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Validity and sensitivity of a pen computer battery of performance tests

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This study compared administration of performance tests and visual analogue scales (VAS) using a newly developed pen computer (PenC) battery with established tests using either pencil-and-paper (PP) or conventional computer. The performance of 47 subjects (23 male, age 18–45 years, weight 51–112 kg) was compared on the two systems after a dose of ethanol (0.8 g/kg up to a maximum of 60 g for males, 50 g for females) or placebo in a double-blind two-period randomized crossover study. Mean (SD) blood ethanol concentrations (breathalyser) were 94.5 mg/100 ml (21.9) at the start of the test battery (30 min post-drink) and 80.2 (13.0) at the end of the battery (75 min post-drink). Ethanol effects were found in all tests, with most outcome measures showing significant slowing or loss of accuracy. Results from the Rapid Visual Information Processing, Sentence Verification and Continuous Attention tasks show that the ethanol–placebo difference and the statistical significance of this difference are in close correspondence for the two modes of administration. The pen computer versions of these tasks may therefore be used as direct replacements for the previous versions. Digit–Symbol and maze tasks did not correspond so closely both showing differences in the speed-accuracy trade-off between the two modes. These tests, however, are sensitive to the effects of ethanol, and may be useful in their own right. Principal component analysis suggested that VAS may be grouped into two factors: (1) 'functional integrity', including measures of alertness and perceived proficiency, and (2) 'mood', including happiness and sociability. Factor 1 showed substantial effects of ethanol, while factor 2 was unchanged. There was close agreement between the results from PP and PenC for both factors as well as for the Sober-Drunk scale, which showed the expected effects of ethanol. Thus pen computer VAS perform in a similar way to the PP versions.

Key words: cognitive testing; maze tasks; pen computers; psychomotor performance; reaction times; validation

Introduction

Performance testing is widely used in psychopharmacology to provide objective evidence of changes in central nervous system function due to drugs. Most commonly, the changes are impairments, such as those associated with sedative drugs, but improvements in performance due to stimulants are also of interest (Tiplady, 1991a).

The automated presentation of such tests using either a computer or dedicated test equipment has become commonplace in recent years. The advantages of such presentation over the older methods of pencil-and-paper (PP) or experimenter-administered tests include: (i) standardization of presentation of test stimuli; (ii) accurate timing of individual responses; (iii) automated data handling, eliminating tedious and error-prone manual scoring, measurement and data entry; and, in some cases, (iv) the ability to generate new random sets of test materials for repeated use.

However, not all tests lend themselves to this approach. For example, maze tests and various types of visual search tasks either require a PP approach, or are most naturally carried out in this way. Similarly, visual analogue scales (VAS), a standard method of assessing subjective changes, are generally carried out as PP measures. Maze tests seem to be much less commonly used than they were before the advent of personal computers, although they are sensitive measures of drug effects (Frewer and Lader, 1993; Fagan *et al.*, 1994). This may be related to the inconvenience of using paper-based tasks compared to tasks that can readily be automated.

More recently, a new type of computer system has become available – the pen computer (PenC). This accepts information in the form of strokes or taps with a special pen or stylus on the screen. This makes it possible to automate PP tasks in a simple and natural way. At the same time, some tests that are easily presented on a conventional computer (BBC) can also be set up on a pen system, to produce an integrated battery of different types of test. Such a system is typically very portable: the device used in the present study, the Apple MessagePad MP2000 weighs approximately 700 g, has a screen dimension of 12.5×8.5 cm, and is equally suitable for taking to a patient's bedside in a hospital setting, or for use in a psychological laboratory (Tseng *et al.*, 1998).

It is necessary to compare the performance of subjects on this new system with that on previous versions of the tests, or on tests assessing similar functions. Since it is change in performance due to drugs that is of interest rather than absolute scores, an appropriate form of validation is to assess changes with a drug treatment whose effects are well known. This is a form of criterion-related validation (Anastasi, 1988). The present study used ethanol for this purpose, at a dose of 0.8 g/kg, compared to placebo. Previous studies have shown that this dose of ethanol produces a slowing of approximately 10% on information processing tasks, reliable impairments to memory and attention and very marked subjective effects, while being well-tolerated (Newman *et al.*, 1997; Tiplady *et al.*, 1998).

The test battery included measures targeted at three main areas of performance: Attention; Psychomotor; and Cognitive; as well as Subjective. In each area, a pen-based test (or tests) was compared to an established task – either using PP or a BBC. The attention task chosen was the Continuous Attention Task (Tiplady, 1992). Psychomotor performance was assessed using maze tasks (Gibson, 1978). Sentence Verification (Baddeley, 1981) was used as the main cognitive measure. In addition, two tests which assess a combination of abilities were included as they are widely used in psychopharmacology – Rapid Visual Information Processing (Wesnes and Warburton, 1983) and Digit–Symbol substitution (Wechsler, 1958; McLeod *et al.*, 1982; Mattila and Mattila-Evenden, 1997).

Validity of the pen computer tests was assessed by comparing the magnitude of the ethanol-placebo difference for each outcome measure on the PenC with the corresponding difference for BBC or PP. Sensitivity was assessed by comparing the variability of these difference scores, and the resulting statistical significances.

Methods

Design

The study used a double-blind two-period within-subjects crossover design. In each main session, volunteers received either ethanol or placebo in randomized order. Tests were administered between 30 and 75 min post-drink. The order of test administration was randomized between subjects. The same test order was used for both sessions for a particular volunteer.

Each test in the battery was presented in two forms: the PenC and the previously used version, either PP or BBC.

Subjects

Fifty volunteers were recruited of whom 48 completed the study procedures. One volunteer felt unwell during the ethanol session, did not drink all of the study drink and was excluded from analysis. Of the 47 subjects included in the analysis, 23 were male, 24 female. They were aged 18–45 years (mean 22.8), weighed 51–112 kg (mean 69.7), and their height ranged from 140–198 cm (mean 172).

Assessments

Continuous Attention Task

Patterns consisting of 3×3 arrangements of light and dark squares were flashed onto the computer screen at intervals of 1.5–2.5 s. The task was to respond by a button press (BBC) or a tap on the screen (PenC) whenever two consecutive shapes were the same. A total of 241 patterns was presented with 40 repetitions (Tiplady, 1992).

Rapid Visual Information Processing

A sequence of digits appeared one at a time on the computer screen at a rate of 100 per min. The task was to detect three consecutive odd digits or three consecutive even digits and respond by a button press (BBC) or a tap on the screen (PenC) as quickly as possible. The task lasted 10 min (Bakan, 1959; Wesnes and Warburton, 1983).

Sentence Verification

A series of sentences appeared on the computer screen, e.g. ‘Bicycles have wheels’ or ‘Pigs have wings’. A YES or NO response was made to indicate whether the sentence was true or false as rapidly as possible by a button press (BBC) or a tap on the screen (PenC). Each sentence remained on the screen until the response was made. Fifty sentences were presented (Baddeley, 1981).

Gibson spiral maze (paper)

This maze consisted of a white path bounded by a black spiral, with circular obstacles. The pencil was placed at the centre of the spiral and the path traced around the spiral as rapidly as possible while avoiding the black sides and the obstacles. Time taken was recorded with a stopwatch (Gibson, 1978).

Rectangular maze (PenC)

A light path appeared on the PenC screen against a dark background, as shown in Fig. 1. The pen was placed on the star. When a bell sounded, the subject traced the path to the flag as quickly as possible, while trying to stay within the light track.

Digit–Symbol substitution (paper)

Nine symbols were matched to the digits 1–9 in a key at the top of the page. A random sequence of digits was printed in a grid on the sheet, and the task was to write the corresponding symbol under each digit as quickly as possible. The task lasted for 90 s (Wechsler, 1958).

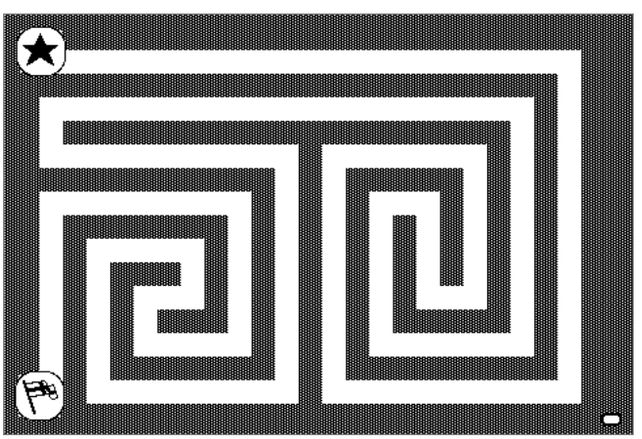

Figure 1 Sample screen from the rectangular maze as set up on the pen computer. The volunteer used a pen to track through the maze from the star to the flag, going as quickly and as accurately as possible

Digit–Symbol yes–no (PenC)

Nine symbols were matched to the digits 1–9 in a key at the top of the PenC screen. Below this, digit–symbol pairs appeared one at a time, and the task was to tap the YES or NO on the screen as rapidly as possible to indicate whether the digit and symbol corresponded. Each digit–symbol pair remained visible until the response was made. Fifty stimuli were presented (Mattila and Mattila-Evenden, 1997; Tiplady *et al.*, 1999).

VAS

Scales consisted of 100 mm lines, the ends of which were marked with semantic opposites (e.g. 'Alert–Drowsy', or 'Sober–Drunk'). Twenty-four scales were used, the 16 described by Bond and Lader (1974) and a further eight that have been found useful in psychopharmacological research. Paper scales were printed 12 to a page, while for the PenC, scales appeared individually on the screen. A single mark was made across each line to indicate the feelings at that time:

Equipment

PenC tasks were presented on the Apple MessagePad MP2000. Conventional computer tasks were administered on a BBC microcomputer Model B with a custom-built response box (Tiplady, 1985). Breath alcohol readings were taken with a Lion Alcolmeter model S-D2 (Lion Laboratories, Barry, South Glamorgan, UK).

Procedures

Each volunteer first took part in a familiarization session in which the test procedures were demonstrated and all tests were carried out at least twice. They then took part in two main sessions, spaced at least 4 days apart.

Subjects were instructed not to use tobacco during test days from 2 h before the beginning of the test session until the end of all procedures, and to take no alcohol from 24 h before the start of the test session until the end of the day. They were instructed to drink a maximum of one cup of tea or coffee at breakfast (to be the same on each test day), and thereafter to abstain from caffeine-containing drinks until the completion of the session. No food was to be consumed for at least 4 h before the beginning of the session.

In the two main sessions, a short test battery was first administered, and volunteers then received a drink consisting of either ethanol in the form of vodka or water, mixed with an equal quantity of orange concentrate. The dose of ethanol was 0.8 g/kg, up to a maximum of 60 g total for males, 50 g for females. Volunteers sucked a Tyrozet lozenge (containing the local anaesthetic benzocaine) before consuming the drink, which was sprayed with a peppermint breath freshener to disguise the taste. The drink was consumed within 10 min. The complete battery of tests was then administered between 30 and 75 min post-drink.

Breathalyser readings were taken before the drink and at the beginning and end of the test battery.

Statistical analysis

Objective tests

Analysis of Variance (SAS, PROC, GLM) was applied to each outcome measure to determine: (i) the magnitude and SE of the ethanol/placebo difference; and (ii) the significance of the ethanol effect. Correlation coefficients between measurements for the two forms of administration were also computed for those tests where the outcome measures for the two forms corresponded (Continuous Attention; Rapid Visual Information Processing; Sentence Verification).

Table 1 Summary of performance on cognitive and psychomotor tasks after placebo and ethanol

Test measure	Placebo	Ethanol	Significance
Continuous Attention Task			
BBC: Error Index	0.154 (0.131)	0.196 (0.166)	*
PenC: Error Index	0.129 (0.162)	0.173 (0.194)	**
Digit–Symbol tasks			
PP: *n* correct/90 s	76.1 (10.9)	66.2 (10.4)	***
PP: *n* incorrect	0.043 (0.204)	0.191 (0.449)	*
PenC: response time (s)	1.41 (0.20)	1.53 (0.23)	***
PenC: *n* incorrect	0.70 (0.78)	1.66 (1.45)	***
Maze tasks			
Gibson (PP): total time (s)	25.7 (6.8)	27.3 (7.6)	**
Gibson (PP): Error Score	14.3 (7.6)	20.1 (12.2)	***
PenC: total time (s)	20.8 (11.7)	21.0 (12.7)	NS
PenC: *n* errors	3.62 (3.02)	6.11 (4.58)	***
PenC: % correct	96.2 (4.6)	90.4 (16.3)	*
Rapid Visual Information Processing			
BBC: *n* correct	47.8 (14.0)	40.5 (13.6)	***
BBC: response time (ms)	445 (59)	489 (69)	***
BBC: *n* incorrect (false alarms)	4.57 (5.58)	7.96 (11.69)	NS
PenC: *n* correct	48.3 (16.1)	39.0 (14.7)	***
PenC: response time (ms)	638 (70)	678 (79)	***
PenC: *n* incorrect (false alarms)	3.07 (5.11)	4.20 (5.81)	NS
Sentence Verification			
BBC: response time (s)	1.22 (0.25)	1.30 (0.24)	**
BBC: *n* incorrect	1.40 (1.22)	2.60 (2.13)	***
PenC: response time (s)	1.60 (0.26)	1.69 (0.27)	**
PenC: *n* incorrect	0.79 (0.86)	2.04 (1.76)	***

Figures are mean values (SD). NS, not significant. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

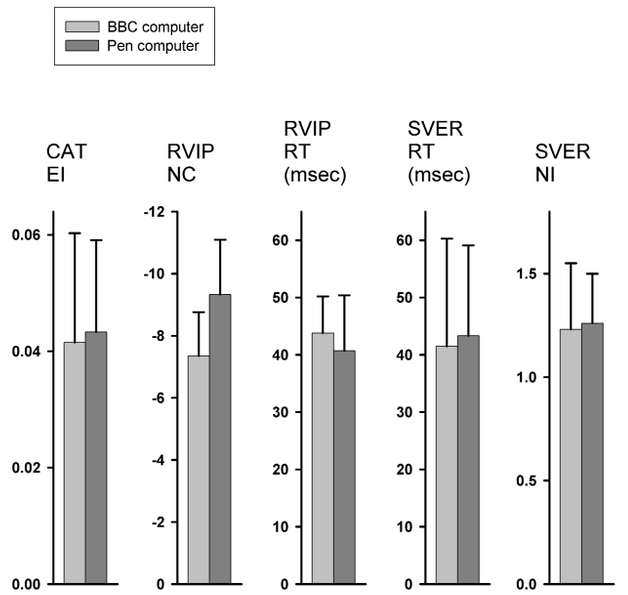

Figure 2 Ethanol–placebo differences for BBC (light grey) and PenC (dark grey) tests. Mean values are shown with the error bars indicating SE. All changes are plotted to indicate impairment in the same direction. CAT, Continuous Attention Task; RVIP, Rapid Visual Information Processing; SVER, Sentence Verification; EI, Error Index; NC, Number Correct; RT, Response Time; NI, Number Incorrect

VAS

Placebo data for the 16 scales described by (Bond and Lader, 1974) were first subjected to a principal components analysis with varimax rotation. In this analysis, the 'Withdrawn–Gregarious' scale was replaced by 'Sociable–Unsociable', because this was considered easier for the volunteers to understand. Scores from the derived factors were then compared in a similar way to the test measures above. The Sober–Drunk scale was analysed separately.

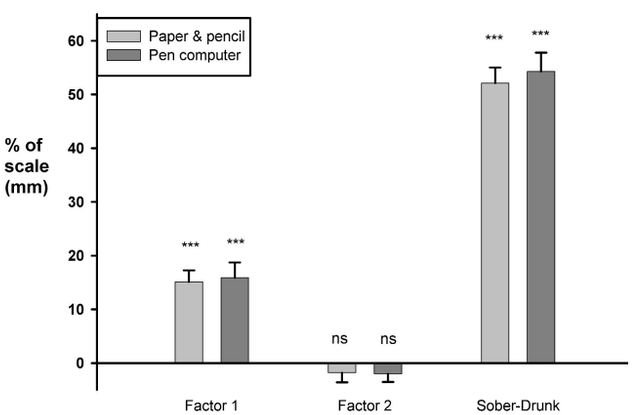

Figure 3 Ethanol–placebo differences for BBC (light grey) and PenC (dark grey) VAS. Mean values are shown with the error bars indicating SE. ***$p < 0.001$; ns, not significant. All changes are plotted to indicate 'impairment' – drowsy, clumsy, sad, drunk, etc. – in the upward direction. Factor 1, functional integrity; Factor 2, mood

Results

The mean (SD) blood ethanol concentrations during the ethanol sessions were 94.5 (21.9) mg/100 ml at the beginning of the test battery and 80.2 (13.0) mg/100 ml at the end of the battery. All pre-drink values and those during the placebo sessions were zero.

The magnitude of ethanol effects and the statistical significance of all test measures from the cognitive/psychomotor battery are shown in Table 1. The great majority of measures showed significant effects of ethanol, and all tests showed significance for at least one outcome measure. All significant effects were in the direction of slowing of responses or of reduced accuracy. The only test measures not to show ethanol effects were total time on the rectangular maze (PenC), in contrast with the Gibson spiral maze which did show significant slowing; and the number of incorrect responses (false alarms) on the Rapid Visual information Processing task (both PenC and BBC). The error rate on the PenC version of the Digit–Symbol task was substantially higher in both ethanol and placebo conditions than that for the PP version. Response times were in general longer for PenC than for comparable BBC measures (Sentence Verification and Rapid Visual Information Processing).

The correlation coefficients between BBC and PenC scores obtained from the Analysis of Variance were: Continuous Attention Task Error Index 0.608; Rapid Visual Information Processing (RVIP) Number Correct 0.813; RVIP Response Time 0.788; Sentence Verification (SVER) Response Time 0.652; and SVER Number Incorrect 0.355; Sober–Drunk VAS 0.854.

Comparisons of the magnitude and variability of the ethanol-induced changes in performance as measured by BBC and PenC are shown in Fig. 2. Both effect size and SD are similar for the two modes of test presentation.

VAS were grouped into two factors: (1) Drowsy, Feeble, Muzzy, Clumsy, Lethargic, Mentally Slow, Dreamy, Incompetent, Bored; (2) Excited, Discontented, Troubled, Tense, Sad, Antagonistic, Unsociable. Analysis of the ethanol effects on these factors and on the Sober–Drunk scale are shown in Fig. 3. The results from the PenC are closely similar to the paper data in terms of raw scores, effects of ethanol and variability.

Discussion

The expected effects of ethanol on performance were clearly evident in this study, and were demonstrated by both established and PenC tests. Responses on most tasks were slowed, and errors increased.

Congruent tests

In three tests – Continuous Attention, Rapid Visual Information Processing and Sentence Verification – the outcome measures correspond closely between the two forms of administration. The magnitude of the changes in test performance produced by ethanol are closely similar for these outcome measures, as can be seen from Fig. 2. Both slowing and increases in errors show similar changes in both PenC and BBC versions of the task. Figure 2 also shows that the variability of these ethanol–placebo differences is similar for the two forms of administration

Another way of looking at test sensitivity is to compare

significance levels found for ethanol effects between the two modes of presentation. These should be the same if the two modes are equivalent. Of the six outcome measures in this group of tests, five show the same conventional level of significance for the two modes, while one test measure (Continuous Attention Error Index) differs by one level ($p < 0.01$ for PenC; $p < 0.05$ for BBC). Thus the results are also in good agreement here.

Although the results for ethanol–placebo differences are very similar between the two modes of presentation, there are some differences in absolute scores. Thus, for the Rapid Visual information Processing task, responses on the pen computer take approximately 200 ms longer on the pen computer than on the BBC (Table 1). In most psychopharmacological work, it is a comparison between conditions, not absolute values that are of interest, and so this difference is not important provided that it represents a constant shift across the range of values. That this is the case here is indicated by the fact that slowing due to ethanol is closely similar for the two modes of presentation (Fig. 2). Although not important in the present context, this shift in values would need to be taken into account if such tests were used in situations where comparisons to population norms were required.

Taken together, these results indicate that in this group of tests – Rapid Visual Information Processing, Continuous Attention, and Sentence Verification – the PenC versions of the tests are closely similar to the BBC versions, and can be substituted for them in psychopharmacological investigations.

Non-congruent tasks

The Digit–Symbol and maze tasks as set up for the PenC do not correspond exactly to the previous PP versions. There have been many proposals for automating Digit–Symbol tasks. McLeod *et al.* (1982) used patterns in a 3×3 grid as symbols, the patterns being entered on the numeric keypad of the computer. Another approach is to replace the writing of a symbol on the page with the pressing of a numbered button in response to a symbol presented on the screen (Tiplady, 1991b; Tiplady *et al.*, 1992; Mattila *et al.*, 1994). The variant used here is based on a suggestion made by Mattila and Mattila-Evenden (1997), who reduced the motor component of the task to a simple YES/NO response, while retaining the elements of visual search and stimulus matching in the original task.

Performance on the Digit–Symbol YES/NO task differed from that on its PP equivalent in showing substantially higher rates of errors. Whereas for the PP task, error rates even on ethanol were less than 0.2 on average, indicating that at least 80% of volunteers made no errors at all, rates around one order of magnitude higher were seen for the automated task. While both speed of performance and errors were significantly impaired by ethanol, the slowing due to ethanol was markedly less for the PenC YES/NO task than for the PP version (8.5 versus 13%). A similar difference between the two modes of administration was previously reported with ethanol (Tiplady *et al.*, 1999).

In the case of the maze tasks, the response mode – drawing a track through the maze – is similar in the two versions, but the shape of the maze is different, to accommodate the relatively small screen size of the PenC. While errors increased very significantly for both the Gibson spiral maze (PP) and the rectangular maze (PenC), speed was affected only for the paper maze. This could perhaps reflect the lack of obstacles in the pen computer maze, making errors less apparent to the subject.

These data indicate that unlike the Congruent tests discussed above, the PenC maze and Digit–Symbol tasks cannot be considered exact equivalents to the paper versions. While they cannot be used as direct substitutes for the originals, they do show good sensitivity to ethanol, and may be suitable for use in such studies in their own right. Further work will be needed to establish whether or not these tests measure similar functions to the corresponding PP tests.

One area where PenC administration may offer particular advantages over PP is in the analysis of detailed performance in the tasks. A number of aspects of the microstructure of performance could be analysed, such as variations in the velocity of tracing of a maze, and the speed with which errors are recognized and corrected. A full implementation of the Digit–Symbol substitution task with drawing of the symbols on the screen could be built, and this would be of particular interest in allowing an assessment of the quality of the symbols produced. No attempt has been made to pursue this approach in the present application, because it was felt necessary to establish the value of using PenC in this area, but future work will address this.

VAS

VAS are frequently grouped into factors on the basis of a principal components analysis (Bond and Lader, 1974; Herbert *et al.*, 1976). The two factors obtained here are closely similar to those of Herbert *et al.* (1976).

The naming of the factors raises interesting points. Factor 1 is very similar to that named ‘Alertness’ by previous authors. This does not seem to capture the common features of a group that includes ‘Clumsy’, ‘Feeble’ and ‘Incompetent’, and we have preferred to refer to this as ‘Functional Integrity’. Similarly ‘Tranquillity’ seems rather too specific for factor 2, and we prefer ‘Mood’.

Analysis of the factor scores, and of the Sober–Drunk individual scale, show very closely similar results between paper and PenC (Fig. 3). Mean difference scores agree within approximately 2 mm, and there is in this case good agreement for raw scores as well as for ethanol-induced changes between PenC and paper assessments. Thus, VAS on the PenC are closely comparable to the corresponding paper scales.

Conclusions

All tasks in both PenC and BBC or paper versions were sensitive to the effects of ethanol. Comparison of the modes of administration showed that while the maze and Digit–Symbol tasks may be suitable for use in performance batteries, they cannot be regarded as simple substitutes for the paper versions. The other tasks – Continuous Attention, Sentence Verification, Rapid Visual Information Processing, and VAS – may be regarded as equivalent to the existing conventional computer tasks for the purposes of detection of drug-induced impairment.

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References

Anastasi A (1988) Psychological testing, 6th edn. Macmillan, New York

Baddeley A D (1981) The cognitive psychology of everyday life. Br J Psychol *72*: 257–269

Bakan P (1959) Extroversion–introversion and improvement in an auditory vigilance task. Br J Psychol *50*: 325–332

Bond A, Lader M (1974) The use of analogue scales in rating subjective feelings. Br J Med Psychol *47*: 211–218

Fagan D, Tiplady B, Scott D B (1994) Effects of ethanol on psychomotor performance under steady-state conditions. J Psychopharmacol *8*: 75–80

Frewer L J, Lader M (1993) The effects of nefazodone, imipramine and placebo, alone and combined with alcohol, in normal subjects. Int Clin Psychopharmacol *8*: 13–20

Gibson H B (1978) Manual to the Gibson spiral maze, 2nd edn. Hodder and Stoughton Educational, Sevenoaks, UK

Herbert M, Johns M W, Dore C (1976) Factor analysis of analogue scales measuring subjective feelings before and after sleep. Br J Med Psychol *49*: 373–379

Mattila M J, Aranko K, Mattila M E, Paakkari I (1994) Effects of psychotropic drugs on digit substitution: comparison of the computerized symbol-digit substitution and traditional digit-symbol substitution tests. J Psychopharmacol *8*: 81–87

Mattila M J, Mattila-Evenden M E (1997) Effects of alcohol and hypnosedative drugs on digit-symbol substitution: comparison of two different computerized tests. J Psychopharmacol *11*: 313–317

McLeod D R, Griffiths R R, Bigelow G E, Yingling J (1982) An automated version of the digit symbol substitution test (DSST). Behav Res Meth Instrument *14*: 463–466

Newman D, Speake D J, Armstrong P J, Tiplady B (1997) Effects of ethanol on control of attention. Hum Psychopharmacol *12*: 235–241

Tiplady B (1985) An automated test battery for the detection of changes in mental function and psychomotor performance. Br J Clin Pharmacol *20*: 305P

Tiplady B (1991a) Psychometric screening of new drugs. In Nimmo W, Tucker G T (eds), Clinical measurement in drug evaluation, pp. 57–71. Wolfe Medical, London

Tiplady B (1991b) Development of a test battery for the measurement of changes in psychological performance. Br J Clin Pharmacol *32*: 667P

Tiplady B (1992) Continuous attention: rationale and discriminant validation of a test designed for use in psychopharmacology. Behav Res Meth Instrument Comput *24*: 16–21

Tiplady B, Faineteau H, Loganathan A, Spiegelberg M, Taylor Z, Wright P (1998) Effects of ethanol and temazepam on performance in memory and psychomotor tasks: a dose–response comparison. Hum Psychopharmacol *13*: 285–291

Tiplady B, Harding C, McLean D, Ortner C, Porter K, Wright P (1999) Effects of ethanol and temazepam on episodic and semantic memory: a dose–response comparison. Hum Psychopharmacol *14*: 263–269

Tiplady B, Sinclair W A, Morrison L M M (1992) Effects of nitrous oxide on psychological performance, Psychopharmacol Bull *28*: 207–211

Tseng H-M., Tiplady B, Macleod H A, Wright P (1998) Computer anxiety: a comparison of pen-based personal digital assistants, conventional computer, and paper assessments of mood and performance. Br J Psychol *89*: 599–610

Wechsler D (1958) The measurement and appraisal of human intelligence, 4th edn. Williams and Wilkins, Baltimore, MD

Wesnes K, Warburton D M (1983) Effects of smoking on rapid visual information processing performance. Neuropsychobiology *9*: 223–229