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Variable-Interval Probe Test as a Tool for Repeated Measurements of Spatial Memory in the Water Maze

Alicja L. Markowska, Jeffrey M. Long, Christopher T. Johnson, and David S. Olton

Probe tests provide an important additional converging operation to identify the characteristics of cognitive processes being assessed by other behavioral measures. We introduce a new procedure using a variable-interval (VI) probe test to assess spatial memory in the water maze. Three groups of rats were trained in spatial discrimination with traditional platform trials. For the probe trials, 2 groups had no-platform (NP) probe trials in which the escape platform was unavailable for the entire trial. The 3rd group had variable interval (VI) probe trials, in which the escape platform was available only after a VI. The VI probe trial was a more sensitive measure of spatial memory than was the NP probe trial and was useful for repeated measurements of spatial memory, a characteristic not readily attainable with the NP probe trial.

Obtaining multiple measures of performance is necessary to distinguish between variables that affect performance itself and those that affect the measuring instrument (Garner, Hake, & Eriksen, 1956; Platt, 1964; Waldrop, 1990a, 1990b). A probe test can be an effective procedure to provide an independent measure of performance. Although the characteristics of a probe test have not received a formal, systematic analysis, these tests are regularly used in many different settings (Olton, 1979). For our analysis, probe tests of spatial knowledge were the focus. Typically, an animal is trained to move from a start location to a goal, and some appropriate measure of performance is obtained during this procedure. The procedure is subsequently changed to provide an independent assessment of performance.

An effective procedure to assess spatial memory is the spatial discrimination in the Morris water maze. For the regular platform trials, a submerged escape platform is placed in the tank; the rat locates and escapes onto this platform (Gage, Dunnett, & Bjorklund, 1989; Gallagher & Burwell, 1989; Markowska et al., 1989; Morris, 1984; Morris, Anderson, Lynch, & Baudry, 1986; Whishaw, O'Connor, & Dunnet, 1985). For the traditional probe trials, the escape platform is removed from the tank for the entire trial. Consequently, the rat is unable to escape from the water. The tendency of the rat to remain near the location where the escape platform had been during platform trials is a measure of spatial memory for the platform location. The amount of time spent in the quadrant containing the platform, and the number of times each of these locations is crossed, are measures of performance during the probe trial.

One difficulty with this traditional no-platform (NP) probe trial is the fact that the response–reinforcement contingencies during the NP probe trial are different from those during the platform trials. During platform trials, the optimal strategy is to go to the goal location and escape on the platform. During NP probe trials, the escape platform is not present anywhere in the tank, and the optimal strategy for the rat is unclear. If, after reaching the goal location and not finding the escape platform, the rat is either uncertain about the location of the platform or is certain that the platform is not present in the usual goal location, then the optimal strategy is to avoid the previous goal location and go elsewhere in the tank to see whether escape is possible by some other means. In any case, the NP probe trial becomes an extinction trial with contingencies that are different from those for the platform trial.

One way to overcome this difficulty in the NP probe trial is to change the procedure so that the contingencies that are present during platform trials are also present during probe trials. In this experiment we introduced such a procedure: the variable-interval (VI) probe trial. As in the NP probe trial, the escape platform is unavailable to the rat at the beginning of the trial. However, after some VI of time, the escape platform is made available so that the rat can escape on it. Because the interval during which the escape platform is unavailable is variable and unpredictable, the optimal strategy during the VI probe trial is the same as that during the platform trials; the rat is to go directly to the location of the platform and remain there until the platform is available.

This experiment was designed to determine the extent to which the VI probe trial can be used repeatedly during acquisition and to compare performance with the different types of probe trials. If this new procedure is to have advantages compared with the traditional NP probe trials, it must be able to obtain accurate repeated measurements that are at least as sensitive to spatial memory as those in the NP probe trials.

Alicja L. Markowska, Jeffrey M. Long (now at the Department of Psychology, University of Utah), Christopher T. Johnson, and David S. Olton, Neuromnemonics Laboratory, Department of Psychology, Johns Hopkins University.

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Correspondence concerning this article should be addressed to Alicja L. Markowska, Neuromnemonics Laboratory, Department of Psychology, Johns Hopkins University, Baltimore, Maryland 21218.

Method

Subjects

Fischer-344 male rats, 4 months old at the start of behavioral testing, were housed in hanging cages with food and water available ad lib in a colony room with a 12:12 light–dark (LD) cycle. Three groups were included: NP6,12; NP1–12; and VI1–12. In the abbreviations of the groups, the letters identify the type of probe trial, and the numbers indicate the sessions in which the probe trials were given. All behavioral testing occurred during the light portion of the LD cycle.

Apparatus

The tank, made of galvanized metal, was 1.8 m in diameter and 60 cm high. It was filled to a depth of 35 cm with water maintained at 24 ± 1 °C by a heater (Visitherm). White nontoxic watercolor paint (Rich Art) was added to the water to make it opaque. The inside of the tank was painted white. The tank was divided into four quadrants (northeast, northwest, southeast, and southwest) by two imaginary perpendicular lines crossing in the center of the tank. A tracking system (HVS Image Analysis VP-112) was used to record data. A camera (Burl) was mounted 1.4 m above the surface of the water and was connected to a microprocessor. Illumination was provided by four 40-W light bulbs mounted in a circle 1.2 m above the surface of the water. The tank was located at one end of a small rectangular room with a variety of visual cues, distal (on the wall) and proximal (on the rim of the tank).

The *escape platform* (also called the *platform* for brevity) was made of transparent plastic (Lucite). The top surface was 10 cm^2, with holes, 1 cm in diameter, that provided the rat with an easier grip. The escape platform could be raised and lowered by a cable that was not visible to the rat. In the raised position, the top of the escape platform was 1 cm below the surface of the water, available to the rat. In the lowered position, it was 19 cm below the surface of the water, therefore unavailable to the rat.

For the straight swim procedure (see the next section), an alley, 100 cm long, was made by two pieces of transparent plastic (Lucite) parallel to each other and 15 cm apart. Both extended 26 cm above the surface of the water.

The *start platform* was made of Lucite. It was shaped like a step, with the horizontal area 14 cm × 10 cm, attached to a vertical piece that could be hung on the edge of the tank. When hanging on the tank, the start platform was just above the surface of the water.

Procedure

Straight Swim

In this procedure rats were trained to swim in the water and climb on the escape platform. No spatial discrimination was required because the alley was sufficiently narrow that the rat had to hit the escape platform at the end. One end of the Lucite alley was placed against the edge of the tank. The escape platform was placed in the raised position at the other end of the alley. Black curtains around the tank eliminated the visual cues that were used for the subsequent place discrimination.

For each trial, the rat was placed on the start platform. The start platform was slowly lowered into the water by the edge of the tank, and the rat was allowed to swim down the alley, climb onto the escape platform, and remain on it for 10 s. The rat was then removed by the experimenter and placed in a holding cage for an intertrial interval (ITI) of approximately 3 min. Five trials were given each session. Two sessions were given each day for 2 consecutive days, with an intersession interval (ISI) of approximately two hr. Each rat was monitored throughout testing for signs of hypothermia.

Place Discrimination

Three types of trials were used: the platform trial, the NP probe trial, and the VI probe trial. For each platform trial, the escape platform was placed in the same location, 40 cm from the edge of the tank and was in the raised position with its top 1 cm below the surface of the water. The three quadrants not containing the escape platform were used for the starting locations. The rat, on the start platform and facing the center of the tank, was lowered into the water near the rim of the tank. For each trial, one of the three start locations was chosen in a counterbalanced sequence so that each location was used once in each successive block of three trials. After reaching the escape platform, the rat was allowed to remain on it for 10 s, picked up by the experimenter, and returned to the holding cage for the ITI of about 3 min.

For each NP probe trial, the escape platform was in its lowered position, unavailable to the rat, for the entire trial (60 s). At the end of the trial, the rat was removed by hand.

For each VI probe trial, the escape platform remained in the lowered position for a VI of time during the trial. At the end of the interval, the escape platform was raised and made available to the rat. Four intervals (10, 20, 30, and 40 s) were used, with each interval being used once in each block of four sessions. Three blocks of sessions, each with a different sequence of intervals, were used. The actual intervals in the 12 sessions were as follows: 10, 30, 20, 40, 40, 20, 30, 10, 40, 10, 30, and 20. Data were collected during the VI.

All three groups of rats were given two sessions per day for 6 days, with an ISI of approximately 2 hr. For all three groups, the first 5 trials of every session were platform trials. The differences in the procedures were as follows: For the NP6,12 trials, the first 6 trials of each session were platform trials, and the NP probe trial was given as the 7th trial for Sessions 6 and 12. For the NP1–12 trials, the 6th trial of each session was an NP probe trial. For the VI1–12 trials, the 6th trial of each session was a VI probe trial.

Platform trials: Measures of performance. *Swim time* was the time between leaving the start location and climbing onto the escape platform. A shorter swim time indicated better performance. *Swim distance* was the distance swum, in centimeters, from the start location to the escape platform. A shorter distance indicated better performance. *Heading angle* was the deviation between the actual direction of the rat when leaving the edge of the tank and a straight line from the start location to the escape platform. A smaller heading angle indicated better performance.

Probe trials: Measures of performance. *Quadrant time* was the percentage of time spent in the quadrant with the escape platform. A higher quadrant time indicated better performance. *Annulus-40 time* was a similar measure for the percentage of time spent in an annulus with a diameter of 40 cm, centered where the center of the escape platform had been on the platform trials. A higher annulus time indicated a better performance. *Platform crossings* were the number of crossings over the escape platform location. A greater number of crossings indicated better performance.

Data Analyses

For the platform trials, the data are presented as a mean value for each group in each session plus or minus the standard error of the mean. For the probe trials, the mean for each group plus or minus the standard error of the mean is reported. For statistical analyses, two-way analyses of variance (ANOVAs; Groups × Sessions) with repeated measures were performed for all six measures of performance using Systat software. When statistical significance was obtained for main effects or for interactions, we performed post hoc analyses using contrast tests.

Results

Straight Swim

All rats swam quickly to the escape platform, even during the first few trials, and decreased their response time even more with training. During the first session, the mean swim time was 13 ± 5 s; by the 10th trial, it reached an asymptotic performance of 3 ± 0.2 s.

Platform Trials

For all three groups, for all three measures, performance improved substantially in the first few sessions, slightly in the middle sessions, and reached asymptotic performance in the last sessions (see Figure 1, left side).

Swim time. Mean swim time in the first session for the three groups ranged from 34 ± 3 s to 39 ± 3 s (see Figure 1, top left). It decreased to 3 ± 0.3 s, 6 ± 1.7 s, and 4 ± 0.5 s in the NP6,12, NP1–12, and VI1–12 groups, respectively. A two-way ANOVA showed a main effect of groups, $F(2, 29) = 7.7, p < .01$, sessions, $F(11, 319) = 121.8, p < .001$, and a significant interaction, $F(22, 319) = 1.6, p < .05$. The VI1–12 rats were better than the NP1–12 rats ($p < .02$), but not different from the NP6,12 rats, in overall performance. Specifically, the groups were not different in the first session. Afterward, the VI1–12 rats were superior to the NP1–12 rats in all sessions ($.005 < p < .05$), except 6, 8, 9, and 12, and to the NP6,12 rats in Session 2. NP6,12 rats were better than NP1–12 rats in overall performance ($p < .001$), specifically in Sessions 3–5 and Sessions 10–11 ($.001 < p < .05$).

Swim distance. The mean swim distance in the first session for the three groups ranged from 1,011 ± 47 cm to 1,137 ± 113 cm and decreased to 67 ± 10 cm, 99 ± 28 cm, and 110 ± 4 cm for the NP6,12, NP1–12, and VI1–12 rats, respectively, in the last session (see Figure 1, middle left). A significant effect of sessions, $F(11, 319) = 160.7, p < .001$, indicated a decrease in the swim distance with continuing training.

Heading angle. The mean heading angle in the first session ranged from 49 ± 4° to 62 ± 3° and decreased to 19 ± 3°, 16 ± 3°, and 10 ± 3° for the NP6,12, NP1–12, and VI1–12 groups, respectively, in the last session (see Figure 1, bottom left). An ANOVA showed a significant effect of groups, $F(2, 29) = 4.5$, $p < .05$, sessions, $F(11, 319) = 46.3, p < .001$, and a significant interaction, $F(22, 319) = 2.3, p < .001$. The VI1–12 rats were more accurate than were NP1–12 rats only at the start of the training (Session 1; $p < .05$), and in Session 10 ($p < .005$). The VI1–12 rats were superior to the NP6,12 rats in overall performance ($p < .02$), specifically in Sessions 1, 3, and 12 ($.01 < p < .05$).

Probe Trials

Probe Trials 6 and 12: A Comparison Across Groups

For all three measures (see Figure 1, right side), performance was more accurate in the VI probe trials as compared with the NP probe trials.

Quadrant time. In Session 6, the mean percentage of quadrant time was 58 ± 3, 29 ± 5, and 72 ± 5 for the NP6,12, NP1–12, and VI1–12 groups, respectively (see Figure 1, top right). In Session 12, the respective mean values were 44 ± 3%, 28 ± 3%, and 83 ± 4%. An ANOVA (Groups × Sessions) showed a main effect of groups, $F(2, 29) = 49.4, p < .001$, and a significant interaction, $F(2, 29) = 8.0, p < .005$. In Session 6, VI1–12 rats were more accurate than were NP6,12 ($p < .05$) and NP1–12 rats ($p < .001$). From Session 6 to Session 12, the performance of the VI1–12 rats improved, whereas the performance of the NP groups declined. Therefore, in Session 12 ($ps < .001$), the difference between the VI group and the NP groups was greater than in Session 6. NP6,12 rats were more accurate than were NP1–12 rats in Sessions 6 and 12 ($ps < .001$).

Annulus-40 time. The pattern of results in this measure was similar to the pattern just described for quadrant time (see Figure 1, middle right). In Session 6, the mean value was 61 ± 2%, 31 ± 3%, and 75 ± 5% for the NP6,12, NP1–12, and VI1–12 groups, respectively. In Session 12, the respective values were 45 ± 4%, 25 ± 3%, and 84 ± 3%. An ANOVA (Groups × Sessions 6 and 12) showed main effects of groups, $F(2, 29) = 82.7$, $p < .001$, and a significant interaction, $F(2, 29) = 6.9, p < .005$. VI1–12 rats spent more time than did NP6,12 rats ($.001 < p < .02$) and more than NP1–12 rats ($.001 < p < .02$) in Sessions 6 and 12. However, in Session 12 ($p < .001$), the difference between the VI group and the NP groups was greater than in Session 6 ($p < .02$). NP6,12 rats were more accurate than were NP1–12 rats in Sessions 6 and 12 ($ps < .001$).

Platform crossings. The pattern of results in this measure was similar to the pattern just described for quadrant time and annulus-40 time (see Figure 1, bottom right). NP6,12, NP1–12, and VI1–12 rats had mean values of 4.5 ± 0.8, 2 ± 0.3, and 6.2 ± 1.2, respectively, in Session 6 and 3.2 ± 0.3, 1.6 ± 0.5, and 6.5 ± 1.1, respectively, in Session 12 (see Figure 1, bottom right). The only significant difference was between groups, $F(2, 29) = 11.6, p < .001$. In Session 6, VI1–12 rats had more crossings than did NP1–12 rats ($p < .005$). In Session 12, VI1–12 rats had more crossings than did NP1–12 rats ($p < .001$) and NP6,12 rats ($p < .05$). NP6,12 rats had more crossings than did NP1–12 rats in Session 6 ($p < .05$), but not in Session 12.

Probe Trials in Sessions 1–12: A Comparison Between VI1–12 and NP1–12

Of particular importance was the contrast in performance with repeated probe trials for VI1–12 and NP1–12 rats across the sessions. For the three respective measures of performance (quadrant time, annulus = 40 time, and platform crossings), an ANOVA (Group × Session) indicated a main effect of groups, $F(1, 21) = 35.8, p < .001$, $F(1, 21) = 150.0, p < .001$, and $F(1, 21) = 43.4, p < .001$; sessions, $F(11, 165) = 6.5, p < .001$, $F(11, 231) = 18.9, p < .001$, and $F(11, 231) = 4.7, p < .001$; and a significant interaction, $F(11, 231) = 8.2, p < .001$, $F(11, 231) = 16.2, p < .001$, and $F(11, 231) = 3.2, p < .001$. VI1–12 was more accurate than NP1–12 ($ps < .001$). For the VI probe trials, performance consistently improved and reached an asymptotic level. For the NP probe trials, performance steadily decreased; for the NP1–12 group, it returned to the initial chance levels for the correct quadrant measure (25%).

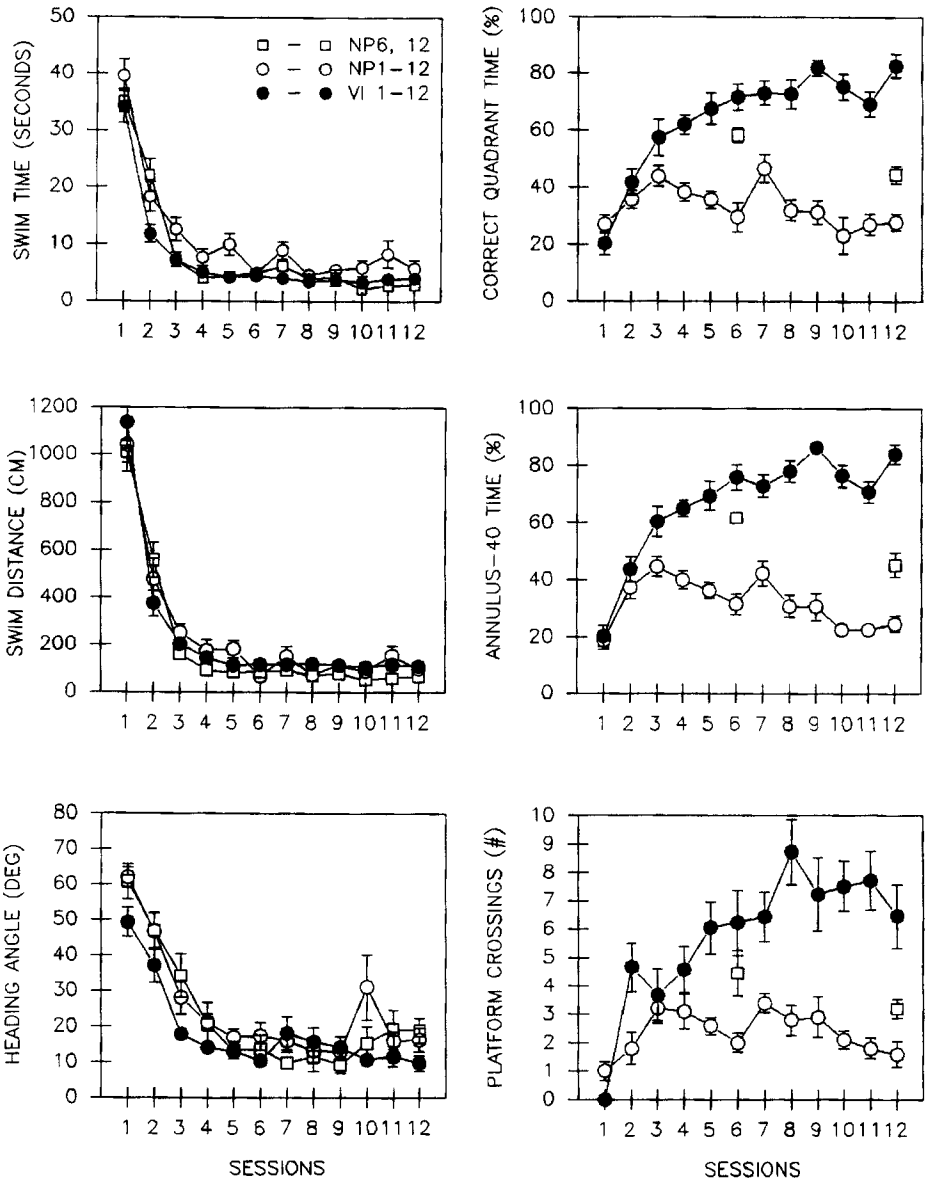


Figure 1. The mean and standard error of the mean for each response measure (vertical axis) for each of the 12 sessions (horizontal axis). (The left side shows performance during platform trials. The graphs depict, in order, swim time, swim distance, and heading angle. The right side shows performance during probe trials. The graphs depict, in order, quadrant time, annulus-40 time, and platform crossings. The no-probe 1–12 [NP1–12] and variable-interval 1–12 [VI1–12] rats both had one probe trial in each test session and consequently have a data point for each of the 12 test sessions. NP6,12 rats had only two probe trials, one each in Session 6 and Session 12. Consequently, data are available for only two points for this group.)

Probe Trials in Session 6 and Session 12: A Comparison Within Groups

For NP6,12 rats, accurate spatial memory was demonstrated in both probe trials. Quadrant time and annulus-40 time decreased from Session 6 to Session 12 (ANOVA; $.03 < p < .04$).

For NP1–12 rats, the pattern of results in this group was similar to that described for NP6,12 rats. With continued training, annulus-40 time decreased.

VI1–12 rats had the best scores of the three groups. The performance expressed by two measures—quadrant time and annulus-40 time—improved from Session 6 to Session 12 ($ps < .03$).

Discussion

Place discrimination as assessed by performance in the water maze has provided important information in many different areas of behavioral neuroscience. The original procedures were creative and made important contributions. However, as with any behavioral task, subsequent developments can improve its usefulness.

The VI probe trial introduced here has two advantages. First, this procedure was a more sensitive measure of spatial memory than was the NP probe trial procedure, as indicated by the superior performance of the VI1–12 group as compared with the two NP groups. Second, this procedure could be used repeatedly during the entire testing procedure, as indicated by the continued high level of performance on the repeated VI probe trials as compared with the decreasing level of performance on the repeated NP probe trials.

The previously used NP probe trials had no escape platform available during the entire trial, and the rat was removed by hand at the end of the trial regardless of its position in the tank (Gage et al., 1989; Gallagher & Burwell, 1989; Morris, 1984; Morris et al., 1986). Although, the NP probe trial can be successful for a few probe trials, the response–reinforcement contingencies of the NP probe trial are different from those in the usual platform trial and permit the rat to learn that if the escape platform is not encountered during the first visit to the usual position, it is not available throughout the rest of the trial. Consequently, remaining in the vicinity of the escape platform has no advantage to the rat, and its performance during multiple probe trials may underestimate the accuracy of its discrimination.

By contrast, the optimal strategy on the VI probe trials, like that on the platform trials, was to go directly to the location of the escape platform and remain there until the platform was available to escape from the water. An escape platform that can be raised from the low position to the upper position can have applications in other types of place discrimination (Buresova, Krekule, Zahalka, & Bures, 1985).

The intervals for the VI probe trials varied in order to prevent the rat from predicting the exact time the platform was raised. Performance was consistent with all intervals, and the scores did not fluctuate significantly with the length of the probe trial.

The stability and accuracy of performance on the VI probe trials were striking, indicating that they provide a sensitive and repeatable measure of spatial memory in the Morris water maze. More generally, in the context of multiple measures of cognitive abilities, these results suggest that maintaining the same response–reinforcement contingencies on probe trials as on regular trials can have significant advantages.

Four other modifications of the traditional experimental procedures used in the place discrimination were incorporated to improve the ability to obtain a sensitive measure of place discrimination.

1. The shaping in the straight swim procedure was designed to minimize the impact of variables other than information about the location of the platform. Previous experiments gave the rats little if any experience in the general test procedures prior to assessing performance in the place discrimination itself (Gage et al., 1989; Gallagher & Burwell, 1989; Whishaw et al., 1985). Consequently, performance during the initial trials of the place discrimination was probably influenced by many variables, such as learning to swim in the water, learning that escape was not possible around the edge of the tank or by diving under the water, learning to remain on the escape platform once it was reached, and so forth. By contrast, the shaping process in the straight swim procedures used in this experiment gave the rat information about the general testing procedures but did not provide information about the location of the escape platform during the subsequent place discrimination. Because all of the basic procedures were learned during the straight swim, performance in the subsequent place discrimination task should have been a more selective and sensitive measure of discriminability than in the previous test procedures that did not incorporate shaping prior to testing.

2. A new dependent variable—annulus-40 time—was designed to be a more sensitive measure of the accuracy of place discrimination during the probe trial than the previous measure of quadrant time. During the time that the escape platform is unavailable on probe trials, the tendency of the rat to remain in the location of the escape platform can be used to assess the accuracy of spatial discrimination. Quadrant time, the percentage of the total test time that is spent in the quadrant that had the escape platform during platform trials, has been an effective dependent variable during probe trials. However, the quadrant is a large area, and the time spent in the quadrant but at a different distances from the escape platform may not be a homogenous measure of the memory of the platform's location. Annulus-40 time, which measures performance in an area more closely related to the escape platform's location, may be a more sensitive measure than quadrant time.

In this experiment, the values for annulus-40 time and quadrant time were similar in pattern. Annulus-40 time was slightly greater than quadrant time (from 2% to 6%), indicating that young rats with good memory, such as those used in this study, search for the escape platform in an area closely related to the correct location rather than in more distant areas. Further variation in the size of the annulus may be a useful index of behavior. Indeed, parametric manipulation of the size of the annulus may provide all of the advantages inherent in parametric manipulations of task difficulty (Olton, 1991; Olton & Markowska, 1988, 1992; Olton & Shapiro, 1992). If the performance of two groups of rats is similar with a large annulus, representing minimal task demand, but different with a small annulus, representing a difficult task demand, this interaction would suggest that the reason for this difference in performance is specifically the ability to remember the exact platform's location.

3. A start platform, rather than the experimenter's hand, was used to lower the rat into the water. This technique provided greater consistency for the start of the trial and should have reduced variability in performance inherent in the previously used procedure.

4. The rat was placed in the tank at the start location facing toward the center of the tank rather than toward the edge of the tank. When placed facing the edge of the tank, the rat had to turn around before being able to use many of the spatial stimuli identifying the location of the escape platform. The direction of the turn can substantially influence the measure of performance, adding undesired variability. Starting the rat facing toward the center of the tank reduces this variability.

Identifying the cognitive changes mediating the better performance of the VI probe group requires additional work. Some evaluation of the relative merits of two alternative explanations are possible with our data. During the probe trials, the VI group had a better performance than did the NP groups for all three measures: quadrant time, annulus-40 time,

and platform crossings. The better performance of the VI group as compared with the NP group might have been due to better memory of the platform's location or to a more effective search strategy. Distinguishing between these two alternative explanations can be done with data from platform trials. If the VI group had better memory than did the NP groups for the platform's location, then during platform trials the performance of the VI group should have been better than that of the NP group. If the VI group had equal memory as the NP groups for the platform's location, then during platform trials the performance of the VI group should have been equivalent to that of the NP groups. The three measures of performance during platform trials had different patterns of results. For swim time, the VI1–12 group was superior to the NP1–12 group. For swim distance, the groups were equivalent. For heading angle, the results are difficult to interpret because even in the first session of platform trials, prior to any probe trial, the VI group had better performance than did the NP groups. Assessing the influence of the probe trial on performance is difficult given this variability in performance in the first session. Consequently, tentative support can be provided for the hypothesis that the VI group had better spatial memory than did the NP group, but the evidence is not strong.

In summary, maintaining the same response–reinforcement contingencies on probe trials as on regular platform trials produced the procedure for the VI probe trial, which provided two advantages as compared with the usual NP probe trial: more accurate performance and repeated use. The VI probe trial can provide important additional information to that obtained in the usual platform trials, and the success of this measure illustrates some general principles that can be used in designing any probe test.

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