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Psychopathology in methamphetamine-dependent adults 3 years after treatment

Suzette Glasner-Edwards, PhD¹, Larssa J. Mooney, MD¹, Patricia Marinelli-Casey, PhD¹, Maureen Hillhouse, PhD¹, Alfonso Ang, PhD², Richard A. Rawson, PhD¹, and The Methamphetamine Treatment Project Corporate Authors^{1,*}

¹UCLA Department of Psychiatry, Integrated Substance Abuse Programs, Los Angeles, USA

²UCLA Department of Family Medicine, Los Angeles, USA

Abstract

Introduction and Aims—Although psychiatric symptoms are frequently observed in methamphetamine (MA) users, little is known about the prevalence of psychiatric disorders in MA-dependent individuals. This is the first study to examine the association of psychiatric disorders with substance use and psychosocial functioning in a large sample of MA users 3 years after treatment. We predicted that psychiatric diagnoses and severity would be associated with substance use and poorer overall functioning over the 3 year post-treatment course.

Design and Methods—Participants (N = 526) received psychosocial treatment for MA dependence as part of the Methamphetamine Treatment Project and were reassessed for psychosocial functioning and substance use at a mean of 3 years after treatment initiation. DSM-IV psychiatric diagnoses were assessed at follow-up using the Mini-International Neuropsychiatric Interview. Psychosocial functioning was assessed using the Addiction Severity Index.

Results—Overall, 48.1% of the sample met criteria for a current or past psychiatric disorder other than a substance use disorder. Consistent with prior reports from clinical samples of cocaine users, this rate was largely accounted for by mood disorders, anxiety disorders and antisocial personality. Those with an Axis I psychiatric disorder evidenced increased MA use and greater functional impairment over time relative to those without a psychiatric disorder.

Discussion and Conclusions—This initial investigation of psychiatric diagnoses in MA users after treatment indicates elevated rates of Axis I and II disorders in this population and underscores the need for integrated psychiatric assessment and intervention in drug abuse treatment settings. [Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, Hillhouse M, Ang A, Rawson RA, The Methamphetamine Treatment Project Corporate Authors. Psychopathology in methamphetamine-dependent adults 3 years after treatment.

Correspondence to Dr Suzette Glasner-Edwards, Integrated Substance Abuse Programs, David Geffen School of Medicine at UCLA, Semel Institute for Neuroscience and Human Behavior, 1640 S. Sepulveda Blvd., Suite 200, Los Angeles, CA 90024, USA. Tel: +310 267-5206; Fax: +310 312-0538; sglasner@ucla.edu.

*Methamphetamine Treatment Project Corporate Authors: M. Douglas Anglin PhD, Joseph Balabis BA, Richard Bradway, Alison Hamilton Brown PhD, Cynthia Burke PhD, Darrell Christian PhD, Judith Cohen PhD, MPH, Florentina Cosmineanu MS, Alice Dickow BA, Melissa Donaldson, Yvonne Frazier, Thomas E. Freese PhD, Cheryl Gallagher MA, Gantt P. Galloway PharmD, Vikas Gulati BS, James Herrell PhD, MPH, Kathryn Horner BA, Alice Huber PhD, Martin Y Iguchi PhD, Russell H. Lord, EdD, Michael J. McCann MA, Sam Minsky MFT, Pat Morrissey MA, MFT, Jeanne Obert MFT, MSM, Susan Pennell MA, Chris Reiber PhD, MPH, Norman Rodrigues, Jr, Janice Stalcup MSN, Dr PH, S Alex Stalcup MD, Ewa S. Stamper PhD., Janice Stimson, PsyD, Sarah Turcotte Manser MA, Denna Vandersloot MEd, Ahndrea Weiner MS, MFT, Kathryn Woodward BA, Joan Zweben PhD. Suzette Glasner-Edwards PhD, Larissa J. Mooney MD, Patricia Marinelli-Casey PhD, Maureen Hillhouse PhD, Alfonso Ang PhD, Richard A. Rawson PhD, the Methamphetamine Treatment Project Corporate Authors, UCLA Integrated Substance Abuse Programs.

Introduction

Psychiatric disorders are highly prevalent among substance-dependent individuals, and are associated with greater psychosocial impairment and poorer clinical course and treatment outcomes [1–3]. Over the past two decades, several large epidemiologic studies have shown a strong and consistent relationship between drug dependence and both mood and anxiety disorders [4–6]. Prevalence rates of these disorders in cocaine-dependent adults are particularly high, with estimates of lifetime mood disorders exceeding 60% and anxiety disorders ranging between 45% and 50% in this population [6]. Of the personality disorders, antisocial personality disorder (ASPD) is more strongly associated with substance dependence than other Axis II diagnoses [7,8]. In parallel with epidemiologic survey data, a large body of clinical literature in psychostimulant users established that cocaine dependence is highly associated with mood and anxiety disorders [9]. Nevertheless, despite the fact that methamphetamine (MA) users are more likely to have a psychiatric diagnosis than cocaine users [10], little research has been conducted on psychiatric comorbidity among MA-, relative to cocaine-dependent patients; extant literature in MA-dependent patients has focused largely on characterising psychiatric symptoms rather than disorders [11]. The present investigation is the first to characterise the frequency of various psychiatric diagnoses in MA-dependent adults following treatment for MA dependence.

Despite the high risk of psychopathology in amphetamine users [6,12], the relationship of psychiatric syndromes to clinical course and treatment outcomes has been more widely studied in cocaine than MA users. Nevertheless, findings from these studies are inconsistent. Depression, the most common comorbid psychiatric disorder in substance-dependent adults [7] is associated with poorer substance use outcomes in cocaine users 2 years post-treatment, yet during treatment, abstinence rates and adherence were found to be better among those with depression relative to non-depressed patients [13]. Other studies have found that post-treatment substance use outcomes are no different for cocaine users with and without concomitant mood or anxiety disorders [14,15]. Nevertheless, longitudinal studies have importantly shown that sustained improvement in psychiatric symptoms in cocaine users varies as a function of cocaine abstinence duration [16].

In this paper, we present findings from a 3-year follow-up of MA-dependent adults who participated in the Methamphetamine Treatment Project (MTP). The purpose of this study is to describe the psychiatric status of MA users 3 years post-treatment, focusing on the following issues: (i) describing the rates of psychiatric diagnoses; (ii) examining the demographic, clinical and substance use characteristics of those with and without psychiatric diagnoses; and (iii) evaluating the relationship between psychiatric diagnoses and substance use and psychosocial functioning over the 3-year post-treatment course.

Method

Subjects

Participants were 526 MA-dependent adults who took part in the MTP, a randomised, controlled trial of psychosocial treatments for MA dependence described elsewhere [17,18]. The current investigation was designed after MTP was completed to examine the post-treatment clinical course of MTP participants who had provided written permission to be contacted for follow-ups. For the present investigation, attempts were made by phone and in writing to contact all participants who consented for follow-up. For the original MTP, treatment-seeking MA users age >18 were recruited from outpatient treatment programs in California, Montana and Hawaii. Individuals were excluded if they: showed medical impairment that compromised their safety as a participant; required medical detoxification from any substances; or psychiatric impairment that warranted hospitalisation or primary

treatment. After complete description of the study to the subjects, informed consent was obtained.

The sample was assessed at baseline, treatment discharge and at a mean of 3.1 years ($SD = 0.48$) after treatment completion. The full follow-up battery consisted of a medical examination, a psychiatric diagnostic interview, a psychosocial interview and administration of self-report questionnaires. Of the 587 participants who were interviewed for the follow-up study, 61 did not complete the psychiatric diagnostic component of the interview for various reasons, including: having moved out of the area, constraints owing to incarceration, inability to schedule a convenient appointment, and/or declining this portion of the assessment. Thus, the final sample included 526 participants.

Procedures and instruments

Trained interviewers conducted face-to-face assessments with participants at pretreatment, discharge and follow-up. The Addiction Severity Index (ASI) provides composite scores in seven functional domains (alcohol, drug, psychiatric, medical, legal, family, employment) [19]. The Life Experiences Timeline interview (LET) [20] was used to quantify MA use in the follow-up period. The LET, a measure adapted from the Natural History Interview [21] assesses substance use history using a month-by-month timeline that links substance use to life events.

The Mini-International Neuropsychiatric Interview (MINI) [22], a brief structured diagnostic interview for assessing DSM-IV psychiatric disorders was administered at follow-up. The MINI includes diagnostic interview questions to assess affective, anxiety, substance use, eating, psychotic disorders and ASPD (but no other Axis II disorders). In the original MTP study, it was the judgment of the protocol development team that administration of a structured DSM-IV diagnostic interview would generate excessive cost and burden on the participants. Thus, the MINI was added to the study assessment battery at 3-year follow-up.

Statistical analysis

MA use was quantified as the number of months during which use occurred in the follow-up period, measured by the LET. Chi-squared tests and odds ratios were used to compare prevalence rates of each disorder and diagnostic category by demographic and substance use characteristics (e.g., route of administration). Linear regression was used to examine the effects of multiple psychiatric diagnoses on MA use frequency during follow-up. Linear mixed effects models with main effects of time and psychiatric diagnosis and the interaction among these variables were used to compare ASI scores for those with and without psychopathology across base-line, treatment-end and 3-year follow-up.

Results

Demographic characteristics

Demographic characteristics of the original MTP sample are described elsewhere [17]. At 3-year follow-up, the sample was predominantly female (60%; $N = 316$) with an average age of 33.4 years ($SD = 8.0$). The majority of the participants were Caucasian (69%; $N = 362$); high school (47%; $N = 249$) or college (33%; $N = 176$) educated and employed (60%; $N = 316$). A total of 23% ($N = 119$) were married, and 36% ($N = 190$) were divorced or separated. At baseline, participants reported using MA an average of 11.9 days out of the past 30 ($SD = 9.6$). The preferred route of administration was smoking (63%), followed by intravenous injecting (27%) and intranasal use (9%).

Psychiatric diagnoses of MA-dependent adults 3 years post-treatment

For clarity, all references to 'Axis I psychiatric disorders' refer to disorders other than a substance use disorder. When current and past (i.e., lifetime) Axis I psychiatric disorders were collapsed to form a single dichotomous variable indicating the presence of any mental disorder, 48% of the sample met criteria for a disorder. Similarly, current and past disorders were collapsed for each major Axis I psychiatric diagnostic category (mood, anxiety, psychosis, eating disorders). Mood disorders, present in 34.2% of the sample, accounted for the largest proportion of diagnoses, followed by anxiety (26.2%), psychosis (12.9%) and eating (2.5%) disorders. Table 1 presents the frequencies of current and lifetime diagnoses in the sample. Notably, nearly one-third (28.7%) of the sample reported having made one or more suicide attempts (SA) in their lifetime.

Demographic characteristics and route of MA administration by psychiatric disorders

Chi-squared tests and odds ratios were used to compare prevalence rates of each disorder and diagnostic category by each of the following variables: sex, marital status (married versus not), race (Caucasian vs. non-Caucasian), education (less than high school vs. high school vs. greater than high school) and route of MA administration. The results of these contrasts are presented in Tables 2 and 3.

Women evidenced a higher prevalence rate of any Axis I psychiatric disorder (51.5%; $N = 163$) than men (42.8%; $N = 90$), although the difference was marginally significant, $\chi^2 = 3.84$, d.f. = 1, $P = 0.05$. A significantly greater proportion of women met criteria for an anxiety disorder (30.3%; $N = 96$) relative to men (20.0%; $N = 42$), $\chi^2 = 7.02$, d.f. = 1, $P < 0.01$. Prevalence rates across diagnostic categories did not differ significantly as a function of marital status nor by level of education. For ASPD, there were no differences by sex, race or marital status; however, the prevalence of ASPD was greater among participants with less education, $\chi^2 = 11.22$, d.f. = 1, $P < 0.01$.

Regarding route of MA administration, the odds of being an injecting user were highest among those with a mood disorder and lowest among those with a psychotic disorder (see Table 3).

Association of psychiatric diagnoses 3 years post-treatment with MA use during follow-up

Those with an Axis I psychiatric diagnosis reported significantly greater frequency of MA use during follow-up ($M = 15.5$ months; $SD = 0.8$) compared with those without a diagnosis ($M = 12.8$ months, $SD = 0.8$), $t = -2.05$, d.f. = 521, $P = 0.03$, whereas the reverse was true of those with ASPD, who reported using less frequently than those without ASPD ($M = 11.9$ vs. $M = 14.8$ months, $t = 2.0$, d.f. = 523, $P = 0.03$). When diagnostic groups were examined, those with mood, anxiety and eating disorders each reported significantly more frequent MA use during follow-up than those without these diagnoses. However, MA use frequency during follow-up was not significantly different between those with and without psychotic disorders.

Effects of multiple diagnoses at follow-up on post-treatment substance use

When all Axis I psychiatric diagnoses were examined, 31.7% of the sample met criteria for none, 27.0% for one, 16.9% for two and 24.6% for three or more current or lifetime disorders. A linear regression indicated that MA use frequency during follow-up increased significantly as a function of the number of psychiatric diagnoses, $b = 0.68$, $SE = 0.29$; $P = 0.02$. Likewise, those with SA history met criteria for more psychiatric diagnoses ($M = 3.1$, $SD = 2.2$) than those without such history ($M = 1.2$, $SD = 1.7$), $t = -10.8$, d.f. = 524, $P < 0.0001$.

Association of Axis I psychiatric diagnoses at follow-up with post-treatment functioning

The ASI composite scores at baseline, discharge and follow-up for those with and without current or life-time Axis I psychiatric disorders are plotted in Figure 1, and the results of mixed model linear regressions testing the effects of time, psychiatric diagnosis and their interaction on ASI scores are provided in Table 4. Controlling for demographics, pre-treatment MA use frequency and route of MA administration, a significant time $\times$ diagnosis interaction emerged on three of the seven ASI composites (alcohol, drug and psychiatric). All interactions indicated that the group with an Axis I psychiatric diagnosis reported problems of significantly greater severity over time. Likewise, those with an Axis I psychiatric disorder were significantly more likely to report SA history (OR = 3.6, 95% confidence interval -2.4, 5.4) relative to those without a psychiatric diagnosis. By contrast, the odds of prior SA were not significantly different among those with and without ASPD (OR = 1.3, 95% confidence interval -0.9, 2.1).

Discussion

In a sample of adults interviewed 3 years after treatment for MA dependence, this study showed similar findings to those reported in other clinical [9,23,24] and community samples [6,8] demonstrating increased rates of psychiatric disorders in substance using populations and poorer clinical outcomes in those with comorbidity. This study, which is the first to characterise the rates and effects of psychopathology on substance use and psychosocial functioning post-treatment in MA users, differed from previous reports of comorbidity among cocaine users [9] by reporting on current in addition to lifetime diagnostic rates.

Prevalence rates of psychiatric illness in MA users

Although findings from this study generally concur with prior work in cocaine users in showing overall high rates of psychiatric disorders, some variations were observed in the magnitude of elevation in specific categories. In the present study, the overall rate of current and lifetime psychiatric diagnoses was 48%, falling in the mid-range of estimates in prior reports of cocaine treatment samples, which range between 21% and 73% [9,24]. The observed rates of affective disorders were lower than that reported in prior studies [8,9,12], whereas anxiety, psychotic and ASPD were observed at substantially higher rates than those previously reported in cocaine users [7,25].

The rates of lifetime (24.5%) and current (22.2%) affective disorders in the present study were noteworthy, given that prior clinical and community studies of cocaine, amphetamine and MA users yielded nearly twice that rate [8,9,12]. These discrepancies are likely attributable to differences in study populations, time points of assessment (i.e. proximity to substance use) and diagnostic methods used. Moreover, although current affective disorders were present at a rate of 44.3% in the largest clinical study to date of cocaine users [9], this was largely accounted for by chronic minor mood disorders. By contrast, in the present study, MDD, present in 15.2% of our sample, accounted for the majority of current affective disorders at a rate more than triple that observed in cocaine users (4.9%).

Given that anxiety and psychotic symptoms are among the most commonly reported psychiatric complaints among MA users [18], it is not surprising that the rate of current anxiety and psychotic disorders in this sample were substantially higher than that reported in community and clinical samples of cocaine users [7,9,25]. ASPD was the most prominent comorbid psychiatric diagnosis observed in this study, present in 28.7% of the sample. This rate was similar to that found in treatment-seeking cocaine users when drug abuse exclusion criteria were not applied to the ASPD diagnosis [9], which is of interest given that the

diagnostic instrument used in this study, like the DSM-IV, does not discount substance-related behaviours when diagnosing ASPD.

Association of psychiatric diagnoses with post-treatment substance use and functioning

Consistent with literature showing poorer post-treatment functioning associated with comorbidity [26], psychiatrically ill patients in this study reported more frequent MA use during follow-up and evidenced poorer functioning across multiple domains. When specific psychiatric illnesses were examined, mood, anxiety and eating disorders were associated with greater MA use, whereas psychotic disorders were not. Patients with ASPD-evidenced less MA use during follow-up relative to those without ASPD. Generally, studies investigating the impact of ASPD on the clinical course of substance dependence have yielded mixed findings [3,27,28]. Although studies of ASPD in MA users are limited, the present findings replicate a prior report in which cocaine users with ASPD showed better post-treatment use outcomes than those without ASPD [29]; however, at least one other study found that ASPD was unrelated to post-treatment cocaine use [30].

The high lifetime rate of SA in this study (28.7%) replicates findings from prior studies of treatment-seeking cocaine and MA users [9,12]. SA rates in patients with substance use disorders (SUDs) are exceeded only by those of patients with mood disorders, and comorbidity increases SA risk [31]. Likewise, the presence of multiple psychiatric diagnoses increased the risk of SA incrementally.

Limitations

This study had several potential limitations. First, the MINI does not distinguish substance-induced from primary psychiatric syndromes and does not determine order of onset of substance use relative to psychiatric diagnoses; thus, further investigation is needed to understand the causal relationships between MA use and psychiatric disorders. Moreover, because the MINI provides limited information concerning lifetime diagnoses, the lifetime prevalence of most psychiatric disorders in MA users remains to be characterised. Second, as psychiatric diagnoses were assessed at 3-year follow-up rather than at treatment entry, the potential effects of pre-existing diagnoses on clinical course and treatment outcomes are unknown. Moreover, although participants who were and were not successfully followed for the 3-year post-treatment assessment did not differ on key measures of baseline addiction and psychiatric severity, it remains possible that psychiatric disorders, which were not measured at baseline impacted the follow-up rate in this study. Third, as patients with psychiatric conditions severe enough to warrant primary treatment or hospitalisation were excluded from study participation, prevalence rates of psychiatric diagnoses were likely underestimated. Fourth, although the effects of different types of psychosocial treatment on post-treatment substance use were not the focus of this investigation, studies are needed to determine whether such treatment effects differ between those MA users with and without psychopathology. Finally, this study did not include objective measures of drug or alcohol use to corroborate self-report.

Conclusions

The present study findings have a number of clinical and research implications. The increased rates of major depression, anxiety and psychotic disorders in this sample of MA users are substantial, posing significant challenges to clinicians given the known association between psychiatric illness and complicated course, poorer prognosis and treatment outcomes [32,33] replicated in this report. Based on the original MTP findings, the Matrix Model is a highly effective psychosocial intervention for MA users, with positive effects on MA use relative to treatment as usual during the active 16-week intervention. Nevertheless, this approach does not thoroughly address concurrent psychiatric symptomatology;

according to the current study, comprehensive and integrated intervention strategies addressing both SUDs and psychiatric disorders [32,34] are indicated for MA using populations with corresponding clinical investigations to determine and refine optimal, disorder-specific approaches. Future epidemiological and clinical research specific to MA using populations is warranted to further understand and address the MA use—psychopathology relationship.

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Figure 1. Mean Addiction Severity Index (ASI) Composite scores as a function of time among MA-dependent adults with ($N = 179$; upper panel) and without ($N = 347$; lower panel) an Axis I disorder at 3-year follow-up.

Table 1

Current and lifetime rates of psychiatric disorders in MA-dependent adults 3 years post-treatment

Characteristic (N = 526)	No. (%)	
	Current	Lifetime
Any psychiatric disorder (excluding drug disorders, alcoholism)	179 (34.0)	182 (34.6)
Affective disorders		
Major depression	80 (15.2)	***
Major depression, recurrent	***	48 (9.1)
Dysthymic disorder	19 (3.6)	***
Mania	21 (3.9)	45 (8.5)
Hypomania	13 (2.4)	49 (9.3)
Any affective disorder	117 (22.2)	129 (24.5)
Anxiety disorders		
Panic disorder	14 (2.6)	43 (8.1)
Agoraphobia	14 (2.6)	***
Social anxiety disorder	45 (8.5)	***
Generalised anxiety disorder	65 (12.3)	***
Obsessive-compulsive disorder	40 (7.6)	***
Post-traumatic stress disorder	31 (5.8)	***
Any anxiety disorder	123 (23.4)	***
Eating disorders		
Anorexia nervosa	0 (0.0)	***
Bulimia nervosa	13 (2.4)	***
Psychotic disorders	26 (4.9)	67 (12.7)
Antisocial personality disorder	***	136 (25.8)
Suicide attempts	***	151 (28.7)

Denotes diagnostic information that is not assessed using the Mini-International Diagnostic Interview.

Table 2

Rates of current psychiatric disorders in MA-dependent adults 3 years after treatment by demographic subgroups

Disorder	Gender, %		Race, %			Education, %		
	M (N = 210)	F (N = 226)	W (N = 362)	NW (N = 164)	<HS (N = 101)	HS (N = 249)	>HS (N = 176)	
Major depressive disorder	11.4	17.7*	15.7	14.0	16.8	12.8	17.6	
Dysthymic disorder	3.3	3.8	4.1	2.4	4.9	4.0	2.2	
Mania	3.8	4.1	3.3	5.4	3.9	4.4	3.4	
Hypomania	1.4	3.1	2.7	1.8	0.9	1.6	4.5	
Panic disorder	2.3	2.8	1.6	4.8*	3.9	3.2	1.1	
Agoraphobia	1.4	3.4	3.3	1.2	3.9	2.0	2.8	
Social anxiety disorder	5.2	10.7*	8.5	8.5	12.8	5.6	10.2	
Generalized anxiety disorder	10.0	13.9	12.7	11.5	11.8	12.0	13.0	
OCD	5.7	8.8	8.8	4.8	4.9	6.4	10.8	
PTSD	4.2	6.9	5.2	7.3	7.9	5.2	5.6	
Bulimia nervosa	1.9	2.8	1.6	4.2	3.9	0.8	3.9	
Psychotic disorders	5.7	4.4	4.1	6.7	5.9	4.4	5.1	
Antisocial personality	26.6	25.3	24.3	29.2	37.6	25.7	19.3*	

* $P < 0.05$ by χ^2 . M, male; F, female; W, white; NW, non-white; HS, high school; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder.

Table 3

Odds of psychiatric diagnoses 3 years after treatment for MA dependence by route of administration

Type of disorder	N	Route of Administration		
		Injector (n = 143)	Smoker (n = 331)	Intranasal (n = 49)
		Odds ratio (CI)	Odds ratio (CI)	Odds ratio CI)
Any mental disorder	179	1.8 (1.2–2.7)	0.6 (0.4–0.9)	0.7 (0.3–1.3)
Any mood disorder	117	1.8 (1.2–2.7)	0.5 (0.4–0.8)	1.0 (0.5–1.8)
Any anxiety disorder	123	1.5 (0.9–2.2)	0.7 (0.4–1.0)	0.9 (0.4–1.7)
Eating disorder	13	1.1 (0.3–3.9)	0.4 (0.1–1.4)	3.0 (0.8–11.4)
Psychotic disorder	26	0.8 (0.4–1.4)	1.2 (0.7–2.1)	0.7 (0.2–1.9)

CI, 95% confidence interval.

Changes in psychosocial, psychiatric and substance-related impairment among MA-dependent adults at 3-year follow-up: linear mixed-effects models

Table 4

Scale	Axis I Diagnosis		Time		Axis I X Time	
	b	P	b	P	b	P
Addiction severity index						
Psychiatric composite	0.07	0.02	-0.01	<0.001	0.01	<0.01
Medical composite	0.06	0.01	0.00	0.48	0.00	0.58
Employment composite	0.00	0.96	-0.02	<0.001	0.00	0.51
Alcohol composite	0.00	0.78	-0.01	<0.001	0.01	0.04
Drug composite	0.00	0.70	-0.03	<0.001	0.01	<0.01
Legal composite	0.00	0.86	-0.03	<0.001	0.00	0.42
Family composite	0.02	0.10	-0.03	<0.001	0.00	0.27