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Educational Attainment is not a Good Proxy for Cognitive Function in Methamphetamine Dependence

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Abstract

We sought to test the hypothesis that methamphetamine use interferes with both the quantity and quality of one's education, such that the years of education obtained by methamphetamine dependent individuals serves to underestimate general cognitive functioning and overestimate the quality of academic learning. Thirty-six methamphetamine-dependent participants and 42 healthy comparison subjects completed cognitive tests and self-report measures in Los Angeles, California. An overall cognitive battery score was used to assess general cognition, and vocabulary knowledge was used as a proxy for the quality of academic learning. Linear regression procedures were used for analyses. Supporting the hypothesis that methamphetamine use interferes with the quantity of education, we found that a) earlier onset of methamphetamine use was associated with fewer years of education ($p < .01$); b) using a normative model developed in healthy participants, methamphetamine-dependent participants had lower educational attainment than predicted from their demographics and performance on the cognitive battery score ($p < .01$); and c) greater differences between methamphetamine-dependent participants' predicted and actual educational attainment were associated with an earlier onset of MA use ($p \leq .01$). Supporting the hypothesis that methamphetamine use interferes with the quality of education, years of education received prior to the onset of methamphetamine use was a better predictor of a proxy for academic learning, vocabulary knowledge, than was the total years of education obtained. Results support the hypothesis that methamphetamine use interferes with the quantity and quality of educational exposure, leading to under- and overestimation of cognitive function and academic learning, respectively.

Keywords

methamphetamine; education; cognition; onset; estimation

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1.1 Introduction

Studies have found that individuals who use methamphetamine (MA) tend to have lower levels of education than individuals who do not use MA (Herman-Stahl et al., 2007; Kobori et al., 2009), including several studies of cognition and/or brain function which compared MA dependent individuals to healthy control subjects (Gonzalez et al., 2007; Ghahremani et al., 2011; Hoffman et al., 2006; London et al., 2005; Salo et al., 2007; Salo et al., 2002; Scott et al., 2007; Simon et al., 2010). In these neurocognitive studies, it is common practice to statistically control for the effects of education when examining the primary cognitive or neurological variables of interest, so as not to attribute group differences to MA dependence which are in fact driven by differences in educational level. The interest in accounting for education in these analyses is often not in the service of education *per se*, but rather, in using education as a proxy to control for group differences in pre-morbid cognition and/or exposure to cognitively enriching circumstances.

At best, controlling for educational level in these analyses assumes that: a) MA dependence and educational level are unrelated constructs, or b) any relationship between MA dependence and education is driven by *premorbid* effects of education on the development of MA dependence; in other words, lower educational level (or its proxy construct) predisposes an individual to become MA dependent, not vice versa. Tacit in the use of educational corrections is the notion that MA usage does not have an effect on educational attainment or exposure, because if it did, correcting for level of education would potentially remove variance which is attributable to MA dependence itself.

Despite the implicit assumption that MA dependence does not impact educational exposure, it is noteworthy that MA and other substance use disorders are commonly considered developmental disorders (Rawson et al., 2007; Compton et al., 2007; Chambers et al., 2003), with MA use often beginning in the late teen years (Hser et al., 2008; Rawson et al., 2007). As such, it is possible that MA use could affect educational engagement and subsequent educational attainment, particularly at secondary and post-secondary educational levels. Indeed, longitudinal data from South Africa have shown that MA use in high school prospectively predicts school drop out one year later (Pluddemann et al., 2010). There have been similar findings for polysubstance use in the United States, with increases in use during adolescence having been found to prospectively predict lower educational attainment in young adulthood (King et al., 2006).

If the constellation of MA usage does affect educational experiences, it is conceivable that this could occur in at least two ways. First, MA may interfere with the *quantity* of educational attainment. In this scenario, although an individual may have the requisite cognitive abilities to go further in school, because of MA use, this potential is cut short. In this situation, years of education would generally *underestimate* cognitive function. This would not preclude the common finding that MA dependent subjects generally have lower cognitive functioning than healthy comparison participants (e.g., Scott et al., 2007); rather, it would suggest that even within lower cognitive levels, education would under-predict performance.

A second possibility is that MA use could interfere with the *quality* of education. In this scenario, although the individual is still enrolled in school, MA use affects the quality of the learning which occurs. This could occur from tardiness, absences, inadequate focus or understanding of instruction, failure to do homework, or other related factors. Given this situation, the overall years of education obtained would *overestimate* the learning of the individual. This would tend to be particularly true of academic skills and cognitive abilities which are highly related to educational exposure.

Despite evidence that MA is associated with reduced educational attainment, we are aware of no studies which have examined the accuracy of educational attainment as a proxy for cognitive function in MA dependence. To address this gap in the literature, we conducted a cross-sectional analysis of 36 MA-dependent participants and 42 control subjects who were assessed on a cognitive battery previously shown to be sensitive to MA-associated cognitive dysfunction (Simon et al., 2004; Simon et al., 2010). Hypotheses were separated into those suggesting that MA interferes with the *quantity* of education, and those suggesting that MA interferes with the *quality* of education:

MA use interferes with the quantity of education

1a) The onset of MA use will be positively associated with years of education, indicating that those who began using MA at an earlier age will have less education.

1b) When compared with a normative model of the relationship between cognitive functioning and educational attainment developed in healthy control subjects, MA dependent subjects will have significantly lower education than predicted from their current cognitive scores. Further, the degree to which their actual and predicted education differ will be correlated with the age of onset of MA use, indicating that those who began to use MA at an earlier age will have a greater discrepancy between actual and predicted educational levels.

1c) If results suggest that years of education is an inaccurate estimate of cognition in MA dependence, we further hypothesize that parental education may be a stronger correlate of cognitive function in MA dependent individuals than personal levels of education. We expect that this pattern will be in contrast to that observed in healthy control participants, in which personal education will be more strongly related to cognition than parental education. Because we are underpowered to test a difference between correlations, we considered this hypothesis exploratory.

MA use interferes with the quality of educational exposure

2) If MA use interferes with the quality of one's education, the years of education obtained before MA use may be a better indicator of the quality of one's learning than the total years of education received. To address this possibility, we hypothesize that a proxy for academic learning, vocabulary knowledge, will be more strongly related to the years of education received before MA use than the total years of education obtained.

2.1 Methods

2.1.1 Participants

The participants were 36 MA-dependent subjects who were not seeking treatment and 42 healthy control subjects. The majority of subjects (71%) participated in a previously published study of early abstinence and cognition (Simon et al., 2010), while smaller subsets completed previous studies of brain structure/function (Berman et al., 2007; London et al., 2005; Thompson et al., 2004). All participants were fluent in English and were administered the Structured Clinical Interview for the DSM-IV (SCID) for Axis I diagnosis (First et al., 1995). *Exclusion criteria*, based on interview, physician-conducted history, physical examination and laboratory tests, were: neurological disease (e.g., stroke, head trauma with loss of consciousness > 30 min); frank structural brain abnormalities on MRI; systemic disease; cardiovascular disease; pulmonary disease; HIV infection (HIV1/HIV2 antibody screen); abnormal laboratory tests (hematocrit, plasma electrolytes, markers for hepatic and renal function); use of psychotropic medications; diagnosis of current abuse or dependence for any substance other than MA, marijuana or nicotine; and any current non-substance-induced Axis I psychiatric conditions (with the exception of one MA subject with current social phobia). Qualified participants with cognitive data indicative of a lack of effort during examination were also excluded (i.e., Trails A performance ≥ 63 seconds, see (Iverson et al., 2002), or below chance performance on multiple choice measures; n = 3).

Participants in the MA group all met DSM-IV criteria for current MA dependence and used MA regularly (at least 3 times per week or twice a week binges for an average of 6.4 years (S.D.=6.5)); they also tested positive for MA in urinalysis at the time of enrollment. Five MA-dependent participants additionally met criteria for current marijuana dependence (n = 2) or abuse (n = 3).

In addition to the previously mentioned exclusion criteria, control participants were stimulant-naïve and did not meet criteria for any current Axis I conditions (substance-related or psychiatric), nor did they have more than experimental use (2-3 times in life) of any illicit substance other than marijuana. They used marijuana or drank alcohol to intoxication on less than 5 of the 30 days before testing. These relatively stringent exclusion criteria were applied to the control group because these subjects were primarily included as means to examine the normative relationship between education and the cognitive battery score. Characteristics of the participants are provided in Table 1.

2.1.2 Measures

Admission & Intake Form—This instrument collects demographic information, years of education, medical information (e.g., to check eligibility), and detailed drug use history.

Cognitive battery—The cognitive battery used was similar to that of Simon et al. (2010), and included measures of processing speed, attention, learning/memory, working memory, and executive functioning. Specific tests included the Trailmaking Test (Part A and B; Reitan, 1958), Stroop Color-Word Test (Golden, 1978), Digit Symbol Coding from the WAIS-R (Wechsler, 1981), Backward Digit Span (Woodcock and Johnson, 1977), Missing

Digit Span (Simon et al., 2004; patterned after Buschke, 1963), Selective Reminding Test (Buschke, 1963), Repeated Memory Test- Pictures (Simon et al., 2004; based on stimuli from Snodgrass and Vanderwart, 1980), Controlled Oral Word Fluency (FAS, Borkowski et al., 1967), Logical Problems (Simon et al., 2004), and Discrimination Learning (Simon et al., 2004; similar to Concept Learning from Woodcock and Johnson, 1977). Similar to Simon et al. (2010), an overall cognitive battery score was created by centering and scaling each of the test scores based on the mean and standard deviation of the control group and then averaging the resulting standardized scores (tests on which lower scores indicated better performance were multiplied by -1 to keep the directionality of the measures consistent). It should be noted that standardizing the test scores to the control sample is simply a scale change, designed to put equal weights on the measures in the composite score. It does not affect our ability to differentiate relationships by group or otherwise represent self-referential use of the data. See Simon et al. (2004) for further description of the individual cognitive tests.

Shipley-Hartford Institute of Living Scale-Vocabulary Test—(Shipley, 1940): A 40-item multiple-choice test of vocabulary knowledge which requires the examinee to select the best synonym for various vocabulary words. We used this test as an estimate of academic learning because tests of vocabulary have been shown to have higher correlations with education in normative samples than numerous other cognitive tests (Heaton et al., 1996; Kaufman et al., 1988; Reitan and Wolfson, 1996). In addition, similar measures of reading/vocabulary have been shown to be correlated with academic achievement (Qian, 2002; Wilkinson, 1993), as well as the quality of education in terms of pupil expenditures, teacher experiences, and pupil-teacher ratio (Hedges, 1994). For this reason, measures of reading/vocabulary have been used to assess the quality of one's education independent from the total years of education obtained (Manly et al., 2002; O'Bryant et al., 2007).

2.1.3 Procedure

Participants were recruited through internet and print advertisements in the greater Los Angeles area. After receiving a detailed description of the protocol, participants provided written informed consent, following the guidelines of the UCLA Office for Protection of Research Subjects. All MA subjects resided at the UCLA General Clinical Research Center (GCRC), in which abstinence from all drugs (aside from nicotine) was confirmed by regular urine drug screens and breathalyzer tests. Control subjects were also tested via urine screen/ breathalyzer for drug use prior to assessments, but did not reside at the GCRC. Inclusion/ exclusion and demographic information were obtained at intake. The cognitive battery was administered after MA participants were on the unit for 3 to 14 days, allowing MA to clear from their system. No participant was positive for MA or any other drug (except nicotine) on the cognitive testing day(s). All MA subjects self-reported at least 4 days abstinence at testing (range 4 to 15 days; note that although all MA subjects tested positive at enrollment, they need not have used MA on the actual enrollment day). No effects of withdrawal have been noted on cognition in this timeframe (Simon et al., 2010; Perez et al., 2008), and days of abstinence were unrelated to the cognitive battery score in correlational and median split analyses (p's > .10).

3.1 Results

Hypothesis 1: MA use interferes with the quantity of education

Hypothesis 1a: Earlier onset of MA use will be associated with fewer years of education—Linear regression was used to assess the relationship between MA use onset and years of education, while controlling for age, gender and ethnicity. In separate analyses, both the age at which participants began using MA ($t(28) = 3.03$, $p = .005$), and the age at which participants began using MA frequently (at least 3 times per week, or twice weekly binges, $t(28) = 4.97$, $p = .000$), were positively related to years of attained education. Demonstration of these effects is depicted in Figure 1, which shows the bivariate correlation between the age of first MA use and years of education.

Hypothesis 1b: When compared with a normative model developed in control subjects, MA dependent subjects will have significantly lower education than predicted from their current cognitive scores, and the degree to which their actual and predicted education differ will be correlated with the age of onset of MA use—In the healthy comparison participants, years of education was regressed onto the cognitive battery score, with age, gender and ethnicity also included as predictors. The resulting estimated model was used to predict years of education in the MA dependent sample from their cognitive battery scores and demographics. Using a paired t-test, the years of education predicted from cognition and demographics was significantly different from the participants' actual years of education ($t(35) = -3.13$, $p = .003$), with a mean difference score of 1.05. This indicates that, on average, the MA dependent subjects had one year less education than predicted from their cognition and demographics. Lastly, we correlated the difference between actual and predicted education in the MA group with the age at which subjects first used MA and the age at which they began to use MA frequently; both correlations were significant ($r = -.42$, $p = .011$ and $r = -.56$, $p = .000$, respectively), indicating that those subjects who began to use MA at an earlier age had a larger discrepancy between their real and predicted educational level (see Figure 2).

Exploratory hypothesis 1c: MA dependent subjects will show a stronger relationship between parental education and cognition than between personal education and cognition, a reverse of the pattern of relationships seen in healthy control subjects—The preceding analyses suggested that years of education is an inaccurate estimate of general cognitive function in MA dependence. Therefore, in MA dependent individuals, familial educational background may be a better predictor of one's general cognitive function than personal levels of education. We hypothesized that this would be in contrast to control subjects, who would show the strongest relationship between personal educational levels and cognition. In the MA subjects, the correlation between personal years of education and the cognitive battery score was $r = .28$ ($p = .094$), while the correlation between mother's education and the cognitive battery score was $r = .36$ ($p = .034$). In contrast, in the control subjects, the correlation between personal years of education and the cognitive battery score was $r = .39$ ($p = .010$), and the correlation between mother's education and the cognitive battery score was $r = .14$ ($p = .377$). Mother's education was used in these analyses because the MA dependent subjects often had no relationship with their fathers.

Hypothesis 2: MA use interferes with the quality of educational exposure

Hypothesis 2: In MA dependent subjects, a proxy for academic learning, vocabulary knowledge, will be more strongly related to the years of education received before MA use than the total years of education obtained—If MA use affects the quality of educational exposure, the learning which occurs prior to MA use may be qualitatively different than that following MA use. Based on the standard timeline of the American education system (e.g., 8th grade average age 13 to 14, 9th grade average age 14 to 15, etc.; National Center for Education Statistics (NCES, 2001)), we defined a new variable which was the estimated maximum number of years of education each MA participant received prior to first using MA. If the participant began using MA *after* they had already stopped going to school, their pre-MA years of education were equivalent to their total years of education. In this sample, 13 of 36 MA participants started using MA before completing their education.

We next sought to determine whether the original or MA-adjusted measure of education had a stronger relationship with a test of vocabulary (Shipley, 1940). Using linear regression with vocabulary scores as the dependent variable, we first controlled for age, gender and ethnicity as a fixed block (R^2 = .46, p = .004), followed by stepwise entry of education and MA-adjusted education. Only the MA-adjusted education variable (Beta = .84, t = 3.23, R^2 = .61, R^2 change = .15, p = .003) was retained in the model. The original education variable was excluded from the model as its fit was inferior to the MA-adjusted variable.

4.1 Discussion

We hypothesized that MA use during adolescence may interfere with both the *quantity* and *quality* of one's education. Our results support both conceptualizations. With respect to educational *quantity*, we hypothesized that years of education may underestimate general cognitive function because MA use interferes with educational attainment, even though some MA users may have the cognitive potential to receive further education. Our results supported this hypothesis. Age of onset of MA use (whether measured as first use or start of frequent use) was positively correlated with years of education ($p < .01$), indicating that participants who began to use MA at an earlier age obtained fewer years of education. Second, using a normative model developed in healthy control participants, the actual educational level of MA dependent participants was significantly lower (approximately 1 year less) than predicted from their current cognitive functioning and demographic characteristics. Further, the earlier that participants began using MA, the larger the discrepancy between their actual and predicted educational levels. Third, given evidence that years of education is an inaccurate estimate of general cognitive function in MA dependence, we hypothesized that maternal education would be a stronger correlate of cognition in MA-dependent subjects than personal education. Although we did not formally test for a difference in correlations due to a lack of power, the descriptive statistics were suggestive: the relationship between cognition and personal education was slightly lower than between cognition and mother's education in MA subjects (r = .28 vs. r = .36). In contrast, this pattern was reversed in the healthy control subjects (r = .39 vs. r = .14, respectively).

We also found evidence to suggest that MA use may interfere with the *quality* of one's education. Specifically, using a test of vocabulary knowledge as a proxy for academic learning, we hypothesized that the years of education received before the onset of MA use would be more strongly related to vocabulary scores than the total years of education obtained. This hypothesis was supported. In a stepwise regression controlling for demographic characteristics, the years of education received before MA use was a better predictor of vocabulary scores than the total years of education obtained.

4.1.2 Summary and Limitations

This research suggests that MA use interferes with how much education one attains as well as the quality of that education. As a result, the years of education MA dependent individuals obtain tend to underestimate general cognitive function while overestimating academic learning. This is in notable contrast to the relationships expected in typically developing individuals, in which years of education is positively associated with both general cognitive function and measures of academic learning (Heaton et al., 1996).

These data indicate that educational attainment should be used cautiously as a covariate in studies of MA dependence. We recommend that authors first attempt to clarify the purpose of using education as a covariate in a given analysis. If the intent is to use education as an estimate of general cognitive function, we recommend that actual tests of cognitive function be used if possible (e.g., abbreviated measures of intelligence like the Wechsler Abbreviated Scale of Intelligence, Wechsler, 1999). If cognitive tests are unavailable, our data suggest that parental education may be a better estimate of general cognitive function in MA dependent subjects than personal levels of education, although replication of our findings would be desirable prior to use of this strategy. On the other hand, if cognitive measures are available and the intent is to control for exposure to learning environments, research suggests that use of vocabulary/pronunciation tests may be more suitable than educational attainment for this purpose (Manly et al., 2002; O'Bryant et al., 2007). However, we also recommend that authors examine their own data to investigate the extent to which education may be associated with MA use. Examining the pattern of relationships between MA use onset, education, parental education, vocabulary scores and cognitive performance in the MA-dependent sample may reveal the most appropriate nuisance variable of interest.

Limitations of this research should be acknowledged. Given the cross-sectional nature of our study, the relationships found between the onset of MA use and education may not reflect causal relationships; instead, the onset of MA use may be correlated with some other variable which accounts for the results. For example, early drug use may be associated with several factors that can affect educational exposure, such as impeded social development, early engagement in adult roles such as parenthood and/or full time work, and peer social norms that are contrary to academic success (King et al., 2006). Socioeconomic status (SES) may also covary with both drug usage and educational attainment. Although the MA and control subjects in our study did not significantly differ in mother's educational level ($p > .10$), we did not have a comprehensive measure of SES and we cannot conclude that the MA and control subjects were equivalent in SES level. In addition, the MA subjects in our study were more likely to use marijuana than the control subjects ($p = .04$), although this use was generally mild. However, when we adjusted all the analyses for the age of first marijuana use, the pattern of results was unchanged (all p's $\leq .05$).

Although other authors have also used tests of vocabulary as a proxy for the quality of academic learning (Manly et al., 2002; O'Bryant et al., 2007), performance on vocabulary tests is likely to be determined by more than the quality of academic learning, including factors such as innate language capacity and the social environment in which one develops. In this respect, it is possible that the MA subjects had a longstanding weakness in the verbal-language domain which accounts for both lower vocabulary performance and a predilection for early drug use.

However, regardless of the causal factors underlying the relationships found between onset of MA use and education, it is clear that the years of education attained by our MA-dependent participants do not relate to cognitive and academic variables as typically expected. Our data suggest that the years of education obtained by MA- dependent individuals tends to underestimate general cognitive functioning but overestimate academic learning.

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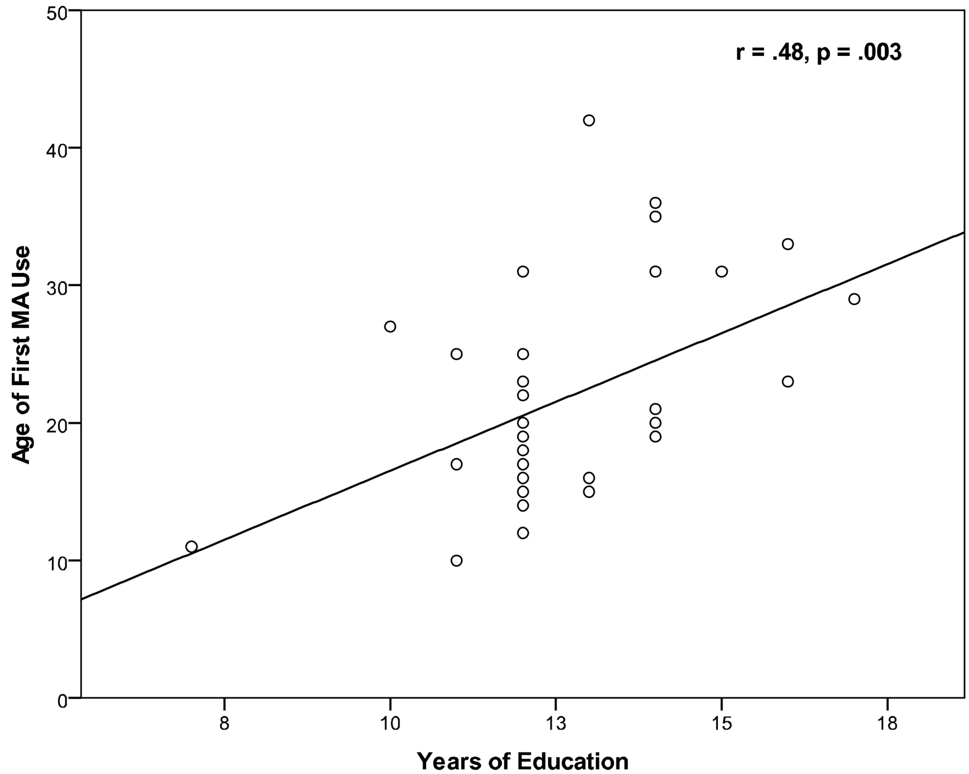

Figure 1. Relationship between age of first use of methamphetamine (MA) and years of education

Note: N = 36 MA-dependent participants. Pearson correlation. Correlation does not covary for demographic characteristics. The participant with 7 years of education in the lower left corner of the graph did not unduly influence the relationship according to several standardized measures (Cook's Distance, Leverage, DfFits, DfBeta), and the correlation remained statistically significant when this data point was removed from analysis ($p = .010$).

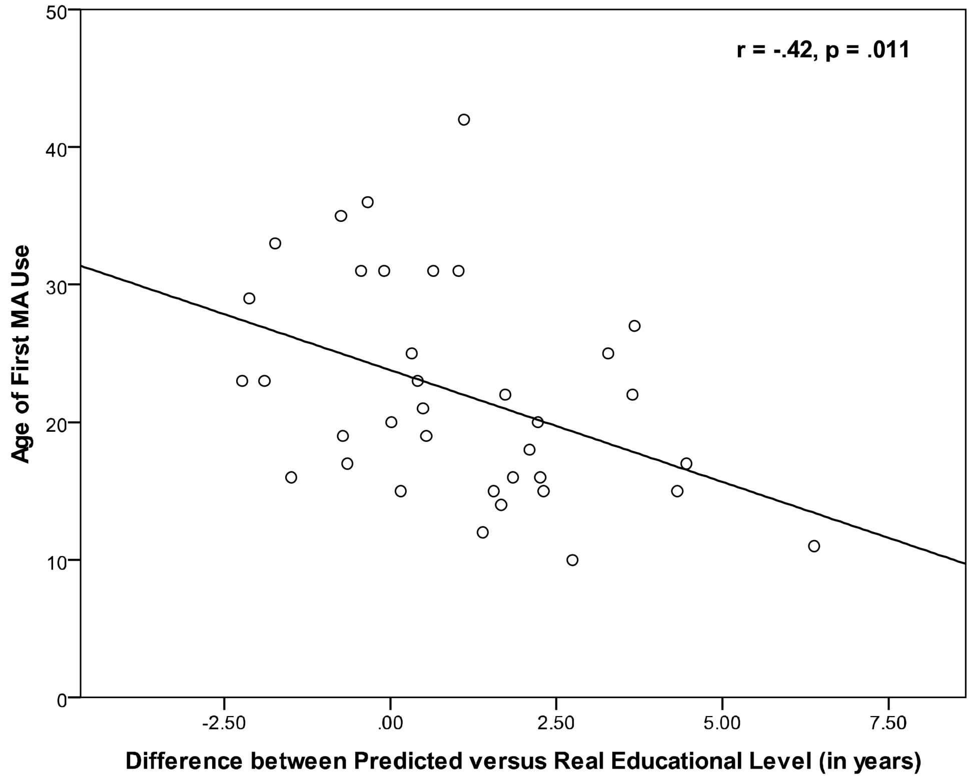

Figure 2. Relationship between age of first use of methamphetamine (MA) and the difference between predicted versus actual years of education

Note: N = 36 MA-dependent participants. Pearson correlation. Predicted education was predicted from cognitive battery scores and demographic characteristics (age, gender, ethnicity), using a regression model developed in healthy comparison subjects (N = 42). Positive difference scores indicate that predicted education was greater than actual years of education, while negative difference scores indicate that predicted education was less than actual years of education. Results show that larger (positive) difference scores were associated with a younger onset of MA use.

Table 1

Characteristics of Research Participants

	Control	MA-Dependent
Sample size	42	36
Age	31.6 ± 9.0	32.5 ±7.6
Education (yrs.)	15.0 ± 2.1	12.8 ± 1.9
Mother's education (yrs.)	14.4 ± 3.2	13.3 ± 2.4
Ethnicity		
Caucasian	26	20
African Am.	6	2
Hispanic	2	9
Asian/Pacific Islander	6	2
Other	2	3
Gender		
Male	19	24
Female	23	12
Years of frequent MA use	--	6.4 ± 6.5
Grams MA/week	--	3.8 ± 4.8
Days abstinent from MA at cognitive testing	--	7.5 ± 2.7
Days used marijuana In last 30 days	0.3 ±1.1	3.4 ± 6.9
Vocabulary score	31.4 ± 3.5	26.3 ± 5.5
Cognitive battery score	.00 ± .54	−.65 ± .48

Note. Where appropriate, values are means ± SD. Vocabulary score = Shipley-Hartford Vocabulary test; Years of frequent MA use = years using MA at least 3 times per week, or twice weekly binges.