activities among MA users. Elevated IIV, as defined by RT variability, has been observed and linked to poor cognitive prognosis (i.e., decline and/or incipient cognitive disorder diagnosis) in several populations such as ADHD (e.g., Tamm et al., 2012), HIV (Ettenhofer et al., 2010), aging (e.g., Bielak et al., 2010; Hultsch et al., 2002), Parkinson's disease (Burton et al., 2006; De Frias et al., 2012), and traumatic brain injury (Burton et al., 2002). Notably, IIV may also identify those at risk difficulty with performing important everyday functions that require regulation of behavior over time. One striking example with considerable consequences is driving, which is a complex activity that draws heavily on stability, consistency, and vigilance for success. Recent evidence has shown that aging drivers perform poorly in a driving simulator across speed and traffic volume settings, characterized by greater variability in driving outcomes (i.e., maintaining proper headway and lane position; Bunce et al., 2012). Reaction time speed has long been associated with driving performance in numerous populations (e.g., aging; Anstey et al., 2005), and it is likely that RT variability, or IIV, would also relate to poor driving performance. Unsafe driving and an elevated rate of traffic violation and accidents have been observed among MA users (e.g., Logan, 1996), which may be due to the interference of high RT IIV on driving ability.

In addition to daily functioning difficulties, elevated IIV among MA users may be associated with behaviors involved in the addiction cycle itself. That is, an individual with elevated IIV might also evidence greater problematic drug use behaviors than someone with better consistency in RT responding. Given that the mechanism purportedly underlying elevated expression of IIV is cognitive dyscontrol, in the same way that MA-users poorly regulate speed of responding on a sustained attention task they may also have difficulty controlling various aspects of drug use relating to initiating drug use, density and duration of use, and maintaining abstinence from drug use. That is, control of drug behavior likely requires consistent focus and effort toward that goal, particularly when immersed in an environment full of drug-related cues and opportunities, and inconsistency in effort and focus could lead to greater frequency or quantity of use, and could result in greater propensity for relapse. Moreover, in much the same way that more recent use of stimulants results in increased speed of RT responding (Toomey et al., 2003), greater RT IIV may also be observed in the context of more recent use.

Based on the evidence above the present study aimed to take a hypothesis-driven approach to examining the profile of IIV in MA users. To demonstrate the hypothesized MA-related IIV elevation, the performance of a group of MA-dependent individuals was investigated relative to a non-MA using comparison group in controlled analyses. A proportion of the sample was HIV+ (proportions within the two study groups were comparable), and therefore HIV status was included in the evaluation of this hypothesis, which allows for generalizability to prior work and to the larger population of MA users given the comorbidity of HIV and MA use. Within the MA-dependent group, the cognitive correlates of IIV were examined, and it was hypothesized that IIV would be significantly associated with a domain summary score measuring executive functions given that poor cognitive control purportedly underlies elevated IIV expression. MA use parameters were also explored as correlates of IIV in the MA-dependent group. Additionally, IIV was expected to be a unique predictor of everyday functioning outcomes in the MA-using group as defined by self-report (i.e., daily functioning problems and cognitive complaints) and laboratory (i.e., tests of functional capacity, including instrumental activities of daily living and driving) measures.

2. Method

2.1. Participants

Participants for the present study were community-dwelling individuals recruited via advertisements and targeted outreach from the San Diego area (including outpatients recruited from substance use clinics) into the larger, ongoing Translational Methamphetamine Research Center (TMARC) study, which broadly investigates the independent and combined CNS effects of MA and HIV infection. TMARC was approved by the UCSD human research protections program, and all participants provided written, informed consent. The present study sample represents a subset of the TMARC sample comprising 35 MA-dependent participants (MA+) and 55 comparison participants who had never met criteria for MA dependence (MA-). Only male participants were included in the study because very few female participants were available in the larger MA+ TMARC sample, limiting the ability to account for potential influence of gender in the subset. All MA-dependent participants met criteria for MA dependence within the past 18 months as determined by the Composite International Diagnostic Interview (CIDI v. 2.1; World Health Organization, 1998), and their lifetime MA use history was fully characterized using a timeline follow-back interview, which yielded the variables shown in Table 1. Exclusion criteria for both groups included histories of severe psychiatric (e.g., schizophrenia) or neurologic illness (e.g., seizure disorders), or a verbal IQ estimate <80 based on the Reading subtest of the Wide Range Achievement Test – 4th edition (WRAT-IV; Wilkinson and Robertson, 2006). Participants were also excluded for hepatitis C infection, histories of alcohol dependence within the past year, other drug dependence within the past 5 years, and drug abuse within the past year, or lifetime history of Attention-Deficit/Hyperactivity Disorder. Exceptions to these exclusion criteria included a history of alcohol abuse or marijuana abuse/dependence given their high comorbidity rate in MA-dependence. Although there was not a required minimum number of days of abstinence from alcohol or substances use prior to testing, participants were not assessed if their Breathalyzer or urine toxicology screenings were positive on the day of testing. This necessitated approximately 72 h since last MA use in the MA group, and the duration of abstinence from other substances varied based on their respective rates of metabolism. HIV serostatus was determined by enzyme-linked immunosorbent assays and confirmed by a Western Blot test.

Sample characteristics are displayed in Table 1. To minimize the likelihood that demographic, psychiatric, medical (i.e., HIV), and substance use factors commonly comorbid with MA use would confound our findings, the MA- comparison group was recruited to have similar levels of exposure to these factors. As such, the groups were comparable with the exception of significantly fewer years of education, greater current depressive symptoms (i.e., Beck Depression Inventory-II; Beck et al., 1996), and higher rates of "Other Substance Use Disorder" diagnoses (i.e., remote abuse or dependence for alcohol, cocaine or opioids) in the MA+ group relative to the MA- group. Of note, the groups were comparable with regard to the proportion of individuals with HIV infection, and when the subsets of individuals with HIV were compared across MA status, their HIV disease characteristics were comparable as well ($ps > 0.05$, as shown in Table 1).