ventricular pressure, and (vi) provides pharmacokinetic data similar to that obtained in man. This primate model may be useful for long-term physiologic, neurochemical, chemotherapeutic, and neurotoxicological evaluations.

JAMES H. WOOD*
DAVID G. POPLACK
WERNER A. BLEYER
AYUB K. OMMAYA†
Surgical Neurology Branch, National Institute of Neurological and Communicative Disorders and Stroke, and *Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20014,* and *Children's Orthopedic Hospital, Seattle, Washington*

References and Notes

1. R. A. Ratcheson and A. K. Ommaya, *N. Engl. J. Med.* **279**, 1025 (1968).
2. W. R. Shapiro, D. F. Young, B. M. Mehta, *ibid.* **293**, 161 (1975).
3. W. Feldberg and S. L. Sherwood, *J. Physiol. (London)* **120**, 3P (1953); *ibid.* **123**, 148 (1954).
4. P. C. Merker, M. D. Walker, E. P. Richardson, R. F. Shepard, *Excerpta Med. Int. Congr. Ser. No. 311, Proc. Eur. Soc. Study Drug Toxic.* **15**, 3 (1973).
5. T. J. Haley and R. W. Dickinson, *J. Am. Pharm. Assoc.* **45**, 432 (1956); A. C. Palmer, *J. Physiol. (London)* **149**, 209 (1959).
6. M. J. Bresnan *et al.*, *Trans. Am. Neurol. Assoc.* **97**, 204 (1972).
7. A. K. Ommaya, *Lancet* **1963-II**, 983 (1963).
8. J. H. Wood, D. G. Poplack, W. J. Flor, E. N. Gunby, A. K. Ommaya, in preparation.
9. G. DiChiro, S. M. Larson, T. Harrington, G. S. Johnston, M. V. Green, C. J. Swann, *Acta Radiol.* **14**, 379 (1973).
10. S. M. Larson, G. S. Johnston, A. K. Ommaya, A. E. Jones, G. DiChiro, *J. Am. Med. Assoc.* **224**, 853 (1973).
11. A. S. Fleischer, J. M. Patton, G. T. Tindall, *Surg. Neurol.* **3**, 309 (1975).
12. C. DiRocco, D. G. McLone, T. Shimoje, A. S. Raimondi, *J. Neurosurg.* **42**, 683 (1975).
13. J. R. Bertino and G. A. Fischer, *Methods Med. Res.* **10**, 297 (1964).
14. H. J. Hoffman, E. B. Hendrick, R. P. Humphreys, *J. Neurosurg.* **44**, 256 (1976).
15. We thank M. Kostolich, A. Stearns, C. Hawkins, and C. Seay for their technical assistance.
* Present address: Division of Neurosurgery, University of Pennsylvania, 3400 Spruce Street, Philadelphia 19104.
† Reprint requests should be sent to A.K.O., Surgical Neurology Branch, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20014.
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Memory for Lists of Sounds by the Bottle-Nosed Dolphin: Convergence of Memory Processes with Humans?

Abstract. *After listening to a list of as many as six discriminably different 2-second sounds, a bottle-nosed dolphin classified a subsequent probe sound as either "old" (from the list) or "new." The probability of recognizing an old probe was close to 1.0 if it matched the most recent sound in the list and decreased sigmoidally for successively earlier list sounds. Memory span was estimated to be at least four sounds. Overall probabilities of correctly classifying old and new probes corresponded closely, as if recognition decisions were made according to an optimum maximum likelihood criterion. The data bore many similarities to data obtained from humans tested on probe recognition tasks.*

Almost all experiments on short-term (immediate) memory in animals have been limited to the study of single-item retention, such as the ability to recognize among alternative visual stimuli the one item previously seen (*1*). Results from these experiments have provided important information on time-dependent processes in animal memory and on the effects of irrelevant activities or stimulation during the retention interval on recognition performance. However, they have contributed little information on more complex memory characteristics, such as storage modes, memory scanning rates, span of memory, and retrieval and decision strategies, characteristics that may be better assessed by tasks requiring the retention of multiple, serially occurring items. Such tasks have so far been limited to a few investigations of the ability of monkeys to reproduce in their response sequence the serial order of occurrence of two or three prior stimuli (*2*).

We now present results of tests of item recognition memory of a bottle-nosed dolphin, *Tursiops truncatus*, using serial lists of sounds as long as six items. In concept and method, these tests closely followed serial probe recognition tests given humans (*3, 4*). In the probe recognition test, a list of unique items is presented and followed by a single probe item, which is either an "old" item from the list or a "new" item. The task is to classify the probe correctly as old or new, a memory dependent process. The dolphin studied easily learned the requirements of the multiple-sound probe recognition task, and classified probes as old or new with great accuracy. These capabilities gave further evidence of the impressive auditory learning skills of *T. truncatus* (*5*). Overall, our results for the dolphin were similar to results obtained from human subjects in probe recognition tasks and revealed many of the same capabilities and constraints observed in human performance.

The dolphin tested, an adult female of 11 to 13 years named Keakiko, was the subject in earlier studies of single-item auditory retention (*6, 7*). We tested her twice daily in her seawater tank (diameter, 15.2 m) at the University of Hawaii. Each testing consisted of 30 to 48 discrete probe recognition trials (intertrial interval, 30 seconds). At the beginning of a trial the dolphin heard a highly familiar sound cue. In response, she swam through a channel of four vertically suspended ropes and pressed a "start" paddle 1 m beyond the channel exit, turning the sound cue off. Four seconds later, while passively stationed underwater facing the start paddle, she heard a list of k discriminably different sounds (k = 1, 2, ..., 6) projected from an underwater speaker (Chesapeake J9) located 1.2 m beyond the start paddle. Each sound was 2 seconds long, and successive sounds were separated by 0.5-second silent intervals. After a 1- or 4-second pause, the probe sound, 2 seconds long, was projected from one of two peripheral J9 speakers positioned 1.6 m to the left and right of the center speaker, diagonally facing the start paddle. Adjacent to each peripheral speaker was a response paddle. To respond "old sound (Yes)" the dolphin swam to the peripheral speaker that projected the probe and pressed the adjacent paddle. To respond "new sound (No)" she swam to the silent speaker, the one that projected no sound, and pressed the adjacent paddle. All correct responses immediately yielded a short (0.5-second) familiar conditioned reinforcer sound and then a thrown-fish reward. These were omitted after incorrect responses. Old and new probe sounds occurred with equal probability, each type occurring equally often at each peripheral speaker.

Testing began with single-sound recognition trials (k = 1), a procedure in which the animal was previously trained (*7*), and then proceeded serially, with all testing of k-sound lists completed before testing of $k + 1$ sound lists was begun. Transfer from a list of k sounds to a list of $k + 1$ sounds was accomplished by gradually increasing the duration of the added sound over 30 to 50 training trials until its final value of 2 seconds was reached; transfer was always completed without any disruption in performance.

The sounds in a list, as well as the probe, were selected from a pool of 600 discriminably different sounds that composed six different classes of sounds of 100 sounds each (*8*). The sounds were generated by oscillators (Wavetek) controlled by a minicomputer. A list of k

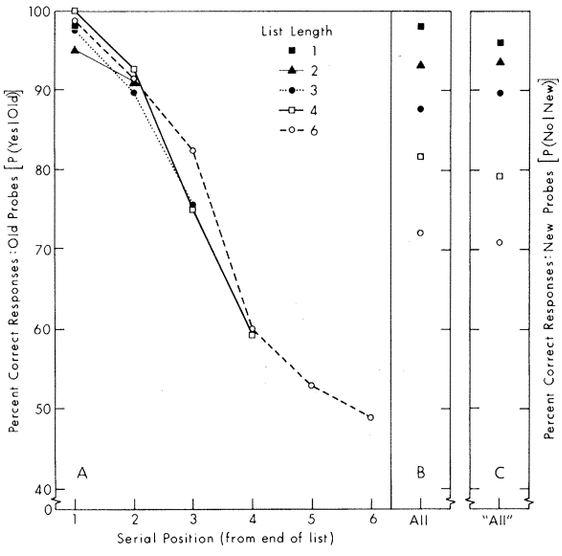

Fig. 1. (A) The percentage of correct recognitions of old probe sounds at each serial position for each length list. Serial positions are shown by relative recency of occurrence from end of list, so that serial position 1 is the most recent (last) sound in each list. (B) Data from (A) summed over all serial positions. (C) The percentage of correct recognitions of new probe sounds for each length list. There are, of course, no serial position data for new probe sounds.

sounds consisted of k different sound classes, with all possible permutations of the six sound classes being used across successive lists of a given size. All 100 sounds in a class were used once before any was repeated (*9*). Except in the case of six-sound lists, a new probe sound was always of a different sound class than any used in the list.

An old probe sound was equally likely to match a sound in any of the serial positions of the list. Figure 1A shows, for each length list, except five sounds, the percentage of correct classifications of old probe sounds [P(Yes|Old)] as a function of the old probe's serial position in the original list (*10*). Since probe delay was not a significant variable (*10*), the data were based on combined observations at the 1- and 4-second delays between the end of the list and the probe item; the minimum number of observations per data point were 397, 264, 204, 108, and 81 for lists of 1, 2, 3, 4, and 6 sounds, respectively.

The curves for the various length lists overlap and a pronounced "recency" effect is seen (Fig. 1A). The data resemble, in both absolute and relative terms, results for four human subjects in a probe recognition task using spoken lists of three-digit numbers (*3*). For six-item lists, the human subjects averaged 99.7, 97.7, 81.3, 72.0, 43.7, and 45.3 percent correct classifications of old items from the most recent to the earliest serial position, respectively (*11*).

Our current data, together with earlier tests of retention of single sounds by the bottle-nosed dolphin (*6, 7*), indicate that auditory memory traces may remain unaltered over long retention intervals unless degraded by newly arriving sounds. We cannot say how memory for the sounds heard is maintained over time by the dolphin in the absence of auditory interference, but so far there seems no reason to suppose it is necessarily by an active rehearsal process. In human studies, when the covert verbal rehearsal of list items is poorly controlled, the first item in the list tends to be remembered especially well (*12*). Figure 1A shows no such primacy effect.

Some information-processing models of human memory have postulated that incoming items are processed and stored serially in a buffer mechanism of limited item capacity, and that newly arriving items may degrade, shunt, and eventually displace older items (*13*). This serial nature of the buffer yields the recency effect, which favors newer items in memory tests (*14*). The buffer's item capacity, that is, the subject's memory span, can be estimated by the location on the abscissa of the asymptote of the recency curve. The recency effect in our data is interpretable within a buffer model. The location of the asymptote in Figure 1A would suggest that this bottle-nosed dolphin's memory span for discriminably different 2-second sounds paced at 0.5-second intervals was at least 4 sounds.

Within lists of each length, the percentages of correct recognitions of old and new probe sounds were very similar and decreased together as the list length-ened (Fig. 1, B and C). The dolphin thus classified probes without bias, as if using a maximum likelihood optimum decision criterion (*15*). The decrease in correct classifications of new probe sounds (increase in "false alarm" rate) as list length increased, together with the continued symmetry of error rates for old and new probe sounds, demonstrates that, although discriminability between old and new probes decreased with increased list length, the decision criterion remained unchanged. Similar increases in false alarm rate with increased list length are found in human data, although criterion shifts may sometimes occur as the list lengthens (*16*).

The human data are extensive and complex and we have here described only some broad functional similarities to it. Nevertheless, obtaining these similarities within a paradigm closely following that used with humans encourages the view that we may be dealing with much the same underlying conceptual phenomena discussed in human memory work, implying a convergence of some memory control processes in dolphin and human, both highly sophisticated species acoustically.

ROGER K. R. THOMPSON
LOUIS M. HERMAN*
Department of Psychology,
University of Hawaii, Honolulu 96822

References and Notes

1. See reviews of L. E. Jarrard and S. L. Moise [in *Cognitive Processes in Nonhuman Primates*, L. E. Jarrard, Ed. (Academic Press, New York, 1971), p. 1] and M. R. D'Amato [in *The Psychology of Learning and Motivation: Advances in Research and Theory*, G. H. Bower, Ed. (Academic Press, New York, 1973), vol. 7, p. 227]. "Short-term" memory is used here in the operational sense, referring to the presentation of an item or items generally once, and then testing for retention immediately or after delays of seconds or minutes. The other sense, the conceptual distinction between short-term (transient) and long-term (permanent) memory traces, is not intended.
2. J. V. Devine and L. C. Jones, *Behav. Res. Methods Instrum.* **7**, 438 (1975); J. H. Dewson III and A. Cowey, *Nature (London)* **222**, 695 (1969); _____, L. Weiskrantz, *Exp. Neurol.* **28**, 529 (1970).
3. W. A. Wickelgren and D. A. Norman, *J. Math. Psychol.* **3**, 316 (1966).
4. W. A. Wickelgren, *ibid.* **7**, 219 (1970).
5. For a review of complex learning and memory skills in delphinidae, see L. M. Herman, *Behaviors of the Dolphins*, L. M. Herman, Ed. (Wiley, New York, in press).
6. L. M. Herman, *Anim. Learn Behav.* **3**, 43 (1975); _____, J. A. Gordon, *J. Exp. Anal. Behav.* **21**, 19 (1974).
7. L. M. Herman, R. K. R. Thompson, M. J. Yunker, *Proceedings of the Western Psychological Association's 55th Annual Convention* (1975 Suppl.), abst., p. 4.
8. The six sound classes were continuous frequency signals, frequency modulated tones, amplitude modulated tones, a mixture of two different continuous frequency signals, a mixture of a pulsed tone and a continuous frequency signal, and a signal discretely shifting twice per second between two different continuous frequency values. The frequency components of the 100 different sounds in each class ranged from 2 to 100 khz with adjacent frequency values separated by at least seven just-noticeable differences (JND's), as extrapolated from frequency discrimination data [R. K. R. Thompson and L. M. Herman, *J. Acoust. Soc. Am.* **57**, 943 (1975)], for the present subject. All sounds were projected at sensation levels of 40 to 60 db, based on extrapolations from auditory threshold data for *T. truncatus* [C. S. Johnson, in *Marine Bioacoustics*, W. N. Tavolga, Ed. (Academic Press, New York, 1967), vol. 2, p. 247], and calibration data for the J9 transducers in our tank.
9. To minimize within-list similarity, absolute frequencies of the different sounds in a list were separated by at least 140 JND's. Using 600 discriminably different sounds circumvented the problem of temporal interference effects occurring when small sets of highly familiar stimuli

are repeatedly used (*6*). The minimum 140-JND criterion was also applied to a new probe item to ensure that it differed substantially in frequency from list items.

10. After the experiment was completed, we discovered that, for five-sound lists, serial position and the delay value preceding the probe had been inadvertently confounded: because of a programming error, the 4-second delay occurred much more frequently at serial positions 1 and 2 than at 3, 4, and 5; the opposite was true for the 1-second delay. This confounding resulted in a spuriously highly significant delay effect ($\chi^2 = 18.4$, $P < .0001$) and may have also been responsible for a significant bias toward responding "old" ($\chi^2 = 8.9$, $P < .005$). For all other list lengths, the two delay values occurred equally often at each serial position, and the differences in their effects were small and nonsignificant ($P > .05$). Also, no significant response bias occurred in any of these other list lengths. The five-sound-list data for serial positions 1 through 5–96.6, 92.2, 82.4, 68.5, and 61.1 percent correct responses, respectively–nevertheless showed the same general trends seen in Fig. 1A, though their absolute values were elevated because of the bias toward responding "old." When the data were corrected for bias [according to techniques described by D. M. Green and J. A. Swets, *Signal Detection Theory and Psychophysics* (Wiley, New York, 1966)], the adjusted percentages of correct responses across the five serial positions—95.4, 91.1, 79.1, 62.0, and 53.3 percent—fell very close to the plotted values for other data in Fig. 1A.
11. Absolute values for human data may vary considerably across studies depending on the type of material to be remembered, though the recency effect will continue to be shown. Recognition probabilities for lists of single letters (*4*) substantially exceeded the values listed here, but recognition probability for the first continuous frequency signal in a list of similar signals, as studied by D. W. Massaro [*J. Exp. Psychol.* **83**, 238 (1970)], fell well below the listed values.
12. N. C. Waugh and D. A. Norman, *Psychol. Rev.* **72**, 89 (1965). For humans, the primacy effect in a serial list can sometimes be eliminated by instructions to attend serially to each new item presented and to avoid thinking of earlier ones.
13. R. C. Atkinson and R. M. Shiffrin, in *The Psychology of Learning and Memory: Advances in Research and Theory*, K. W. Spence and J. A. Spence, Eds. (Academic Press, New York, 1968), vol. 2, p. 89.
14. B. B. Murdock, Jr., *Human Memory: Theory and Data* (Erlbaum, Potomac, Md., 1974).
15. If our experiment is conceptualized in terms of signal detection concepts (*14*), and a strength (item familiarity) theory is used for recognition memory (*3*), old and new probe items form independent but partially overlapping normal distributions (with equal variances and with a difference of d′ in the means) along a decision axis in which old (previously heard) probes have greater mean strength (familiarity) than new probes. With equal probability of old and new probe items and a symmetrical payoff matrix, the maximum likelihood criterion would be located at the intersection of the ordinates of the two distributions. If this criterion is then used in recognition decisions, unbiased responding will result, as indeed happened.
16. See C. A. Boneau and J. L. Cole [*Psychol. Rev.* **74**, 123 (1967)] for a discussion of the use of the maximum likelihood criterion when trial-by-trial information on the accuracy of responses is available, as is the case in most animal studies including the present one; and E. A. C. Thomas and D. Legge [*ibid.* **27**, 65 (1970)] on the use of a probability matching criterion (matching the ratio of the responses in each category to the a priori ratio of occurrence of the categories) when trial-by-trial information is not available, as is the case in many human studies.
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* Reprint requests should be sent to L.M.H.

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Dopamine-Sensitive Adenylate Cyclase: Location in Substantia Nigra

Abstract. *A dopamine-sensitive adenylate cyclase with characteristics similar to those measured in the striatum is present in the rat substantia nigra. Destruction of dopamine cell bodies by intranigral 6-hydroxydopamine application failed to abolish the response of nigral adenylate cyclase to dopamine. In contrast, brain hemitransection between the striatum and substantia nigra, or a more circumscribed lesion of striatonigral pathways, abolished the dopamine stimulation of adenylate cyclase in the substantia nigra. These results suggest that dopamine receptors within the substantia nigra are not located on dopamine cell bodies but are associated with a pathway, containing γ-aminobutyric acid or substance P, which projects from forebrain structures to the substantia nigra.*

The substantia nigra (SN) is a strategic relay center for the modulation of dopamine (DA) function in the central nervous system (*1*). Dopamine-containing efferent projections from the SN have been extensively characterized (*2*). In addition, neurons containing γ-aminobutyric acid (GABA) (*3*), substance P (*4*), acetylcholine (*5, 6*), and serotonin (*7*) have been found in the SN, but relatively little is known about the synaptic interactions of these neurons.

In an effort to unravel possible sites of interneuronal regulation in the SN, we pursued the idea that DA, released from nigral dendrites (*8*), may interact with receptors in the immediate vicinity. Since DA receptors are apparently associated with a DA-sensitive adenylate cyclase (*9*), and since the presence of such an adenylate cyclase has been demonstrated in the SN (*10*), it is likely that DA serves a neuromodulatory function in this region. The suggestion has been made that in the SN DA may influence the activity of the very same neurons from which it is released by interacting with dendritic or somatic DA receptors, which have been termed autoreceptors (*11*). Alternatively, it is likely that nondopaminergic neuronal components in the SN may contain receptors for this transmitter.

On the basis of measurements of DA-sensitive adenylate cyclase activity, we now provide evidence that most, if not all, nigral DA receptors are present in cells other than DA neurons. In the first series of experiments, rats received unilateral nigral injections (Fig. 1) of 6-hydroxydopamine (6-OHDA) and were killed 10 to 15 days later to study the adenylate cyclase activity of the SN. To ascertain the extent of DA neuron destruction caused by 6-OHDA, we assayed tyrosine hydroxylase (TH) activity in the striatum, a terminal projection area of nigral DA neurons.

In homogenates of untreated SN, the threshold concentration of DA for stimulation of adenosine 3′,5′-monophosphate (cyclic AMP) synthesis was $10^{-6}M$ (Fig. 1); with $5 \times 10^{-6}M$ DA, stimulation was virtually maximal. Norepinephrine (NE) was approximately ten times less potent than DA; threshold stimulation was obtained at $10^{-5}M$ NE.

In homogenates of 6-OHDA–treated SN, the absolute and relative potencies of both DA and NE did not significantly differ from values obtained in untreated controls (Fig. 1). Since the 6-OHDA treatment resulted in an 80 to 90 percent loss of striatal TH (Fig. 1), the data demonstrate that in the SN the presence of DA-sensitive adenylate cyclase is independent of the amount of DA cell bodies.

In a second series of experiments a complete cerebral hemitransection at the diencephalic-mesencephalic junction was performed in rats 7 days before they were killed (*12*). In the SN of the lesioned side, the basal activity of adenylate cyclase (30 ± 2.0 pmole mg^{-1} min^{-1}) was comparable to that of the intact side (28 ± 1.5 pmole mg^{-1} min^{-1}). In homogenates of the SN from the intact side, DA ($10^{-5}M$) produced a nearly twofold increase in cyclic AMP synthesis (54 ± 4.1 pmole mg^{-1} min^{-1}). In contrast, DA failed to stimulate the adenylate cyclase activity of SN from the lesioned side (38 ± 4.2 pmole mg^{-1} min^{-1}). When the hemitransection was done posterior to the SN (*13*), DA stimulation of adenylate cyclase was not significantly altered.

These results provide biochemical evidence that DA-dependent adenylate cyclase is located in neurons connecting the forebrain with the SN. Since our data tend to exclude the possibility that DA-dependent adenylate cyclase is directly associated with DA cell bodies or dendrites (*14*), a third series of experiments was performed to determine more specifically what population of SN neurons contains the major proportion of DA-sensitive adenylate cyclase. One of the most significant biochemical changes reported in the SN after hemitransection is the loss of GABA and its synthesizing en-