Comparison of the effects of dexamphetamine and 1-benzylpiperazine in former addicts

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The effects of 1-benzylpiperazine and dexamphetamine on normal volunteers were recently reported (Munro-Faure, Peck, Pullin & Young, 1971). Both compounds produced similar effects on heart rate and systolic blood pressure, and performance in tapping and an auditory vigilance test (Wilkinson, 1969). The latter proved highly sensitive, while measurement of subjective effects assessed using an adjective check list, in drug naive subjects proved much less sensitive. The present investigation was undertaken to compare the effects of the two compounds in subjects formerly addicted to amphetamine and similar drugs. The attitude of this population to the effects produced by 1-benzylpiperazine might be of value in predicting possible abuse of this compound.

The experiment was conducted on eighteen volunteers, eight male and ten female aged 16 to 50, with extensive experience of amphetamine-like drugs. Subjects received all three treatments, dexamphetamine sulphate, 10 mg; 1-benzylpiperazine hydrochloride, 100 mg; and lactose placebo, on three occasions, and were studied in groups of three at weekly intervals. One subject defaulted after two treatments. All drugs were administered orally on an empty stomach in identical capsules under double blind conditions according to a design based on a completely balanced block replicated 3 times.

Subjects completed a questionnaire designed to ascertain whether they felt drug effects, and if so whether these were similar to those produced by amphetamine-like drugs, and whether they liked the effects. Answers were scored on a 0–4 scale and the questionnaire completed 1, 2 and 4 h after drug administration. Behavioural changes were rated by a single observer using a psychiatric rating scale (Malamud, Hoagland, & Kaufman, 1946), and also using a simple questionnaire designed to record changes in behaviour similar in type to those seen after amphetamine-like drugs. Radial pulse, blood pressure (measured with a sphygmomanometer) and pupil diameter (measured with a transparent rule) were recorded under standardized conditions. The results were submitted to an analysis of variance, and the degree of change ascribable to the various treatments evaluated.

In the subjects' questionnaire the scores to questions indicating an amphetamine-like effect and a liking for this effect were highest after 1-benzylpiperazine, lower after dexamphetamine and lowest after the placebo. The highest scores after the drugs and greatest difference from placebo occurred 2 h after administration. The difference between both drugs and placebo and also the difference between the two active drugs was significant ($P < 0{\cdot}001$).

Objective assessment of behaviour using the psychiatric rating scale revealed a difference between both drugs and placebo ($P < 0{\cdot}001$) on the excitation scale, but no difference between the two drugs ($P > 0{\cdot}05$). The simple questionnaire gave a similar result. The rise in pulse rate was greater after both drugs than after the placebo ($P < 0{\cdot}001$) but the difference between the two drugs was not significant ($P > 0{\cdot}05$). The rise in blood pressure after both drugs was significantly greater than that after the placebo on both systolic blood pressure ($P < 0{\cdot}001$) and diastolic blood pressure ($P < 0{\cdot}05$). There was no significant difference between the effects of dexam-

phetamine and placebo on pupil diameter, but the dilatation after 1-benzylpiperazine was greater than that after the placebo ($P < 0.001$).

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Clinical pharmacology of chlorpromazine

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Chlorpromazine has been extensively used in psychiatric treatment over the last 20 years, but its clinical pharmacology remains imperfectly understood. In particular, relationships between plasma concentrations, and physiological and behavioural effects have not been fully evaluated.

In the present study ten drug-free patients requiring phenothiazine treatment received oral chlorpromazine (100 mg) at intervals of 8 h in liquid form. No other drug was given except nitrazepam at night if needed. The patients were first evaluated on the day before treatment, at 10.00 hours. Testing was then carried out on the 4th, 8th, 15th, 22nd, 29th and 36th or 43rd days of treatment and consisted of: (a) blood samples for chlorpromazine estimation at 0, 2, 4 and 6 h after the dose; (b) blood pressure and pulse rate (sitting and standing), pupil size, sweat gland activity and electroencephalogram (e.e.g.) at these times; (c) salivary secretion, e.e.g. auditory evoked response, simple auditory reaction time and handwriting tests at the 2-h point only (10.00 h); and (d) clinical ratings between the 2nd and 4th hours.

After an initial rise in the first 8–15 days, plasma concentrations dropped markedly, as we have previously reported (Curry, Lader, Mould & Sakalis, 1971). The changes were reflected by some of the peripheral measurements. Correlations were computed within each subject, between concentration, physiological measures, and clinical ratings. They were pooled using z transformations (see Table 1). Clinical changes over the first fortnight showed a tenuous relationship with drug concentrations, and there was no correlation during the decreasing phase.

TABLE 1. *Intra-patient correlations between plasma concentration and other variables*

	r	P
Pupil size	−0·4605	<0·001
Pulse rate (standing)	0·3021	<0·001
Blood pressure (sitting systolic)	−0·2603	<0·001
Blood pressure (sitting diastolic)	−0·2114	<0·01
Palmar skin conductance	−0·1906	<0·01
Salivary secretion	−0·3646	<0·05
e.e.g. 4·0–7·5 Hz percentage	0·3912	<0·05