Pattern of cannabis use in ecstasy polydrug users: moderate cannabis use may compensate for self-rated aggression and somatic symptoms

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Cannabis is one of the most common 'co-drugs' for ecstasy users. The aim of the present study was to explore self-reported psychobiological problems in ecstasy polydrug users in relation to their pattern of cannabis use. Two hundred and eighty ecstasy polydrug users were allocated into five cannabis groups according to the frequency of their cannabis use. The control group comprised 121 alcohol-tobacco users. There were no significant group differences with regard to age, diagnosed family psychiatric history and level of self-rated stress experienced during 6 months prior to the study. The present study produced three main findings: (a) Ecstasy users with no concomitant use of cannabis displayed more self-rated aggression and somatic symptoms compared with ecstasy users who were smoking cannabis on a monthly or weekly basis. (b) Ecstasy users who reported heavy cannabis use in the past displayed higher paranoid symptoms compared with ecstasy weekly and daily cannabis users. (c) Former heavy cannabis users were the most likely to complain of a variety of ecstasy related long-term problems. In conclusion, moderate cannabis use may help to ameliorate or mask MDMA-induced aggressivity and somatic symptoms. However, this study confirms that heavy cannabis and ecstasy use is associated with several psychobiological problems, which may emerge after a period of abstinence from both drugs. Copyright © 2005 John Wiley & Sons, Ltd.

key words — ecstasy; MDMA; cannabis; aggression; paranoia; somatization

INTRODUCTION

Cannabis is one of the most common drugs taken alongside or in addition to ecstasy (co-drug) in regular ecstasy users (Topp et al., 1999; Boys et al., 1997). Winstock et al. (2000) showed that 82% of young people in a magazine survey were using cannabis with ecstasy or during the comedown. Another investigation at dance events in Edinburgh (Riley et al., 2001) revealed that although 48.4% of the attendees were consuming cannabis, these users classified it as a ‘secondary’ dance-drug, in contrast to ecstasy and stimulants that were considered as ‘primary’ dance-drugs. Cannabis is often taken during the comedown to compensate for feelings of agitation, muscular tension, anxiety and depression which can predominate after using MDMA (Williamson et al., 1997; Parrott et al., 2000).

Several studies have investigated the crucial role of cannabis use when investigating the cognitive and psychological effects of MDMA use (McCardle et al., 2004; Gouzoulis-Mayfrank et al., 2002; Lieb et al., 2002; Daumann et al., 2001). It is extremely difficult to predict the effects generated by the interaction of several psychoactive drugs, however, some attempts have been made in order to dissociate between the impact of cannabis and ecstasy on memory functioning. For instance, Rodgers et al. (2001) found that cannabis was associated with more self-reported ‘every day’ memory, internally cued and short-term prospective memory problems, whereas ecstasy was correlated with higher rates of long-term prospective memory problems. Conversely, other recent studies

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have suggested that most long-term psychological problems may in fact be related to cannabis rather than MDMA use (Morgan et al., 2002; Daumann et al., 2004). In contrast, cannabinoids have been found to prevent acute hyperthermia and to protect partially against the 5-HT depletions following MDMA administration, which would suggest that co-use of cannabis and MDMA may protect against the negative effects of serotoninergic modulation (anxiety, depression and other psychobiological problems) and/or neurotoxicity induced by MDMA (Morley et al., 2004; Parrott et al., 2004a). In line with this hypothesis, animal research has demonstrated that cannabinoids have antioxidant, excitotoxicity prevention, anti-inflammatory and other potentially protective properties (Grundy et al., 2002; Hampson et al., 2000). Furthermore, cannabidiol (CBD), a non-psutotropic constituent of cannabis, has been found to have antianxiety and antipsychotic properties (Sethi et al., 1986; Mechoulam et al., 2002; Parrott et al., 2004a).

However, anxiety and panic attacks are the most common adverse effects of cannabis intoxication and these reactions were found to be potentiated by stress (Patel et al., 2004). Furthermore, a 6-year longitudinal study found that weekly or more frequent cannabis use in teenage girls predicted later depression and anxiety; though depression and anxiety were not associated with either weekly or daily cannabis use. This finding supports an aetiological link between cannabis and psychological problems rather than the self-medication hypothesis (Patton et al., 2002). In conclusion, the long-term effects of cannabis use are still unclear, and to date very few attempts have been made to explore the consequences of combined use of ecstasy and cannabis.

The aim of this investigation was to explore self-reported psychobiological problems in ecstasy polydrug users in relation to their pattern of cannabis use. Based on previous studies, ecstasy users who were current daily cannabis users were expected to display high pathology scores compared with ecstasy users with less intense or no cannabis use.

METHODS

Participants

Preliminary analysis on the present data set was presented as a poster published as an abstract (Milani et al., 2002).

Participants were contacted in clubs, colleges and other venues where young people congregate; they were informed about the aims of the research and invited to take part in the study. The principal investigator went through the questionnaires together with each participant and made sure that the instructions were clear. When possible, questionnaires were completed in situ; alternatively they were sent via a pre-paid envelope provided by the researcher. All participants signed a consent form and the study was approved by the University of East London ethics committee. The authors have not gained or lost any financial or other kind of interests from the results of the present studies.

The ecstasy user sample comprised 280 participants (152 male and 128 females, average age 24.8 ± 4.7): 44 no-cannabis users (not currently using cannabis and had used on less than 20 occasions in their lifetime), 70 current monthly users (maximum twice per month), 31 current weekly users (every weekend), 103 current daily users, 32 former heavy users (not using for at least 12 months, but had used on a daily basis in the past). The control group consisted of 121 individuals who only used alcohol/tobacco (39 males and 82 females, average age 24.8 ± 5.9). There were significantly more men than women in the daily cannabis users group, and more women than men in the alcohol/tobacco user control group (overall gender difference: C6/C6 20.46, p = 0.001). There were no significant age differences between the groups (Table 2). Table 1 displays the group means, standard deviations and Kruskal–Wallis test findings for lifetime drug consumption.

Materials

(1) A brief personal history questionnaire included:

- Demographic details;
- Personal psychiatric history; in this session participants were asked if they had ever been treated for any of the following problems (Yes/No): alcohol and/or drug dependence, anxiety/panic attacks, depression, obsessive-compulsive disorders, schizophrenia/paranoia. If so, they were asked to provide details and to specify whether psychiatric problems were related to their drug use.
- A brief family psychiatric history; as above, participants were asked to report whether any member of their first degree relatives family had ever been treated for any psychiatric disorder, and to provide details.
- One question asked whether participants had ever ‘been hospitalized for brain injuries’ (Yes/No)

(2) A 3-point self-rated item was used as an indication of level of stress during the last 6 months: ‘How stressful had life been in the last 6 months?’
months? (1) More than usual; (2) As normal; (3) Less than usual.

(3) A modified UEL drug use questionnaire was used to assess lifetime drug use. The original questionnaire (Parrott et al., 2001) was modified in order to include other drugs such as: GHB, fluoxetine and viagra. In addition, estimated lifetime consumption and monthly use of cannabis were also investigated.

(4) A detailed ecstasy use questionnaire investigated ecstasy dose and regimen variables (first and last time of use, usual and largest number of tablets taken on a single occasion) drugs of co-use, subjective short-term and long-term physical, psychological and cognitive adverse effects; (dependence and tolerance were also investigated).

(5) The brief symptoms inventory BSI (Derogatis and Melisaratos, 1983) was used to assess psychological well-being. This standardized checklist assesses nine symptom dimensions (somatization, obsessive-compulsiveness, interpersonal sensitivity, depression, anxiety, anger-hostility, paranoid ideation, phobic anxiety and psychoticism) and the global indexes of psychological distress (global severity index, positive symptom total and positive symptom distress index). Responses indicated how participants felt over the past 4 weeks when not under the effects of drugs.

Analysis

All statistical procedures were performed using SPSS version 10.00 (SPSS Inc., Chicago, IL).

Chi-square or likelihood test (when expected values were less than 5) were used to compare frequencies across groups; when the absolute value of the standardized residual for a category exceeded 2.00, then it was concluded that that cell made a major contribution to a significant result (Grimm, 1993).

Group differences regarding drug use were analysed using both ANOVA and Kruskal–Wallis tests.

A multiple analyses of variance was run on the total sample in order to compare the ecstasy/cannabis group with alcohol-tobacco users. When Leven’s test of variance was significant, a Kruskal–Wallis analysis was carried out to back up results obtained with parametric tests. One-sample independent t-tests were employed to contrast present scores with Derogatis’ outpatients psychiatric raw scores (Derogatis and Melisaratos, 1983). BSI scores were transformed into t-scores for comparison against Derogatis’ norms (Derogatis and Melisaratos, 1983).

Multiple analysis of covariance and Bonferroni corrected post-hoc comparisons were carried out on the ecstasy sample to control for ecstasy and other drug use measures. BSI-dimensions were entered as independent variables, the cannabis group as factor and the drug dose and regimen variables as covariates. Variables were included in the analysis only if the assumption of normality and homogeneity of regression were met; partial correlations between excluded factors and psychological dimensions were run in order to identify any significant associations.

RESULTS

Drug use

Daily and former heavy cannabis users reported the heaviest ecstasy lifetime consumption, and a larger number of ecstasy tablets taken on a single occasion compared with the other groups (Table 1). Former heavy cannabis users stopped using ecstasy for a significantly longer period compared with daily cannabis users, and they had used it for a longer period compared with no-cannabis, monthly and weekly cannabis users.

As presented in Figure 1, the extent of polydrug use was associated with the extent of cannabis use. Former heavy cannabis users consumed the widest range of drugs in their lifetime (linear polynomial function significant at $F_{(4,275)} = 58.08, p < 0.001$).

Monthly, daily and no-cannabis users were drinking significantly more alcohol and smoking more tobacco compared with the alcohol/tobacco group (the overall ANOVA was $F_{(5,393)} = 6.86, p < 0.001$ and $F_{(5,393)} = 9.13, p < 0.001$ respectively). In the ecstasy sample, there was no significant difference in alcohol and tobacco use among cannabis groups. Since Leven’s test showed unequal variances, parametric as well as non-parametric tests were used to test differences in lifetime polydrug use. Multiple ANOVA detected significant group differences for cocaine use only ($F_{(4,264)} = 4.82, p = 0.001$), post-hoc pair comparisons showed that former heavy cannabis users consumed more cocaine compared with all the other groups. However, Kruskal–Wallis analysis detected significant group differences for amphetamine, LSD and magic mushrooms, cocaine and solvents (see Table 2). No significant group difference was detected for GHB, and fluoxetine and viagra.

The likelihood ratio test revealed that there was a significant difference in the pattern of co-drug use across cannabis groups ($c = 75.75, p < 0.001$); specifically, significantly more daily cannabis users were taking stimulants together with ecstasy compared with the other groups (see Table 2, for frequencies and
standard residuals). On the contrary, no-cannabis or monthly cannabis users were more likely to take ecstasy only, or ecstasy and alcohol, compared with daily cannabis users.

**Family and personal psychiatric history**

Overall, about half of the sample reported that at least one member of their immediate family had been medicated for psychiatric disorders. The most common disturbances were anxiety and depression. A likelihood ratio test showed no significant group effect of psychiatric disorders diagnosed in participants' families.

Overall, 117/395 participants (29.6%) had been treated for psychiatric disorders, of whom 21 (5.3%) were addictive disorders. The highest prevalence was found in the former heavy cannabis users (74.2%), whereas the lowest was in the alcohol/tobacco user controls (10.6%). The likelihood ratio test revealed that in the former heavy cannabis users and daily cannabis users there were significantly more participants who were treated for addictive disorders compared with alcohol/tobacco user controls and weekly cannabis users (Table 4). The highest prevalence of anxiety disorders was also in the former heavy cannabis user group, and this was significantly higher than in the controls.

**Level of stress**

A Kruskal–Wallis test showed no significant group differences with regard to the level of stress experienced in the 6 months prior to the interview.
The overall result for the likelihood ratio test was: $\chi^2(20, 267) = 75.75, p = 0.000$;

**Bold**: cells that made a major contribution to the significant result (absolute value of St. Residual > 2).

**NS**: non significant.

**Table 2.** Means, standard deviations and $p$ values for lifetime drug consumption (estimated number of occasions)

<table>
<thead>
<tr>
<th>Cannabis use</th>
<th>Ecstasy only</th>
<th>Ecstasy + alcohol</th>
<th>Ecstasy + cannabis</th>
<th>Ecstasy + alcohol and cannabis</th>
<th>Ecstasy + stimulants and cannabis</th>
<th>Ecstasy + multiple polydrug ketamine, LSD, stimulants …</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No-cannabis</td>
<td>n(%)</td>
<td>Std. Residual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly</td>
<td>16 (38.1)</td>
<td>2.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>42 (100)</td>
</tr>
<tr>
<td></td>
<td>Std. Residual</td>
<td>2.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>0.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>−1.8</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly</td>
<td>21 (31.8)</td>
<td>1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>66 (100)</td>
</tr>
<tr>
<td></td>
<td>Std. Residual</td>
<td>1.1</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>−0.5</td>
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<tr>
<td></td>
<td></td>
<td>−0.7</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>−1.9</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>−0.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly</td>
<td>6 (20.0)</td>
<td>−0.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30 (100.0)</td>
</tr>
<tr>
<td></td>
<td>Std. Residual</td>
<td>−1.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>1.3</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>−0.4</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>9 (9.1)</td>
<td>−2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>99 (100)</td>
</tr>
<tr>
<td></td>
<td>Std. Residual</td>
<td>−1.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former heavy users</td>
<td>n(%)</td>
<td>7 (23.3)</td>
<td>5 (16.7)</td>
<td>6 (20.0)</td>
<td>2 (6.7)</td>
<td>4 (13.3)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td></td>
<td>Std. Residual</td>
<td>0.1</td>
<td>0.5</td>
<td>1.1</td>
<td>−0.8</td>
<td>−1.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Total</td>
<td>59 (22.1)</td>
<td>35 (13.1)</td>
<td>34 (12.7)</td>
<td>32 (12.0)</td>
<td>63 (23.6)</td>
<td>44 (16.5)</td>
<td>267 (100.0)</td>
</tr>
</tbody>
</table>

The overall result for the likelihood ratio test was: $\chi^2(20, 267) = 75.75, p = 0.000$;

**Bold**: cells that made a major contribution to the significant result (absolute value of St. Residual > 2).

**NS**: non significant.

**Table 3.** Ecstasy users sample: pattern of co-drug use in relation to cannabis use

<table>
<thead>
<tr>
<th>Alcohol or drug dependence</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Obsessive-compulsive disorders</th>
<th>Schizophrenia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No-cannabis</td>
<td>n(%)</td>
<td>Std. Residual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly</td>
<td>3 (14.3)</td>
<td>0.6</td>
<td>0.0</td>
<td>1.4</td>
<td>−0.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly</td>
<td>2 (3.0)</td>
<td>−0.8</td>
<td>0.9</td>
<td>0.6</td>
<td>−0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>0 (0)</td>
<td>−1.3</td>
<td>−0.2</td>
<td>−1.1</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former heavy cannabis</td>
<td>9 (8.7)</td>
<td>1.5</td>
<td>0.2</td>
<td>0.8</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol/tobacco users</td>
<td>n(%)</td>
<td>Std. Residual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 (19.4)</td>
<td>3.4</td>
<td>3.1</td>
<td>1.4</td>
<td>−0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21 (5.3)</td>
<td>−2.2</td>
<td>−2.3</td>
<td>−2.1</td>
<td>−1.1</td>
</tr>
</tbody>
</table>

The overall result for the likelihood ratio test was: $\chi^2(20, 267) = 75.75, p = 0.000$;

**Bold**: cells that made a major contribution to the significant result (absolute value of St. Residual > 2).

### Table 5. Mean scores, standard deviations and MANOVA for ecstasy-cannabis users and non-drug user control group

<table>
<thead>
<tr>
<th></th>
<th>Controls (0)</th>
<th>No-cannabis (1)</th>
<th>Monthly use (2)</th>
<th>Weekly use (3)</th>
<th>Daily use (4)</th>
<th>Former heavy use (5)</th>
<th>p</th>
<th>Pair comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Somatization</strong></td>
<td>0.56 ± 0.61</td>
<td>1.05 ± 0.80</td>
<td>1.63 ± 0.84</td>
<td>1.21 ± 0.77</td>
<td>1.17 ± 0.77</td>
<td>1.16 ± 0.88</td>
<td>0.81</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>O.C.D.</strong></td>
<td>1.04 ± 0.79</td>
<td>1.63 ± 0.84</td>
<td>1.77 ± 0.92</td>
<td>1.40 ± 0.86</td>
<td>1.55 ± 0.88</td>
<td>1.50 ± 0.85</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Interpersonal</strong></td>
<td>0.56 ± 0.61</td>
<td>1.05 ± 0.80</td>
<td>1.63 ± 0.84</td>
<td>1.21 ± 0.77</td>
<td>1.17 ± 0.77</td>
<td>1.16 ± 0.88</td>
<td>0.81</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td>0.73 ± 0.77</td>
<td>1.07 ± 0.87</td>
<td>1.12 ± 0.95</td>
<td>0.95 ± 0.82</td>
<td>1.05 ± 0.92</td>
<td>1.00 ± 0.89</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>0.69 ± 0.67</td>
<td>1.07 ± 0.87</td>
<td>1.12 ± 0.95</td>
<td>0.95 ± 0.82</td>
<td>1.05 ± 0.92</td>
<td>1.00 ± 0.89</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Anger-hostility</strong></td>
<td>0.73 ± 0.77</td>
<td>1.07 ± 0.87</td>
<td>1.12 ± 0.95</td>
<td>0.95 ± 0.82</td>
<td>1.05 ± 0.92</td>
<td>1.00 ± 0.89</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Paranoid ideation</strong></td>
<td>0.83 ± 0.76</td>
<td>1.09 ± 0.88</td>
<td>1.11 ± 0.95</td>
<td>0.95 ± 0.82</td>
<td>1.05 ± 0.92</td>
<td>1.00 ± 0.89</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>Psychoticism</strong></td>
<td>0.75 ± 0.75</td>
<td>1.05 ± 0.88</td>
<td>1.11 ± 0.95</td>
<td>0.95 ± 0.82</td>
<td>1.05 ± 0.92</td>
<td>1.00 ± 0.89</td>
<td>0.85</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>GSI</strong></td>
<td>23.11 ± 3.11</td>
<td>32.26 ± 4.26</td>
<td>25.38 ± 3.35</td>
<td>19.54 ± 2.64</td>
<td>17.64 ± 2.54</td>
<td>17.01 ± 2.44</td>
<td>0.54</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>PST</strong></td>
<td>1.59 ± 1.69</td>
<td>1.71 ± 1.64</td>
<td>1.78 ± 1.62</td>
<td>1.54 ± 1.54</td>
<td>1.54 ± 1.54</td>
<td>1.54 ± 1.54</td>
<td>0.54</td>
<td>0.2 &lt; 1</td>
</tr>
<tr>
<td><strong>PSTDI</strong></td>
<td>1.59 ± 1.69</td>
<td>1.71 ± 1.64</td>
<td>1.78 ± 1.62</td>
<td>1.54 ± 1.54</td>
<td>1.54 ± 1.54</td>
<td>1.54 ± 1.54</td>
<td>0.54</td>
<td>0.2 &lt; 1</td>
</tr>
</tbody>
</table>

*Pairwise comparisons (Bonferroni corrected); significance level at 0.05.

### Psychological assessment

**Comparison with alcohol/tobacco.** A multiple analysis of variance (MANOVA) was run in order to compare ecstasy sample scores (divided by cannabis groups) with the alcohol/tobacco users group. Group means, standard deviations and statistical findings are displayed in Table 5.

The overall MANOVA was significant for somatization, obsessive-compulsive disorders, anxiety, anger-hostility, paranoid ideation and psychoticism. Paired comparisons showed that levels of obsessive-compulsive disorders, anger-hostility and psychoticism reported by the ecstasy no-cannabis users were significantly higher compared with the alcohol/tobacco user group. The non-cannabis user group displayed higher anger-hostility compared with the monthly and weekly cannabis users; and higher somatization in comparison with the monthly cannabis users. The heavy past cannabis users reported higher paranoid ideation symptoms compared with the controls and the daily cannabis users. All general indexes showed a significant group effect, but post hoc Tukey pairwise comparisons (Bonferroni corrected) were significant for the GSI and PST only. In both cases, non-cannabis, daily and former heavy cannabis users scored higher than the controls (Table 5).

Given the unequal sample size, Kruskal–Wallis tests were run for subscales that displayed a significant Levene’s test of equality of variance. Results of the non-parametric tests were similar to the parametric ones (somatization $c = 21.770$, $p < 0.001$, anger-hostility $c = 12.388$, $p = 0.015$, paranoid ideation $c = 10.756$, $p = 0.029$) with the exception of phobic anxiety $c = 10.132$, $p = 0.038$.

**Comparisons with Derogatis normative groups.** The BSI dimensions showed a significant group effect compared with the Derogatis (1983) psychiatric out-patient sample norms. Scores for somatization and obsessive-compulsive disorders were similar to the psychiatric norms. Whereas the anxiety, phobic anxiety and psychoticism scores were all significantly lower than the psychiatric sample. The former heavy cannabis users reported elevated anger-hostility, paranoid ideation and positive symptoms distress index (non-significantly different from psychiatric out-patient norms). The no-cannabis users’ anger-hostility dimension was also close to psychiatric norms.

BSI dimensions were also plotted against the non-patients’ norms. All dimensions were within 1 standard deviation from the normative means. The highest standardized scores were reported by the
non-cannabis users on the somatization and anger-hostility dimension and by the former heavy cannabis users on the paranoid ideation scale. Interestingly, alcohol/tobacco users, weekly and monthly cannabis users, reported scores equal to or below the means (data not shown).

Ecstasy user sample: Multiple Analysis of Covariance (MANCOVA). A multiple ANCOVA was run within the ecstasy sample to control for drug use factors. Cannabis group was entered as a factor. Covariates included gender, period of ecstasy use, amphetamine, LSD, ketamine and cocaine use. The BSI-subscaler and general indexes (global severity index, positive symptom total and positive symptom distress index) were the dependent variables. Lifetime dose of ecstasy consumption, the usual number of tablets, the last time of ecstasy use, the usual number of tablets taken in one occasion, the extent of polydrug use, could not be included as covariates because they broke the assumption of homogeneity of regression slope.

Group differences were significant for anger-hostility \(F(4, 244) = 4.67, p = 0.001\); somatization \(F(4, 244) = 2.51, p = 0.034\) and paranoid ideation \(F(4, 244) = 2.90, p = 0.031\). Tukey pairwise comparisons revealed that the no-cannabis users reported significantly higher somatization compared with the monthly cannabis users and significantly higher anger-hostility scores compared with both the monthly and the weekly cannabis users. Moreover, the former heavy cannabis users scored significantly higher than the weekly and the daily cannabis users on the paranoid ideation sub-scale. Among the general indexes, only the PST (positive symptoms total) was significant, with the no-cannabis users reporting higher score compared with the monthly cannabis users \(F(4, 244) = 2.92 p = 0.022\).

Gender, period of ecstasy use, LSD, cocaine and amphetamine lifetime consumption were not significantly associated with any BSI dimensions.

Partial correlations were run on the ecstasy sample to explore the relationship between somatization, anger-hostility, paranoid ideation, general indexes and ecstasy dose and regimen variables (lifetime dose of ecstasy consumption, the usual number of tablets, the last time of ecstasy use, the usual number of tablets taken in one occasion), controlling for extent of polydrug use. The analysis revealed that somatization and anger-hostility were positively correlated with the usual number of tablets taken in one occasion \((r = 0.16, p = 0.012; r = 0.14, p = 0.029, respectively); paranoid ideation was associated with the usual number of ecstasy tablets taken in one occasion \((r = 0.18, p = 0.003);\) and the last time of ecstasy use \((r = 0.15, p = 0.022)\).

Subjective reports: physical, psychological and cognitive long-term problems following ecstasy use

Participants were asked to report whether, according to their perception, they experienced long-term (for more than 6 months) physical, psychological or cognitive problems following ecstasy use. Examples of long term psychological problems were: ‘anxiety when thinking about a bad trip on E’, ‘paranoia, stress, panic . . .’ ‘panic attacks since taking e’, ‘depression, mood swings, no drive, lazziness’. Reported at least one psychological or physical problem as a consequence of their ecstasy use; specifically 27/27 said that they were suffering from long-term ecstasy-related physical disturbances. The most common complaint was chronic tiredness and lowered immunity (5/27). Other physical disturbances were: headache (2/23), muscular pain/backache (2/23), irregular eating and sleeping (2/23). Interestingly, two people said that they developed ‘visual distortions’ and ‘long term visual problems’. Ten people did not specify what physical problems they were suffering from. One participant thought they had developed poor circulation following ecstasy use, and another one blamed ecstasy for kidney stones. Overall, 56/271 (20.7%) of the ecstasy users complained of long-term psychological problems; the most common were: depression (24 out of 56 complaints), anxiety (11/56), mood swings (8/56), panic attacks (8/56), paranoia (7/56). Of these, 12/56 reported multiple problems (e.g. depression and anxiety, anxiety panic attacks, depression and paranoia). Fifty-nine out of 270 ecstasy users stated that they developed long-term cognitive problems, although 5 out of 19 daily cannabis users thought that they were also related to cannabis use. The most frequent complaint was ‘memory loss’ 26(59), 7 specified that they had short term memory, 6 were not sure that their problems were ecstasy related. The second most frequent disturbance was ‘lack of concentration’ and difficulties sustaining attention for a long period of time (13/59). The above proportions include the overlap of those participants reporting more than one category of long-term problems: 11/83 respondents complained of both physical and cognitive disturbances, 12/83 had psychological as well as cognitive problems and 10 people out of 83 reported a combination of physical, psychological and cognitive problems. Interestingly, there was a significantly larger proportion of people complaining.
of long-term problems (physical, psychological and cognitive) in the former heavy cannabis group, compared with all other groups, including the current daily users (Figure 2).

DISCUSSION

The primary aim of this investigation was to explore patterns of cannabis use in a cohort of ecstasy polydrug users and to investigate the possible psychobehavioral implications. The present study generated three main findings: (a) against the initial hypothesis, ecstasy users with no concomitant use of cannabis displayed more self-rated aggression and somatic symptoms compared with ecstasy users who were smoking cannabis on a monthly or weekly basis; (b) ecstasy users who reported heavy cannabis use in the past displayed higher paranoid symptoms compared with ecstasy weekly cannabis users; (c) former heavy cannabis users were the most likely to complain of ecstasy related long-term physical, psychological and cognitive problems.

Consistent with previous studies (Winstock et al., 2000; Riley et al., 2001; Scholey et al., 2004) a large proportion of the ecstasy users sample were using cannabis regularly at the time of the interview (25% daily and 8% weekly). However, about 11% of the respondents stated that they were not using cannabis at the time of the interview and they had only tried it a few times in their lifetime. Another 8% of the ecstasy user sample reported that they had smoked heavily for a few years in the past, but gave up cannabis at least one year prior to the interview. The intensity of cannabis use (current or past) reflected the extent of ecstasy polynegative use. Nevertheless, daily cannabis users were more likely to co-use ecstasy and stimulants compared with the former heavy cannabis users; this may indicate a change in the style of drug taking, as the latter generally had a longer period of ecstasy abstinence (on average 1.5 years) compared with the first group.

In agreement with previous self-rated studies (Parrott et al., 2001; Schifano, 2000; Morgan, 2000; Parrott et al., 2000) the ecstasy/cannabis polydrug user groups displayed higher pathology scores compared with the alcohol/tobacco user controls on several BSI dimensions: somatization, obsessive-compulsive disorders, anxiety, anger-hostility, paranoid ideation, psychotism, general distress index (GSI) and the positive symptoms total (PST). However, against our initial hypothesis, ecstasy users with no concomitant use of cannabis and who had never been frequent cannabis users in the past displayed the highest pathology scores on all the above mentioned subscales, with the exception of paranoid ideation (where ecstasy users with former heavy cannabis use reported the highest scores). There were no significant differences in the prevalence of diagnosed psychiatric disorders (including alcohol/drug addiction) in the immediate family among ecstasy/cannabis user groups and alcohol/tobacco user controls. Only 2.5% of the total sample had suffered a minor brain injury and these were equally distributed among groups (including controls). Additionally, there were no group differences with regard to the level of stress experienced in the 6 months prior to the interview. Hence, it is likely that drug use contributed significantly to the differences between ecstasy/cannabis users and alcohol/tobacco users.

Separate analyses were run within the ecstasy sample: after controlling for gender, period of ecstasy use, amphetamine, LSD and cocaine use, only anger-hostility, somatization and paranoid ideation displayed an overall cannabis group effect. Interestingly, ecstasy users with no concomitant use of cannabis had significantly more aggressive symptoms in comparison with ecstasy users with monthly or weekly cannabis consumption; they also reported more somatic symptoms in comparison with ecstasy monthly cannabis users. Differences in anger-hostility were highly significant ($p = 0.001$ after controlling for ecstasy and other drug use). Partial correlations showed that both somatization and anger were associated with large numbers of ecstasy tablets being taken in a single occasion; and this association was significant even after controlling for the extent of polydrug use. This is...
consistent with Milani et al. (2000) who found anger-hostility scores to be associated with the usual and the maximum number of tablets taken in a single occasion. Previous studies have also found that ecstasy use is linked to residual (Verheyden et al., 2002; Curran et al., 2004) or short-term (Gerra et al., 2000) self-rated aggression. Importantly, Curran et al. (2004) corroborated self-report findings with results based on cognitive measures; in their study, 4 days after MDMA consumption, ecstasy users were cognitively biased towards aggressive rather than neutral sentences, whereas controls showed the opposite pattern; moreover, the extent of MDMA use was positively correlated with the level of aggressive interpretative bias. Furthermore, anger and impulsiveness was found to be one of the reasons for stopping MDMA use (Verheyden et al., 2003). Furthermore, in Gerra et al. (2001), ecstasy users displayed higher experimentally induced aggressive behaviour compared with the controls; moreover, the extent of ecstasy use was associated with aggressive responses. However, the long-term findings are more inconclusive. In Curran et al. (2004) study, 7 days after MDMA consumption, ecstasy users’ self-rated aggression dropped to the same level as the controls. Nevertheless, Curran and Verheyden (2003) had previously found that both ex and current ecstasy users self-reported higher aggression compared with the controls, with the former users scoring higher than the current users. In addition, there was a positive correlation between the last time of MDMA use and physical aggression. Milani et al. (2000) found the same correlation in a sample of heavy ecstasy users. In contrast, direct aggressiveness decreased after 1 year of MDMA abstinence in Gerra et al. (2000) longitudinal study. These contrasts might be due to the fact that diverse measures were used to assess aggression; moreover, some of the characteristics of the MDMA and control groups varied between these studies. From a pharmacological perspective, increased levels of 5-HT have been shown to decrease aggressive behaviour (Moskowitz et al., 2003) confirming that deficits in 5-HT can lead to aggression (Cleare and Bond, 1995). There is experimental evidence of MDMA induced 5-HT depletion in ecstasy users (McCann et al., 2000; Semple et al., 1999), it is therefore conceivable that ecstasy users may experience enhanced aggressivity.

Although all the above mentioned studies made an attempt to control for other drug use, other findings suggest that cannabis, rather than MDMA, is responsible for the elevated anger displayed by ecstasy polydrug users (Thomasius et al., 2003; Morgan, 2000; Daumann et al., 2001). However, this was not entirely replicated by a subsequent study of Daumann et al. (2004) where, in contrast with other SCL-90 dimensions, the anger-hostility subscale displayed no significant difference between cannabis users and 18 months cannabis abstinent participants. Furthermore, the extent of cannabis use was negatively associated with non-planning impulsivity. Likewise, Milani et al. (2000) found an inverse relationship between the extent of cannabis consumption and anger-hostility scores. In the present sample, the pattern of ecstasy polydrug use for the no-cannabis user group was similar to that of monthly and weekly cannabis users. Hence, it is probable that the frequency of cannabis use accounts for the group differences found on the anger-hostility and somatization dimensions. To summarize, ecstasy with concomitant moderate cannabis use may be associated with less aggressivity and somatic symptoms in comparison with ecstasy use only.

The above findings are consistent with the known anxiolytic, sedative and analgesic properties of cannabis (Sethi et al., 1986; Grotenhermen, 2004; Block et al., 1998). These effects are well known to the many recreational drug users who smoke cannabis after MDMA and other stimulants use in order to compensate for residual effects (Boys et al., 1997; Williamson et al., 1997; Parrott, 2001; Cole and Sumnall, 2003). However, the present study suggests that moderate cannabis use may also prevent aggressive and somatic symptoms from emerging in the long-term; results from the anger-hostility subscale were particularly pronounced.

Various pharmacological mechanisms may be related to these findings. Cannabinoids have been found to have antioxidant properties (Grundy, 2002; Hampson et al., 2000). Morley et al. (2004) has recently proven that cannabinoids prevent acute MDMA-induced hyperthermia and partially prevent 5-HTP depletion effects and anxiety in rats. The fact that cannabis may reduce hyperthermia may have important implications especially when ecstasy is taken under hot and crowded conditions typical of raves and dance clubs (Parrott, 2002; Parrott, in press) as a high temperature enhances ecstasy-induced neurotoxic effects (Dafters and Biello, 2003; Malberg and Seiden, 1998). One possibility is that these mechanisms may partially explain the low psychobehavioural problems reported by ecstasy users with moderate cannabis use. However, heavy cannabis usage did not show the same effect, this might be due to the fact that as cannabis addiction can lead to aggressive behaviour (Haney et al., 2004; Hoaken and Stewart, 2003; Budney et al., 2003; Aharonovich...
et al., 2001; Walfish et al., 2001). Furthermore, cannabis use was aetiologically linked to the onset of schizophrenia and psychotic episodes (Smit et al., 2004; Verdoux and Tournier, 2004; Arsenault et al., 2004), thus the higher level of hostility might be due to increased paranoid ideation (Chaudry et al., 1991).

In the present study, former heavy cannabis consumption was associated with significantly higher paranoid ideation compared with weekly and daily cannabis use. Moreover, paranoid ideation was correlated with the number of tablets normally taken in one occasion. This is in line with studies that found a strong association between ecstasy consumption and the onset of severe paranoid symptoms (see Parrott, 2001, Soar et al., 2001 for review). Therefore, it can be argued that differences between former heavy cannabis users and weekly cannabis users were linked to the extent of cannabis and ecstasy use. However, it is not clear why the ecstasy/no-cannabis and the ecstasy/monthly cannabis users did not display lower paranoid ideation than the weekly/ecstasy cannabis users. Additionally, the ecstasy/former heavy cannabis users reported more paranoid symptoms in comparison with the ecstasy/daily cannabis users. Interestingly, the two groups had similar lifetime cannabis consumption and ecstasy polydrug use regimen variables except for the last time of ecstasy and cannabis use. Moreover, the period of abstinence from ecstasy was positively correlated to paranoid ideation, indicating that the longer the time since ecstasy was taken, the higher the scores. Paradoxically, a longer period of ecstasy abstinence might partially explain the higher level of paranoia reported by the former heavy cannabis users.

Interestingly, in agreement with the results on the paranoid ideation subscale, subjective reports revealed that the former heavy cannabis users were more problematic compared with the other groups, including the current daily cannabis users. Participants were expressly asked to report whether they had experienced any physical, psychological or cognitive problems following their ecstasy consumption, 30% of the total ecstasy user sample complained of some sort of ecstasy-related long-term problems. The most common ecstasy-related psychological problems were depression, anxiety, panic attacks and paranoia. As far as the cognitive complaints are concerned, many of the participants reported loss of memory, difficulty concentrating and sustaining attention.

These reports are in line with several studies which found impaired cognitive functioning in ecstasy (Parrott, 2001). Previous work has also shown that cannabis use can potentially impair cognition, both acutely and as a consequence of long-term usage (Parrott et al., 2004; Curran et al., 2002). A recent on-line survey found differential effects of ecstasy and cannabis on self-reported memory problems (Rodgers et al., 2001). In relation to physical disturbances, chronic tiredness and low immunity were the most common problems reported by the former heavy cannabis user group. This is consistent with numerous reports of the arousal and psychomotor lowering effects of cannabis (Pertwee, 1990), and with evidence demonstrating immunosuppressive effects of Δ⁹-tetrahydrocannabinol (THC) and other cannabinoids (Klein et al., 2001). MDMA has also been proven to permanently affect the immune system in animals (Pacifici et al., 2002). However, it is difficult to be specific about the influence of MDMA or cannabis on the above complaints, as it is likely that physical, psychological and cognitive problems are interrelated. For example, depressive illness is often characterized by cognitive disruption (Austin et al., 2001) and depression is also purported to negatively modulate immunity and, therefore, well-being (Irwin, 2001). Accordingly, a proportion of ecstasy users (33 out of 278) reported an overlap of physical, psychological and cognitive disturbances. In summary, subjective reports suggest that ecstasy polydrug use including cannabis, can be associated with a variety of long-term problems, however, it is not clear why former rather than current heavy cannabis users self-reported more psychobiological disturbances.

At least five hypotheses can be proposed: (1) cannabis acute effects may obscure psychobiological problems in ecstasy with daily cannabis use. This may imply a self-therapeutic use of cannabis (Ogborne et al., 2000; Hambrecht and Hafner, 2000; Grant and Pickering, 1998). However, the self-medication hypothesis of cannabis use was not supported by a recent 4 year longitudinal study (Henquet et al., 2005). (2) Awareness of problems may develop after a period of abstinence. Since only self-reported measures were used, the participant’s harm perception should also be taken into account, as this may be reflected in their self-rating. It is also conceivable that individuals who are still conducting a heavy drug-using lifestyle prefer not to think about the long-term consequences of their behaviour. (3) Former heavy cannabis users may have consumed a more potent kind of cannabis in comparison with daily cannabis users. In fact, there is an increased variety of cannabis containing different percentages of tetrahydrocannabinol. For example the percentage of tetrahydrocannabinol in Super-Skunk (or Nederwiet; Paris and Tran, 1998) is three or more times higher in comparison...
with ‘normal’ cannabis, and some users have reported psychotic experiences after the use of relatively small quantities (Wylie et al., 1995). This factor may also be implicated in the high paranoid ideation reported by this group. (4) Former heavy cannabis users may have stopped using both cannabis and ecstasy following the onset of psychobiological problems, which may have been exacerbated or caused by their drug use. In agreement with this explanation, the psychiatric personal history revealed that in this group there was a high percentage of diagnosed anxiety, depression and addictive disorders. Accordingly, Verheyden et al. (2003) found that the most common reason to quit ecstasy use was mental illness or fear of it. Although this is probably the most likely hypothesis, a fifth explanation could be offered. (5) The onset of psychobiological problems may occur following a period of abstinence from ecstasy and cannabis polydrug use. This pattern is consistent with findings from Curran and Verheyden study (Curran and Verheyden, 2003) in which increased self-rated aggression was found after a period of abstinence from ecstasy. Additionally, Milani et al. (unpublished data) detected a direct correlation between anger, anxiety and depression and last time of ecstasy was found in the heavy ecstasy user group. At least two other studies are in line with this hypothesis. In Thomasius et al. (2003) ex but not current users displayed significantly elevated somatization, anger-hostility, anxiety, phobic anxiety, paranoid ideation and psychoticism; furthermore in Morgan (2000) only ex users exhibited impaired RBMT (Rivermead behavioural memory test) recall performance in comparison with polydrug no-ecstasy users. In conclusion, it is likely that the interaction among all the above mentioned factors contributed to the present findings.

This study has a number of methodological limitations: the cross-sectional design does not enable the causal link between the onset of psychobiological problems and drug use to be verified. Nevertheless, some information with regard to family and personal mental health were collected and these indicated that the heavy ecstasy/cannabis users were more likely to have suffered from psychological disturbances preceding their drug use; in contrast premorbid psycho-pathology did not explain the differences between ecstasy no-cannabis and ecstasy moderate cannabis users. A longitudinal study would help to clarify the relationship between psychological disorders and drug use. Another important limitation of this study is that the pattern of drug use relied on self-report data. Furthermore, no objective psychological assessment was used. Nevertheless, as an indication of clinical relevance, the present values were compared with the scores of Derogatis (1983) norms. The highest pathology scores in our sample were similar to the outpatients psychiatric scores. Most importantly, similar findings have been replicated over the years in several independent samples (Parrott et al., 2001; Schifano, 2000; Morgan, 2000; Parrott et al., 2000). Further longitudinal studies are needed to confirm the above hypothesis. Combining self-rated measures with clinical interviews as well as physiological and cognitive assessments would be recommended. It would be also important to collect more detailed cannabis use data, including the kind of cannabis that the participants had used. This would give a more reliable indication of the intensity of THC consumption.

In summary, heavy, but not moderate, cannabis use was associated with extensive polydrug use. Despite several important methodological limitations, this study contributes to a better understanding of the complex interaction between ecstasy and cannabis use. The present findings suggest two main hypotheses: (1) moderate cannabis use may compensate for some ecstasy-related psychobiological problems, especially subjective aggression and somatization; (2) psychobiological problems may emerge after a period of abstinence from ecstasy and cannabis polydrug use.

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