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Individual differences in mood reactions to *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 *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 *d*-amphetamine and then again after 90 min. The results showed significant psychoticism × *d*–amphetamine interactions for both drug doses: *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 *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.

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

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 *et al.*, 1999). These subjective feelings have a parallel in improved cognitive performance, including learning and visual coordination (Carrol *et al.*, 1982), reaction time, vigilance and memory performance (Rapaport *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 *et al.*, 1972; Angrist *et al.*, 1974). In addition, amphetamine administered at non-psychotomimetic doses can provoke or exacerbate psychotic symptoms in schizophrenic patients (Lieberman *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 *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 *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.

Psychoticism

A number of lines of evidence point to the putative association of amphetamine and psychoticism. 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 psychoticism/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 Eysencks' 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. Volunteers 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 [$F(2,59) = 66.93$, $Mse = 19.27$, $p < 0.001$ (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, $F(2,59) = 3.55$, $Mse = 27.17$, $p < 0.05$, which was lower in 5 mg ($M = 7.73$, 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 (*p*s > 0.05). ΔEA and ΔTA were uncorrelated ($p > 0.05$), 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 ($r = –.28$, $p < 0.05$).

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 (*p*s > 0.05).

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

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

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

	N	P	L	NS	HA	RD
E	–0.27*	–0.23	0.16	0.29*	–0.59**	0.49**
N		0.08	–0.26*	0.04	0.46**	–0.17
P			–0.26*	0.17	0.13	–0.01
L				–0.32*	–0.15	0.09
NS					–0.29*	0.16
HA						–0.31*

* p <0.05; ** p <0.01.

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

		Mean	*SD*	*n*
Energetic arousal				
	Placebo	–0.14	4.21	21
	5 mg AMP	–0.27	4.05	22
	10 mg AMP	–0.55	3.84	20
Tense arousal				
	Placebo	–0.19	4.46	21
	5 mg AMP	–1.54	2.40	22
	10 mg AMP	–0.30	4.14	20
Hedonic tones				
	Placebo	–0.62	3.46	21
	5 mg AMP	–0.14	3.37	22
	10 mg AMP	0.80	2.14	20

Amphetamine × 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 × psychoticism. A further analysis was conducted on a contrast between 5 and 10 mg (ignoring placebo). This psychoticism × 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 Δmood [$F(3,36) = 0.07$, not significant]. Therefore, the two doses were collapsed into a single level of AMP for further univariate analysis of the Δmood change scores. Comparing placebo versus the combined AMP group, the psychoticism AMP effect [$F(3,57) = 4.74$, $p < 0.01$] was significant. Follow-up univariate ANOVAs revealed the following.

Energetic arousal. ΔEA [$F(1,59) = 7.29$, $Mse = 14.45$, $p < 0.01$] related to increasing levels of psychoticism in placebo being associated with increased energetic arousal; AMP served to abolish this positive association (Fig. 1).

Tense arousal. ΔTA [$F(1,59) = 6.47$, $Mse = 13.11$, $p < 0.02$] related to increasing levels of Psychoticism being associated with reduced

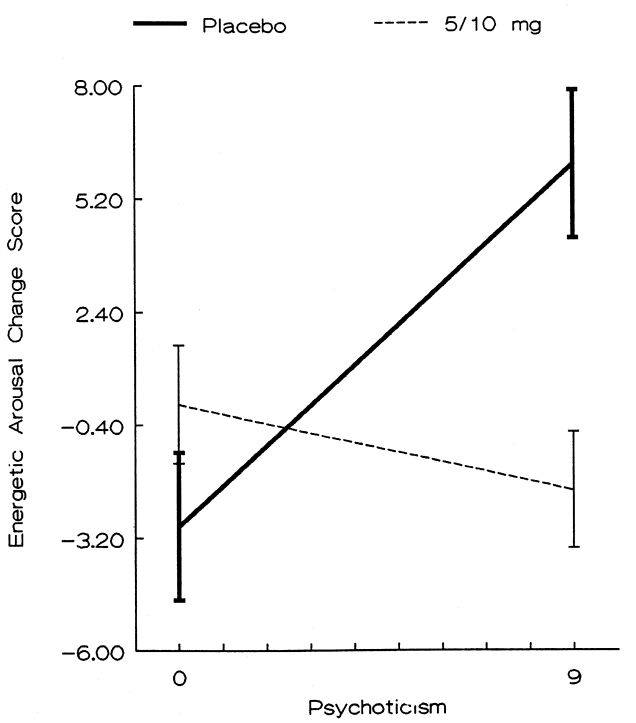

Figure 1 Regression slopes (unstandardized; ± 1 SEM) showing the relationship between (EPQ) psychoticism and energetic arousal change (ΔEA) under placebo (β = 0.58, $p < 0.001$) and combined (5 and 10 mg) *d*-amphetamine (β = –0.12, not significant) groups (+Δ, increase in score; –Δ, decrease in score)

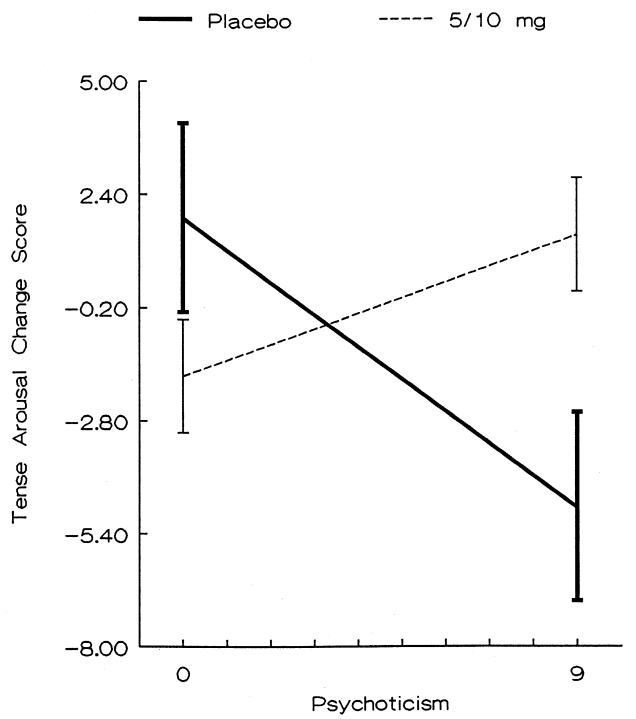

Figure 2 Regression slopes (unstandardized; ± 1 SEM) showing the relationship between (EPQ) psychoticism and tense arousal change (ΔTA) under placebo (β = –0.41, $p = 0.07$) and combined (5 and 10 mg) *d*-amphetamine (β = 0.22, not significant) groups (+Δ, increase in score; –Δ, decrease in score)

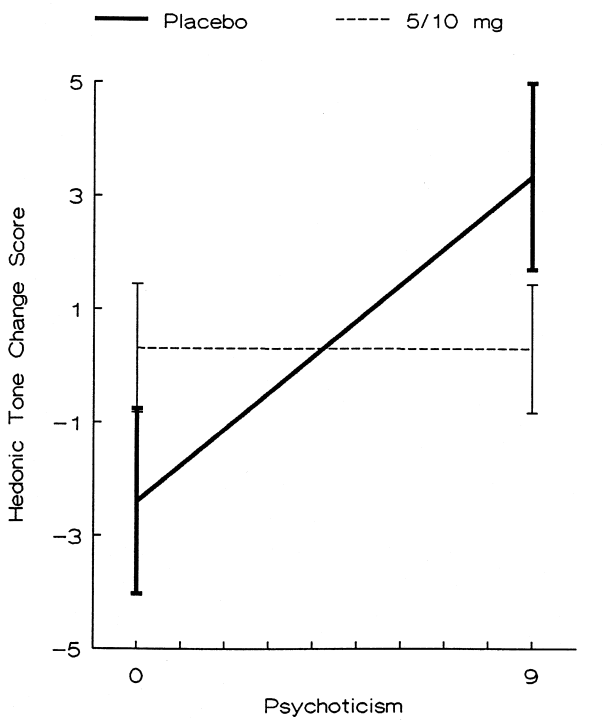

Figure 3 Regression slopes (unstandardized; ± 1 SEM) showing the relationship between (EPQ) psychoticism and hedonic tone change (ΔHT) under placebo (β = 0.45, $p < 0.05$) and combined (5 and 10 mg) *d*-amphetamine (β = –0.01, not significant) groups (+Δ, increase in score; –Δ, decrease in score)

tense arousal in placebo; in AMP, increasing levels of Psychoticism were associated with increased tense arousal (Fig. 2).

Hedonic tone. ΔHT [$F(1,59) = 3.22$, $Mse = 8.90$, $p = 0.08$] 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. ΔEA [$F(1,59) = 5.04$, $Mse = 14.45$, $p < 0.05$] 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. ΔTA [$F(1,59) = 6.79$, $Mse = 13.11$, $p < 0.05$] 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. ΔHT [$F(1,59) = 4.93$, $Mse = 8.90$, $p < 0.05$] 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 × 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, administrated 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, specificially 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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References

Angrist B M, Gershon S (1970) The phenomenology of experimentally induced amphetamine psychosis: preliminary observation. Biol Psychiatry *2*: 95–107

Angrist B, Sathananthan G, Wilk S, Gershon S (1974) Amphetamine psychosis: behavioural and chemical aspects. J Psychiat Res *11*: 13

Baruch I, Hemsley D R, Gray J, A. (1988a) Latent inhibition and 'psychotic proneness' in normal subjects. Person Indiv Diff *9*: 777–784

Baruch I, Hemsley D R, Gray J A (1988b) Differential performance of acute and chronic schizophrenics in a latent inhibition task. J Nerv Ment Dis *176*: 598–606

Bell R, Hepper P G (1987) Catecholamines and aggression in animals. Behav Brain Res *23*: 1–21

Benjamin J, Li L, Patterson C, Greenberg B D, Murphy D L, Hamer D H (1996) Population and familial association between the D4 dopamine receptor gene and measures of novelty seeking. Nature Genet *12*: 81–84

Bissonnette V, Ickes W, Berstein I, Knowles E (1990) Personality moderating variables: a warning about statistical artefact and a comparison of analytic techniques. J Person *58*: 657–587

Carlsson A (1988) The current status of the dopamine hypothesis of schizophrenia. Neuropsychopharmacology *1*: 179–203

Carrol E N, Zuckerman M, Vogel W H (1982) A test of the optimal level of arousal theory of sensation seeking. J Person Soc Psychol *42*: 572–575

Chait L D (1993) Factors influencing the reinforcing and subjective effects of *d*-amphetamine in humans. Behav Pharmacol *4*: 191–199

Claridge G (1997) Eysenck's contribution to understanding psychopathology. In Nyborg H (ed), The scientific study of human nature: tribute to Hans J. Eysenck at 80, pp. 364–387. Elsevier Sciences, London

Cloninger C R (1986) A unified biosocial theory of personality and its role in the development of anxiety states. Psychiatr Dev *3*: 167–226

Cloninger C R (1987) Neurogenetic adaptive mechanisms in alcoholism. Science *236*: 410–416

Cloninger C R (1989) The tridimensional personality questionnaire. Department of Psychiatry and Genetics, Washington University School of Medicine

Cohen J (1968) Multiple regression as a general data-analytic system. Psych Bull *70*: 426–443

Corr P J, Kumari V (1997) Sociability/impulsivity and attenuated dopaminergic arousal: critical flicker/fusion frequency and procedural learning. Person Indiv Diff *22*: 805–815

Corr P J, Pickering A D, Gray J A (1995) Personality and reinforcement in associative and instrumental learning. Person Indiv Diff *19*: 47–71

Depue R A, Collins P F (1999) Neurobiology of the structure of personality: dopamine, facilitation of incentive motivation, and extraversion. Behav Brain Sci *22*: 491–533

Ebstein R P, Novick O, Umansky R, Priel B, Osher Y, Blaine D, Bennett E R, Nemanov L, Katz M, Bemaker R H (1996) Dopamine D4 receptor (D4DR) exon III polymorphism associated with the human personality trait of novelty seeking. Nature Genet *12*: 78–80

Ellinwood E H (1967) Amphetamine psychosis I: description of the individuals and process. J Nerv Ment Dis *144*: 273

Eysenck H J (1992) The definition and measurement of psychoticism. Person Indiv Diff *13*: 757–785

Eysenck H J, Eysenck S B G (1964) Eysenck personality inventory. University of London Press, London

Eysenck H J, Eysenck S B G (1975) Manual of the Eysenck personality questionniare (adults). Hodder and Stoughton, London

Eysenck H J, Eysenck S B G (1976) Psychoticism as a dimension of personality. Hodder and Stoughton, London

Fischer H, Wik G, Fredrikson M (1997) Extraversion, neuroticism and brain function: a PET study of personality. Person Indiv Diff *23*: 345–353

Fleming K, Bigelow L B, Weinberger D R, Goldberg T E (1995) Neuropsychological effects of amphetamine may correlate with personality characteristics. Psychopharmacol Bull *31*: 357–362

Gelernter J, Kranzler H, Coccaro E, Siever L, New A, Mulgrew C L (1997) D4 dopamine-receptor (DRD4) alleles and novelty seeking in substance-dependent personality-disorder, and control subjects. Am J Hum Genet *61*: 1144–1152

Gray N S, Pickering A D, Hemsley D R, Dawling S, Gray J A (1992) Abolition of latent inhibition by a single 5 mg dose of *d*-amphetamine in man. Psychopharmacology *107*: 425–430

Gray N S, Pickering A D, Gray J A (1994) Psychoticism and dopamine D2 binding in the basal ganglia using single-photon emission tomography. Person Indiv Diff *17*: 431–434

Griffin J D, Cavanaugh J, Held J, Oates J A (1972) Dextro-amphetamine: evaluation of psychomimetic properties in man. Arch Gen Psychiatry *26*: 97–100

Gupta B S (1970) The effects of extraversion and stimulant and depressant drugs on verbal conditioning. Acta Psychologia *34*: 505–510

Hutchison K E, Wood M D, Swift R (1999) Personality factors moderate subjective and psychophysiological responses to *d*-amphetamine in humans. Exp Clin Psychoharmacol *7*: 493–501

Kumari V, Corr P J, Wilson G D, Kaviani H, Thornton J C, Checkley S A, Gray J A (1996) Personality and modulation of the startle reflex by emotionally toned filmclips. Person Indiv Diff *21*: 1029–1041

Kavoussi R J, Coccaro E F (1993) The amphetamine challenge test correlates with affective lability in healthy volunteers. Psychiat Res *48*: 219–228

Lieberman J A, Kinon B J, Loebel A D (1990) Dopaminergic mechanism in idiopathic and drug-induced psychosis. Schiz Bull *16*: 97–109

Lubow R R, Ingbergsachs Y, Zalsteunorda N, Gewirtz J C (1992) Latent inhibition in low and high psychotic-prone normal subjects. Person Indiv Diff *13*: 563–572

Matthews G, Jones D M, Chamberlain A G (1990) Refining the measurement of mood: the UWIST mood adjective checklist. Br J Psychol *81*: 17–42

Noble E P, Ozkaragoz T Z, Ritchie T L, Zhang _ X, Belin T R, Sparkes R S (1998) D-2 and D-4 dopamine receptor polymorphisms and personality. Am J Med Genet *81*: 257–267

Rapaport J L, Buchsbaum M S, Weingarten H, Zahn T P, Ludlow C, Mikkelsen E J (1980) Dextroamphetamine: its cognitive and behavioural effects in normal and hyperactive boys. Arch Gen Psychiatry *37*: 933–943

Sander T, Harms H, Dufeu P, Kuhn S, Rommelspacher H, Schmidt L G (1997) Dopamine D4 receptor exon III alleles and variations of novelty seeking in alcoholics. Am J Med Genet *74*: 483–487

Sullivan P F, Fifield W J, Kennedy M A, Mulder R T, Sellman J D, Joyce P R (1998) No association between novelty seeking and the type 4 dopmaine receptor gene (DRD4) in two New Zealand samples. Am J Psychiatry *155*: 98–101

Tecce J J, Cole J O (1974) Amphetamine effects in man: paradoxical drowsiness and lowered electrical brain activity (CNV). Science *185*: 451–453

Thayer R E (1989) The biopsychology of mood and arousal. Oxford University Press, Oxford

Thornton J C, Dawe S, Lee C, Capstick C, Corr P J, Cotter P, Frangou S, Gray N S, Russell M A H, Gray J A (1996) Effects of nicotine and amphetamine on latent inhibition in human subjects. Psychopharmacology *127*: 164–173

Wan S H, Matin S B, Azarnoff D L (1978) Kinetics, salivary excretion and amphetamine isomers, and effect of urinary PH. Clin Pharmacol Ther *23*: 585–590

Zuckerman M (1991) Psychobiology of personality. Cambridge University Press, Cambridge

Zuckerman M, Eysenck S B G, Eysenck H J (1978) Sensation seeking in England and America: cross-cultural, age, and sex comparisons. J Consult Clin Psych *46*: 139–149