HHS Public Access

Author manuscript

Behav Brain Res. Author manuscript; available in PMC 2023 June 03.

Published in final edited form as:

Behav Brain Res. 2022 June 03; 427: 113876. doi:10.1016/j.bbr.2022.113876.

Applying the Addictions Neuroclinical Assessment to Derive Neurofunctional Domains in Individuals Who Use Methamphetamine

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Abstract

The Addictions Neuroclinical Assessment (ANA) was proposed as a neuroscience-informed clinical framework to understand heterogeneity in addiction encompassing dysfunction in three domains: incentive salience, negative emotionality, and executive functions. The ANA has been validated in the alcohol field but has not been extended to other substances. Thus, the objective of the current study was to replicate and extend the ANA framework to methamphetamine use disorder. Non-treatment seeking individuals (N = 185) who reported regular methamphetamine use completed a deep phenotyping battery comprising self-report and behavioral measures that assessed methamphetamine craving and emotional withdrawal symptoms, mood and anxiety symptomatology, risk-taking behaviors, working memory, attention, and impulsivity. Factor analytic techniques were used in an iterative manner to derive latent factors that explained biobehavioral variation in the sample. The relationship between factor scores and demographic and clinical indicators of methamphetamine use were examined to assess the construct validity of the latent factors. Deep phenotyping combined with factor analytic techniques implicated three intercorrelated neurofunctional domains that map on to the proposed ANA domains: incentive salience, negative emotionality, and executive function. Each of the domains were associated with demographic and clinical indicators of methamphetamine use providing initial support for their construct validity. The ANA framework holds promise for explaining heterogeneity in addiction by identifying neuroscience-informed phenotypes. Knowledge from the ANA framework may be applied to advance precision medicine and inform medications development for a host of substance use disorders, particularly those with no approved pharmacotherapy such as methamphetamine.

Keywords

methamphetamine use disorder; phenotyping; addiction; neuroscience; neurofunctional domains; Addictions Neuroclinical Assessment

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1. Introduction

Methamphetamine is a powerful, highly addictive psychoactive stimulant that is developing into its own epidemic in the United States [1, 2]. According to 2017 National Survey on Drug Use and Health (NSDUH) ~1.6 million people reported using methamphetamine in the past year, and 774,000 people reported using it in the past month [3]. Despite its growing prevalence and far-reaching negative consequences [4, 5], there are currently no approved medications to reduce the misuse of, or prolong abstinence from, methamphetamine in individuals with methamphetamine use disorder [6, 7]. While our understanding of the neurobiological effects of addictive substances, such as methamphetamine, has advanced in the last few decades, these insights have not translated into clinical practice [7–9]. This may be due, at least part, to the fact that diagnostic criteria for substance use disorders are outcome-based rather than process-based [10]. This is in contrast with most other medical diagnoses and is not necessarily useful for heterogeneous disorders [11].

In order to address this issue, there have been calls for the field of psychiatry to move towards a transdiagnostic and neuroscience-based framework to foster development of psychiatric nosology based on pathophysiology rather than clinical presentation. The Research Domain Criteria (RDoC) from the National Institute of Mental Health is one such initiative that is intended to advance the goal of a neuroscience-based research framework for psychiatric diseases [12]. Inspired by the RDoC, an Alcohol Addiction RDoC was proposed as a framework wherein specific functional domains can be prioritized [13]. As a compliment to these research frameworks, the Addictions Neuroclinical Assessment was proposed as a clinical framework for the assessment of addictions [11]. The ANA captures information in three of the five RDoC domains.

In its development, the ANA leveraged deep phenotyping with factor analytic methods to construct core neurofunctional domains. These domains have received initial empirical replication and validation in the alcohol field [14–17] but have not been extended to other substances, such as methamphetamine. The ANA posits three neurofunctional domains that can be leveraged to understand heterogeneity in addiction, incentive salience, negative emotionality, and executive (dys)function [11]. These domains have been derived across independent alcohol-focused laboratories using a combination of clinical, behavioral, and self-report measures that assess the aforementioned underlying constructs.

While the ANA presents new opportunities to fill the translational gap between behavioral and biological phenotypes, it is critical that the ANA framework be extended to substances beyond alcohol. Thus, the purpose of the current study was to conduct a secondary analysis of a methamphetamine study conducted in our laboratory [18] wherein methamphetamine users were phenotyped using a battery of well-validated scales and behavioral tasks that are all conceptually related to the previously proposed ANA dimensions. In order to derive a factor solution that is both quantitatively and theoretically sound, scales were subjected to sequential factor analytic work. To validate the resulting factor structure, scores on each factor were associated with several demographic and clinical indicators of methamphetamine use. We hypothesized that the derived latent factors would correspond

to the three ANA domains: incentive salience, negative emotionality, and executive dysfunction.

2. Material and methods

2.1 Participants

Non-treatment seeking individuals who regularly use methamphetamine were recruited from the Greater Los Angeles area. Inclusion criteria consisted of the following: (1) English fluency; (2) aged 18–50; and (3) ability to produce a methamphetamine positive urine prior to study entry. Exclusion criteria included the following: (1) in treatment for methamphetamine dependence, a history of treatment in the 30 days before enrollment, or treatment seeking; (2) current (last 12 months) DSM-IV diagnosis of drug dependence other than methamphetamine; (3) lifetime DSM-IV diagnosis of schizophrenia, bipolar disorder, or any psychotic disorder; (4) current major depressive disorder with suicidal ideation; and (5) current use of psychoactive drug, other than marijuana and methamphetamine, determined by toxicology screen.

2.2 Procedures

Participants were recruited from the community through radio, Internet, and newspaper advertisements. Interested individuals called into the laboratory and completed a brief phone screen to assess for eligibility. Following the phone screen, eligible individuals were invited to the lab for an in-person assessment. During the assessment, participants provided a urine sample for verification of recent methamphetamine use and completed a detailed battery of questionnaires, behavioral tasks, and interviews to assess for individual differences, methamphetamine and other substance use. Participants received $50 for participating in the assessment visit.

2.3. Measures

Eligible participants were invited to the laboratory to complete a phenotypic battery consisting of sociodemographic (i.e., age, sex, race), clinical, and behavioral measures. Individual differences measures included the Fagerstrőm Test for Nicotine Dependence (FTND) [19] to assess cigarette smoking severity, and the Drug Use Questionnaire [20] to measure cannabis use.

Latent factors were derived using measures assessing negative emotional symptoms of methamphetamine withdrawal (Methamphetamine Withdrawal Questionnaire; MAWQ [21]), methamphetamine craving (Methamphetamine Urge Questionnaire; MAUQ adapted from published and validated studies of craving assessment [22]), anxiety symptomatology (Beck Anxiety Inventory; BAI [23]), depressive symptomology (Beck Depression Inventory; BDI-II [24]), risk attitudes (Domain-specific Risk-attitude Scale; DOSPERT [25]), behavioral inhibition (The Stop Signal Task; SST [26]), attention and working memory (Digit Span; [27]), impulsivity (Barratt Impulsivity Scale; BIS-11; [28]), and delay discounting (Monetary Choice Questionnaire; MCQ; [29]).

The construct validity of the latent factors was assessed by an interview-based assessment of methamphetamine use over the previous 30 days using the Timeline Followback; [30]. The Structured Clinical Interview for DSM-IV (SCID) was administered by a master's level clinician to determine age at first methamphetamine use and assess for current methamphetamine abuse and dependence symptoms.

2.4 Statistical Analyses

2.4.1 Exploratory Factor Analysis (EFA).—A covariance matrix was constructed from individual level data in order to follow the pairwise deletion of missing data rule [31]. Pairwise deletion allows participants to contribute to the model if they had data on at least one indicator variable. EFA was used to identify latent factors underlying the above measures. Analyses were conducted using PROC FACTOR in SAS 9.4 using an oblique promax rotation, which assumes that latent factors are correlated. This assumption is supported and has been validated by previous work in the alcohol field [32]. Variables with a loading ≥ 0.40 were considered to load on particular factor [31]. Factors that had eigenvalues greater than 1, in combination with scree tests, suggested that factors were meaningful. An EFA solution was considered unsatisfactory if it included a factor that was composed of less than three measures. Weighted factor scores were then computed for each participant from the acceptable EFA to indicate their standing on each latent factor. Factor scores were then used as response variables in subsequent analyses. Cronbach's alpha (a) was calculated as a measure of internal consistency for each measure included in the factor analysis [33]. It is important to note that EFA/confirmatory factor analysis cross-validation could not be performed because separating our sample would have reduced that number of participants on these measures below the recommended minimum per measure in factor analysis [31, 34].

2.4.2. Construct Validity Analyses.—Demographic and clinical predictors were used to examine the construct validity of the derived latent factors. Specifically, we examined the association between the latent factors and the following variables: sex, age, age at first methamphetamine use, DSM-IV methamphetamine abuse and dependence symptom counts, and the number of methamphetamine use days over the past 30 days. These analyses were used to examine the validity of the extracted factor scores as they relate to a host of demographic and methamphetamine-related variables.

3. Results

3.1 Sample

The sample consisted of 185 individuals. Demographic and clinical characteristics of this sample have previously been reported in [18]. Approximately 71.86% of the sample were male, and 40.00% were Non-Hispanic White and 39.46% were Latino. The mean age of participants was 35.62 (SD = 8.75). The mean number of methamphetamine use days in the past 30 days was 19.11 (SD=8.89). Participants had an average combined DSM-IV methamphetamine abuse and dependence symptom count of 6.90 (SD = 2.47). The mean number of drinking days was 6.14 (SD = 8.87) and the mean number of drinks per drinking day was 4.18 (SD = 3.24). Mean nicotine dependence score as assessed via the FTND was 5.51 (2.47). In regard to cannabis use, 72 (38.92%) participants reported never using

cannabis, 32 (17.30%) participants reported using cannabis once or twice ever, 13 (7.02%) participants reported using cannabis once a month, 26 (14.05%) participants reported using cannabis once a week, 31 (16.76%) participants reported using cannabis more than once a week, and 10 (5.41%) participants reported using cannabis every day.

3.2 Exploratory Factor Analyses

An initial EFA was conducted using all of the variables available in the deep phenotyping battery described above. The scree plot from the first EFA revealed variance discontinuities that suggested five latent factors. The pattern matrix providing the factor loadings and reflecting the correlation coefficients between each variable and each rotated factor is provided in Table 1. The first factor accounted for 58.10% of the variance, with an Eigenvalue of 7.21, and was primarily composed of the BDI, BAI, emotional symptoms from the MAWQ, and the BIS subscales. The second factor accounted for 21.72% of the variance, with an Eigenvalue of 2.69, and was primarily composed of 5 items from the MAUQ and the craving symptom form the MAWQ. The third factor accounted for 9.04% of the variance, with an Eigenvalue of 1.12, and was primarily composed of both Digit Span subscales and DOSPERT. No additional factors crossed the critical Eigenvalue threshold of 1.0. Descriptive statistics on the indicator variables appear in Table 2.

Based on the results of this initial EFA, selected measures and items were removed from the model if they did not load on any of the three extracted factors. Specifically, the following scales and items with defuse loadings were removed from the subsequent EFA: (1) the second item from the MAUQ, (2) both SST items, and (3) delay discounting.

A subsequent EFA was conducted extracting a three-factor solution. The pattern matrix providing the factor loadings and reflecting the correlation coefficients between each variable and each rotated factor is provided in Table 3. The first factor accounted for 63.10% of the variance, with an Eigenvalue of 7.17, and was primarily composed of the BDI, BAI, emotional symptoms from the MAWQ, and the BIS subscales. We interpret this first factor as a negative emotionality domain given that the highest factor loadings reflect depressive and anxiety symptomatology, as well as negative emotional symptoms of methamphetamine withdrawal. The second factor accounted for 23.58% of the variance, with an Eigenvalue of 2.68, and was primarily composed of items from the MAUQ and the craving item from the MAWQ. We interpret this second factor to very closely parallel the incentive salience domain proposed in the ANA. The third factor accounted for 8.97% of the variance, with an Eigenvalue of 1.02, and was primarily composed of both Digit Span subscales and DOSPERT. This third factor is highly indicative of the executive function domain in the ANA. Subsequent factors accounted for small proportions of variance with negligible Eigenvalues.

The correlations between the factors varied in strength (Negative emotionality and Incentive salience correlation coefficient = 0.40, Negative emotionality and Executive function correlation coefficient = −0.08, and Incentive salience and Executive function correlation coefficient = 0.04).

3.3 Construct Validity

The relationship between the ANA domains and demographic and methamphetamine use characteristics are presented in Table 4. Higher scores on the negative emotionality domain were significantly and positively related to methamphetamine use disorder symptom count, and trend level associations were also found for age at first methamphetamine use and methamphetamine use days in the past 30 days. Higher scores on the incentive salience domain were significantly and positively associated with methamphetamine use disorder symptom counts and methamphetamine use days in the past 30 days. Higher scores on the executive function factor were significantly associated with younger age, and a trend-level negative relationship was found for age at fist methamphetamine use.

4. Discussion

The current study provides a robust replication of ANA domains in a sample of individuals who use methamphetamine. Using deep phenotyping and factor analytic techniques, we were able to derive intercorrelated neurofunctional domains that map on to the proposed ANA domains: incentive salience, negative emotionality, and executive function. Each of the domains were associated with demographic and clinical indicators of methamphetamine use providing initial support for their construct validity. To our knowledge, this is the first study extending the ANA framework in a sample of individuals who use methamphetamine.

The negative emotionality domain explained the largest amount of variability in the sample. Consistent with the ANA framework, the negative emotionality domain was primarily composed of depression and anxiety symptomatology, as well as emotional methamphetamine withdrawal symptoms. Trait impulsivity also loaded on this factor; albeit the factor loadings were considerably weaker compared to the aforementioned measures. While trait impulsivity is considered a stable personality trait relevant to addiction, it is distinct from state impulsivities, such as impulsive choice (i.e., delay discounting), which are proposed to share definitional and neurobiological overlap with executive functions [35]. In the negative emotionality domain, it may be the case that higher levels of trait impulsivity may increase vulnerability to rumination and recurrence of negative affect episodes, which has been documented among cigarette smokers [36]. Depression and anxiety frequently co-occur in individuals with methamphetamine use disorder [37, 38] with recurrent drug use being a compensatory behavior to alleviate negative emotional symptoms [39]. In support of this view, negative emotionality may potentiate methamphetamine craving in a similar manner to what has been demonstrated for cocaine [40]. Indeed, our laboratory showed a positive relationship between depression/anxiety symptoms and methamphetamine craving that occurred in a sex-specific manner [41]. With respect to methamphetamine use disorder and co-occurring depression, dual diagnosis worsens the overall prognosis and confounds treatment outcomes [42].

The incentive salience domain explained the second most amount of variability in the sample. Items associated with methamphetamine urge and craving primarily loaded on this domain. As such, this domain reflects motivation for methamphetamine that is characterized by “wanting” (i.e., desire or craving) which sensitizes and drives further drug use even as the drug’s hedonic value (i.e., “liking”) decreases [43, 44]. Craving has been posited as

an intermediate phenotype of addictions that predicts the development and maintenance of substance use disorders and treatment response [45, 46]. In a sample of individuals with MUD, craving intensity predicted subsequent methamphetamine use in the following week [47] as well as during the treatment period [48].

The executive function domain explained the least amount of variability in the sample. Measures reflecting risk-taking, attention, and working memory loaded on this domain. Neurocognitive deficits are well-documented in individuals who use methamphetamine compared to healthy controls with notable deficits in executive function and memory [49, 50]. Importantly, executive functions may influence treatment outcomes among individuals with methamphetamine use disorder. For example, recent work from our laboratory found that the opioid receptor antagonist naltrexone decreased subjective responses to methamphetamine and craving more readily in individuals with low executive function compared to those with high executive function [51].

Our results also provide initial validation of construct validity of the ANA domains in relation to methamphetamine severity measures. Negative emotionality had the most robust associations with methamphetamine use variables, followed by the incentive salience domain, and then executive function domain. Sex and age did not have robust associations with negative emotionality or incentive salience; however, as expected age did negatively correlate with executive function. The associations between methamphetamine use variables and ANA domains provide support for the construct validity of the ANA domains among individuals who use methamphetamine.

The ANA domains derived from the current study are highly consistent with ANA domains derived in alcohol studies. In the alcohol literature, the negative emotionality domain is primarily weighted by high factor loadings on self-report depression and anxiety measures [14, 15, 17, 32]. Across ANA alcohol studies, the incentive salience domain is primarily weighted on assessments that capture drive and urge to drink alcohol [16, 17, 32]; however, the actual measures used vary across studies. The least amount of consistency relates to measures used to derive the executive function domain. Kwako and colleagues [32] showed that the executive function domain was heavily weighted on trait impulsivity subscales and personality traits (i.e., conscientiousness and premeditation). Our laboratory found heavier weighting for working memory, attention, and delay discounting measures [17]. The lack of consistency between these studies may be that our study lacked in-depth assessments of personality traits. The same may be true for the executive function domain derived in the current study. As such, further elucidating the measures that load on executive function would be a worthwhile endeavor for future work. As a whole, the derived ANA domains reported in the current study replicate and extend previous ANA work to a sample of individuals who use methamphetamine. Based on the current work, it is reasonable to posit that the ANA framework can be extended to other substance use disorders.

It is possible that the ANA domains can be leveraged to advance precision medicine for methamphetamine use disorder using pharmacological and/or behavioral treatments. Indeed, behavioral treatments for this disorder have shown modest efficacy [52]. Since individuals with high incentive salience are likely to have greater craving for methamphetamine, it

is likely that these individuals may benefit more from a treatment specifically targeting craving and reward from methamphetamine. Effective treatment options that have been shown to reduce methamphetamine craving include contingency management [53], aerobic exercise [54], repetitive transcranial magnetic stimulation targeting the frontal regions [55], and the pharmacotherapy naltrexone [56]. In the negative emotionality domain, treatments that address mood disturbances and methamphetamine use concurrently may benefit individuals with high negative emotionality. Interventions that may target negative emotionality in methamphetamine include cognitive behavioral therapy [57], behavioral activation [58], aerobic exercise [59], and real-time functional magnetic resonance imaging neurofeedback [60]. Individuals with a large degree of executive dysfunction may respond better to contingency management and/or cognitive remediation with tasks that involve memory, attention, or executive function in order to restore impairments caused by excessive methamphetamine use [61].

The results of the current study should be viewed in light of the study's strengths and limitations. Strengths include a deeply phenotyped clinical sample and the use of well-validated self-report measures and behavioral tasks. Limitations include the use of measures requiring retrospective recall and a relatively modest sample size for structural equation modeling. Specifically, the sample size prevented us from splitting the sample into discovery and replication datasets needed to conduct a confirmatory factor analysis. Thus, there is a critical need to replicate these findings in a larger sample of individuals who use methamphetamine. In addition, the exclusion criteria used (i.e., treatment seeking, psychiatric disorders, psychiatric medications, etc.) may limit generalizability. Nonetheless, the current study provides the first independent replication and extension of the ANA framework to methamphetamine.

The ANA framework holds promise for explaining heterogeneity in addiction by identifying neuroscience-informed phenotypes. While the field is beginning to validate the ANA domains across substances, one critical future direction is to maximize its clinical application. It may be possible that ANA phenotypes can be leveraged to identify and refine addiction biomarkers. In addition, knowledge from the ANA framework may also be applied to advance precision medicine and inform medications development for a host of substance use disorders, particularly those with no approved pharmacotherapy such as methamphetamine.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This study was supported by funds from the National Institute on Alcohol Abuse and Alcoholism (K24AA025704 to LAR; F32AA029288 to SJN).

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Table 1.

Pattern matrix for the initial factor analysis using measures from the phenotypic battery[a]

	Latent Factors (Eigenvalues / % Variance Explained)		
	Factor 1 7.21 / 58.10%	**Factor 2 2.69 / 21.72%**	**Factor 3 1.12 / 9.04%**
BDI Total Score	**0.829**	−0.029	0.032
BAI Total Score	**0.756**	0.018	0.093
MAWQ - Anger	**0.727**	0.030	0.059
MAWQ - Anxious/Nervous	**0.818**	−0.035	0.095
MAWQ - Craving	**0.436**	**0.411**	−0.078
MAWQ - Depressed	**0.824**	−0.008	−0.048
MAWQ - Irritable	**0.854**	−0.092	−0.010
MAWQ - No Motivation	**0.757**	−0.013	−0.101
MAWQ - Loss of interest/pleasure	**0.758**	0.033	−0.145
MAUQ - All I want to do now is use MA	0.019	**0.666**	−0.097
MAUQ - I do not need to use MA right now	−0.113	−0.048	−0.171
MAUQ - It would be difficult to turn down MA this minute	−0.013	**0.712**	0.153
MAUQ - Having MA now would make things seem just perfect	−0.014	**0.756**	−0.012
MAUQ - I want to use MA so bad I can almost feel it	0.053	**0.792**	−0.062
MAUQ - Nothing would be better than having MA right now	0.052	**0.838**	0.009
MAUQ - If I had a chance to use MA, I don’t think I would use it	0.169	**-0.520**	−0.137
MAUQ - I crave MA right now	0.016	**0.770**	−0.043
BIS Constraint	**-0.400**	−0.028	0.179
BIS Impulsivity	**0.619**	0.013	0.310
DOSPERT Total Score	0.190	0.138	**0.455**
Digit Span Forward	−0.077	−0.020	**0.565**
Digit Span Backward	−0.039	0.042	**0.602**
SST – Mean Go Reaction Time	0.171	−0.055	0.206
SST - Mean Stop Signal Delay	0.028	−0.001	−0.079
Delay Discounting ln(k)	0.004	0.077	−0.100

[a]Boldface indicates factor loadings ≥ 0.40.

BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; MAWQ, Methamphetamine Withdrawal Questionnaire; MAUQ, Methamphetamine Urge Questionnaire, BIS = Barratt Impulsiveness Scale; DOSPERT, Domain Specific Risk Taking Scale; SST, Stop Signal Task.

Table 2.

Descriptive statistics on indicator variables.

Measure	Total Sample (N=185)			
	N	Mean	SD	Cronbach's α
BDI Total[a]	185	13.80	10.50	0.92
BAI Total[b]	185	9.94	10.09	0.93
MAWQ Total[c]	184	15.32	11.67	0.91
MAWQ - Anger	184	0.60	0.87	
MAWQ - Anxious/Nervous	184	1.01	0.99	
MAWQ - Craving	184	1.18	1.02	
MAWQ - Depressed	184	0.75	0.95	
MAWQ - Irritable	184	0.90	0.97	
MAWQ - No Motivation	184	0.73	0.94	
MAWQ - Loss of interest/pleasure	184	0.63	0.90	
MAUQ Total[d]	185	22.21	10.44	0.70
MAUQ - All I want to do now is use MA	185	3.07	1.98	
MAUQ - I do not need to use MA right now	185	2.95	2.07	
MAUQ - It would be difficult to turn down MA this minute	185	3.82	2.20	
MAUQ - Having MA now would make things seem just perfect	185	2.74	2.16	
MAUQ - I want to use MA so bad I can almost feel it	185	2.06	2.07	
MAUQ - Nothing would be better than having MA right now	185	2.27	2.05	
MAUQ - If I had a chance to use MA, I don't think I would use it	185	1.81	2.09	
MAUQ - I crave MA right now	185	3.04	2.08	
BIS[e]				
Constraint	180	16.03	4.02	0.81
Impulsivity	177	13.96	4.52	0.82
DOSPERT[f]	137	100.50	30.40	0.88
Not assessed	48			
Digit Span[g]				

Table 3.

Pattern matrix for the final factor analysis using measures from the phenotypic battery[a]

	Latent Factors (Eigenvalues / % Variance Explained)		
	Factor 1 7.17 / 63.10%	**Factor 2 2.68 / 23.58%**	**Factor 3 1.02 / 8.97%**
BDI Total Score	**0.829**	−0.031	0.020
BAI Total Score	**0.757**	0.018	0.078
MAWQ - Anger	**0.728**	0.029	0.051
MAWQ - Anxious/Nervous	**0.823**	−0.039	0.095
MAWQ - Craving	**0.430**	**0.413**	−0.081
MAWQ - Depressed	**0.826**	−0.011	−0.040
MAWQ - Irritable	**0.852**	−0.090	−0.028
MAWQ - No Motivation	**0.759**	−0.017	−0.085
MAWQ - Loss of interest/pleasure	**0.754**	0.030	−0.150
MAUQ - All I want to do now is use MA	0.017	**0.661**	−0.087
MAUQ - It would be difficult to turn down MA this minute	−0.005	**0.707**	0.180
MAUQ - Having MA now would make things seem just perfect	−0.018	**0.757**	−0.006
MAUQ - I want to use MA so bad I can almost feel it	0.046	**0.796**	−0.070
MAUQ - Nothing would be better than having MA right now	0.049	**0.840**	0.006
MAUQ - If I had a chance to use MA, I don’t think I would use it	0.166	**-0.516**	−0.121
MAUQ - I crave MA right now	0.022	**0.763**	−0.024
BIS Constraint	**-0.403**	−0.026	0.189
BIS Impulsivity	**0.618**	0.019	0.284
DOSPERT Total Score	0.190	0.144	**0.426**
Digit Span Forward	−0.063	−0.022	**0.567**
Digit Span Backward	−0.020	0.036	**0.618**

[a]Boldface indicates factor loadings ≥ 0.40.

BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; MAWQ, Methamphetamine Withdrawal Questionnaire; MAUQ, Methamphetamine Urge Questionnaire, BIS = Barratt Impulsiveness Scale; DOSPERT, Domain Specific Risk-Taking Scale.

Table 4.

Relationship between ANA domains and demographic and methamphetamine (MA) use variables.[a]

	Negative Emotionality		Incentive Salience		Executive Functions	
	r	**p-value**	***r***	**p-value**	***r***	**p-value**
Sex[b]	−0.043	0.640	0.017	0.849	−0.074	0.417
Age	−0.062	0.481	0.004	0.962	**-0.210**	**0.021**
Age at first MA use	*−0.157*	*0.080*	−0.049	0.584	*−0.179*	*0.052*
MA symptom count	**0.369**	**<0.0001**	**0.316**	**0.0003**	0.110	0.230
30-day TLFB MA Use Days	*0.151*	*0.090*	**0.193**	**0.030**	0.063	0.488

TLFB = Timeline Follow-back.

[a]Estimates are measures of association. Values in boldface indicate significant relationships on each domain. Values in italics indicate trend-level significance ($p \leq 0.09$)

[b]Sex (0=Male, 1=Female)