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The Effect of Vasopressin on Memory in the Healthy Elderly

Robert D. Nebes, Charles F. Reynolds III, and Lisa C. Horn

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Abstract. The effect that vasopressin has upon memory in young and old males was tested in a double-blind crossover study. There were two 1-week medication periods; during one, subjects received 60 μg of vasopressin daily; during the other, placebo. Reaction time tasks were used to measure their speed of retrieval from: short-term memory (STM), long-term memory (LTM), and semantic memory (SM). While vasopressin did not affect SM retrieval time or simple vocal reaction time, it did reduce memory comparison time and perceptual-motor time in STM and retrieval time in LTM. The degree of facilitation was similar in young and old.

Key Words. Vasopressin, aging, short-term memory, long-term memory.

Vasopressin, a pituitary hormone long known for its peripheral antidiuretic action, has recently been found also to alter central nervous system function. Rats deficient in vasopressin, due either to a genetic trait or to hypophysectomy, exhibit a learning deficit that can be remedied by administration of vasopressin (De Wied et al., 1975; De Wied and Gispen, 1977). Normal animals show a similar improvement in avoidance learning when given this neurohormone (Cooper et al., 1980). Vasopressin also facilitates performance in healthy humans (Legros and Gilot, 1978; Weingartner et al., 1981*a*; Beckwith et al., 1982), especially on tests requiring memory. Results with cognitively impaired individuals have been less consistent. Although patients suffering from depression (Gold et al., 1979; Weingartner et al., 1981*a*) and mild senile dementia (Delwaide et al., 1980; Weingartner et al., 1981*b*) have shown some improvement with vasopressin, others with severe head trauma (Jenkins et al., 1979) and alcoholic amnesia (Blake et al., 1978; Tinklenberg et al., 1981) have not.

Some investigators (De Wied and Van Ree, 1982) have suggested that vasopressin may be effective only in persons with a mild cognitive decrement. One population that would fit this description is the healthy elderly. Many aspects of information processing (e.g., attention and memory) decline with advancing age (Salthouse, 1982) and there is preliminary evidence that vasopressin may reduce some of these age-related deficits, both in animals (Cooper et al., 1980) and in man (Legros and Gilot, 1978). In the present experiment, we sought to examine further the ability of vasopressin to facilitate cognition in both young and older healthy men. Given their generally lower level of performance, it was hypothesized that the older subjects might show a greater improvement than the young.

Robert D. Nebes, Ph.D., Charles F. Reynolds III, M.D., and Lisa C. Horn, B.S., are at the Western Psychiatric Institute and Clinic, University of Pittsburgh, 3811 O'Hara St., Pittsburgh, PA 15213, USA. (Reprint requests to Dr. R.D. Nebes.)

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The second aim of this experiment was to determine the nature of the mental operation(s) affected by vasopressin. Most previous studies have used complex tasks in which it was not possible to specify the exact processing stage being influenced by this hormone. Thus, at present, there are a variety of suggested sites of action for vasopressin: attention (Gold et al., 1979), encoding of information into memory (Weingartner et al., 1981*a*), memory consolidation (Legros and Gilot, 1978), and most commonly, memory retrieval (Weingartner et al., 1981*b*). There is, however, no evidence that allows one to distinguish between these possibilities.

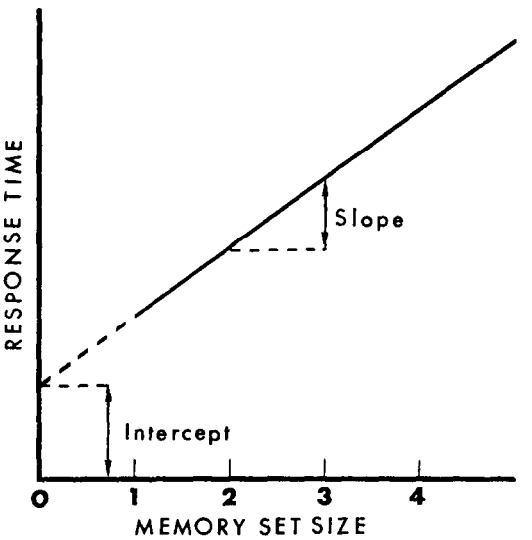
The present experiment was designed to examine whether vasopressin specifically facilitates memory retrieval, or whether its influence is more general, also affecting perceptual and motor operations. The tasks were based on the information-processing model of cognition that distinguishes between several distinct forms of memory. Short-term memory is viewed as a temporary maintenance of small amounts (four to seven items) of information in conscious awareness, while long-term memory is a relatively permanent store holding large amounts of information. A distinction has been drawn between two types of long-term memory: episodic and semantic (Tulving, 1972). Episodic memory comprises events defined by a personally dated context, while semantic memory is a thesaurus of organized knowledge about words, concepts, and their relations. Thus, the knowledge that "canary" refers to a small yellow bird involves semantic memory, while recalling that "canary" appeared among a set of 20 stimulus words seen an hour earlier involves episodic memory.

This study examined the effect that vasopressin has upon all three of these theoretically distinct forms of memory. The Sternberg (1975) paradigm was used to test short-term memory. In this procedure, the subject holds a varying number of items in memory and on each trial must decide whether a given stimulus is a member of that memory set. Performance on this task is postulated to consist of a series of operations: identification of the stimulus, serial comparison of the stimulus to each item in the memory set, a yes/no decision, and organization of an appropriate motor response. Response time has been shown to rise linearly (see Fig. 1) as the number of items in the memory set increases (Sternberg, 1975). The *slope* of this function (i.e., the average increase in response time per item added to the memory set) yields an estimate of memory comparison time, whereas the intercept (i.e., the projected response time at a set size of 0) is thought to represent a combination of perceptual and motor processes, distinct from memory. Thus, if vasopressin selectively facilitates memory retrieval, its effect should be more obvious in the slope of this function, whereas if its influence is on the perceptual or motor stages of the task, then it should be more apparent in the intercept.

The episodic long-term memory task used here required the subject first to memorize pairs of items. Then on each trial, he was presented with the first item of a pair. One condition measured the time he needed just to identify this item, while the other condition measured the time necessary to recall the associated item. If vasopressin reduces memory retrieval time, then its effect should be evident only in the second condition; if it affects the perceptual-motor stages, it should facilitate response time in both conditions.

In the semantic memory task, the subject was given a semantic category and had to

Fig. 1. Relationship between response time and the size of the memory set in the short-term memory task



respond with a member of that category beginning with a specified letter. The letters were chosen so as to elicit typical and atypical members of the category. For example, for "fruit" the letter "A" would elicit a common fruit such as apple, while the letter "L" would elicit a less common fruit—lemon or lime. If vasopressin improves search through semantic memory, then it should be especially effective with letters requiring generation of atypical items which generally take longer to retrieve.

In summary, the overall goals of this experiment were (1) to confirm that vasopressin does in fact facilitate the performance of healthy adults on cognitive tasks; (2) to determine whether this effect is greater in older individuals; and (3) to define the exact psychological operation(s) affected by the drug.

Methods

Subjects. The subjects in this study were 48 healthy community-resident male volunteers, half of whom were between the ages of 20 and 30 (mean age = 23.6) and half between 60 and 70 (mean age = 66.0). The subjects had at least a high school degree; the average number of years of education was 16.5 for the young and 16.8 for the old. All subjects were native English speakers. Of the elderly, 12 were retired, while the other 12 were still employed. Four of the younger subjects were employed; the rest were in school. Individuals with a history of diabetes, renal or cardiovascular disease, psychiatric or neurological illness, or with a blood pressure in excess of 150/90 were excluded from the study. All subjects had a complete medical examination and an SMA-15 chemistry screen. Every subject scored 28/30 or above the Mini-Mental Status examination (Folstein et al., 1975).

The experiment used a randomized, double-blind, crossover design with two 8-day medication periods separated by a 1-month washout. During one medication period, subjects took

30 μg of DDAVP (a synthetic form of 8 arginine-vasopressin) intranasally b.i.d. (10 μg b.i.d. on day 1, 20 μg b.i.d. on day 2, and 30 μg b.i.d. on days 3-8). During the other period, they took an equivalent amount of placebo (vehicle solution). Half of the subjects in each age group received DDAVP during their first medication period, while the rest received placebo. During both periods, subjects were allowed to drink no more than 1500 ml of fluid daily and were required to abstain from alcohol. They were told not to smoke within 24 hours of being tested. They were also required to come into the laboratory for daily measurements of blood pressure, weight, and serum sodium/potassium in order to reduce the risk of hyponatremia.

Each subject took part in five test sessions: an initial practice session, and sessions at the beginning (before taking any medication) and end of each medication period. A test session lasted approximately 90 minutes. There were four main psychological tasks, all of which used vocal response time as their primary measure. In all tasks, presentation of a visual stimulus (digits or letters, each approximately 12 mm high by 8 mm wide) in a three-channel tachistoscope started a millisecond timer which was stopped by a voice key triggered by the subject's spoken answer.

The first task measured simple vocal reaction time (RT). The subject heard a ½-second tone followed by a delay of 750, 1250, or 1750 msec, after which an "X" flashed on the screen for 250 msec. The subject had merely to respond as soon as he saw the "X" by saying "Po." The various delays were given in a random order. There were a total of 30 trials, divided into two sets of 15 trials, one set at the beginning of the test session, the other set at the end. This division allowed us to detect any major effect of subject fatigue.

The order in which the next three tests were given was counterbalanced across subjects. The *short-term memory* task measured the speed with which a subject decided whether a visually presented digit was a member of a previously memorized set of digits. If it was, the subject said "yes," if not, "no." (Actually, he said "bes" and "bo" in order to equate the initial sound activating the voice key.) The subject was given three series of 48 trials. One series had a memory set of two digits, another a memory set of three digits, another, four digits. Half of the trials in each series required a "yes" response (i.e., the presented digit actually was a member of the memory set), half a "no" response. "Yes" and "no" trials occurred in a random order. The sequence in which the memory-set sizes were given was counterbalanced across subjects. The items in the memory sets were randomly chosen from the digits 0 through 9 and were different for every test session. A practice series of 30 trials, with a memory test size of three, was given before the actual test.

In the *long-term memory* task, the subject first memorized 12 pairs of items, each pair consisting of two letters (a bigram) and a one-syllable word beginning with those letters (e.g., sh and sharp). After he could correctly recall all 12 words upon being shown their first two letters on flashcards, he was given two series of 48 RT trials. On each trial he saw one of the 12 bigrams for 250 msec in the tachistoscope. In one series of trials, he had only to name out loud the two letters he saw as quickly as possible. In the other series, he had to recall and name aloud the *word* associated with that bigram. The sequence in which the letter-naming and associate-recall series were given was counterbalanced across subjects. Different letter bigrams and words were used in each session.

In the *semantic memory* task, the subject was first shown the 12 semantic categories to be used in that session. He was then given a series of tachistoscopic trials in each of which he first saw one of the categories for 2,000 msec, followed by a 500 msec delay; a single letter then appeared for 250 msec. His task was to think of a word from that category beginning with that letter and to say its name aloud as quickly as possible. For example, if he saw "fruit" followed by "P," he could say "peach" or "pear," etc. He had 15 seconds to respond, after which the trial was ended. Each category was used twice, once with a letter designed to elicit a common (i.e., high dominance) member of the category, the other, an uncommon (low dominance) member. The categories were presented in a random order within a session, and different categories, all chosen from Battig and Montague (1969), were used for each session.

In addition to the four RT tasks, two other measures were given. The subject completed the KDS 1 and 2 self-rating scales (Kupfer et al., 1972), a screening test for psychiatric symptoms,

and a questionnaire which asked him to rate how much change, if any, he had noticed in his everyday memory (e.g., remembering appointments or people's names) during the preceding medication week.

Results

Before beginning the analysis, we examined the distribution of the raw data and found that several of the measures showed either extreme outliers, or an obvious skewness which, if ignored, would have seriously affected the analysis. We corrected for these problems by transforming the data when necessary to achieve a relative degree of normality. A repeated measures analysis of variance (ANOVA) with covariance was then performed. The study design involved test sessions both before starting the medication (pretreatment) and after completing the 8 days of medication (treatment) for both the placebo and the drug periods. To control for any differences between the pretreatment scores for the placebo and drug periods, a regression was performed using pretreatment scores to obtain residuals for the treatment scores in each period. This served as a measure of the treatment effect. The procedure controlled for initial level effects (including that produced by age) and ensured that a common regression was used across treatments. The grand mean was then added back into each residual so that subsequent analysis would provide ordinary means adjusted for initial level, thus allowing us to see any change due to treatment. The scores were then analyzed by a repeated measures ANOVA with treatment (placebo vs. DDAVP) as a within-subject factor, and age and order (of placebo-drug treatment periods) as between-subject factors.

In the short-term memory task, we calculated for each subject the linear function that described the relationship between the number of items in the memory set and the amount of time the subject took to decide whether the stimulus was a member of the set. The linear fit of these functions was generally between 90 and 99%. The slope and intercept of this function for "yes" and "no" responses served as the data for the analysis. While the slope and intercept represent different cognitive constructs that are theoretically independent (memory-comparison time and encoding-response time, respectively), in practice they were correlated. In order to test each construct uncontaminated by the other, when regressional residuals were obtained for each, the other was used as an additional covariate (i.e., slope covaried for intercept, and vice versa).

Analysis of the slope data showed a significant medication effect (a decrease in slope) for the "yes" responses ($F = 4.35$; $df = 1, 44$; $p < 0.05$) but not for the "no" responses ($F = 2.80$; $df = 1, 44$; $p > 0.11$). While the drug effect on the slope measures was larger in the older subjects (see Table 1), the medication by age interaction did not quite reach significance ($p > 0.08$). The intercept was significantly affected (i.e., decreased) by medication for both "yes" ($F = 5.14$; $df = 1, 44$; $p < 0.03$) and "no" responses ($F = 4.22$; $df = 1, 44$; $p < 0.05$). There were no significant effects of age (which is to be expected given the adjustment of the latencies for initial session performance) or order, nor did these factors interact with the medication effect. While the errors on the short-term memory task were too few to analyze, there was no indication of a speed-accuracy trade-off, as the percentage of errors increased with memory set size just as did response time. The error rate for the placebo and drug sessions was almost

Table 1. Mean latencies and (standard deviations) for the second session of the placebo and drug (DDAVP) periods, adjusted for first sesson latencies

	"STM"—slope measure			
	"Yes" response		"No" response	
	Placebo	Drug	Placebo	Drug
Old	92 (23)	73 (28)	74 (21)	63 (24)
Young	78 (18)	77 (14)	65 (19)	63 (13)
	"STM"—intercept measure			
	"Yes" response		"No" response	
	Placebo	Drug	Placebo	Drug
Old	444 (64)	391 (85)	485 (61)	457 (71)
Young	409 (56)	398 (38)	471 (62)	450 (42)

identical (3.8% vs. 4.2%) and, therefore, the decrease in RT with DDAVP was not due to a higher error rate while on the drug.

On the long-term episodic memory task, two scores were obtained for each subject: (1) mean time to name the stimulus letters and (2) mean time to retrieve from memory the word associated with those letters (see Table 2). There was no effect of medication on the letter-naming condition ($F = 0.3$; $df = 1, 44$), whereas on the associate-recall condition there was a significant medication effect ($F = 6.11$; $df = 1, 44$; $p < 0.02$), the subjects being faster while on DDAVP. Again, there was no effect of age or of order, nor did these factors interact with medication effect. There was no indication of any age by medication effect. The error rates on the long-term memory task were fairly low (less than 4%), and therefore were not analyzed. There was, however, no evidence of a speed-accuracy trade-off; the slight increase in errors that occurred from the pretreatment to the treatment session was actually somewhat smaller in the vasopressin period than in the placebo period.

In the semantic-memory task, there was no effect of medicaton on the retrieval of either high dominance or low dominance items from the given categories, nor were there any other main effects or interactions. However, the error rate for the semantic memory task was quite high, especially for the low dominance items (approximately 11% for high dominance items and 25% for low dominance items). Most of these errors were defaults (the subject did not make a response within 15 seconds, especially on the low dominance trials. This makes interpretation of the response-time data somewhat questionable.

On the final measure, simple vocal response time, we first compared latencies for trials given at the beginning of the test session to those given at the end. Since there was no difference, we combined the two trial sets for each individual and used the combined results for the main analysis. Here, there was no medication effect, nor were there any other main effects or interactions. The mean response time for the elderly

Table 2. Mean latencies and (standard deviations) for the second session of the placebo and drug (DDAVP) periods, adjusted for first sesson latencies

	Long-term memory			
	Letter-naming condition		Associate-recall condition	
	Placebo	Drug	Placebo	Drug
Old	514 (77)	511 (76)	637 (51)	610 (53)
Young	508 (62)	508 (82)	627 (56)	592 (48)

	Semantic memory			
	High dominance		Low dominance	
	Placebo	Drug	Placebo	Drug
Old	1488 (538)	1445 (680)	2136 (914)	2300 (1048)
Young	1301 (681)	1194 (445)	2247 (1042)	2076 (857)

was 300 msec on the placebo trials, and 295 msec on the drug trials, while for the young these times were 293 and 290 msec.

Thus, overall, DDAVP reduced response time significantly on both short- and long-term episodic memory measures, but did not affect semantic memory or simple response time. The order in which the drug and placebo were given did not have any effect, and the amount of memory facilitation produced by DDAVP was similar in the younger and older subjects.

To determine whether this effect of DDAVP on episodic memory was due to a facilitation of memory retrieval processes, we conducted a second analysis, which directly compared the magnitude of the drug effect within each episodic memory task on measures which did, and did not, require retrieval. This analysis involved constructing specific contrasts, using the zero-centered residual scores of improvement. Each contrast was made by subtracting the improvement on drug for one form of the task from the improvement on drug for the other, after normalizing to create a common standard deviation. In the short-term memory (STM) task, we compared the size of the drug effect on the slope (a measure of memory search) and intercept (a measure of nonretrieval operations). There was no significant difference in the effect that vasopressin had on these two measures for either "yes" ($t = 0.25$, $df = 47$) or "no" ($t = 0.43$, $df = 47$) responses. In the long-term memory (LTM) task, the comparison was between the associate recall and the letter-naming conditions. Again, there was no significant difference between the two conditions in the size of the effect produced by vasopressin ($t = 1.33$, $df = 47$, $p > 0.2$).

On the questionnaire asking subjects to rate any change they noticed in their everyday memory performance over the treatment period, almost all of the subjects marked "no change" for both the placebo and the vasopressin periods. On the KDS 1 & 2, the median difference in scores between the placebo and vasopressin weeks was 0

for all five scales (depression, anxiety, organicity, mania, and cognitive disorganization).

On the physical measures taken, the young showed a small rise in weight (0.14 kg) during the period they received the vasopressin and a loss (0.36 kg) while on placebo (probably due to the fluid restriction). Weight in the elderly declined in both periods, but less so in the vasopressin periods (0.41 vs. 0.1 kg). Serum sodium levels showed a slight decrease during the vasopressin periods in both age groups, but this was less than one mEq/l. Blood pressure actually fell during the treatment periods, especially while the subjects were on vasopressin (on the average, a decrease of 3.6/1.6 mmHg).

Discussion

One of the major goals of this study was to determine the specificity of vasopressin's action on mental functioning. Recent reports (Tinklenberg et al., 1982; Gash and Thomas, 1983) have suggested that vasopressin affects human performance through nonspecific mechanisms, such as enhancement of the general level of arousal, rather than by facilitating some particular mental operation. The present data do not support this concept of diffuse action. Rather, while vasopressin did facilitate the processing of information in our subjects, its effects were restricted to certain tasks—those testing short-term memory and long-term episodic memory. There was no evidence that vasopressin influenced simple vocal response time. Such an effect might be expected if this drug produced a generalized activation of all cognitive functions. While there were relatively few trials on this task, the small standard deviations found (between 13 and 30 msec) make it unlikely that excessive intersubject variability is masking a true drug effect here.

Vasopressin also did not significantly affect the speed with which subjects retrieved information from semantic memory (SM). There are several possible reasons for this lack of effect. First, the latency results from the tasks are suspect due both to the large number of errors, and to the substantial intrasubject and intersubject variability in the response times. These data problems may be obscuring a true drug effect on this task. There was, however, no evidence in the error data that subjects showed any improvement while on the drug. Another potential explanation involves an experimental factor which distinguishes the SM task from the two tasks that did show a drug effect (i.e., STM and LTM). In the SM task there was no need to learn new material, i.e., the subject had only to recall overlearned information. By contrast, in both the STM and LTM tasks, the subjects were given new material during the test session that they had to hold in memory. It may be, therefore, that vasopressin has an effect only on tasks that require the encoding and storage of new information, rather than those which involve solely memory retrieval. It should be noted, however, that Weingartner et al. (1981*b*) did find vasopressin to facilitate retrieval from SM in a verbal fluency task.

The issue of whether vasopressin affects only retrieval or also other cognitive operations was also examined within the STM and LTM paradigms. The memory tasks were designed to test whether the action of vasopressin was specific to the retrieval stage of that form of memory. In the STM task, if vasopressin facilitated only memory search and comparison, then it should have affected only the slope of the function which related memory set size to response time. Any drug effect on the

encoding of information, or on the decision or motor execution stages, should be evident as a medication effect on the intercept of this function. If this framework is used, our present results suggest that vasopressin influences *both* retrieval and nonretrieval stages of STM. Both the slope and the intercept of the function were reduced by the medication, and there was no significant difference between these two measures in the size of the drug-induced reduction. The results of the LTM task are less clear. In the first analysis, which examined the associate recall (requiring retrieval) and the letter-naming (no retrieval) conditions separately, vasopressin had a significant effect on response time only when the subject had to retrieve a word associated with the presented letter pair, and not when he had just to identify the letters. However, when the size of the medication effect on these two conditions was directly compared in the second analysis, the difference did not quite reach significance. Thus, the results of the LTM task are not clear as to the relative effect that the drug has on the retrieval and perceptual identification stages of long-term episodic memory.

Another goal of this study was to determine whether elderly subjects, because of their generally suboptimal level of cognitive efficiency, would show a greater drug-related improvement than the young. There was, however, no indication in the data of a differential effect of vasopressin on the two age groups. Although older subjects were generally slower on all the tasks than were the young (this difference is not reflected in the means of Tables 1 and 2 due to the covarying for the initial level of performance), both age groups improved equally while on the drug. It should, however, be pointed out that due to our medical criteria, the older subjects in this study were probably healthier than the average person of their age. An older group with greater physical and cognitive problems might have given different results, although the present older subjects certainly were substantially slower in retrieving information and making decisions than were the young.

Overall, the results of this study strengthen recent claims that vasopressin facilitates cognitive performance in normal humans. The data also suggest that this facilitation is specific to certain mental functions, and is not the result of a generalized change in the level of arousal. Vasopressin improved response speed on tests of episodic memory, but had no significant effect on a similarly complex and demanding test of semantic memory, nor did it affect a simple perceptual-motor task.

It is, of course, possible that the action of vasopressin is not specific to STM and LTM, but rather that these measures are just more sensitive than are the SM and simple response time measures to what is actually a general facilitation of cognition. One aspect of the present data which argues against this possibility is the pattern of correlations found between the test scores in the drug period. Scores on the measures affected by vasopressin (i.e., STM slope and intercept, LTM associate recall) were only slightly correlated ($r = 0.09$ to 0.23) with scores on the measures not affected by the drug (i.e., simple response time, SM). None of these correlations were significant. This result does not support the presence of a general effect of vasopressin with the various cognitive tasks differing only in their sensitivity to this effect. However, in order to confirm the cognitive specificity of vasopressin's action, it will be necessary to determine the effect of this drug on other measures of the same psychological functions. It is not clear from the present work exactly which stage(s) of episodic memory

function vasopressin is affecting. We found evidence of a drug-related increase in the speed both of memory retrieval and nonretrieval (possibly encoding) operations. Further work will be necessary to determine the exact psychological site of action. Finally, there was no evidence for any differential effect of vasopressin on young and older subjects, despite the differences in their level of cognitive functioning.

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References

Battig, W.F., and Montague, W.E. Category norms for verbal items in 56 categories. *Journal of Experimental Psychology Monographs,* **80,** 1 (1969).

Beckwith, B.E., Petros, T., Kanaan-Beckwith, S., Couk, D.I., and Haug, R.J. Vasopressin analog (DDAVP) facilitates concept learning in human males. *Peptides,* **3,** 627 (1982).

Blake, D.R., Dodd, M.J., and Grimley, E.J. Vasopressin in amnesia. *Lancet,* **I,** 608 (1978).

Cooper, R.L., McNamara, M.C., Thompson, W.G., and Marsh, G.R. Vasopressin modulation of learning and memory in the rat. In: Poon, L.W., ed. *Aging in the 1980's.* American Psychological Association, Washington, DC (1980).

Delwaide, P.J., Devoitille, J.M., and Ylieff, M. Acute effect of drugs upon memory of patients with senile dementia. *Acta Psychiatrica Belgica,* **80,** 748 (1980).

De Wied, D., Bohus, B., Urban, I., and van Wimersma-Greidanus, T.B. Memory deficit in rats with diabetes insipidus. *Brain Research,* **85,** 152 (1975).

De Wied, D., and Gispen, W.H. Behavioral effects of peptides. In: Gainer, H., ed. *Peptides in Neurobiology.* Plenum Press, New York (1977).

De Wied, D., and van Ree, J.M. Neuropeptides, mental performance and aging. *Life Sciences,* **31,** 709 (1982).

Folstein, M.F., Folstein, S.E., and McHugh, P.R. Mini-Mental State: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research,* **12,** 189 (1975).

Gash, D.M., and Thomas, G.T. What is the importance of vasopressin in memory processes? *Trends in Neurosciences,* **6,** 197 (1983).

Gold, P.W., Weingartner, H., Ballenger, J.C., Goodwin, F.K., and Post, R.M. Effects of 1-desamo-8-*d*-arginine vasopressin on behavior and cognition in primary affective disorder. *Lancet,* **II,** 992 (1979).

Jenkins, J.S., Mather, H.M., Coughlan, A.K., and Jenkins, D.G. Desmopressin in post-traumatic amnesia. *Lancet,* **II,** 1924 (1979).

Kupfer, D.J., Detre, T.P., and Amdur, M.J. KDS-1 scale for symptom discrimination. *Psychological Reports,* **30,** 915 (1972).

Legros, J.J., and Gilot, P. Vasopressin and memory in the human. In: Gotto, A.M., Jr., Peck E.J., Jr., and Boyd, A.B. III, eds. *Brain Peptides: A New Endocrinology.* Elsevier/North-Holland Biomedical Press, New York (1978).

Salthouse, T.A. *Adult Cognition.* Springer-Verlag, New York (1982).

Sternberg, S. Memory scanning: New findings and current controversies. *Quarterly Journal of Experimental Psychology,* **27,** 1 (1975).

Tinklenberg, J.R., Pfefferbaum, A., and Berger, P.A. 1-Desamino-*d*-arginine vasopressin (DDAVP) in cognitively impaired patients. *Psychopharmacolgoy Bulletin,* **17,** 206 (1981).

Tinklenberg, J.R., Pigache, R., Pfefferbaum, A., and Berger, P.A. Vasopressin peptides and dementia. In: Corkin, S., Davis, K.L., Growdin, J.H., Usdin, E., and Wurtman, R.J., eds. *Alzheimer's Disease: A Report of Progress in Research.* Raven Press, New York (1982).

Tulving, E. Episodic and semantic memory. In: Tulving, E., and Donaldson, W., eds. *Organization of Memory.* Academic Press, New York (1972).

Weingartner, H., Gold, P., Ballenger J.C., Smallberg, S.A., Summers, R., Rubinow, D.R., Post, R.M., and Goodwin, F.K. Effects of vasopressin on human memory functions. *Science,* **211,** 601 (1981*a*).

Weingartner, H., Kaye, W., Gold, P., Smallberg, S., Peterson, R., Gillin, J.C., and Ebert, M. Vasopressin treatment of cognitive dysfunction in progressive dementia. *Life Sciences,* **29,** 2721 (1981*b*).