A NOVEL AUTOMATED TOUCHSCREEN PROCEDURE FOR ASSESSING LEARNING IN THE RAT USING COMPUTER GRAPillC STIMULI

Timothy J. Bussey, Janice L. Muir and Trevor W. Robbins

Department of Experimental Psychology, University of Cambridge, Cambridge, CB2 3EB, U.K.

(Accepted July 6, 1994)

SUMMARY

A new computer-automated touchscreen testing procedure for studying learning in the rat, allowing the presentation of nonspatial computer graphic stimuli, is described. Data from three tasks implemented in the apparatus (8-pair concurrent discrimination learning, visuospatial conditional rule learning, and nonspatial nonmatching-to-sample) are presented. The advantages of the technique are discussed, including the utility of such a method within the framework of a comparative neuropsychological approach, the ability to compare performance in nonspatial tasks with their spatial analogues, the ease of training rats to attend and respond to stimuli in the apparatus, and the advantages of automation over more labour-intensive options such as presenting junk objects or two-dimensional stimuli in mazes, or the Lashley jumping stand.

KEY WORDS: Discrimination, Nonmatching-to-sample, Touchscreen, Learning, Memory, Rat.

INTRODUCTION

A popular research strategy is to compare cognitive performance of brain-damaged human patients with animal models of their disorders, using tasks designed to assess specitic psychological functions. This enterprise is greatly facilitated when the tasks are as similar as possible across species, and very difficult when they are not (14). Thus, researchers have begun to develop techniques whereby humans and monkeys may be tested on tasks in which the task parameters and stimuli are, as near as possible, identical (13). These tasks typically involve the use of 'junk objects' in the Wisconsin General Test Apparatus. Procedures have also been developed to allow the use of junk objects with rats (1, 6, 9).

CCC 0893-6609/94/050103-08

However, such methods, as well as mazes and the classic Lashley jumping stand, much used in the study of discrimination learning in the rat, suffer from their labour-intensive nature.

The assessment of learning and memory in humans generally involves rather different testing methods such as card-sorting, pencil and paper tests, paired associate learning tests or response button tasks. However, a powerful and innovative development for testing humans involves the use of a touchsensitive screen, so that feedback can rapidly be provided for responses to computer graphic stimuli presented on a video display unit (5, 11). A particular advantage of this method is that there is a reduced requirement for additional cognitive processing that mediates performance when stimuli and responses are spatially separate (3). Similar methods have been used in primates (2) and indeed it has been possible to study performance in the same tasks in humans, marmosets and rhesus monkeys (8). However, the predominant methodology for cognitive assessment of the rat relies on the use of spatial stimuli, in foraging (7) or escape (4) paradigms. The usefulness of this species would be enhanced further if more powerful procedures were developed for measuring discrimination learning and memory using stimuli with defined perceptual features that can be presented in an automated manner.

In this study, we present a new apparatus and method for testing rats which utilises computer graphic stimuli presented on a touch-sensitive screen. It has been known for some time that rats are able to attend and respond to such computer graphic stimuli (Bussey, Saksida and Wilkie, unpublished observations). The apparatus used in the present study capitalises on this ability, to allow the implementation of a variety of spatial and nonspatial tasks. Data from three such tasks are presented: 8pair concurrent discrimination learning, visuospatial conditional rule learning, and nonspatial nonmatching-to-sample. Each of these tasks has been shown to be important for defining the neural substrates of learning and memory in monkeys and humans (eg., 13).

MATERIALS AND METHODS

Subjects: Seven experimentally naive male Lister hooded rats (Olac, Bicester, U.K.), weighing between 320 and 350 grams at the beginning of the experiment, were housed in pairs in a temperature controlled room (minimum 22C) on a 12hr light/12hr dark cycle (light on 0700). They were provided with free access to water, and by means of a restricted feeding regimen were maintained throughout the experiment at 90% of their free feeding weight.

Apparatus: The apparatus, shown in Figure I (built in the Department of Experimental Psychology, University of Cambridge), consisted of a testing chamber and video display unit (VDU) housed within a wooden sound-attenuating box, fitted with a fan for ventilation and masking of extraneous noise. The inner chamber measured 48cm x 30cm x 30cm, and consisted of a metal frame, clear Perspex walls, and an aluminium floor. A 3W houselight and a tone generator were attached to the ceiling of the chamber. Located centrally on the wall at the rear of the chamber was a food magazine attached to a pellet dispenser (Campclen Inst.) situated outside of the sound-attenuating box. The magazine could be illuminated by a standard 3W bulb. Animals gained access to the magazine via a hinged Perspex panel monitored by a microswitch. A pressure-sensitive area of floor measuring 14cm x lOcm and located directly in front of the food magazine was attached to a microswitch in order to detect the presence of the rat when in this area of the testing chamber. The VDU, on which the stimuli were presented, was located at the other end of the chamber. Surrounding the VDU was a 'touchscreen' attachment

(Microvitec Touch-tech 501), an array of horizontally and vertically placed photocells which detected the location of pokes to the VDU screen. A black Perspex 'mask' was attached to the face of the VDU, approximately 2 cm from the surface of the display. This mask served to block access to the VDU display except through response windows each measuring 6cm high x 8cm wide. A shelf extending 7cm from the surface of the Perspex mask was positioned just beneath the response windows, approximately 15cm from the tloor of the chamber. The shelf was supported by springs to prevent attempts by animals to climb onto it. The combined effect of the response windows and the shelf was to force the animal to stop, rear up, and stretch toward the stimuli with a head-on approach, thus facilitating the rats' attention to the stimuli. The stimuli used in the tasks consisted of coloured shapes, lines and patterns (see Figure 2). The apparatus was controlled and monitored by a BBC Master series microcomputer, using programs written by TJB in BBC BASIC.

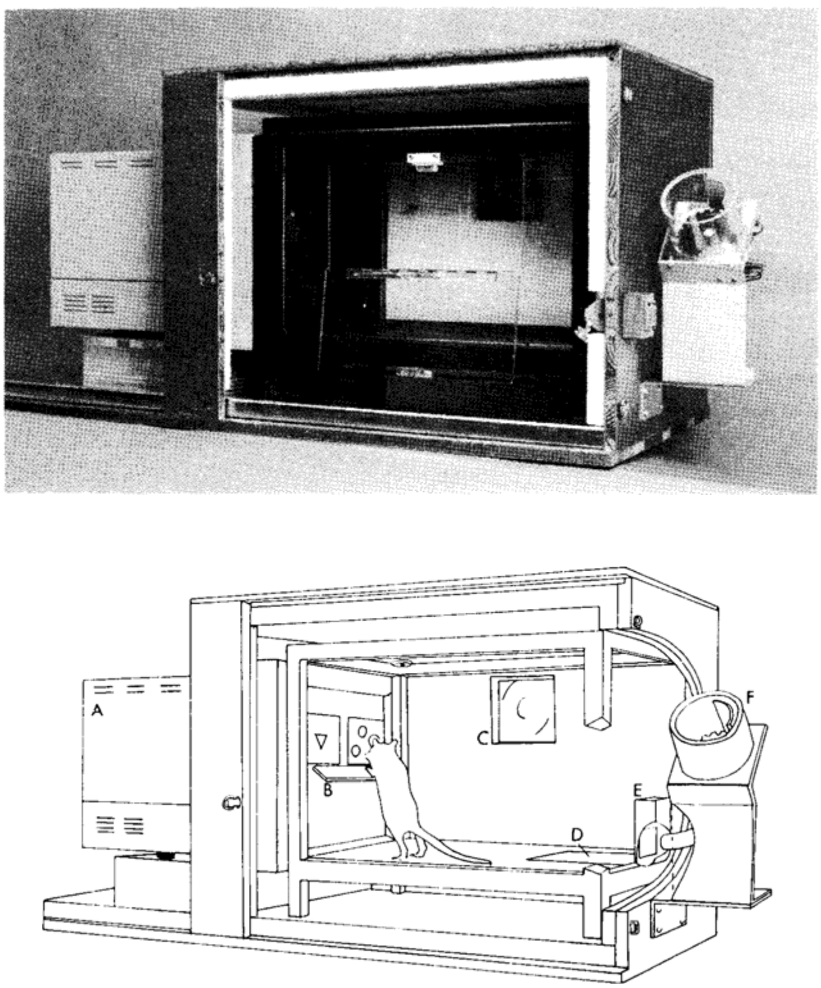

Figure 1. Photograph and line drawing of the apparatus. A=video display unit, B=Perspex 'mask' with response windows and 'shelf, C=fan, D=pressure-sensitive tloor panel, E=magazine, F = pellet dispenser. Illustration by Brian Fromant, Dept. of Experimental Psychology, Cambridge.

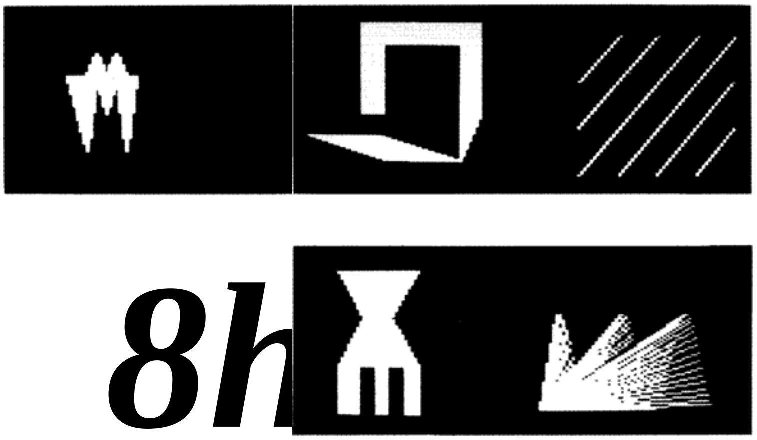

Figure 2. Representative coloured shape, line and pattern stimuli.

General Behavioural Procedures: In each of the three behavioural tasks described below, each trial began with the presentation of the stimuli, contingent upon the animal being located on the rear t100r panel following a 5 sec inter-trial interval. The rat was then required to approach the VDU display and select a stimulus by responding to it directly via a nose-poke. Correct responses were followed by the disappearance of the stimuli and the presentation of a 1 sec, 4KHz tone, concomitant with illumination of the magazine light and delivery of a sucrose pellet (45mg dustless; Bioserve, Inc., NJ) into the magazine. Incorrect responses resulted in the disappearance of the stimuli and the houselight being extinguished for a "time-out" period of 5 sec. In the event that a rat developed a spatial response bias (defined as > 70% responses to the left or right window within a session), a correction procedure was implemented such that following an incorrect response, the stimulus contiguration for that trial was represented until the rat responded correctly. For the 8-pair concurrent discrimination task, the number of trials per session was increased appropriately during correction sessions such that each of the eight stimulus pairs was presented at least 15 times (see below). Each rat typically required only one or two correction sessions.

Pretraining: Pretraining consisted of four sessions. During the tirst 15 min session, the magazine panel was taped open to allow animals free access to food pellets which were delivered on a PI 20 schedule together with illumination of the magazine light and presentation of the tone. The second and third sessions were identical to the tirst with the exception that the magazine panel was now untaped so that the animal was required to press the magzine panel in order to gain access to the food pellets. During the fourth session, rats were trained to respond to the VDU display. During each of the 50 trials a large yellow square was randomly presented in one of the response windows. The square remained on the screen until the rat responded to it, after which the rat was rewarded with magazine light, tone, and sucrose pellet. Following pretraining, rats were tested on one of three tasks: 8-pair concurrent discriminations, visuospatial conditional rule learning, or nonspatial nonmatching-to-sample.

Eight-pair Concurrent Discrimination task: Rats were required to learn the correct, reinforced stimulus in each of eight pairs. Each of the 8 stimulus pairs was presented 15 times during a session giving a total of 120 trials per session. The sequence of presentation of stimulus pairs for each session was determined in a pseudorandom fashion. Each stimulus appeared in the left and right windows an approximately equal number of times (7 lefts and 8 rights for one stimulus of each pair, 8 lefts and 7 rights for the other). The correct stimulus in each pair was the same for each rat.

Visuospatial Conditional Rule Learning task: Rats were required to learn a rule of the type, "If Stimulus A then go left, if Stimulus B then go right". For this task, a 3-window mask was used. The three windows were raised the same distance from the tloor, one located centrally, the other two located to the right and left of the central window. A trial began with the presentation of one of two discriminative stimuli, determined pseudorandomly, in the central window. The rat was required to make a nose-poke to this stimulus. Immediately following the disappearance of the discriminative stimulus, two white squares appeared in the left and right windows. A nose poke to the appropriate square (left or right, depending on the discriminative stimulus) was rewarded as above; an incorrect response was punished with a time-out. Each session consisted of 100 trials.

Nonmatching-to-sample task: In this task, a nonmatching procedure with two repeating stimuli was used. A 3-window mask was used, with two windows as for the 8-pair concurrent discrimination task (the 'choice windows'), and one window located centrally below the shelf (the 'sample window'). A trial began with the presentation of a sample stimulus in the sample window. Following a nose-poke response to this stimulus, the sample disappeared from the sample window, and was re-presented in one of the two choice windows, along with the second stimulus in the other choice window. A response to the nonmatching stimulus was rewarded with light, tone and pellet. A response to the sample stimulus was punished with a time-out. The sample stimulus, and the location of the correct stimulus, was determined pseudorandomly on each trial. A session consisted of 100 trials.

RESULTS

Discrimination learning for each of the three tasks is shown in Figure 3. In the 8-pair concurrent discrimination task, performance was characterised by a smooth, negatively accelerated function. Both rats attained a weak criterion of learning (59%, a level of pertimnance statistically just above chance ($p < .05$) for 120 trials, on two consecutive sessions), within the first ten sessions (mean=5.0). The more stringent learning criterion of 85% correct on two consecutive days was achieved in an average of 9.5 sessions, and asymptotic performance was about 90%. The learning functions for both the visuospatial conditional and nonmatching-to-sample tasks were more gradual and incremental than in the case of the concurrent discrimination learning task. The weak criterion of learning (61 % for 100 trials, $p < .05$) was achieved for the former tasks in an average of 5.5 and 12.6 sessions respectively, whereas the more stringent criterion of 80% on two consecutive days was reached in an average of 15.5 and 44.7 sessions respectively, subsequent performance stabilising at about this level.

DISCUSSION

We have demonstrated a novel touchscreen testing method which enables rats to discriminate computer graphic stimuli in several distinct paradigms t(Jr measuring learning and memory. To our knowledge, this is the first example of an automated method for recording responses made by the rat to nonspatial, two-dimensional visual stimuli in a discrimination learning context. In extensions of this work we have found that rats are able to demonstrate serial reversal learning and are able to remember the spatial location of a stimulus across a delay (delayed nonmatching-to-position) in our apparatus (Bussey, Muir and Robbins, unpublished observations). While other workers have trained rats to respond to spatial stimuli presented on a VDU using a pressure-sensitive "Touch Window" apparatus (10), the present method allows for direct comparison between performance in tasks requiring discrimination of visual features (eg. delayed nonmatching-to-sample), as well as their spatial analogues (ie. delayed nonmatching-to-position).

Historically, it has proven to be notoriously difficult to train rats to attend adequately to two-dimensional stimuli, and experimenters have had to go to some lengths to achieve this end (12). In the present study, this has been accomplished through the use of at least three important features of the

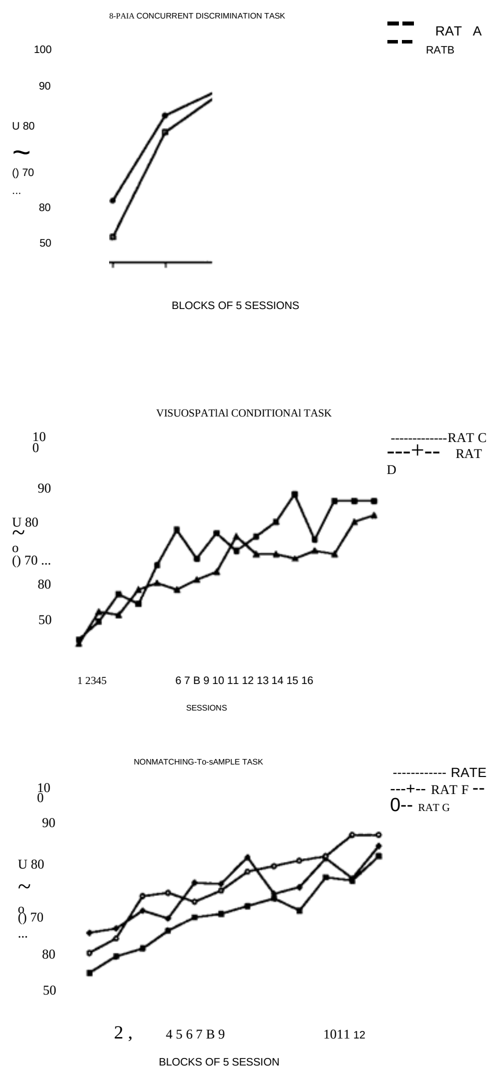

Figure 3. Acquisition curves for individual rats on each of the three tasks: 8-pair concurrent discrimination (top), conditional rule learning (middle) and nonmatching-to-sample (bottom).

apparatus: (i) a pressure-sensitive Hoor panel used to ensure that the rat is positioned centrally, at the rear of the apparatus, before the stimuli are presented, (ii) a 'mask' which allows access to the stimuli only through windows just larger than the stimuli themselves, thus forcing a 'head-on' approach, and hence appropriate orientation, to the stimuli, and (iii) a 'shelf' below these windows which forces the animal to stop in front of the stimuli, rear, and stretch toward a stimulus in order to make its response. Indeed, we have found that only when all of these features are in place does training on these tasks proceed at a sufficient rate as to be experimentally feasible, and at least comparable to similar tasks in non-automated paradigms employing three-dimensional 'junk objects'. Furthermore, the preliminary training required in this apparatus is minimal, as the methodology capitalises on the fact that exploration via nose-poking (in the service of sniffing) is the rats' natural response to novel stimuli in the environment.

Attention to the stimulus is also facilitated as a consequence of the stimulus-directed mode of responding employed in our method, in which the stimulus material that guides the decision of the subject also guides the response. This was an important consideration in the design of the human touchscreen method, as it removed the necessity for the subject to divide his or her attention across two spatial locations, one for stimulus and one for response. This is especially relevant for certain patient groups, for example those with Alzheimer's disease, known to exhibit impairments in divided attention. Of course, such considerations are equally important in animal neuropsychology (3). A further advantage of this feature is that since the animal is able to respond directly to a stimulus, it is positioned such that the stimulus is present directly in the animal's tield of vision during the conditioned reinforcer (tone) signalling the delivery of food, thus facilitating stimulus-reward learning. Furthermore, the stimuli used in this method are purely visual, precluding the use of other modalities such as touch and smell. One criticism of procedures using 3-dimensional objects or mazes is that olfactory and tactile cues may be used.

Finally, the automated nature of this procedure confers considerable advantages, for example, in the on-line collection and analysis of a wide range of performance measures such as latencies and premature responses, the automatic filing of data into an expanding data base, the removal of experimenter bias, consistency and precision in task parameters such as inter-trial intervals and delays, and the reduction of experimenter time and effort.

The development of this touchscreen testing method for the rat stemmed from our interest in the comparative approach to neuropsychology. In our laboratory, we routinely test patient groups and monkeys on identical tests using a computerised touchscreen method (8). The ability to test rats on such tasks should prove extremely valuable: rats are the laboratory animal of choice for initial neurobiological investigations and pharmacological screening because of their convenience, availability, low cost and the existence of a large data base for this species. Furthermore, the relative simplicity of the rat brain facilitates the study of basic principles of brain-behaviour interactions, making the rat a species worthy of neuropsychological study in its own right.

This work was supported by a Well come Trust Programme Grant. TJB was supported by a Commonwealth Scholarship. The authors would like to thank Brian Fromant for his illustration of the apparatus.

REFERENCES

1 Aggleton, J.P., Kentridge, R.W. and Sembi, S. (1992) Behav. Brain Res. 48, 103.
2 Gaffan, D., Saunders, R.C., Gaffan, E.A., Harrison, S., Shields, C. and Owen, MJ. (1984) Quart. J. Exper. Psycho\. 36B, 173.
3 Meyer, D.R., Treichler, F.R. and Meyer, P.M. (1965) In: Behavior of Nonhuman Primates (Vo\. 1), A.M. Schrier, H.F. Harlow and F. Stollnitz (eds). Academic Press, New York, p. 1.
4 Morris, R.G.M. (1981) Learning and Motivation 12,239.
5 Morris, R.G., Evenden, J.L., Sahakian, BJ. and Robbins T.W. (1986) In: Cognitive Neurochemistry, S. Stahl, S.D. Iversen and E. Goodman (eds). Oxford University Press, p. 21.
6 Mumby, D.G., Pinel, J.PJ. and Wood, E.R. (1990) Psychobiology 18(3),321.
7 Olton, D.S. (1979) American Psychologist 34(7), 583.
8 Roberts, A.C. and Sahakian, BJ. (1993) In: Behavioural Neuroscience: A Practical Approach (Vo\.I), A. Sahgal (ed). Oxford University Press, p. 165.
9 Rothblat, L.A. and Hayes, L.L. (1987) Behav. Neurosci. 101(4),587.
10 Sahgal, A. and Steckler, T. (1994) 1. Neurosci Methods (in press).
11 Sahakian, B.1. and Owen, A. (1990) 1. Royal Soc. Med. 85, 399.
12 Sutherland, N .S. and Mackintosh, N J. (1971) Mechanisms of Animal Discrimination Learning, Academic Press, London.
13 Squire, L.R., Zola-Morgan, S. and Chen, K.S. (1988) Behav. Neurosci. 102,210.
14 Weiskrantz, L. (1977) Brit. J. Psycho\. 68,431.