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Working memory predicts methamphetamine hair concentration over the course of treatment: moderating effect of impulsivity and implications for dual-systems model

Adam J. Rubenis[1], Rebecca E. Fitzpatrick[1], Dan I. Lubman[2,3] & Antonio Verdejo-Garcia[1]

Monash Institute of Cognitive and Clinical Neurosciences, Monash University, Clayton, VIC 3800, Australia[1], Turning Point, Eastern Health, Fitzroy, VIC 3065, Australia[2] and Eastern Health Clinical School, Monash University, Fitzroy, VIC 3065, Australia[3]

ABSTRACT

High impulsivity and poor executive function are characteristic of methamphetamine use disorder. High arousal in the impulsive system has been proposed to compromise the executive system's regulating ability (i.e. the dual-systems model). While interaction between these variables may partly explain poor treatment outcomes associated with methamphetamine use disorder, previous research has tended to examine each factor separately. We investigated whether high impulsivity (measured with an impulsive choice task) and poor executive function (measured with a working memory task) predict methamphetamine use (determined by hair sample) in the 6 weeks following treatment commencement. We also investigated whether impulsive choice moderates the relationship between working memory and methamphetamine use. One hundred and eight individuals with methamphetamine use disorder (75 percent male) were tested within 3 weeks of commencing treatment; 80 (74 percent) were followed up 6 weeks following baseline testing. Cognitive measures significantly predicted drug use after controlling for nuisance variables. Working memory was a significant predictor, while impulsive choice was not. The interaction model included working memory as a predictor and impulsive choice as a moderator. This model was significant, as was the interaction term. Working memory significantly predicted levels of methamphetamine use in early treatment, and impulsive choice moderated this relationship. Those with working memory deficits are particularly vulnerable to using greater amounts of methamphetamine. As working memory increased methamphetamine use decreased among individuals with low/medium delay discounting. Pre-treatment cognitive testing may identify patients at high risk, while remediation of working memory function may be a treatment target for reducing methamphetamine use.

Keywords dual systems, executive function, impulsivity, methamphetamine use disorder, working memory.

Correspondence to: Antonio Verdejo-Garcia, Monash Institute of Cognitive and Clinical Neurosciences, Monash University, 18 Innovation Walk, Clayton, VIC 3800, Australia. E-mail: antonio.verdejo@monash.edu

INTRODUCTION

Methamphetamine is a highly addictive stimulant, used by an estimated 24 million people worldwide (United Nations Office on Drugs and Crime, 2016). Methamphetamine use disorder (MUD) is placing an increasing burden on health care services globally (Courtney & Ray 2014; Lubman *et al.* 2016; McKetin *et al.* in press). Psychosocial approaches are the predominant treatment for individuals with MUD; however, treatment engagement is often poor with frequent periods of relapse (McKetin *et al.* 2012). Furthermore, current predictors of relapse cannot be measured at treatment commencement (length of treatment/engagement post-treatment; Brecht & Herbeck 2014) or are unfeasible in clinical practice (neuroimaging measurements of brain activity; Gowin *et al.* 2015). Nevertheless, objective measures of cognitive function have shown excellent predictive value in relation to treatment outcomes for individuals with MUD (Chen, Chen, & Wang 2015). Additionally, cognitive deficits can be simultaneously accommodated (e.g. developing strategies to adapt to patient-specific strengths and weaknesses) and rehabilitated (e.g. group-based cognitive remediation; Sofuoglu *et al.* 2016) in treatment.

The role of cognitive dysfunction in MUD can be partly understood through the dual-systems model, in which the top-down cognitive control system is compromised, while the bottom-up reward-driven system is sensitized (McClure & Bickel 2014). These systems are underpinned by the cognitive constructs of impulsivity (reward-driven behaviour) and executive function (cognitive control; Bickel *et al.* 2012). Impulsivity refers to a preference for short-term rewards and engaging in behaviour without adequate foresight (Stevens *et al.* 2014). This reward-driven behaviour is characterized by impulsive choice (the preference for smaller immediate rewards over larger, delayed rewards), which is analogous to the decisions made regarding drug use (Khurana *et al.* 2017). The top-down system of cognitive control is underpinned by working memory, the ability to temporarily store, access and manipulate a limited amount of information and to manage incoming stimuli (Baddeley 2012). Deficits are reflected in diminished cognitive control in substance-dependent individuals (Brooks 2016). Here, working memory fails to exert control over distracting, arousing stimuli (Okon-Singer *et al.* 2015), such as impulsive urges to use substances (Khurana *et al.* 2017). Therefore, high levels of reward-driven behaviour to use substances, combined with deficiencies in the ability to inhibit these impulses can 'hardwire' drug use and potentially explain the high levels of relapse among individuals with substance use disorders.

Both impulsivity and working memory are individually predictive of substance use and are consistently impaired in individuals with MUD (Ellis *et al.* 2016; Zhong *et al.* 2016). There is a strong theoretical rationale for the link between impulsivity, working memory and drug use in individuals with MUD; however, past research has been limited. Nejtek *et al.* (2013) studied methamphetamine-dependent and cocaine-dependent individuals in treatment. Impulsive choice at baseline predicted the number of positive urine screens over the 20-week study period. More recently, Chen *et al.* (2015) found that impulsive choice significantly predicted dropout in individuals with MUD in a 12-week psychologically based relapse prevention programme.

Similarly, few studies have directly addressed the link between working memory and MUD outcomes; however, this is emerging as a highly relevant area for understanding recovery trajectories (Bickel *et al.* 2011). In individuals with MUD, Dean *et al.* (2009) found distinct working memory performance in those who completed psychological and pharmacological treatment and those who did not. Working memory also predicted treatment outcomes among users of other stimulants. For example, cognitive (Patterson *et al.* 2010) and neuroimaging (Loughead *et al.* 2015) measures of working memory were significantly predictive of nicotine relapse during a counselling intervention. In cocaine-dependent individuals, neuroimaging measures of cognitive control significantly predicted self-reported days of use at 3-month follow-up (Marhe, van de Wetering, & Franken 2013) and number of positive urine samples across 16 weeks of psychological and pharmacological treatment (Moeller *et al.* 2010).

Both elements of the dual-systems model (impulsivity and working memory) are individually predictive of stimulant relapse (Moeller *et al.* 2010; Nejtek *et al.* 2013). However, previous studies have not examined their interactive effect (Bickel *et al.* 2012). Consistent with the interactional nature of the dual-systems model, improvements in working memory reduce the level of impulsive choice in stimulant users (Bickel *et al.* 2011), while individuals with MUD have exhibited significantly reduced impulsivity following working memory improvements (Brooks *et al.* 2017). These findings suggest that greater cognitive control (working memory) enhances the ability to manage incoming impulsive urges. Furthermore, those with compromised working memory are likely to have problems regulating impulsive urges, with greater difficulty as levels of impulsivity increase (Houben, Wiers, & Jansen 2011). In addition, previous studies have not examined cognitive predictors in relation to the intensity of stimulant use during treatment. This is critical, as previous research has found a dose–response relationship between methamphetamine use and poorer outcomes (Lappin *et al.* 2016; McKetin *et al.* 2016).

This study aimed to examine the longitudinal association between performance in cognitive measures of working memory and impulsivity (reflecting the function of the top-down system and the bottom-up system, respectively) and levels of methamphetamine use among people with MUD during early treatment. Cognitive measures were conducted within the first 3 weeks of treatment, and levels of methamphetamine use over a 6-week follow-up period were quantified with hair toxicology. We hypothesized that poorer working memory and heightened impulsivity would longitudinally predict levels of methamphetamine use. Furthermore, we predicted that impulsivity would moderate the relationship between working memory and methamphetamine use, according to the dual-systems model.

MATERIALS AND METHODS

Design

We conducted a longitudinal cohort study. Participants with MUD underwent a cognitive battery within the first 3 weeks of commencing treatment and provided a hair sample in a follow-up session 6 weeks later. We examined the longitudinal link between baseline cognitive functioning and levels of methamphetamine use at the 6-week follow-up.

Participants

The sample comprised 108 adults meeting criteria for MUD (age, M = 31.1, SD = 7.2, 81 male participants) recruited through public and private inpatient and outpatient detoxification, counselling and rehabilitation facilities in Melbourne, Australia. The sample size was determined a priori, with 80 percent power and $\alpha = 0.05$, assuming a moderate effect size and allowing for 30 percent attrition, based on the findings of similar longitudinal studies conducted in people with methamphetamine use disorder (e.g. Simon *et al.* 2010).

The selection criteria for participants were defined as follows: aged between 18 and 55 years, meeting DSM-IV criteria for MUD measured with the Structured Clinical Interview for the DSM-IV (First et al., 1996) and being abstinent for at least 2 days and a maximum of 3 weeks indicated by self-report and confirmed by clinicians, to minimize between-subjects variability on cognitive performance due to abstinence duration. Participants were excluded if they reported a loss of consciousness for more than 30 min, a history of major depression, bipolar disorder, psychotic disorder, intellectual disability or dependence on substances other than methamphetamine, alcohol or cannabis (as determined by the Structured Clinical Interview for the DSM-IV).

Procedures

The Eastern Health Human Research Ethics Committee approved the study (E52/1213). Recruitment was conducted between April 2015 and December 2016. People with MUD commencing treatment were introduced to the study by one of their primary clinicians, prior to screening and consenting by one of the researchers. In the baseline session, participants were tested on measures of impulsivity and working memory. Experimenters took a hair sample at the follow-up session 6 weeks later. Seventy-nine participants (73 percent of the sample) provided the hair sample at the follow-up session. The remaining 29 participants were unreachable (n = 28) or refused to provide a sample (n = 1). After completing both sessions, participants were provided with a $AUD40 gift card and a report of their cognitive performance. The first two authors, who have postgraduate training in clinical assessment methods, conducted all assessments.

Measures

Background measures

Wechsler Abbreviated Scale of Intelligence—Second Edition (WASI-II): This measure briefly assesses general cognitive functioning and consists of four tasks. These tasks incorporate performance IQ (visuospatial abilities) and verbal IQ (language comprehension and expression). Our study used a two-task estimate of IQ, using Vocabulary and Matrix Reasoning tasks. This measure is highly valid and reliable (Wechsler & Hsiao-pin 2011).

Severity of Dependence Scale (SDS): This 5-item self-report measure provides an indication of an individual's level of dependence on a substance. Questions are rated on a 4-point scale (e.g. 'Did you wish you could stop?' from 'Never/almost never' to 'Always/nearly always'). The SDS is valid and reliable in drug-dependent populations (Gossop *et al.* 1995). Our study used the methamphetamine, cannabis and alcohol versions of the SDS. The cannabis score was used as a nuisance variable because a substantial proportion of individuals with MUD also use cannabis (Lubman *et al.* 2016).

Centre for Epidemiological Studies Depression Scale (CES-D): This scale is a 20-item self-report measure of physical and emotional correlates of low mood. Questions are rated on a 4-point scale, based on the frequency of symptom occurrence (e.g. 'I talked less than usual' from 'Rarely or none of the time—less than 1 day' to 'Most or all of the time—5 to 7 days'). Ratings are assigned a number from 0 to 3 (items 4, 8, 12 and 16 are reverse scored); higher scores are indicative of greater symptomatology. The CES-D shows high validity and reliability (Orme, Reis, & Herz 1986). This measure was used as a nuisance variable to account for low mood.

Socio-economic Indexes for Areas (Australian Bureau of Statistics 2011): These data rank postal-coded areas in Australia according to socio-economic status (considering income, employment and education). Each postal code is categorized into a decile from 1 to 10 (from most disadvantaged to most advantaged).

Cognitive measures

Impulsive choice

Delay Discounting Task (DDT): The DDT measures the tendency to discount the value of a reward as it becomes temporally distant. This was measured by the 27-item questionnaire developed by Kirby, Petry, & Bickel (1999). Participants are presented with hypothetical monetary options—an amount to be received immediately and a larger amount to be received after a delay. This measure has been found to be highly reliable and valid (Kirby *et al.* 1999). The main performance index is the k value, a number that indicates how rapidly monetary value is degraded for each participant—larger values indicate greater impulsivity.

Working memory

Digit Span Sequencing (Wechsler & Hsiao-pin 2011): This task measures the ability to hold multiple pieces of information in mind for a brief period. An examiner reads out a sequence of unrelated numbers at a rate of 1 second per item (e.g. 1, 4, 3 and 7). After the examiner has finished the sequence, the participant repeats back the numbers in the same order. The length of numbers to be

repeated becomes longer as the task continues. Each sequence is considered one item, and a trial consists of two items. The task ends when a participant's response is incorrect for both items within a trial. There are three components of the task—forwards repetition, backwards repetition and sequencing (rearranging the numbers in order from lowest to highest). We chose this task over more complex and longer measures of working memory to increase the feasibility of the assessment in the clinical setting, while maintaining excellent reliability and validity (Wechsler & Hsiao-pin 2011). The main performance index in our study was the longest digit span sequence achieved. In factor analysis, this index loads on both attentional and executive functioning domains and exhibits greater validity to measure working memory than forward or backward variants that load on attentional function alone (Vogel *et al.* 2015).

Outcome measures

Methamphetamine concentration in hair: A single strand of 1 cm from the root (approximate length of hair growth in 1 month) from each participant was analysed using gas chromatography–mass spectrometry (Meng et al., 2009). Gas chromatography–mass spectrometry provides a quantitative measure of methamphetamine concentration in hair, expressed in ng/mg. This metric provides an objective, continuous measure of the intensity of methamphetamine use over the first month of treatment (i.e. period between baseline and follow-up) and has been recommended by expert consensus guidelines as the most appropriate technique to measure long periods of drug use in addiction treatment research (Donovan *et al.* 2012).
Timeline Followback (Sobell & Sobell 1996): This self-report measure of drug use consists of a calendar on which a participant marks a *u* on each day that they used the relevant substance. We used it to obtain a baseline measure of methamphetamine use in the last month before treatment and to cross-validate methamphetamine hair concentration values at follow-up.

Statistical analysis

We used IBM SPSS (version 21.0) to compute statistical analysis. Data were initially explored for missing data and outliers, as well as data distribution. There were no outliers in the predictor variables. Pairwise deletion was used for three missing data values in the *k* parameter (Enders 2010). Most variables met assumptions for linear multiple regression, but levels of methamphetamine use (ng/mg) were log-transformed to fit an appropriate distribution of errors.

We conducted a hierarchical regression analysis to determine whether impulsivity and working memory predict levels of methamphetamine use after controlling for nuisance variables (age, gender, IQ estimate, socio-economic status decile, CES-D depression scores, SDS methamphetamine use severity score and SDS cannabis use severity score). The nuisance variables were entered in the first block, followed by impulsivity (DDT *k* value) and working memory (longest digit span sequencing score) in a second block. The statistics of interest were the change in *F* and *P* values after entry of impulsivity and working memory predictors and the *Beta* values of individual predictors in the final model.

We subsequently conducted a moderation analysis to determine if the relationship between working memory and methamphetamine use was moderated by impulsivity. This analysis was conducted using Hayes' PROCESS macro for SPSS (Hayes 2012). This macro uses a path analysis approach with ordinary least squares regression to estimate continuous outcomes (i.e. methamphetamine use), in which predictor variables are mean-centred before analysis. The interaction term is the product of the predictor and moderator terms—its significance is tested in the regression model. 'Simple slopes' analysis graphically represents the extent to which two cases that differ by one unit on the predictor (i.e. working memory) will differ on the outcome (i.e. methamphetamine use) at low, medium and high levels of the moderator (i.e. delay discounting).

RESULTS

Preliminary analyses

Demographic and clinical characteristics of the sample are shown in Table 1. The majority of the sample was male and unemployed, and the average daily dose was 0.75 g.

Preliminary analyses were conducted to account for the potential influence of drug use patterns on cognitive predictors. Time since last use of methamphetamine at baseline testing and methamphetamine use characteristics (route of administration, average daily usage and days used in month prior to testing) were not significantly correlated with cognitive predictors ($r_{max} = -0.17$, all $P > 0.05$).

A bivariate correlation was conducted to assess the consistency between methamphetamine concentration in hair and self-reported methamphetamine use indicated by the Timeline Followback at follow-up. Results showed a significant correlation ($r = 0.46$, $P < 0.001$), supporting the reliability of the quantitative hair measure.

Link between cognition and longitudinal methamphetamine use

Table 2 shows the results of the regression model. The nuisance variables (age, gender, IQ, socio-economic status decile, depression score, methamphetamine dependence severity score and cannabis dependence severity score) explained 3.6 percent of the variance in methamphetamine use at follow-up, $F(7, 68) = 1.40$, $P = 0.220$. The addition of DDT *k* value and longest digit

Table 1 Demographic and clinical characteristic of the MUD sample (N = 108).

	Mean/n (percent)	*SD*
Age	31.1	7.2
Sex (M/F)	81.0 (75.0)	
Years of education	13.0	2.4
IQ estimate	96.1	11.0
Unemployed	77.0 (71.3)	
Smokers	87.0 (80.6)	
Cigarettes per month	414.4	260.0
Daily level of MA use (g)	0.75	0.62
Days of MA use in month prior to treatment	22.1	9.3
Years of MA use prior to treatment	6.9	4.9
Age commenced MA use	23.8	8.1
MA route of administration		
Smoking	76.0 (70.4)	
Intravenous	25.0 (23.1)	
Multiple routes	7.0 (6.5)	
Ever used MA intravenously	45.0 (41.7)	
MA SDS	11.1	3.1
Cannabis use	54.0 (50.0)	
Cannabis use disorder	27.0 (25.0)	
Cannabis SDS	2.7	4.3
Alcohol use	59.0 (54.6)	
Alcohol use disorder	9.0 (8.3)	
Alcohol SDS	1.7	3.3
CES-D score	28.3	12.3
Clinical measures	*Mean*	*SD*
Delay discounting k value	0.06	0.07
DS longest digit span sequencing	5.57	1.18
Concentration of methamphetamine in hair (ng/mg)	6.06	14.20

Note: CES-D = Centre for Epidemiologic Studies Depression Scale; DS = digit span; MA = methamphetamine; SDS = Severity of Dependence Scale.

Table 2 Hierarchical multiple regression examining the predictive value of impulsivity and working memory on methamphetamine use.

Outcome	*Methamphetamine concentration in hair*		
	FΔ	*β*	*Sig.*
Block 1	1.40		0.220
Age		0.19	0.103
Gender		0.01	0.919
IQ estimate		−0.02	0.855
SES decile		−0.04	0.719
CES-D		−0.01	0.912
SDS methamphetamine		−0.14	0.258
SDS cannabis		−0.25	0.033
Block 2	4.20		0.019
Age		0.16	0.145
Gender		−0.04	0.705
IQ estimate		0.12	0.416
SES decile		−0.06	0.650
CES-D		−0.02	0.839
SDS methamphetamine		−0.10	0.379
SDS cannabis		−0.23	0.040
DDT k value		−0.06	0.594
LDSS		−0.35	0.007

Note: CES-D = Centre for Epidemiologic Studies Depression Scale; DDT = Delay Discounting Task; LDSS = longest digit span sequencing; SES = socio-economic status decile, Socio-economic Indexes for Areas; SDS = Severity of Dependence Scale.

span sequencing significantly improved the predictive value of the model $F\Delta(2, 66) = 4.20$, $P = 0.019$, and resulted in a significant model $F(9, 66) = 2.12$, $P = 0.040$. Cognitive variables explained an additional 8.3 percent of the variance in the dependent variable. DDT k value ($\beta = -0.06$, $P = 0.594$) was not a significant predictor, however longest digit span sequencing ($\beta = -0.35$, $P = 0.007$) emerged as significant.

Moderation analysis

The interaction model included longest digit span sequencing as the predictor, DDT k value as the moderator and cannabis dependence severity as a covariate, as this was the only nuisance variable that was a significant predictor in the regression model. The interaction model was statistically significant $F(4, 71) = 6.37$, $P < 0.001$, as was the interaction term, $t(71) = 2.22$, $P = 0.029$. Longest digit span sequencing was a significant predictor, $t(71) = -2.57$, $P = 0.012$; DDT k value was not, $t(71) = -0.93$, $P = 0.357$. Figure 1 shows the simple slopes analysis of methamphetamine use—predicted by working memory and delay discounting at low or high levels. The relationship between working memory and methamphetamine use changed as a function of delay discounting rates. As working memory increased, methamphetamine use significantly decreased among individuals with low and medium delay discounting groups, but this relationship was not significant among individuals with high discounting. As illustrated in Table 3, in the low delay discounting group, every unit increase in working memory performance predicted a 0.62-unit decrease in methamphetamine use; in the medium group, there was a decrease of 0.38 units.

Discussion

This study examined if cognitive performance in tests of working memory and impulsivity at treatment commencement predicted levels of methamphetamine use over the following 6 weeks of treatment. We found that working memory performance significantly

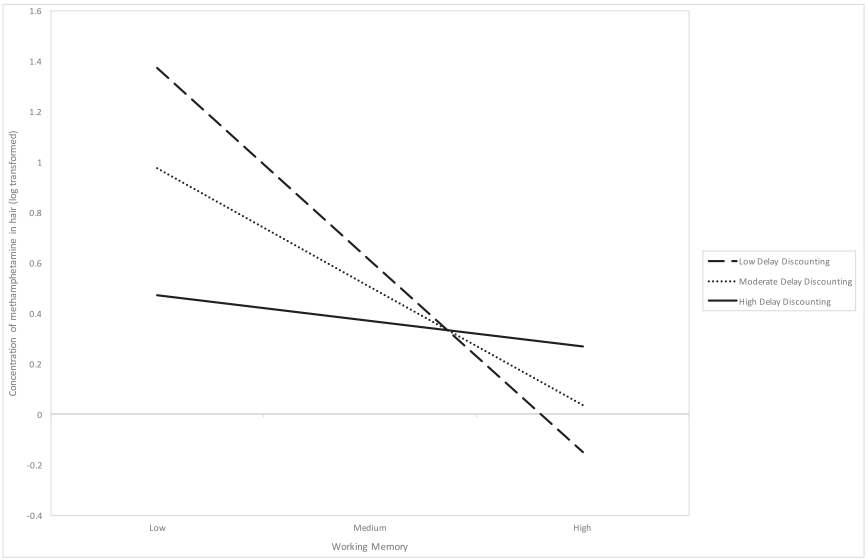

Figure 1 The interaction between different levels of delay discounting and working memory performance on concentration of methamphetamine in hair. NB: High delay discounting reflects more impulsivity.

Table 3 The moderating effect of impulsivity on working memory and methamphetamine concentration in hair relationship.

Delay discounting group	*β*	*Sig.*
Low	−0.62	$P = 0.002$
Average	−0.38	$P = 0.012$
High	−0.08	$P = 0.677$

predicted levels of methamphetamine use measured by hair toxicology. Although impulsivity did not directly predict methamphetamine use, it moderated the relationship between working memory and methamphetamine levels (i.e. among users with low to moderate levels of impulsivity, better working memory was associated with less methamphetamine use).

Findings regarding working memory are consistent with previous research linking such deficits with increased stimulant use (Moeller *et al.* 2010; Marhe *et al.* 2013). We found that this link generalizes to methamphetamine use in early recovery. These findings can be understood in the context of working memory's role in broader executive functioning, which includes involvement in representation of self-regulatory goals, control of attention towards goal-relevant stimuli and regulation of desires and cravings (Hofmann, Schmeichel, & Baddeley 2012). Those with significant working memory dysfunction may have difficulty in regulating habits and impulses (even of mild intensity) to engage in drug use. Previous research has suggested that a high load on working memory results in greater vulnerability to decisions providing short-term benefit, such as drug use (Fridberg, Gerst, & Finn 2013). Those with poorer working memory functioning may more readily experience a substantial cognitive load that interferes with self-regulatory goals, such as maintaining abstinence.

Results were not consistent with previous work that associated impulsivity and methamphetamine use (Nejtek *et al.* 2013; Chen *et al.* 2015). However, these studies utilized measures of impulsive decision-making (Iowa Gambling Task; Nejtek *et al.* 2013) and self-reported impulsivity (Barratt Impulsiveness Scale; Chen *et al.* 2015) rather than delay discounting. Indeed, scores on these same measures differed significantly among cocaine-dependent individuals according to hair-indexed changes in use over a 1-year period, while delay discounting did not (Hulka *et al.* 2015). Furthermore, findings that directly link delay discounting with prognosis have measured length of abstinence/treatment retention rather than drug use intensity (Stevens *et al.* 2015). From a theoretical perspective, our findings are partly consistent with the dual-systems approach (McClure & Bickel 2014). Impairment in top-down cognitive control (working memory) significantly predicted higher levels of drug use in early recovery. However, this relationship was not moderated by high levels of delay discounting, which were used as a proxy of the reward-impulsive system. High rates of delay discounting may significantly impact the initial decision to leave a treatment setting and recommence drug use (Stevens *et al.* 2015), but it has not been consistently associated with measures of drug relapse (Dominguez-Salas *et al.* 2016). In the current study, low and medium levels of delay discounting significantly moderated the relationship between working memory and methamphetamine use. Participants with lower levels of delay discounting showed a significant reduction in drug use as working memory performance increased. Individuals with MUD

who place greater value on long-term outcomes may remain engaged in treatment, while a greater working memory capacity may allow the management of a greater cognitive load and focus on long-term goals such as abstinence (Hofmann *et al.* 2012).

Our findings need to be considered in the context of a number of limitations. There were a small number of participants that reported cannabis and/or alcohol use disorder or met criteria for a major depressive episode at the time of testing. However, the inclusion of these participants allowed for a sample that is representative of treatment-seeking individuals with MUD (Lubman *et al.* 2016), and the impact of these variables was controlled in statistical analysis. Although rates of smoking methamphetamine (~70 percent) were higher in the current sample than in the most recently available Australian data (~40 percent; Australian Institute of Health and Welfare, 2013), this likely reflects the increasing prevalence of the crystal form of the drug in the Australian population, which is typically smoked (Degenhardt *et al.* 2016). The impact of route of administration was also controlled for statistically. The study's follow-up period was also brief at 6 weeks, and while an extended follow-up would allow for examination of longer-term predictors of relapse, the current study incorporates the period of the greatest relapse vulnerability (Brecht & Herbeck 2014).

Despite these limitations, our findings have important clinical implications. Individuals with MUD entering treatment with working memory deficits appear to be particularly vulnerable to relapse and higher levels of use. Additionally, those with low to moderate levels of impulsive choice and intact working memory are likely to use less methamphetamine following treatment. Pretreatment cognitive testing may help categorize patients that require additional support and those at lower risk. Furthermore, individuals with impaired working memory are likely to benefit from learning specific strategies to manage a reduced cognitive capacity (e.g. list making and taking notes on a mobile phone), which may allow more considered decision making in relation to methamphetamine use, in combination with behavioural strategies (e.g. leaving a situation where drugs may be present). Furthermore, the cognitive domain of working memory has been specifically identified as a candidate for rehabilitation in substance dependence due to its broad impact on functioning and relapse (Bickel *et al.* 2011). Working memory training has been effective in improving decision making in individuals with MUD (Brooks *et al.* 2017) and reducing consumption in alcohol-dependent individuals (Houben *et al.* 2011). From a neurobiological perspective, impulsivity and working memory are associated with lower levels of dopamine availability in the basal ganglia in people with MUD (Dobbs, Lemos, & Alvarez 2017). However, when such individuals receive working memory training, reduced levels of impulsivity are accompanied by increased bilateral basal ganglia volume (Brooks *et al.* 2016). These findings reflect potential neurobiological drivers of the behavioural outcomes observed in the current study.

Our study demonstrates that working memory, and its interaction with impulsivity, predicts levels of methamphetamine use during early treatment. These findings support the trialling of adjunctive cognitive remediation interventions focused on working memory for treatment-seeking individuals with MUD.

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Disclosure/Conflict of Interest

All authors declare no competing interests.

Authors Contribution

All authors were responsible for the study concept and design. AVG and DL facilitated recruitment of participants. AR and RF were responsible for recruitment and data collection. AR and AVG were responsible for data analysis and interpretation of results. AR drafted the manuscript; AVG and DL provided intellectual input. All authors critically analysed the manuscript prior to submission.

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