Posterolateral hypothalamic and midbrain central gray lesions impair visual and spatial reversal learning: Further additions to the "general learning system" of the rodent brain

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It has been assumed that the components of the rodent's "general learning system" (a group of brain structures essential for normal acquisition of a wide range of laboratory tasks) can roughly be identified by determining which lesion placements within the rat brain will lead to defective acquisition of a spatial discrimination habit and its reversal as well as a brightness discrimination habit and its reversal. The results of this experiment suggest that the regions of the posterolateral hypothalamus and mesencephalic central gray, but not the regions of the nucleus accumbens, septofornix, medial supraoptic area, or ventromedial hypothalamus, qualify as components of the general learning system.

This study is an extension of a series of lesion experiments (Thompson, 1982a, 1982b) aimed at identifying the "general learning system" (an ensemble of neural structures conceived to play a significant role in the acquisition of a broad spectrum of laboratory tasks) of the rodent brain. While the composition of the general learning system (GLS) cannot be fully established until it has been shown that a lesion to each component part impedes acquisition of a wide variety of laboratory tasks, a reasonably good estimate of its makeup can be obtained by determining which structures of the rat brain, when individually damaged, would induce significant learning impairments on the following four problems: a simple position (vestibular-proprioceptive-kinesthetic) discrimination habit and its reversal and a white-black (visual) discrimination habit and its reversal. Choosing these four problems to identify the constituents of the GLS was based upon earlier lesion studies which showed that those brain structures found to be critical for *retention* of both visual and vestibular-proprioceptive-kinesthetic discrimination habits were also found to be critical for retention of such learned activities as a complex maze, latch-box problems, and avoidance responses (Thompson, 1982c).

Of the 23 different cortical and subcortical sites previously found to be critical for original and re-

versal learning of a position habit, only 10 were found to be critical for original and reversal learning of a white-black discrimination habit (Thompson, 1982a, 1982b). These 10 sites included the occipital cortex, globus pallidus, ventrolateral thalamus, lateral thalamus, parafascicular nucleus, substantia nigra, red nucleus, interpeduncular-central tegmental complex, median raphe, and pontine reticular formation. When these data were compared with other findings, it was proposed that all of the foregoing structures, except the occipital cortex,¹ qualify as components of the GLS.

In the current study, six additional regions of the rat brain were investigated in relation to their possible inclusion within the GLS. Bilateral damage to any one of these regions (nucleus accumbens, septofornix, medial supraoptic hypothalamus, ventromedial hypothalamus, posterolateral hypothalamus, and mesencephalic central gray) has previously been shown to retard acquisition and reversal of a position habit formed in a single-unit T-maze (Thompson, 1983). Any one of the foregoing brain sites found to be critical for acquisition and reversal of a white-black discrimination habit would, according to the argument presented above, qualify as a component of the GLS.

METHOD

Subjects and Surgery

The completion of this study was facilitated by cooperation of the Board of Directors and Staff of the Rehabilitation Center for Brain Dysfunction. The authors are affiliated with the Department of Physical Medicine and Rehabilitation of the University of California Irvine Medical Center. Requests for reprints should be sent to Robert Thompson, Fairview State Hospital, 2501 Harbor Boulevard, Costa Mesa, California 92626.

Twenty-seven male Sprague-Dawley albino rats (90-120 days old), under deep chloral-hydrate anesthesia (250 mg/kg), sustained bilateral damage to the nucleus accumbens, septofornix, medial supraoptic hypothalamus, ventromedial hypothalamus, postero-

lateral hypothalamus, or mesencephalic central gray. The lesions were made stereotactically by passing a constant anodal current (1.5-3.0 mA) for 5-10 sec through an implanted stainless steel electrode with 1.0-1.5 mm of the tip exposed. The size and locus of the lesions of the various experimental groups were intended to be comparable to those received by the corresponding groups investigated earlier in connection with acquisition of the position discrimination habits (Thompson, 1983). The eight sham-operated control rats underwent the same surgical procedure as the experimental rats, save for drilling of the skull and insertion of the lesion electrode.

Following surgery, the animals were usually housed, two per cage, in medium-size wire cages containing a constant supply of food pellets and water. Throughout the recovery period, the animals were handled for approximately 5 min on every 3rd day. Preliminary training in the visual discrimination apparatus was begun 3 weeks postsurgically. On the day prior to preliminary training, the vibrissae of each animal were shaved (see Thompson, 1982a).

Apparatus

A two-choice Thompson-Bryant discrimination box, utilizing the motive of escape-avoidance of footshock, was employed (see Thompson, 1978a). All parts of the grid floor were connected to an alternating-current source adjusted to provide footshocks ranging from 1.0 to 1.8 mA. Two pairs of stimulus cards mounted on wooden blocks were used in the apparatus. One pair (two medium-gray cards) was employed for the purpose of training the animals to push aside a card in order to gain access to the goalbox. The second pair consisted of a white card and a black card.

Procedure

Original Learning

Formal training on the white (positive)-black (negative) discrimination problem began 24 h after the completion of preliminary training (see Thompson, 1982b). An approach response to the unlocked white card admitted the animal to the goalbox, whereas an approach response to the adjacent locked black card (error) was punished by footshock. If an error was committed (approach to the black card which brought the animal's forefeet in contact with the charged grid section that extended 8.0 cm in front of the black card), the animal was forced to respond to the white card in order to gain access to the goalbox. The position of the white (and black) card was changed from the left to the right window in a sequence mixed with single- and double-alternation runs. Eight to 12 trials were given daily with an inter-trial interval of 50-75 sec. The criterion of learning consisted of either a "perfect" or a "near-perfect" run of correct responses with a probability of occurrence of less than .05 (Runnells, Thompson, & Runnells, 1968), followed by at least 75% correct responding in the subsequent block of 8 trials given on the next day. If the criterion was not reached within 100 trials, the animals involved received no further training on the original problem and were not required to learn the reversal problem.

The specific training procedure was as follows: The rat was placed in the startbox, and the startbox door was raised. Failure to leave the startbox within 5 sec was followed by brief footshocks. No further footshocks were given unless the rat made an error or failed to make a choice of one of the stimulus cards within 5 sec. The animal was allowed to remain in the goalbox for 10 sec, after which it was transferred to a restraining cage to await the next trial. The animals were usually run in squads of two.

Reversal Learning

On the day following attainment of the criterion of learning on the original problem, the animals began training on the reversal problem—black card positive vs. white card negative. The training procedure was the same as that followed in original learning, and

postoperative training was terminated when the animal reached the criterion of learning.

Histology

Each brain-damaged rat was killed with an overdose of chloral hydrate. Its vascular system was then perfused with normal saline followed by 10% Formalin, and the brain was removed and stored in 10% Formalin for 2-4 days. Each brain was then blocked, frozen, and sectioned frontally at 90 μ . Every fourth section through the lesioned area was retained and subsequently photographed at 12 $\times$ by using the section as a negative film in an enlarger.

Measurements of Performance

Learning measures consisted of both trials to criterion and initial errors to criterion. A third measure (total errors to criterion) was also included because it was not uncommon for an animal on a given trial to retreat from the charged grid section below the negative card and then approach the negative card a second (third, fourth, etc.) time, each approach response resulting in footshock. Thus, total errors to criterion referred to the sum of approaches to the negative card that resulted in footshock.

As discussed earlier (Thompson, 1982a), a "reversal learning deficit" cannot necessarily be inferred from the finding that a given brain-damaged group was significantly inferior to the controls in learning the reversal problem. However, such a deficit would be indicated by the finding that a given brain-damaged group committed proportionately more errors (or required proportionately more trials) in learning the reversal problem, as opposed to the original problem, than the controls. Thus, individual "savings scores"—[(original learning score - reversal learning score)/original learning score] $\times$ 100—were computed for each measure of performance.

RESULTS

Original and Reversal Learning

Table 1 shows the three measures of performance on the original and reversal problems for all groups. These data will be discussed in terms of the site of brain damage.

Control Group

All sham-operated control subjects learned the original problem within 32 trials. On the reversal problem, the slowest control animal required 60 trials to reach the criterion of learning. Based on the Wilcoxon test for paired replicates, the reversal problem was significantly more difficult to master than the original problem in terms of all three measures of performance ($ps < .01$).

Nucleus Accumbens Group

Three animals sustained multiple bilateral electrolytic lesions in the region of the nucleus accumbens (Figure 1). While these animals were somewhat retarded in learning the original problem, they rapidly acquired the reversal problem. The Mann-Whitney U test disclosed that none of the differences in performance measures between this group and the controls approached statistical significance.

Table 1
Mean Learning Scores on the Original and Reversal Problems for All Groups

Group	Original Problem				Reversal Problem			
	N	Trials	Initial Errors	Total Errors	N	Trials	Initial Errors	Total Errors
Control	8	24.3	12.4	18.4	8	41.9	24.9	34.6
Nucleus Accumbens	3	33.7	16.0	24.3	3	34.3	20.8	33.3
Septofornix	6	33.3	16.2	24.3	5	22.6*	12.8*	23.4
Medial Supraoptic Area	3	31.3	16.7	24.7	3	29.0	19.7	28.0
Ventromedial Hypothalamus	4	23.2	10.2	16.2	4	30.0	19.2	42.2
Posterolateral Hypothalamus	6	30.7	14.7	26.2*	6	49.2	28.5	48.2*
Midbrain Central Gray	5	43.0*	20.6*	31.4*	5	57.2*	33.0*	38.2

*Differed from the controls at least at the .05 level.

Figure 1. Photographs of unstained sections showing lesions of the nucleus accumbens in three rats.

Septofornix Group

The region of the septofornix was extensively damaged in six rats. One of these rats failed to learn the original problem within 100 trials (Figure 2). In contrast, the remaining five readily learned both the original and reversal problems. (Figure 3 shows the lesion in one of these rats.) In fact, they mastered the reversal problem at a significantly faster rate than the controls. [Interestingly, these five animals averaged only 10.2 initial errors in learning the original problem; the difference between this score and that of the controls approached statistical significance ($p = .10$).]

It is important to mention that the atypical rat of this group was highly emotional. Throughout training, this animal strongly resisted handling, bit the experimenter's glove, and, despite being delayed in the startbox, ran speedily toward the stimulus cards when the startbox door was raised.

Hypothalamic Groups

Medial supraoptic region. The three rats with bilateral lesions to the medial supraoptic area (Figure 4), like the group with damage to the nucleus accumbens, tended to learn the original problem more slowly than the controls, but mastered the reversal problem somewhat faster than the controls. None of the differences, however, approached statistical significance.

Ventromedial region. Four animals sustained bilateral lesions to the ventromedial hypothalamic area that encroached only slightly upon the mammillary bodies. Figure 5 shows the lesions in three rats of this group. This group was virtually indistinguishable from the controls in learning the original problem. While these animals tended to earn better learning scores on the reversal problem than the controls, only the difference in the trials-to-criterion measure approached statistical significance ($p = .10$).

Posterolateral region. Six animals suffered bilateral damage to the medial forebrain bundle at mid-tubular levels. Figure 6 shows the lesion in one of these rats. In terms of total errors to criterion, this

Figure 2. Photographs of three unstained sections showing a lesion of the septofornix in the rat that failed to learn the original discrimination.

Figure 3. Photographs of three unstained sections showing a lesion of the septofornix in one rat that rapidly learned the original and reversal problems.

group was significantly retarded in acquiring both the original and reversal problems.

Mesencephalic Central Gray Group

The central gray and surrounding tegmentum were damaged to varying degrees in five rats. In no case did the lesions invade the underlying oculomotor complex. Figure 7 shows the lesion in one of these rats. This group was significantly inferior to the controls in learning both visual discrimination tasks.

Reversal Learning Deficit

Table 2 presents the means of the savings scores that were used to determine the presence and extent of a reversal learning deficit. Surprisingly, most of the experimental groups examined in this study earned better savings scores than the controls. Significant facilitation of reversal learning, as reflected by at least one measure of performance, was observed in the groups with lesions to either the septofornix or

Figure 4. Photographs of unstained sections showing lesions of the medial supraoptic area in three rats.

medial supraoptic area. A marginally significant facilitory effect in terms of initial errors to criterion ($p = .10$) was observed in the group with lesions to the nucleus accumbens. (No such facilitory effect was evident in any of the 23 brain-damaged groups examined in the earlier studies—Thompson, 1982a, 1982b.)

Escape-Avoidance Behavior

Only 2 of the 27 brain-damaged animals consistently required more than one or two footshocks to force escape responses from the startbox and/or

Figure 5. Photographs of unstained sections showing lesions of the ventromedial hypothalamus in three rats.

choice chamber. Both of these animals suffered the largest lesions to the posterolateral hypothalamus. One was the poorest learner of the group, while the second was immediately behind the best learner of the group.

Extremely rapid running from the startbox toward the goalbox constituted another aberrant escape-avoidance response. This behavior appeared in five of the control animals and in eight of the brain-damaged animals (one with medial supraoptic, two with septofornix, and five with central gray lesions). In most cases, running speed was greatly reduced by the routine imposition of a delay of 10-20 sec be-

Figure 6. Photographs of three unstained sections showing a lesion of the posterolateral hypothalamus in one rat.

tween placing the animal into the startbox and raising the startbox door.

Other Behavioral Observations

All brain-damaged (and control) animals appeared healthy and alert at the time preliminary training was instituted. The three animals (each with posterolateral hypothalamic lesions) that exhibited eating and drinking disturbances beyond the 3rd post-surgical day gradually recovered these behaviors when provided with sweetened wet mash in the home cage.

Throughout postoperative testing, the majority

of animals with lesions to the nucleus accumbens, septofornix, medial supraoptic area, ventromedial hypothalamus, or posterolateral hypothalamus strongly resisted handling and bit the experimenter's glove. This "irritability," which also led to fighting with cage mates, made it necessary to house each of these animals in a separate cage.

DISCUSSION

General Findings

It was not surprising that bilateral posterolateral hypothalamic lesions were found to retard acqui-

Figure 7. Photographs of three unstained sections showing a lesion of the mesencephalic central gray in one rat.

tion of a white-black discrimination habit (and its reversal) in the white rat. Previous work on retention of visual discrimination tasks has revealed that at least 50% of the subjects with posterolateral hypothalamic damage committed *more* errors in relearning the tasks than they committed during preoperative training (Thompson, 1976; Thompson & Spiliotis, 1981). On the other hand, it was totally unexpected that bilateral lesions in the vicinity of the mesencephalic central gray would retard original and reversal learning of a white-black discrimination problem. According to earlier findings (Thompson, 1976; Thompson & Spiliotis, 1981), relatively localized central gray lesions do not produce any marked de-

leterious effects on preoperatively learned brightness or pattern discrimination habits in the rat. However, it would be premature to conclude that the region of the midbrain central gray is more concerned with learning than with retention of visual tasks, since the lesions of the current study were appreciably larger than those examined in the retention studies. Interestingly, Myers (1964) reported that cats with midbrain lesions destroying much of the central gray substance were seriously deficient in relearning pattern discrimination problems.

Schwartzbaum and Donovan (1968) have previously shown that rats with septal lesions do not exhibit a deficit in either original or reversal learning of

Table 2
Mean Savings Scores for All Groups

Group	N	Trials		Initial Errors		Total Errors	
		Mean	Range	Mean	Range	Mean	Range
Control	8	-84.0	-186 to 16	-103.5	-200 to -29	-90.6	-553 to -23
Nucleus Accumbens	3	-6.3	-19 to 17	-37.7	-70 to -5	-50.0	-81 to 6
Septofornix	5	15.0	-77 to 48	-28.8*	-100 to 17	-42.2	-150 to 32
Medial Supraoptic Area	3	12.3*	-19 to 33	-15.7*	-48 to 11	-20.3*	-46 to 13
Ventromedial Hypothalamus	4	-33.3	-75 to 19	-92.3	-167 to 39	-148.8	-277 to -54
Posterolateral Hypothalamus	6	-68.2	-115 to -38	-95.3	-117 to -73	-90.5	-163 to -11
Midbrain Central Gray	5	-69.0	-240 to 23	-77.8	-230 to -10	-49.0	-215 to 2

*Differed from the controls at least at the .05 level.

a brightness discrimination habit. Our findings agree with their results, at least to the extent that damage to the septofornix does not adversely affect visual discrimination learning. However, our lesioned rats clearly learned the reversal problem faster than the controls. This is a remarkable finding when it is considered that rats with damage to the septal area show a profound disturbance in learning the reversal of spatial (Schwartzbaum & Donovick, 1968; Thompson, 1983) as well as kinesthetic (Gittelson & Donovick, 1968) discrimination habits. That this facilitation of visual discrimination reversal learning in the septofornix-lesioned rat is probably not the result of chance is indicated by the fact that two independent studies have shown that monkeys with transection of the fornix likewise learn visual (object) discrimination reversal problems faster than controls (see Zola & Mahut, 1973).

It is important to note that hippocampal-lesioned rats have not been observed to show facilitation of visual reversal learning (Becker & Olton, 1980; Samuels, 1972; Silveira & Kimble, 1968; Thompson, 1982a), although one study has disclosed that these brain-damaged rats learn the original visual discrimination problem faster than controls (Sara & David-Remacle, 1981). On the other hand, the present study has revealed a significant (or marginally significant) facilitation of visual reversal learning in those groups with damage to the ventromedial hypothalamus, medial supraoptic area, or nucleus accumbens. In light of these findings, it is conceivable that the paradoxical effect of septal lesions on visual reversal learning may be more related to disruption of a hypothalamic mechanism than to disruption of a hippocampal mechanism. This interpretation, however, must be viewed with caution, since monkeys with anterior or ventromedial hypothalamic lesions apparently exhibit deficits in original and reversal learning of visual discrimination problems (Rosvold, 1972).

General Learning System

It has previously been proposed that the regions of the globus pallidus, ventrolateral thalamus, lateral thalamus, parafascicular nucleus, substantia nigra,

red nucleus, interpeduncular-central tegmental area, median raphe, and pontine reticular formation are components of the general learning system (GLS) of the rodent brain. This proposal was based not only upon the findings that selective lesions to these regions impair original and reversal learning of both visual and spatial discrimination habits, but upon lesion data related to learning (or relearning) of other tasks as well (Thompson, 1982a, 1982b). According to the results of the present investigation, the regions of the posterolateral hypothalamus and mesencephalic central gray must also be considered as possible components of the GLS.

In light of earlier findings, it appears quite reasonable to include the posterolateral hypothalamus within the GLS. Rats with bilateral damage to this area have been reported to exhibit relearning disturbances (errors to relearn postoperatively being greater, in many cases, than errors to learn pre-operatively) on a variety of laboratory tasks, including visual discriminations (Thompson, 1976), an incline plane discrimination (Thompson, Arabie, & Sisk, 1976), a three-cul maze (Thompson, 1974), latch-box problems (Thompson, Gates, & Gross, 1979), and active (and passive) avoidance responses (Thompson, 1978b).

On the other hand, justifying the inclusion of the midbrain central gray area within the GLS is hindered by the fact that rats with lesions of this area have not been found to exhibit relearning disturbances on a three-cul maze (Thompson, 1974), latch-box problems (Thompson et al., 1979), or avoidance responses (Thompson, 1978b). These data, however, may be irrelevant to the extent that it is not uncommon that a given brain lesion will be found to have little effect on retention, although it may seriously impair acquisition (see, e.g., Brady, Schreiner, Geller, & Kling, 1954, and Ranje & Ungerstedt, 1977). In view of this possibility, we initiated a study of the effects of midbrain central gray lesions in rats on acquisition of an active avoidance response, an incline plane discrimination, a three-cul maze, and several latch-box problems (Thompson, Gallardo, & Yu, Note 1). To date, the findings clearly indicate that these lesions do indeed retard acquisition of a

wide range of laboratory tasks. On the strength of these data, we have decided to include the midbrain central gray region within the GLS of the rodent brain (see Figure 8).

It should be emphasized that the current composition of the GLS shown in Figure 8 is an outcome of the study of 37 different lesion placements in cortical and subcortical areas. Eight of these lesion placements failed to impair original and/or reversal learning of a spatial discrimination habit,² 17 failed to impair original and/or reversal learning of a visual discrimination habit, although they did impair original and reversal learning of the spatial discrimination habit,³ and only 12 (11 are shown in Figure 8, the 12th being the occipital cortex⁴) impaired acquisition of all four discrimination tasks. Obviously, subsequent studies may lead to the expansion of the GLS. It is very likely, for example, that the ventral tegmental area and the entopeduncular nucleus will qualify as components of the GLS (see Thompson, 1982c). On the other hand, the GLS shown in Figure 8 may have to be abridged in the event that future lesion studies fail to implicate one or more of its constituent parts in the acquisition of other kinds of laboratory tasks.

While other interpretations are possible, we favor the notion that the GLS constitutes the major part of a neural mechanism that exerts an organizing effect on the brain on both the sensory and motor sides (Thompson, 1982b).⁵ With respect to learning, this organizing effect may take the form of an "anticipatory set," as conceived by Sperry (1955). Several reasons for linking anticipatory sets with the GLS have previously been discussed (Thompson, 1982b).

If subsequent studies confirm the central role of the GLS of the rodent brain in acquiring various

laboratory tasks, then the question arises concerning the existence (and morphology) of such a system in higher mammalian forms, including humans. On different grounds, several investigators have referred to the presence of a subcortical mechanism that integrates (Kilmer, McCulloch, & Blum, 1968; Penfield, 1954), controls (Levy & Trevarthen, 1976), organizes (MacKay, 1966), and/or sustains (Hassler, 1978) the activities of the brain of man, but the neural substrata underlying these hypothetical processes remain to be identified. Perhaps further studies into the nature of "subcortical dementia" in man (Albert, 1978) will shed some light on the morphology of this neural system. Lesion studies dealing with brainstem mechanisms underlying learning in the monkey would constitute a more direct approach to this problem. However, the size of the lesions investigated will undoubtedly be a critical factor, judging from the rather inconclusive results arising from relatively small brainstem lesions in monkeys (Thompson & Myers, 1971).

REFERENCE NOTE

1. Thompson, R., Gallardo, K., Yu, J. Unpublished observations, 1983.

REFERENCES

- ALBERT, M. L. Subcortical dementia. In R. Katzman, R. D. Terry, & K. L. Bick (Eds.), *Alzheimer's disease: Senile dementia and related disorders*. New York: Raven Press, 1978.
- ARBUTHNOTT, G. W., MITCHELL, G. W., TULLOCH, M. J., & WRIGHT, A. K. Efferent pathways from lateral hypothalamic neurons. *Journal of Physiology* (London), 1976, **263**, 131-132P.
- BARBARESI, P., CONTI, F., & MANZONI, T. Axonal branching in the periaqueductal gray projections to the thalamus: A fluorescent retrograde double-labeling study in the cat. *Brain Research*, 1982, **252**, 137-141.
- BECKER, J. T., & OLTON, D. S. Object discrimination by rats: The role of frontal and hippocampal systems in retention and reversal. *Physiology & Behavior*, 1980, **24**, 33-38.
- BRADY, J. V., SCHREINER, L., GELLER, I., & KLING, A. Subcortical mechanisms in emotional behavior: The effect of rhinencephalic injury upon the acquisition and retention of a conditioned avoidance response in cats. *Journal of Comparative and Physiological Psychology*, 1954, **47**, 179-186.
- ESTES, W. K. *Learning theory and mental development*. New York: Academic Press, 1970.
- FINGER, S., COHEN, M., & ALONGI, R. Role of somatosensory cortical Areas 1 and 2 in tactile discrimination in the rat. *International Journal of Psychobiology*, 1972, **2**, 93-102.
- FINGER, S., & FROMMER, G. P. Effects of cortical lesions on tactile discrimination graded in difficulty. *Life Sciences*, 1968, **7**, 897-904.
- GABRIEL, S., FREER, B., & FINGER, S. Brain damage and the overlearning reversal effect. *Physiological Psychology*, 1979, **7**, 327-332.
- GITTELSON, P. L., & DONOVICK, P. J. The effects of septal lesions on the learning and reversal of a kinesthetic discrimination. *Psychonomic Science*, 1968, **13**, 137-138.
- HASSLER, R. Interaction of reticular activating system for vigilance and the thalamocortical and pallidal systems for directing awareness and attention under striatal control. In P. A. Buser & A. Rougeul-Buser (Eds.), *Cerebral correlates of conscious experience*. Amsterdam: Elsevier/North Holland, 1978.

Figure 8. Components of the general learning system (cross-hatched areas) shown at frontal levels of the brainstem of the rat. Abbreviations: CG = mesencephalic central gray, GP = globus pallidus, IC = interpeduncular-central tegmental complex, L = lateral thalamus, LH = posterolateral hypothalamus, MR = median raphe, PF = parafascicular nucleus, PRF = pontine reticular formation, RN = red nucleus, SN = substantia nigra, VL = ventrolateral thalamus.

- HOPKINS, D. A., & NIESSEN, L. W. Substantia nigra projections to the reticular formation, superior colliculus and central gray in the rat, cat and monkey. *Neuroscience Letters*, 1976, 2, 253-259.
- KILMER, W. L., MCCULLOCH, W. S., & BLUM, J. An embodiment of some vertebrate command and control principles. *Currents in Modern Biology*, 1968, 2, 81-97.
- LEVY, J., & TREVARTHEN, C. Metacognition of hemispheric function in human split-brain patients. *Journal of Experimental Psychology: Human Perception and Performance*, 1976, 2, 299-312.
- MACKEY, D. M. Conscious control of action. In J. C. Eccles (Ed.), *Brain and conscious experience*. New York: Springer-Verlag, 1966.
- MYERS, R. E. Visual deficits after lesions of brain stem tegmentum in cats. *Archives of Neurology*, 1964, 11, 73-90.
- PENFIELD, W. Mechanisms of voluntary movement. *Brain*, 1954, 77, 1-17.
- RANJE, C., & UNGERSTEDT, U. Lack of acquisition in dopamine denervated animals tested in an underwater Y-maze. *Brain Research*, 1977, 134, 95-111.
- ROSVALD, H. E. The frontal lobe system: Cortico-subcortical interrelationships. *Acta Neurobiologiae Experimentalis*, 1972, 32, 439-460.
- RUNNELS, L. K., THOMPSON, R., & RUNNELS, P. Near-perfect runs as a learning criterion. *Journal of Mathematical Psychology*, 1968, 5, 362-368.
- SAMUELS, I. Hippocampal lesions in the rat: Effects on spatial and visual habits. *Physiology & Behavior*, 1972, 8, 1093-1098.
- SARA, S. J., & DAVID-REMACLE, M. Discrimination avoidance learning in hippocampal and cortical rats: Acquisition rate, behavioral strategies, and long-term retention. *Physiological Psychology*, 1981, 9, 37-48.
- SCHWARTZBAUM, J. S., & DONOVICK, P. J. Discrimination reversal and spatial alternation associated with septal and caudate dysfunction in rats. *Journal of Comparative and Physiological Psychology*, 1968, 65, 83-92.
- SHERMAN, B. S., HOEHLER, F. K., & BUEGER, A. A. Instrumental avoidance conditioning of increased leg lowering in the spinal rat. *Physiology & Behavior*, 1982, 25, 123-128.
- SHIOSAKA, S., TOHYAMA, M., TAKAGI, H., TAKAHASHI, Y., SAITOH, Y., SAKUMOTO, T., NAKAGAWA, H., & SHIMIZU, N. Ascending and descending components of the medial fore-brain bundle in the rat as demonstrated by the horseradish peroxidase-blue reaction. *Experimental Brain Research*, 1980, 39, 377-388.
- SILVEIRA, J. M., & KIMBLE, D. P. Brightness discrimination and reversal in hippocampally-lesioned rats. *Physiology & Behavior*, 1968, 3, 625-630.
- SPEERY, R. W. On the neural basis of the conditioned response. *British Journal of Animal Behaviour*, 1955, 3, 41-44.
- THOMPSON, R. Localization of the "maze memory system" in the white rat. *Physiological Psychology*, 1974, 2, 1-17.
- THOMPSON, R. Stereotaxic mapping of brainstem areas critical for memory of visual discrimination habits in the rat. *Physiological Psychology*, 1976, 4, 1-10.
- THOMPSON, R. *A behavioral atlas of the rat brain*. New York: Oxford University Press, 1978. (a)
- THOMPSON, R. Localization of a "passive avoidance memory system" in the white rat. *Physiological Psychology*, 1978, 6, 263-274. (b)
- THOMPSON, R. Brain lesions impairing visual and spatial reversal learning in rats: Components of the "general learning system" of the rodent brain. *Physiological Psychology*, 1982, 10, 186-198. (a)
- THOMPSON, R. Impaired visual and spatial reversal learning in brain-damaged rats: Additional components of the "general learning system" of the rodent brain. *Physiological Psychology*, 1982, 10, 293-305. (b)
- THOMPSON, R. Functional organization of the rat brain. In J. Orbach (Ed.), *Neuropsychology after Lashley*. Hillsdale, N.J.: Erlbaum, 1982. (c)
- THOMPSON, R. Abnormal learning and forgetting of individual spatial reversal problems in brain-damaged rats. *Physiological Psychology*, 1983, 11, 35-46.
- THOMPSON, R., ARABIE, G. J., & SISK, G. B. Localization of the "incline plane discrimination memory system" in the white rat. *Physiological Psychology*, 1976, 4, 311-324.
- THOMPSON, R., GATES, C. E., & GROSS, S. A. Thalamic regions critical for retention of skilled movements in the rat. *Physiological Psychology*, 1979, 7, 7-21.
- THOMPSON, R., & MYERS, R. E. Brainstem mechanisms underlying visually guided responses in the rhesus monkey. *Journal of Comparative and Physiological Psychology*, 1971, 74, 479-512.
- THOMPSON, R., & SPILLOTIS, P. H. Subcortical lesions and retention of a brightness discrimination in the rat: Appetitive vs. aversive motivation. *Physiological Psychology*, 1981, 9, 63-67.
- ZOLA, S. M., & MAHUT, H. Paradoxical facilitation of object reversal learning after transection of the fornix in monkeys. *Neuropsychologia*, 1973, 11, 217-284.

NOTES

1. Bilateral destruction of the occipital cortex does not appear to retard acquisition of either a tactile discrimination (Finger, Cohen, & Alongi, 1972; Finger & Frommer, 1968; Gabriel, Freer, & Finger, 1979) or an incline plane discrimination (Thompson, 1982a) problem in the rat.
2. The eight structures include the amygdala, ventrobasal thalamus, nucleus posterior thalami, zona incerta, pretectal area, superior colliculus, dorsomedial mesencephalic reticular formation, and cerebellar cortex (Thompson, 1983).
3. The 17 structures include the olfactory bulb, frontal cortex, parietal cortex, anterior cingulate cortex, posterior cingulate cortex, dorsal hippocampus, ventral hippocampus, septofornix, nucleus accumbens septi, rostral caudoputamen, anteromedial hypothalamus, anterolateral hypothalamus, ventromedial hypothalamus, mammillary bodies, anterior thalamus, ventromedial thalamus, and dorsomedial thalamus (Thompson, 1982a, 1982b, 1983, present study).
4. It is conceivable that acquisition of such tasks as passive avoidance, taste aversions, and eyelid conditioning may not be retarded by selective lesions to certain components of the GLS. The finding that conditioning can take place in the spinal rat (see, e.g., Sherman, Hoehler, & Buerger, 1982) indicates that learning of some tasks can proceed in the absence of the entire GLS. These exceptions, however, do not alter the relative importance of the GLS to the extent that it contains 11 brain sites that are potentially more involved in the general learning process than the 26 brain sites that have been excluded from the GLS. The fact that mental retardates can acquire a simple conditioned response as fast as control subjects (Estes, 1970) does not detract from the severity of the otherwise global learning impairment exhibited by the former.
5. The remarkable degree of interconnectivity existing among the original nine components of the GLS has been discussed earlier (Thompson, 1982b). This feature of the GLS is largely retained, despite the inclusion of the posterolateral hypothalamus and mesencephalic central gray. Both of these structures, for example, appear to be connected with the substantia nigra (Arbuthnott, Mitchell, Tulloch, & Wright, 1976; Hopkins & Niessen, 1976) as well as the parafascicular nucleus (Barbaresi, Conti, & Manzoni, 1982; Shiosaka, Tohyama, Takagi, Takahashi, Saitoh, Sakumoto, Nakagawa, & Shimizu, 1980).