Original Article

Effects of *d*-Amphetamine and Haloperidol on Modulation of the Human Acoustic Startle Response

Hossein Kaviani, PhD [1,2]

1 Psychiatry and Psychology Research Center, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran
2 Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author:
Hossein Kaviani,
Associated Professor of Clinical Psychology, Psychiatry and Psychology Research Center, Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Sciences, South Kargar Avenue, Tehran 13337, Iran
Email: h.kaviani@usa.com
Telephone: +98-21-55412222
Fax: +98-21-55419113

Objective: This study aimed to examine the effects of haloperidol and amphetamine on human startle response modulated by emotionally-toned film clips.
Method: Sixty participants, in two groups (one receiving haloperidol and the other receiving amphetamine) were tested using electromyography (EMG) to measure eye-blink muscle (orbicular oculi) while different emotions were induced by six 2-minute film clips.
Results: An affective rating shows the negative and positive effects of the two drugs on emotional reactivity, neither amphetamine nor haloperidol had any impact on the modulation of the startle response.
Conclusion: The methodological and theoretical aspects of the study and findings will be discussed.

Keywords:
Haloperidol, Dextramphetamine, Startle reaction, Humans, Psychoacoustic

Iran J Psychiatry 2006; 1: 19-26

Dopamine appears to instigate approach behavior and to mediate reward (1). An association has been suggested between dopamine and tendencies to approach, forage, and explore the environment or to experience positive affect states (2,3). A very wide range of substances have pronounced excitatory or inhibitory effects on the dopamine system and subsequently, on behavior and emotion (4,5). Systematic administration of dopamine antagonists, in experimental animals has been shown to cause reductions in the frequency of rearing, jumping, and ambulation behaviors; higher doses can reduce animals to a cataleptic state. Initial interpretations considered such global retardation to reflect motor impairment (6-8). However, more systematic experimental studies suggested that dopamine blockade not only diminishes spontaneous activity (9,10) but may also produce anhedonia, an absence of the capacity to experience pleasure (11), and a decrease in behavioral responsiveness (12). If dopamine antagonists interfere with goal-directed actions and stimulus-reward association learning, then it is expected that dopamine agonists would enhance these phenomena. This expectation has been supported by a decade of research (13, 14). Amphetamine is a powerful stimulant and is thought to produce effects like energization because it potentiates the release of dopamine and decreases its reuptake. Therefore, it can temporarily increase the levels of dopamine in the synaptic cleft (15). Amphetamine has several effects on behavior as a stimulant and also as an anorexic substance (4). Amphetamine in low doses is known to produce euphoria, positive mood, and feelings of friendliness, alertness, energy and mental activity (15, 16). Haloperidol is a neuroleptic drug which is used in the treatment of schizophrenia and related psychiatric disorders. It is not only a potent antagonist of dopamine D2 receptors, but also blocks alpha adrenoreceptors (16). Haloperidol has been found to increase reaction time (RT) during attentional search, consistent with an effect on the dopaminergic mesostriatal system.

This mechanism is thought to be involved in motor or response output too (17). As discussed by Berlyne in 1981, the anti-dopaminergic properties of the neuroleptic drugs are also demonstrated in behavioral experiments in which these substances have been found to potently antagonize the effects of drugs such as apomorphine and amphetamine. Haloperidol produced decreases in pulse-alone startle response in rats in a study by Mansbach et al. in 1988; however to date, no studies have examined whether dopaminergic manipulations influence affective modulation of the startle response in human beings. In the present study, we examined the effects of acute administration of an indirect dopamine-agonist, *d*-amphetamine (5mg), and a non-selective dopamine receptor antagonist, haloperidol (5mg), on the affective modulation of the human acoustic startle response in a healthy population. It is expected that *d*-amphetamine would induce positive hedonic tone (1), and enhance the emotional impact of positive film-clips resulting in a greater response inhibition during the positive film-clips as compared to during the neutral film-clips. Conversely, it was predicted that haloperidol would reduce arousal and emotional hedonic tone (18), and therefore decrease the emotional impact of the film-clips on startle modulation, particularly response inhibition. In the present study, scales to measure the state of mood were taken to see (i) whether dopamine (as manipulated by drug administration) plays a role in the regulation of mood

and (ii) whether alterations in startle modulation can be found when mood is thus manipulated. Scales to measure personality were also taken to explore the role of personality in mediating the effects of drug administration on startle modulation.

The effects of amphetamine on performance and arousal/emotion are especially relevant to Eysenck's arousal-based, Gray's, and Consigner's reinforcement-based, neurophysiologic models of personality (19, 20, 21, 22, 5). However, the precise relationship between personality factors and the effects of amphetamine has yet to be clarified.

Eysenck's theory hypothesized that amphetamine should have performance effects comparable to those of other agents of arousal induction such as caffeine. The fact that amphetamine potentiates the release of noradrenaline and slows its reuptake, suggests that it is amply equipped to act as an agent of arousal induction. If amphetamine has effects comparable to caffeine, then it must also have some effects on the energetic and tense arousal, with possible secondary effects on hedonic tone(19,20).

Gray's theory associates the dopamine potentiating properties of amphetamine with the Behavioural Approach System (BAS), which is charged with the emotional aspects of motor programming, namely, goal direction and incentive motivation (21,5).

Release of dopamine in nucleus accumbens in particular has been linked to the action of many drugs of abuse (1), indicating that it is the release of dopamine in nucleus accumbens that is associated with the positive affect caused by these drugs. Gray's model therefore predicts that impulsivity (neurotic-extraversion), as the factor corresponding to the BAS, should be related to the effects of amphetamine. Given the reinforcement basis of Gray's model, amphetamine should be reflected in changed hedonic tone scores, with possible secondary effects on the energetic/tense arousal. Consigner's model of personality associates dopamine with the personality dimension of novelty seeking (NS), which in this model reflects heritable differences in a behavioural activation system (similar to Gray's BAS); a second personality dimension, reward dependence (RD), is associated with nor adrenaline (23).

Therefore, the effects of amphetamine as a potent dopamine and nor adrenaline agonist may be manifested by either novelty seeking or reward dependence behaviours.

Material and Method (Experiment 1)

Subjects

Sixty right-handed healthy male subjects (age 18-45 years with a mean of 74.97 kg in weight) were recruited by advertisements or referrals from our healthy subjects. Before being accepted, all potential subjects were screened on a semi-structured basis, for thyroid dysfunction, glaucoma, heart-disease, hypo/ hypertension, a background of severe psychiatric problems, anorexia, violent or rapid mood changes, regular medical prescription, alcohol dependency, and drug abuse (ascertained by urine analysis). All subjects signed a consent form approved by the Ethical Committee.

Experimental Design and Procedure

Subjects were randomly assigned to one of the drug groups (placebo, *d*-amphetamine, and haloperidol), with equal sample sizes (n = 20). Placebo (empty capsule), *d*-amphetamine (5 mg) and haloperidol (5 mg) all were administered orally in identical capsules. Drug latency periods were determined according to previous studies; 90 minutes in the case of *d*-amphetamine (24) and 3 hours in the case of haloperidol (25,26). In order to be able to run the study double-blind, all subjects were given two capsules, one at minute 0 and the other 90 minutes after. Thus, subjects in the placebo group were given two placebo capsules; while those in the *d*-amphetamine and haloperidol groups were given one placebo capsule and the other containing 5mg *d*-amphetamine or 5mg haloperidol, respectively. Table 1 demonstrates the schedule of drug administration.

Table 1. The schedule and timing design of drug administration for the placebo, *d*-amphetamine, and haloperidol groups

Group Time(min)	Placebo group	*d*-Amphetamine group	Haloperidol
0	Placebo	Placebo	Haloperidol
90	Placebo	*d*-amphetamine	Placebo

All subjects were given the first drug/placebo capsule between 9.30 and 11.00 a.m. to control for possible differential effects on drug metabolism due to the time of day. Similarly, the study sample was restricted to males only, to reduce another potential source of variance. Subjects were tested 195 to 210 min after taking the first tablet. After taking the drugs and before taking part in this experiment, subjects had participated in another experiment (including latent inhibition tasks), performed approximately 15 min before. In summary, subjects received occasional bursts of noise through the headphones, while viewing a series of film-clips. The electrodes were then attached. Affective ratings were obtained during the intervals between clips in each of the two sessions.

Apparatus and Materials

The film-set (the same as the one used in previous studies in our lab) consisted of 9 clips separated by blank intervals (dark blue screen) of 10-25 seconds long (27-30). The first three clips were used only to familiarize subjects with the experience procedure. The last six clips, used to induce emotions experimentally, were presented in two blocks and in the order N (neutral), P (pleasant), U (unpleasant), N, U, P.

Each film-clip lasted about 2 minutes. The set, shown on a Sharp video recorder (VC-A30HM) connected to a Sharp color TV monitor, 20 Inch (DV-5101 A), was viewed from a distance of 2m. The acoustic startle stimuli (consisted of a 50ms presentation of a 92.5-dB

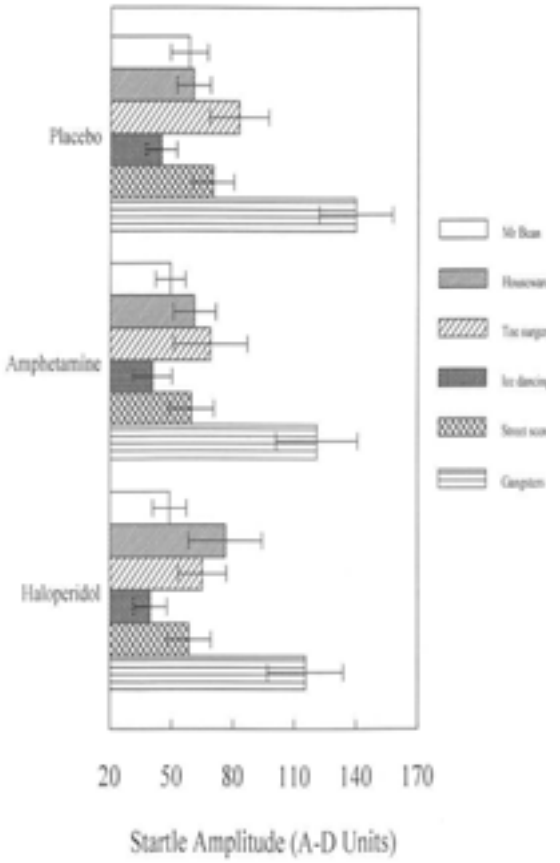

Figure 1. Mean affective ratings (±1 standard error of the mean) for two blocks of film-clips in the three drug groups.

(A) burst of white noise, with quasi-instantaneous rise time) were superimposed on the sound tracks (ranging from 40 to 60 dB) of the film clips, at relatively low sound level, and presented monaurally via head- phones (Telephonics TDH-39P).

Three startle stimuli were presented during each clip (total = 27). To increase unpredictability, the startle stimuli were presented with varying inter-stimulus intervals of 20 to 90 seconds after the onset of clip. The responses to the last 18 acoustic startle stimuli (during the last six clips) were included in the analyses, excluding the responses to the first 9 acoustic stimuli (during the first three clips which were only for habituation).

To record electromyographic (EMG) activity of the orbicular oculi muscle, two 6-mm disc electrodes (Ag/AgCl) filled with electrolyte paste (SLE, Croydon, UK) were placed approximately 1 cm below the middle of the lower eyelid and 1 cm below the outer corner of the right eye, so that the second electrode was about 1 cm lateral and slightly higher than the first but both were parallel to the lower rim of the eyelid. An additional, ground electrode was placed behind the right ear over the mastoid. Raw EMG signals were recorded, amplified, filtered, stored, and analyzed by a computerized startle response monitoring system (SR Instruments, San Diego, California). The analytic program treats the first 20ms after presentation of each startle stimulus as a baseline for that trial. Based on this baseline, it then calculates latency (msec) to startle onset and peak EMG amplitude (in arbitrary analogue-to-digital units; 1 unit equals 1.2 microvolts, SR-Lab Program) over the 95msec following startle onset. Trials with an unstable baseline (shift > 20 units) were eliminated. Samples were taken at 1 millisecond (1 KHz sampling rate). The lower band pass alternative provided by the apparatus (0 - 500 Hz) was used throughout the experiment. (There is also a built-in standard 50-cycle filter.) With respect to the 1.2 mV per A/D unit, SD Instruments describe the logic as follows: "The A/D board is set for voltages from 0-5 volts. For maximal resolution a board with '12 bit' resolution was used, which divided the 5 volts into 4095 'A/D units'. Therefore a 1.2 millivolt input to the card is reported as 1 A/D unit (5 divided by 4095)".

To be consistent with previous studies in our lab (27, 30, 31, 32) the scoring criteria were identical. Trials were rejected if there was evidence of excessive activity (including evidence of a premature eye-blink) during the baseline period. They were also rejected if there was no evidence of an eye-blink having been evoked by the startle probe. Altogether, 16.35% of trials were excluded on one or other of these criteria. Subjects were excluded from analysis if they showed missing data on all three startle probes within any one of the film clip.

The affective content of each clip was rated as each clip ended (during the blank interval) on a single 11-point (-5 to +5) scale, from extremely unpleasant (e.g. depressed, disgusted, angry, anxious; scored as -5), through neutral (scored as 0) to extremely pleasant (e.g. happy, relaxed; scored as +5).

Mood and Personality Measures

In order to examine drug effects on self-reported mood, the UWIST Mood Adjective Checklist (33) was used twice, before taking the drug and 3 hrs after taking the first capsule. This checklist provides measures of energetic arousal (EA), tense arousal (TA), and hedonic tone (HT). To measure personality traits, short form of the Temperament and Character Inventory (TCI) was administered; this provides measures of novelty seeking [NS], harm avoidance [HA], reward dependence [RD], persistence [P], self-directiveness [SD], cooperation [C], and self-transcendence [ST] (23). From these subscales only NS, HA, and RD were chosen for analysis because they were the dimensions meant to assess temperamental traits. The Eysenck Personality Scales (EPS) (34) was also administered; it measures extraversion (E), neuroticism (N), and psychoticism (P).

Results (Experiment 1)

Affective Rating

Figure 1 represents mean affective ratings (error bars indicate ± 1 standard error of the mean) for two blocks in the three drug groups.

The data were analysed by a three-way [Drug (placebo, amphetamine, and haloperidol) × Block (blocks 1 and) × Valence (pleasant, neutral, and unpleasant)] MANOVA with Block and Valence as within-subjects variables and

Table 2. Mean (±1 standard error of mean) baseline EMG activity (a-D Units) for the two blocks in three drug groups

		Placebo	Amphetamine	Haloperidol
	Pleasant	24.65 (4.95)	25.30 (3.64)	21.67 (2.81)
Block 1	Neutral	12.25 (1.13)	16.57 (3.55)	15.63 (2.79)
	Unpleasant	17.50 (1.85)	16.80 (1.63)	18.38 (3.26)
	Pleasant	11.97 (1.57)	13.48 (1.52)	12.25 (1.84)
Block 2	Neutral	12.48 (1.29)	12.78 (1.35)	17.47 (2.68)
	Unpleasant	14.17 (1.79)	13.82 (1.42)	14.23 (2.29)

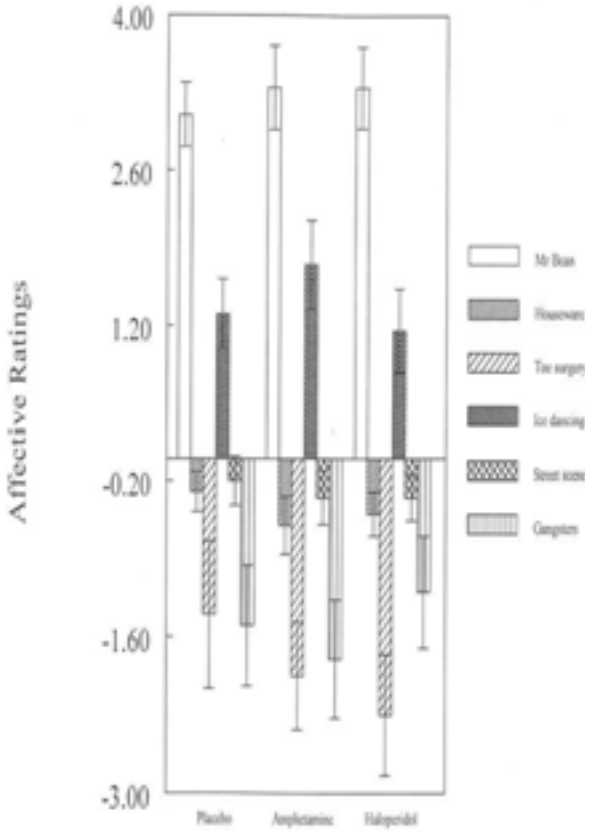

Figure 2. Mean startle amplitude (±1 standard error of the mean) for two blocks of film-clips in the three drug groups.

Drug as a between-subjects factor. There was a highly significant effect of Valence, F [2, 56]=106.66, p<0.0001), but also a significant Block×Valence effect (F [2, 56] =31.02, p<0.001) (see Figure1), suggesting that subjects found the Mr Bean clip more pleasant and the Toe Surgery clip more unpleasant than the Ice Dancing and Gangsters clips, respectively.

Therefore, in order to detect Valence and Drug effects in each block, the data were analysed for each block separately by a two-way MANOVA, with Valence as a within-subjects and Drug as a between-subjects factor. The results showed an overall significant Valence effect in both blocks (Block 1: F[2, 56]=149.97, p<0.001; Block 2: F[2, 56]=26.04, p<0.001), with a highly significant linear trend (Block 1: t=12.20, p<0.00001; Block: t=6.17, p<0.00001). No Valence Drug effect was found in either of the blocks, suggesting that the effects of *d*-amphetamine and haloperidol on subjective ratings were trivial and similar to those observed with the placebo.

Startle Amplitude

Figure 2 shows mean startle amplitudes (error bars indicate ±1 standard error of the mean) for the two blocks in the three drug groups.

The data were subjected to the same statistical analysis as described above for affective ratings. Ten cases were excluded from analysis because of missing amplitude data. A significant Block×Valence effect was found (F [2, 46]=19.34, p<0.001). This finding suggests that the contents of the two blocks differentially modified startle responses. When analysing the data for the two blocks separately, six cases in block 1 and five cases in block 2 were rejected from analyses due to missing data. The findings showed that there was a significant overall Valence effect in both blocks (Block 1: F[2, 50]=3.18, p=0.05; Block 2: F[2, 51]=35.30, p<0.001), with a linear trend (Block 1: t=2.25, p<0.05; Block 2: t=8.41, p<0.0001). Significant response inhibition by the pleasant (t[54]=4.13, p<0.001) and a significant augmentation by the unpleasant clip (t[58]=6.87, p<0.001) appeared only in block 2; no significant differences were obtained in block 1. No significant Drug×Valence effect was found in either of the blocks.

Baseline EMG

Mean baseline EMG (1 standard error of the mean) for the pleasant, neutral, and unpleasant clips in blocks, separately for the three drug groups are shown in Table 2. The same statistical analyses were used. A significant Block×Valence effect was found (F[2, 56]=5.98, p<0.01), suggesting that the two blocks had different arousal impact on the subjects.

The results showed a significant overall Valence effect for block 1 (F[2, 56]=5.18, p<0.01), with a quadratic trend (*t*=2.91, p<0.01), showing that the tension of orbicular oculi during Mr Bean and Toe surgery was higher than during the neutral clip (house ware); no significant Valence effect was found for block 2. No significant Drug×Valence effect was observed in either of the blocks.

Table 3. Mean (±1 standard error of mean) latency to onset (ms) for the two blocks in the three drug groups

		Placebo	Amphetamine	Haloperidol
Block 1	Pleasant	43.46 (2.62)	40.26 (2.41)	40.16 (3.18)
	Neutral	49.28 (3.65)	51.07 (3.61)	44.19 (3.41)
	Unpleasant	45.32 (2.45)	43.79 (3.04)	48.03 (2.89)
Block 2	Pleasant	49.93 (2.79)	53.13 (4.00)	51.38 (4.76)
	Neutral	45.18 (1.75)	44.16 (2.52)	44.36 (2.87)
	Unpleasant	40.60 (2.30)	44.16 (2.52)	38.30 (1.88)

Table 4. The summary analyses for *t*-test over UWIST measures, Energetic Arousal (EA), Hedonic Tone (HT), and Tense Arousal (TA) in the three groups (df = 19)

Group		Before Drug	Before Experiment		
		Mean (±SEM)	Mean (±SEM)	*t*-value	*p*
Placebo	EA	23.10 (1.01)	22.45 (1.45)	.52	.68
	HT	28.00 (0.624)	28.30 (0.78)	.48	.63
	TA	13.35 (0.95)	12.20 (1.20)	1.15	.27
Amphetamine	EA	23.00 (0.96)	23.55 (0.92)	.57	.57
	HT	27.30 (0.79)	28.75 (0.75)	1.74	.10
	TA	14.40 (0.98)	11.40 (0.66)	3.74	.001*
Haloperidol	EA	21.60 (0.95)	20.35 (0.98)	1.06	.30
	HT	27.25 (0.54)	24.50 (1.11)	2.79	.01*
	TA	14.75 (0.71)	14.35 (1.16)	.32	.75

*** p<0.05, significant**

Latency to Onset

Table 3 shows mean latency to response onset (1 standard error) for the two blocks in the three drug groups. Data wee analysed by the same statistical analyses as described in the previous sections. Ten cases were rejected from analysis due to missing baseline EMG data.

A significant Block×Valence effect was found (F[2, 46]=19.66, p<0.001). When analysing the data of the two blocks, six cases in block 1 and five cases in block 2 were rejected owing to missing data. There was a significant overall Valence effect in both blocks (Block 1: F[2, 50]=4.47, p<0.02; Block 2: F[2, 51]=16.05, p<0.001), with a quadratic trend for block 1 (t=2.06, p<0.05), but a linear trend for block 2 (t=5.48, p<0.0001). In block 1, latencies during the unpleasant and pleasant clips were smaller than during the neutral clip. In block 2, latencies during the unpleasant clip were smaller but latencies during the pleasant clip were larger than those during the neutral clip. Again no significant Drug×Valence effect was found in either of the blocks. main effect of Valence (F[2, 17]=39.23, p<0.001).

Mood Adjectives

The summary statistics for the scores on energetic arousal (EA), hedonic tone (HT), and tense arousal (TA) of the UWIST Mood Adjective Checklist, obtainedbefore and three hours after taking the drug, are presented in Table 4.

In order to detect changes in the UWIST measures, Energetic Arousal (EA), Hedonic Tone (HT), and Tense Arousal (TA), as a function of drug, the data on each measure were subjected to a two-way (3×2: Drug Group [placebo, amphetamine, and haloperidol]×Time [before and after taking the drug]) MANOVA, with Time as a within-subjects and Drug Group as a between-subjects factor. The results showed no significant Time or Drug Group x Time effects for the Energetic Arousal measure. Although there was a significant Time effect for the Tense Arousal measure (F[1, 57]=6.49, $p < .02$), no significant Drug Group×Time effect was observed. For the Hedonic Tone measure, there was a significant Drug Group×Time effect (F[2, 57]=6.88, p<0.005). The data were further analysed by a two-way drug]) MANOVA, with Time as a within-subjects and Drug Group as a between-subjects factor. No Drug Group×Time effect was found for amphetamine in any measure. There were no significant Time effects except for Tense Arousal (F[1, 38]=10.51, p<0.005). The analysis for the haloperidol group showed significant results only for the Hedonic Tone scores; there was a significant Group×Time effect (F[1, 38]=6.85, p<0.02),

confirming that haloperidol lowered subjects' hedonic tone scores.

Personality Traits and Startle Measures

For each chosen (see Method) personality measure from the Eysenck Personality Scales (EPS) and Temperament and Character Inventory (TCI), the study sample was divided by median split into low and high groups; the median score was included in the low group. Table 5 presents the descriptive statistics for the personality measures.

The startle data (amplitude, baseline EMG, and latency to onset) over each block were separately subjected to a three-way (Drug [placebo, amphetamine, and haloperidol]×Valence [pleasant, neutral, and unpleasant] ×Personality Trait [low group and high group]) MANOVA with Valence as a within-subjects factor, and Drug and Personality Trait as between-subject factors. The data were re-analysed after a logarithmic transform on reporting significant results. This reanalysis was made due to an observed positive correlation between mean startle measures and their variance.

Next, the data in each drug group were separately analysed by a two-way (Valence [pleasant, neutral, and unpleasant]×Personality Trait [low group and high group]) MANOVA with Valence as a within-subjects variable and Personality Trait as a between-subjects factor.

No significant effects were found for startle amplitude or affective measures in interaction with any of the personality dimensions.

Material and Method (Experiment 2)

As already described, no effect of amphetamine was found on startle modulation in Experiment 1. Subjects of Experiment 1 had, however, participated in another experiment prior to taking part in the startle experiment.

To examine the possibility whether this affected the results (due to a small drug response window), Experiment 2 was conducted in such a way that startle measures were taken exactly 90 min following amphetamine administration.

Subjects

Ten male subjects (age-range 18-45 years; mean weight 72.50 kg) were tested.

Experimental Design and Procedure

In order to re-examine, the effects of *d*-amphetamine (5 mg) on the startle response, subjects were tested 90 min after taking the drug. The data on ten subjects from the placebo Group of Experiment 1, matched for age, were used as controls. The experimental design and procedure were identical to Experiment 1, except that Experiment 2 could not be run double-blind.

Apparatus and Materials

These were identical to those described in Experiment 1.

Results (Experiment 2)

Affective Ratings

The affective ratings data in the additional group (n=10) for placebo and amphetamine were analysed by a three-way (Drug [placebo and amphetamine]×Block [block 1 and block 2] ×Valence [pleasant, neutral, and unpleasant]) MANOVA, with Block and Valence as within-subjects factors and Drug as a between-subjects factor. The results showed no significant Drug × Valence effect, although there was a highly significant main effect of Valence ($F[2, 17]=39.23$, $p<0.001$). No significant Valence×Block effect was observed in this experiment.

Startle Amplitude

The data were treated by the same statistical analysis method as described above for affective ratings. The results revealed no significant Drug effect, but a significant main effect of Valence ($F[2, 16]=20.19$, $p<0.001$). No significant Block×Valence effect was observed.

Base Line EMG and Latency to Onset

The same statistical analyses were employed as described for previous Results sections. No significant main or interaction effects were found.

Table 5. Summary descriptive statistics for the personality measures

	Mean	Median	SD	Range
EPS: Extroversion (E)	15.41	16.00	4.97	2-23
EPS: Neuroticism (N)	9.85	9.00	6.28	0-24
EPS: Psychoticism (P)	8.69	7.00	5.83	0-28
TCI: Novelty Seeking (NS)	10.56	10.00	3.37	4-17
TCI: Harm Avoidance (HA)	6.93	6.00	4.64	0-18
TCI: Reward Dependence (RD)	8.73	9.00	2.94	1-15

Discussion

This study was designed to examine the effects of a dopamine agonist (*d*-amphetamine) and a dopamine antagonist (haloperidol) on the modulated startle blink response, looking at personality measures that might possibly interact with the drugs' effects. The major finding of Experiment 1 and 2 is that neither amphetamine nor haloperidol had any impact on the modulation of the startle response. Both drugs were given in doses which had significant but small effects on mood. Amphetamine in the dose used resulted in a significant reduction in the summary measure tense arousal (see Table 3) as a result of changes in the ratings for nervous, tense, jittery, and anxious (versus relaxed, composed, restful, and calm). Haloperidol resulted in a small but significant reduction in hedonic tone as a result of changes in ratings for happy, cheerful, satisfied, and contented (versus dissatisfied, sorry, depressed, and sad). Mood ratings showed that subjects in the haloperidol group experienced decreased hedonic tone three hours after administering drug (before the experiment). Since the rating of tense arousal in the haloperidol group was not significantly different from the placebo group, the reduction in hedonic tone in people taking haloperidol implies that they experienced a depressed-like mood.

The present study shows that drug treatments which block (haloperidol) or indirectly stimulate (amphetamine) dopamine receptors in doses sufficient to have subtle effects on mood, have no significant effect on the modulation of the startle reflex in man. However, larger doses might have such an effect.

The significant valence effect for baseline EMG in block 1 could be an artefact of changes in facial muscles caused by smiling and laughing in response to Mr Bean clip (comic) and disgust mimicry in response to Toe surgery (degusting). These changes could have been the cause of increases in baseline EMG during Mr Bean and Toe surgery compared to the neutral clip, leading to the quadratic trend, which was observed in this experiment.

The results on startle amplitude support this idea that the two blocks differently modulate startle reflex. This point was further supported by the analyses over affective ratings, showing significant interaction between Valence and Block. Moreover, affective ratings showed that both the pleasant and unpleasant film-clips in block 1 induced stronger affect than those in block 2. However, the startle amplitude data showed an overall significant valence effect in both blocks.

In conclusion, no significant drug effect on startle amplitude was found in this experiment. Although the dosage of haloperidol in this study seems sufficient to affect hedonic tone, amphetamine did not appear to influence this measure. Therefore, one possible reason for the failure to observe any effect of amphetamine might be that the dose was too low. Therefore, a replication of this study is required with larger doses. The robust effect of film material in manipulating mood and emotions may account for the similar response of subjects in the two different drug groups (dopamine agonist versus dopamine receptor antagonist) and the placebo group.

Reference:

1. Di Chiara. The role of dopamine in drug abuse viewed from the perspective of its role in motivation. *Drug Alcohol Depend* 1995; 38: 95-137.
2. Gray J A. *The psychology of fear and stress*. Cambridge: Cambridge University Press; 1987.
3. Panksepp J. Towards a general psychobiological theory of emotions. *Behav Brain Sci* 1982;5: 407-22.
4. Iversen SD, Iversen LL. *Behavioral pharmacology*. Oxford: Oxford University Press; 1975.
5. Gray JA. *Neural systems, emotion and personality. In Madden J eds. Neurobiology Learning, Emotion and Affect, IV*. New York: Raven Press; 1991.
6. Delong MR, Strick PL. Relation of basal ganglia, cerebellum, and motor cortex units to ramp and ballistic movement. *Brain Res* 1974; 71: 327-35.
7. Marshall JF, Teitelbaum P. Further analysis of sensory inattention following lateral hypothalamic damage in rats. *J Physiol Psychol* 1974; 86: 375-95.
8. Beckstead RM, Domesick VB, Nauta WJ. Efferent connections of the substantia nigra and ventral tegmental area in the rat. *Brain Res*. 1979 19;175:191-217.
9. Janssen PA, Niemegeers CJ, Schellekens KH. Is it possible to predict the clinical effects of neuroleptic drugs (major tranquillizers) from animal data? *Arzneimittelforschung* 1966; 16 :339-46.
10. Acquas E, Carboni E, Leone P, Di Chiara G. SCH 23390 blocks drug-conditioned place-preference and place-aversion: anhedonia (lack of reward) or apathy (lack of motivation) after dopamine-receptor blockade? *Psychopharmacology* 1989; 99: 151-5.
11. Wise RA. Neuroleptic and operant behavior: the anhedonia hypothesis. *Behav Brain Sci* 1982; 5: 39-87.
12. Bindra D. A motivational view of learning, performance, and behavior modification. *Psychol Rev* 1974; 81: 199-213.
13. Dackis CA, Gold MS. Bromocriptine as treatment of cocaine abuse. *Lancet* 1985; 1:1151-2
14. Lawford BR, Young RM, Rowell JA, Qualichefski J, Fletcher BH, Syndulku K, et al. Bromocriptine in treatment of alcoholics with the D_2 dopamine receptor A_1 allele. *Nat Med* 1995; 1: 337-41.
15. Zuckerman M. *Psychobiology of personality*. New York: Cambridge Univerity Press; 1991.
16. Baldessarini RJ. *Drug and treatment of psychiatric disorders: depression and mania. In Molinoff PB, Ruddon RW eds. Goodman & Gilman's, the Pharmacological Basis of Therapeutics*. New York: McGraw-Hill; 1996.
17. Coull JT, Sahakian BJ, Middleton HC, Young AH, Park SB, McShane RH, Cowen PJ, Robbins TW. Differential effects of clonidine, haloperidol, diazepam and tryptophan depletion on focused attention and attentional search. *Psychopharmacology* 1995; 121: 222-30.
18. Deniker P. Psychophysiologic aspects of the new chemotherapeutic drugs in psychiatry; some practical features of neuroleptics in order to screen new drugs. *J Nerv Ment Dis* 1956; 124: 371-6.
19. Eysenck HJ. *The dynamics of anxiety and hysteria*. New York: Prauger; 1957.

20. Eysenck HJ. *The biological basis of personality.* Illinois: Charles C. Thomas; 1967.
21. Gray JA. *The psychology of fear and stress*. New York: McGraw Hill;1971.
22. Cloninger CR. A systematic method for clinical description and classification of personality variants. *Arch Gen Psychiatry* 1987;44:573-88.
23. Cloninger CR, Svrakic DM. Personality dimensions as conceptual framework for explaining variation in normal, neurotic, and personality disordred behavior. In Burrows GD, Noyes R, Roth M eds. *Handbook of anxiety*. Netherlands: Elsevier;1993.
24. Gray NS, Pickering AD, Hemsley DR, Dawling S, Gray JA. Abolition of latent inhibition by a single 5 mg dose of d-amphetamine in man. *Psychopharmacology*.1992;107: 425-30
25. Nordstrom AL, Farde L, Halldin C. Time course of D2-dopamine receptor occupancy examined by PET after single oral doses of haloperidol. *Psychopharmacology* 1992; 106: 433-38.
26. Magliozzi JR, Doran AR, Gietzen DW, Olson AM, Maclin EL, Tuason VB. Effects of single dose haloperidol administration on plasma homovanillic acid levels in normal subjects. *Psychiatry Res* 1993; 47: 141-9.
27. Kaviani H, Gray JA, Checkley SA, Kumari V, Corr PJ, Wilson GD. Modulation of the acoustic startle reflex by emotionally-toned filmclips. *Psychophysiology* 1996; 33: S49(Abstract).
28. Kaviani H, Gray JA, Checkley SA, Kumari V, Corr PJ, Wilson GD. Modulation of the acoustic startle reflex by emotionally-toned video sequences. *J Psychophysiol* 1996; 33: S49(Abstract).
29. Kaviani H, Gray JA, Checkley SA, Kumari V, Corr PJ, Wilson GD. The use of affect-toned odours to modulate acoustic startle reflex . *Psychophysiology* 1996; 33: S49(Abstract).
30. Kaviani H, Gray JA, Checkley SA, Kumari V, Wilson GD. Modulation of the acoustic startle reflex by emotionally-toned filmclips. *Int J Psychophysiol* 1999; 32: 47-54.
31. Corr PJ, Wilson GD, Fotiadou M, Kumari V, Gray NS, Checkley S, et al. Personality and affective modulation of the startle reflex. *Pers Individ Dif* 1995; 19: 543-553.
32. Kumari V, Cotter P, Corr PJ, Gray JA, Checkley SA. Effect of clonidine on the human acoustic startle reflex. *Psychopharmacology* 1996; 123: 353-360.
33. Matthews G, Jones DM, Chamberlain AG. Refining the measurement of mood: the UWIST Mood Adjective Checklist. *Br J Psychol* 1990; 81: 17-42.
34. Eysenck HJ, Eysenck SBG. *Manual of the Eysenck Personality Scales*. London: Hodder and Stoughton; 1991.