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THE EFFECTS OF LOW DOSES OF DIAZEPAM ON HUMAN PERFORMANCE IN GROUP ADMINISTERED TASKS

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1 The effects of diazepam in 5 mg dosage were assessed on a range of psychological tasks. Seventy-eight healthy subjects were tested in an independent groups design; subjects were randomly assigned to either control, placebo or drug group. Treatments were administered orally under double blind conditions.

2 Auditory vigilance performance was unimpaired, in terms of (a) correct detections, (b) false alarms or (c) the subjects' estimates of the duration of the task.

3 The short term retention of digit strings was impaired by diazepam ($P < 0.05$), especially for those digits presented in the middle of the sequence.

4 Searching for a few letters among many was significantly impaired by diazepam ($P < 0.01$).

5 Diazepam had no effect on performance at a mental arithmetic task; neither was there a placebo effect.

6 Results were discussed in the light of the characteristics of drug sensitive tasks. It was concluded that characteristics such as feedback of results, monotony, and memory load are more likely to be drug sensitive when in combination than in isolation.

Introduction

The assessment of psychological impairment by benzodiazepine drugs in laboratory tasks has been mainly concerned with the response to large doses. Even with large doses, significant effects have been test-specific, with drugs appearing to influence some tests and not others. McNair (1973) classified 97 studies concerned with the effects of anti-anxiety drugs on performance into four categories: high, average, low and indeterminate sensitivity. The resulting table was not impressive. Not only did the high sensitivity tasks have a low record of producing significant results, but they were not easily distinguishable, in psychological terms, from the insensitive ones. For example, the learning of paired associates was a highly sensitive task, but the learning of nonsense syllables was an insensitive one. Both tasks have common functional characteristics and it may be that the effect of anti-anxiety drugs on performance may be less dependent on the faculty involved, like 'learning' and 'memory', than on quite subtle differences in the demands placed upon the subject.

While McNair (1973) points out obvious procedural and design faults, his 'vox populi' of studies cannot do justice to the complex interaction of task demands and drug effects. The categorization of tasks on the basis of strength of effect is in itself a flawed approach: those tasks found to be in the low or the high sensitivity group were represented by far fewer studies than those classified as being of average sensitivity.

The dosage required to produce effects in man has shared the mixed fortunes of task sensitivity. Jäättelä, Männistö, Paatero & Tuomisto (1971), on the one hand, showed impairment in digit symbol substitution and short term memory after a relatively small dose (10 mg) of diazepam, while on the other, Haffner, Mørland, Setekleiv, Strømsaether, Danielson, Frivik & Dybing (1973) found no effect on psychological tests with up to 20 mg of diazepam. In both these cases tests were relatively short and it may be that the length of the task is a crucial feature in determining the sensitivity. Despite McNair's (1973) protestations that his 'biggest losers' in terms of sensitive tasks were 'rather odious', it seems likely that protracted, repetitive and boring tasks will be more sensitive than short, entertaining or engrossing ones. Wilkinson (1965), in reviewing the sensitivity of tasks performed in stress conditions such as noise and loss of sleep, notes that the adverse effects of stress upon performance may only become apparent when the subject has been engaged in the task for some period of time. Such a notion may be equally applicable to drug effects. Hart, Hill, Bye, Wilkinson & Peck (1976), for example, found that relatively small doses of diazepam (5 mg) produced significant impairment in a number of tasks, among them a short term memory task, a digit symbol substitution task and an auditory vigilance task. Long tasks lack the novelty and challenge of short ones and are more likely to reflect the subjects' performance outside the laboratory. Data on tasks of this sort are particularly useful in view of ubiquity of low dosages of diazepam in ambulatory patients engaged in repetitive industrial tasks.

Allied with the need to increase the length of tasks and consequently the length of time a subject spends in the laboratory is the need to decrease the tedium for the experimenter and the expense in running these experiments. Most tasks employed to date have required the testing of one or, at most, a handful of individuals at one time. This increases the duration of the proposed experiment, and inevitably leads to small sample sizes. There are a number of advantages in using large numbers of subjects which group testing allows: the possibility, for example, of using different sets of subjects for each drug treatment, avoiding the need to 'balance out' the experience of the subject with the task. With this in mind, the tasks in the present study were chosen on the basis of allowing their administration to large groups of subjects at the same time.

The present study is concerned with the effects of a relatively small dose of diazepam (in dosages comparable to those often employed in the treatment of mild anxiety states) on performance. The tasks were chosen as being representative of the kinds of functions commonly found in practical situations: such as searching, listening, and remembering.

Methods

Subjects

Seventy-eight students, males and females, took part in the study. No attempt was made to control smoking between experimental tasks but subjects were asked to refrain from drinking alcohol during the one-day study. All subjects were given a standard light lunch. Subjects were assigned either to a control, placebo or experimental group.

Drugs

The experimental group was given soft gelatin capsules containing 5 mg diazepam. The placebo group was given lactose filled dummy capsules. All capsules were given at 09.00 on the day of the experiment.

Physical arrangements

Subjects were seated some 1 m apart and visually separated by screens. Watches were removed from subjects and all clocks covered up at the beginning of the experiment. A background of 'white' noise (at 70 dB) was played during the execution of the tasks involving visually presented materials which masked out auditory cues.

Design

A total of four tasks were completed by each subject on his/her experimental day. Forty of the subjects performed the experiment on day I and thirty-eight of the subjects performed the experiment on day II a week later.

Subjects performed four tasks: short term memory, auditory vigilance, letter cancellation and mental arithmetic. These tasks were divided into experimental blocks where tasks were performed successively. Vigilance formed block I, Memory, Cancellation and Arithmetic formed block 2. On any one day the subject group was split in half; half the subjects performed the blocks in the order Block I–Block 2, the other half of the subjects performed the tasks in the order Block 2–Block I. This incomplete balancing of task order went some way to alleviate effects of time of performance of the tasks.

Schedule of tasks

(i) *'Bakan' auditory vigilance.* This was a version of the Vigilance test devised by Bakan (e.g. 1959). The test lasted 1 h during which subjects listened to digits spoken at a rate of one per second. The subjects' task was to detect a particular combination of three successive digits amongst a background of non-signal digits. Specifically, subjects had to detect three successive odd and unequal digits e.g. 759. There were ten randomly occurring signals in each 12 min period of the task. Subjects reported the detection of a signal by writing the three digits down. Correct detections and false reports were available for each 12 min period of the task. At the end of this task subjects were asked how long they thought the task had lasted.

(ii) *A short-term memory task* consisting of the recall of auditorily presented nine-digit sequences. Subjects heard sixty nine-digit sequences in all. As soon as each sequence ended subjects had to write down the digits from memory in their order of presentation. Ten seconds was allowed for response. Error scores were available for each digit: performance scores were thus available for each serial position in an archetypal list.

(iii) *Visual search.* Subjects were asked to search systematically through pages of letters looking for instances of two target letters. Subjects were given fifteen pages containing letters in a twenty by twenty matrix. There were four targets randomly scattered on

Table 1a Vigilance: Mean number of correct detections and total numbers of false positives

	Correct detections					False positives
Min into task	*1–12*	*13–24*	*25–36*	*37–48*	*49–60*	
Control	8.12	6.73	6.46	6.69	5.73	74
Placebo	7.35	6.50	6.73	6.50	6.58	91
Drug	7.19	6.23	6.77	6.54	6.15	85

Table 1b Vigilance: Mean estimated duration of the vigilance task (min)

Control	*Placebo*	*Drug*
42.61	33.61	35.14

each page. The task lasted 15 min and scores were of the numbers of letters checked.

(iv) *Mental arithmetic.* Subjects were asked to work through as many instances as they could of a three digit by two digit multiplication in the 15 min allotted. Response sheets contained sixty items. Scores were taken of the number of attempts and number of errors.

Results

(i) *Vigilance.* Data for correct detections and false positives are given in Table 1a. Correct detections were subjected to a two way analysis of variance with the drug treatment as a 'between' factor and time-into-task as a 'within' factor (Winer, 1970). Neither the drug treatment ($F=0.95$, d.f.$=2/75$) nor its interactions ($F=1.30$; d.f.$=8/300$) was significant ($P>0.05$). The main effect of time-into-task showed the usual significant decline in correct detections as the task proceeded ($F=21.14$; d.f.$=4/300$; $P<0.001$). False positives, in a one way analysis of variance, showed a non-significant drug treatment effect ($F=0.38$; d.f.$=2/75$). There was no effect of drug treatment on time estimation ($F=2.29$; d.f.$=2/75$) (Table 1b) though estimations were usually less than 'clock time'.

(ii) *Short term memory.* Error data were subjected to a two way analysis of variance: drug treatment (between) and serial position (within). A main effect of drug treatment failed to reach significance ($F=1.94$; d.f.$=2/75$, $P<0.15$) but there was a significant drug × serial position interaction ($F=1.65$; d.f.$=16/600$; $P<0.05$). Figure 1 illustrates the form of this interaction: short term memory was worse in the drug condition than in both the placebo and control conditions, particularly in the medial serial positions. Subjects seem to remember the beginning and end of the digit sequences quite well in all conditions, but the middle digits in a sequence are particularly susceptible to disruption by diazepam.

(iii) *Visual search* (Table 2). Data in the form of number of letters searched (to the nearest hundred) were subjected to a one-way analysis of variance for the drug treatments and gave a significant main effect due to drug treatment ($F=8.19$; d.f.$=2/75$; $P<0.01$). Subjects searched significantly fewer letters in the drug group than in either placebo or control groups. Subsequent comparisons of pairs of treatments indicated that this significant F ratio arose from a significant difference between placebo and drug groups ($t=3.73$; d.f.$=50$; $P<0.01$) and the control and drug groups ($t=3.71$; d.f.$=50$; $P<0.01$). There were no significant differences between the placebo and control groups ($t=0.18$; d.f.$=50$; $P>0.05$).

(iv) *Mental arithmetic* (Table 3). None of the treatments had an effect upon mental arithmetic either in terms of Attempts ($F=0.84$, d.f.$=2/75$); Errors ($F=0.08$, d.f.$=2/75$); or Errors as a percentage of Attempts ($F=1.98$, d.f.$=2/75$).

Discussion

The results indicate that a dosage of diazepam commonly prescribed in the treatment of anxiety states is capable of producing impairment in some mental tasks. The strongest effects in the experiment consist of a derogatory effect of diazepam upon short term retention and upon visual search. Before embarking on a discussion of the positive findings it is worth remarking on some of the features of those tasks that showed no effect.

The absence of any effect upon the Vigilance task is perhaps the most surprising especially in view of the known sensitivity of such tasks to environmental stressors (see, for example, Broadbent, 1971). The only study involving auditory vigilance after diazepam which has come to light is one by Hart *et al.* (1976). Their vigilance task seemed particularly sensitive to diazepam, with a 2.5 mg dose producing deleterious effects upon correct detections. The 'Wilkinson auditory vigilance test' which they employed involved the detection of occasionally appearing short tones among a large number of long ones. It may be that the nature of the task would account for the difference: the simpler stimuli might make the Wilkinson task more tedious or boring, while in contrast, the Bakan task might be seen as intrinsically

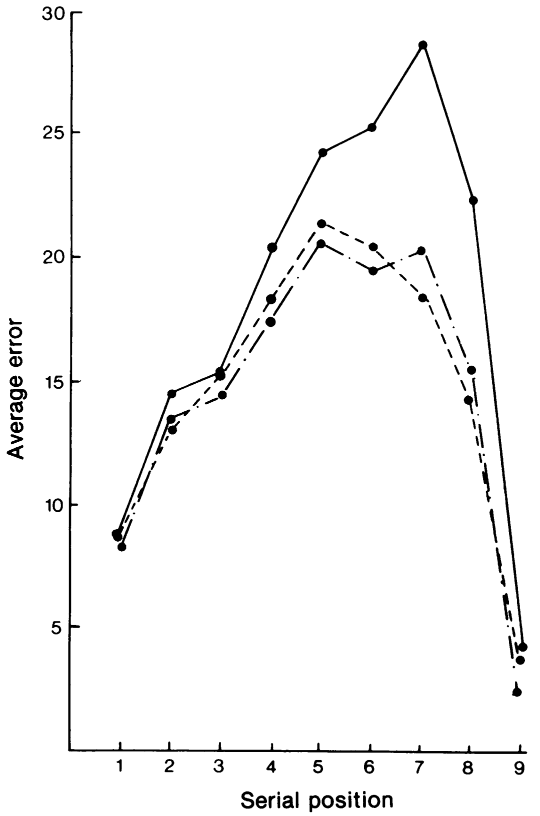

Figure 1 Average error for each presentation position in short term memory. The solid line indicates data from the drug group. The dashed lines represent the placebo and control groups.

more interesting and challenging and hence less boring. Lack of effects in other types of vigilance tasks are not without precedent: Linnoila & Mattila (1973) found no effect of a 5 mg dose of diazepam on a dial watching task. Their task involved several activities with the consequence that subjects found it interesting. Their vigilance task was also visual, and Hart *et al.* (1976) see this as being an important causative factor. These results cannot be accounted for purely in terms of modality, as Hart *et al.* (1976) imply, since the present study finds effects in the visual search task and an auditory short term retention task.

A likely candidate for explaining the absence of effect with auditory vigilance in the present study is group testing. Subjects may have gained non-verbal auditory cues from those around them about the presence of a signal. Thus subjects who may have been drug affected could pick up cues from other members of the placebo or control groups by hearing the rustle of paper as they wrote down their responses. These cues might have helped in the detection of signals. In order to avoid this problem we would suggest in group testing situations using the Bakan task that different subjects are asked to look for different signals.

The absence of any effect of the drug upon mental arithmetic is less straightforwardly explained. Few cues should have been available from their fellow subjects, either visual or auditory (in the latter case white noise masking was effective). The case of mental arithmetic is especially problematical in view of the common features it shares with those tasks in this study that *are* sensitive: the mental arithmetic task is visual and self paced like the search task; it contains a component of short term memory like our test of retention. This task may have been sufficiently challenging to engage and motivate the drug affected subjects, and thus lessen the impact of the drug effects.

Subjects' short term retention was significantly impaired by diazepam. Those items most easily lost as a result of drug administration are the ones from the middle of a list. The impact of this finding is unclear. The data are novel in establishing the precise point in the digit sequence where performance breaks down. Both Hart *et al.* (1976) and Jäättelä *et al.* (1971) failed to provide such a detailed analysis of their data. Despite the apparent superficiality of such a task it is by now widely recognized that the recall of digit strings involves a number of complex processes (cf. Crowder & Morton, 1969).

The substantial changes in the visual search task are in marked contrast to those of Hart *et al.* (1976) who found no significant effects due to diazepam in a similar task, despite the task's apparent sensitivity to the effects of both loud noise (e.g. Woodhead, 1964); and circadian variation in performance (Blake, 1971; Preston, Bateman, Short & Wilkinson, 1973). Hart *et al.* (1976) argue that the task they used was comparatively interesting. In their case subjects searched for instances of five letters whilst in the present study the subject searched for two letters. The search for five

Table 2 Visual search: Average number of letters searched

Control	*Placebo*	*Drug*
8346	7709	5972

Table 3 Mental arithmetic: Average number of attempts and errors

	Control	*Placebo*	*Drug*
Attempts	35.65	38.46	36.42
Errors	5.07	4.73	4.70

letters might have proved to be more interesting than the search for two letters.

What can be said of the general characteristics of drug sensitive tasks? In the present study no single factor seems to differentiate sensitive from insensitive tasks. While mental arithmetic was insensitive it contains components of self pacing and short term memory which were the characteristics of two of the sensitive tasks. Vigilance was paced and contained an element of short term memory.

Hart *et al.* (1976) argue that tasks that are sensitive to low doses of diazepam are (a) prolonged and monotonous, (b) provide no feedback of results and finally (c) require 'a short term memory function'. Evidence from the present study casts doubt on all three of these criteria. The vigilance task is high on (a) and fairly high on (c) but is insensitive to the drug. Mental arithmetic is high on (b) and (c) yet is insensitive. Visual search, on the other hand, provides little of (b) and (c) yet is sensitive. Short term memory runs true to form by being high on (c) and sensitive. Unlike Hart *et al.* (1976), we consider the short term memory task employed in this study to have a high degree of feedback results (i.e. low on (b)). The reader can no doubt testify to this next time he tries to remember an unfamiliar telephone number: one is all too aware of being forgetful in everyday life. Indeed some of the EEG and short term memory changes observed in our laboratory (Jones, Gale & Smallbone, 1977) have been accounted for in terms of the especially strong feedback available to the subject in memory tasks.

This study has served to illustrate the advantages and possible pitfalls in the assessment of human performance by group administered tasks, after clinically typical doses of diazepam. In addition the experiment produced novel data of the locus of memory deficit with an unexpectedly robust finding that visual search was sensitive to the drug. It seems likely that a particular combination of properties of psychological tests, rather than single characteristics alone, will provide a prescription for tests sensitive to anti-anxiety drugs.

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