# THE ROZELLE TEST BATTERY

A computerised testing instrument for visuomotor and cognitive performance

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## **SUMMARY**

One of the research instruments currently in use at the National Drug and Alcohol Research Centre is the Rozelle Test Battery. This report is intended to provide a primary reference to that instrument, to describe the tests, the programming environment in which they were realised, and the considerations which led to the choice of tests, equipment and environment. The six original tests were intended to provide a broad range of performance indices sensitive to selected drug effects. The extent to which these intentions were realised is discussed for each case, and some indication of the future development planned is provided.

## **ACKNOWLEDGEMENTS**

I would like to thank Dr. G.B. Chesher, Ms. M. Gomel, Prof. G.A. Starmer and Mr. D. Mascord, who all contributed to the development of the test battery in many ways. The initial work was funded by the NSW Drug and Alcohol Authority while the author was at the Psychopharmacology Research Unit of the University of Sydney.

#### Introduction

This report describes the Rozelle Test Battery, why it was constructed, and a selection of the empirical results which have been obtained through its use. It is written to provide a complete, up-to-date reference on the entire test battery. Additionally, this report offers an introduction to the rationale upon which the individual tests, and the entire program environment, are based.

### Computerised testing

An enormous number computerised testing instruments have appeared during the last 10 to 15 years (Kennedy, Baltzley, Wilkes & Kuntz, 1989). The ease with which microcomputers can be programmed to control laboratory equipment and collect data has produced a variety of testing programs (e.g. Kennedy, Baltzley, Wilkes & Kuntz, 1989). Some of these attempt to translate existing instruments into the computer format, while others have introduced novel tests, some of which would be difficult or impossible to realise outside that format. While this trend has led to a general improvement in the ease of presenting tests and collecting the resulting data, a number of difficulties have emerged. These range from problems with the actual hardware used to flaws in the design of the tests themselves. A great deal of the development of the Rozelle Test Battery was addressed to these concerns.

## Hardware considerations

Testing programs realised on computers which are expensive and hard to obtain may severely limit the applicability of the tests. In many cases, tests designed for computers are dependent upon unique hardware interfaces which cannot be easily and cheaply reproduced by other investigators. It would obviously be preferable for the computers used to be cheap, reliable, and easily obtained,

provided they are adequate. Any peripheral devices necessary to operate the tests should either be easily built and well-documented, or proprietary products which are readily available.

#### Software considerations

Testing programs are sometimes written using exotic programming languages and/or proprietary compilers which are not available to the user. Apart from the obvious problems of attempting to modify a test without the source code or the tools used to produce the final programs, it is rare for programs of such limited distribution and testing to be free of errors. It is highly desirable to program, whenever possible, in the languages which are provided with the machine, or are available from the same distributors.

The user interface of testing programs ranges from those which compare favourably with commercial software to others which definitely challenge the operator's ability. A great deal of testing is actually administered by relatively untrained research assistants. and facilitating the use of the programs through an intuitively obvious interface should be a prime consideration. As the interface tends to differ considerably between test batteries, it would also be desirable to have a consistent interface across a range of tests. Additionally, the very difficulty and expense collecting data makes that correspondingly valuable. Every effort should be made to allow the resulting programs to recover from commonly encountered errors without the loss of data.

#### Test design

A central concern to many designers of tests, whether or not these were intended to be presented by computers, has been the presumed reliability of the tests. This is typically assessed in two ways; a theoretical reliability computed using the number of items on the test and their inter-correlation, and a variety of empirically determined

test/test or test/retest reliability measures (Cronbach, 1964). While the former method has proven adequate in the development of multi-dimensional scales of personality and the like, it has severe limitations when applied to the testing of drug effects.

The effect of many drugs is temporary, even ephemeral. The use of extended tests may allow these effects to change considerably or even dissipate to an undetectable level during the testing While maintaining adequate reliability, it is advantageous to limit the duration of the test to a period within which the drug effect is relatively stable. A less obvious consideration is the effect on the subject of a long, uninteresting test. A great deal of evidence has accumulated to support the notion that the most important effects of drugs on human behaviour are modulated by the motivational state of the user. It may therefore be futile to attempt to assess the effect of a drug in a laboratory situation which produces a markedly different motivational state from that accompanying behaviour outside the laboratory setting. The fact that such changes in motivation might lead to a violation of one of the assumptions underlying the coefficient reliability (viz. the of consistency of the inter-item correlation coefficient) is usually ignored.

## Data management

The microcomputer is a powerful tool for collecting data. However, its potential in this respect may easily lead to the accumulation of a vast amount of information which is exceedingly difficult to analyse or interpret. The response to this in some cases has been to subject the data to reduction within the testing program itself. These techniques produce a more compact output, but may predefine the intial analysis, and perhaps the interpretation, of the data. For instance, restricting the output to the mean and

variance of a number of observations would prevent the assessment of any linear trend across those observations.

## The Rozelle Test Battery

In 1984, a grant from the NSW Drug and Alcohol Authority was awarded to Dr. Chesher and Dr. J.C. Crawford to develop a series of tests to assess the effects of both therapeutic and recreational drugs on human performance. This project was carried out by the Psychopharmacology Research Unit (PRU - Department of Pharmacology, University of Sydney) at the Rozelle Hospital. The Rozelle Test Battery resulted from continuing work on the tests initially developed.

#### Hardware

It was decided to develop the initial test battery on the *Apple IIe* microcomputers which were available in the laboratory, and which are widely distributed and relatively cheap.

One advantage of the Apple IIe microcomputer is its open architecture which allows the use of quite simple input/output (I/O) devices. The entire computer, and its operating software are thoroughly documented, and a large number of proprietary products are available to enhance the machine's capabilities. While the design is certainly dated, the machine proved adequate for the task.

The test battery was eventually completed using only a proprietary timer card (Timemaster II H.O.), which was necessary for the real time data acquisition, and a subject response board and control wheel in addition to the standard microcomputer. The response board was designed to simulate an Apple IIe keypad, and the control wheel interfaced with the 'game' port of the Apple IIe. At the time of writing, at least one other testing centre (School of Underwater Medicine, RAN, Sydney) has successfully constructed the accessory equipment.

#### User Interface

The user interface was menu-driven to facilitate the use of the tests, and included programmable test orders which would run without the intervention of the operator. All operations from initial subject data entry to display of the test data were programmed to operate within a consistent environment.

## **Program Environment**

All programs were written in standard Applesoft BASIC and/or 6502 Assembly language using the Apple Assembler 1.0. The use of assembly language was necessary to produce adequate performance in programs involving graphic animation, and to manage the real-time data acquisition. It was unnecessary to compile the sections of the programs written in BASIC, and these are easily modified by a reasonably competent programmer.

The parameter passing conventions between the programs managing the user interface and those running the tests are consistent across all tests, and allow the inclusion and/or deletion of tests. This flexibility has fostered continuing development of the battery, enabling the production of tailored test sequences for differing experimental applications.

## Data management

In most experimental situations, data is collected by case, and this was reflected in the data management adopted. All data filenames were derived from a single root word, usually the subject's name. After entering the subject's name (or other root word) once on a data disk, the filenames are generated automatically, obviating the possibility of misspelt data filenames. The data collected in any test was preserved in its raw form in the data file, and only reduced by programs designed to display the data. In all cases,

the original raw data remained accessible to the investigator.

All programs were written with routines to recover from the most common errors in data storage; i.e. full data disks, corrupted or improperly formatted data disks, or data disks not properly inserted into the drive.

The data collected from each test was chosen through examination of the results of a number of piloting and testing sessions in addition to any prior notions about the appropriate variables to be measured. While this has produced tests which tend to measure a restricted range of variables on any given test, the design of the tests facilitates alteration of the programs if additional variables are required for a particular experimental purpose.

## Procedure of testing

typically been The tests have administered in darkened, sound-attenuated booths, with the subject wearing headphones. White noise of approximately 80 dB intensity is constantly presented via the headphones. The headphones are also used to deliver the various auditory feedback signals which the programs produce. In the current equipment, the white noise generator and amplifier circuitry is mounted within the subject response board. Subjects are given an initial practice run, in which shortened versions of each test are presented. The experimenter verbally guides the subject through these, answering any questions to supplement the onscreen instructions which are provided. The practice versions of each test vary in length, with those tests which are easiest to understand (e.g. the Mackworth Clock) having quite brief introductions. Subsequent testing runs are conducted with the subject alone in the booth. As each test must be started by a button press from the subject, the sequence may be interrupted between tests if this is necessary.

#### Individual tests

The tests which have been developed thus far range from visuomotor performance tests to those assessing various aspects of cognitive functioning. Each test will be treated separately in terms of its proposed aims, the theoretical indications leading to its development, and its success in detecting drug effects, using ethanol as the prototypical psychotropic drug. The tests have successfully been used to study the effects of a wide range of psychoactive drugs. Recreational drugs such as ethanol and marijuana, as well as therapeutic drugs (chemotherapy agents, anti-epileptics. benzodiazepines, antihistamines, barbiturates and lithium) have all been shown to affect performance in one or more of the tests.

## **Digit Symbol Substitution Test**

When two sets of symbols are arbitrarily paired, the ability to rapidly substitute a symbol from one set when presented with its associate has proven to be a useful measure of speed and accuracy (Wechsler, 1958). Typically, the pairing is presented as a table in which the two sets of symbols are arranged in two parallel rows. The subject may merely scan the table, which is always visible, or attempt to memorise the association of symbols to In either case, the speed and accuracy of responding is not only a useful test of the subject's functioning, but is reliably sensitive to moderate levels of recreational drugs such as ethanol.

This test was adapted from the test of the same name used on the Wechsler Adult Intelligence Scale. A row of symbols is displayed above the digits from 1 to 9, and in a box below this, one of the symbols appears. The pairing of digits and symbols is randomised on each run of the test. The subject is required to press the number key on the response board corresponding to that symbol. The progression of symbols continues for 120

seconds. The reaction time and correctness is recorded for each response.

The Digit Symbol test has consistently shown increased reaction time for correct responses after subjects have consumed ethanol to a BAC of .05% (Starmer & Mascord, Note 4; Mascord, Starmer, Smith & Whitfield, Note 3 - see Figure 1).

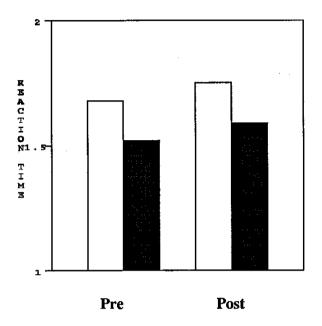


Figure 1 - Digit symbol reaction time before and after .54g/kg ethanol. Mascord & Starmer, Note 2 (open bars) - Starmer & Mascord, Note 4 (solid bars).

#### **Mackworth Clock**

The Mackworth Clock Test (Mackworth, 1948) is widely accepted as a standard vigilance test. The fundamental rationale for such a test is the simulation of a task in which infrequent target stimuli must be detected within an exceedingly repetitive sequence of similar non-targets. Both the ability to detect a non-salient target, and to maintain concentration in an impoverished stimulus environment are severely tested. Either momentary lapses of attention brought about by drowsiness or reduced vigilance to the detection of targets should result in a decrease in the proportion of targets reported.

In this version of the test, a circular 🦛

arrangement of 24 dots is displayed, and each dot "flashes" in clockwise sequence. The stimulus onset asynchrony (SOA) between successive flashes is 0.5 seconds. A target is defined as a jump of one dot in the sequence. The subject must maintain constant attention on the display to detect targets. When a target is detected, the subject is required to press any key on the response panel. Recalling that the test is typically conducted in a darkened, sound-attentuated environment, with masking noise delivered through the subject's headphones, it is obvious that minimal stimulation is available.

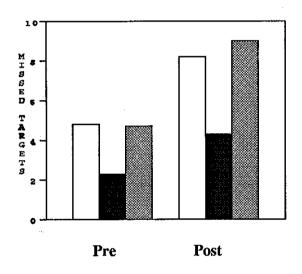


Figure 2 - Number of missed targets before and after .75g/kg ethanol for three groups (Chesher et al, 1989).

effects of ethanol concentration in such a task are well known. The success in detecting targets shows a pronounced decrement with intoxicating doses of ethanol (Chesher, Lemon, Gomel & Murphy, 1989 - see Figure 2). While the reaction time has often been increased under a dose of ethanol on the present test battery, the principal measure of interest has been the number of missed targets. This has resulted from the fact that the Mackworth Clock has invariably been administered in combination with other tests which are . more sensitive indices of reaction time.

## Sternberg Test

Since Sternberg's (1966) original paper describing an apparently linear increase with size of set in the time taken to establish membership of a probe digit in a small set of previously presented digits, this test has found extensive use outside the study of such mental The subject is required to remember an arbitrary set of digits for a short time, and to search that set for the presence of one or more probe digits. The speed with which this is done, for various set sizes, might be expected to vary with the dose of a drug like ethanol, which is known to affect both short term memory (Miller & Dolan, 1974; Ryback, 1973) and simple reaction time (Chesher, Dauncey, Crawford & Horn, 1986).

In the Sternberg Test, a message indicating the upcoming trial appears on the screen, followed by a set of digits presented in sequential order, each digit displayed for 1.5 seconds. The size of the set has previously been specified in a parameter file, and the program randomises the 10 available digits and chooses the test digit. After another message, the test digit is displayed until the subject presses either the "YES" or "NO" button, to record their decision as to whether the test digit was a member of the preceding set. This sequence is repeated for a number of trials, usually 30, with 10 sets each of 3, 4 and 5 digits.

The Sternberg test intially showed little promise as a performance test. However, when the test was modified so that larger sets were available, and multiple probe digits were presented for each memory set, better results were obtained. While the learning curve of the modified Sternberg test has masked the effects of ethanol on reaction time to correct answers, the number of errors has been shown to be sensitive to levels as low as .05% BAC (Mascord & Starmer, Note 2). Figures 3 illustrates the change in correct responses for the test after moderate doses of ethanol.

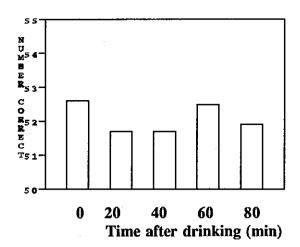


Figure 3 - Number of correct responses on the Sternberg Test after .54g/kg ethanol (Mascord & Starmer, Note 2).

#### "Little man" Test

The ability to determine left and right in another person's frame of reference is an important landmark in development (Piaget & Inhelder, 1956) as well as an index of brain function, particularly of the parietal area (Goodglass Such tests have and Kaplan, 1979). previously used other persons, or relatively detailed representations of people, upon which judgements were made. versions of a test which required left-right judgements were examined at the PRU before work on the present test was commenced. In both tests. the representations were quite schematic, leading to some difficulty in discriminating the front from the rear of the figure. Worse still, the information differentiating the right "hand" from the left (upon which the judgement was to be made) was minimal.

In the test, a cartoon-style figure appears on the screen, holding a large glass of beer in one hand. The subject is required to press a "RIGHT" or "LEFT" button to indicate which hand of the figure holds the beer. The figure may be oriented head-up or head-down, and may be facing toward the subject or away. The subject may adopt a strategy of mentally

rotating the figure to an orientation in which the judgement is relatively easy (e.g. head-up, facing away from the subject), or some other transformation. Subjects almost invariably report a rotation or similar strategy when questioned.

The original "Little Man" test showed suggestive, but unreliable effects with drugs such as ethanol. It was considered that two factors contributed to this. The number of trials (20) was insufficient to provide reliability, as this only contained 10 of the difficult head-down trials. Also, the learning curve varied considerably between individuals, and did not appear to approximate the negatively accelerated ideal. Performance tended to change in fairly large steps, as subjects learned more effective strategies, and the strategies that subjects apply to the solution appear to have a marked effect on assessed performance (Mascord & Starmer, Note 2). As these strategies are evolved on an individual basis, their effects on performance are apparent at different times for different individuals. Figures 4 and 5 show the reaction times and proportion of correct responses which have been recorded before and after moderate doses of ethanol.

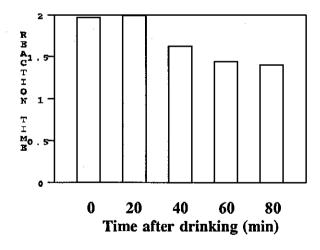


Figure 4 - Reaction time in seconds on the "Little Man" test after a .54g/kg dose of ethanol (Mascord & Starmer, Note 2)

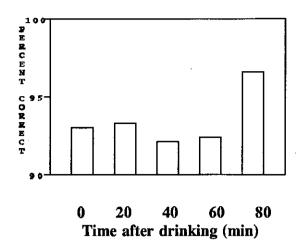


Figure 5 - Percent correct responses on the "Little Man" test after a .54g/kg dose of ethanol (Mascord & Starmer, Note 2).

The task of mental rotation alone may prove to be valuable as a performance test, and a modified version with two figures has been programmed. This is currently being assessed for use in examining event related potentials (ERPs).

## **Tracking Test**

Visuomotor coordination is not only a valuable index of generalised ability, but is also useful in the initial diagnosis of neurological disorders, and is often impaired by psychotropic drugs. are two broad types of tracking tasks in use, termed pursuit and compensatory. In a pursuit tracking task, the subject attempts to trace the same path as a freely moving object. A compensatory tracking task imposes movements upon an object, and the subject attempts to reduce these movements to a minimum by some form of control which opposes the movements. A useful analogy to the control required in these two tasks is that of driving an automobile. Compensatory tracking corresponds to the steering corrections made in order to keep the vehicle travelling within the lane on a straight road, while pursuit tracking simulates the task of remaining within the lane of a winding road. Although exceedingly sensitive compensatory tracking tasks have been devised (Jex, McDonnell & Phatak, 1966), it was decided to use a pursuit task in the present battery. This type of task tends to be more familiar to the average subject, and is thus learned more rapidly.

Two vertical lines approximately 17mm high and 20mm apart are displayed at about the center of the screen. A small rectangle approximately 6 x 4mm is also displayed, its horizontal position controlled by the steering wheel placed in front of the subject. When the subject presses a key, the lines begin to move horizontally, reversing direction at irregular intervals. The subject is instructed to keep the small rectangle between the two vertical lines. The program monitors the subject's performance, and adjusts the speed of the moving lines to approach a prespecified error rate. This is essentially a "branched" testing strategy (Cronbach, 1964), and enables a more reliable estimate of performance with a smaller number of items. In this test, the "items" may be considered the intervals at which performance is monitored. When the rectangle moves outside the lines, a beeping sound is heard in the subject's headphones. This error feedback appears to be quite important in focussing the attention of the subject upon the task, and curtailing any lapses of attention.

Each time the program checks the performance of the subject, the speed which is set is recorded. Whenever the small rectangle moves outside the lines, the time is recorded. When the rectangle is brought back within the lines, both the time and the maximum excursion is recorded.

The mean speed at which the lines move over the final 10 monitoring intervals is represent the thought to maximum performance of which the subject is capable at that time. The speed is recorded as a delay between screen movements, so that numerical increases represent poorer performance. This terminal speed has reliably been sensitive to ethanol at BACs starting at .04% (Mascord, Starmer, Smith & Whitfield, Note 4). Figure 6 shows a selection of experimental results obtained using the tracking test.

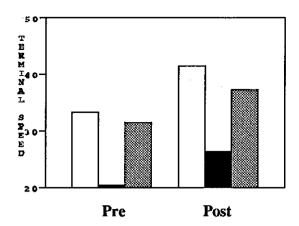


Figure 6 - Terminal speed attained on the tracking test before and after alcohol. The mean BACs on the post test were ORAL (open bars) .067; STEADY-STATE (solid bars) .068; INTRAVENOUS (hatched bars) .055 (Mascord et al, submitted).

The mean time off target, and mean maximum excursion are also recorded, and have shown some potential for distinguishing drug effects in the divided attention task, described below.

#### Divided Attention Task

One of the major problems in tasks such as motor vehicle driving is the allocation of attentional appropriate resources to various aspects of the task. Whether this is metaphorically represented as divided attention, time-sharing or parallel processing, the essential problem remains one of processing all necessary stimulus input and responding effectively. It has become evident that in motor vehicle accidents associated with ethanol use, it is the selective neglect of some aspects of the task which is commonly reported as contributing to the accident, rather than a general degradation of performance (McLean, Holubowycz & Sandow, 1971). It has been argued elsewhere (Lemon, Mascord & Starmer, Note 1) that the perceived difficulty of the component tasks, their relative attentional demands. and the provision of error feedback are all crucial factors in the subject's allocation of attentional resources. This allocation in turn affects the performance on task components in ways which may compromise assumptions made about the relevance of the test to activities such as motor vehicle driving.

The Rozelle Divided Attention Task (RDAT) uses the previously described pursuit tracking as the central task. The only alteration made to this component of the task has been an increase in the error rate allowed. This was done primarily to allow the maximum tracking speed attained in both tests to be roughly comparable for any given subject. It was discovered empirically that doubling the error rate compensated for the additional difficulty imposed by the second task.

At each corner of the visual display unit a circle approximately 15 mm in diameter is displayed. Within each circle is a diametrical line in one of four orientations; horizontal, vertical or either oblique, one of which is designated the target. This allows some control over the difficulty of the peripheral task, as the discrimination of oblique lines has been shown to be more difficult than that of orthogonal (Triesman, 1982). When a target orientation appears, the subject is required to press the button on a panel of four which corresponds to the position of the target on the screen. When a correct keypress is made, the line orientation changes to a non-target, and a short beep of a higher frequency than the error sound (2kHz) signals the correct response.

The program records the time at which each target was presented and when each keypress was made by the subject, in addition to the information collected by the tracking task.

The Divided attention test has been shown to be sensitive to ethanol at .05% BAC both in overall performance (Lemon, Starmer & Mascord, Note 1; Mascord & Starmer, Note 2) and in its individual components (Starmer & Mascord, Note 4). Figure 7 illustrates the effect of ethanol on performance on the RDAT. Overall performance is computed by standardising the scores on both components

of the test, and adding the two component scores. In all scores, a numerical increase indicates poorer performance.

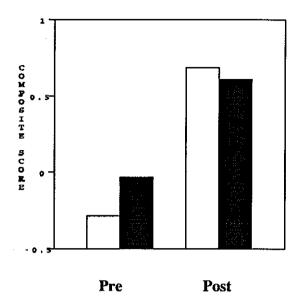


Figure 7 - Composite scores on the Rozelle Divided Attention Task before and after 0.54 g/kg ethanol (open bars - Lemon, Starmer & Mascord, Note 1; solid bars - Mascord & Starmer, Note 2).

## **Gomel Task Shift**

The Divided Attention Task uses two concurrent tasks to test the subject's ability to allocate attentional resources. The Gomel Task Shift, in contrast, presents two alternating tasks to examine the extent to which the subject is able to rapidly change task analysis and response determination. This ability has been linked to frontal lobe functioning (Milner, 1964), as well as being a commonly global reported deficit in neuropsychological assessment (Goodglass and Kaplan, 1979).

One component task is digit echoing, in which a single digit appears on the visual display unit, and the subject is required to press the corresponding number key on the response board. The second task is a set membership decision similar to the Sternberg task. A nonsense word of from three to seven consonants is presented at the beginning of the trial,

which the subject is asked to remember. In the first phase of the test, letters appear successively on the screen, and the subject is required to press a "YES" key if the letter is a member of the word, or a "NO" key if it is not. This phase allows a determination of the subject's average time to respond. In the second phase, the letter trials are spaced so that several trials of digit echoing occur between each set membership trial. In this way, a measure of the ease with which the subject switches between the two tasks is obtained. The ratio of reaction times on the letter-only trials, to that of trials where the letters are interspersed with digits, should indicate the relative difficulty of this shift. The difficulty of performing the two tasks is quite different; it was proposed that the ability to shift to the easier task would be likely to survive under more severe drug effects (or brain damage) than that to the harder task. If a given subject encountered equal difficulty with both shifts, this might indicate a general deficit in altering mental set.

The Gomel Task Shift test has been evaluated as a performance test, but thus far the difficulties of collecting sufficient data within a short enough interval to be useful in testing drug effects have limited its usefulness. The suitability of this test for the assessment of cognitive functioning using longer test times is proceeding.

#### **Visual Analog Scales**

Self report scales are often used in the drug research field, to collect data about perceived drug effects, cognitive functioning, and motivational states. As mentioned previously, these effects may not be stable over any great length of time, and it is essential to gather such self reports when they are most meaningful.

A program to present a series of questions using a visual analog response scale was included to sample these variables while the subject is still in the test situation. Since the same response board is used as for the tests, continuity is ensured between the testing situation and the subject's assessment of their own state or performance.

Up to twenty questions are programmed, with endpoint descriptors, and ten of these question files are available for testing at any time. Each set of questions is associated with a particular automatic order of testing, and may be programmed to run at any point within that sequence of Thus different questions may be asked on different testing occasions. Each question appears at the centre of the screen, with the endpoint descriptors and a row of digits from 0 to 9 beneath it. Pressing any numeric key on the response board places an asterisk above the corresponding digit. The subject may decide to press another numeric key to change the position of the asterisk, or the "YES" key to record the response. These instructions are presented above each question on the screen. The final response is recorded for each question. A typical question screen is illustrated below.

PRESS THE NUMBER WHICH BEST REPRESENTS YOUR ANSWER. PRESS "YES" WHEN DECIDED.

HOW DRUNK DO YOU FEEL?

NOT AT ALL VERY

\*
0 1 2 3 4 5 6 7 8 9

The visual analog scales have been successfully used to obtain subjects' reports of the effects of drugs on both performance and their perceived affective state (Mascord & Starmer, Notes 2 and 3).

The Rozelle Test Battery was originally developed as a means of assessing the acute and chronic effects of various drugs

on human performance. The tests sample a broad range of abilities, and do so with sufficient sensitivity to reveal the effects of a variety of drugs on those abilities. Continuing use and development of the tests may reveal additional areas of use, both in the study of drug effects, and other influences on human performance.

#### RESEARCH NOTES

- 1. Lemon, J.A., Mascord, D.J. & Starmer, G.A. (unpublished manuscript) A comparison of performance on two divided attention tasks after two moderate doses of ethanol.
- 2. Mascord, D.J. & Starmer, G.A. (unpublished manuscript) Subjective and objective measures of acute tolerance.
- 3. Mascord, D.J. & Starmer, G.A. (manuscript in preparation) Comparisons between subjective and objective measures of the effect of ethanol on performance on visuomotor and cognitive tasks.
- 4. Starmer, G.A. & Mascord, D.J. (manuscript in preparation) Visuomotor performance and mood across the menstrual cycle.

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