Individual differences in mood reactions to \textit{d-}amphetamine: a test of three personality factors

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Individual differences in self-reported mood following either 5 mg or 10 mg \textit{d-}amphetamine challenge were examined in order to test the modifying role of three factors of personality, viz., the Eysencks' psychoticism, Cloninger's novelty seeking, and Depue and Collins' extraversion. In a double-blind study, mood measures (energetic arousal, tense arousal, and hedonic tone) were taken immediately following a single-dose of \textit{d-}amphetamine and then again after 90 min. The results showed significant \textit{psychoticism} \textit{\times d-}amphetamine interactions for both drug doses: \textit{d-}amphetamine increased energetic arousal and hedonic tone, and reduced tense arousal, only in low psychoticism individuals; in high psychoticism individuals, it led to lowered energetic arousal and hedonic tone, and increased tense arousal. Neither novelty seeking nor extraversion modified the effects of \textit{d-}amphetamine. These data suggest a link between psychoticism and dopaminergic functioning, although they do not rule out the involvement of other transmitter systems (e.g. noradrenergic). In common with other studies, such findings point to the important role that well-established factors of personality play in accounting for individual differences in reactions to psychoactive drugs. It is concluded that the routine inclusion of personality measures in future psychopharmacological studies may help to refine the characterization of drug effects.

\textit{Key words: amphetamine; extraversion; individual differences; mood; novelty seeking; paradoxical effects; psychosis-proneness; psychoticism; substance abuse}

\textbf{Introduction}

Amphetamine is a prototypic psychomotor stimulant that potentiates the release of both dopamine and noradrenaline. Its behavioural profile depends upon both dose and mode of administration. At acute low doses, it produces euphoria, positive affect, feelings of friendliness, alertness, energy and mental activity (Hutchison \textit{et al.}, 1999). These subjective feelings have a parallel in improved cognitive performance, including learning and visual coordination (Carrol \textit{et al.}, 1982), reaction time, vigilance and memory performance (Rapaport \textit{et al.}, 1980).

However, negative effects of amphetamine are also found, including aggression (Bell and Hepper, 1987) and psychosis (Ellinwood, 1967; Angrist and Gershon, 1970; Griffin \textit{et al.}, 1972; Angrist \textit{et al.}, 1974). In addition, amphetamine administered at non-psychotomimetic doses can provoke or exacerbate psychotic symptoms in schizophrenic patients (Lieberman \textit{et al.}, 1990). Both aggression and psychosis can be reversed by administration of the dopamine antagonist, haloperidol (see Zuckerman, 1991), suggesting that the effects of amphetamine are, to a significant extent, dopamine mediated.

There are also marked individual differences in reactions to amphetamine challenge (Chait, 1993). For example, Tecce and Cole (1974), studying the effects of 10 mg \textit{d-}amphetamine on the electrophysiological wave negative contingent variation (CNV), reported that 65% of individuals became drowsy, while 35% of individuals become more alert. Although such findings point to important individual differences in reactions to amphetamine challenge, the modifying role of well-established factors of personality has not yet been characterized.

In this article, we examine the effects of two (single) low doses of \textit{d-}amphetamine (5 and 10 mg) on self-reported mood, and contrast three candidate factors of personality that may account for these individual differences, viz. (1) psychoticism, (2) novelty seeking, and (3) extraversion.

\textbf{Psychoticism}

A number of lines of evidence point to the putative association of amphetamine and psychosis. The relationship between amphetamine and psychosis/aggression is similar to that observed between psychoticism and psychosis-proneness/aggression (Eysenck, 1992). Empirical evidence supports this putative association: (1) hyper-dopaminergic activity is related to positive symptoms in schizophrenia (Carlsson, 1988); (2) amphetamine has been shown to produce schizophrenic-like cognitive deficits on experimental tasks (e.g. disrupted latent inhibition, LI) in normal...
volunteers (e.g. Gray et al., 1992; Thornton et al., 1996); and (3) latent inhibition is disrupted in high psychoticism individuals (Baruch et al., 1988a; Lubow et al., 1992), as well as in acute schizophrenics (Baruch et al., 1988b). Furthermore, as stated earlier, amphetamine can lead to psychosis and aggression, and psychoticism seems to be a risk factor for both psychosis and aggressive antisocial behaviour (Eysenck and Eysenck, 1976; although there remains debate over the psychotism/psychosis link; e.g. Claridge, 1997). The association of psychoticism and central dopaminergic functioning has been supported using single-photon emission tomography (Gray et al., 1994), suggesting that psychoticism has a dopaminergic basis. To the extent that amphetamine potentiates dopaminergic functioning, a prima facie case may be made for psychoticism being associated with individual differences in reactions to amphetamine challenge. However, to date, no study has reported a psychoticism–amphetamine interaction.

It is possible that high psychoticism individuals have chronic (trait-like) hyper-dopaminergic functioning. As high psychoticism is associated with negative mood, including irritation and aggression, it may be hypothesized that increasing levels of dopamine (via amphetamine challenge) would lead to increased (hyper-dopamine-related) negative mood states. In contrast, low psychoticism individuals, putatively in a hypo-dopaminergic condition, may benefit from this dopamine agonism, leading to an improvement in mood state.

Novelty seeking

Other data suggest that novelty seeking may modify the effects of amphetamine. This personality factor represents one of three main temperament factors in Cloninger’s (1986) neurobehavioural model of personality, which purports to explain three genetically independent dimensions. Novelty seeking relates to the tendency towards exploratory behaviour and intense excitement in response to novel stimuli; reward dependence, the tendency to respond intensively to reward and succorance and to learn to maintain rewarded behaviour; and harm avoidance, the tendency to respond intensively to aversive stimuli and to learn to avoid punishment, novelty and non-reward passively.

Recent molecular genetics research has reported associations between measures of novelty seeking and a dopamine receptor gene (D4DR) (e.g. Benjamin et al., 1996; Ebstein et al., 1996; Noble et al., 1998) but, there have also been failures to replicate these promising associations (e.g. Gelernter et al., 1997; Sander et al., 1997; Sullivan et al., 1998). However, because psychoticism has not been measured in these molecular genetic studies, it is not known whether this factor has a higher affinity than novelty seeking with the D4DR gene (psychoticism and novelty seeking traits are highly positively correlated; Corr et al., 1995).

Fleming et al. (1995) reported that, for one of several measures of cognitive performance (i.e. verbal memory), amphetamine disrupted performance in high novelty seeking individuals, but improved performance in low novelty seeking individuals. Hutchison et al. (1999) found that a subscale of the Sensation Seeking Scale (SSS; Zuckerman et al., 1978), disinhibition, not novelty seeking, significantly moderated the effects of (20 mg) d-amphetamine on self-reported mood (although there was a weak trend for novelty seeking in this study).

On the basis of the findings of Fleming et al. (1995), we may predict that, in a similar manner to psychoticism, amphetamine should increase negative mood states in high novelty seeking individuals; while, in contrast, low novelty seeking individuals may benefit from amphetamine challenge. However, on the basis of a weak trend in the data of Hutchison et al. (1999), it could also be predicted that, consistent with Cloninger’s theory, that high novelty seeking individuals should show improved mood under amphetamine challenge. This latter prediction is consistent with the association of novelty seeking to vulnerability to substance abuse.

Extraversion

Extraversion may also be considered a potentially important modifying factor. For example, Depue and Collins (1999) developed an elegant neurobiological model of personality and positive incentive motivation that argues for extraversion being considered the trait underlying dopamine functioning. Fischer et al. (1997), using positron emission tomography, found significant associations between extraversion and areas of the brain rich in dopamine terminals. Gupta (1970) found that, in a verbal operant conditioning paradigm, extraversion and amphetamine interacted, with extraverted individuals showing better conditioning under amphetamine, introverted individuals worse conditioning. However, Gupta’s results are difficult to interpret because the measure of extraversion used (taken from the Eysenck Personality Inventory; Eysenck and Eysenck, 1964) contained, in addition to sociability, elements of impulsivity, which in the Eysenck’s later version of their questionnaire [i.e. the Eysenck Personality Questionnaire (EPQ); see below] have largely been removed, with much of impulsivity’s variance migrating to psychoticism. However, the sociability component of extraversion has been found to modify the effects of the dopamine antagonist, haloperidol (Corr and Kumari, 1997), indicating the direct involvement of extraversion. In the light of previous work relating level of arousal to hedonic tone (inverted-U), amphetamine should improve mood in (low arousal) extraverted individuals, perhaps lowering it in (over-aroused) introverted individuals.

Mood was chosen as the main variable of interest as it may be conceptualized in biopsychological terms, exerting a broad range of influences on behaviour (Thayer, 1989). Also, mood measures provide a convenient means by which to index central systems of drug-induced activation. Psychometric research indicates that three basic mood dimensions capture the majority of variance in self-report instruments: energetic arousal and hedonic tone (which measure different aspects of positive affect), and tense arousal (which measures negative affect) (Matthews et al., 1990). Given the vagaries of the effects of low doses of amphetamine on mood, it was decided to use two (5 and 10 mg) doses for completeness (Tecce and Cole, 1974, found significant paradoxical effects with 10 mg). We also examined possible gender effects (Hutchison et al., 1999).

Methods and materials

Participants

Sixty-three volunteers, 32 males (mean age = 29.91 years, SD = 5.58) and 31 females (mean age = 27.26, SD = 6.09) participated. Volunteers were recruited through local newspaper advertisements, and all underwent a full medical screening prior to
the testing session. Voluntees were excluded from the study if they had medical contraindications to d-amphetamine (i.e. thyroid dysfunction, glaucoma, anorexia, allergies, Parkinsonism, bowel or muscle problems, heart or liver disease, hypotension or hypertension, violent or rapid mood changes, psychiatric illness, drug or alcohol dependency, lactation or if they were pregnant), as assessed by a physician, or evidence of recent use of certain drugs (morphine, methadone, cannabis, cocaine, and drugs from the amphetamine and benzodiazepine groups), as assessed by a urine screen. Participants' weights were within the normal range and evenly distributed over the drug conditions. Volunteers received £50.00 for their participation.

Psychometric measures

The UWIST Mood Adjective Checklist (UMACL: Matthews et al., 1990), which measures Energetic Arousal (EA), Tense Arousal (TA), and Hedonic Tone (HT), was used to index self-reported mood. High EA and HT reflect positive emotions, TA negative emotion (Thayer, 1989).

The Eysenck Personality Questionnaire (EPQ; Eysenck and Eysenck, 1975) was used to measure Extraversion (E), Neuroticism (N), Psychoticism (P), and response distortion (Lie, L). N is a well-known measure of personality that is strongly associated with anxiety, negative emotionality and general dysphoria. The Tridimensional Personality Questionnaire (TPQ) (Cloninger, 1989) was used to measure Harm Avoidance (HA), Reward Dependence (RD), and Novelty Seeking (NS) (it may also be scored for a fourth factor, Persistence, that is taken from the fourth subfactor, RD4, of RD). TPQ factors correlate with EPQ factors (Corr et al., 1995); for example, HA is positively correlated with N, negatively with E. No exclusion criteria were applied to the random sampling of personality variables.

Design

Participants were tested twice on the mood measures, once immediately following (0, 5 or 10 mg) d-amphetamine (AMP) administration, and once again after 90 min. Each participant received one of three doses of AMP (either two empty capsules (placebo); one 5 mg capsule (5 mg, and one placebo); or two 5 mg capsules (10 mg) dexamphetamine) in a double-blind design (opaque gelatine capsules were used in all conditions). Twenty-two participants were randomly assigned to each AMP condition, counterbalancing for gender. Incomplete or unscorable questionnaires were found for three participants, reducing data to 21 in placebo (male/female ratio: 11/10) 22 in 5 mg AMP (10/12), and 20 in 10 mg AMP (11/9).

AMP dose and administration was based upon Gray et al. (1992), who showed that AMP plasma levels (expressed in μg units) significantly differed between 0, 5 and 10 mg. Following the analysis procedure reported in Gray et al. (1992), we found a significant difference in AMP plasma levels between the drug groups \(F(2,59) = 66.93, \text{MSE} = 19.27, p < 0.001\) (placebo mean = 0, SD = 0; 5 mg = 7.24, 4.70; 10 mg = 15.86, 6.05).

Procedure

Upon arrival, participants were informed that they would be required to swallow capsules which might contain a stimulant drug; the possible side-effects of amphetamine (tension, irritation, etc.) were explained; and they then signed a consent form. Blood pressure and pulse, rate monitoring by a research nurse, then began, and following the taking of these first readings, the mood and personality questionnaires were issued (order: UMACL, EPQ, TPQ), and participants swallowed the capsules. The UMACL mood scales took a few minutes to complete; the EPQ and TPQ approximately 10 min (all questionnaires were completed with 15 min of the capsules being swallowed). The UMACL was issued for a second time, approximately 90 min after drug administration.

Oral administration of amphetamine is known to produce highest plasma concentrations around 90 min (Wan et al., 1978); however, levels start to ascend long before this time, leading to behavioural effects from approximately 30 min. In this study, it was not expected that amphetamine effects would start to be seen much before 30 min, by which time all psychometric measures have been taken. The procedures of the study were approved by the Ethics Committee of the Institute of Psychiatry/Maudsley Hospital.

Statistical analysis

Mood difference (Δmood) scores comprised the main dependent measures (a +Δ represented a pre-post increase in mood score; a –Δ a reduction in mood score). Two-way multivariate analysis of variance (MANOVA) was used to analyse simultaneously ΔEA (energetic arousal), ΔTA (tension arousal) and ΔHT (hedonic change). Each MANOVA model contained one personality measure (psychoticism, novelty seeking, or extraversion; entered as continuous variables), and two a priori contrasts on the AMP factor (i.e. placebo versus 5 mg; and placebo versus 10 mg). Entering personality as a continuous variable is comparable to moderated multiple regression, and is preferable to taking median splits on the personality scales because of the preservation of statistical power (Cohen, 1968) and the reduction of statistical artefact (Bissonnette et al., 1990).

Results

Table 1 shows the means and standard deviations for the EPQ, TPQ and (time 1) UMACL mood measures, and correlations between personality and mood scores at the start of the experiment. There were no significant differences in personality scores between the drug conditions, save for neuroticism, \(F(2,59) = 3.55, \text{MSE} = 27.17\), \(p < 0.05\), which was lower in 5 mg (\(M = 7.73, \text{SD} = 4.59\)) than in either placebo (11.24, 5.06) or 10 mg (11.56, 6.00). Table 2 provides the intercorrelations of the personality variables. Psychoticism, extraversion and novelty seeking were only very weakly correlated.

Age and gender were not correlated with any of the Δmood scores (\(ps > 0.05\)). ΔEA and ΔTA were uncorrelated (\(ps > 0.05\)), indicating that these two measures of arousal were independent factors; ΔHT was positively, but weakly, correlated with ΔEA (\(r = 0.25\), \(p < 0.05\)) and negatively with ΔTA (\(r = –0.28\), \(p < 0.05\)).

Effects of amphetamine

Table 3 gives descriptive statistics for Δmood in each AMP condition. In order to examine the effects of AMP, and possible effects of gender, a two-way (3 AMP × 2 gender) multivariate analysis of variance (MANOVA) was conducted with the three mood change measures comprising the dependent variables. There were no main or interactions effects (\(ps > 0.05\)).
Psychoticism interactions with the placebo vs. 5 mg \( [F(3,55) = 2.91, p < 0.05] \) and the placebo versus 10 mg \( [F(3,55) = 3.75, p < 0.02] \) contrasts were significant. The main effect of Psychoticism was nonsignificant \( [F(3,55) = 0.64] \).

A further analysis was conducted on a contrast between 5 and 10 mg (ignoring placebo). This psychoticism \( \times \) AMP effect was nonsignificant \( [F(3,36) = 0.26] \) indicating that the interaction of psychoticism with AMP did not differ at the two doses. Also, the AMP (5 versus 10) levels had very similar effects on \( \Delta \)mood \( [F(3,36) = 0.07, \text{ not significant}] \). Therefore, the two doses were collapsed into a single level of AMP for further univariate analysis of the \( \Delta \)mood change scores.

Table 1 Means and standard deviations (SD) for EPQ and pre–test UMACL ratings, and personality-mood Pearson correlations

<table>
<thead>
<tr>
<th>EPQ</th>
<th>Mean</th>
<th>SD</th>
<th>EA</th>
<th>TA</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extraversion</td>
<td>13.85</td>
<td>5.33</td>
<td>0.17</td>
<td>-0.22</td>
<td>0.38**</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>10.10</td>
<td>5.43</td>
<td>-0.29*</td>
<td>0.38**</td>
<td>-0.40**</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>3.17</td>
<td>1.93</td>
<td>-0.23</td>
<td>0.04</td>
<td>-0.22</td>
</tr>
<tr>
<td>Lie</td>
<td>6.42</td>
<td>3.49</td>
<td>0.36**</td>
<td>-0.25*</td>
<td>0.24</td>
</tr>
<tr>
<td>TPQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novelty seeking</td>
<td>18.76</td>
<td>4.89</td>
<td>-0.07</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>12.81</td>
<td>5.87</td>
<td>-0.08</td>
<td>0.33**</td>
<td>-0.24</td>
</tr>
<tr>
<td>Reward dependence</td>
<td>17.46</td>
<td>5.13</td>
<td>0.17</td>
<td>-0.05</td>
<td>0.18</td>
</tr>
<tr>
<td>UMACL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energetic arousal (EA)</td>
<td>21.76</td>
<td>3.49</td>
<td>–</td>
<td>-0.19</td>
<td>0.36**</td>
</tr>
<tr>
<td>Tense arousal (TA)</td>
<td>16.60</td>
<td>4.72</td>
<td>–</td>
<td>–</td>
<td>-0.57**</td>
</tr>
<tr>
<td>Hedonic tone (HT)</td>
<td>25.83</td>
<td>3.92</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

EPQ, Eysenck Personality Questionnaire; TPQ, Tridimensional Personality Questionnaire; UMACL, UWIST Mood Adjective Checklist.

\* \( p < 0.05 \); \** \( p < 0.01 \).

Table 2 Pearson correlations for personality variables

<table>
<thead>
<tr>
<th>N</th>
<th>P</th>
<th>L</th>
<th>NS</th>
<th>HA</th>
<th>RD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.27*</td>
<td>-0.23</td>
<td>0.16</td>
<td>0.29*</td>
<td>-0.59**</td>
</tr>
<tr>
<td>E</td>
<td>0.08</td>
<td>-0.26*</td>
<td>0.04</td>
<td>0.46**</td>
<td>-0.17</td>
</tr>
<tr>
<td>N</td>
<td>-0.26*</td>
<td>0.17</td>
<td>0.13</td>
<td>-0.01</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>-0.32*</td>
<td>-0.15</td>
<td>0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>-0.29*</td>
<td>-0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NS</td>
<td>-0.31*</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HA</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

\* \( p < 0.05 \); \** \( p < 0.01 \).

Table 3 Means and standard deviations (SD) for mood changes scores in placebo and \( \delta \)-amphetamine (AMP) groups

<table>
<thead>
<tr>
<th>Energetic arousal</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-0.14</td>
<td>4.21</td>
<td>21</td>
</tr>
<tr>
<td>5 mg AMP</td>
<td>-0.27</td>
<td>4.05</td>
<td>22</td>
</tr>
<tr>
<td>10 mg AMP</td>
<td>-0.55</td>
<td>3.84</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tense arousal</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-0.19</td>
<td>4.46</td>
<td>21</td>
</tr>
<tr>
<td>5 mg AMP</td>
<td>-1.54</td>
<td>2.40</td>
<td>22</td>
</tr>
<tr>
<td>10 mg AMP</td>
<td>-0.30</td>
<td>4.14</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hedonic tones</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-0.62</td>
<td>3.46</td>
<td>21</td>
</tr>
<tr>
<td>5 mg AMP</td>
<td>-0.14</td>
<td>3.37</td>
<td>22</td>
</tr>
<tr>
<td>10 mg AMP</td>
<td>0.80</td>
<td>2.14</td>
<td>20</td>
</tr>
</tbody>
</table>

Amphetamine \( \times \) personality

Psychoticism

Psychoticism interactions with the placebo vs. 5 mg \( [F(3,55) = 2.91, p < 0.05] \) and the placebo versus 10 mg \( [F(3,55) = 3.75, p < 0.02] \) contrasts were significant. The main effect of Psychoticism was nonsignificant \( [F(3,55) = 0.64] \).

Combined AMP groups \( \times \) psychoticism. A further analysis was conducted on a contrast between 5 and 10 mg (ignoring placebo). This psychoticism \( \times \) AMP effect was nonsignificant \( [F(3,36) = 0.26] \) indicating that the interaction of psychoticism with AMP did not differ at the two doses. Also, the AMP (5 versus 10) levels had very similar effects on \( \Delta \)mood \( [F(3,36) = 0.07, \text{ not significant}] \).

Figure 1 Regression slopes (unstandardized; \( \pm 1 \) SEM) showing the relationship between (EPQ) psychoticism and energetic arousal change (\( \Delta \)EA) under placebo (\( \beta = 0.58, p < 0.001 \)) and combined (5 and 10 mg) \( \delta \)-amphetamine (\( \beta = -0.12, \text{ not significant} \)) groups (+\( \Delta \), increase in score; -\( \Delta \), decrease in score).
tense arousal in placebo; in AMP, increasing levels of Psychoticism were associated with increased tense arousal (Fig. 2).

**Hedonic tone.** $\Delta HT \ [F(1, 59) = 3.22, Mse = 8.90, p = 0.08]$ related to increasing levels of Psychoticism in placebo being associated with increased hedonic tone, while low Psychoticism scores were associated with reduced hedonic tone; in AMP, low psychoticism scorers showed improved hedonic tone, high psychoticism scorers impaired hedonic tone (Fig. 3).

In addition, the main effect of placebo versus the combined AMP group was significant $[F(3, 57) = 4.45, p < 0.01]$ although these main effects were small in magnitude and dependent on the effects of psychoticism. Follow-up univariate ANOVAs revealed the following effects.

**Energetic arousal.** $\Delta EA \ [F(1, 59) = 5.04, Mse = 14.45, p < 0.05]$ related to a larger energetic arousal reduction in AMP ($M = -0.40$, SD = 3.91) than in the placebo ($M = -0.14$, SD = 4.21) group.

**Tense arousal.** $\Delta TA \ [F(1, 59) = 6.79, Mse = 13.11, p < 0.05]$ related to a larger tense arousal reduction in AMP ($M = -0.95$, SD = 3.36) than in the placebo ($M = -0.19$, SD = 4.46) group.

**Hedonic tone.** $\Delta HT \ [F(1, 59) = 4.93, Mse = 8.90, p < 0.05]$ related to an increase in hedonic tone in the AMP ($M = 0.31$, SD = 2.86), as compared to a reduction in the placebo ($M = -0.62$, SD = 3.46) group.

**Novelty seeking**

Novelty seeking interactions with placebo versus 5 mg $[F(3, 55) = 0.615]$ and placebo versus 10 mg $[F(3, 55) = 0.548]$ contrasts were nonsignificant. Neither main effects of AMP nor novelty seeking were significant.

**Extraversion**

Extraversion interactions with placebo versus 5 mg $[F(3, 54) = 0.06]$ and placebo versus 10 mg, $[F(3, 54) = 0.51]$ contrasts were nonsignificant. Neither main effects of AMP nor extraversion were significant.

**Other personality factors**

For completeness, all other available personality variables (i.e. EPQ Neuroticism; and TPQ Reward Dependence, Harm Avoidance, and Persistence) were entered into identical analyses to the above. None of these analyses revealed any personality $\times$ AMP contrast effects that even approached statistical significance.

**Discussion**

The purpose of this experiment was to examine individual differences in reactions to $d$-amphetamine on self-reported mood in order to contrast the modifying effects of three candidate personality factors, viz. psychoticism, novelty seeking, and extraversion. Only psychoticism received support; there was not even a hint of an effect for the other personality factors measured.
Irrespective of dose, in placebo, psychoticism was positively related to energy and hedonic tone increments, and tension decrements; in d-amphetamine, these effects were either abolished or reversed. This pattern of effects is indicative of a curvilinear relationship, such that too much stimulation is perceived as aversive by high psychoticism individuals; in contrast, d-amphetamine induced stimulation was perceived as pleasurable by low psychoticism individuals (relative to placebo, they showed improved energy and hedonic tone, and reduced tension). These effects are consistent with Tecce and Cole's (1974) observation of paradoxical reactions of amphetamine, producing arousal in some individuals, drowsiness in others. Kavoussi and Coccaro (1993) reported that amphetamine produces a dysphoric response in emotionally volatile individuals; these authors suggested that this negative response might be important in personality disorder. In this regard, it is interesting to note that the trait of psychoticism is closely associated with antisocial, aggressive and volatile behaviour (Eysenck and Eysenck, 1976; Eysenck, 1992).

Although the effects of d-amphetamine are consistent with a dopaminergic mechanism of action, the involvement of other systems, particularly noradrenergic ones, cannot be ruled out. If amphetamine affected noradrenergic systems then we might have expected a significant effect of extraversion, which is the best predictor of individual differences in level of arousal (Corr and Kumari, 1997), or indeed reward dependence which is considered by Cloninger (1987) to reflect noradrenergic functioning. But neither personality factor interacted with the d-amphetamine challenge.

The fact that high psychoticism individuals in placebo showed an increase in positive mood over the course of the experiment may be attributed to two causes. First, putative hyper-dopaminergic functioning may predispose these individuals to perceive the testing environment as pleasurable (in the present experiment, it was nonthreatening, and participants were put at their ease); and, second, this putative effect may have interacted with an expectancy effect. Participants were informed that they might be given a drug that produces elation, positive mood, etc. As high psychoticism is related to sensation seeking and a willingness to take dangerous drugs (Eysenck and Eysenck, 1976), perhaps this putative dopamine × expectancy effect was responsible for the increased hedonic tone and energetic arousal, and decreased tension (high psychoticism and positive incentive motivation have been shown to be related; Kumari et al., 1996). In contrast, participants low in psychoticism, without the benefit of a high (trait) dopaminergic functioning and expectancy effects, may have perceived the testing environment as less pleasant and rather stressful. The reversal of these effects under d-amphetamine indicates that high psychoticism individuals have labile dopaminergic circuits, which might account for their comorbidity of aggression and psychosis-proneness.

The possibility that the association of psychoticism and mood change may have been a result of d-amphetamine altering both sets of scores may be discounted. The psychoticism scale was completed within the first 5 min of drug administration, with most of the psychoticism items being answered before the end of this period. In addition, psychoticism scores were not higher in the drug conditions.

It is possible that analysis of lower-order traits of extraversion (e.g. agency; Depue and Collins, 1999), would have yielded significant results. Also, manipulation of central dopaminergic states by different pharmacological agents, administered by a chronic preparation, may have led to significant effects of both extraversion and novelty seeking. Future research should explore these possibilities. In any event, the present data point to the conclusion that the effects on mood of low doses of d-amphetamine, administered by an acute preparation, are modified by psychoticism, not extraversion or novelty seeking.

Elucidation of individual differences in reactions to psychoactive drugs may be especially important in relation to substance abuse (Chait, 1993). Although definition of the addictive personality has remained elusive, there is evidence that certain aspects of personality are of aetiological significance, specifically those related to the impulsivity/disinhibition continuum (Hutchison et al., 1999). It is theoretically significant that psychoticism is closely related to this disinhibitory continuum. However, previously Hutchison et al. (1999) found that high scores on the Disinhibition scale (Zuckerman et al., 1978) were related to higher levels of self-reported stimulation, elation and positive affect. It is therefore a possibility that this impulsivity/disinhibition continuum is composed of one factor (disinhibition) that relates to euphoric reactions to amphetamine, and is therefore a risk factor for substance abuse, and a second factor (psychoticism) that relates to dysphoric reactions to amphetamine, and is therefore a risk factor for aggression and psychosis. Further research is needed to tease apart these possibilities.

The findings of the present study, in agreement with previous reports, point to the important role that well-established factors of personality play in accounting for individual differences in reactions to psychoactive drugs. In addition to the reduction in the error term, inclusion of personality measures in future psychopharmacological studies may contribute to the characterization of drug effects, including what are sometimes seen as paradoxical reactions, as well as leading to a better understanding of the transmitter specificity of personality factors. This strategy may be especially valuable in attempts to clarify the vulnerability of certain personality groups to psychiatric disorder.

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