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## Angry cognitive bias, trait aggression and impulsivity in substance users

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**Abstract** *Rationale:* According to cognitive theory, people who are aggressive expect angry responses to ambiguous situations. Increased aggression has been reported a few days or weeks following use of MDMA (ecstasy). This may relate to low 5-HT release, and so a 5-HT challenge may increase cognitive bias towards anger differentially in MDMA users and non-users. *Objectives:* To investigate whether: (1) measures of anger and aggression will correlate with processing time of angry material and with generation of aggressive responses and (2) tryptophan challenge in people abstinent from MDMA and controls will affect angry cognitive bias. *Methods:* Thirty-two current MDMA users abstinent for 3 weeks, 32 ex-users abstinent for longer than 1 year and 32 non-MDMA substance users were recruited. Trait measures were administered before and state measures before and 5 h after an amino acid drink, depleted or augmented with tryptophan. After the drink, subjects undertook a computer task, which involved reading ambiguous short stories. Reading times to a key sentence describing an angry or non-angry reaction were recorded and subjects wrote a continuing sentence for half the stories. *Results:* Subjects were faster to process angry than non-angry reactions, indicating the presence of angry cognitive bias. Trait anger and aggression were correlated with processing time of angry relative to non-angry reactions, particularly in the current users. Impulsivity was correlated with non-specific speed of response. Subjects wrote more aggressive sentences after an angry reaction. Tryptophan depletion tended to increase aggressive content. Trait aggression was correlated with

aggressive content following non-angry reactions. *Conclusions:* Evidence of angry cognitive bias was shown in this group of substance users, which was not specific to MDMA use. People high on trait aggression were more likely to expect an angry reaction to an ambiguous situation and to generate more written aggression when this did not occur.

**Keywords** MDMA · Abstinent · Aggression · Anger · Impulsivity · Cognitive bias

### Introduction

Ecstasy or MDMA ( $\pm$ 3,4-methylenedioxymethamphetamine) has become a popular recreational drug among young people. Its use has increased substantially over the past few years, and this increase is particularly noticeable in younger age groups and among women (Schuster et al. 1998). Users describe taking ecstasy recreationally in order to enhance mood and closeness to others in a dance culture, and experimental studies have confirmed these generally positive acute effects (Vollenweider et al. 1998; Liechti et al. 2000). However, it is well established that other drugs taken for their mood-enhancing qualities, such as amphetamines and cocaine, result in an offset period in which mood worsens (Kosten et al. 1998). A novel study designed to investigate whether MDMA also resulted in residual effects on mood (Curran and Travill 1997) compared subjects who were regular users of MDMA to subjects who regularly used alcohol. Their mood was measured when they had taken ecstasy or alcohol during an evening's clubbing, the following day and 4 days later. While the alcohol group showed some lowering of mood the next day, they had completely recovered by 4 days, whereas the MDMA group had persistent low mood 4 days later. The authors attributed this effect to a depletion in 5-HT which could either be temporary following the acute elevation caused by MDMA or more permanent due to neurotoxic effects.

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As well as an association with depression, there is a wide body of literature relating deficiencies in central 5-HT function to affective aggression in both clinical and preclinical samples (Brown et al. 1982; Coccaro 1989). Hormonal responses to challenge doses with a 5-HT compound such as fenfluramine have also been shown to inversely correlate with scores on aggression questionnaires in healthy volunteers (Cleare and Bond 1997; Manuck et al. 1998). Most of the human work has been correlational but the technique of tryptophan depletion has been used to study the effects of acutely lowering central levels of 5-HT on aggressive feelings and behaviour in several studies (Bond and Wingrove 2001). A clear relationship between depletion and increased anger and aggression was found, and these effects were greater in those with higher trait hostility scores. Thus, the depletion of 5-HT following acute MDMA use might not only result in increased feelings of low mood but also of anger and aggression. A recent study investigated changes in current mood, including feelings of aggression and anger in male and female users immediately following and 4 days after MDMA use (Verheyden et al. 2002). They found that feelings of aggression as well as depression and discontent were increased 4 days after the use of MDMA. The effects on depression were greater in females and correlated with the amount of MDMA taken 4 days previously. Increased feelings of aggression were shown in both men and women and correlated with the amount taken 4 days previously in men. There were no associations with length or lifetime consumption of MDMA and so these results support a temporary rather than a neurotoxic effect.

Elevated scores on subscales of the Buss Durkee Hostility Inventory (BDHI) have also been found in MDMA users who had been abstinent for 3 weeks (Gerra et al. 1998). However, this work, like much of the substance abuse literature, relies on self-report scales with resultant problems of demand characteristics. Gerra et al. (2001) therefore used a laboratory aggression task to examine behavioural aggression in MDMA users compared to healthy controls. The MDMA users not only rated themselves as more aggressive on the BDHI but also subtracted more points (representing money) from their opponent on the Point Subtraction Aggression Paradigm. An alternative strategy would be to look at anger indirectly by examining cognitive bias in an information processing task. Although this approach has been used to study both anxiety and depression, few studies have yet examined anger. However, there is some evidence that people who are high on trait anger do involuntarily allocate attention towards anger-related cues. For example, high trait anger has been found to be associated with an attentional bias towards angry faces in a modified Stroop task (van Honk et al. 2001) and towards anger-related words in a visual search task (Cohen et al. 1998), although the latter effect was only found following anger induction.

Material ambiguous with respect to aggressive content has also been presented in the form of short stories which

participants are asked to complete (Rule et al. 1987). Using such a technique, people high on trait measures of aggression have been found to be more likely to write aggressive endings to ambiguous short stories (Dill et al. 1997). It is also possible to use a more objective measure of time taken to read critical sentences during the presentation of such stories. Readers develop mental models of situations described in the text that they are reading which aid comprehension of the text (Bower and Morrow 1990). Most of the work supporting this proposition has been concerned with events and settings; but, in a series of experiments, Gernsbacher et al. (1992) demonstrated that it also applied to information about a fictional character's emotional state. Subjects were shown to take less time to process information that matched the character's emotional state. In the current study, a reading time task was therefore used to examine the time it took to process a sentence describing an angry relative to a non-angry reaction to a series of ambiguous anger-provoking short stories. Previously, we have found trait anger to be correlated with relatively faster processing of sentences describing angry reactions (Wingrove and Bond, unpublished observations). As well as measuring processing time, we scored the additional sentences generated by participants to half of the stories for aggressive content. Current MDMA users who had been abstinent for 3 weeks (refer to: Gerra et al. 1998), ex-users who had stopped using at least a year previously and substance user controls who had never used MDMA were compared. To explore the role of 5-HT in angry responding in the three groups of participants, a tryptophan depletion/enhancement strategy was used. The subjects in each group were randomly assigned to either depletion or enhancement, and the task was carried out 6 h after the drink.

## Materials and methods

### Subjects

Three groups of male volunteers aged between 18 years and 40 years were recruited by advertisement: (1) regular users who had taken MDMA more than 20 times over the past year; (2) ex-users, i.e. regular users who had not taken MDMA for at least 1 year; and (3) controls who had never taken MDMA but were regular users of alcohol and cannabis. Exclusion criteria were current use of any psychotropic medication or any use of opiates. In addition, volunteers agreed to abstain from MDMA and LSD for 3 weeks and from alcohol for 24 h before the test day. They were paid £5 (pounds sterling) per hour for participating in the study. All volunteers gave written informed consent, and the study was approved by the institutional ethics committee.

### Design and drugs

A double-blind independent groups design was employed in which half the subjects in each group were randomly assigned to receive a 100-g drink of 15 amino acids either depleted or augmented with tryptophan.

## Rating scales

Anger was assessed using the Multidimensional Anger Inventory (MAI; Siegel 1986), aggression using the Aggression Questionnaire (Buss and Perry 1992) and impulsivity using the Barratt Impulsiveness Scale (BIS-11; Patton et al. 1995). The Beck Depression Inventory (BDI; Beck et al. 1988) and the trait version of the State Trait Anxiety Inventory (STAI; Spielberger et al. 1970) were used to exclude those with very high scores. Current mood was assessed with the Mood Rating Scale (MRS; Bond and Lader 1974) which yields three factors: alertness, contentedness and calmness, the Anger Rating Scale (ARS; Bond and Lader 1986) and the State Impulsivity Scale (STIMP; Wingrove and Bond 1997), which each produce a mean score.

## Stories task

The task was based on the method described by Gernsbacher et al. (1992). Twelve short stories were constructed, each six to nine sentences long. These were a subset of 48 used in another study (Wingrove and Bond, unpublished observations). The stories were presented on a computer screen. First the name of the main character appeared on the screen. The participant was instructed to press the space bar on a keyboard to get the first sentence of the story and, then, when they had read the first sentence, to press the space bar again to get the second sentence, and so on. After half the stories, the question, "what does [name of main character] do next?" appeared on the screen. Participants were then required to write a one-sentence ending to the story on a paper form placed on the table beside them. Each story related a situation involving the main character named at the start. The target sentence then described his or her reaction to that situation. To reduce the possibility that participants would anticipate the end of the story, some continued with a further one or two sentences after the target sentence. The situations were chosen so that anger would be a plausible but not inevitable reaction. For each story, two different target sentences were prepared, one angry and one non-angry. Twelve neutral filler stories, designed to be as devoid of emotional content as possible, were also prepared. The final set consisted of 24 stories: 12 neutral filler stories, presented alternately with 12 ambiguous anger-provoking stories, half with an angry ending and half with a non-angry ending, starting with an additional neutral story. Requests for endings occurred in quasi-random order, and followed 6 of the filler and 6 of the ambiguous stories.

## Procedure

The subjects attended the laboratory on two occasions. On the first occasion, they had a full psychiatric history taken, signed the consent form, filled in a substance-use questionnaire, completed the National Adult Reading Test (NART; Nelson 1982) and the other trait questionnaires. Subjects with a positive psychiatric history, a score of more than 32 errors on the NART, 30 on the BDI or 60 on the STAI-Trait were excluded. On the test day, each participant came to the laboratory after an overnight fast and was tested individually. They completed the MRS, ARS and STIMP and were then given a drink containing a mixture of amino acids, which either contained no tryptophan (depleted) or had 10.3 g tryptophan added (augmented). The constituents and quantities used were exactly the same as detailed in the study by Young et al. (1985). Five hours later, they completed the MRS, ARS and STIMP again, alongside several cognitive assessments (Curran and Verheyden 2003). At 6 h, the participant was read standard instructions for the stories task and completed a practice set of six stories to ensure that they understood the task. They then completed the main task, which took approximately 20 min.

## Analysis of data

A two-way analysis of variance (ANOVA) was used to examine the differences between conditions and groups and the interaction. However, no differences were found between tryptophan conditions or interaction with group and so the data for the two conditions was combined and one-way ANOVA was used to examine the differences between groups. A repeated-measures analysis with time as the within-subject factor and group and condition as the between-subjects factors was used to examine changes from pre- to post-drink between groups. Post-hoc comparisons were examined using the Bonferroni test. The mean response times for angry endings (RTA) and non-angry endings (RTN) for each participant were used to calculate a standardised difference:  $RTD = (RTN - RTA) / (RTA + RTN)$ . Spearman rank order correlations were calculated between the trait and state measures and the measures of response time and aggressive content.

## Results

### Participants

Ninety-six participants took part in the study: 32 in each group. The groups did not differ on the NART (mean=112.1). There was a significant difference on age ( $F_{2,90}=3.27$ ,  $P<0.05$ ). The ex-users (mean=27.8) were slightly older than the controls (mean=23.9) but not different from the current users (mean=25.2).

### Drug use

The participants in all groups had similar rates of consumption for cannabis, alcohol and nicotine. They had been drinking for between 7.7 years and 9.5 years, smoking cigarettes for 6–8.4 years and cannabis for 6.7–7.4 years. They drank on 10.6–18.2 days per month and consumed between 5.6–7.2 units each time. The current users drank significantly more per occasion than the ex-users ( $P<0.05$ ) but were not different from controls. The participants smoked 7.1–7.8 cigarettes per day and smoked on 17.7–18.7 days per month. They smoked cannabis on 14.1–17.5 days per month and consumed 0.6–0.7 ounces per month. The current and ex-users of MDMA reported some use of cocaine, amphetamines and LSD, but this use was not regular. None of the controls used any other drugs. The current users had been using MDMA for  $4.3 \pm 2.9$  years. They used it on  $3.5 \pm 1.8$  days per month and took an average of  $2.6 \pm 0.9$  tablets per session. Their estimated lifetime use was  $527.8 \pm 734.5$  tablets. They stopped using it for  $39 \pm 22.6$  days pre-study. The ex-users had used MDMA for  $3.5 \pm 2.6$  years and had stopped using  $2.4 \pm 1.8$  years ago. They had used it on  $7 \pm 4.3$  days per month and had taken  $2.4 \pm 1.4$  tablets per session. Their estimated lifetime use was  $1105.85 \pm 1923.03$  tablets. There was no difference between current and ex-users in years of MDMA use or amount taken per session, but the ex-users had used MDMA more frequently than the current users ( $P<0.001$ ).

**Table 1** Mean  $\pm$  standard deviations of scores on trait measures and reading time for current users, ex-users, controls, and for the total sample

|                                     | Current users<br><i>n</i> =32  | Ex-users<br><i>n</i> =32       | Controls<br><i>n</i> =32 | Total<br><i>n</i> =96 |
|-------------------------------------|--------------------------------|--------------------------------|--------------------------|-----------------------|
| Multidimensional anger inventory    |                                |                                |                          |                       |
| Anger-arousal                       | 17.34 $\pm$ 5.38               | 20.30 $\pm$ 7.25               | 16.63 $\pm$ 6.37         | 18.04 $\pm$ 6.49      |
| Range                               | 21.61 $\pm$ 4.17               | 22.57 $\pm$ 4.92               | 21.66 $\pm$ 4.51         | 21.94 $\pm$ 4.51      |
| Hostile outlook                     | 11.97 $\pm$ 2.86               | 11.60 $\pm$ 3.38               | 12.22 $\pm$ 3.41         | 11.94 $\pm$ 3.20      |
| Anger-in                            | 11.50 $\pm$ 3.81               | 13.60 $\pm$ 4.09               | 11.63 $\pm$ 3.55         | 12.21 $\pm$ 3.90*     |
| Anger-out                           | 5.84 $\pm$ 0.85                | 6.11 $\pm$ 1.12                | 5.88 $\pm$ 1.29          | 5.94 $\pm$ 1.10       |
| Total                               | 64.97 $\pm$ 12.53              | 71.27 $\pm$ 15.82              | 64.97 $\pm$ 13.71        | 67.00 $\pm$ 14.22     |
| Aggression questionnaire            |                                |                                |                          |                       |
| Physical                            | 21.69 $\pm$ 7.81               | 23.63 $\pm$ 6.25               | 19.94 $\pm$ 5.98         | 21.71 $\pm$ 6.83      |
| Verbal                              | 16.00 $\pm$ 3.67               | 15.67 $\pm$ 3.52               | 16.00 $\pm$ 3.96         | 15.89 $\pm$ 3.69      |
| Anger                               | 16.78 $\pm$ 5.10               | 19.33 $\pm$ 5.90               | 16.34 $\pm$ 4.67         | 17.45 $\pm$ 5.34      |
| Hostility                           | 18.16 $\pm$ 4.59               | 21.03 $\pm$ 7.15 <sup>a</sup>  | 17.09 $\pm$ 9.67         | 18.71 $\pm$ 5.81*     |
| Total                               | 72.63 $\pm$ 15.25              | 79.67 $\pm$ 17.12 <sup>a</sup> | 69.38 $\pm$ 12.86        | 73.77 $\pm$ 15.56*    |
| Barratt impulsivity scale           |                                |                                |                          |                       |
| Non-planning                        | 26.75 $\pm$ 6.55               | 22.87 $\pm$ 7.51               | 22.97 $\pm$ 7.05         | 24.24 $\pm$ 7.20*     |
| Motor                               | 19.16 $\pm$ 5.06 <sup>b</sup>  | 19.10 $\pm$ 5.89 <sup>a</sup>  | 15.42 $\pm$ 5.39         | 17.89 $\pm$ 5.67*     |
| Cognitive                           | 13.94 $\pm$ 5.01               | 15.67 $\pm$ 5.31               | 12.65 $\pm$ 4.53         | 14.06 $\pm$ 5.06      |
| Total                               | 59.84 $\pm$ 13.83 <sup>b</sup> | 57.63 $\pm$ 14.49              | 51.03 $\pm$ 14.29        | 56.19 $\pm$ 14.55*    |
| Stories task                        |                                |                                |                          |                       |
| Reading time—angry endings (ms)     | 1924.5 $\pm$ 861.7             | 1969.7 $\pm$ 611.1             | 1593.8 $\pm$ 661.6       | 1830.8 $\pm$ 730.4    |
| Reading time—non-angry endings (ms) | 2074.3 $\pm$ 866.7             | 2242.4 $\pm$ 864.9             | 1681.3 $\pm$ 452.8       | 2001.9 $\pm$ 783.4    |

<sup>a</sup> Ex users versus controls  $P<0.05$

<sup>b</sup> Current users versus controls  $P<0.05$

## Rating scales

The scores on the measures of anger, aggression and impulsivity are shown in Table 1. There were no differences between groups on the total MAI or the subscales. The just significant effect on “anger-in” ( $F_{2,90}=3.09$ ,  $P<0.05$ ) did not discriminate significantly between groups. There was a significant difference between groups on the total AQ ( $F_{2,91}=3.72$ ,  $P<0.03$ ) and on the hostility subscale ( $F_{2,91}=4.03$ ,  $P<0.03$ ). The ex-users scored higher than the controls on both measures. There were significant differences between groups on the total BIS-11 ( $F_{2,90}=3.26$ ,  $P<0.05$ ) and on the non-planning ( $F_{2,90}=3.11$ ,  $P<0.05$ ) and motor subscales ( $F_{2,90}=4.79$ ,  $P<0.02$ ). The current users scored higher than the controls on the total scale ( $P<0.05$ ) and both the current and the ex-users scored higher than the controls ( $P<0.03$ ) on motor impulsivity. The effect on non-planning did not discriminate significantly between groups.

## Current feelings

A significant change from time 1 to time 2 was shown for the alertness and calmness factors of the MRS (Table 2). All participants felt more sedated ( $F_{1,90}=6.29$ ,  $P<0.02$ ) and calmer ( $F_{1,90}=5.49$ ,  $P<0.03$ ) at time 2. There were no significant interactions with group or condition. Values at time 2 were used in the correlations.

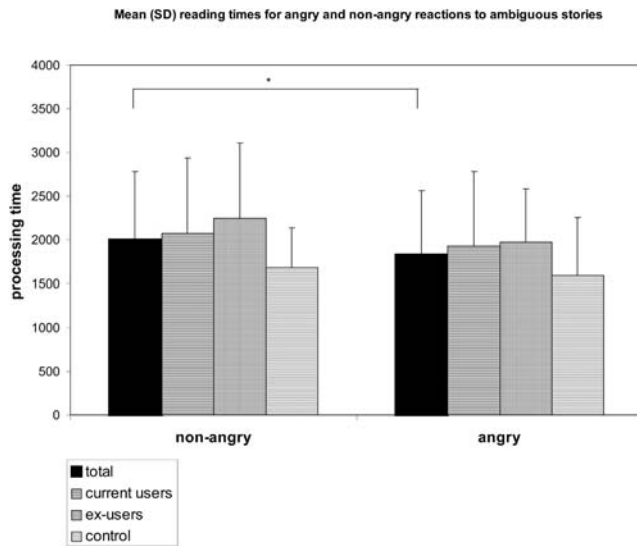
**Table 2** Mean  $\pm$  standard deviations of current mood scores for the total sample before and after the amino acid drink

| Measure                 | Pre-drink         | Post-drink        |
|-------------------------|-------------------|-------------------|
| Anger rating scale      |                   |                   |
| Mean                    | 25.26 $\pm$ 14.30 | 25.14 $\pm$ 13.39 |
| Mood rating scale       |                   |                   |
| Alertness—sedation      | 38.68 $\pm$ 17.49 | 43.02 $\pm$ 15.99 |
| Content—discontent      | 31.02 $\pm$ 14.88 | 31.06 $\pm$ 13.19 |
| Calmness—anxiety        | 30.83 $\pm$ 15.01 | 26.64 $\pm$ 14.97 |
| State impulsivity scale |                   |                   |
| Mean                    | 34.93 $\pm$ 13.85 | 36.18 $\pm$ 13.43 |

## Stories task—reading time

There was a significant difference between the reading times for the angry and non-angry reactions ( $F_{1,91}=7.42$ ,  $P<0.01$ ). Participants were faster to process the angry reactions (Fig. 1). There was also a significant difference between groups ( $F_{2,91}=4.18$ ,  $P<0.02$ ) but no interaction between reading time and group. The ex-users took longer to respond than the controls ( $P<0.02$ ) but were not different from current users. There were no significant differences between groups on the standardised difference measure which was calculated for each participant.





**Fig. 1** Mean ( $\pm$ SD) response times to angry and non-angry reactions to ambiguous stories in the current users, ex-users, controls and the total sample

### Correlations with reading time

The correlations between the questionnaire measures and the reading times for the different reactions were examined in each group and in the total sample.

#### Reading time—angry reactions

In the current users, there were significant negative correlations between reading time and MAI—anger arousal ( $r=-0.44$ ,  $P=0.013$ ), MAI—range ( $r=-0.39$ ,  $P=0.034$ ), MAI—hostility ( $r=-0.47$ ,  $P=0.008$ ), MAI—total ( $r=-0.46$ ,  $P<0.013$ ), BIS—motor ( $r=-0.40$ ,  $P<0.024$ ), BIS—cognitive ( $r=-0.42$ ,  $P=0.019$ ) and BIS—total ( $r=-0.44$ ,  $P=0.014$ ). In the controls, there were significant negative correlations between reading time and MAI—range ( $r=-0.52$ ,  $P=0.003$ ), MAI—hostility ( $r=-0.36$ ,  $P=0.046$ ), BIS—cognitive ( $r=-0.40$ ,  $P=0.03$ ), discontent ( $r=-0.39$ ,  $P=0.028$ ) and anger ( $r=-0.49$ ,  $P=0.006$ ) at the time of testing. There were no significant correlations in the ex-users. When the groups were combined, there were significant negative correlations between response time and two of the MAI subscales, range of situations ( $r=-0.23$ ,  $P<0.03$ ) and hostility ( $r=-0.39$ ,  $P<0.001$ ), and with current anger ( $r=-0.25$ ,  $P<0.014$ ) and impulsivity on the STIMP ( $r=-0.21$ ,  $P<0.041$ ).

#### Reading time—non-angry reactions

In the current users, there were significant negative correlations between reading time and MAI—hostility ( $r=-0.36$ ,  $P=0.047$ ) and the BIS—total ( $r=-0.36$ ,  $P=0.046$ ). In the controls, there were significant negative correlations between reading time and MAI—range ( $r=-0.40$ ,

**Table 3** Correlations between reading time difference scores and measures of anger, aggression and impulsivity

|                                         | Current users | Ex-users | Controls | Total    |
|-----------------------------------------|---------------|----------|----------|----------|
| <b>Multidimensional anger inventory</b> |               |          |          |          |
| Anger arousal                           | 0.351*        | 0.031    | 0.172    | 0.208*   |
| Range of situations                     | 0.369*        | 0.028    | 0.303†   | 0.225*   |
| Hostility                               | 0.369*        | 0.063    | 0.263    | 0.247*   |
| Anger in                                | 0.152         | -0.01    | 0.107    | 0.106    |
| Anger out                               | 0.163         | -0.314†  | -0.234   | 0.114    |
| Total                                   | 0.404*        | 0.020    | 0.182    | 0.231*   |
| <b>Aggression questionnaire</b>         |               |          |          |          |
| Physical                                | 0.235         | 0.239    | 0.205    | 0.194    |
| Verbal                                  | 0.198         | 0.296    | 0.155    | 0.216*   |
| Anger                                   | 0.318†        | 0.201    | 0.273    | 0.261*   |
| Hostility                               | 0.358*        | -0.193   | 0.101    | 0.056    |
| Total                                   | 0.382*        | 0.157    | 0.290    | 0.266*-* |
| <b>Anger rating scale</b>               |               |          |          |          |
| Mean                                    | 0.151         | 0.142    | 0.409*   | 0.197†   |
| <b>Barratt impulsivity scale</b>        |               |          |          |          |
| Non-planning                            | 0.004         | 0.009    | 0.194    | 0.037    |
| Motor                                   | 0.153         | 0.071    | 0.151    | 0.131    |
| Cognitive                               | 0.284         | 0.114    | 0.000    | 0.163    |
| Total                                   | 0.163         | 0.06     | 0.116    | 0.132    |

\* $P<0.05$

\*\* $P<0.01$

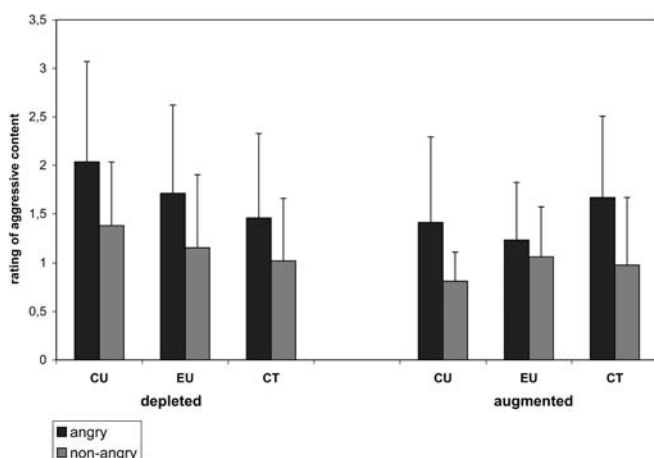
$P=0.025$ ) and BIS—cognitive ( $r=-0.49$ ,  $P<0.007$ ). There were no significant correlations in the ex-users. When the groups were combined, there were significant negative correlations between reading time and the MAI hostility subscale ( $r=-0.3$ ,  $P=0.003$ ) and current impulsivity on the STIMP ( $r=-0.213$ ,  $P=0.042$ ).

#### Reading time—standardised difference

In the current users, there were significant correlations between reading time and several of the MAI and AQ scales and in the controls, with current discontent ( $r=0.40$ ,  $P=0.028$ ) and anger. When the groups were combined, there were significant correlations between reading time and the MAI total score and with three of the subscales, the AQ total and two of the subscales and a trend with current anger (Table 3).

### Correlations with frequency and dose of MDMA

In the current users, neither frequency nor dose of MDMA used was significantly correlated with reading time. In the ex-users, reading time (standardised difference) was correlated with amount of MDMA used per session ( $r=0.38$ ,  $P=0.04$ ) but not with frequency of use. Within this group, people who had taken the highest dose of MDMA per session showed the fastest corrected reading times.



**Fig. 2** Mean ( $\pm$ SD) ratings for aggressive content in the continuing sentences after angry and non-angry reactions in the current users, ex-users and controls after tryptophan depletion and augmentation

### Subject-generated sentences

The continuing sentences, which the participants were asked to write for half of the stories, were rated by two independent raters. The raters were asked to rate the stories for aggressive content (0–4). Of the 12 stories, 9 contained some aggression in the responses. Good agreement between raters was shown. Cronbach alpha ranged between 0.71 and 0.87, and so the mean of the two ratings was taken. When the mean ratings of aggressive content of the sentences following the angry and non-angry reactions were compared, there was a significant difference between reactions ( $F_{1,84}=31.92$ ,  $P<0.0001$ ) but no interaction with group or condition. The rating was higher for the angry reactions in all groups (Fig. 2). There was a tendency for a difference between conditions ( $F_{1,84}=3.68$ ,  $P=0.059$ ) but no interaction with group. Participants in the depleted condition tended to generate more aggressive continuing sentences to all the ambiguous stories.

### Correlations with aggressive content

The relationships between the scores for the different types of sentences (all those containing emotion, angry reaction, non-angry reaction and neutral content) and current mood, reading time, the MAI and the AQ were calculated both in the total sample and in the different groups. All groups showed individual significant correlations between the MAI and AQ scales and aggressive content in the subject generated continuing sentences to emotional stories with non-angry reactions, and this pattern is clearly seen in the total sample (Table 4). Participants with either an angry disposition or who were feeling angry at the time generated aggression particularly when this had not been expressed as a reaction in the story. Aggressive content in these sentences also corre-

**Table 4** Relationship between mean ratings of aggressive content in story endings and questionnaire measures of anger and aggression in total sample

|                                  | All ambiguous stories | Angry reactions | Non-angry reactions | Neutral stories |
|----------------------------------|-----------------------|-----------------|---------------------|-----------------|
| Multidimensional anger inventory |                       |                 |                     |                 |
| Anger arousal                    |                       |                 | 0.371***            |                 |
| Range                            |                       |                 | 0.239*              |                 |
| Hostile outlook                  | 0.297**               |                 | 0.373***            | 0.251*          |
| Anger-in                         | 0.213*                |                 | 0.424***            |                 |
| Anger-out                        |                       |                 |                     |                 |
| Total score                      | 0.190                 |                 | 0.422***            |                 |
| Aggression questionnaire         |                       |                 |                     |                 |
| Anger                            |                       |                 | 0.250*              | 0.271*          |
| Physical                         |                       |                 | 0.228*              |                 |
| Verbal                           | 0.281**               |                 | 0.317**             |                 |
| Hostility                        |                       |                 | 0.259*              |                 |
| Total                            | 0.199                 |                 | 0.361***            |                 |
| Anger rating scale               |                       |                 |                     |                 |
| Total                            | 0.252*                | 0.180           | 0.299**             |                 |

\* $P<0.05$

\*\* $P<0.01$

\*\*\* $P<0.001$

lated significantly with the standardised difference reading time ( $r=0.37$ ,  $P<0.05$ ) in the current users. The faster they were to process (agree with) an angry reaction, the higher the aggressive content in continuations of ambiguous stories with non-angry reactions. However, in the controls, the standardised difference reading time correlated significantly with aggressive content in sentences written at the end of neutral stories ( $r=0.42$ ,  $P<0.05$ ). The faster they were to respond to an angry reaction, the higher the aggressive content in continuations of stories containing no aggression.

## Discussion

This study used a novel measure of cognitive bias to investigate the relationship between anger and aggression and depletion of 5-HT by tryptophan challenge in a young group of substance users. In fact, there were few differences attributable to prior use of MDMA, but cognitive bias was found to relate to both trait and state measures of aggression in substance users.

The groups were well matched on most measures. All groups reported similar levels of cannabis, alcohol and cigarette use and, although the MDMA groups had experimented more with other drugs, this use was infrequent and the major difference between the groups was their current or previous use of ecstasy. The groups did not differ on measures of anger but the ex-users scored higher than the controls on trait aggression. This is in contrast to a previous longitudinal study which found that aggression and irritability scores in ecstasy users decreased after approximately 1 year of abstinence (Gerra

et al. 2000). However, it is difficult to make comparisons in a between-groups study. Our ex-users had had more exposure to MDMA, and aggression ratings have been shown to relate to extent of exposure to MDMA and to be higher in those who use more (Parrott et al. 2000). There were differences between groups on trait impulsivity. Both MDMA groups scored higher on motor impulsivity and the current users were also higher than controls on the total scale. This confirms previous work linking MDMA use to higher scores on measures of impulsivity (Morgan 1998; Parrott et al. 2000; Tuchtenhagen et al. 2000). Impulsivity is often associated with substance misuse itself, but MDMA users have been found to be more impulsive than polydrug users in a study specifically investigating this topic (Morgan 1998). The groups did not differ on current mood, but all subjects felt more sedated and calm at the time that testing took place.

In the current study, subjects read stories describing ambiguous situations to which a central character had either an angry reaction or a non-angry, alternative emotional reaction. The subjects were quicker to respond to the angry than the non-angry reactions and there were no differences between groups. Readers have been shown to form mental representations of fictional characters' emotional states (Gernsbacher et al. 1992) and, therefore, take less time to process information that matches this perception. This result then indicates that these participants as a whole were more likely to expect an angry than an alternative emotional reaction to an ambiguous situation. We did not have a non-substance user control group in the current study, but this pattern of results is in contrast to our previous study which showed a group of healthy young volunteers to have shorter processing times for, and therefore to expect, non-angry reactions (Wingrove and Bond, unpublished observations). Anger may therefore have had more salience for the present young group of substance users. This is in agreement with other studies that have found abstinent substance users to behave more aggressively than non-substance users using controls (Allen et al. 1997; Gerra et al. 2001). We did not use a group of non-substance users in this study. In fact, we chose our groups to be as similar as possible on all variables except MDMA use, as extremely healthy controls, e.g. members of hospital staff (Gerra et al. 2001) are likely to be different from substance users on other variables which may account for differences on tasks measuring anger or aggression. However, in future studies it would be worth trying to recruit non-substance users from the same source as users, if possible. The ex-users took longer to respond to all stories which may indicate a general slowing in performance with respect to emotional material in this group.

The relationship between trait anger and aggression and the time to process the reactions was examined. Both anger and aggression were associated with faster reading of sentences describing angry reactions to ambiguous anger provoking situations, relative to non-angry reactions. This indicates that those with angrier dispositions or ready accessibility to aggressive cognitions were more

likely to be anticipating angry reactions on the part of the fictional characters they were reading about and confirms the results of our previous study (Wingrove and Bond, unpublished observations). Interestingly, this relationship was strongest in the current users and they contributed most to the relationship in the total sample. The experiment was carried out when these participants had stopped taking ecstasy for a period of 3 weeks. It may be that angry cognitions and hostile expectancies are most salient in this abstinence state. The acute effects of MDMA are mainly positive and last for several hours (Vollenweider et al. 1998; Liechti et al. 2000) but residual symptoms can be identified during the following 24 h (Vollenweider et al. 1998) and negative effects on mood (Curran and Travill 1997; Parrott and Lasky 1998) and increased feelings of anger and aggression (Verheyden et al. 2002) have been shown to persist for several days after recreational use. The current participants were all male and, in the latter study, increased feelings of aggression in men were correlated with the amount of MDMA taken 4 days previously but were not associated with length or lifetime consumption. This was interpreted as lending support to a temporary rather than a neurotoxic effect and, in agreement with this, in the current study the ex-users, who had been abstinent for a minimum of 1 year, showed the lowest correlations. It should be noted that the time since stopping ecstasy in the EU group was very varied and ranged from 1 year to 7 years; thus, this group may be more heterogeneous than the other groups. The correlation between the dose of MDMA that they reported usually taking and faster relative processing speeds for angry endings suggests that angry reactions were more readily accessible to ex-users who habitually took the highest doses. However, there was no significant relationship with dose in the current users.

There were also relationships between processing time of both types of story ending and the trait and state measures. People with a disposition to feel angry or to behave impulsively tended to read both types of emotional reaction to ambiguous situations faster. There was also a relationship with current mood in the controls. Those who felt more angry, discontented or impulsive at the time of testing read both types of reaction faster. However, impulsivity was not associated with the standardised difference between the endings. Although both state and trait impulsivity are therefore associated with the more rapid processing of emotional material, this is not specific to anger. Previous studies investigating measures of impulsivity have found poor relationships between self-report and performance measures (Gerbing et al. 1987; Wingrove and Bond 1997; Morgan 1998), but this may be because these studies have largely used behavioural tasks without any emotional content. It may be necessary to design novel processing tasks to explore this relationship further.

The participants were asked to write a continuing sentence to half of the stories presented and the content of these sentences was rated for aggression. Subjects in all groups generated more aggressive continuing sentences to

stories describing angry relative to non-angry reactions. This provides evidence of a conscious or unconscious priming effect (Todorov and Bargh 2002). Aggressive thoughts and feelings were made more available by prior exposure to an angry response to an ambiguous situation. These stories did not require a personal interpretation and, therefore, the influence of trait factors was relatively small. However, there were across-group correlations between trait and state measures of aggression and anger and aggressive content in subject-generated sentences to emotional stories describing non-angry reactions. Subjects with either an angry disposition or who were feeling angry at the time of testing generated more aggressive content in response to ambiguous stories, particularly when anger had not been expressed as a reaction to the situation. Previous work has shown trait aggression to be related to aggressive responses to different types of ambiguous and even neutral material (Dodge 1980; Dill et al. 1997).

Relationships between subject-generated aggressive content in the sentences and reading time were also found within two of the groups. Current users who processed angry endings to the stories relatively faster were more likely to write aggressive continuations to the stories with non-angry endings. Controls who processed angry endings to the stories relatively faster were more likely to write aggressive continuations to the neutral stories. This provides further confirmation that processing time in this task is a valid measure of hostile cognitive bias. It is important to recognise that cultural factors may also be important in endings generated to this sort of task, which emphasises the need to control as many demographic factors as possible between subject groups.

It is perhaps surprising that the acute 5-HT manipulation had little effect. There were no effects on anger or reading times. Although tryptophan depletion has been shown to increase anger (Cleare and Bond 1995; Finn et al. 1998), this effect was confined to groups with high scores on trait aggression or hostility and the current subjects were not selected for trait aggressiveness. There was a tendency for the subjects in the depleted condition to generate more aggression in their continuing sentences to the ambiguous stories containing both types of reaction and this effect merits further investigation. It suggests that the acute decrease in central levels of 5-HT produced by tryptophan depletion may increase accessibility to aggressive thoughts in ambiguous situations.

Ecstasy users have been found to feel more angry a few days after using the drug (Verheyden et al. 2002) but, in the current study, MDMA users did not show greater effects on a task measuring angry cognitive bias than non-users. There are two possible explanations for this. First, it might be that 3 weeks or more abstinence is too long to reveal such an effect. A recent study has shown aggressive mood to be increased after 4 days abstinence but to remit by 7 days (Curran et al., 2003). Our testing period may therefore have been too late to measure subtle cognitive distortions. Second, the use of cannabis may be an important factor. Withdrawal from daily cannabis use

has been associated with behavioural aggression after both 3 days' and 7 days' abstinence (Kouri et al. 1999). Experimental studies of oral and smoked formulations of  $\Delta^9$ -tetrahydrocannabinol (THC) have revealed mood symptoms including increased irritability, anxiety and restlessness to occur on abstinence (Haney et al. 1999a, 1999b). Cannabis use was fairly well matched across groups and so abstinence from cannabis before the study day may have made angry thoughts more accessible in all the participants. Further studies are needed to test these hypotheses.

## References

- Allen TJ, Moeller FG, Rhoades HM, Cherek DR (1997) Subjects with a history of drug dependence are more aggressive than subjects with no drug use history. *Drug Alcohol Depend* 46:95–103
- Beck AT, Steer R, Garbin M (1988) Psychometric properties of the Beck Depression Inventory: 25 years of evaluation. *Clin Psychol Rev* 8:77–100
- Bond AJ, Lader ML (1974) The use of analogue scales in rating subjective feelings. *Br J Med Psychol* 47:211–218
- Bond AJ, Lader MH (1986) A method to elicit aggressive feelings and behaviour via provocation. *Biol Psychol* 22:69–79
- Bond AJ, Wingrove J (2001) The role of serotonin in the modulation of aggression: studies using tryptophan manipulation. In: Martinez M (ed) *Prevention and control of aggression and the impact on its victims*. Kluwer Academic/Plenum Publishers, London
- Bower GH, Morrow DG (1990) Mental models in narrative comprehension. *Science* 247:44–48
- Brown GL, Ebert MH, Goyer PF, Jimerson DC, Klein WJ, Bunney WE, Goodwin FK (1982) Aggression, suicide, and serotonin relationships to CSF metabolites. *Am J Psychiatry* 139:741–745
- Buss AH, Perry M (1992) The aggression questionnaire. *J Pers Soc Psychol* 63:452–459
- Cleare AJ, Bond AJ (1995) The effects of tryptophan depletion and enhancement on subjective and behavioural aggression in normal subjects: evidence for role of 5-HT in control of aggression. *Psychopharmacology* 118:72–81
- Cleare AJ, Bond AJ (1997) Does central serotonergic function correlate inversely with aggression? A study using D-fenfluramine in healthy subjects. *Psychiatry Res* 69:89–95
- Coccaro EF (1989) Central serotonin and impulsive aggression. *Br J Psychiatry* 155:52–62
- Cohen DJ, Eckhart CI, Schagat KD (1998) Attention allocation and habituation to anger-related stimuli during a visual search task. *Aggress Behav* 24:399–409
- Curran HV, Travill RA (1997) Mood and cognitive effects of 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'): week-end 'high' followed by midweek 'low'. *Addiction* 92:821–831
- Curran HV, Verheyden SL (2003) Altered response to tryptophan supplementation after long-term abstinence from MDMA ('Ecstasy') is highly correlated with human memory function. *Psychopharmacology* DOI 10.1007/s00213-003-1463-5
- Curran HV, Rees H, Hoare T, Hoshi R, Bond A (2003) Empathy and aggression: two faces of ecstasy? A study of interpretative cognitive bias and mood change in ecstasy users. *Psychopharmacology* (in press)
- Dill KE, Anderson CA, Anderson KB, Deuser WE (1997) Effects of aggressive personality on social expectations and social perceptions. *J Res Pers* 31:272–292
- Dodge KA (1980) Social cognition and children's aggressive behavior. *Child Dev* 51:162–170
- Finn PR, Young SN, Pihl RO, Ervin FR (1998) The effects of acute plasma tryptophan manipulation on hostile mood: the influence of trait hostility. *Aggress Behav* 24:173–185



- Gerbing DW, Ahadi SA, Patton JH (1987) Towards a conceptualization of impulsivity: components across the behavioral and self-report domains. *Multivariate Behav Res* 22:357–379
- Gernsbacher MA, Goldsmith HH, Robertson RRW (1992) Do readers represent characters' emotional states? *Cogn Emotion* 6:89–111
- Gerra G, Zaimovic A, Giucastro G, Maestri D, Monica C, Sartori R, Caccavari R, Delsignore R (1998) Serotonergic function after ( $\pm$ )3,4-methylenedioxymethamphetamine ("ecstasy") in humans. *Int Clin Psychopharmacol* 13:1–9
- Gerra G, Zaimovic A, Rizzi O, Timpano M, Neri E, Marzocchi GF, Delsignore R, Brambilla F (2000) Long-lasting effects of  $\pm$ 3,4-methylenedioxymethamphetamine (ecstasy) on serotonin function in humans. *Biol Psychiatry* 47:127–136
- Gerra G, Zaimovic A, Ampollini R, Giusti F, Delsignore R, Raggi MA, Laviola G, Macchia T, Brambilla F (2001) Experimentally induced aggressive behavior in subjects with 3,4-methylenedioxymethamphetamine ("Ecstasy") use history. *Psychobiological correlates*. *J Subst Abuse* 13:471–491
- Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW (1999a) Abstinence symptoms following oral THC administration to humans. *Psychopharmacology* 141:385–394
- Haney M, Ward AS, Comer SD, Foltin RW, Fischman MW (1999b) Abstinence symptoms following smoked marijuana in humans. *Psychopharmacology* 141:395–404
- Kosten TR, Markou A, Koob GF (1998) Depression and stimulant dependence: neurobiology and pharmacotherapy. *J Nerv Ment Dis* 186:737–745
- Kouri EM, Pope HG Jr, Lukas SE (1999) Changes in aggressive behavior during withdrawal from long-term marijuana use. *Psychopharmacology* 143:302–308
- Liechti ME, Baumann C, Gamma A, Vollenweider FX (2000) Acute psychological effects of 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy") are attenuated by the serotonin uptake inhibitor citalopram. *Neuropsychopharmacology* 22:513–521
- Manuck SB, Flory JD, McCaffery JM, Matthews KA, Mann JJ, Muldoon MF (1998) Aggression, impulsivity, and central nervous system serotonergic responsivity in a nonpatient sample. *Neuropsychopharmacology* 19:287–299
- Morgan MJ (1998) Recreational use of Ecstasy (MDMA) is associated with elevated impulsivity. *Neuropsychopharmacology* 19:252–264
- Nelson HE (1982) The national adult reading test (NART): test manual. NFER-Nelson, Windsor, UK
- Parrott AC, Lasky J (1998) Ecstasy (MDMA) effects upon mood and cognition: before, during and after a Saturday night dance. *Psychopharmacology* 139:261–268
- Parrott AC, Sisk E, Turner JJD (2000) Psychobiological problems in heavy "ecstasy" (MDMA) polydrug users. *Drug Alcohol Depend* 60:105–110
- Patton JH, Stanford MS, Barratt ES (1995) Factor structure of the Barratt Impulsiveness Scale. *J Clin Psychol* 51:768–774
- Rule BG, Taylor BR, Dobbs AR (1987) Priming effects of heat on aggressive thoughts. *Soc Cogn* 5:131–143
- Schuster P, Lieb R, Lamertz C, Wittchen HU (1998) Is the use of ecstasy and hallucinogens increasing? *Eur Addict Res* 4:75–82
- Siegel JM (1986) The multidimensional anger inventory. *J Pers Soc Psychol* 51:191–200
- Spielberger CD, Gorsuch RL, Lushene RE (1970) Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto
- Todorov A, Bargh JA (2002) Automatic sources of aggression. *Aggress Violent Behav* 7:53–68
- Tuchenhagen F, Daumann J, Norra C, Gobbele R, Becker S, Pelz S, Sass H, Buchner H, Gouzoulis-Mayfrank E (2000) High-intensity dependence of auditory evoked dipole source activity indicates decreased serotonergic activity in abstinent ecstasy (MDMA) users. *Neuropsychopharmacology* 22:608–617
- Van Honk J, Tuiten A, de Haan E, van den Hout M, Stem H (2001) Attentional biases for angry faces: relationships to trait anger and anxiety. *Cogn Emotion* 15:279–297
- Verheyden SL, Hadfield J, Calin T, Curran HV (2002) Sub-acute effects of MDMA (3,4 methylenedioxymethamphetamine, "ecstasy") on mood: evidence of gender differences. *Psychopharmacology* 161:23–31
- Vollenweider FX, Gamma A, Liechti M, Huber T (1998) Psychological and cardiovascular effects and short-term sequelae of MDMA ("ecstasy") in MDMA-naïve healthy volunteers. *Neuropsychopharmacology* 19:241–251
- Wingrove J, Bond AJ (1997) Impulsivity: a state as well as trait variable. Does mood awareness explain low correlations between trait and behavioural measures of impulsivity? *Pers Individual Diff* 22:333–339
- Young SN, Smith SE, Pihl RO, Ervin FR (1985) Tryptophan depletion causes a rapid lowering of mood in normal males. *Psychopharmacology* 87:173–177