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Simultaneous use of alcohol with methamphetamine but not ecstasy linked with aggression among young adult stimulant users

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Abstract

Introduction: Illicit stimulants are often combined with alcohol in nightlife entertainment districts, an environment where aggressive behaviour commonly occurs. While alcohol and methamphetamine use are each associated with aggressive behaviour, relatively little is known about the impact of the combined use of alcohol and amphetamine-type stimulants (i.e., ecstasy [MDMA] and methamphetamine) on aggression. Method: Analysis of longitudinal data from a population-based sample of Australian young adult amphetamine-type stimulant users (n=248) to examine: (a) prevalence and timing of simultaneous alcohol and amphetamine-type stimulant use and (b) predictors of ecstasy- and methamphetamine-related aggression and hostility. Prediction models of ecstasy- and methamphetamine-related aggression and hostility were developed using multivariate logistic regression.

Results: Simultaneous alcohol consumption and amphetamine-type stimulant use was prevalent, with drinking generally occurring before consuming amphetamine-type stimulants and while ‘high’. Methamphetamine-related aggression and hostility was significantly associated with recurrent risky simultaneous methamphetamine and alcohol use (Adjusted Odds Ratio [AOR] 2.74, 95% CI 1.09-6.89), a high frequency and increasing use methamphetamine trajectory (AOR 7.23, 95% CI 1.27-41.03), and high trait aggression (AOR 5.78, 95% CI 2.53-13.20). In contrast, only trait aggression (moderate: AOR 3.01, 95% CI 1.55-5.84; high: AOR 5.02, 95% CI 2.38-10.61) was associated with ecstasy-related aggression and hostility. Conclusions: These findings indicate a link between risky patterns of simultaneous alcohol and methamphetamine use and methamphetamine-related
aggression and hostility, independent of separate use of alcohol, methamphetamine and cannabis, trait aggression, psychosis, and gender. The policy challenges of amphetamine-type stimulant and alcohol use require a targeted, multidisciplinary approach.

Key words
Ecstasy, Methamphetamine, Amphetamine-type Stimulants, Alcohol, Aggression, Young Adult
1. Introduction

Violence among young adults often occurs in and around licensed venues in nightlife entertainment districts (NEDs) [1, 2]. These settings are inextricably linked with both drinking and illicit substance use, including use of amphetamine-type stimulants (ATS; i.e., ecstasy [MDMA] and methamphetamine). Illicit stimulants, such as ATS, are often combined with alcohol in NEDs in the context of a ‘big night out’ [3]. In a study of Canadian rave attendees, 45.2% of ecstasy users and 39.3% of amphetamine users had combined alcohol with ecstasy and amphetamines, respectively [4]. While alcohol and methamphetamine use are each associated with aggression under certain circumstances [5-9], relatively little is known about the impact of their combined use on aggression.

1.1 Simultaneous amphetamine-type stimulant and alcohol use

The use of other substances, particularly alcohol and cannabis, is common among ATS users [10-12]. Substances may be combined for various reasons, including to produce pleasurable effects, to extend, enhance, or intensify effects, and to mitigate negative effects [13]. Specifically, combined alcohol and ATS use may produce longer-lasting euphoria than separate use [14] and may mitigate some unwanted ATS use effects (e.g., anxiety, agitation, and restlessness) [15]. ATS use may also facilitate high-volume alcohol consumption, as ATS-intoxicated individuals are potentially able to consume alcohol without experiencing its usual sedative effects [14]. A recent study observed that ecstasy users who consumed illicit stimulants on a night out drank excessively, consuming a median of 20 standard drinks [16]. While a growing body of research suggests alcohol and drug combinations may result in greater harms than their separate use [15, 17, 18], little is known about potential consequences of simultaneous ATS and alcohol use [19].
1.2 Drinking, amphetamine-type stimulant use, and aggression

Numerous studies have separately examined the relationship between either alcohol or methamphetamine use and aggression. Both substances affect cognitive functioning, increasing the likelihood that environmental stimuli will be perceived as threatening [20-22], and each affects impulsivity regulation and responses to perceived threats [23-27]. A recent Australian study suggests alcohol consumption may account for part of the association between methamphetamine use and violence [28], raising the possibility that alcohol and methamphetamine may interact to produce a profile of aggressive behaviour that differs from those arising from separate use. This aligns with research examining combined alcohol and cocaine use, which indicates that co-use may have synergistic effects on aggression [29, 30]. However, the relationship between combined alcohol and methamphetamine use and aggression has not been examined.

In contrast, evidence is mixed regarding ecstasy use and aggression. While there is evidence of subacute effects, with ecstasy linked with increased aggression 3-4 days post-consumption [31, 32], this association may be confounded by sleep factors (e.g., hours and quality of sleep) [33, 34]. Further, there is little evidence supporting an association between ecstasy use and long-term increases in aggression [35].

1.3 Current study

This study adds to the scarce research examining the relationship between simultaneous alcohol and ATS use and aggression, using a population-based sample of Australian young adult ATS users to address the following questions:

1. How prevalent is simultaneous alcohol and ATS use among young adult ATS users?
2. Are patterns of simultaneous alcohol and ATS use associated with ATS-attributed aggression and hostility, adjusting for ATS use trajectories, cannabis use, alcohol use, trait aggression, psychosis, and gender?

2. Methods

2.1 Participants

The Natural History Study of Drug Use (NHSDU) is a prospective study of a population-based sample of young adult ATS users in South-East Queensland, Australia, which commenced in 2009. A one-page drug use screening questionnaire was mailed to 12,079 young adults (aged 19-23 years) randomly selected from the Brisbane and Gold Coast electoral roll (response rate: 49.9%). Using these screening data, a sampling frame was developed from which an ATS-user group (used ecstasy or methamphetamine ≥3 times within the last 12 months; n=352) was recruited. This method is described in detail elsewhere [36]. All participants provided informed consent and the study protocol was approved by the University of Queensland’s Behavioural and Social Sciences Ethical Review Committee (approval number: 2007-001-367).

Data are drawn from the baseline face-to-face interview (n=352), 6-month online survey (n=335), 12-month face-to-face interview (n=315), 30-month online survey (n=319), and 4.5-year face-to-face interview (n=274; 77.8% of baseline sample). In the current study, 104 cases (29.5%) were excluded due to missing data, including 92 participants who did not complete follow-up waves and 12 participants who were missing relevant data, resulting in the present sample (n=248).

Excluded participants were more likely, compared with the present sample, to be male (59.6% cf. 45.6%; $\chi^2=5.79$, $p<0.05$) but did not differ significantly by age ($t=1.12$, ns),
baseline employment ($\chi^2=0.23$, ns), last month ecstasy (43.0% cf. 46.8%, $\chi^2=0.41$, ns) or methamphetamine use (12.0% cf. 14.6%, $\chi^2=0.40$, ns) at baseline, or mean total lifetime consumption of ecstasy pills at baseline (180.1 pills cf. 194.3 pills; $z=-0.98$, ns). They were less likely to have consumed alcohol in the last month at baseline (92.0% cf. 98.0%; $\chi^2=7.10$, $p<0.01$), but among those who had consumed alcohol, there was no difference in the mean number of standard drinks (defined as any portion containing 10 grams of alcohol [37]) consumed (8.80 cf. 7.71 standard drinks; $z=-1.04$, ns).

2.2 Measures

2.2.1 Aggression and hostility during ecstasy and methamphetamine use (outcome)

As part of a set of questions assessing subjective effects, participants reported whether they experienced feelings of aggression or hostility from using (a) ecstasy and (b) methamphetamine at three waves – baseline (timeframe: ever), 12 months (timeframe: last 12 months), and 4.5 years (timeframe: last 12 months). Dichotomous variables were created for ecstasy- and methamphetamine-related aggression and hostility (experienced feelings of aggression or hostility at any wave vs. never experienced).

2.2.2 Timing of alcohol consumption during ecstasy and methamphetamine use

Timing of alcohol consumption was measured at three waves. At baseline (timeframe: ever) and 12 months (timeframe: last 12 months), participants who had used ecstasy or methamphetamine reported if they usually consumed alcohol during their episodes of use of that drug (i.e., did not usually drink, usually drank while ‘up’ on ecstasy/methamphetamine, usually drank while ‘coming-down’). At 30 months, participants reported if they consumed alcohol on their most recent ecstasy and methamphetamine use
episodes in the last 12 months (i.e., did not drink, drank before taking, drank while up, drank while coming-down).

From these data, two variables were created to capture recurrent ‘risky’ patterns of simultaneous alcohol use during ecstasy and methamphetamine use (categories: 1. no risky simultaneous use, 2. risky simultaneous use at 1 wave, and 3. risky simultaneous use at 2-3 waves). Risky simultaneous use was defined as consuming alcohol both while up and while coming-down as this likely involves extended drinking episodes.

2.2.3 Ecstasy and methamphetamine use trajectories

The number of days of ecstasy and methamphetamine use in the last 31 days was measured at baseline, 6 months, 12 months, and 30 months, and recoded as ‘no recent use’, ‘occasional use (1-2 times a month)’, ‘frequent use (3-4 times a month)’, and ‘very frequent use (≥5 times a month)’. K-means cluster analysis with Euclidean distance as the measure of similarity was used to identify ecstasy and methamphetamine trajectory groups based on these ordinal variables. This method was chosen as there is a lack of etiological evidence to inform the selection of covariates or criteria for group allocation, as required by other analytic methods [38]. For ecstasy and methamphetamine, four cluster groups were specified, based on previous research [38, 39]. For both variables, two contiguous clusters were combined to form an intermediate cluster, resulting in three trajectory groups (see Appendix A):

- Ecstasy: 1. ‘very infrequent use’ (n=84), 2. ‘regular and declining use’ (n=138), and 3. ‘high frequency and declining use’ (n=20);
- Methamphetamine: 1. ‘very infrequent use’ (n=159), 2. ‘low regular use’ (n=54), and 3. ‘high frequency and increasing use’ (n=10).
Despite small numbers in the high frequency and increasing use methamphetamine trajectory, all groups were retained as they appear to reflect population patterns of use [40]. The ecstasy use trajectories effectively discriminate between usage levels, as corroborated by measures of lifetime quantity of use and ecstasy dependence [41].

2.2.4 Cannabis use

The number of days of cannabis use in the last 31 days was measured at baseline, 12 months, and 30 months. Binary variables were created for each time point (≥weekly use [4 or more days of use] vs. <weekly use), from which a measure of recurrent weekly use was derived (categories: 1. no weekly use at any wave, 2. weekly use at 1 wave, and 3. weekly use at 2-3 waves).

2.2.5 Binge alcohol consumption

At baseline, 12 months, 30 months, and 4.5 years, participants reported the number of standard drinks they usually consumed on days of drinking in the last 31 days, with reference to a chart displaying the number of standard drinks in different alcoholic beverage servings. Dichotomous variables were created for binge alcohol consumption at each wave based on recognised thresholds (i.e., ≥5 standard drinks on a single occasion [37]). A measure was created to capture recurrent binge consumption (categories: 1. no binge alcohol consumption, 2. binge consumption at 1-2 waves, and 3. binge consumption at 3-4 waves).
2.2.6 Trait aggression

Trait aggression was measured at 4.5 years using the Buss Perry Aggression Questionnaire’s physical aggression subscale [42], which asks respondents to rate how characteristic a number of statements are of them. This questionnaire has been used widely in research examining aggression and substance use [43-45]. The physical aggression subscale has high internal consistency (Cronbach’s alpha 0.82 to 0.85 [42, 46, 47]) and test-retest reliability (0.80 [42]), and is strongly related to direct measures of physical aggression [46].

2.2.7 Psychosis

Past 12-month psychosis was measured at baseline using a brief psychosis screening instrument based on core elements of the Composite International Diagnostic Interview Schizophrenia module, including symptom domains of thought interference, ideas of reference or persecution, and grandiose beliefs [48]. A score of ≥3 across 7 items was used to identify potential cases of psychosis [48].

2.3 Analysis

We conducted longitudinal analyses, comprising variables measured across multiple time points (i.e., ecstasy- and methamphetamine-related aggression and hostility, risky simultaneous alcohol and ATS use, ATS-use trajectories, cannabis use, and risky alcohol use). Separate prediction models of ecstasy- and methamphetamine-related aggression and hostility were developed using multivariate logistic regression, reporting unadjusted and adjusted estimated odds ratios. These models examine a number of potential predictors, including risky simultaneous alcohol and ATS use. Data were analysed using Stata/SE Version 13.1.
3. Results

3.1 Sample characteristics

Socio-demographic characteristics of the sample are presented in Table 1. A majority had completed tertiary education, after 30 months of follow-up, and were employed either part- or full-time.

With regard to subjective effects of aggression or hostility, 45.5% of ecstasy users (n=242) and 41.7% of methamphetamine users (n=223) reported experiencing these effects from their ecstasy and methamphetamine use, respectively, at least once during the study period.

Table 1. Socio-demographic characteristics of young adult amphetamine-type stimulant user sample (n=248)

<table>
<thead>
<tr>
<th>Age at baseline</th>
<th>Mean (Standard Deviation)</th>
<th>20.86 years (1.21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>Range</td>
<td>19-23 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>54.44%</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>45.56%</td>
</tr>
<tr>
<td>Education at baseline</td>
<td>Completed high school</td>
<td>71.37%</td>
</tr>
<tr>
<td>Tertiary education&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Completed tertiary education</td>
<td>72.58%</td>
</tr>
<tr>
<td>Employment at baseline</td>
<td>Unemployed</td>
<td>13.71%</td>
</tr>
<tr>
<td></td>
<td>Part-time employment</td>
<td>40.32%</td>
</tr>
<tr>
<td></td>
<td>Full-time employment</td>
<td>45.97%</td>
</tr>
<tr>
<td>Employment at 4 ½ years</td>
<td>Unemployed</td>
<td>14.52%</td>
</tr>
<tr>
<td></td>
<td>Part-time employment</td>
<td>22.18%</td>
</tr>
<tr>
<td></td>
<td>Full-time employment</td>
<td>63.31%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Measured at baseline and 30-month follow-up; tertiary education refers to university, Technical and Further Education (TAFE), or trade qualification

3.2 Prevalence of simultaneous alcohol and amphetamine-type stimulant use

At baseline, 92.9% of ecstasy users (n=241) and 80.7% of methamphetamine users (n=197) usually consumed alcohol while using ecstasy and methamphetamine, respectively. These high rates continued; at 12 months, 96.3% of recent ecstasy users (used in last 12 months;
n=187) and 84.4% of recent methamphetamine users (n=101) had usually consumed alcohol during their episodes of use. At 30 months, 97.9% and 89.7% of recent ecstasy (n=145) and methamphetamine users (n=87) had consumed alcohol on their most recent episode of use.

3.3 Timing of alcohol consumption during amphetamine-type stimulant use

Among ecstasy users (n=242), 31.4% engaged in risky simultaneous alcohol and ecstasy use (i.e. used alcohol while ‘up’ on ecstasy and while coming-down) at one study wave and 28.5% did so at multiple waves. Among methamphetamine users (n=223), 30.9% engaged in risky simultaneous alcohol and methamphetamine use at one wave and 19.7% did so at multiple waves. Overall, alcohol use was more commonly used while up than it was while coming-down from ATS. At multiple study waves, 76.0% of ecstasy users had used alcohol while up on ecstasy and 41.3% of methamphetamine users had used while up on methamphetamine, compared with 29.8% while coming down from ecstasy and 19.7% while coming down from methamphetamine. Additional data collected at the 30-month follow-up, relating to occasions of ecstasy (n=145) and methamphetamine use (n=87) in the last 12 months, indicate that drinking alcohol before consuming ecstasy (75.2%) and methamphetamine (64.4%) was also common. Those who drank before ATS use (ecstasy: n=109; methamphetamine: n=56) also tended to drink while up (ecstasy: 71.6%; methamphetamine: 75.0%), but less commonly drank while coming down (ecstasy: 24.8%; methamphetamine: 39.3%).

3.4 Predictors of ecstasy- and methamphetamine-related aggression and hostility

Tables 2 and 3 present results for prediction models of ecstasy- and methamphetamine-related aggression and hostility, developed using multivariate logistic regression and
Simultaneous alcohol and methamphetamine use linked with aggression among young adults

reporting unadjusted and adjusted odds ratios and 95% confidence intervals. Both moderate and high trait aggression were associated with ecstasy-related aggression and hostility in unadjusted and adjusted analyses. A marginally non-significant association (p=0.065) for the high frequency and declining ecstasy trajectory was fully attenuated in the adjusted model. No significant associations were found between ecstasy-related aggression and hostility and risky simultaneous ecstasy and alcohol use, cannabis use, risky alcohol use, psychosis, or gender.

Table 2. Prediction model of ecstasy-related aggression and hostility* (n=242)

<table>
<thead>
<tr>
<th>Risky simultaneous ecstasy and alcohol use</th>
<th>n</th>
<th>Unadjusted ORs (95% CI)</th>
<th>Adjusted b ORs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risky simultaneous use at 1 wave</td>
<td>76</td>
<td>1.47 (0.80-2.70)</td>
<td>1.37 (0.69-2.66)</td>
</tr>
<tr>
<td>Risky simultaneous use at 2-3 waves</td>
<td>69</td>
<td>1.60 (0.86-2.98)</td>
<td>1.38 (0.68-2.79)</td>
</tr>
<tr>
<td>Ecstasy use trajectory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular and declining use</td>
<td>138</td>
<td>1.14 (0.66-1.98)</td>
<td>1.03 (0.56-1.91)</td>
</tr>
<tr>
<td>High frequency and declining use</td>
<td>20</td>
<td>2.60 (0.94-7.18)†</td>
<td>2.16 (0.72-6.47)</td>
</tr>
<tr>
<td>Cannabis use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly use at 1 wave</td>
<td>33</td>
<td>0.64 (0.29-1.43)</td>
<td>0.56 (0.23-1.33)</td>
</tr>
<tr>
<td>Weekly use at 2-3 waves</td>
<td>72</td>
<td>1.52 (0.85-2.69)</td>
<td>1.22 (0.64-2.32)</td>
</tr>
<tr>
<td>Risky alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risky use at 1-2 waves</td>
<td>94</td>
<td>1.77 (0.67-4.70)</td>
<td>1.27 (0.44-3.71)</td>
</tr>
<tr>
<td>Risky use at 3-4 waves</td>
<td>125</td>
<td>2.25 (0.86-5.84)</td>
<td>1.34 (0.46-3.93)</td>
</tr>
<tr>
<td>Trait aggression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>65</td>
<td>2.83 (1.51-5.30)**</td>
<td>3.01 (1.55-5.84)**</td>
</tr>
<tr>
<td>High</td>
<td>57</td>
<td>5.71 (2.86-11.40)***</td>
<td>5.02 (2.38-10.61)***</td>
</tr>
<tr>
<td>Psychosis</td>
<td>12</td>
<td>2.51 (0.73-8.57)</td>
<td>1.63 (0.44-6.13)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>111</td>
<td>1.55 (0.93-2.59)</td>
<td>0.91 (0.50-1.67)</td>
</tr>
</tbody>
</table>

† p=0.065, ** p<0.01, *** p<0.001

* Experienced feelings of aggression or hostility attributed to ecstasy use at baseline, 12 months, or 4.5 years (n=110); b Prediction model using multivariate logistic regression, reporting odds ratios adjusted for all other variables in the model; c Risky simultaneous ecstasy and alcohol use defined as consuming alcohol while up on ecstasy and while coming down from ecstasy; measured at baseline, 12 months, and 30 months; reference category is no risky simultaneous ecstasy and alcohol use at any of the three time points; d Trajectory groups developed using k-means cluster analysis; reference category is 'very infrequent use'; e Days of cannabis use in the last month measured at baseline, 12 months, and 30 months; weekly cannabis use defined as four or more days of use in the last month; reference category is no weekly cannabis use at any of the three waves; † Risky alcohol use defined as usually consuming ≥5 standard drinks on days of drinking in the last month; measured at baseline, 12 months, 30 months, and 4.5 years; reference category is no risky alcohol use at any of the four time points; f Trait aggression measured using the Buss Perry Aggressive Questionnaire for physical aggression; categories are low (scores range from 6.4-13.6), moderate (scores range from 14.3-20.0), and high (scores range from 27.06-37.9); † Past 12-month psychosis measured using a 7-item brief psychosis screener, with scores of ≥3 categorised as potential cases of psychosis.
In contrast, risky simultaneous methamphetamine and alcohol use was significantly associated with methamphetamine-related aggression and hostility in unadjusted and adjusted analyses (Table 3). Methamphetamine users who engaged in risky simultaneous use (i.e., consumed alcohol while up and while coming-down) at 2-3 study waves had almost three times the relative odds of methamphetamine-related aggression and hostility (AOR 2.74, 95% CI 1.09-6.89, p<0.05), compared to users who did not engage in risky simultaneous use. The high frequency and increasing use methamphetamine trajectory and high trait aggression were also significantly associated with feelings of aggression and hostility.

Associations for the regular low use methamphetamine trajectory, recurrent weekly cannabis use, and gender were attenuated in the adjusted analyses. Risky alcohol use and psychosis were not associated with methamphetamine-related aggression and hostility.

Table 3. Prediction model of methamphetamine-related aggression and hostility\(^a\) (n=223)

<table>
<thead>
<tr>
<th>Risky simultaneous methamphetamine and alcohol use(^c)</th>
<th>n</th>
<th>Unadjusted ORs (95% CI)</th>
<th>Adjusted(^b) ORs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risky simultaneous use at 1 wave</td>
<td>69</td>
<td>1.46 (0.78-2.74)</td>
<td>1.45 (0.70-3.01)</td>
</tr>
<tr>
<td>Risky simultaneous use at 2-3 waves</td>
<td>44</td>
<td>4.59 (2.17-9.73)(^***)</td>
<td>2.74 (1.09-6.89)(^*)</td>
</tr>
<tr>
<td>Methamphetamine use trajectory(^d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular low use</td>
<td>54</td>
<td>2.62 (1.39-4.93)(^**)</td>
<td>2.02 (0.92-4.42)</td>
</tr>
<tr>
<td>High frequency and increasing use</td>
<td>10</td>
<td>7.78 (1.60-37.91)(^*)</td>
<td>7.23 (1.27-41.03)(^*)</td>
</tr>
<tr>
<td>Cannabis use(^e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly use at 1 wave</td>
<td>33</td>
<td>0.95 (0.42-2.15)</td>
<td>0.70 (0.28-1.80)</td>
</tr>
<tr>
<td>Weekly use at 2-3 waves</td>
<td>71</td>
<td>2.60 (1.42-4.76)(^**)</td>
<td>1.64 (0.80-3.40)</td>
</tr>
<tr>
<td>Risky alcohol use(^f)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risky use at 1-2 waves</td>
<td>87</td>
<td>1.00 (0.36-2.75)</td>
<td>0.53 (0.17-1.68)</td>
</tr>
<tr>
<td>Risky use at 3-4 waves</td>
<td>115</td>
<td>1.97 (0.74-5.23)</td>
<td>0.94 (0.30-2.92)</td>
</tr>
<tr>
<td>Trait aggression(^g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>63</td>
<td>1.93 (1.00-3.75)(^†)</td>
<td>1.57 (0.74-3.32)</td>
</tr>
<tr>
<td>High</td>
<td>55</td>
<td>6.70 (3.25-13.83)(^***)</td>
<td>5.78 (2.53-13.20)(^***)</td>
</tr>
<tr>
<td>Psychosis(^h)</td>
<td>12</td>
<td>1.00 (0.31-3.25)</td>
<td>0.64 (0.16-2.66)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>103</td>
<td>2.47 (1.43-4.27)(^**)</td>
<td>1.38 (0.70-2.74)</td>
</tr>
</tbody>
</table>

\(^a\) Experienced feelings of aggression or hostility attributed to methamphetamine use at baseline, 12 months, or 4.5 years (n=93); \(^b\) Prediction model using multivariate logistic regression, reporting odds ratios adjusted for all other variables in the model; \(^c\) Risky simultaneous methamphetamine and alcohol use defined as consuming alcohol while up on methamphetamine and while coming-down from methamphetamine; measured at baseline, 12 months, and 30 months; reference category is no risky simultaneous methamphetamine and alcohol use; \(^d\) Regular low use = ≤ 1 methamphetamine use wave; \(^e\) Recurrent weekly cannabis use = weekly use at 1, 2, or 3 waves; \(^f\) Risky alcohol use defined as consuming alcohol while up on methamphetamine and while coming-down from methamphetamine; measured at baseline, 12 months, and 30 months; reference category is no risky alcohol use; \(^g\) Trait aggression = moderate or high; \(^h\) Psychosis = yes or no.
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4. Discussion

Alcohol consumption was a ubiquitous feature of ATS use in this population-based sample. Recurrent risky simultaneous alcohol and methamphetamine use (i.e., drinking alcohol while intoxicated on methamphetamine and while coming-down at 2-3 waves of the study) was associated with methamphetamine-related aggression and hostility, indicating that risky simultaneous alcohol and methamphetamine use increases the likelihood of aggression among young adults. This association was independent of patterns of alcohol, methamphetamine, and cannabis use, trait aggression, psychosis, and gender. In contrast, there was no association between risky simultaneous alcohol and ecstasy use and ecstasy-related aggression and hostility.

Alcohol was predominantly consumed before and during ATS use episodes, rather than while coming-down, which aligns with US research [4, 49, 50]. However, a significant minority did drink while coming-down from ATS. The timing of alcohol consumption is important as it may reflect motives for combined use. Young adults who consume alcohol while coming-down may have different motives (e.g., drinking to cope with depressive symptoms of coming-down) than those who only drink prior to and during ATS use. They may also use alcohol as a coping mechanism in other scenarios. Further investigation of the timing of alcohol consumption during ATS use, including the associated motives, is warranted.
A likely explanatory mechanism for the association between risky simultaneous alcohol and methamphetamine use and methamphetamine-related aggression and hostility relates to the physiology of use. Our findings are consistent with evidence concerning physiological effects of both methamphetamine and alcohol use on aggression, including an observed dose-response relationship [24, 28]. There may be an additive effect of alcohol and methamphetamine use on aggression; however, more research examining the rate and severity of aggression is required to confirm this.

The high frequency and increasing methamphetamine use trajectory was also associated with methamphetamine-related aggression and hostility. This finding adds to previous research linking frequent methamphetamine use and violent behaviour [28], by pointing to the possible contribution of persistent patterns of use. Further, our findings indicate that trait aggression plays an important role. For males, the occurrence of this trait, and more intensive substance use patterns, appears to explain their higher rates of methamphetamine-related aggression and hostility. No association was found between psychosis and methamphetamine-related aggression and hostility, which is consistent with research involving dependent methamphetamine users [28]. Lastly, the association with recurrent weekly cannabis use was attenuated in the full model, which may reflect overlap in methamphetamine and cannabis use patterns.

Research should also consider the potential impact of the social-environmental context and substance use outcome expectancies. Alcohol and illicit stimulants are commonly combined in licensed venues [3] and both environmental characteristics of these settings [51, 52] and outcome expectancies regarding alcohol consumption in these settings [53] can increase the risk of violence. However, the social context of use is unlikely to be a
sufficient explanatory factor, given that ecstasy and methamphetamine use overwhelmingly occurs in similar settings for this young adult population.

The lack of association between ecstasy-related aggression and hostility and simultaneous ecstasy and alcohol use, risky drinking, and ecstasy use trajectories is consistent with previous evidence [33-35]. The marginal association between ecstasy use and aggression, which was attenuated in the full model, could be accounted for by the polydrug use profile of higher-risk ecstasy users. Only trait aggression was associated with ecstasy-related aggression and hostility, which is perhaps not surprising, as expressions of aggression run counter to commonly reported subjective effects of ecstasy use (e.g., feelings of empathy and social bonding [54, 55]).

4.1 Implications

Our study contributes to understandings of the relationship between alcohol use, methamphetamine use, and aggression, which have predominantly focused on separate relationships for these substances. While high-volume alcohol consumption has previously been shown to increase the likelihood of aggressive behaviour among dependent methamphetamine users [28], co-use of alcohol and methamphetamine has not been explicitly examined. Our findings show a link between simultaneous alcohol and methamphetamine use and methamphetamine-related aggression and hostility, independent of a number of potential predictors including separate patterns of alcohol and methamphetamine use, trait aggression, psychosis, and gender. Further, our findings build on previous research indicating that ecstasy does not appear to be linked with aggression, showing this is still the case when combined with alcohol.
The link between alcohol, methamphetamine, and aggression is a concern for both public health and law enforcement, particularly given the high prevalence of drinking during ATS use in this population-based sample. The interlinking of these issues indicates that the policy challenges of ATS and alcohol use by young adults should be approached in an integrated manner. Engagement in risky behaviours in public settings, such as NEDs, likely increases the risk of police contact, which may present an important opportunity for engaging with this group. Australian police have taken an active role in areas of public health related to substance use – such as police diversion for cannabis users [56] – and there may be greater scope for police involvement in provision of harm reduction resources, including drug and alcohol service referrals. However, harm reduction resources should reflect normative patterns of use. While our findings show that simultaneous alcohol and ATS use is prevalent among young adult ATS users, there is currently a lack of harm reduction resources specifically targeting this issue.

4.2 Limitations

Study limitations should be acknowledged. Firstly, the accuracy of self-report can be impacted by concerns around stigma and illegality of behaviour. However, this is likely mitigated in a longitudinal study with high participant retention. Secondly, our measures of ATS-related feelings of aggression and hostility do not necessarily correspond to incidents of aggressive behaviour. Forthcoming analyses from this study will examine such incidents. Thirdly, the cluster analytic method used may potentially have resulted in higher rates of trajectory misclassification compared with other analytic methods. Fourthly, ATS users in this study were drawn from a population sample of predominantly recreational users. Consequently, our findings may differ from samples of more problematic ATS users. Lastly,
while we adjusted for trait aggression, psychosis, and gender, our results could potentially be explained by confounding factors not examined in this study, including factors relating to the social-environmental setting and substance use outcome expectancies. Further, we had limited capacity to examine use of other substances (e.g., cocaine) due to the low frequency of use in this sample.

5. Conclusion

Drinking is a ubiquitous feature of ecstasy and methamphetamine use in this population of Australian young adult amphetamine-type stimulant users. Combined alcohol and amphetamine-type stimulant use is an emerging area of concern for public health and law enforcement and has been linked with increased harms compared to the separate use of these substances. This study adds to the growing literature, with our findings indicating a link between risky simultaneous alcohol and methamphetamine use and methamphetamine-related aggression and hostility, independent of patterns of alcohol, methamphetamine, and cannabis use, trait aggression, psychosis, and gender. The interlinking of issues of drinking, methamphetamine use, and aggression highlights that the policy challenges of amphetamine-type stimulant and alcohol use by young adults may need to be approached collaboratively by both public health and law enforcement.
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Figure A1. Ecstasy use trajectories over a 30-month period

Note: Mean days of ecstasy use refers to the number of days that ecstasy was used during the last month at each time interval. Trajectory groups were developed using k-means cluster analysis.
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Figure A2. Methamphetamine use trajectories over a 30-month period

Note: Mean days of methamphetamine use refers to the number of days that ecstasy was used during the last month at each time interval. Trajectory groups were developed using k-means cluster analysis.
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Contributors

All authors contributed to the development of this research. AS and JMN conceived of the present study. HW, RK, and ML contributed to the development of the study. EML reviewed the literature. EML conducted the statistical analysis with assistance from AS. EML wrote the first draft of the manuscript and all authors contributed to and approved the final manuscript.

Conflict of Interest

All authors declare that they have no conflicts of interest.

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Highlights

- Alcohol consumption is a ubiquitous feature of amphetamine-type stimulant use
- Risky simultaneous alcohol and methamphetamine use is linked with aggression
- No association found between simultaneous use of alcohol and ecstasy and aggression
- Policy challenges of alcohol and amphetamine-type stimulant use are interlinked