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Does methamphetamine use increase violent behaviour? Evidence from a prospective longitudinal study

Running title: Methamphetamine use and violence

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Abstract

**Aims:** To determine whether violent behaviour increases during periods of methamphetamine use and whether this is due to methamphetamine-induced psychotic symptoms. **Design:** A fixed-effects (within-subject) analysis of four non-contiguous one-month observation periods from a longitudinal prospective cohort study. **Setting:** Sydney and Brisbane, Australia.

**Participants:** A total of 278 participants aged 16 years or older who met DSM-IV criteria for methamphetamine dependence on entry to the study but who did not meet DSM-IV criteria for lifetime schizophrenia or mania. **Measurements:** Violent behaviour was defined as severe hostility in the past month on the Brief Psychiatric Rating Scale (BPRS) (corresponding to assault / damage to property). Days of methamphetamine and other substance use in the past month were assessed using the Opiate Treatment Index. Positive psychotic symptoms in the past month were identified using the BPRS. **Findings:** There was a dose-related increase in violent behaviour when an individual was using methamphetamine compared to when they were not after adjusting for other substance use and socio-demographics (cf. no use in the past month: 1-15 days of use OR 2.8, 95% CI 1.6 – 4.9; 16+ days of use OR 9.5, 95% CI 4.8 – 19.1). The odds of violent behaviour were further increased by psychotic symptoms (OR 2.0, 95% CI 1.1 – 3.6) which accounted for 22-30% of violent behaviour related to methamphetamine use. Heavy alcohol consumption also increased the risk of violent behaviour (OR 3.1, 95% CI 1.4 – 7.0) and accounted 12-18% of the violence risk related to methamphetamine use. **Conclusions:** There was a dose-related increase in violent behaviour during periods of methamphetamine use that was largely independent of the violence risk associated with psychotic symptoms.
Introduction

Methamphetamine (aka ‘ice’ or ‘crystal meth’) is notorious for its association with violent behaviour (1, 2). Epidemics of use have been marked by rises in assaults and violent crime and case reports have implicated the drug in homicides (2-4). Violence associated with methamphetamine use is characterised by its capricious and often bizarre nature, this seeming to be fuelled by methamphetamine-induced paranoia (5). With between 14 and 53 million users of the drug worldwide (6), the potential capacity of methamphetamine to incite violence is a significant public health concern.

Despite its reputation, evidence falls short of showing a causal link between methamphetamine use and violence (1). Epidemiological evidence is based on case reports of methamphetamine users behaving violently (3, 4, 7), high rates of methamphetamine use among violent offenders (8), and cross sectional studies that show higher rates of violence among people who use the drug compared to those who do not (9-11). It is not clear from these studies whether methamphetamine use causes violent behaviour or whether people who use the drug are otherwise predisposed to violence (Figure 1). Violent behaviour among people who use methamphetamine could be accounted for by premorbid risk factors for violence that are common in illicit drug using populations (12-14). In particular, the childhood antecedent to antisocial personality disorder, conduct disorder, is predictive of both later substance use and later violent offending (15, 16).

One way to overcome confounding by pre-morbid risk factors is to use a within-subject, or ‘fixed effects’, analysis of longitudinal panel data. This type of analysis examines the likelihood of an event (in this case, violent behaviour) during periods when an individual is exposed to a risk factor (e.g., methamphetamine use) relative to when they are not exposed to that risk factor. Examining changes within individuals over time eliminates confounding by pre-existing individual characteristics and other time-invariant factors (e.g., heritable traits,
personality, gender, prior adverse life events) in so far as these factors do not change over the course of the study. Factors that vary during this time (e.g., changes in other drug use) need to be adjusted for, as in any conventional regression analysis. Fixed effects analysis is commonly applied within the econometrics literature (17), and to a lesser extent within public health research (18-20), to eliminate the confound of premorbid factors.

A potentially important mediating factor for methamphetamine-related violence is the paranoid psychotic state that the drug can induce (5, 21) (Figure 1). There is a dose-response increase in psychotic symptoms during periods of methamphetamine use (22) and these symptoms often co-occur with high levels of hostility (23). Psychosis is known to increase the risk of violence, this being related to the capacity of delusions to incite anger, increase a person’s perception of threat in their environment and their propensity to misinterpret events (4, 24, 25). Understanding whether psychotic symptoms are responsible for methamphetamine-related violent behaviour is important because it will determine whether the risk of violence is confined to people who have methamphetamine psychosis or whether the risk extends to the broader population of methamphetamine users.

The aim of the current study was to determine the risk of violent behaviour attributable to methamphetamine use net of premorbid risk factors. We achieve this by applying a within-subject (fixed effects) analysis to longitudinal panel data from a prospective cohort of methamphetamine users (26). As noted above, in this design each participant acts as their own control, avoiding confounding by premorbid factors that do not change during the study. The relationship between methamphetamine use and violent behaviour was assessed over four discrete non-contiguous one-month periods, while adjusting for concurrent changes in other drug use and socio-demographics. We also examined whether psychotic symptoms exacerbated the risk of violent behaviour, and whether this could account for the relationship between methamphetamine use and violent behaviour.
Method

Participants and procedure

A total of 278 participants met DSM-IV criteria for methamphetamine dependence on entry to the study and none met DSM-IV criteria for lifetime schizophrenia or mania. DSM-IV diagnoses were assessed using the Composite International Diagnostic Interview (CIDI) (27). Participants were selected from the Methamphetamine Treatment Evaluation Study (MATES) cohort (28). The MATES cohort included 400 people entering community-based drug treatment services in Sydney and Brisbane, Australia, for methamphetamine use, and 101 methamphetamine users from Sydney who were not in treatment (i.e., recruited through needle and syringe programs and outreach services) and who screened positive for dependence on methamphetamine. Other inclusion criteria for MATES were being at least 16 years old, comprehension of English, being willing to participate in follow-up interviews, and not having been in methamphetamine treatment, other inpatient drug treatment, or in prison, in the month prior to entering the study.

From the MATES cohort, 17 participants were excluded because they did not meet DSM-IV criteria for methamphetamine dependence on recruitment. A further 59 participants were excluded because they met DSM-IV criteria for either lifetime schizophrenia or a lifetime manic episode, and 138 participants were excluded because this diagnostic information was not available (i.e., these participants did not partake in the follow-up interviews when these diagnoses were made). Finally, nine further participants were excluded because they had not used methamphetamine during any of the one-month periods analysed in the current study.
A structured interview schedule was administered at baseline and at each follow-up (3 months, 1 year and 3 years after the baseline interview). Recruitment of the cohort took place in 2006 and 2007, while follow-up interviews spanned the period from 2006 to 2010. Interviews were conducted face-to-face or by phone. All participants were volunteers who provided informed consent, and who were reimbursed for their time and travel expenses (up to AUD40 per interview). All of the participants (N = 330) were re-interviewed at 3 months and 12 months after entry to the cohort, and 82% (n = 271) were interviewed at 3 years. Participants who dropped out at 3 years did not differ significantly from other participants on methamphetamine use (1-15 days: 44 vs. 40%; 16+ days 22% vs. 16%) or violent behaviour (24% vs. 19%). The current study used data on past month outcomes measured at each of these four time points, totaling 1,261 months of data for all of the participants combined.

**Time-varying measures**

The following measures were taken for the past month at each of the four time points in the study.

*Violent behaviour:* Violent behaviour was defined as a score of 6 or 7 on the BPRS hostility item in the past month. The BPRS is a semi-structured psychiatric interview that is used to rate the severity of various psychiatric symptoms on a scale of 1 to 7, with a score of 1 reflecting no symptom present, scores of 2-3 representing mild/sub-clinical symptoms, and scores of 4+ indicating clinically significant / pathological symptoms (29) – these being rated as either moderate (scores 4 or 5) or severe (scores of 6 or 7). The probes and anchor point ratings for the BPRS hostility item can be found in the online Appendix S1. The anchor point rating for a score of 6 is, “has assaulted others, but with no harm likely (e.g., slapped or pushed) OR destroyed property (e.g., knocked over furniture, broken windows)”; and for a score of 7, “has attacked others with the definite possibility of harming them, or with actual
harm (e.g., assault with a hammer or weapon”). The BPRS is specifically designed to monitor psychiatric symptom severity over time and is widely used in clinical trials (30). Published quality assurance procedures, which we adopted in our study, ensure high levels of inter-rater reliability and can be maintained when the scale is used by trained interviewers with pre-doctoral degrees (30). Ratings in our study were made by trained interviewers (honors level psychology graduates or equivalent) and weekly meetings were held to review BPRS ratings in order to maintain inter-rater agreement and avoid rater drift (30). A selection of interviews from the MATES cohort (28) (n = 64) were audio-recorded and rated by a second interviewer for inter-rater reliability. Inter-rater agreement for our definition of violent behaviour was 94%, yielding a kappa of 0.86.

Methamphetamine use: Days of methamphetamine use in the past four weeks was measured using the Opiate Treatment Index (31). Self-reported abstinence from methamphetamine use was confirmed in a sub-sample of the entire MATES cohort (n = 83) using hair toxicology, with false reporting of abstinence occurring in only 6% of cases (detailed elsewhere (28)). Main route of methamphetamine administration (oral, intranasal, smoked, intravenous) during the past four weeks was also recorded.

Other substance use: Days of use in the past four weeks was measured for other substances, including cannabis, heroin, cocaine, ecstasy, hallucinogens, alcohol and tobacco.

Psychotic symptoms: Psychotic symptoms were defined as a score of four or greater on any of the BPRS items of suspiciousness, unusual thought content or hallucinations, in the past month (29). This definition of psychotic symptoms has been used previously to assess psychotic symptoms in methamphetamine-using samples (32) and yielded inter-rater agreement of 93% and a kappa of 0.86 in this sample (33).
Socio-demographics: These included unemployment, living alone and unstable accommodation (no fixed address, living in a boarding house/shelter, refuge or other temporary accommodation).

Time-invariant measures

Time-invariant measures were age, sex, duration of methamphetamine use and primary route of methamphetamine administration on recruitment, and a diagnosis of childhood conduct disorder (assessed using a modified version of the Diagnostic Interview Schedule (34)).

Design and statistical analysis

Data were analysed using Stata SE version 11.2 (35). All tests were two-sided with significance set at p < 0.05. A random effects logit model (xtlogit) was used assess the relationship between methamphetamine use and violent behaviour over time. The fixed effects model option was used to determine the within-subject effect for methamphetamine use on violent behaviour. The influence of time-invariant factors on violent behaviour were assessed using a random effects model in which the between-subject effect (the mean score for each participant over their observation period) and the within-subject effect (the difference between the participant’s score at each time point and their mean score for the observation period) were modelled separately. Modification of the effect of methamphetamine use on violent behaviour was tested using an interaction contrast between the time-invariant factor and the within-subject effect contrast for methamphetamine use.

The main outcome measure was violent behaviour in the past month. The main predictor variable was days of methamphetamine use in the past month (no use, 1-15 days, 16+ days). Time-varying covariates were psychotic symptoms, other substance use and socio-demographic factors.
To assess the extent to which the relationship between methamphetamine on hostility was mediated by psychotic symptoms the ‘explained fraction’ approach, as described by Whitehead et al. (36), was used: \[
\frac{(OR_a - 1) - (OR_b - 1)}{(OR_a - 1)}
\] where OR\(_a\) represented the odds ratio for the unadjusted relationship between methamphetamine use and hostility, and OR\(_b\) the relationship between methamphetamine use and violent behaviour after adjusting for psychotic symptoms.

**Results**

*Characteristics of the sample*

Participants had a mean age of 31.7 years (SD 8.1 years). The majority were male (72%), single (72%) and unemployed (78%). Most were Australian born (89%) and nominated English as their preferred language (96%). They had a median of 10 years of schooling (range 6 –12), 44% had completed a tertiary technical or trade qualification and 6% had completed a university degree. The majority (76%) had a history of conduct disorder.

All participants met DSM-IV criteria for methamphetamine dependence in the year prior to entering the study; they had used the drug for a mean of 13.1 years (SD 7.9 years) and 72% usually injected it. Methamphetamine use occurred during 58% of all observed months. During months of methamphetamine use, participants used the drug on a median of 8 days (range 1 – 28 days) and injection was typically their main route of administration (79% cf. 14% smoking and 6% snorting or swallowing). Other substance use consisted primarily of tobacco (89% of months, median of 28 days of use), cannabis (57% of months, median of 20 days use), and alcohol (62% of months, median of 6 days use), with other substance use being less common.
Half (51%) of the sample reported violent behaviour during at least one of the observed months, and hostility was present during 20% of the observed months in total (49% of these involved a BPRS score of 6 and 51% a score of 7). Psychotic symptoms occurred amongst 60% of the sample during at least one of the observed months, and psychotic symptoms were present for 25% of the observed months. The relationship between methamphetamine use and psychotic symptoms is documented elsewhere (33).

**Changes in violent behaviour during periods of methamphetamine use**

Violent behaviour was 6.2 times more likely to occur when a participant was using methamphetamine relative to when they were not using the drug (95% CI 3.8 – 10.2, p < 0.001). This relationship was dose-dependent, with low use (< 16 days in the past month) increasing the odds of violent behaviour 4-fold and heavier use (16+ days in the past month) producing a 15-fold increase (Table 1).

The relationship between methamphetamine use and violent behaviour persisted after adjustment for other drug use and socio-demographic variables (model 1, Table 1). Heavy alcohol use (16+ days use in the past month) was the only other factor that remained significantly predictive of violent behaviour in this model. Model 2 (Table 1) shows the relationship between methamphetamine use and violent behaviour adjusting only for heavy alcohol consumption; lower levels of methamphetamine use (1-15 days) tripled the odds of violent behaviour and heavy use (16+ days) predicted a 13-fold increase. Using the explained fraction approach described by Whitehead et al. (36) we compared the odds ratio for methamphetamine use and violent behaviour in model 2 to the unadjusted odds ratio and found that heavy alcohol use accounted for 18% of the relationship between low methamphetamine use (1-15 days) and violent behaviour [(3.8-1) – (3.3-1)](3.8-1)] and 12%
of the relationship between high methamphetamine use (16+ days) and violent behaviour 
\[((14.7-1) – (13.1-1))/(14.7-1)\].

Adding psychotic symptoms to this model showed that they further increased the odds of 
vviolent behaviour (model 3, Table 1). The relationship between methamphetamine use and 
vviolent behaviour was only slightly attenuated. Comparing the odds ratio of 
methamphetamine use and violent behaviour in models 2 and 3 (36) showed that psychotic 
symptoms accounted for 22% of the relationship between low methamphetamine use levels 
(1-15 days) \[((3.3-1) – (2.8-1))/(3.3-1)\] and violent behaviour, and 30% of the of the 
relationship between heavy methamphetamine use levels (16+ days) and violent behaviour 
\[((13.1-1) – (9.5-1))/(13.1-1)\].

The predicted probability of violent behaviour derived from model 3 is shown in Figure 2. 
Without psychotic symptoms, the probability of violent behaviour was 9% when participants 
were not using methamphetamine, rising to 24% during periods of low use (< 16 days) and 
52% during periods of heavy use (16+ days). Psychotic symptoms increased the probability of 
vviolent behaviour across all levels of methamphetamine use. There was no significant 
interaction effect between methamphetamine use and psychotic symptoms (OR 1.0, 95% CI 
0.9 – 1.1, p = 0.482).

Table 1 and Figure 2 about here.

The role of time-invariant factors in predicting violence

Conduct disorder increased the overall risk of violent behaviour (OR 1.9, 95% CI 1.1 – 3.6, p 
= 0.037) but did not modify the relationship between methamphetamine use and violent 
behaviour. The risk of violent behaviour declined with age, but heavy methamphetamine use 
(16+ days) produced a slightly greater increase in the odds of violent behaviour among older
participants (age by 16+ days use interaction: OR 1.1 95% CI 1.0 – 1.2, p = 0.033). Other
time-invariant measures were not related to violent behaviour (p > 0.05, analyses not shown).

**Discussion**

There was a clear dose-response increase in violent behaviour when participants were using
methamphetamine compared to when they were not using the drug. This effect was especially
large for frequent methamphetamine use (i.e., 16+ days of use in the past month), which
increased the odds of violent behaviour 10-fold (cf. 3-fold with less frequent use) after
adjusting for shifts in other drug use, socio-demographics and psychotic symptoms. Although
psychotic symptoms significantly exacerbated the risk of violent behaviour, the relationship
between methamphetamine use and violent behaviour was largely independent of psychotic
symptoms, suggesting a direct relationship between the drug and violent behaviour. Heavy
alcohol consumption also increased the risk of violent behaviour, but it accounted for only 12-
18% of the relationship between methamphetamine use and violence.

These findings indicate that violence is a key harm associated with methamphetamine use,
with the probability of violent behaviour increasing from 10% during periods of abstinence to
60% during periods of heavy methamphetamine use. Violent behaviour was characterised
mostly by interpersonal violence, ranging from altercations that led to fights to seemingly
unprovoked physical attacks. Efforts are needed to quantify the impact of this interpersonal
violence on assault rates. Our findings also fortify reports of violent behaviour associated with
methamphetamine emergency presentations (37, 38), and highlight the need to adequately
resource such services to manage methamphetamine-related violence (39, 40). Generic
protocols for psychiatric emergencies (e.g. Castle et al. (41)) may not be adequate or
appropriate for use in this context (42). Although the evidence base for treating
methamphetamine dependence is limited (43, 44), existing effective interventions (e.g.,
structured psychological and behavioural interventions (43)) need to be promoted and made accessible.

These results support the existence of a causal relationship between methamphetamine use and violent behaviour by showing that this relationship cannot be accounted for by premorbid risk factors for violence among people who use the drug. We also adjusted for concurrent shifts in other drug use and several indicators of social adversity (unstable accommodation, unemployment, living alone) and found that these could not better explain the relationship between methamphetamine use and violence. However, we cannot confirm the direction of the relationship between methamphetamine use and violence (i.e., whether methamphetamine use increased violence or violence increased methamphetamine use). Nor can we confirm the mechanism underpinning this relationship. The pharmacological mechanisms posited to underpin methamphetamine-related violence are monoamine dysregulation within the fronto-limbic pathway with chronic use (45) and the sympathetic arousal (fight-or-flight response) during acute intoxication (46, 47). However, we cannot eliminate the potential contribution of non-pharmacological factors (e.g., economically motivated violent crime) or factors closely linked to methamphetamine use (e.g., sleep deprivation, hypoglycaemia, cognitive impairment or acquired brain injury) to violent behaviour.

One question raised by our research is whether premorbid risk factors for violence, such as conduct disorder, are necessary for methamphetamine use to precipitate violent behaviour. That is, whether the drug is having a disinhibiting effect on people predisposed to violence, or whether it is capable of inciting violent behaviour in people who are not predisposed to such behaviour. We failed to find evidence that methamphetamine’s effect on violence was dependent on people having conduct disorder, but we were limited in our capacity to detect such an effect because the vast majority of our sample had a history of conduct disorder. As is the case with alcohol (48), we found some evidence that the relationship between
methamphetamine and violent behaviour was dependent on an individual’s characteristics, in that older users of the drug, who were generally less likely to engage in violent behaviour than their younger peers, were comparatively more vulnerable to the methamphetamine’s effect on violent behaviour.

Although heavy alcohol consumption increased the risk of violence, it accounted for only a small component of the relationship between methamphetamine use and violence (12-18%) and it had a much smaller effect on violent behaviour than did methamphetamine use. This raises an important question about the contribution of methamphetamine use to violence among young adults who “binge drink”, who often co-consume stimulants with alcohol (49). While the relationship between alcohol use and violence is well-established (20, 48), the potential combined effect of alcohol and stimulant use on violent behaviour has not been well-researched.

The current findings are specific to chronic methamphetamine users and should not be generalized to other populations, including recreational stimulant users, whose drug use is less frequent and who have fewer premorbid risk factors for violence. In order to examine the whether the relationship between methamphetamine use and violence was due to psychotic symptoms produced by the drug, we also needed to exclude participants who had a diagnosis of schizophrenia or mania from our sample (and a further 138 participants for whom this diagnostic information was not available). We therefore cannot make inferences about the effect of methamphetamine on violence in people with primary psychotic disorders.

Our definition of violent behaviour corresponded broadly to self-reported assaults and/or damage to property, this being gleaned from a semi-structured psychiatric interview (the BPRS). Definitions and measures of violent behaviour vary considerably across research studies (50), but the BPRS was ideal for our study because it is a clinically valid instrument.
that assesses changes in psychiatric symptom severity across time. However, it relies on accurate event recollection, which may be impaired with methamphetamine and other heavy substance use (30). Note that our definition of violent behaviour would not necessarily correspond to violent offending.

In conclusion, violent behaviour is a key harm associated with the use of methamphetamine. A better understanding of how methamphetamine use contributes to the level of violence within the community is needed. Resources that identify and manage methamphetamine-related violence are essential within clinical and frontline settings that have regular contact with methamphetamine-using populations, particularly those services that manage individuals with methamphetamine psychosis. Further research is needed to elucidate the mechanism underpinning the relationship between methamphetamine use and violent behaviour in chronic users of the drug.
Disclosure and acknowledgement

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Appendices

Appendix S1. Brief Psychiatric Rating Scale hostility item
<table>
<thead>
<tr>
<th>Table 1. The relationship between violent behaviour and methamphetamine use, other substance use, socio-demographics and psychotic symptoms.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months with violent behaviour</td>
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<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>No use (ref)</td>
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<tr>
<td>1-15 days</td>
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<tr>
<td>16-28 days</td>
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<tr>
<td>Cannabis use, No. (%)</td>
</tr>
<tr>
<td>No use (ref)</td>
</tr>
<tr>
<td>1-15 days</td>
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<tr>
<td>16-28 days</td>
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<tr>
<td>Alcohol use, No. (%)</td>
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<tr>
<td>No use (ref)</td>
</tr>
<tr>
<td>1-15 days</td>
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<tr>
<td>16-28 days</td>
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<tr>
<td>Other drugs used, No. (%)</td>
</tr>
<tr>
<td>Tobacco</td>
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<tr>
<td>Ecstasy</td>
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<tr>
<td>Hallucinogen</td>
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<td>Cocaine</td>
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<tr>
<td>Heroin</td>
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<tr>
<td>Benzodiazepines</td>
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<tr>
<td>Socio-demographics, No. (%)</td>
</tr>
<tr>
<td>Unemployed</td>
</tr>
<tr>
<td>Unstable accommodation</td>
</tr>
<tr>
<td>Living alone</td>
</tr>
<tr>
<td>Psychotic symptoms, No. (%)</td>
</tr>
</tbody>
</table>

Note. Empty cells indicate variables not included in the model.

<sup>a</sup> Simultaneous fixed effects regression including all substance use and socio-demographic variables

<sup>b</sup> Simultaneous fixed effects regression including only substance use and socio-demographic variables that showed evidence of a relationship with hostility in Model 1.

<sup>c</sup> Simultaneous fixed effects regression including variables in Model 2 together with psychotic symptoms
d Relative to less than 16 days of use

Figure 1. The posited relationship between premorbid factors, methamphetamine use, methamphetamine-induced psychotic symptoms and violent behaviour.
Figure 2. Probability of violent behaviour in the past month predicted from Model 3 by days of methamphetamine use and psychotic symptoms.
References


