Memory impairment in now abstinent MDMA users and continued users: A longitudinal follow-up

Abstract—The authors further investigated the functional consequences of continued neurotoxicity of (±)3,4-methylenedioxymethamphetamine (MDMA) use. Fifteen participants who were previously given a brief neuropsychological battery were tested for a third time 2 years after baseline. At 2 years, seven participants were still using MDMA, whereas eight participants had become abstinent from MDMA since 1-year testing. Current users demonstrated further declines in memory ability; former users improved on several memory measures or remained static in performance.

NEUROLOGY 2006;66:740–741

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(±)3,4-Methylenedioxymethamphetamine (MDMA or "Ecstasy") has neurotoxic effects on the serotonergic system in both animals and humans.[1,2] The serotonergic system may play an important role in learning and memory systems.[3] We previously assessed the longitudinal effect of MDMA use on memory and overall cognitive functioning over the course of 1 year.[4] We found impaired retrospective explicit memory, whereas performance on prospective memory measures remained intact. Moreover, the results of that study[4] indicated that vocabulary and explicit verbal recall ability may be adversely affected by the frequency of MDMA use and that the ability to immediately recall a previously navigated route may be related to the duration of MDMA use. This study concluded that continued use of MDMA produces progressive impairment in memory functioning over time. An appropriate follow-up question to these results is whether these observed impairments can persist in discontinued users and continued users.

Accordingly, 2 years after baseline, these same participants were assessed once more on the same neuropsychological battery of tests. Approximately half of the participants (n = 8) had reportedly ceased using MDMA since their 1-year assessment. Therefore, we sought to assess whether the memory impairment exhibited by the former MDMA users had subsided or remained static and whether the continued MDMA users had sustained further decline in memory function.

Methods. Fifteen MDMA users, both current and former, participated in this study. Details regarding the inclusion and exclusion criteria have been described in detail previously.[4] Informed consent was obtained from all participants. All were tested a third time at 2 years after baseline after having been assessed at baseline and 1 year after baseline. No attrition occurred over the 24 months; however, 8 of the 15 participants had ceased using MDMA since the 1-year testing date. Overall, the former user group had been abstinent for at least 32 weeks at the time of testing.

Participants completed a brief battery of neuropsychological tests. The following measures were included in the test battery: the Wechsler Adult Intelligence Scale III (WAIS-III) Vocabulary and Block Design subtests as well as the Rivermead Behavioral Memory Test (RBMT). Descriptions of the subtests of the RBMT have been described previously in detail.[4]

Results. Using either independent samples t tests or Fisher exact tests (one-tailed), where appropriate, retrospective analyses revealed a difference in age between the user groups ($p < 0.05$). The current and former user groups had mean ages of 29.0 (SD = 2.8) and 19.9 (SD = 3.4) at baseline. There were no significant differences found in any other demographic variables, characteristic MDMA use, or "other drug use" at any point in the study. However, it is important to note that "duration of MDMA use" at baseline and at 1-year testing approached significance, which is not surprising in keeping with the age differences between the user groups.

Longitudinal analyses. In keeping with the age difference between the former and current user groups, it is important to note that the remaining statistical tests were performed solely within and not between user groups. At the 2-year follow-up, test scores either remained static or improved for the former user group, whereas test scores declined for the current user group (table). In declining order of effect for the former user group, paired sample t tests revealed improvements on total RBMT score (Cohen's $d = 1.94$; $p < 0.01$), RBMT story immediate (Cohen's $d = 0.83$, $p < 0.05$), WAIS-III Vocabulary (Cohen's $d = 0.35$; $p < 0.01$), and WAIS-III Block Design (Cohen's $d = 0.32$; $p < 0.05$). For the current user group, declines in performance were seen on total RBMT score (Cohen's $d = 2.96$; $p < 0.001$), RBMT route delayed (Cohen's $d = 2.67$; $p < 0.05$), RBMT pictures (Cohen's $d = 2.56$; $p < 0.05$), RBMT faces (Cohen's $d = 1.75$; $p < 0.05$), RBMT route immediate (Cohen's $d = 1.69$; $p < 0.01$), RBMT story immediate (Cohen's $d = 1.45$; $p < 0.01$), RBMT appointment (Cohen's $d = 1.33$; $p < 0.05$), RBMT first/second name (Cohen's $d = 1.00$; $p < 0.01$), and WAIS-III Vocabulary (Cohen's $d = 0.30$; $p < 0.01$). In keeping with the methods of the previous study, interaction effects were computed in terms of change scores (2-year − 1-year) and their correlative relationship to the characteristic MDMA use of the current user group. These effects were not computed for the former user group because their characteristic MDMA use is not applicable. Relationships were observed between RBMT

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Disclosure: The authors report no conflicts of interest.

Received September 6, 2005. Accepted in final form November 8, 2005.

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Table *Neuropsychological results at 1-year and 2-year follow-up*

	Current users					Former users				
Test measure	1 Year*	2 Years*	*d*	*t*	*p*	1 Year*	2 Years*	*d*	*t*	*p*
WAIS-III Vocabulary	50.1 (9.4)	47.4 (8.3)	0.30	3.49	<0.01	55.5 (4.8)	57.3 (5.5)	0.35	−3.56	<0.01
WAIS-III Block Design	46.9 (9.6)	44.0 (9.8)	0.30	2.14	NS	49.8 (9.8)	52.8 (8.7)	0.32	−2.68	<0.05
RBMT										
First/second name	1.4 (1.0)	0.7 (0.4)	1.00	3.87	<0.01	1.3 (1.0)	1.6 (0.7)	0.35	−1.43	NS
Belonging	1.3 (1.0)	0.7 (1.0)	0.06	1.55	NS	1.3 (1.0)	2.0 (0.0)	1.40	−2.05	NS
Appointment	1.4 (1.0)	0.4 (0.5)	1.33	3.24	<0.05	1.8 (0.7)	2.0 (0.0)	0.57	−1.00	NS
Pictures	1.6 (0.8)	0.7 (1.0)	2.56	2.52	<0.05	2.0 (0.0)	1.8 (0.5)	0.80	1.53	NS
Story (I)	0.9 (0.7)	0.1 (0.4)	1.45	3.87	<0.01	1.3 (0.7)	1.8 (0.5)	0.83	−2.65	<0.05
Story (D)	0.9 (0.7)	0.4 (0.5)	0.83	2.12	NS	1.6 (0.7)	1.8 (0.5)	0.33	−0.55	NS
Faces	2.0 (0.0)	1.3 (0.8)	1.75	2.50	<0.05	1.9 (0.4)	2.0 (0.0)	0.50	−1.00	NS
Route (I)	1.7 (0.8)	0.6 (0.5)	1.69	4.38	<0.01	1.5 (1.0)	1.8 (0.5)	0.40	−1.53	NS
Route (D)	1.4 (1.0)	0.6 (0.5)	2.67	3.28	<0.05	1.5 (1.0)	2.0 (0.0)	1.00	−1.53	NS
Message	0.7 (0.8)	0.3 (0.5)	1.54	1.44	NS	1.9 (0.4)	2.0 (0.0)	0.50	−1.00	NS
Orientation	2.0 (0.0)	1.7 (0.5)	1.20	1.55	NS	2.0 (0.0)	2.0 (0.0)	0.00	–	–
Date	2.0 (0.0)	1.6 (0.5)	1.60	2.12	NS	2.0 (0.0)	2.0 (0.0)	0.00	–	–
Total	17.4 (2.6)	9.1 (3.0)	2.96	9.02	<0.001	19.9 (2.5)	22.9 (0.6)	1.94	−3.24	<0.01

* Scores are mean (SD).

WAIS-III = Wechsler Adult Intelligence Scale III; RBMT = Rivermead Behavioral Memory Test; I = immediate; D = delayed.

belongings performance and number of times MDMA was used ($r = 0.76$, $p < 0.05$), RBMT belongings performance and duration of MDMA use ($r = 0.81$, $p < 0.05$), RBMT orientation performance and number of times MDMA was used ($r = 0.76$, $p < 0.05$), and RBMT orientation performance and duration of MDMA use ($r = 0.81$, $p < 0.05$).

Discussion. Evidence for neuropsychological impairment in MDMA users using cross-sectional methodology is abundant,[5,6] while the inherent limitations that can be drawn from such inquiry are known. We have previously investigated the functional consequences of continued MDMA use using a longitudinal design and found evidence for progressive neuropsychological impairment. At this time, longitudinal data on neuropsychological functioning after both continued and discontinued use is scarce with the exception of a recent study,[7] which found that subjects who stopped MDMA use after their baseline examination did not improve, and subjects who continued MDMA use did not deteriorate in terms of test performance. In contrast, the current study, which draws on both baseline and previous follow-up evaluations, found that continued users had further declines in memory ability, whereas former users improved on several memory measures or remained static in performance. It is important to note some limitations in the current research, however. There was a significant difference in age between the abstinent and continued user groups as well as a trend toward difference in duration of use. Accordingly, the effects of age and accumulated MDMA exposure may explain some of the differences in memory performance observed. Notwithstanding these limitations, both the current study and a previous case report tend to suggest that the effects of MDMA may be reversible.[8] However, there does seem to be some evidence that intensive MDMA use may result in persistent, but not progressive, neuropsychological compromise.

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