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Sparing of Function Following Early Lesions
of Selected Limbic Structures

by

Andy Molino

Thesis presented to the Faculty of
Graduate Studies of Carleton University
in partial fulfillment of the require-
ments for the degree of Doctor of
Philosophy.

DEPARTMENT OF PSYCHOLOGY

CARLETON UNIVERSITY

Ottawa, May 29, 1973.

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The undersigned recommend to the Faculty
of Graduate Studies acceptance of the thesis
"Sparing of Function Following Early Lesions
of Selected Limbic Structures"
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fulfillment of the requirements for the
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Ottawa, May 29, 1973.

ABSTRACT

An attempt was made in this study to determine the extent of functional sparing following infant subcortical lesions. Male Wistar rats received bilateral lesions of the amygdala, septum, posteroventral hippocampus (PH), anterodorsal hippocampus (AH), or frontal neocortex either as infants (at 10 days of age) or as adults (at 60 days of age). Normal and anesthetized control animals were also used. All animals in the infant conditions were weighed once per week from 10 days of age to 63 days of age, and then again at histology. Testing for these animals began at 70 days of age. Animals in the adult conditions were weighed once per week from 10 days to 113 days, and then again at histology. Testing for these animals began at 120 days. The major tasks used were the ability to acquire a two-way active avoidance response (CAR), and a conditioned emotional response (CER). Following the CAR and CER, supplementary measures were taken, involving activity levels in an activity wheel and open-field, and exploration and social interaction measures in the open field. At histology the adrenal, thyroids, and testes of animals which had been tested were removed and weighed, and these weights compared to those of littermates which had received similar lesions but which had not been tested.

Both infant and adult amygdala and septal lesions significantly and permanently retarded normal weight gain. In addition, adult amygdala lesions severely retarded CER and CAR acquisition. Adult

sental lesions had a slight debilitating effect on CER acquisition, and a significant facilitatory effect on CAR acquisition. Adult PH lesions significantly retarded CER acquisition, and had a significant facilitatory effect on CAR acquisition. Adult AH and frontal neocortical lesions had no effect on any of the measures taken in this study. Animals with infant-accrued amygdala lesions showed no snaring for the CER task, but displayed excellent snaring for the CAR. Infant sental-operated animals showed little snaring on either the CER or CAR, performing in a fashion similar to their adult-operated counterparts, while animals with infant-accrued PH lesions showed excellent snaring on both tasks, performing in a fashion similar to the control animals. Infant AH and frontal neocortical lesions had no effect on any of the measures taken in this study. The task-specific snaring effects were explained as being due to some form of structural or functional reorganization which is possible following infant lesions, but not following adult lesions.

Lesion and snaring effects were observed on the activity, exploration, social interaction, and glandular measures, but these effects failed to follow any consistent pattern.

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INTRODUCTION

This study was an attempt to determine the degree of sparing of function following infant lesions of selected limbic structures. The phrases "sparing of function" and "selected limbic structures" implicitly assume that the brain is composed of relatively distinct parts, and that these parts serve different functions. These are concepts which underlie the doctrine of localization of function, a doctrine which has been of central importance since the inception of physiological psychology. Since this doctrine is of such importance, a short history of the controversies surrounding the doctrine should precede a literature review dealing with sparing of function.

Historical Overview¹

The first modern approach to both the nature of functions, or faculties, and their localizations was provided by Franz Joseph Gall (1758-1828), a neuroanatomist and the father of phrenology. The prevailing view among epistemologists before the time of Gall was that the relevant faculties of the brain were understanding, the will, imagination, memory, and so on. Gall rejected this view outright, and regarded the functions of the brain as being functions of biological significance, and as being those which would lead to an adaptation of the organism to its environment. His arguments took psychology out of

1. Information for this historical review has been taken primarily from Young (1970), with additional information also from Boring (1950), Chaplin & Krawiec (1968), and Marx & Hillix (1963).

the realm of philosophy and put it into the realm of general biology. Gall's greatest contribution to psychology was his insistence that understanding the functions of the brain involved two facets: identifying the functions (through naturalistic observation rather than philosophic speculation), and localizing them within the brain.

Generally speaking, Gall's theory of phrenology held that the various behaviours and talents possessed by individuals implied the existence of a faculty or function in the brain to govern each of these behaviours. Each of these faculties, in turn, had as its seat a separate cerebral organ. The degree to which a faculty expressed itself depended on the activity and size of its cerebral organ, which was reflected in the size of the cranial prominence or bump overlying that organ. Unfortunately, Gall misused the scientific method which he strongly advocated, often using anecdotal information to support his theory. His ideas, however, did spur a great deal of research which became the basis of modern psychology.

Technical and methodological improvements towards the end of Gall's life allowed sensory-motor physiologists more direct manipulation of the nervous system (e.g., ablation and electrical stimulation). However, the approach taken by these scientists towards psychology and physiology was influenced by philosophical constraints. The widespread acceptance of Cartesian dualism (i.e., the doctrine which holds that the mind is an unextended, indivisible entity, while the body is extended and divisible), for example, greatly influenced the interpretation of research findings. Three physiologists who were affected in just such

a way were Flourens, Magendie, and Mueller.

In the early 1820's Pierre Flourens took advantage of advances in ablation techniques to study the functions of the brain, primarily as an attempt to disprove the theories of Gall. Flourens proceeded on the assumption that if removal of cerebral tissue resulted in the disappearance of a certain behaviour, then the removed tissue is responsible for that behaviour in the normal animal. Flourens relied exclusively on observation to determine behavioural change, and although this method led to the classical findings of the regulatory functions of the cerebellum in muscular coordination and the localization of the respiratory center in the medulla oblongata, it also led him to reject the doctrine of localization of function. His ablation techniques involved successive slicing of the cortex, ignoring the possible existence of distinct cortical organs. Consequently the ablation typically resulted in defects in all the behaviours he observed, and led him to conclude that the cortex is the organ of the unitary mind, and that its functions are indivisible.

Magendie, a contemporary of Flourens, made his major contribution to psychology by experimentally demonstrating (Bell's anatomical observation) that the anterior spinal roots are motor in function, while the posterior nerve roots are sensory. The importance of this demonstration is that it separated the analysis of the lower nervous structures from the analysis of the brain, releasing the investigation of at least those structures from the classical philosophical constraints. The remainder of the 19th century saw the application of the sensory-motor Bell-Magendie

Law to successively higher regions of the nervous system, culminating in its application to the functioning of the cortex.

Johannes Mueller was another exponent of the experimental method during this period (1820-1850). Mueller also rejected Gall's faculty psychology and the theory of localization of function. He confirmed and extended Magendie's findings, and suggested that the lower sensory-motor centers are the instruments of the mind, although the mind's cortical organ supposedly had no direct connection with them.

Once the Bell-Magendie Law was well established among physiologists it needed a theoretical context to bring it into contact with psychology. This theoretical context was provided by Alexander Bain, who combined the sensory-motor physiology of the Bell-Magendie Law with the principles of association psychology. Association psychologists before the time of Bain (1860) were strictly philosophers. They rejected the classical Cartesian view of a unitary mind and argued that mental substances could be broken down into atomic units. Complex mental processes were supposedly built up from sensations by habit or repetition. Bain rejected the faculty psychology of phrenology and extended the sensory-motor paradigm to subcortical structures so that the thalamus was considered the highest sensory center and the corpus striatum the highest motor center.

Herbert Spencer, another associationist and contemporary of Bain's, extended the work of Bain and provided psychology with a new foundation in evolutionary biology. Spencer had been a keen student of phrenology, but was influenced by the association psychologists.

One important idea which he retained from phrenology, however, was the view that the mind is an instrument of adaptation. He regarded learning as being a continuous adjustment of the internal integration of the mind to the external integration of the environment. Experiences, he believed, resulted in ideas which are continuously superimposed upon each other, modifying the nervous system. These modifications can then be transmitted through heredity. In connection with this theory Spencer argued that comparative and developmental studies rather than philosophical and introspective analysis would better serve to help understand the functions of the brain. Another major contribution made by Spencer was that he reintroduced the concept of localization of function, which by this time had been severely criticized and had fallen into disrepute. Unlike Gall, however, Spencer showed a great amount of foresight in opposing attempts to demarcate specific organs in the brain and then assigning functions to these organs.

Hughlings Jackson was greatly influenced by Spencer, and he applied Spencer's theory of evolution to his own theory of the structure and function of the nervous system. Jackson extended the Bell-Magendie Law to the cortex and combined it with Spencer's theory of localization of function. In place of Gall's faculties localized in specific organs, Jackson saw cortical areas acting as centers for coordinating complex sensory-motor processes. Jackson, however, still influenced by the constraints of Cartesian dualism, was led to propose a doctrine of psychophysical parallelism. According to this doctrine the functions of the nervous system were strictly sensory-motor, but its physiological processes were paralleled by ideas of sensation and movement.

Two major discoveries occurred within Jackson's lifetime which had a profound effect on the position of psychologists with regard to the localization of brain function. In 1861 Paul Broca, through a series of post-mortem examinations, established that the faculty of speech was localized in the third frontal convolution. In 1870 two German physicians, Gustav Fritsch and Eduard Hitzig, demonstrated the electrical excitability of the cortex. They showed that electrical stimulation of discrete cortical regions could produce combined muscular contractions, and were able to map five motor areas in the dog brain using this technique. Although these results tended to support localization of function, their support of Cartesian dualism influenced their interpretation of these results. Fritsch and Hitzig claimed that their findings left room for nonmotor cortical areas which could serve as the organ of the mind, or of psychological functions. These functions, they felt, could also eventually be localized.

With the findings of Fritsch and Hitzig, and subsequent replications by various researchers, the doctrine of localization of function soon became widely accepted, and the search for cortical centers became the focal point of psychological research. Further improvements in stimulation and ablation techniques led to several classical findings, as the centers for vision, hearing, touch, etc., were more or less determined. At the center of these developments was a physician named David Ferrier, who started publishing his experiments in 1873. He verified and extended the work of Fritsch and Hitzig, mapping out 15 cortical motor areas and specifying cortical areas of the five senses.

His extensive work in the area of sensory-motor localization led him to conclude that mental operations were merely the subjective side of sensory-motor processes. All of behaviour, therefore, was explained in terms of sensation and motion. This represented the final extension of the Bell-Magendie Law, which became an all-embracing explanation in both physiology and psychology.

Unfortunately, despite the advances in the physical sciences after Gall, no one thought of providing a psychophysiological explanation to account for how an animal adapts to its environment. In rejecting Gall's phrenology, the scientists and philosophers of the 19th century also rejected his goals: to relate the striking characteristics and behaviours of men and animals to the functions of the brain, and to determine the biological and adaptive significance of these functions. No one thought of determining what the sensory-motor elements should be required to explain.

Another major stumbling block for researchers of the 19th century was the lack of a suitable technique for experimentally evaluating the effects of treatments such as ablations. The dawn of the 20th century, however, saw this difficulty overcome to a large extent by advances in experimental animal psychology. With the publication of Thorndike's dissertation in 1898 came the development of new methods for testing animal learning and sensory discrimination. By 1902 Shepherd I. Franz had already started applying these techniques to the study of the functions of the frontal lobes, and it was not long before he started expressing serious doubts about the validity of a doctrine which subscribed to a

strict localization of sensory and motor cortical regions. Learning, memory, intelligence, and "mental processes" soon replaced simple sensory and motor functions as the focal points of psychophysiological research.

The strategy of applying methods for testing animal learning and sensory discrimination to the study of the brain was passed on by Franz to his student, Karl S. Lashley. Although Lashley started his career as a staunch behaviourist, studying with J.B. Watson, he had the opportunity to work with Franz and, by 1917, had adapted Franz's methods for studying localization of brain functions. Lashley's research is generally considered as having been conducted to demonstrate that there is no localization of function, and that the effects of cortical lesions on learning are directly proportional to the size of the lesions. The results of his research led Lashley to formulate the theories of equipotentiality and mass action. The theory of equipotentiality stated that "one part of the cortex is essentially equal to another with respect to the contribution to tasks like maze learning"; while the theory of mass action stated that "the efficiency of learning depends upon the total mass of cortex left functioning" (both quotations taken from Marx & Hillix, 1963, p. 153). Unfortunately, in choosing the maze to test for learning and retention, Lashley committed an error very similar to that made by Flourens, who indiscriminately sliced successive layers off the cortex. Maze-learning taps a variety of modalities and neural mechanisms, and it would be expected that the larger the lesion the larger the number of neural mechanisms disrupted, and the larger the deficit obtained. It should be noted, however, that

Lashley himself stressed the existence of some form of localization of function; what he denied was that localization should explain all of behaviour.

The question of localization of function is far from being resolved. Whether or not localization does exist seems to depend on what one means by "function". If one is searching for specific sensory-motor areas, or areas of the brain which subserve biologically adaptive processes, then localization does seem to exist to a certain extent (e.g., the respiratory center can be localized in the medulla oblongata; the center for articulate speech in man can be localized in the third convolution of the frontal lobe of the left hemisphere). However, if one is searching for the neural processes which subserve learning and memory, then it would be inaccurate to speak of such functions as being localized in specific areas of the brain. At present it appears that the electrophysiological and/or chemical changes which take place during learning are not centered in any specific region of the brain, but are probably the functional attribute of several (if not all) areas of the brain. Ablation (and stimulation) techniques have revealed that certain areas of the brain appear to play a dominant role in learning, retention, and recall in specific situations, and other areas of the brain playing a dominant role in other situations. Removal of the occipital cortex, for example, has been shown to produce memory deficits for simple brightness discriminations without affecting acquisition of those discriminations, in both cats (Smith, 1937) and monkeys (Kluver, 1936). Also, deficits in memory for roughness discriminations have been reported

for rats following ablation of the somesthetic cortex (Zubeck, 1951); relearning the discriminations by the same animals took approximately the same number of trials as the original preoperative acquisition. Furthermore, subcortical areas have been shown to be directly involved in certain types of learning, retention, and recall. Hippocampal lesions, for example, appear to affect acquisition in situations that require short-term memory (e.g., Kimble 1963 reported deficits in the acquisition of successive but not simultaneous discriminations following hippocampal lesions in rats).

Lashley's experimental results, and his theories, had a germinal effect on psychophysiological investigations of functional localization and, it was out of such investigations that evolved the first studies concerned with recovery and sparing of function. Researchers using the ablation technique to determine cortical localization (e.g., Kennard, 1936) found that, if their animals were tested repeatedly over a period of time, they often recovered from the adverse effects of the ablations. Consequently, recovery and sparing of function soon became a topic of interest for its own sake.

Since studies of functional recovery stemmed directly from investigations of localization of function, most of the studies which have been conducted in the area of recovery of function have dealt with cortical rather than subcortical damage. The following subsection, then, is a review of the relevant research which has been conducted over the last 40 years to investigate recovery and sparing of function following early cortical damage.

It is perhaps necessary at this point, however, to differentiate and define what is meant by the term "sparing of function" and "recovery of function". Lesions incurred in infancy do not always have the same effect as lesions incurred in adulthood. Whether one refers to this phenomenon as sparing or recovery of function depends in large part on the manner in which one views the question. If one is interested in whether or not a particular function has been spared in an adult animal operated on in infancy, and not in how or why the function was spared, then the phenomenon could be referred to as sparing of function. However, if one is interested in how or why that phenomenon was spared (i.e., was it due to some form of reorganization or regrowth), or attempts to determine whether the function was affected immediately postoperative, then the phenomenon could be referred to as recovery of function. The present author has chosen to use the term sparing of function since the animals in this study were only tested in adulthood, after a prolonged period of rest following infant surgery; no attempt was made to determine whether any behavioural deficits were present immediately postoperative.

The meaning of the term "function" in the present context should also be elucidated. When working with ablation techniques we can only make limited inferences about the manner in which the brain, or some particular area of the brain, works. For example, if destruction of a particular area of the brain results in the disappearance of a certain faculty of which a normal animal is capable (e.g., it stops eating, or drinking, or is unable to acquire a conditioned emotional response), then one may be able to make some inferences about the function of the

damaged portion of the brain in the normal animal. Different inferences could be made if the brain damage results in the appearance of some unusual behaviours (e.g., overeating, hyperactivity). These inferences can then lead to more detailed investigations using a greater variety of techniques (e.g., chemical, electrophysiological, or anatomical investigations).

Early Cortical Lesions

Beach (1938) reported that female rats which had received various cortical lesions as infants were superior at executing complex maternal behaviour patterns when compared with animals which had received similar lesions as adults. Furthermore, the extent to which the infant-operates were superior was found to be a function of the amount of cortical tissue destroyed and age at the time of surgery. Similarly, Kennard (1936, 1938, 1940, 1942, 1944) demonstrated that the extent of recovery of sensory-motor coordination following various ablations of motor, premotor, and parietal areas in monkeys is a decreasing function of age at the time of operation.

A similar age-loss relationship following neonatal cortical lesions was demonstrated by Tsang (1937, a, b). Rats, hemidecorticated in infancy, were tested as adults on a maze-learning task. His results indicated that, although these rats showed retarded maze-learning when compared to normals, their performance was still significantly superior to that of rats operated as adults. Tsang concluded that cortical lesions suffered in infancy are much less detrimental than similar

lesions suffered at an adult age. He suggested that the infant brain, unlike the adult brain, has a high degree of functional plasticity, and can affect good integration with a minimum of brain tissue. He claimed that, due to the high functional plasticity of the infant brain tissue, a prompt readjustment of functional patterns can easily be achieved, while this is not possible with adult animals because of their functional rigidity. He did not, however, explain how this functional reorganization can take place in the infant brain.

Schwartz (1964) subjected one-day old rat pups to posterior cortical ablations or sham operations, and raised them in environments that afforded either maximum or minimum opportunity for perceptual and motor experience. When testing the animals as adults on a Hebb-Williams maze, he found that the neonatal lesions resulted in a learning deficit if the infants had been reared in a deprived environment. The deleterious effects of the neonatal lesions, however, were significantly offset by the enriched early environment. Landsell (1953) conducted a similar study in which rats reared in a complex environment were subjected to either early or late anterior, posterior, or total unilateral cortical lesions. These animals were also tested in an apparatus which was very similar to a Hebb-Williams maze. Anterior cortical lesions were found to have no effect on either infant- or adult- operates, while posterior cortical lesions had the most profound effect on both groups. Infant-operates with posterior cortical lesions, however, still performed significantly better than adult-operates with similar lesions.

Sharlock, Tucker, and Strominger (1963) showed that cats which

had received large bilateral ablations of the auditory cortex between the seventh and 10th day after birth were able to acquire auditory discriminations which could not be acquired by cats which had sustained similar brain damage at maturity. Similar sparing of function has also been reported for roughness discrimination following lesions of the somesthetic cortex in cats (Benjamin & Thompson, 1959), for pattern discrimination following removal of the visual neocortex in cats (Doty, 1961; Wetzel, Thompson, Horel, & Meyer, 1965) and rats (Tsang, 1937, b), and for object discrimination following combined lesions of the frontal and posterior association cortex in monkeys (Kling & Tucker, 1968).

Harlow, Blumquist, Thompson, Schiltz, & Harlow (1968) found that the deficits suffered by rhesus monkeys in their ability to perform delayed-responses increased as a function of increases in age at the time they were subjected to bilateral frontal lobe lesions. The authors suggested that the increase in age is paralleled by an increase in the ability of these animals to perform delayed-responses, and that the more advanced this ability is at the time of surgery, the greater the deficits incurred by the animals. The results of their study showed that animals lobectomized at five days of age performed short delays without sign of deficit. Animals lobectomized at five months, when the ability is present to some extent, were slightly, but not significantly inferior to controls. Animals lobectomized at 18 or 24 months, when the ability is approaching an optimal level, both performed in an identical manner - significantly below the normal animals.

Bauer and Hughes (1970) conducted a series of studies investigating

the nature of visual and non-visual behavioural changes resulting from removal of visual neocortex in neonatal and adult rats. Their results indicated that removal of cortical visual areas in mature rats interferes with visual and non-visual behaviours in a wide range of situations, whereas neonatal lesions allow sparing of visual capacity. Early striate lesions, for example, did not abolish depth perception, as measured on a visual cliff, while adult striate lesions did. However, Bauer and Hughes found that, in rats, visual pattern discrimination was not spared, whereas such sparing has been reported following similar neonatal lesions in cats (Wetzel et al., 1965).

Some additional evidence contradictory to sparing of function following early cortical lesions was provided by Thompson (1966). Unlike most studies in the area of functional sparing, this particular study tested the performance of neocortically-ablated and normal kittens on a three-choice delayed-response task shortly after the ablations had been produced in the experimental animals, without waiting for any of the kittens to reach adulthood. The performance of these kittens was then compared to that of neocortically-ablated and normal adult cats on the same task. The ablations were all in the area of the orbitofrontal cortex. Results showed that the rate of learning of the infant-ablation group was the same as that of the adult-ablation group. Rate of learning for the infant-normal group was the same as that of the adult-normal group. Furthermore, rate of learning of the two operated groups was significantly inferior to that of the two normal groups. This is one study which could have determined whether functional recovery would

take place by testing the animals repeatedly as they became progressively older. Unfortunately, Thompson failed to do so. Consequently, the only inference which can be made from this study is that the role of the orbitofrontal cortex on a delayed-response task is not spared following infant destruction of that area in cats. Whether or not that function can be recovered or compensated for at a later age cannot be inferred from their results. Therefore, although the results of this particular study contradict the findings of previous studies with respect to sparing of function following early cortical lesions, they do not necessarily eliminate the possibility of functional recovery.

Task complexity, a variable which most authors have chosen to ignore, is probably one of the most important factors to consider when evaluating recovery or sparing of function. Several studies with infant monkeys, for example, have shown that the degree of functional sparing following neonatal brain injury may be related to task difficulty as well as age at time of lesion. On the one hand, for example, Akert, Orth, Harlow, and Schiltz (1960) and Harlow, Akert, and Schiltz (1964) observed excellent recovery on a delayed-response task following lesions of the frontal association cortex at five days or five months of age. Similar lesions, however, affected moderate to severe losses if inflicted at one or two years of age, respectively. Tucker and Kling (1967), on the other hand, performed bilateral ablations of the frontal association cortex on infant monkeys prior to the 35th postnatal day, and on adult monkeys three years of age. The animals were later tested on a colour-discrimination, and delayed-response and delayed-alternation tasks.

Both groups learned the colour-discrimination with equal facility, and both groups were equally impaired in delayed-alternation performance. The performance of the early-frontal group, however, was superior to that of the adult-frontal group on the delayed-response tests. Furthermore, these differences in delayed-response performance between the two frontal groups were not due to differences in size or locus of surface lesions, or retrograde thalamic degeneration. The authors concluded that the sparing of the delayed-response capacity in the early-frontal animals might be due to cerebral maturation or a compensatory neural regeneration. These findings were replicated by Kling and Tucker (1968) who found, in addition, that combined lesions of frontal association cortex and posterior association cortex in the neonatal monkey also resulted in sparing of delayed-response performance as well as object discrimination. Adult-operates were severely impaired on both tasks. However, combined lesions of frontal association cortex and caudate nucleus resulted in failure on the delayed-response task in both infant- and adult-operates.

Raisler and Harlow (1965) also failed to find any deficit in delayed-response performance in three groups of adult monkeys which had received bilateral lesions of the posterior association cortex as infants. The lesions had been produced in the groups at 130, 370, and 900 days of age, respectively. The study did, however, report consistent deviations from normal patterned-strings performance and a deficit in object-quality discrimination learning in the 900-day group. The authors suggested that their results support the hypothesis that sparing

of function following ablation of the posterior association cortex is related to task complexity as well as age at time of operation.

Lenneberg (1968), in a literature review, reported that a similar pattern of sparing of function followed early cortical lesions in humans. He hypothesized that, although cells and tissues are differentiated at a certain time, they may not reach their final form and function until a short time thereafter. A lesion suffered before this final stage may, in some cases, be compensated for by internal readjustments or compensatory growth, because not all structures reach this final stage of differentiation at the same time. However, once the final stage of differentiation has been achieved, compensation is no longer possible. An abnormality in one part of the brain can thus be compensated for by other parts to a degree that depends on their stage of differentiation. Borrowing the term from embryology, Lenneberg referred to the final stage of differentiation as the process of "determination". He cited, as an example, the fact that determination with respect to language takes place in the second decade. Lesions suffered (in the appropriate cortical area) before this time usually spare that particular function, while later lesions frequently leave permanent deficits.

Goldman and her associates (Goldman, Rosvold, & Mishkin, 1970, a, b) presented evidence suggesting that the role of the orbitofrontal cortex in delayed-response performance, unlike the role of the frontal association cortex, is not spared following removal of those two regions in infant monkeys two months old. Lesions restricted to the frontal

association cortex failed to produce deficits on delayed-response performance similar to the deficits observed following identical lesions in adult monkeys. Such deficits were observed, however, when the early lesions included removal of the orbitofrontal cortex. These results were interpreted as suggesting that the orbitofrontal and frontal association cortical regions belong to different neuro-behavioral systems which develop ontogenetically at different rates.

That sparing of function is possible following early cortical lesions is corroborated by existing anatomical and neurochemical data. Bogolepov and Popova (1967) investigated the cytoarchitecture and neuronal structure of the cerebral cortex of adult rats and rats two, seven, 14, and 21 days of age, using both light and electron microscopy. They found the cytoarchitecture and neuronal structure of the two-day old rats to be poorly differentiated. The microscopic constituents of cytoplasm and nucleus were incomplete and the interneuronal connections were so poorly developed that synapses were seldom observed in the newborn rat. Not until the second week after birth, when the cerebral cortex had acquired the features of the adult animal with respect to its cytoarchitecture and neuronal structure, did any significant increase occur in the number of synapses and in the intricacy of the synaptic structures themselves. Similarly, Jacobson (1963) reported that myelin formation appears first in the spinal cord and then progresses to the brainstem, diencephalon, and finally to the telencephalon. Robinson (1967, 1968) found that increases in the neurotransmitter levels and their metabolizing enzymes followed a similar pattern of

development.

In general, then, the results of studies concerned with recovery and sparing of function following early cortical lesions are relatively consistent and well documented. The general trend appears to be that the effects of early cortical damage are not as debilitating as the effects of similar damage accrued in adulthood, except when relatively difficult tasks are used to evaluate these effects. There are, of course, findings which contradict this general trend. Thompson (1966), for example, was cited, and it was suggested that the reason his findings were different was that he tested for immediate sparing following neonatal lesions, but failed to test for eventual recovery.

The above discussion has thusfar concerned itself primarily with the cortex, and with the role of various cortical areas in certain learning and behavioural situations. The present study, however, was concerned with sparing of function following early (i.e., early in life; in infancy) subcortical lesions, and, more specifically, early lesions to areas of the limbic system, which is briefly described in the following subsection.

The Limbic System

In 1937 James W. Papez suggested that a set of interconnected cortical and subcortical structures surrounding the diencephalon were responsible for the initiation of emotional behaviour. This set of structures, which eventually came to be known as the limbic system, had, for more than a century before the time of Papez, been considered to be involved almost exclusively with olfaction. Papez' theory initially

failed to attract a great deal of experimental attention. Following the second World War, however, the theoretical implications of the theory were revived and extended by Paul D. MacLean (1949). Since that time, a legion of experimenters have studied the limbic system, attempting to delimit the various limbic structures, their interconnections, and the role they play in learning, attention and motivation.

Exactly which structures should be included when discussing the limbic system is still a topic of debate. Generally, the system is thought to consist of two basic divisions, cortical and subcortical. The cortical regions which are typically included are the cingulate gyrus, the hippocampal gyrus, and the pyriform lobe. The subcortical regions which are typically included are the fornix, hippocampus, septum, amygdala, and the mamillary bodies. Some authorities, however, would also include the hypothalamic nuclei, the nonspecific nuclei of the thalamus, the olfactory bulbs, and the temporal lobe as part of the limbic system.

In the nearly three decades which have followed MacLean's reformulation of Papez' theory of emotions, the vast number of studies which have dealt with limbic centers have been plagued with the problem of interpreting the nature of emotional behaviours in animals. Experimenters have, therefore, developed learning methods which can yield more objective indices of animal emotionality. Such techniques, for example, employ an emotional state as a drive to stimulate a learned escape or avoidance response. The assumption on which such techniques are based is that if an animal escapes or avoids, then it is experiencing

fear or anxiety, and the act of escaping or avoiding is an objective index of emotion. Such an assumption is certainly an oversimplification of the situation. Researchers have, for example, believed that limbic centers play an important role in actual learning acquisition and retention ever since Penfield and Milner (1958) suggested that hippocampal mechanisms are responsible for the initial storage of memory traces. Therefore, research on the limbic system has, since then, concerned itself not only with emotion, but also with learning, attention, and motivation.

The following subsection is a brief review of studies which have dealt with limbic lesions. The review is limited to those studies which have concerned themselves with those limbic areas known as the amygdala, septum or hippocampus, since it is with these areas that the present investigation was primarily concerned.

Limbic Lesions

The presence of an intact amygdala, septum, and hippocampus has been found necessary for the acquisition or retention of several fear-motivated tasks. Retarded acquisition and retention of a conditioned emotional response (CER), for example, have been reported in the rat following bilateral lesions of the amygdala (Kellicut & Schwartzbaum, 1963; McIntyre & Molino, 1972; Suboski, Marquis, Black, & Platenius, 1970), septum (Brady & Nauta, 1953, 1955; Harvey, Jacobson, & Hunt, 1961; Harvey, Lints, & Jacobson, 1965; Trafton, 1967), and hippocampus (Brady, 1958; Brady & Hunt, 1955; Nadel, 1968), and following stimulation of the amygdala (Goddard, 1964, b; Lidsky & Slotnick, 1970), septum

(Brady & Conrad, 1960), and hippocampus (Shinkman & Kaufman, 1972).

Amygdala lesions have also generally been reported to cause active avoidance (CAR) deficits in cats (Brady, Schreiner, Geller, & Kling, 1954; Horvath, 1963; Kling, Orback, Schwartz, & Towne, 1960) and rats (DiCara, 1966; King, 1958; McNew & Thompson, 1966; Robinson, 1963; Suboski et al., 1970; Weiskrantz, 1956). Septal lesions, on the other hand have usually been shown to result in facilitated two-way active avoidance acquisition (Donovick, 1968; Fox, Kimble, & Lickey, 1964; Garber & Simons, 1968; Green, Beatty, & Schwartzbaum, 1967; Green & Schwartz, 1968; Hamilton, 1970; Kenyon & Kriekhaus, 1965; King 1958; Kriekhaus, Simmons, Thomas, & Kenyon, 1964; Meyer, Johnson, & Vaughn, 1970; Schwartzbaum, Green, Beatty, & Thompson, 1967; Sodetz, 1970; Trafton, 1967; Usher & Lambie, 1969; Van Hoeson, MacDougall, Mitchell, 1969; Zucker, 1965). Active avoidance acquisition following hippocampal lesions has been found to be both facilitated (Antelman & Brown, 1972; Blanchard & Fial, 1970; Douglas & Moore, 1961; Green et al., 1967; Isaacson, Douglas, & Moore, 1961; Nadel, 1968) and retarded (Cosino & Lash, 1969; Kimura, 1958; Liss, 1968; McNew & Thompson, 1966; Nadel, 1968).

Several theories have been forwarded in an attempt to explain these findings. Some authors, in attempting to explain the functions of the amygdala, have suggested that an intact amygdala is required for normal emotional responsiveness (Kluver & Bucy, 1938; Plotnick, 1968; Robinson, 1963; White, 1971). Those deficits which are observed in amygdalectomized animals, they explain, can be attributed to a reduction

in emotional responsiveness. According to this hypothesis, amygdalectomized animals are poor at learning fear-motivated responses because they are not afraid, or at least less afraid than normal animals. Findings from research which has thusfar specifically examined the emotional responsiveness of amygdalectomized animals have been relatively inconsistent. On the one hand, amygdalectomized dogs (Fuller, Rosvold, & Pribram 1957) and monkeys (Rosvold, Mirsky, & Pribram, 1954; Thompson, Schwartzbaum, & Harlow, 1968) have been shown to be capable of emitting normal or accentuated fear responses in social situations. On the other hand, some authors have reported amygdalectomized animals to show increased rage threshold (Schreiner & Kling, 1953; Shealy & Peele, 1957) and decreased CER (Brady et al., 1954), and aggressiveness in wild rats (Galef, 1970).

A second theory of amygdala function views the amygdala as aiding in the formation of the association of a neutral stimulus to a noxious event (Egger, 1972; Gloor, 1972; Goddard, 1964, a; Pelligrino, 1968; Weiskrantz, 1956). According to this theory, an amygdalectomized animal is incapable of forming the appropriate associations between a conditioned stimulus (CS) and an unconditioned stimulus (UCS). Failure to form this association then results in a failure on the part of the amygdalectomized animal to alter its behaviour according to the demands of the environmental contingencies. Gloor (1972) has suggested that the amygdala aids in the establishment of this associations by acting as a link between the information stored in the neocortex and the basic drive mechanisms centered in the hypothalamus. Destruction of the

amygdala, then, eliminates this vital link, making it difficult or impossible for the association to be formed.

Although several hypotheses have been forwarded to explain septal function, two of them appear to be most widely accepted. The first theory suggests that the septum exerts an inhibitory influence on learned responses, and that removal of this inhibitory influence through septal destruction releases those behaviours which are highest in habit strength for a particular situation (Douglas, 1966; Gerbrandt, 1965; Hamilton, 1970; Kaada, Rasmussen, & Kvein, 1962; McCleary, 1961, 1966; Schwartzbaum et al., 1964). Removal of that inhibitory septal influence, then, makes it difficult for an animal to suppress a response which is high in habit strength, so as to be able to acquire new responses. If the situation happens to call for only the response which is highest in habit strength, then a septal animal will perform better than a normal one.

The second widely accepted theory of septal function hypothesizes that the septum serves to dampen the increment in response strength normally caused by a reinforcement, thus allowing a normal animal to acquire new responses (Fried, 1969, 1970; Zucker, 1965; Zucker & McCleary, 1964). A given reinforcement, then, would produce a greater increment in response strength in animals with septal lesions, allowing these animals to overrespond to motivating (noxious or appetitive) stimuli, while impairing their ability to suppress previously reinforced responses.

Several theories of hippocampal function have suggested that

the hippocampus plays a major role in the control of attentional processes through the inhibitory modulation of sensory input (Douglas, 1967; Douglas & Pribram, 1966; Isaacson, 1966; Kimble, 1968). According to Jarrad (1973), this is accomplished by the inhibitory action of the hippocampus on lower structures which serve to control arousal and activation levels which affect the manner in which an animal reacts to the environment. According to this theory, when an animal is placed in a learning situation the hippocampus inhibits the animal's attention to, or reception of, the stimulus which normally initiates a response, especially when that response is no longer appropriate. According to Kimble (1968) the purpose of this inhibitory hippocampal action is to allow an animal to decouple its attention to new or more important stimuli. Therefore, if the environmental contingencies are rearranged, or if a more important stimulus is introduced, an animal with hippocampal damage is unable to focus its attention on it. If the situation happens to be one in which an animal is required to focus its attention on only one stimulus, then the animal with hippocampal damage can focus a greater amount of its attention on it than a normal animal.

The theories which have just been discussed are by no means the only ones which have been forwarded to explain the functions of the amygdala, septum, and hippocampus. Nor are these theories without serious flaws. However, the primary purpose of the present study was not to investigate the range of functions of these limbic areas, but rather to determine the degree of functional sparing which occurs following early destruction of the regions. These hypotheses have been

presented because they appear, at present, to best explain the functions of the areas in question. Furthermore, the brief literature review of limbic lesions concerned itself with only two learning situations: the CER and the CAR. Again, this was done because these were the two major tasks which were used in the present study. These tasks were chosen because of the relative abundance and consistency of experimental data concerned with the effects of limbic lesions in these two situations. Destruction of the amygdala, septum, and hippocampus has produced a variety of effects in non-learning situations, some of which will be briefly discussed in the following paragraphs. These effects were also investigated as supplementary measures in the present study.

Adult limbic lesions have, for example, also been found to alter activity and exploration levels, social interaction, and endocrine regulation. Activity levels have been shown to be enhanced in a variety of situations (e.g., activity wheel, activity cage, open field) following bilateral lesions of the amygdala (Allikments & Lapin, 1967; Anderson, 1967; 1970; Corman, Meyer, & Meyer, 1967; Schreinger & Kling, 1953; Schwartzbaum & Gay, 1966), and the hippocampus (Blanchard, Blanchard, & Fial, 1970; Douglas & Isaacson, 1964; Green et al., 1967; Kimble, 1963; Leaton, 1965; Means, 1971; Roberts, Dember, & Brodwick, 1962; Sengstake, 1968; Teitlebaum & Milner, 1963). Inconsistent findings, however, have been reported following septal lesions. Some authors, for example, have reported that septal lesions resulted in hypoactivity in situations not conducive to exploratory behaviour, such as small enclosures (Zucker, 1965), home cages (Thomas, Moore, Harvey, & Hunt, 1959), and running

wheels (Anderson, 1970; Douglas & Raphelson, 1966; Kaada & Bruiland, 1960). On the other hand, animals with septal lesions have been reported to be hyperactive in situations which facilitate exploratory behaviour, such as mazes (Nielson, McIver, & Boswell, 1965), and in two-way shuttle box avoidance tasks (Dalby, 1970; Donovanick, 1968; Green et al., 1967; Schwartzbaum et al., 1967) when the activity was measured during the intertrial intervals. The activity data derived from open-field tests for animals with septal lesions are inconsistent, with authors reporting both decreased activity (Schwartzbaum & Gay, 1966; Corman et al., 1967) and increased activity (Donovick & Wakeman, 1969). Increased exploratory activity in rats has also been reported following bilateral septal lesions (Douglas & Raphelson, 1966) and hippocampal lesions (Leaton, 1965; Nadel, 1968; Roberts et al., 1962; Sengstake, 1968).

Rats have been found to display a great deal of social cohesiveness. Latané and his associates (Echman, Meltzer, & Latané, 1969; Latané, 1969) found that rats placed in pairs in an open-field were highly gregarious, staying much closer together than expected by chance. To make certain that his results were valid, Latané (1969) compared the attractive power of an empty cage, a caged rat, and a freely moving partner. Again, rats tested together showed a high degree of gregariousness. Social cohesiveness in rats has also been demonstrated by Jonason and Enloe (1971), who tested their animals both before and after producing bilateral amygdala or septal lesions. Results showed that amygdala lesions decreased social cohesiveness, while septal lesions had the opposite effect. These results have been verified by

other studies investigating the effects of bilateral septal lesions in rats (Bunnell, Fleshner, & Fleshner, 1966; Bunnell & Smith, 1966) and bilateral amygdala lesions in rats (Bunnell, 1966; Green & Kling, 1960), cats (Green & Kling, 1960), dogs (Fonberg, 1969), and monkeys (Fuller, et al., 1957; Green & Kling, 1960; Plotnick, 1967, 1968; Rosvold, 1954; Weiskrantz, 1956).

Finally, it has been suggested that the limbic system plays an important role in endocrine regulation via the hypothalamic-anterior pituitary system (see Seggi, 1971). Although the exact nature of this relationship is not entirely clear, direct and indirect hypothalamic afferents have been shown to exit from the amygdala (Cowan, Guillery, & Powell, 1964;), septum (Raisman, 1966), and hippocampus (Feldman, 1962; Jacobson, 1968; Nauta, 1956; Raisman, Cowan, & Powell, 1966). Furthermore, bilateral septal lesions have also been shown to result in adrenal hypertrophy (Bohus, 1961; Endroczi & Lissak, 1960; Montgomery & Berkut, 1969; Seggie, 1968; Usher, Kasper, & Birmingham, 1967), and in the interruption of normal thyroid functioning (Usher, Kasper, & Birmingham, 1967). Similarly, bilateral amygdala lesions have been shown to result in adrenal hypertrophy (Greer & Yamada, 1960; Kling et al., 1960; Koikegami, Fuse, Hiroki, Kazami, & Kageyama, 1958; Koikegami, Fuse, Yokoyama, Watanabe, & Watanabe, 1955; Martin, Endroczi & Bata, 1958), and testicular atrophy (Greer & Yamada, 1960; Kling et al., 1960). In addition, Levine and Mullins (1966) have proposed that the presence of certain hormones (sex, thyroid, adrenal) at certain critical stages of development exert a direct and permanent effect on

the nervous system and subsequent psychophysical processes, and that disruption of the hormonal balance of the newborn animal will have a profound effect on both the nervous system and these psychophysical processes.

As was previously mentioned, the present study investigated sparing of function following early limbic lesions. The number of studies which have been conducted in this particular area of concentration is relatively small. The study of recovery and sparing of function following early subcortical damage evolved as an extension of the study of recovery and sparing of function following early cortical damage, and from the study of the effects of subcortical damage in adult animals. The following subsection, then, will briefly review those studies which have already examined recovery or sparing of function following early subcortical damage.

Early Subcortical Lesions

Kling and his associates (Green & Kling, 1961; Kling, 1962, 1966, 1966; Kling & Green, 1967) found that amygdala lesions in the infant cat, rat, and monkey did not result in changes in affective, sexual, or oral behaviour commonly seen after similar lesions in adults of these species. These studies, however, were concerned primarily with comparing the short-term effects of early amygdala lesions with the short-term effects of amygdala lesions produced in adult animals. In most cases their infant-operated animals were sacrificed before reaching maturity and consequently the long-term effects of the lesions were not investigated. In those animals which were not sacrificed before reaching puberty, some aspects of the amygdectomy syndrome (Kluver & Bucy, 1938;

Weiskrantz, 1956), such as changes in affective, sexual, or oral behaviour, became prominent at puberty. Hence, although these studies demonstrate a lack of immediate effect following neonatally-sustained amygdala lesions it is believed by the authors that their results suggest that the behaviour exhibited by animals with such lesions is largely dependent on the maturational level of the undamaged tissue. One consistent effect which Kling and his associates reported was precocious ovarian stimulation following neonatal lesions in female cats. The same effect was also observed in rats by Elwers and Critchlow (1960) who found that amygdala lesions produced in 18- to 20-day-old rat pups also resulted in precocious ovarian stimulation.

For the most part, however, the results of other studies which have dealt with early amygdala lesions fail to corroborate those of Kling and his associates. Thompson, et al. (1969), for example, subjected infant rhesus monkeys to bilateral amygdala lesions and compared them in group and individual situations with sham operated controls. A certain amount of sparing did take place, in the sense that animals with amygdala lesions did not display behaviour patterns which are typically observed in animals which had received similar lesions as adults (i.e., changes in affective, sexual, and oral behaviour). However, significant differences in the expression of fear responses did develop during the year following surgery, with the amygdalectomized animals generally appearing less disturbed by novel stimuli than control animals. Furthermore, as the monkeys grew older, the amygdalectomized animals made more and more fear responses in group situations than

control animals.

Green (1970) studied the effects of infant lesions of the ventromedial nucleus of the hypothalamus (VMH) on activity level. Infant-lesion animals observed before puberty showed no changes in activity level, while adult-lesion animals were hypoactive. However, if the infant-lesion animals were observed after puberty, they, too, displayed the effect. In addition Frohman and Bernardis (1968) found VMH lesions in weanling rats resulted in a decrease in linear growth accompanied by less pronounced changes in body weight. Although there was no significant increase in food intake, there was an increase in body fat, an effect similar to that observed following VMH lesions in adult animals (Teitlebaum & Epstein, 1962). Furthermore, hyperinsulinemia, another effect observed following adult VMH lesions (Hales & Kenedy, 1964) was also observed in the infant-operates of Frohman and Bernardis.

Kling and Tucker (1968) observed sparing of function in infant-operated monkeys following frontal and/or posterior cortical lesions. However, if the early frontal lesions were combined with early caudate lesions (Kling & Tucker, 1967), both infant and adult monkeys were seriously retarded on a delayed-response task. Moreover, the infant frontal-caudate animals failed to thrive and displayed growth and somatomotor deficiencies, as well as hyperactivity and postoperative seizures. The authors concluded that early reflexive, biologically adaptive responses are mediated largely by subcortical mechanisms, with some degree of cortical representation. They also suggested that their results support a centrencephalic theory of cerebral organization, and

that the nature of the connections between cortical and subcortical areas is such as to allow subcortical areas to compensate for cortical damage, while not allowing the reverse to occur.

Hicks and D'Amato (1970) hemispherectomized infant rats within 12 to 28 hours after birth, and adult rats six and one-half to 10 weeks of age. The animals were then tested daily, starting the day following surgery, for the first several weeks following surgery, and then less often during the subsequent months. Removal of half of the forebrain and diencephalon resulted in the loss of tactile placing opposite the ablation in both infant- and adult-operates. Also lost to both groups were the ability to discriminate visual patterns, and to visually gauge variable jumping distances. However, loss of the tactile placing in the infant-operates did not occur until the 17th day. Also, stride was impaired in adult-, but not infant-hemispherectomized animals. Interestingly, the infant-operates were found to have developed an additional, small, uncrossed corticospinal tract, which the authors suggest may account for the spared stride component in these animals.

Isaacson and his associates (Isaacson, Nonneman, & Schmaltz, 1968; Nonneman & Isaacson, 1973) have thus far been the only ones to investigate the effects of early hippocampal lesions. These researchers investigated the anatomical and behavioural effects produced by hippocampal damage in cats at various stages of development. Their results showed that, for some problems such as differential reinforcement of low rates of responding (DRL) and discrimination-reversal performance, destruction of the hippocampus in the neonate produced less behavioural debilitation

than at other ages. On the other hand, passive avoidance performance was equally impaired regardless of age at hippocampal destruction, indicating that degree of impairment shown by animals with lesions made early in life is specific to the task. Hippocampal lesions at six weeks of age had the same effect as neonatal destruction on DRL performance, but were as severe as adult lesions on a discrimination-reversal task, runway extinction, and passive avoidance. Hippocampal damage at three months produced the same degree of behavioural impairment, on all tasks, as lesions made in adults. Histological examination two to four years after neonatal hippocampal damage revealed a good deal of hippocampal tissue still present. The authors suggested that this was due to the spreading of the remaining hippocampal tissue to take the place of the damaged tissue, rather than to the re-establishment of cell division after the lesion.

Johnson (1971, 1972) conducted an extensive investigation into what could probably be considered both recovery and sparing of function following infant septal lesions in rats. Infant-operates received bilateral septal lesions at seven days of age, and were subsequently compared to sham-operated littermates for emotionality and open-field behaviours at 21, 42, 63, and 90 days of age. According to Johnson, the infant septal lesions resulted in a permanent hyperemotionality similar to that observed following adult septal lesions. The emotionality ratings for the normal animals, however, increased over time, so that, although the infant septal animals were "hyperemotional" when compared to control animals at 21 and 42 days of age, the differences in emotionality between

experimental and control animals by 63 days was very slight, questioning the idea of permanence. The infant-operates were also found to be hyperactive in the open-field when tested prior to 63 days of age, but hypoactive when tested beyond that time. Johnson suggested that this reversal may be related to sexual maturation, although another explanation may be more pragmatic. As was mentioned earlier (p.27), septal lesions have resulted in hypoactivity in situation not conducive to exploratory behaviour (e.g., Zucker, 1965). Although the open-field may be a situation conducive to exploratory behaviour, repeated exposure to it may cause an animal to become habituated to it, transforming the open-field into an environment which is not so conducive to exploratory behaviour. This, then, rather than sexual maturity, could also explain the shift from hyperactivity to hypoactivity by the infant septal animals at 63 days of age.

When the infant-operated septal animals were 90 days of age, Johnson compared their performance on an active avoidance task, fixed-ratio responding (FR), and social interaction with the performance of adult normal and adult-operated septal rats. Adult- and infant-septal animals performed in similar fashion, displaying enhanced social facilitation when compared with control animals.

To summarize, then, it appears that no consistent pattern of sparing of function is found following early subcortical damage. Existing data is scarce and inconsistent. Certain studies (Kling et al.) have reported sparing of function following early lesions, while others (Thompson et al., 1969; Kling & Tucker, 1967; Johnson, 1972) have shown

that early subcortical destruction is just as serious as late subcortical destruction. Others still (Isaacson et al., 1968, Nooneman & Isaacson, 1973) have shown that the degree of sparing may vary from task to task.

The Present Study

The present study examined the degree of sparing of function following infant bilateral lesions of the amygdala, septum, anterior dorsal hippocampus (AH), and posterior ventral hippocampus (PH) of rats. These areas were chosen to acquire additional information about the capacity of the limbic system to display sparing of function following early destruction and with the intention that this information might reveal some of the mysteries of limbic organization and function. The effects of total hippocampal lesions were not investigated because of control problems which would have been created as a result of such large lesions.

The two major tasks on which the animals were tested were the ability to acquire a conditioned emotional response, and the ability to acquire a two-way active avoidance response. Additional measures were also made of activity and exploration levels, social interaction, and glandular and body weight change. Early- and late-operated animals underwent surgery at 10 and 60 days of age, respectively, and were tested starting at 70 and 120 days, respectively. This created a discrepancy between the two basic conditions with respect to age at time of testing. It would have been more desirable to control for both recovery time and age at time of testing. However, evidence indicates that there is no reliable difference in rats from post-weanling infancy

to adulthood in aversion and detection thresholds for shock stimuli (Campbell, 1967), in the acquisition of a passive or active avoidance task (Campbell, 1967; Feigley & Spear, 1970; Spear, 1971) or in the ability to display the "Kamin Effect" (Klein & Spear, 1969). It should be noted, however, that Paré (1969) found that aversion thresholds in rats were influenced by body weights, with lighter animals having lower shock thresholds than heavier animals. Age did not influence aversion thresholds per se, but indirectly influenced them to the extent that animals of different ages have different body weights. The maximum intensity used by Paré, however, was .09 mA, which was much lower than the intensity used in the present study, i.e., 0.7 mA. It was thought that using this high intensity would greatly reduce the variability between animals of different body weights.

The major hypothesis of the present study was that the infant limbic lesions would not be followed by the same degree of sparing of function as is commonly observed following infant cortical lesions. This hypothesis was based on the theory that subcortical structures, being phylogenetically older than cortical areas, are also ontogenetically older, reaching maturity within the individual first (Isaacson, Douglas, Lubar, & Schmaltz, 1971; Milner, 1970). Subcortical structures are derived from the phylogenetically older paleopallium and archipallium while cortical tissue is derived from the phylogenetically newer neopallium. The embryonic development of certain organisms, including man, appears to parallel phylogenetic development, and, at birth, the neocortex of many organisms has not yet reached its full functional maturity. The dendritic and axonic development of cells in the rat

cortex, for example, for at least one month after birth (Bogolepov & Popova, 1967; Isaacson et al., 1971). As a result, early cortical lesions may in fact be destroying cortical regions which have not reached functional maturity, allowing the mechanisms associated with these regions to be compensated for by other regions of the brain. Early subcortical destruction, on the other hand, may be eliminating regions which are already functionally mature at birth, or shortly thereafter, so that the mechanisms associated with these areas cannot be compensated for.

Furthermore, since the limbic system has been implicated in the regulation of endocrine function, it was also hypothesized that these early limbic lesions would influence the physiological development of the subjects.

METHOD

Subjects

Twenty-four, pregnant, Wistar albino rats were purchased from Woodlyn Farms (Guelph, Ontario). Specifications were that the animals be not more than 14 days pregnant on arrival, and that they had had at least one litter prior to that pregnancy. Each female was individually housed in a plastic breeding cage and, after delivery, remained with the pups until weaning at 21 days after birth. Following weaning, the mothers were placed in colony cages for a minimum of two weeks before being mated again with albino stud rats which had been previously acquired from the same breeders. Three females and one male were placed together in a colony cage for a period of 15 days, at which point the females were removed to individual breeding cages once more.

When the pups were five days of age they were sexed on the basis of the ano-genital space (male, 6-4mm; female 4-2mm). Female pups were destroyed, and the remaining male litters were randomly culled so as not to exceed eight pups per litter. The remaining pups were then housed with their littermates and mothers until 21 days of age. At that point the mothers were removed, but the litters were kept together until reaching 30 days of age, when each animal was caged individually and maintained on ad lib. food and water until one week prior to the initiation of training.

A total of 273 male albino rats, taken from 61 litters were used in the main experiment. Of the 273 animals, 16 died before behavioural data collection was begun. Ten of these animals died in early infancy of causes which were unrelated to any of the experimental treat-

ments. Three animals died during surgery (Two infants and one adult), apparently from an overdose of anesthetic, while three adult animals died several days after receiving bilateral amygdala lesions. Data for two additional animals had to be discarded at the end of the study because of inaccurately placed lesions. Data for the main experiment, therefore, was collected from 255 animals.

Design

At ten days of age each animal was weighed for the first time and randomly assigned to one of 14 groups shown in Table 1. Each of these groups was later divided into two subgroups, with animals being randomly assigned to either a "test" condition or a "nontest" condition. All except the early-operated groups had 10 animals assigned to the test condition. Early-operated groups had 14 animals assigned to the test condition because higher rates of lesion inaccuracy and mortality were anticipated under early-operated conditions. All animals in the test condition were subsequently subjected to the battery of tests described below. Animals in the non-test condition were not subjected to any of the behavioural tests, but were food deprived, in a manner similar to their counterparts in the test condition, starting at 63 or 113 days of age, depending on whether they were in an "early" or "late" group, respectively.

Surgical and Histological Procedures

All surgery on the infants was performed while the animals were under Metophane anesthesia, using a Krieg (#51200) stereotaxic instrument with a special 3/8 in. diameter toothbar. Measurements for the toothbar, which was on the same plain as the earbars, were adapted

TABLE 1

Names of Groups, Age at Surgery and First Testing Date, and Number of Animals Per Group.

Name of Group (Locus of Lesion)	Age (in days) at Surgery	Age (in days) at First Testing	Final "N" for Test Condition	Final "N" for Non-Test Condition
Early Amygdala (EA)	10	70	14	8
Late Amygdala (LA)	60	120	8	8
Early Septal (ES)	10	70	14	8
Late Septal (LS)	60	120	10	9
Early Anterior Dorsal Hippocampus (EAH)	10	70	14	7
Late Anterior Dorsal Hippocampus (LAH)	60	120	10	8
Early Posterior Ventral Hippocampus (EPH)	10	70	14	8
Late Posterior Ventral Hippocampus (LPH)	60	120	10	8
Early Frontal (EF)	10	70	14	7
Late Frontal (LF)	60	120	10	9
Early Normal Control (ENC)		70	10	9
Late Normal Control (LNC)		120	10	7
Early Anesthetized Control (EAC)		70	10	10
Late Anesthetized Control (LAC)		120	10	9

from Sherwood and Timiras (1970). A plastocene mold was also constructed and fitted to the stereotaxic. The plastocene part of the mold kept the animal's body up far enough to ensure that the head could be maintained in a level position. A small styrofoam block was carved out to act as a mold for the head only. It was inserted into the plastocene at the earbars, in such a way that the earbars could be screwed partially into the styrofoam block to prevent it from moving. Plastocene was also fitted between the toothbar carrier and the floor of the stereotaxic instrument so as to form a small compartment beneath the animal's snout, which allowed for the administration of supplementary anesthetic. A special anal electrode was also constructed for the infants, consisting of a piece of 0.406mm stainless steel wire doubled over. The blunt end of the wire could then be inserted into the anus of the infants to act as a cathode.

On the 10th day after birth each litter was removed from its mother and placed under a heatlamp. Each animal was then weighed and randomly assigned to one of 14 major groups shown in Table 1. If an animal was assigned to a control condition, it was merely earpunched for identification after being weighed. All animals assigned to either of the anesthetized control groups, as well as all animals assigned to an adult-operated condition were weighed, anesthetized with Metophane, and then earpunched. This was done to control for the effects of early anesthetization with Metophane. Animals assigned to early-operated conditions were anesthetized, operated and then earpunched.

The lesion-making procedure for the infant animals was as follows: A Metophane-soaked guaze sponge was placed at the bottom of a 100cc glass beaker. An animal was placed in the beaker, which was then pressed between the hands to form an airtight seal around the open end of the beaker. Each animal was kept in the beaker for two minutes. The animal was then removed from the beaker, placed in the mold, and taped to the stereotaxic instrument with three strands of Scotch brand tape. The animal's mouth was placed around the toothbar and the snout held down with the first piece of tape to help keep the head level. Another strand of tape held the animal's shoulders and forelegs in place, while the third strand was placed around the animal's middle. If an animal began to recover from the anesthetic during surgery, the Metophane-soaked guaze was removed from the beaker and placed in the compartment beneath the animal's snout for approximately 15 seconds.

When the electrolytic lesions had been made, the scalps were sutured with silk (4-0) thread, and the wound soaked with a 1 percent solution of quinine to prevent the mothers from chewing off the sutures. Earpunch wounds were also soaked with the quinine solution. The entire lesion-making procedure took less than 15 minutes per animal. After surgery each animal was replaced under the heatlamp until all animals from that litter became mobile. There was no instance in which a mother refused to take back her pups, or in which a mother chewed the sutures off the scalp-wound of a pup, or of cannibalism after infant surgery.

A pilot study was conducted, prior to the main experiment, to determine lesion coordinates and current parameters to ensure that loci and extent of damage (Immediately post-operative) were similar for infant and adult animals. Forty-six albino Wistar rats, twenty males and twenty-six females, taken from four litters were used in the pilot study. Also used in the pilot study were 10 adult, male Wistar rats which had served as controls in other unrelated experiments. The coordinates and parameters determined in that pilot study are presented in Table 2. All lesions were made using a 0.406mm stainless steel needle which had been insulated with Epoxylite and baked. Surgery on the adult animals was performed on the 60th day after birth under Nembutal anesthesia (60mg/kg). All animals in infant-operated and anesthetized-control groups were re-anesthetized with Nembutal at 60 days of age.

At the end of the study all animals were sacrificed with a lethal dose of Nembutal. The adrenals, thyroid, and testes of each animal were removed and stored in Bouin's solution for a minimum of 72 hours before being weighed. Animals with lesions were perfused through the heart with normal saline and 10% formal saline. The brains were removed, stored in formal saline for at least three days, then frozen and sectioned at 40 μ . Every fifth section was mounted on a slide and stained with cresyl violet.

Body Weights and Intake Measure

Starting at ten days of age all animals were weighed once per week. The infant-operated and infant-control animals started training at 70 days of age and were therefore placed on deprivation (approximately 20 grams of Purina rat chunk per day) at 63 days of age.

TABLE 2

Lesion Coordinates and Current Parameters for All Infant and Adult Lesions.

Group	mm Anterior (A) or Posterior (P) to Bregma	mm Lateral to Bregma	mm Below Skull Surface	Anodal Current	
				Intensity (mA)	Duration (seconds)
EA	0	3.5	6.5	3	25
LA	0	4.5	8.1	3	35
ES x	1(A)	1.5	4.1	3	20
LS x x	2.3 (A)	1.5	5.5	3	30
EAH	2.5 (P)	1.8* 2.8	2.0	2	10
LAH	2.0 (P)	1.8* 2.8	2.8	3	10
EPH	3.3 (P)	4.0	4.0* 3.0	2	10
LPH	3.3 (P)	4.4	5.7* 4.7	3	10
EF	2.3** 3.5 (A) 4.0	2.0	1.0	3	10
LF	4.0** 5.0 (A) 6.0	2.0	2.0	3	15

x electrode carrier was aimed at a 12° angle to the midline
 xx electrode carrier was aimed at a 10° angle to the midline
 * 2 discrete lesions were made on each side
 ** 3 discrete lesions were made on each side

Since animals were no longer weighed after being placed on deprivation, the final weigh date for animals in the infant conditions was at 59 days of age. Similarly, animals in the adult conditions began training at 120 days of age, and were therefore placed on deprivation at 113 days. Therefore, their final weigh date was at 108 days.

Consistent differences in body weights between groups were noticed during the weighing sessions, and an attempt was made to determine whether these differences were due to differential food and water intake. This had not been planned originally, and was at best a crude attempt involving a very small number of animals in each group. Limited observations were taken with the anticipation that they might reveal some gross differences between the groups. The measures taken involved total food and water intake and total boli weight for five animals in each of groups ENC, EAC, EF, and EPH, and for six animals in each of groups EAH, ES, and EA, starting at 40 days of age. Food intake was measured by placing a weighed amount of food in each animal's cage and, at irregular intervals, weighing the food that was left, including the food that had dropped through the bottom of the cage, and replenishing the supply. These differences between food placed in the cage and food left were added up at the end of the week to form one score per animal for food intake. Water intake was similarly determined by replacing the standard water bottles on the cages of these animals with graduated tubes. Total boli weights were also added up at the end of the week. Similar measures were also recorded for

three animals in each of groups LNC, LF, LAH, and LPH, and for four animals in each of groups LPH, LS, and LA starting at 90 days of age.

CER Measures

Apparatus Animals were tested in four Lehigh Valley operant chambers each equipped with a 100-cubic-foot-moved Dayton blower for masking noise and ventilation, and a two-in. speaker. Four Lehigh Valley control units were used to automatically record lever presses, and to deliver a 0.5-second footshock (0.7mA, a.c., RMS). The shock source and counters of each control unit, and a tone generator used to deliver a 50-decibel tone, were triggered by four timers in a specially-constructed separate control box.

Procedure Animals were given 10-minute daily sessions, in which each lever press was reinforced with a 45 mg Noyes pellet. After five days of unassisted lever-press experience, the CS (A three-minute 50-decibel tone) was presented without reinforcement after four minutes of uninterrupted lever pressing. Each animal's response to the unreinforced presentation of the CS was recorded, and each animal was then allowed to remain in the apparatus for three minutes after the offset of the CS. Animals were allowed to bar press without CS presentation on the seventh day.

The CS was presented again on the eighth day after four minutes of lever pressing. It was immediately followed by a 0.5-second footshock, following which each animal was allowed to remain in the apparatus for an additional three minutes. Tone-shock pairings were then presented only on alternate days for the first seven pairings to prevent the

development of a generalized CER to the apparatus, but were then administered every day until each animal received 20 tone-shock pairings. Animals were allowed 10 minutes of uninterrupted lever pressing on days in which no tone-shock was presented.

The learning index was defined as the suppression ratio, or the ratio of the number of presses during the three-minute period preceding the tone (A), to the sum of the presses during the tone (B) plus the presses during the three-minute period preceding the tone ($=A/A+B$). A total suppression score was calculated for each animal by adding its suppression ratios from all tone-shock trials, excluding the first trial. Thus a total suppression may yield a score of 9.5 if an animal continued to press at the same rate during the tone as before the tone on each of the 19 tone-shock trials.

Active Avoidance Measures

Apparatus Animals were tested in a two-compartment shuttle box, which was 12" high x 32" long, and constructed of $\frac{1}{2}$ "-thick plexiglass. Each compartment was 16" long, widening gradually from a three inch-wide passageway to an end-width of $4\frac{3}{4}$ ". The top of the box was hinged in the center to allow accessibility to either compartment. The box was painted a uniform grey throughout, except for one side-wall which had been left clear for observation. A light-bulb (GE #1820) was fixed to the end of each compartment, $1\frac{1}{2}$ " from the top. A Grid floor, made up of $\frac{1}{8}$ " brass rods placed $\frac{1}{2}$ " apart served each compartment. Footshock (0.7 mA d.c.) was delivered from a Lehigh Valley shock source and scrambler.

Procedure Animals were given two daily five-minute adaptation sessions before the daily training sessions which began on the third day. Training sessions consisted of placing an animal (randomly) in one of the two lighted compartments. After 30 seconds, the light in the compartment occupied by the animal was extinguished (CS), while the other light remained on. The animal was then required to shuttle to the lighted compartment within 10 seconds. Failure to do so resulted in the administration of the UCS (footshock) until the animal did escape to the lighted compartment. The CS (light off) remained until the animal avoided or escaped to the safe compartment. When an animal did shuttle within the 10-second time limit, the CS was terminated (light came on again) and no UCS was delivered. Each animal received 20 such trials per day, with 30-second intertrial intervals (ITI). Each ITI was computed from the time the animal shuttled to the safe (lighted) compartment after presentation of the CS, or from the time the animal entered the safe compartment to escape the UCS. Animals were allowed to shuttle freely during the ITI's and, if an animal was straddling the two compartments at the end of an ITI, the next trial was delayed until the animal fully entered one compartment or the other. A stop-watch was used to determine escape and avoidance latencies. The learning criterion was nine out of ten correct responses.

It had been intended to use the number of spontaneous shuttle responses as a form of activity measure. However, it was soon observed that during the training sessions the animals were too frightened to shuttle. Therefore, it was decided to give the animals three additional

testing days, at 10 trials per day, after they had reached criterion, to determine activity levels during the ITI's.

The CER and CAR were the two major tasks used, and it was decided to control for carry-over effects between the two tasks. Therefore, order of presentation of these two tests was counterbalanced for animals in each group, with a two- to four-day rest period between the two tasks.

Activity Wheel

Following both CER and CAR testing, each animal was given a two-day rest period and then placed in one of four activity wheels, housed each in a separate room, for a 24-hour period with food rations and water for the day. To simulate a day-night cycle the activity wheels were kept in light for 12 hours and in dark for 12 hours. The order of the day-night cycle was counter-balanced for animals in each group to control for the novelty effect of the apparatus. Two measurements were taken, one at the end of each cycle.

Open-Field Activity and Exploration Measures

The open-field apparatus consisted of a box with a wooden floor 36" x 36", with 10 in.-high black wooden walls. The floor of the apparatus was marked off in 36 five-in. numbered squares.

Following the period in the activity wheel each animal was rested for a minimum of one day before being tested for activity in the open-field apparatus. Each animal was placed in the centre of the apparatus and the total number of squares entered in a five-min. session

was taken as the index of activity. The exploration index was measured as the percentage of all possible squares entered during the same session.

Social interaction

Social interaction was measured on the day following the open-field activity measure, using the same apparatus. Animals from the same group were tested in pairs for a period of five minutes. Two animals were placed in opposite corners of the open-field, and latency to first contact (LFC), number of physical contacts, and total duration of physical contact between the two animals were recorded during the session. This latter method of measuring social cohesiveness is similar to that employed by Jonason and Enloe (1971). In this case LFC and number of physical contacts were also recorded as supplementary measures.

RESULTS AND DISCUSSION

Histology

Histological observation revealed that one animal in group LA had only a unilateral amygdala lesion, while another animal in the same group had a lesion centered in the internal capsule. Data for both of these animals was discarded. The remaining animals in both early and late amygdala groups all had extensive bilateral lesions of the amygdala which typically destroyed most of the nuclei within the amygdalae. Other structures which were also slightly damaged on occasion, in both early- and late-operated animals, following amygdala damage included the globus pallidus, internal capsule, caudate nucleus, claustrum, external capsule, pyriform cortex, optic tract, stria terminalis, and medial forebrain bundle. The extent of extra-amygdala damage incurred by each animal in groups EA and LA is presented in Appendix 1 and 2, respectively. Representative early and late lesions for all groups are shown in Appendix 49. Early- and late-operated animals in all groups were sacrificed at approximately 130 and 180 days of age, respectively, approximately 120 days after surgery.

Septal lesions were centered in the lateral septal nucleus, and complete destruction of all but the most ventral aspects of this nucleus was the case in every animal. Histological results were the same for infant- and adult-operated animals. Total destruction of the medial septal nucleus was observed in 12 animals in each of groups ES and LS. The remaining septal animals had medial septal damage ranging from slight to extensive. Slight damage to the caudate nucleus,

anterior commissure, medial parolfactory area, diagonal band of Broca, cingulate cortex, accumbens nucleus, fornix, and hippocampal commissure was also observed in some of the animals. One animal in group ES was found to be hydrocephalic, resulting from swelling of the ventricles. Although this animal had no trace of septal tissue, extra-septal damage was not extensive, and its behaviour was not readily distinguishable from that of any other animal in that group. The extent of extra-septal damage incurred by each animal in group ES and LS is presented in Appendix 3 and 4, respectively.

Frontal cortical lesions in both infant and adult animals were approximately one and one-half to two millimeters (mm) wide, and spread three to four mm in a posterior direction from the tip of the frontal cortex. The most medial one mm of the frontal cortex was always spared. Slight damage to the corpus callosum in this region was also observed in animals in both groups EF and LF. The extent of extra-cortical damage for each animal in these two groups is presented in Appendix 5.

Animals in the AH groups were found to have, in addition to damage to the anterodorsal hippocampus, slight damage to the overlying cortex, the corpus callosum, fimbria, dentate gyrus, stria medullaris, and medial habenular nucleus. The extent of extra-hippocampal damage incurred by each animal in groups EAH and LAH is presented in Appendix 6 and 7.

Some animals in the two PH groups were found to have, in addition to posteroventral hippocampal damage, slight damage to the lateral geniculate nucleus, optic tract, corpus callosum, and fimbria. Again,

all extra-hippocampal damage was slight and did not seem to cause any apparent behavioural differences. The extent of extra-hippocampal damage suffered by each animal in groups EPH and LPH is presented in Appendix 8.

Infant cerebral damage, except for damage to the septal area, was more difficult to evaluate than similar damage inflicted on adult animals. When the cortex, hippocampus, or amygdala were damaged in infant animals, the remaining tissue seemed to spread into the damaged area, taking up much of the vacant space. As a result, although the infant and adult lesions appeared identical immediately postoperative, the infant hippocampal, cortical, and amygdala lesions seemed somewhat smaller at histology, several months after the lesions had been made. This tissue spread following infant brain damage seems similar to that reported by Isaacson et al. (1968) following hippocampal lesions in kittens. Although the same amount of time elapsed between the adult lesions and histology, the same type of tissue spread was not observed in the adult-operates. Failure to observe a similar tissue spread in the infant septal-operated animals may have been due to the fact that the space made vacant by septal destruction was occupied by cerebro-spinal fluid from the ventricles, preventing the tissue from adjacent intact structures from moving into the space.

Subjective observation would indicate that the amygdala lesions had the most dramatic effects on both infant and adult animals, but more so on the adults. Infant-operates appeared somewhat retarded in growth, and in the appearance of certain developmental milestones. Their eyes, for example, did not open until after approximately 17

days of age, while other animals opened their eyes at about 14 days of age. Also, their scalp wound took longer to heal, and they retained their downy fur for one to two weeks longer than other animals. Finally, after weaning, the amygdala animals did not appear as well groomed as other animals. Some of these effects can be seen in Appendix 50. The photo presented in this appendix is of two littermates operated on at 10 days of age, and sacrificed at 17 days. The smaller animal had received bilateral amygdala lesions, while the other had received bilateral anterodorsal hippocampal lesions. Animals which received amygdala lesions as adults would typically refuse to eat or drink following surgery, and were all placed on a diet of wet mash for two weeks. It was also observed that these animals became lethargic and ceased grooming themselves for approximately 21 days following surgery. The adult-operated amygdala animals became the most difficult to handle, and remained so until they were sacrificed at approximately 180 days of age. This was not so for the infant-operated animals.

All infant-operated animals were extremely tame and easy to handle, with the infant-operated septal animals being by far the most easy to handle of all groups. Septal "rage", or hyperemotionality was never observed in any of the infant septal animals, but, conversely, was observed in every adult septal animal. This hyperemotionality in the adult septals was present immediately postoperative, and dissipated approximately two weeks after surgery even though these animals were not handled.

CER Measures

The suppression ratio on each tone-shock trial was recorded for each animal. As well, total suppression scores were calculated for each animal by adding the suppression ratios calculated for trials two through 20. Although each animal received 20 tone-shock trials regardless of their performance, an animal was considered as having acquired the CER if it failed to lever press during the tone on two consecutive tone-shock days. This was considered the learning criterion, and total trials to criterion were calculated for each animal. Since neither task-order nor anesthetic effects approached significance on any of the CER measures, both were eliminated as variables from further analyses. This meant that the scores of animals in identical conditions were grouped together regardless of whether these animals had been tested on the CER first or the CAR first. In addition, animals in the early anesthetized control condition (EAC) were grouped with animals in the early normal control condition (ENC) to form one early control group (EC). Similarly animals in LAC and LNC were joined together to form one late control condition (LC).

All analyses of variance calculated in the present study were for unweighted means. The suppression ratios of all groups were compared in an analysis of variance having six treatment levels (locus of lesion), two age-of-treatment levels (early or late), analysed over the last 19 trials. The results of this analysis showed a reliable treatment effect ($F(5, 146) = 33.10; p < .001$), age-of-treatment effect ($F(1, 146) = 4.14; p < .05$), treatment by age-of-treatment interaction

($F(5, 146)=3.71$; $p<.003$), trials effect ($F(18, 2628)=56.04$; $p<.001$), trials by treatment interaction ($F(90, 2628)=2.96$; $p<.001$), and trials by age-of-treatment interaction ($F(18, 1628)=1.84$; $p<.02$). The summary table for this analysis can be found in Appendix 9. All interactions are displayed in Figures 1 and 2. Individual group comparisons of the suppression ratios were then made using a Newman-Keuls Test. The average daily suppression ratio for group EC was .143; for group LC, .116; for EF, .149; for LF, .144; for EAH, .100; for LAH, .160; for EPH, .144; for ES, .236; and for LS, .206. All comparisons between these groups revealed no reliable differences ($p>.05$). The average daily suppression ratio for group LPH was 3.04. The difference between this group and each of the nine former groups was reliable ($p<.05$). No reliable differences were found between groups EA ($\bar{X}=.443$) and LA ($\bar{X}=.463$), but each of these groups was significantly different from each of the other 10 groups ($p<.05$). Animals in groups EA, LA, and LPH appear to have been severely retarded in CER acquisition.

Similar, but not identical results were obtained from analysis of total suppression scores. The distribution of total suppression scores for all animals can be seen in Figures 3 and 4. Total suppression scores for all groups were compared by an analysis of variance having six treatment levels and two age-of-treatment levels. Results showed a significant treatment effect ($F(5, 146)=32.81$; $p<.001$), age-of-treatment effect ($F(1, 146)=4.498$; $p<.04$), and treatment by age-of-treatment interaction ($F(5, 146)=3.61$; $p<.005$). The summary table from this analysis is presented in Appendix 10, and reliable interactions

FIG. 1. Mean suppression ratios over trials 2 to 20 for groups receiving their appropriate treatments as infants.

FIG. 2. Mean suppression ratios over trials 1 to 20 for groups receiving their appropriate treatment as adults.

FIG. 3. Total suppression scores (sum of the ratios over trials 2 to 20) for each animal in all early or infant treated groups. Solid squares indicate animals which acquired the CER. Open squares indicate animals which did not acquire the CER in 20 tone-shock pairings.

FIG. 4. Total suppression scores (sum of the ratios over trials 2 to 20) for each animal in all late or adult treated groups. Solid squares indicate animals which acquired the CER. Open squares indicate animals which did not acquire the CER in 20 tone-shock trials.

can be seen in Appendix 11. The average total suppression ratios for the animals in each of the various groups were: EC=2.37; LC=2.00; EF=2.52; LF=2.71; EAH=1.45; LAH=2.83; EPH=1.81; LPH=5.58; ES=4.29; LS=3.67; EA=8.54; and LA=8.81. Individual comparisons made with a Newman-Keuls Test showed no reliable differences between groups EC, LC, EAH, LAH, EF, LF, EPH, and LS. Total suppression scores for animals in group ES, however, were reliably higher than total suppression scores for animals in groups EPH ($p < .05$). Similarly, group LPH differed reliably from each of groups EC, LC, EAH, LAH, EPH, EF, and LF, with scores for group LPH being significantly higher ($p < .05$). Finally, no reliable differences were obtained between groups EA and LA, with the scores of each of these two groups being significantly higher than the scores of each of the other 10 groups ($p < .05$).

Total days to criterion were compared for all groups by an analysis of variance having six treatment levels and two age-of-treatment levels. Results showed a reliable treatment effect ($F(5, 146) = 19.167$; $p < .001$), age-of-treatment effect ($F(1, 146) = 5.2$; $p < .03$), and treatment by age-of-treatment interaction ($F(5, 146) = 3.79$; $p < .005$). A summary table for this analysis is presented in Appendix 12, and reliable interactions are displayed in Appendix 13. The average number of days to criterion for the various groups were: EC=7.95; LC=7.53; LF=9.00; EAH=6.92; LAH=9.80; EPH=7.28; LPH=16.00; ES=11.42; LS=11.60; EA=20.00; LA=18.00. Individual comparisons made using a Newman-Keuls Test revealed no reliable differences between any of the following groups: EC, LC, EF, LF, EAH, LAH, EPH, ES, and LS. Days to

criterion for animals in group LPH, however, were significantly higher than days to criterion for each of these nine groups ($p < .05$). No reliable differences were found between groups EA and LA. In addition, days to criterion for each of these two groups were reliably higher than mean days to criterion for each of the other groups ($p < .05$), with the only exception being that scores for group LA were not reliably different from scores for group LPH. This seems to have been due to one animal in group LA which reached criterion in four trials, while all other animals in that group failed to reach criterion in 20 trials.

The observation that adult amygdala lesions retard CER acquisition corroborates the findings of previous studies (Kellicut & Schwartzbaum, 1963; McIntyre & Molino, 1972; Suboski et al., 1970), as does the observation that adult posteroventral hippocampal lesions have a similar effect (Brady, 1958; Brady & Hunt, 1955; 1955; Nadel, 1968). It is clear from this experiment, however, that the effects of amygdala damage are relatively more disruptive for CER acquisition than are the effects of hippocampal damage. It is also noteworthy that the differential performance of the two hippocampal groups supports the notion that the hippocampus is a heterogeneous structure (Fried, 1971; Grant & Jarrad 1968; Jacobson, 1968; Kimura, 1958; Nadel, 1968; Raisman, 1969). Although the data fail to support the findings of previous authors which have demonstrated significant retardation in CER acquisition following septal lesions (Brady & Nauta, 1953, 1955; Harvey et al., 1961, 1965; Trafton, 1967), the data do show that the performance of the adult

septal animals was consistently inferior to that of the control animals. Adult frontal cortical and anterodorsal hippocampal lesions appear to have had no reliable effect on CER acquisition.

Failure of all infant-operated animals to acquire the CER suggests that the role or function of the amygdala in CER acquisition was not spared following infant amygdala lesions. Conversely, failure of the infant-operated PH animals to show the same CER deficits as their adult counterparts suggests that the role or function of that particular portion of the brain in CER acquisition was spared following infant PH lesions. Infant-operated septal animals performed at approximately the same level as their adult counterparts, suggesting that, if the septum does play a slight function in CER acquisition, then that function is not spared following infant septal lesions.

CAR Measures

Total number of trials to criterion were calculated for each animal. Again, neither task-order nor anesthetic effects approached significance on any of the CAR measures and were therefore both eliminated as variables from further analyses.

An analysis of variance having six treatment levels and two age-of-treatment levels, compared the trials to criterion for all groups. The results, which are presented in summary form in Appendix 14, revealed a reliable treatment effect ($F(5,129)=13.42$; $p<.001$), and treatment by age-of-treatment interaction ($F(5, 129)=5.19$; $p<.001$), but no reliable age-of-treatment effect ($F(1, 129)<1$). These data are represented in Fig. 5. Inspection of the treatment by age-of-

FIG. 5 Trials to criterion for active avoidance acquisition: treatment by age-of-treatment interactions with age-of-treatment on abscissa.

treatment interaction shows that not all groups failed to display a reliable age-of-treatment effect. Trials to criterion for animals in group LPH, for example, are dramatically less than trials to criterion for animals in group EPH. Also, trials to criterion for animals in group LA are greater than trials to criterion for animals in group EA. Average trials to criterion for the various groups are: EC=174.28; LC=177.50; EF=158.18; LF=165.00; EAH=188.00; LAH=181.00; EPH=181.66; LPH=83.00; ES=82.12; LS=77.00; EA=173.33; LA=261.25. Individual group comparisons of trial to criterion were made using a Newman-Keuls Test. Results revealed no reliable differences between groups EC, LC, EF, LF, EAH, LAH, EA, and EPH, with animals in these groups acquiring the active avoidance at a relatively normal rate. No reliable differences in trials to criterion were found between groups ES, LS, and LPH, with animals in these groups acquiring the active avoidance response at an accelerated pace. Furthermore scores for animals in each of the latter three groups differed significantly from the scores of animals in each of the former eight groups ($p < .05$). In addition, scores for animals in group LA differed reliably from scores for animals in each of the other 11 groups ($p < .05$), with animals in group LA being significantly inferior in CAR acquisition.

The number of trials to first avoidance (more specifically, the first correct avoidance response emitted by an animal after it had received at least two footshocks) were also analysed. It was anticipated that these data might provide some insight about the strategies used by the animals in the various groups to solve the

problem. The results of an analysis of variance having six treatment levels and two age-of-treatment levels revealed no reliable effects of treatment ($F(5, 147) < 1$), or age-of-treatment ($F(1, 147) = 2.98$; $p > .08$) on the number of trials to first avoidance. The average number of trials to first avoidance for the various groups were: EC=37.36; LC=28.1; EF=49.71; LF=33.20; EAH=41.50; LAH=25.8; EPH=47.14; LPH=15.8; ES=22.80; LS=12.50; EA=23.00; LA=45.00. Appendix 15 shows that the trials to first avoidance followed the same basic pattern as trials to criterion.

Escape and avoidance latencies were recorded for each trial. Immediate escape reactions following shock, however, resulted in little between subject variability. As a result, the only escape and avoidance latencies analysed were those recorded for the 10 trials on which each animal reached criterion and the 10 daily trials administered on the three days following criterion acquisition. The avoidance latencies for each of these 10-trial blocks were summed, giving each animal four independent scores. These latency scores were then compared for all groups with an analysis of variance having six treatment levels, two age-of-treatment levels, analysed over four blocks of trials. The results of this analysis revealed a reliable treatment effect ($F(5, 126) = 3.81$; $p < .004$), and age-of-treatment effect ($F(1, 126) = 10.59$; $p < .002$). There was no reliable trials effect ($F(3, 378) < 1$), and no reliable interaction. The summary table for this analysis is presented in Appendix 16, and the data are displayed in Appendix 17. The avoidance latencies (in seconds) for the various groups averaged over four days were: EC=672.41; LC=724.42; EF=609.61; LF=688.67; EAH=698.59; LAH=758.88;

EPH=631.89; LPH=644.79; ES=616.07; LS=694.50; EA=703.72; LA=780.00.

The results of a Newman-Keuls Test comparing total latencies per group revealed no reliable differences between any of the 12 groups.

The results of the active avoidance experiment show that adult amygdala lesions significantly retard active avoidance acquisition, corroborating the results of previous studies (DiCara, 1966; King, 1958; McNew & Thompson, 1966; Robinson, 1963; Suboski et al., 1970; Weiskrantz, 1956). Similarly, the active avoidance acquisition displayed by the adult-operated septal animals supports previous findings (e.g., Schwartzbaum et al., 1967; Trafton, 1967; Zucker, 1965), as does the facilitated active avoidance acquisition displayed by the adult-operated posteroventral hippocampal animals (Antelman & Brown, 1972; Blanchard et al., 1970; Green et al., 1967; Isaacson et al., 1961; Nadel, 1968). Once again, the behavioural discrepancies displayed by the two adult-operated hippocampal groups lends further support to the theory that the hippocampus is a functionally heterogeneous structure. Adult frontal cortical and anterodorsal hippocampal lesions again failed to have a reliable effect on acquisition.

Failure of the infant amygdala lesions to have the same debilitating effect on active avoidance acquisition as the adult amygdala lesions suggests that the functional recovery for active avoidance acquisition did take place following infant amygdala lesions. Infant septal lesions were found to have an identical facilitatory effect on active avoidance acquisition as the adult septal lesions. The results essentially replicate the findings of Johnson (1972) who reported no

functional recovery on a two-way active avoidance task following infant septal lesions. On the other hand, failure of the infant-operated posteroventral hippocampal animals to show the same facilitated active avoidance acquisition as their adult-operated counterparts indicates that functional recovery for active avoidance acquisition did take place following infant posteroventral lesions.

The trials to first avoidance were analysed with the anticipation that they might shed some light on the strategies used by the animals during the course of CAR training. It was expected that animals which were faster at acquiring the CAR might normally be faster at exhibiting their first avoidance response, and vice versa. Therefore, if animals in the groups which showed recovery (EA and EPH) had developed new strategies during the course of CAR training to acquire the appropriate response, it was expected that they might show an abnormal number of trials to first avoidance (more similar to the number of trials to first avoidance shown by their adult-operated counterparts) while yielding a normal trials to criterion score. The results indicate that the trials to first avoidance scores did follow the same basic pattern as the trials to criterion, with groups LS, ES, and LPH yielding the lowest scores, and group LA with the highest score. However, trials to first avoidance scores for groups EA and EPH were normal, reflecting the eventual trials to criterion scores of these two groups rather than resembling the trials to first avoidance scores of the adult-operated counterparts of these two groups. The results, then, suggest that the functional recovery displayed by animals in

groups EA and EPH was probably due to some form of compensation other than the development of new strategies during the course of training.

The significant age-of-treatment effect obtained in the first analysis of the avoidance latencies can be attributed to the fact that animals in the "early" condition avoided consistently faster than their counterparts in the "late" condition. Although a significant treatment effect was also observed in both analyses dealing with the avoidance latencies, the exact nature of this effect is difficult to ascertain since individual group comparisons revealed no reliable differences. The reliable treatment effect does not appear to be due to any single treatment, and is instead probably due to a combination of the high scores displayed by the Amygdala, AH, and Control groups compared to the low scores yielded by the Septal, Frontal, and PH groups.

Body Weights

Animals in the adult conditions were weighed at 10, 17, 24, 31, 38, 45, 52, 59, 66, 73, 80, 87, 94, 101, and 108 days of age, while animals in the infant conditions were similarly weighed, but only to 59 days of age. Anesthetic effects on body weights were negligible, and thus the data from animals in group EAC were joined with those of animals in group ENC to form only one early control group (EC). Similarly, data from animals in LAC were joined with those of animals in LNC to form one adult control condition (LC).

Body weights for animals in the infant conditions can be seen in Fig. 6. A one-way analysis of variance with repeated measures analysed the effects of these six treatment conditions (EC, EF, EAH,

Fig. 6. Treatment by age-of-weighing interaction for body weights for animals which had received their respective treatments as infants.

EPH, ES, and EA) over the eight ages-of-weighing. Results showed a reliable treatment effect ($F(7, 141)=5.38$; $p<.0004$), age-of-weighing effect ($F(7, 987)=5093.12$; $p<.0001$), and treatment by age-of-weighing interaction ($F(35, 987)=4.33$; $p<.0001$). The results of this analysis are summarized in Appendix 18. Individual group comparisons made with a Newman-Keuls Test revealed that weights for animals in group EA were reliably lower than weights for animals in any of the other five infant conditions ($p<.05$). Weights for animals in group ES were reliably lower than weights for animals in groups EC, EF, EAH, and EPH ($p<.05$). All comparisons between groups EC, EAH, EF, and EPH revealed no reliable differences in body weights to 59 days of age.

Terminal weights (i.e., weights at sacrifice) were compared for all animals in the infant conditions by means of a one-way analysis of variance. Results showed a reliable treatment effect ($F(5, 146)=13.33$; $p<.0001$). The mean terminal weights for each group can be seen in Fig. 6. Mean terminal weights for animals in the infant-operated groups were: EC=414.05; EF=414.14; EAH=414.90; EPH=416.27; ES=350.95; EA=373.36. All comparisons made with a Newman-Keuls Test between groups EC, EF, EAH, and EPH revealed no reliable differences in terminal weights between any of these groups. Terminal weights for animals in group ES were reliably smaller than terminal weights for all other groups, including EA ($p<.05$). Terminal weights for animals in group EA were reliably higher than those of animals in group ES, but reliably lower than those of all other infant groups ($p<.05$).

Body weights for animals in the adult-operated groups are presented in Fig. 7. Since these animals were operated on at 60 days of age, body weights were compared by means of two one-way analyses of variance with repeated measures, one to compare body weights before surgery, and the other to compare them after surgery. The first analysis, comparing the first eight scores, revealed normal weight-gain, evidenced by a significant age-of-weighing effect ($F(7, 840) = 2612.45$; $p < .0001$), but no reliable group differences ($F(5, 120) < 1$) or group by age-of-weighing interaction ($F(5, 840) < 1$). The second analysis, comparing the last seven scores, revealed a reliable group effect ($F(5, 120) = 7.84$; $p < .0001$), age-of-weighing effect ($F(6, 720) = 1523.02$; $p < .0001$), and group by age-of-weighing interaction ($F(30, 720) = 5.19$; $p < .0001$). The results of this analysis are summarized in Appendix 19. Individual comparisons made with a Newman-Keuls Test revealed no reliable differences between any of groups LC, LF, LAH, LPH. However, each of these four groups was reliably heavier than group LS ($p < .05$). Furthermore, each of these groups, including LS, were reliably heavier than group LA ($p < .05$).

A one-way analysis of variance compared terminal weights for all adult animals in the six treatment conditions. Results showed a significant treatment effect ($F(5, 120) = 22.36$; $p < .0001$). The mean terminal weights for each group, which can be seen in Fig. 7 were: LC=475.25; LF=471.63; LAH=478.55; LPH=473.22; LS=367.26; LA=425.87. Individual comparisons made with a Newman-Keuls Test revealed no reliable differences between any of groups LC, LF, LAH, and LPH.

Fig. 7. Treatment by age-of-weighing interaction for body weights for animals which had received their respective treatments as adults.

Terminal weights for animals in group LS were significantly smaller than terminal weights of animals in the other five groups, including LA ($p < .05$). Terminal weights for animals in group LA were significantly larger than those of group LS, but significantly smaller than those of animals in any of the other groups ($p < .05$).

From the results described above, it appears that septal and amygdala lesions do influence normal weight gain in the developing rat. Furthermore, these lesions have similar effects at 10 and 60 days of age, suggesting that the mechanisms which were disrupted to cause this abnormal weight gain are already present in early infancy, and continue to function well into adulthood. The immediate effects of amygdala lesions on weight gain are more pronounced than are the immediate effects of septal lesions. This is true for both infant and adult animals. The effects of amygdala destruction, however, quickly stabilize, while the effects of septal lesions become more pronounced over time, and eventually supercede those of amygdala destruction. These findings contradict those previously reported following early septal (Johnson, 1971, 1972) and early amygdala lesions (Kling, 1962, 1965, 1966), which had claimed to find no significant developmental effects in terms of body weights following neonatal lesions (although Johnson did report that the development of certain behaviours was altered following early septal lesions, i.e., open-field behaviour, emotionality, socialization).

Intake Measures

Since consistent differences in body weights had been observed, crude intake measures were taken in an attempt to determine whether these differences were due to differential food and water intake, or to some metabolic disorder caused by the lesion. Total food and water intake and total boli weights were recorded for a seven-day period for five animals from each of groups ENC, EAC, EF, and EPH, and from six animals in each of groups EAH, ES, and EA, starting at 40 days of age. Similar measurements were recorded from three animals in each of groups LNC, LAC, LF, and LAH, and from four animals in each of groups LPH, LS, and LA, starting at 90 days of age. It was noticed while taking the intake measures from the infant animals that the amount of food dropped through the cage varied from animal to animal. Although this observation came too late to allow any such measurement to be taken from the infant-operates, the amount of food dropped through the cage was measured separately for the adult animals involved. Anesthetic effects were again negligible for both infant and adult conditions, and the data for the two control groups were joined together to form one control group for each condition.

One-way analyses of variance revealed no group differences in any of the infant conditions with regard to food intake ($F(5, 32) < 1$), water intake ($F(5, 32) = 1.21$; $p > .300$), or total boli weight ($F(5, 32) < 1$). Average food and water intake and boli weights for the infant groups are presented in Appendix 20. Similar analyses revealed no reliable differences among animals in the adult conditions with regard

to food intake ($F(5, 18)=1.41$; $p>.2$), total boli weight ($F(5, 18)<1$), or food fallen through the cage ($F(5, 18)=1.14$; $p>.300$). A significant effect was obtained however, with regard to water intake among animals in the adult condition ($F(5, 18)=3.76$; $p<.02$). Average water intake (in millilitres) for animals in the adult groups were: LC=288.39; LF=263.16; LAH=277.37; LPH=257.59; LS=372.39; LA=210.77. Individual group comparisons made with a Newman-Keuls Test revealed that the only reliable difference that existed was between groups LS and LA. Average total food and water intake, boli weights, and food fallen through the cage for animals in each of the adult-operated groups are also presented in Appendix 20.

It should be stressed, at this point, that the intake measures recorded in this study were crude, utilizing small sample sizes, and designed to detect only gross differences between the groups.

The data appear to indicate that the infant lesions had no significant effect on food or water intake, or boli weights, suggesting that the lower weight gains displayed by the infant septal and amygdala animals may have been due to metabolic disorders.

The adult lesions failed to have a significant effect on food intake, boli weights, or food fallen through the cage. Failure of the adult amygdala lesions to significantly alter food intake is not consistent with previous findings which had reported either increased (Fuller et al., 1957; Green, Clements & De Groot, 1957; Wood, 1958) or decreased (Brady et al., 1954; Weiskrantz, 1956; Yamada & Greer, 1960) food intake following adult amygdala lesions.

The adult septal animals drank more water, relative to the control animals. Although the data did not attain statistical significance, they are consistent with previous findings which have shown increased water intake following septal lesions (Blass & Hanson, 1970; Donovan & Burrig, 1968; Hamilton, 1970; Harvey & Hunt, 1965; Harvey et al., 1965; Pizzi & Lorens, 1967). The increased water intake displayed by these animals, along with their failure to show a concomitant increase in food intake, suggests that the lower weight gains displayed by these animals may have been due to a metabolic disorder. The adult amygdala lesions caused a decrease in water intake, relative to the control animals. Although these data did not attain statistical significance, this decrease in water intake, along with the failure of these animals to show a concomitant decrease in water intake suggests that the lower weight gains displayed by the amygdala animals may have been due to a metabolic disorder quite different from that caused by the septal lesions.

Activity and Exploration

Spontaneous shuttle responses The number of spontaneous shuttle responses was recorded for each animal for the first two days of habituation, and for the day on which each animal reached criterion plus the three days following criterion acquisition. These measures were interpreted as indices of activity. Anesthetic and task-order effects were negligible and were once again deleted as variables from further analyses. The mean number of spontaneous shuttle responses for animals in the various groups, over each of the six days, are presented in Appendix 21.

Number of shuttle responses for the two habituation days were compared for all groups with an analysis of variance having six treatment levels, two age-of-treatment levels, analysed over two trials. Results showed a significant age-of-treatment effect ($F(1, 126)=12.14$; $p<.001$), and trials effect ($F(1, 126)=52.45$; $p<.0001$). The treatment effect was not reliable ($F(5, 126)<1$), nor were any of the interactions. A summary table for this analysis is presented in Appendix 22. The data are represented in Appendix 23 and 24. The age-of-treatment effect is presented in Fig. 8.

Number of shuttle responses for the last four days were compared for all groups with an analysis of variance with six treatment levels, two age-of-treatment levels, analysed over four trials. Results showed a reliable age-of-treatment effect ($F(1, 126)=33.62$; $p<.0001$). The treatment effect was not significant ($F(5, 126)=1.53$; $p>.1$), nor was the trials effect ($F(3, 378)=1.67$; $p>.1$), nor any of the interactions. A summary table for this analysis is presented in Appendix 25.

Activity wheel Effects of anesthetic and cycle order (day-night/night-day) were negligible and were therefore eliminated as variables from further analyses. Activity scores for all groups were then compared with an analysis of variance having six treatment levels, two age-of-treatment levels, analysed over the two cycles (day and night). Results showed a reliable treatment effect ($F(5, 147)=2.35$; $p<.05$), and treatment by cycle interaction ($F(5, 147)=3.25$; $p<.01$). No reliable age-of-treatment effect ($F(1, 147)<1$), or cycle effect ($F(1, 147)=1.67$; $p>.1$) were obtained. A summary table for this analysis

Fig. 8. Age-of-Treatment effect for animals in the early (infant) and late (adult) conditions. H1=first habituation day; H2=second habituation day; C=day on which animals reached criterion; 1, 2, 3=the three days following criterion acquisition.

is presented in Appendix 26. These data are represented in Fig. 9 and in Appendix 27 and 28. The average number of revolutions per cycle for the animals in the various groups are presented in Appendix 29. Individual comparisons made with a Newman-Keuls Test, however, revealed that the only reliable difference existed between group EA, the most active, and group LS, the least active ($p < .05$). None of the other individual comparisons revealed any statistically significant differences. Despite the fact that no reliable age-of-treatment effects were observed, Fig. 9 shows that animals in group EA tended to be consistently more active than animals in group LA, and that animals in group LS tended to be consistently less active than animals in group ES.

Open-field activity and exploration measures The total number and percentage of squares crossed during a five min. session were recorded for each animal. The former score was interpreted as an activity index, while the latter was interpreted as an exploration index. Anesthetic effects were negligible on both activity and exploration indices and were therefore eliminated as a variable. Activity scores were compared for all groups with an analysis of variance having six treatment levels and two age-of-treatment levels. Results showed a significant treatment effect ($F(5, 147) = 3.80$; $p < .004$), but no significant age-of-treatment effect ($F(1, 147) = 1.37$; $p > .2$) or treatment by age-of-treatment interaction ($F(5, 147) = 1.46$; $p > .2$). A summary of this analysis is presented in Appendix 30. Average activity and exploration scores for animals in the various groups are presented in

Fig.9. Treatment by age-of-treatment interaction for activity wheel scores.

Appendix 29. The treatment by age-of-treatment interaction is presented in Appendix 31. Although the age-of-treatment effect was not significant, inspection of the interaction reveals that the activity scores for all adult-operated amygdala and PH animals were consistently higher than the scores for their infant-operated counterparts. Furthermore, the individual comparisons made with a Newman-Keuls Test showed that the activity scores for group LA were significantly higher than those of every other group except LPH ($p < .05$). All other comparisons revealed no reliable differences.

Exploration levels for each group were compared with another analysis of variance having six treatment levels and two age-of-treatment levels. Results showed a reliable treatment effect ($F(5, 147) = 2.5311$; $p < .03$), but no reliable age-of-treatment effect ($F(5, 147) < 1$), or treatment by age-of-treatment interaction ($F(5, 147) < 1$). A summary of this analysis is presented in Appendix 32. The treatment by age-of-treatment interaction is shown in Appendix 33. Individual comparisons made with a Newman-Keuls Test revealed no reliable differences between any of the 12 groups. Once again, although there was no reliable age-of-treatment effect the scores for adult-operated amygdala animals were consistently higher than the exploration scores of their infant-operated counterparts. Also, both infant and adult septal groups yielded consistently lower open-field exploration scores than any of the other groups, while both infant and adult AH groups yielded consistently higher exploration scores than any of the other groups except LA.

Animals which had received bilateral lesions of the amygdala as adults displayed a normal level of activity in the shuttle box and activity wheel. These same animals, however, were significantly hyperactive in the open-field situation, supporting the findings of previous research (Allikments & Lapin, 1967; Anderson, 1967; Corman et al., 1967; Schriener & Kling, 1953; Schwartzbaum & Gay, 1966). Adult septal animals were consistently hypoactive in the activity wheel and open-field, and yielded lower levels of exploration in the open-field. Although these scores did not attain statistical significance when compared to scores of control animals, they were still in a direction which tended to support the findings of previous studies which had reported hypoactivity following adult septal lesions (Anderson, 1970; Douglas & Raphelson, 1966; Kaada & Bruland, 1960; Thomas et al., 1959; Zucker, 1965). These findings, however, contradict those of other studies which have reported hyperactivity (Dalby, 1970; Donovanick, 1968; Green et al., 1967; Nielson et al., 1965; Schwartzbaum et al., 1967) and increased exploratory activity following bilateral septal lesions (Douglas & Raphelson, 1966). Adult hippocampal lesions also appear to have had an effect on activity level. Animals in group LPH showed normal activity in the shuttle box and activity wheel, but were hyperactive in the open-field. Similarly, animals in group AH showed normal activity in the shuttle box and activity wheel, but showed a higher level of both activity and exploration in the open-field. Although none of these results either were statistically significant when compared to control animals, they were, nevertheless, in a direction

which supports the findings of previous studies which reported animals with hippocampal lesions to be hyperactive (Blanchard et al., 1970; Douglas & Isaacson, 1964; Green et al., 1967; Kimble, 1963; Leaton, 1965; Roberts et al., 1962; Sengstake, 1968; Teitlebaum & Milner, 1963), and to show higher levels of exploration in the open-field (Leaton, 1965; Nadel, 1968; Roberts et al., 1962; Sengstake, 1968).

Age-of-treatment was found to have a reliable effect on activity in the shuttle box, with groups in the "early" conditions being significantly more active than groups in the "late" conditions. This seems to have been strictly an age effect, and does not appear to have been triggered by a differential reaction to the training procedure since it was present on the two habituation days.

No reliable age-of-treatment effect was obtained on activity wheel, open-field activity, or open-field exploration scores. Inspection of the data, however, indicates that on the activity wheel scores the animals in group EA were hyperactive when compared to all other groups, including group LA which showed normal performance. These results are confusing, and imply that it might be possible for early amygdala lesions to have effects not observed after adult amygdala lesions. This is purely speculative, however, since the adult amygdala-operated animals did not display the expected hyperactivity. The opposite situation was found to exist in the open-field activity and exploration scores, where the early-operated amygdala animals performed more like the control animals than their hyperactive, hyperexplorative, adult-operated counterparts, indicating that recovery may have taken place

in that situation.

The early-operated posteroventral hippocampal animals performed like control animals on all activity measures. Failure of animals in group EPH to show the same hyperactivity in the open-field as animals in group LPH indicated that recovery took place for that situation.

Animals which had received septal lesions as infants performed in a fashion very similar to their adult-operated counterparts on the shuttle box activity, open-field exploration, and open-field activity measures. Activity wheel scores produced the largest differences between group ES and Group LS. In that situation animals in group ES failed to display the same hypoactivity as animals in group LS, indicating that a certain amount of recovery may have taken place following the infant septal lesions.

Social Interaction

Three measures of social interaction were recorded at one time: latency to first contact (LFC), total time spent in physical contact, and total number of contacts. Anesthetic effects were negligible and were again eliminated as a variable from further analyses. An analysis of variance having six treatment levels and two age-of-treatment levels was used to analyse LFC scores for all groups. No reliable treatment effects ($F(5, 67)=1.60$; $p<.1$), age-of-treatment effects ($F(1, 67)<.1$), or treatment by age-of-treatment interaction ($F(5, 67)<.1$). A summary table for this analysis is presented in Appendix 34. The treatment by age-of-treatment interaction is presented in Appendix 35. Average LFC scores (in seconds) for animals in each of the various

groups were: EC=38.50; LC=33.60; EF=28.28; LF=53.00; EAH=49.00; LAH=40.00; EPH=18.28; LPH=41.80; ES=59.00; LS=61.40; EA=25.28; LA=16.00.

These data show that, although no reliable treatment effects were obtained, large group differences did exist. The lack of statistical significance may have been due to the small number of observations per group. Similarly, although no reliable age-of-treatment effects were observed, LFC scores for animals in groups LF and LPH were considerably higher than LFC scores for their respective infant-operated counterparts.

Another analysis of variance having six treatment levels and two age-of-treatment levels was used to analyse total time spent in physical contact. Results revealed a reliable age-of-treatment effect ($F(1, 67)=5.37$; $p<.03$) and treatment by age-of-treatment interaction ($F(5, 67)=2.56$; $p<.04$), but no reliable treatment effect ($F(5, 67)=1.61$; $p>.1$). This analysis is summarized in Appendix 36, and the treatment by age-of-treatment interaction is presented in Fig. 10. The average times (in seconds) spent in physical contact by the various groups were: EC=146.80; LC=141.10; EF=166.42; LF=131.60; EAH=148.28; LAH=173.00; EPH=161.57; LPH=110.60; ES=155.42; LS=162.80; EA=156.85; LA=91.00. Individual comparisons made with a Newman-Keuls Test showed that the total time spent in physical contact by animals in group LA was reliably less than that of animals in groups LAH, and LF ($p<.05$). No other individual comparison yielded a reliable difference. Fig. 10 shows a definite lack of lesion effect among animals in the early-operated groups. A lesion effect (expressed as a reliable age-of-treatment effect in the analysis) is present among late-operated

Fig.10. Treatment by age-of-treatment interaction for total time spent in physical contact during testing for social interaction.

animals, however, with animals in group LS and LAH showing more time in physical contact when compared to control animals.

Another analysis of variance having six treatment levels and two age-of-treatment levels was used to analyse the total number of contacts. Results revealed a reliable age-of-treatment effect ($F(1, 67)=12.52$; $p<.002$), but no reliable treatment effect ($F(5, 67)<1$) or treatment by age-of-treatment interaction ($F(5, 67)=1.67$; $p>.3$). This analysis is summarized in Appendix 37, and the treatment by age-of-treatment interaction is presented in Appendix 38. Individual comparisons made with a Newman-Keuls Test revealed no reliable differences between any of the groups. The reliable age-of-treatment effect appears to have been due to the fact that animals in the early conditions consistently displayed a greater number of contacts than animals in the adult conditions.

Age-of-treatment had a reliable effect on time spent in physical contact. This effect seems to have been due to the fact that the animals in groups LA, LPH, and LF spent consistently less time in physical contact than their infant-operated counterparts. Animals in group LS spent only slightly more time in physical contact than animals in group ES, while animals in group LAH spent consistently more time in physical contact than animals in group EAH. It appears that none of the infant lesions had an effect on this measure. Adult lesions, however, had a disruptive effect for animals in groups LA and LPH, and a facilitatory effect for animals in groups LS and LAH. Although these scores did not differ significantly from those of control animals, they do support the findings of previous studies which had shown amygdala

lesions to decrease social interaction (Jonason & Enloe, 1971) and septal lesions to increase social interaction (Jonason & Enloe, 1971; Bunnell & Smith, 1966; Johnson 1972). The effects of hippocampal lesions on social interaction had not previously been examined, but the fact that the AH and PH lesions had opposite effects supports the theory that the hippocampus is a heterogenous structure (e.g., Jacobson, 1968; Raisman, 1966).

The experimental treatments had no statistically significant effects on the LFC scores. There was, however, a great deal of variability between groups, with animals in the amygdala groups showing extremely low scores (i.e., they were fast to make the first contact), and animals in the septal groups showing extremely high LFC scores (i.e., they were slow to make that first contact). These scores closely resemble those obtained on several of the activity measures and may, in fact be reflecting activity level rather than social interaction. This is an interesting finding, especially in light of the fact that this and other studies (e.g., Jonason & Enloe, 1971) have found septal lesions to enhance social interaction and amygdala lesions to disrupt it. It is not unlikely, then, as is suggested by the LFC data, that the lesion effects on social interaction are secondary to the effects on activity level. It seems likely, therefore, that the septal animals took longer to make the initial contact because they were hypoactive, and that this hypoactivity kept them from moving about a great deal after that contact had been made. Conversely, the hyperactive amygdala animals were much faster at making the initial

contact, but were unable to remain in physical contact because of their hyperactivity. Although a similar hyperactivity or hypoactivity was not reflected in the number of contacts, this may have been due to a "floor" effect, as all adult-operated animals showed a small number contacts during the social interaction test session. However, there was a significant age-of-treatment effect, with animals in the "early" conditions consistently displaying a greater number of contacts than animals in the "late" conditions. These results are similar to the results of the shuttle box activity measure, where animals in the "early" groups consistently yielded a greater number of spontaneous shuttle responses than animals in the "late" conditions. These results, then, imply that those effects which have been conventionally interpreted as lesion effects on social interaction may, in fact, be lesion effects on activity level.

Glandular Weights

The weights of the adrenals, thyroid, and testes were recorded for all animals, including those animals in the non-test conditions. Twelve six by two analyses of variance for unweighted means were used to analyses these data. Six of the analyses had six treatment levels and two levels of manipulation - test, non-test, and the other six analyses had six treatment levels and two age-of-treatment levels. Average weights of adrenals, thyroids, and testes for all tested and non-tested groups are presented in Appendix 39.

Adrenals The first analysis compared adrenal weights for all infant groups, including those in the non-test conditions. The results

of this analysis showed that neither treatment ($F(5, 134) < 1$) nor testing effects ($F(1, 134) = 2.96$; $p > .08$) were reliable. The second analysis compared adrenal weights for all adult groups, including those in the non-test condition. The results of this analysis showed that although no reliable treatment effect was observed ($F(5, 116) = 2.26$; $p > .05$), a reliable testing effect did occur ($F(1, 116) = 6.20$; $p < .02$). These results are summarized in Appendix 40, and are represented in Fig. 11. Individual group comparisons made with a Newman-Keuls Test, however, revealed no reliable differences between any of the individual groups. The reliable testing effects appear to have been due to the fact that the tested animals yielded consistently lower adrenal weights than the non-tested animals. This trend was also observed for animals in the "early" conditions, although in that case the testing effects did not attain statistical significance.

The next analysis, comparing adrenal weights for all infant and adult animals in the test conditions, revealed no reliable treatment effect ($F(5, 146) = 1.28$; $p > .2$) or age-of-treatment effect ($F(1, 146) = 1.96$; $p > .1$). Conversely, the analysis comparing adrenal weights for all infant and adult animals in the non-test conditions revealed a reliable treatment effect ($F(5, 104) = 2.49$ $p < .04$), and age-of-treatment effect ($F(1, 104) = 9.09$ $p < .004$). These results are summarized in Appendix 41, and are represented in Fig. 12. Individual group comparisons made with a Newman-Keuls Test revealed no reliable individual group differences. The reliable treatment effect appears to have been due to the fact that animals in the septal and amygdala groups consis-

Fig.11. Treatment by testing/non-testing interaction for adrenal weights for animals in the adult conditions.

Fig.12. Treatment by age-of-treatment interaction for adrenal weights for animals in the non-test conditions.

tently yielded smaller adrenal weights than animals in other groups. The reliable age-of-treatment effect obtained in this analysis seems to have been due to the fact that adrenal weights for animals in the "late" conditions were consistently heavier than adrenal weights of animals in the "early" conditions. Failure to obtain reliable treatment and age-of-treatment effects among animals in the test conditions suggests that the effects of testing confounded the lesion effects.

Thyroid The first analysis compared thyroid weights for all infant groups, including those in the non-test conditions. Results showed a reliable treatment effect ($F(5, 134)=3.55; p<.004$) and testing effect ($F(1, 134)=5.76; p<.02$). These results are summarized in Appendix 42, and represented in Fig. 13. Individual comparisons revealed no reliable group differences. The reliable treatment effect appears to have been due to a combination of the heavy thyroid weights yielded by animals in groups EC and EPH, and the low thyroid weights yielded by animals in the other groups. The reliable testing effect appears to have been due to the fact that animals in the test conditions consistently yielded lower thyroid weights than animals in the non-test conditions. The second analysis compared thyroid weights for all adult groups, including those in the non-test conditions. Results again showed a reliable treatment effect ($F(5, 116)=5.27; p<.001$) and testing effect ($F(1, 116)=4.35; p<.04$). Again, the individual comparisons made with a Newman-Keuls Test failed to show any significant group differences. The reliable treatment effect appears to have been due to a combination of the heavy thyroid weights of groups LC, LF,

Fig.13. Treatment by testing/non-testing interaction for thyroid weights for animals in the infant conditions.

and LAH, and the light weights of groups LPH, LA, and especially LS. The reliable testing effects appear to have been due to the fact that animals in the test groups again yielded consistently lighter thyroid weights than animals in the non-test conditions. These results are summarized in Appendix 43, and represented in Fig. 14.

The next analysis compared the thyroid weights for all infant and adult animals in the test conditions. Results showed a reliable treatment effect ($F(5, 104)=3.46$; $p<.007$), but no reliable treatment age-of-treatment effect ($F(1, 104)=3.41$; $p>.06$). The reliable treatment effect appears to have been due to the relatively low thyroid weights yielded by animals in the septal and amygdala groups. These results are summarized in Appendix 44, and represented in Fig. 15. Individual group comparisons, however, yielded no reliable individual group differences. The analysis which compared the thyroid weights for all infant and adult groups in the non-test conditions revealed a reliable treatment effect ($F(5, 146)=3.61$; $p<.005$) and age-of-treatment effect ($F(1, 146)=6.28$; $p<.02$). The reliable treatment effect appears to have been due to the consistently lower thyroid weights yielded by the animals in the septal and amygdala groups. The age-of-treatment effects appear to have been due to the fact that animals in the adult groups yielded consistently heavier thyroid weight than animals in the infant conditions. Individual comparisons again failed to reveal any reliable individual group differences. These results are summarized in Appendix 45, and represented in Fig. 16.

Fig.14. Treatment by testing/non-testing interaction for thyroid weights for animals in the adult conditions.

Fig.15. Treatment by age-of-treatment interaction for thyroid weights for animals in the test conditions.

Fig.16. Treatment by age-of-treatment interaction for thyroid weights for animals in the non-test conditions.

Testes The first analysis compared testes weights for all infant groups in the test and non-test conditions. Results showed a reliable treatment effect ($F(5, 134)=2.32$; $p<.05$) and testing effect ($F(1, 134)=5.43$; $p<.02$). Again, individual group comparisons made with a Newman-Keuls Test revealed no reliable individual group differences. The source of the reliable treatment effect is difficult to ascertain since no consistent pattern of lesion effect was observed. The only statement that can be made is that animals in the septal and amygdala groups yielded the lowest testes weights. The testing effect seems to have been due to the fact animals in the test condition yielded consistently lower testes weights than animals in the non-test conditions. These results are summarized in Appendix 46, and represented in Fig. 17. The analysis which compared the testes weights for all adult groups in the test and non-test condition also revealed a reliable testing effect ($F(1, 116)=5.94$; $p<.02$), but did not show a reliable treatment effect ($F(5, 116)=1.37$; $p>.2$). These results are summarized in Appendix 47. The individual group comparisons again failed to yield any reliable individual group differences. Although no reliable treatment effect was observed for the adult animals, groups LA and LS once again showed the lowest testes weights. The reliable testing effect again appears to have been due to the fact that animals in the test conditions yielded consistently lower testes weights than animals in non-test conditions.

The next analysis compared testes weights for all adult and infant animals in the tested conditions. The results of this analysis revealed a reliable treatment effect ($F(5, 136)=2.95$; $p<.01$), but no

Fig.17. Treatment by testing/non-testing interaction for testes weights for animals in the infant conditions.

reliable age-of-treatment effect ($F(1, 146) < 1$). These results are summarized in Appendix 48 and represented in Fig. 18. Although a Newman-Keuls Test failed to reveal any reliable group differences, animals in the amygdala and septal groups again yielded the lowest testes weights. A similar analysis compared the testes weights for all adult and infant animals in the non-test conditions. The results of this analysis revealed no reliable treatment effect ($F(5, 104) = 2.19$; $p > .05$) or age-of-treatment effect ($F(1, 104) = 1.57$; $p > .2$). Despite the lack of a reliable treatment effect, animals in the septal and amygdala groups again displayed the lowest testicular weights.

The differential treatment to which animals in the test and non-test conditions were subjected had a similar effect on the glandular weights of animals in both "early" and "late" conditions. In every instance the glandular weights of animals in the test groups were smaller than the glandular weights of animals in the non-test groups. It is difficult to ascertain, however, whether the testing served to lower glandular weights, or whether the prolonged isolation served to raise them. Handling, for example, is typically considered as being stressful for rats, and is generally followed by adrenal hypertrophy. In this study, the animals in the test conditions were extensively and gently handled during the course of training, and for the most part became very placid and easy to handle. Handling did not appear to be stressful in the least for most of the animals in the test conditions. It may be, then, that in this case the prolonged isolation suffered by animals in the non-test conditions was more stressful than the

Fig.18. Treatment by age-of-treatment interaction for testes weights for animals in the test conditions.

handling received by animals in the test conditions.

The only reliable treatment and age-of-treatment effects on adrenal weights were observed among animals in the non-test conditions. Failure to obtain similar reliable effects among animals in the test conditions suggests that these effects may have been confounded by testing effects. The reliable age-of-treatment effects revealed that the adrenal weights of animals in the "early" groups were consistently below those of animals in the "late" groups. It will be recalled that animals in the former condition began training at 60 days of age while animals in the latter conditions began training at 120 days. The results suggest, then, that the younger animals were more susceptible to these handling effects than the older animals.

Several of the analyses showed significant treatment effects and, although the individual comparisons revealed no reliable group differences, the animal with septal and amygdala lesions consistently yielded lower adrenal, thyroid, and testicular weights than animals in the other groups. The fact that animals in the septal and amygdala groups had the lowest adrenal weights is contrary to the findings of previous studies which had reported adrenal hypertrophy following lesions in these areas (Bohus, 1961; Endroczi & Lissack, 1960; Greer & Yamada, 1959; Kling et al., 1960; Koekegami et al., 1955; Martin, 1958; Montgomery & Berkut, 1969; Seggie, 1968; Usher et al., 1967). It should be noted, however, that for the most part these studies were conducted solely for the purpose of investigating the lesion effects on the adrenals. Consequently, the animals in these studies were

generally not subjected to any behavioural training or testing, nor were they maintained for very long periods of time after surgery. Therefore, the lesion effects investigated were relatively more immediate than those investigated in the present study, and were not confounded by effects of handling, training and testing, or prolonged isolation. Furthermore, previous studies have generally shown that the increases in adrenal weights are usually transient, and typically peak at approximately two weeks after surgery in adult-operated animals (Greer & Yamada, 1959; King et al., 1960; Yamada & Greer, 1960).

The observation that animals with amygdala lesions had low thyroid weights is consonant with the findings of previous studies (Koikegami et al, 1955, 1958) which had reported atrophy of the thyroid following amygdala destruction. The low thyroid weights yielded by both septal and amygdala animals, though not statistically significant, may be indicative of an underlying thyroid dysfunction. Deficiencies in thyroxin, the major hormone produced by the thyroid, can cause severe metabolic disorders. There may possibly be a connection, then, between the low thyroid weights found in animals with septal and amygdala lesions and the low body weights yielded by these same animals. Although it is difficult to disprove that this relationship is merely superficial (i.e., the animals were smaller, and therefore their thyroid weights were smaller) and not direct (i.e., thyroid weights were lower because of thyroid dysfunction, and body weights were lower because of the resulting metabolic disorder), the possibility neverthe-

less remains that a thyroid deficiency and resulting metabolic disorder may have been caused by the amygdala and septal lesions. Thyroid activity is almost entirely determined by the secretion of thyrotrophic hormone by the anterior pituitary gland, and both the formation and secretion of thyroxin are affected by this hormone. Although the hypothalamus plays the major role in controlling hypophysial function, the septum and amygdala may very well exert their influence on the anterior pituitary by modulating hypothalamic activity. Damaging the amygdala or septum may have served to remove this modulatory influence from the hypothalamus, with the resulting effects on the thyroid.

The observation that amygdala lesions caused a decrease in testicular weights is consonant with the findings of previous studies (Greer & Yamada, 1960; King et al., 1960; Yamada & Greer, 1959) which had reported testicular atrophy following amygdala lesions. Testicular function, like thyroid function, is under hypophysial control. It is possible, then, that the effects of amygdala and septal lesions on testicular weights may have resulted from the removal of a modulatory influence of these structures from the hypothalamus.

General Discussion And Conclusions

Summary

The major results obtained in the present study can be summarized as follows: 1) Severe deficits in CER and CAR acquisition following adult amygdectomy; 2) Severe deficits in CER acquisition (no sparing), but normal CAR acquisition (sparing) following infant amygdectomy; 3) Slight deficits in CER acquisition, and significant facilitation in CAR acquisition following adult septal lesions; 4) Slight deficits (no sparing) in CER acquisition, and significant facilitation (no sparing) in CAR acquisition following infant septal lesions. 5) Significant deficits in CER acquisition, and significant facilitation in CAR acquisition following adult PH lesions; 6) Normal CER acquisition (sparing), and normal CAR acquisition (sparing) following infant PH lesions.

Sparing/Recovery of Function

The major hypothesis put forth at the start of this study was that the regions of the limbic system would show poorer sparing of function following early damage than is commonly observed following early damage to areas of the cortex. This was expected because it is generally believed that the subcortical portions of the brain are derived from the phylogenetically older paleopallium and archipallium, while cortical tissue is derived from the phylogenetically newer neopallium. Also, since ontogeny does, in many instances, recapitulate phylogeny, then subcortical structures may be more functionally complete at birth or shortly thereafter than cortical areas. Therefore, it was

suggested that early subcortical damage may essentially be eliminating regions which are already functionally mature, and that the mechanisms associated with these regions cannot be compensated for following early damage. Failure of the infant-operated amygdala animals to show sparing of function on the CER task, and of the infant-operated septal animals to show sparing on both CER and CAR tasks supports this hypothesis. However, the excellent sparing shown by the animals in group EA on the CAR task, and by the animals in group EPH on both CER and CAR tasks makes the validity of this hypothesis questionable.

The task-specific effects of sparing of function observed in the present study are not unlike the task-specific sparing effects reported by Isaacson and his associates (Isaacson et al., 1968; Nonne-man & Isaacson, 1973) following early hippocampal aspiration in the cat. Basically, these researchers proposed two theories to explain these task-specific effects. The first explanation suggested that those tasks for which the animal showed sparing of function were solved by the animals' developing new strategies to cope with those problems. An implicit assumption of this explanation is that the early-operated animals had not had as much opportunity as the adult-operated animals to develop definite strategies or tactics to cope with certain problems. As a result, early brain damage was more easily followed by the development of new strategies, an accomplishment too difficult for the adult-operated animals in which definite strategies had already been well established before surgery.

The only behavioural measure recorded in the present study which

could possibly be applied to test this hypothesis was the trial-to-first-avoidance score for each animal in the CAR situation. It was assumed that, if the infant-operated animals were actually developing new strategies during the course of CAR training, then they might not start avoiding at the same time as the control animals, and might, instead, start avoiding sooner or later than the controls. Those infant-operated animals which showed sparing, however, yielded trials-to-first-avoidance scores which were similar to those of the control animals, indicating that the strategies used by those operated animals for solving the problem were probably similar to those used by the control animals, and that these strategies were probably present prior to the start of training. It should be stressed, however, that this was a relatively weak measure, and this first hypothesis should not necessarily be discounted because of these results. This measure could not, for example, account for any new strategies which may have been developed prior to the start of training by those animals which displayed sparing of function.

A slight modification or extension of the first hypothesis could hold that those animals which received lesions as adults were deprived of access to vital early experience, and that this caused the observed deficits or facilitation in performance. Those animals which showed sparing of function, on the other hand, may have had this vital experience after surgery, and may thus have been able to take greater advantage of it. Unfortunately, this hypothesis is extremely difficult to test.

The second explanation offered by Isaacson and his associates, as well as others (e.g., Beach, 1938; Tsang, 1937, a, b), is that some form of functional or structural reorganization takes place, but that this reorganization is more difficult or impossible in the older, more rigid brain. According to this theory, functionally related areas of the brain form a "system" to govern an animal's behaviour in certain situations. If early brain damage destroys a portion of this system, then the remaining tissue can compensate for the damaged area, taking over its functions. This theory has a good deal of experimental support. Several authors, for example, have shown that a decrease in the degree of sparing of function will occur if enough functionally related areas of the brain are destroyed shortly after birth (e.g., Doty, 1961; Goldman et al, 1970, a, b; Kennard, 1938; Kling & Tucker, 1967, 1968). If functionally unrelated areas are destroyed, on the other hand, then the decrease in sparing of function is not observed (Tucker & Kling, 1969).

Existing neuroanatomical evidence could also be interpreted as supporting the possibility of a structural reorganization proposed in this theory. Altman and Das (1965) reported that the number of differentiated granule cells in the dentate gyrus of the rat increases six-fold through cell division between 14 and 28 days of age. Since the dentate is the chief target of the temporoammonic tract, the major source of input to the hippocampus, these authors suggested that hippocampally-related behaviours would not be present in the rat until approximately one month after birth. Furthermore, since Altman

and Das (1967) found that the hippocampus of the guinea pig in a relatively advanced stage of development at birth, they predicted that these animals would possess hippocampally-related behaviours at birth or shortly thereafter. Both of these predictions were tested and supported by Douglas, Peterson, and Douglas (1973), who found that infant rats typically began to display spontaneous alternation at approximately 28 days of age, while in the guinea pig alternation was at a near-adult level within the first 10 days after birth. It seems possible, then, that destruction of a portion of the brain prior to completion of its maturational processes could more easily be followed by some form of structural reorganization than destruction of that same structure after it had achieved its final level of maturation.

This structural reorganization theory of sparing of function may be applied to the results of the present study. It should be stressed, however, that since certain tasks were not compensated for, this structural reorganization is not completely effective in overcoming early damage. This implies, then, that there may exist a portion of a "system" which plays a greater role in certain tasks than other areas of that system, and that destruction of that portion would have a permanent task-specific debilitating effect. If the theory is expanded to include this hypothesis, then the results of the present study suggest that the amygdala plays a major role in the mechanism involved in CER acquisition, and that this mechanism is firmly established in early infancy. Furthermore, the destruction of the amygdala at any time can have a permanent debilitating effect on this mechanism.

A similar argument could be put forth for the septum, especially with regard to active avoidance acquisition, except that in this case the effects are facilitatory. Likewise, it can be argued that the role of the amygdala in active avoidance acquisition was not a major one, nor was the role of the posteroventral hippocampus in either CER or CAR acquisition. As a result, although adult lesions in these areas affected acquisition of these tasks, infant lesions were compensated for by the remaining tissue of the "system" involved.

One obvious extension of the Altman and Das (1965, 1967) and Douglas et al. (1973) studies would be a lesion study to determine if the neurophysiological results would support the neuroanatomical and behavioural findings with regard to hippocampal maturity. Hippocampal lesions in the rat could, for example, be made at various stages of development to determine at which point the bilateral lesions will produce effects similar to those produced in adult animals. If the results of such a study were to demonstrate that lesions made at approximately 28 days of age (and not before) had effects similar to those produced in adult animals, then those results would support the neuroanatomical and behavioural findings. Similar neuroanatomical, behavioural, and neurophysiological studies could then be considered to trace the developmental processes of other subcortical areas.

To summarize, the results of the present study, in conjunction with the results of Isaacson and his associates suggest that several areas of the brain may form "systems" which govern an animal's behaviour in certain situations. Early damage to a portion of such a

system may be compensated for by the remaining parts of the system taking over the function of the damaged area. Furthermore, a certain portion of a system may play a major role in a particular task, and destruction of that portion at any time would have a permanent task-specific debilitating effect.

The question of whether the phenomenon observed in this study is truly sparing of function, and not recovery, is open to debate. The differences between recovery and sparing of function were discussed earlier (p. 11). According to the definitions made at that point, the only inferences which can properly be made from the present results must involve sparing and not recovery of function since there were no tests for functional loss immediately postoperative. However, in light of the preceding interpretation of the results, it seems that whether one terms the phenomenon sparing or recovery may depend on whether one is referring to the function or to the neural mechanisms underlying the function. On the one hand, for example, if one is concerned with whether or not a function is present in an infant-operated adult animal, without being concerned with whether the function was ever destroyed, or with how it was spared, then the phenomenon could be termed sparing of function. On the other hand, if one believes that (the reason) the function is present in the adult animal is because some form of structural or functional reorganization took place following early damage, then the phenomenon could be better termed recovery. An important step which must now be taken in the area of sparing/recovery of function, therefore, is the development of new techniques for testing very young animals. This must be done to determine whether

those deficits which were "spared" following early damage are present immediately postoperative. If such deficits are found, then the term recovery could be used more confidently.

One final point should be made with reference to the fact that infant PH lesions resulted in excellent recovery on both CER and CAR tasks: the possibility exists that the early and late PH lesions were not equivalent. although early and late PH lesions were equivalent immediately postoperative (p214), the late PH lesions did appear larger at histology at the end of the study. A detailed degeneration study would probably best serve to clarify this point.

Glandular Weights

The second hypothesis proposed at the start of this study was that, since the limbic system had been implicated in the regulation of endocrine function, then early limbic lesions would influence the development of the animals involved. This hypothesis was partially supported by the fact that septal and amygdala lesions significantly effected normal weight gain. The fact that these lesions had similar effects at 10 and 60 days of age suggests that development, in this case, be regarded as a continuous process and not one that ends when an animal reaches adulthood. These findings were not surprising, especially in light of the hypothalamic connections of the amygdala (e.g., Cowan et al., 1965) and septum (e.g., Raisman, 1966). The intake measures taken to determine the source of the lesion effects on body weights indicate that these effects were probably due to metabolic disorders. This hypothesis could be better tested by more extensive intake studies and by direct measurement of basal metabolic rates.

The most consistent results obtained from glandular weights measured in this study were that the amygdala and septal lesions caused slight atrophy of the adrenals, thyroid, and testes. Failure, for the most part, of these effects to reach statistical significance was likely due to the fact that these weights are so small to begin with

and the variability so great from animal to animal. More precise lesion effects on the glands could probably be determined by microscopic study of these glands and/or measurement of the level of related hormones within the blood.

It had been suggested earlier that the lesion effects on the glandular weights may have been related to the lesion effects on body weights. It is also possible that the lesion effects on learning may in some way be related to both the effects on body weights and glandular weights, i.e., a lesion may have caused a glandular dysfunction which resulted in a hormonal imbalance, this imbalance in turn resulted in abnormal weight gain and retardation on certain tasks. If this is the case, then it may be possible to compensate experimentally for both the retardation and the abnormal weight gain by compensating for the hormonal imbalance. This is, of course, a purely speculative notion, but testable nevertheless.

The data obtained from the activity, exploration, and social interaction did not follow any specific pattern. The results generally indicated that the task-specific recovery effects observed on the CER and CAR were present in these supplementary measures as well.

Adult Limbic Lesions

The abnormal behaviour displayed by the adult-operated animals may yield some information about the mechanisms which were disrupted by the various limbic lesions. Adult amygdala-operated animals were severely retarded in CER and CAR acquisition. This deficit does not appear to have been due to a general inability to learn, since these

same amygdalectomized animals were able to acquire the leverpress response with normal ease. Nor does the deficit appear to have been due to an insensitivity to footshock, since these animals responded as vigorously as other animals to the noxious stimulus (although specific shock thresholds were not empirically determined).

These effects of amygdalectomy could possibly be explained by two existing theories of amygdala function. The first theory views the amygdala as playing a vital role in an animal's ability to display normal emotional reactivity. This theory regards the deficits as being due to a reduction in the emotional responsiveness of the amygdalectomized animals. Although this theory has been proposed by several authors (e.g., Kluver & Bucy, 1938; Plotnick, 1968; Robinson, 1963; White, 1971) who observed deficits in amygdalectomized animals in their ability to display normal emotional reactivity, the hypothesis has never been adequately investigated. Research which has thus far examined the emotional responsiveness of amygdalectomized animals has been concerned exclusively with the external responses emitted by the animals. Findings from such research have been inconsistent. Amygdalectomized dogs (Fuller, Rosvold, & Pribram, 1957) and monkeys (Thompson et al., 1969; Rosvold, Mirsky, & Pribram, 1954), for example have been shown to be capable of emitting normal or accentuated fear responses in social situations. On the other hand, authors have reported amygdalectomized animals to show increased rage threshold (Schreiner & Kling, 1953; Shealy & Peele, 1957), and decreased CER (Brady et al., 1954) and aggressiveness in wild rats (Galef, 1970).

As yet, however, no study has investigated whether normal autonomic responses are present in amygdalectomized animals. It remains to be determined, for example, whether amygdalectomized animals can manifest autonomic responses which are commonly observed in normal animals in fear-provoking situations (i.e., decrease in heart rate and respiration, and increase in blood pressure). If the amygdalectomized animals do emit the normal autonomic responses while failing to acquire the fear-motivated tasks (e.g., CER, CAR), then this first hypothesis could be discounted since it could be argued that these animals were displaying emotional responsiveness. The hypothesis would be supported, however, if the amygdalectomized animals failed to emit the normal autonomic responses as well as failing to acquire the fear-motivated responses.

The second theory views the amygdalectomized animals as capable of normal emotional responsiveness, but being incapable of forming the appropriate associations between the conditioned stimulus (CS) and unconditioned stimulus (UCS). This explanation is consonant with the commonly held theory that the amygdala somehow aids in the formation of the association of a neutral stimulus with a noxious event (Egger, 1972; Gloor, 1972; Goddard, 1964; Pellegrino, 1968; Weiskrantz, 1956). Although the role played by the amygdala in this association is far from clear. Gloor (1972) claims that the amygdala aids in the establishment of this association by acting as a link between the information stored in the neocortex and the basic drive mechanisms centered in the hypothalamus. According to Gloor, although these mechanisms are

usually activated by unlearned, internal stimuli such as homeostatic imbalances, input from limbic structures such as the amygdala can render these mechanisms more flexible, allowing them to respond to a greater variety of learned, external stimuli. Hypothalamic activity, then, modulated by the amygdala, can activate those mechanisms responsible for the expression of fear, thus endowing a neutral stimulus with emotional connotation. The general idea expressed by this theory can be applied to the experimental findings of this study, although the details of the theory require further investigation. The involvement of the neocortex, for example, to the exclusion of subcortical areas in the storage of cues in fear-related learning situations must be questioned. This is especially so in light of the findings of Carlson (1967), who demonstrated that the emotional and cue components of passive and active avoidance situations can be stored subcortically. The findings of Carlson's study suggest that the theory, as described by Gloor, should be expanded to include subcortical storage of emotional and cue components of learning situations. If this theory is accurate, then one would expect that once the appropriate associations had been formed between the CS and UCS, then amygdalectomy should not disrupt them. This has, in fact, been shown to be the case. Brady et al., (1954) reported that bilateral amygdala lesions disrupted the acquisition of a two-way active avoidance response if the lesions were produced prior to training. Similar lesions produced after the response had been acquired, however, failed to disrupt its retention. Similarly, Weiskrantz (1956) found that amygdala lesions which disrupted the

acquisition of active avoidance and conditioned suppression responses if produced before training, failed to disrupt the retention of these responses if produced after the responses had been established.

If this explanation is applied to the present study, the retarded CER and CAR acquisition observed in the amygdalectomized animals could be attributed to the failure of the animals to associate the relevant cues (i.e., the CS's: tone in the CER and light in the CAR) with the UCS (i.e., footshock). Failure to form this association, then, resulted in a failure on the part of these animals to alter their behaviour (suppress bar-pressing response, or learn to shuttle at appropriate time) as the control animals did.

Which of these two hypotheses can best explain the deficits observed in the amygdalectomized animals could be clarified by studies examining autonomic responses during CER and CAR training, retention of an acquired CER and CAR following amygdectomy, and bar-press rates during various components of a CER session.

The amygdala lesions produced in the present study were large, and typically destroyed most of the amygdaloid complex. It should be noted at this point, however, that this complex is made up of several nuclei, and that these nuclei are suspected of having distinct functions. Attempts have been made to localize specific functions in the various components of the amygdaloid complex (although the results have not always been consistent). Bresnahan and Routtenbert (1972), for example, found that low intensity stimulation (5uA) of the medial amygdaloid nucleus of rats during acquisition of a passive avoidance learning

task disrupted retention of that task. Similar results were not obtained if their stimulating electrodes were centered in other amygdala or non-amygdala areas, suggesting that this nuclear group may subserve some learning function for the avoidance task used in that particular study. Also, Green et al., (1957) found that only lesions restricted to the basal and lateral nuclei of the amygdala of cats resulted in hyperphagia, while lesions restricted to the anterior region of the amygdala resulted in aphagia. Wood (1958), on the other hand, found that hyperphagia was caused only by lesions restricted to the medial and central nuclei of the amygdala. The importance of these results is that they suggest that large amygdala lesions may have multiple effects. The deficits observed following such lesions, then, may result from the disruption of several mechanisms, rather than the disruption of a unitary function.

The adult-operated septal animals of the present study were slightly deficient in withholding a learned bar-press response during the CS in the CER situation (although the deficit was not statistically significant). During CAR testing, however, these same animals learned to avoid the UCS at a significantly accelerated rate. These findings could possibly be explained by either of two current theories of septal function. The first theory proposes that the septum exerts an inhibitory influence on learned responses, and that removal of this inhibitory influence through septal destruction releases those behaviours which are highest in habit strength for a particular situation (Douglas, 1966; Gerbrandt, 1965; Hamilton, 1970; Kaada et al.,

1962; McCleary, 1961, 1966; Schwartzbaum et al., 1964). Removal of this inhibitory influence would make it more difficult for an animal to suppress a response high in habit strength so as to be able to acquire new responses..

If applied to the present findings, this theory would explain that one of the behaviours which was highest in habit strength in the CER situation was the bar-press response. Under normal circumstances, the inhibitory influence of the septum would enable an animal to suppress that response and allow the formation of a CER. Septal destruction, however, removed that inhibitory influence, making it more difficult for an animal to inhibit the bar-press response. Similarly, the behaviour highest in habit strength in the CAR situation was escape from, or avoidance of, the UCS. Again, under normal circumstances that behaviour may have taken longer to become firmly established as an animal would test other competing responses (e.g., attempting to climb out of the apparatus, or trying to claw through the grid floor) in search of the most effective one. Septal destruction, then, removed a certain amount of inhibition from this response, allowing it to become more easily established.

Although this theory could be used to explain the present data, its acceptability is weakened by the fact that septal lesions are not always followed by the type of response disinhibition described above. Sodetz (1970), for example, found that animals with septal lesions exhibited superior acquisition and performance on a Sidman avoidance task (Sidman, 1953). In a Sidman avoidance paradigm, an

an animal is shocked if it withholds a response (e.g., bar-press, or moving to a safe compartment) longer than an interval determined by the experimenter. The most efficient manner of responding in such a situation is for the animal to withhold its response until just before the end of the intershock interval.

A second, and perhaps more appropriate, theory which could be used to explain the present findings hypothesizes that the septum serves to dampen the increment in response strength normally caused by a reinforcement, thus allowing an animal to acquire new responses (Fried, 1969, 1970; Zucker, 1965; Zucker & McCleary, 1964). A given reinforcement, therefore, would produce a greater increment in response strength in animals with septal lesions, causing the animals to overrespond to the motivating (noxious or appetitive) stimuli, while impairing their ability to suppress previously-reinforced responses.

Applied to the present findings, this theory would explain that in the CER situation each food-pellet reinforcement brought about an increment in response strength which was somewhat dampened by the action of the septum. Through septal destruction, then, each reinforcement produced a greater increase in response strength than would normally have occurred. As a result, the animals with septal damage were not as efficient as the normal animals in suppressing the bar-press response. Similarly, in the CAR situation each successful avoidance brought about a much greater increase in the habit strength of that response than would normally have occurred, resulting in a more rapid acquisition of the CAR

These two theories need not be considered mutually exclusive. Rather, it seems more likely that some combination of the two may best serve to explain septal function. Both theories, for example, regard the septum as being part of a central inhibitory system, with the first theory viewing the septum as suppressing learned responses, and the second viewing it as suppressing the reinforcement effects which would strengthen the establishment of a response. It seems reasonable to assume that, in a learning situation, an association is formed between the reinforcement effects and the response that produced them, and that this association must take place at some central location. It is possible, then, that the system exerts its inhibitory influence at that location, acting to dampen the association between response and reinforcement. This inhibitory influence would have an adaptive value for the normal animal, in that it would protect the animal from becoming "fixated" or locked on to the first response that had any positive reinforcing value in a particular situation, leaving the animal free to attempt alternate responses which might prove more beneficial. This inhibitory septal influence is probably achieved through a complex interaction of the septum with the hypothalamus and hippocampus with which it is interconnected (Raisman, 1966). Septal destruction, then, would remove this inhibitory influence, allowing greater increments to occur in the strength of the response-reinforcement association with each response-reinforcement pairing. This combination of the two theories could explain why it is more difficult for animals with septal lesions to give up learned responses when they are no

longer appropriate, since it would predict that these animals had acquired a greater than normal habit strength for reinforced responses. Facilitated rejection of a noxious stimulus, such as increased quinine rejection (Donovick, Burrig, & Zuromski, 1970) and facilitated active avoidance acquisition (e.g., Donovan, 1968; Hamilton, 1969; King, 1958; Trafton, 1970) could be attributed to the relative reinforcing value of neutral stimuli, such as ordinary water or an unelectrified grid, when compared to noxious stimuli such as a quinine solution or footshock. These normally neutral stimuli could then act as reinforcers in the response-reinforcement association which is facilitated by septal destruction.

According to this theory, then, animals with septal lesions should not display as many competing responses during training as control animals. This was, in fact, observed in the present study, particularly during CAR training. Although no attempt was made to record the frequency of competing responses such as attempting to climb out of the apparatus or claw through the grid floor, these behaviors were observed to occur less among the animals with septal lesions than among other animals. A controlled study investigating the frequency of competing responses among animals with septal lesions might yield more information concerning the accuracy of this hypothesis.

The septal lesions produced in the present study were quite

large, generally destroying most of the septal nuclei. Several researchers, however, have suggested that the septum does not serve a unitary function (e.g., Holdstock, 1970; Lubar & Numan, 1973, Schwartzbaum et al., 1967; Van Hoeson et al., 1969) and that those effects which are observed following large septal lesions are probably the result of a combination of several different effects (Fried, 1972). Discrete lesions of the medial septal nucleus, for example, have been shown to increase intertrial activity during two-way active avoidance training (Donovick, 1968), and to disrupt food-motivated DRL performance (Ellen, Wilson, and Powell, 1964), position reversal (Hamilton, 1970), and spatial reversal acquisition (Donovick, 1969; Thompson & Langer, 1963). Passive avoidance deficits (Hamilton et al., 1970) and increased quinine rejection (Donovick et al., 1970) have been observed following lesions restricted to the lateral septal nucleus, while deficits in passive avoidance and position reversal acquisition have been reported following stimulation of the lateral septal nucleus (Kasper, 1965). In addition, Carey (1969) found that rats with lesions restricted to the posterior region of the septum ran more slowly in a straight alley and bar pressed less in a fixed-ratio (FR) schedule for water reinforcement when compared to normal animals; rats with lesions restricted to the anterior region of the septum, on the other hand, ran faster in the straight alley and bar pressed more for water reinforcement when compared to control

animals. Anatomically, the afferent and efferent connections of the different septal regions also vary (Raisman, 1966). It appears that, with the septum, as with the amygdala, large lesions may be producing multiple effects, and the observed behavioural abnormalities may be due to a disruption of several mechanisms rather than a single function.

Existing neuroanatomical (Nauta, 1956; Raisman et al., 1966), neurophysiological (Adey, 1961; Brazier, 1970; Elul, 1964, a, b; MacLean, 1959; Votaw & Lauer, 1963), neurochemical (Grant & Jarrad, 1968; Purpura, 1959), and behavioural (Fried, 1971; Kimura, 1958; Nadel, 1968) evidence suggests that the hippocampus is a heterogeneous structure. Therefore, the finding that AH and PH lesions had differential effects has a good deal of support from previous studies. Since the AH lesions had no observable effects on any of the behavioural measures used in this study its function cannot readily be discussed. Animals with adult-accrued PH lesions, however, were significantly retarded in their ability to acquire the CER, while acquiring the CAR at a significantly accelerated rate. It appears that these findings can be explained by existing theories of hippocampal function. Several authors have suggested that the hippocampus plays a major role in the control of attentional processes through the inhibitory modulation of sensory input (Douglas, 1967; Douglas & Pribram, 1966; Isaacson, 1966; Kimble, 1968). According to Jarrad (1973) this is accomplished by the inhibitory action of

the hippocampus on lower structures which serve to control arousal and activation levels. Damaging the hippocampus, then, alters the general arousal or drive levels which affect the manner in which an animal reacts to the environment.

According to this theory, when an animal is placed in a learning situation the hippocampus inhibits the animal's attention to, or reception of, the stimulus which normally initiates a response, especially when the response is no longer appropriate. According to Kimble (1968), the purpose of this inhibitory hippocampal action is to allow the animal to disengage its attention from one stimulus to a new or more important stimulus. If applied to the CER situation, this theory would explain that in the normal animal the hippocampus works to partially inhibit reception of the relevant stimuli which prompt the animal to lever-press, allowing the animal to devote a certain amount of its attention to other environmental events. Then, when a more important stimulus such as the tone is presented, the animal can readily withdraw its attention from lever pressing. Hippocampal destruction, then, removes this inhibitory effect, allowing the animal to devote a greater amount of attention to the response-controlling stimulus. As a result, if the environmental contingencies are rearranged, or if a more important stimulus is introduced, the animal is unable to focus its attention on it, and continues to lever press. In the CAR situation hippocampal lesions allowed the animal to focus a greater than normal amount of its

attention on the relevant stimulus. In that case, however, it had a beneficial effect since it prevented the animal from focusing its attention on irrelevant stimuli, thus allowing it to acquire the avoidance response more rapidly.

Several studies have shown that the hippocampus is capable of producing this inhibitory effect. The hippocampus has, for example, been shown to be reciprocally interconnected with the brainstem reticular formation and the diffuse thalamic system, exerting an inhibitory influence on the former (Adey, Segundo, & Livingston, 1957; Grastyan, 1959; Guillery, 1955; Nauta, 1953; Redding, 1967), and a facilitatory influence on the latter (Nauta, 1956; Redding, 1967). Kaada, Jansen and Anderson (1953) have shown that cortical activation patterns that are accompanied by behavioral arousal or attention can be elicited by hippocampal stimulation. Feldman (1962) has shown that the hippocampus can regulate input to the hypothalamus from the medial lemniscus. Finally, it has been demonstrated that the hippocampus can modify most sensory input (Adey, et al., 1957; Redding, 1967). There appears to be little doubt, then, that the hippocampus is in a position to exert a great deal of inhibitory control over attentional processes by modulating sensory input. Although the method by which this is accomplished is uncertain, Nauta (1956) has suggested that it may be primarily affected by virtue of neural connection from the hippocampus mediating postsynaptic inhibition onto neurons in the arousal system.

This theory of hippocampal function can explain most of the effects observed in hippocampectomized animals: difficulty in habituating to a novel environment (e.g., Limble, 1963; Leaton, 1965; Sengstake, 1968); deficits in passive avoidance acquisition (e.g., Kimura, 1958; Teitelbaum & Milner, 1963); facilitated active avoidance acquisition (e.g., Isaacson et al., 1961); difficulty in learning successive but not simultaneous discriminations (Kimble, 1963; Lash, 1964); and reversal impairment (Kimble & Kimble, 1965). Additional studies could further examine the validity of this theory. Studies could, for example, investigate the effects of hippocampectomy on habituation to a novel environment, similar to the studies of Leaton, Sengstake, and Kimble cited above. In these proposed studies, however, the animals would be permitted to explore the novel environment before being hippocampectomized, and then returned to the same environment after surgery. If failure to habituate is due to a faulty attention mechanism, the animals hippocampectomized after being permitted to explore the novel environment should not display the typical perseverative exploration (since they had been able to explore the environment with an intact attention mechanism, and had thus had an opportunity to become relatively familiar with it).

This theory could also be tested in a double runway (RW), double goalbox (GB) situation. Amsel and Rousal (1952) trained rats to run in such an apparatus and, after the animals had achieved a stable running rate, withheld the reinforcement in the first GB on

one-half of the trials. On trials in which the reinforcement was absent, the animals showed consistently faster running speeds in RW 2. If the behavioural deficits observed in hippocampectomized animals are due to a faulty attention mechanism (preventing them from being aware of changes in the situational contingencies), then these animals should not display similar increases in running speed in RW 2.

The discussion of hippocampal function has thusfar concerned itself only with the hippocampus as a whole. However, cytoarchitectonically the hippocampus can be divided into various cell fields which are commonly referred to as cell fields CA1, 2, 3, and 4. It may be more accurate, then, to attribute various hippocampal functions to the different cell fields rather than to the hippocampus as a whole. Raisman and his associates (Raisman, 1966; Raisman et al., 1966) have demonstrated, through neurohistological investigations, that the cell fields in the hippocampus of the rat have differential extrahippocampal connections. They have suggested that these cell fields, and the areas with which they are interconnected, form two distinct neuronal systems, one involving primarily cell field CA1, and the other primarily cell fields CA3 and 4. The complex manner in which fields CA2 is arranged made it too difficult to determine its exact projections. Cell field CA1 was found to project to the medial and lateral mamillary nuclei and to the anterior thalamic nuclei. From the anterior thalamic nuclei projections are

relayed to the cingulate gyrus, and from there to the entorhinal area. From the entorhinal area, the projections are sent back to field CA1 to complete one neuronal system. Cell fields CA3-4 were found to send their fibers to the lateral and medial nuclei of the septum, and to the nucleus of the diagonal band. The medial nucleus of the septum and the nucleus of the diagonal band send fibers back to the cell fields CA3 and CA4 to complete the second neuronal system. Raisman et al., (1966) suggest that the dentate gyrus serves primarily as a link between these two neuronal systems.

Although the various cell fields are generally arranged in a complex manner, they are relatively easy to investigate in the rat, in which field CA1 is the outermost layer and lies primarily in the anterodorsal region of the hippocampus; cell fields CA3 and CA4 are located primarily in the caudal half of the hippocampus (Raisman et al., 1966). These two regions correspond roughly to the hippocampal loci destroyed in the present study. Jarrad (1973) has suggested that, although anterodorsal and posteroventral hippocampal lesions do not completely destroy cell fields CA1 and CA3-4, respectively, such lesions could adequately serve to differentiate the functions of these cell fields. If Jarrad's hypothesis is accurate, then the results of the present study suggest that, since the AH lesions had no major effects, destruction of cell field CA1, or a major portion of it, had little effect on any of the tasks used in this study. In addition, the results suggest that

cell fields CA3-4 play an important role in CER and CAR acquisition, and destruction of these cell fields has a disruptive effect on the acquisition of these tasks.

It is difficult to hypothesize what the functions of the various cell fields, and the neuronal systems they comprise, really are. Jarrad (1973) has suggested that since the cells from field CA1 project to the anterior thalamic nuclei and the hypothalamus, then these cells are concerned primarily with incentive and motivation. Indeed, experimental manipulations of this cell field have, in some instances, been shown to affect eating (Milgram, 1969) and drinking (Grant & Jarrad, 1968). Although the anterodorsal hippocampal lesions failed to have a significant effect on food and water intake in the present study, it was mentioned that these measures were rather crude, and Jarrad's hypothesis should not be refuted on the basis of these findings. Jarrad has also suggested that, since cells in fields CA3 and CA4 project to the septum and the diagonal band, then these cells are concerned primarily with response inhibition. Experimental manipulations of these cell fields has been shown to disrupt acquisition of a one-way passive avoidance task (Liss, 1968) and DRL performance (MacDougall, Van Hoesen, & Mitchell, 1969). This hypothesis is supported by the present findings (i.e., retarded CER acquisition and facilitated CAR acquisition). Therefore, it appears that a more molecular approach may be more appropriate for the investigation of hippocampal function.

In conclusion, it appears that adult bilateral lesions of the amygdala, septum, and posteroventral hippocampus had differential effects on CER and CAR acquisition. Interpretations of the functions of these various limbic areas were made within the context of existing theories. Two hypotheses were proposed to explain the effects of the amygdala lesions: 1) An intact amygdala is required for an animal to display normal emotional reactivity; the deficits observed following amygdalotomy are due to a reduction in the emotional responsiveness of the amygdalotomized animals (e.g., Plotnick, 1968; White, 1971). 2) The amygdala aids in the formation of the association formed between a neutral stimulus and a noxious event (e.g., Egger, 1972; Gloor, 1972; Goddard, 1964); amygdalotomy makes it more difficult for an animal to form this association. The septum, it was hypothesized, exerts an inhibitory influence on the formation of the bond between a response and a reinforcement; septal destruction removes this inhibitory influence and facilitates the formation of this bond. This theory was derived from two existing theories of septal function: 1) The septum exerts an inhibitory influence on learned response, and septal destruction releases those behaviours which are highest in habit strength for a particular situation (e.g., Douglas, 1966; Gerbrandt, 1965). 2) The septum serves to dampen the increment in response strength normally caused by a reinforcement; septal destruction allows each reinforcement to produce a greater than normal increment in response strength (e.g., Fried,

1969, 1970; Zucker, 1965).

The theory of hippocampal function supported by the present data is that the hippocampus plays a major role in the control of attentional processes through the inhibitory modulation of sensory input (e.g., Douglas, 1967; Isaacson, 1966); hippocampal lesions affect the manner in which an animal reacts to the environment by altering its general arousal and drive levels.

Finally, it was suggested that, as previous studies have shown, these various limbic areas are not unitary structures, but are made up of various nuclear groups or cell fields. It seems that a more realistic understanding of the structure and functions of the brain could probably be acquired if a more molecular approach was taken in the application of ablation and stimulation techniques to the study of the brain.

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APPENDIX 1

Extra-Amygdala Damage Incurred by Animals in Group EA.

Subject Number	OT	CPU	CI	GP	ST	CLA	EXT CAP	PYR CTX	MFB	Trials to Criterion	
										CER	CAR
1										20	80
2						X	X			20	120
3	X	X								20	*
4	X	X		X	X	X	X	X		20	*
5							X	X		20	170
6	X	X		X	X	X	X	X		20	330
7		X		X	X	X				20	200
8				X	X	X				20	170
9				X					X	20	120
10		X	X							20	300
11					X	X	X		X	20	150
12								X		20	70
13					X	X	X			20	230
14					X	X	X		X	20	140
15	X	X		X	X	X	X		X		
16					X	X	X	X	X		
17					X	X	X		X		
18				X	X	X	X		X		
19			X		X	X	X				
20					X	X	X		X		
21					X	X	X	X	X		
22		X	X		X				X		

Definitions:

OT= optic tract CLA= claustrum
 CPU= caudate nucleus EXT CAP= external capsule
 CI= internal capsule PYR CTX= pyriform cortex
 GP= globus pallidus MFB= medial forebrain bundle
 ST= stria terminalis

* These animals were among the first to be tested in the CAR apparatus. Since a slight modification to the apparatus was made shortly after testing had begun for these animals, their data was discarded from the analyses.

X= Damage was incurred here.

APPENDIX 2

Extra-Amygdala Damage Incurred by Animals in Group LA.

Subject Number										Trials to Criterion	
	OT	CPU	CI	GP	ST	CLA	EXT CAP	PYR CTX	MFB	CER	CAR
1		X	X	X	X	X	X	X	X	20	170
2					X	X	X	X	X	20	180
3	X	X	X	X	X	X	X	X	X	*	*
4					X	X	X	X	X	20	330
5					X	X	X	X	X	**	**
6					X	X	X	X		20	280
7		X			X	X	X			20	400
8		X			X	X	X		X	20	400
9		X			X	X	X	X	X	4	220
10		X		X	X	X	X	X		20	210
11					X	X	X	X	X		
12				X	X	X	X	X	X		
13		X		X	X	X	X		X		
14					X	X	X		X		
15	X				X	X	X	X			
16					X	X	X	X			
17					X	X	X				
18		X			X						

Definitions:

OT= optic tract

CPU= caudate nucleus

CI= internal capsule

GP= globus pallidus

ST= stria terminalis

CLA= claustrum

EXT CAP= external capsule

PYR CTX= pyriform cortex

MFB= medial forebrain bundle

* Data omitted from analyses because one lesion was centered in the internal capsule.

** Data discarded because animal had only a unilateral lesion.

X= Damage was incurred here.

APPENDIX 3

Extra-Septal Damage Incurred by Animals in Group ES.

Subject Number	CC	CING	CPU	DBB	ACB	FX	HC	AC	MPA	Trials to Criterion	
										CER	CAR
1	X	X	X	X	X				X	7	60
2	X		X							6	90
3	X									20	110
4	X	X								20	40
5	X			X			X		X	20	80
6	X	X								8	50
7	X			X		X	X		X	9	80
8	X	X	X	X	X	X	X	X	X	5	120
9	X	X	X	X	X	X	X	X	X	7	80
10	X			X	X	X	X		X	5	120
11	X				X	X	X			20	70
12	X	X		X		X	X		X	6	90
13	X				X	X			X	20	90
14	X		X		X	X			X	7	40
15	X	X		X	X				X		
16	X				X	X	X		X		
17	X					X			X		
18	X	X				X	X		X		
19	X				X	X	X		X		
20					X	X	X		X		
21	X			X	X	X	X		X		
22	X			X	X	X	X	X	X		

Definitions:

CC= corpus callosum

CING= cingulate cortex

CPU= caudate nucleus

DBB= diagonal band of Broca

ACB= accumbens nucleus

FX= fornix

HC= hippocampal commissure

AC= anterior commissure

MPA= medial parolfactory area

X= Damage was incurred here.

APPENDIX 4

Extra-Septal Damage Incurred by Animals in Group LS.

Subject Number	CC	CING	CPU	DBB	ACB	FX	HC	AC	MPA	Trials to Criterion	
										CER	CAR
1	X		X	X	X	X	X			20	80
2	X	X		X		X	X		X	6	80
3	X	X		X	X	X	X	X	X	6	80
4	X	X	X	X	X		X		X	6	60
5	X	X		X	X				X	20	40
6	X	X		X	X				X	8	170
7	X	X		X		X	X	X	X	7	50
8	X	X	X		X	X	X			10	50
9	X	X	X	X	X	X	X		X	20	80
10	X	X		X	X				X	13	80
11	X			X	X	X	X	X	X		
12	X			X	X	X	X		X		
13	X			X	X	X	X	X	X		
14	X	X		X		X			X		
15	X	X		X		X	X		X		
16	X	X		X	X	X	X		X		
17	X	X		X	X	X	X		X		
18	X	X	X	X	X	X	X	X	X		
19	X	X	X	X	X	X	X	X	X		

Definitions:

CC= corpus callosum

CING= cingulate cortex

CPU= caudate nucleus

ABB= diagonal band of Broca

ACB= accumbens nucleus

FX= fornix

HC= hippocampal commissure

AC= anterior commissure

MPA= medial parolfactory area

X= Damage was incurred here.

APPENDIX 5

Extra-Cortical Damage Incurred by Animals in Groups EF and LF.

Group EF		Trials to Criterion		Group LF		Trials to Criterion	
Subject Number	CC	CER	CAR	Subject Number	CC	CER	CAR
1	X	7	120	1	X	4	150
2		4	*	2		12	170
3	X	5	*	3	X	7	400
4	X	3	160	4		20	150
5	X	19	160	5		4	100
6	X	9	170	6	X	15	220
7	X	5	110	7		6	70
8	X	4	140	8		15	150
9		10	180	9		8	80
10	X	**	190	10	X	4	180
11	X	3	100	11	X		
12	X	5	250	12	X		
13	X	6	*	13	X		
14	X	13	160	14	X		
15				15			
16				16			
17				17			
18				18			
19	X			19			
20	X						
21	X						

Definitions:

CC= corpus callosum

* These animals were also among the first to be tested in the CAR apparatus. Their scores were also omitted because of the modification to the apparatus (see Appendix 1).

** The score for this animal was omitted from the analyses because of an equipment breakdown at a crucial point in testing.

X= Damage was incurred here.

APPENDIX 6

Extra-Hippocampal Damage Incurred by Animals in Group EAH.

Subject Number	CTX	CC	FD	FI	LT	MH	Trials to Criterion	
							CER	CAR
1	X	X		X			8	270
2		X					6	220
3		X					8	110
4		X					4	*
5		X	X				7	290
6		X	X				5	*
7	X	X	X				5	160
8		X	X				5	*
9	X	X	X		X		6	160
10		X	X				9	220
11	X	X	X				5	190
12		X			X		7	*
13	X	X	X				15	180
14		X	X				7	180
15	X	X						
16	X	X	X					
17		X	X					
18		X	X					
19	X	X	X					
20	X	X						
21	X	X	X	X		X		

Definitions:

CTX= overlying cortex LT= lateral thalamic nucleus

CC= corpus callosum MH= medial habenular nucleus

FD= dentate gyrus

FI= fimbria

* Scores for these animals were omitted because of the modification to the CAR apparatus (see Appendix 1).

X= Damage was incurred here.

APPENDIX 7

Extra-Hippocampal Damage Incurred by Animals in Group LAH.

Subject Number	CTX	CC	FD	FI	LT	SM	MH	Trials to Criterion	
								CER	CAR
1	X	X	X					12	180
2	X	X	X	X				7	120
3			X	X	X	X	X	7	400
4	X	X						13	180
5	X	X	X					7	230
6	X	X	X		X	X	X	4	110
7	X	X	X	X	X	X		17	170
8		X	X	X	X	X	X	20	170
9	X	X						6	190
10	X	X	X	X	X	X		5	160
11	X	X							
12	X	X	X	X					
13	X	X							
14	X	X	X						
15	X	X							
16	X	X	X						
17	X	X	X		X	X			
18	X	X	X		X	X			

Definitions:

CTX= overlying cortex LT= lateral thalamic nucleus
 CC= corpus callosum SM= stria medullaris
 FD= dentate gyrus MH= medial habenular nucleus
 FI= fimbria

X= Damage was incurred here.

APPENDIX 8

Extra-Hippocampal Damage Incurred by Animals in Groups EPH and LPH

Group EPH					Trials to Criterion		Group LPH					Trials to Criterion	
Subject Number	CC	FI	LG	OT	CER	CAR	Subject Number	CC	FI	LG	OT	CER	CAR
1		X	X		4	*	1		X			20	70
2	X	X			6	180	2				X	9	180
3		X			6	*	3			X		20	60
4	X				5	160	4		X			6	80
5		X			4	160	5		X	X		20	140
6					7	180	6	X	X	X		20	60
7		X	X	X	20	80	7		X	X		6	130
8					5	90	8		X	X		20	100
9	X		X		8	280	9		X	X		19	70
10		X			12	90	10	X	X			20	40
11	X				5	60	11			X			
12		X			9	360	12		X	X			
13	X				5	190	13		X	X			
14			X		6	150	14		X	X	X		
15			X				15		X	X	X		
16							16		X	X			
17							17		X	X	X		
18	X			X			18		X		X		
19	X	X					19	X	X	X	X		
20	X												
21	X												

Definitions:

CC= corpus callosum

FI= fimbria

LG= lateral geniculate

OT= optic tract

* These scores were omitted from the analyses because of the modification to the CAR apparatus (see Appendix 1).

X= Damage was incurred here.

APPENDIX 9

Analysis of Variance of Suppression Ratios of All Groups Over Trials Two to 20.

Source	DF	MS	F	P
Treatment	5	7.85	33.10	.00000
Age-of-Treatment	1	.98	4.14	.04103
Treatment X Age-of-Treatment	5	.88	3.71	.00376
Error 1	146	.23		
Trials	18	.86	56.04	.00000
Treatment X Trials	90	.04	2.96	.00000
Age-of-Treatment X Trials	18	.02	1.84	.01640
Treatment X Age-of-Treatment X Trials	90	.01	.83	.87188
Error 2	2628	.01		

APPENDIX 10

Analysis of Variance of Total Suppression Scores for All Groups.

Source	DF	MS	F	P
Treatment	5	149.81	32.81	.00000
Age-of-Treatment	1	20.54	4.49	.03342
Treatment X Age-of-Treatment	5	16.49	3.61	.00445
Error	146	4.56		

Treatment by Age-of-Treatment Interaction of Total Suppression Scores
Obtained by All Groups in the CER Situation.

APPENDIX 12

Analysis of Variance of Total Number of Trials to Criterion for All Groups in the CER Situation.

Source	DF	MS	F	P
Treatment	5	435.37	19.16	.00000
Age-of-Treatment	1	120.30	5.29	.02145
Treatment X Age-of-Treatment	5	86.11	3.79	.00328
Error	146	22.71		

APPENDIX 13

Treatment by Age-of-Treatment Interaction for Trials to Criterion
Obtained by All Groups in the CER Situation.

APPENDIX 14

Analysis of Variance of Total Number of Trials to Criterion for All Groups in the CAR Situation.

Source	DF	MS	F	P
Treatment	5	50698.18	13.42	.00000
Age-of-Treatment	1	153.42	.04	.53492
Treatment X Age-of-Treatment	5	19604.85	5.19	.00041
Error	129			

APPENDIX 15

Treatment by Age-of-Treatment Interaction for Trials to First Avoidance.

APPENDIX 16

Analysis of Variance of Avoidance Latencies for All Groups in the CAR Situation.

Source	DF	MS	F	P
Treatment	5	164633.12	3.81	.00332
Age-of-Treatment	1	457106.31	10.59	.00185
Treatment X Age-of-Treatment	5	13818.69	.32	.89981
Error 1	126	43151.81		
Trials	3	10154.13	.29	.82785
Treatment X Trials	15	32266.32	.95	.50767
Age-of-Treatment X Trials	3	3970.89	.11	.94925
Treatment X Age-of-Treatment X Trials	15	16450.83	.48	.94798
Error 2	378	33933.20		

Treatment by Age-of-Treatment Interaction for Escape and Avoidance Latencies in the CAR Situation.

APPENDIX 18

Analysis of Variance of Weight Gain among Animals in the Infant Conditions.

Source	DF	MS	F	P
Treatment	5	1.38	5.38	.00030
Error 1	141	.25		
Age-of-Weighing	7	107.83	5093.12	.00000
Treatment X Age-of-Weighing	35	.09	4.33	.00000
Error 2	987	.02		

APPENDIX 19

Analysis of Variance of Weight Gain among Animals in the Adult Conditions, After Operation.

Source	DF	MS	F	P
Treatment	5	94027.06	7.84	.00002
Error 1	120	11986.47		
Age-of-Weighing	6	402661.50	1523.02	.00000
Treatment X Age-of-Weighing	30	1373.54	5.19	.00000
Error 2	720	264.38		

APPENDIX 20

Daily Food and Water Intake, Boli Weights, and Food Dronned Through the Cage, Averaged Over Seven Days.

Group	N	Mean Food Intake (In Grams)	Mean Water Intake (In Mills)	Boli Weights (In Grams)	Food Dronned Through Cage (In Grams)
EA	6	29.0	22.4	21.2	*
ES	6	21.6	35.6	19.8	*
EF	5	21.9	21.8	16.5	*
EPH	5	21.4	29.9	19.4	*
ENC	5	22.6	25.1	15.4	*
EAC	5	23.1	28.4	12.4	*
EAH	5	22.7	29.9	19.5	*
LA	4	28.5	28.8	18.7	3.4
LS	4	27.3	53.2	16.9	3.6
LF	3	26.2	37.6	15.5	2.7
LPH	4	32.4	36.8	21.8	4.6
LNC	3	25.8	39.5	16.9	1.1
LAC	3	23.1	42.9	14.4	0.6
LAH	3	25.8	39.6	17.0	1.4

* This measure was not taken for these groups.

APPENDIX 21

Mean Number of Spontaneous Shuttle Responses Over Days.

Group	N	H1	H2	C	1	2	3
EA	12	12.5	11.0	4.3	4.8	5.3	4.5
ES	14	13.4	7.0	3.5	4.5	3.8	3.5
EPH	12	10.7	9.2	5.0	5.6	6.2	6.2
EAH	10	11.0	7.8	3.1	3.0	3.8	3.5
EF	11	11.9	9.0	5.9	5.0	5.7	5.4
EAC	6	14.5	11.8	5.5	4.5	4.5	4.5
ENC	8	10.8	9.0	5.0	5.0	5.0	6.0
LA	6	9.6	7.6	2.3	2.6	2.8	1.3
LS	10	7.0	4.5	2.8	2.3	2.2	1.3
LPH	10	10.7	7.9	2.9	2.6	3.8	2.8
LAH	9	10.6	7.3	.5	.7	1.5	1.4
LAC	10	9.2	8.6	.8	1.3	1.7	1.0
LNC	10	9.7	7.9	1.7	1.1	1.4	1.6

APPENDIX 22

Analysis of Variance for the Number of Spontaneous Shuttle Responses
for All Groups on the Two Habituation Days in the CAR Situation.

Source	DF	MS	F	P
Treatment	5	25.92	.99	.57802
Age-of-Treatment	1	315.21	12.14	.00102
Treatment X Age-of-Treatment	5	24.67	.95	.54805
Error 1	126	24.95		
Trials	1	473.65	52.45	.00000
Treatment X Trials	5	11.97	1.32	.25641
Age-of-Treatment X Trials	1	2.17	.24	.62995
Treatment X Age-of-Treatment X Trials	5	8.82	.97	.56442
Error 2	126	9.02		

APPENDIX 23

Treatment by Days Interaction for Number of Spontaneous Shuttle Responses for Animals in Infant Conditions. H1=First Habituation Day; H2=Second Habituation Day; C=Day on Which Animals Reached Criterion; 1,2,3=Three Days Following Criterion Acquisition.

APPENDIX 24

Treatment by Days Interaction for Number of Spontaneous Shuttle Responses for Animals in Adult Conditions. H1=First Habituation Day; H2=Second Habituation Day; C=Day on Which Animals Reached Criterion; 1,2,3=Three Days Following Criterion Acquisition.

APPENDIX 25

Analysis of Variance for the Number of Spontaneous Shuttle Responses
for All Groups on the Last Four Days in the CAR Situation.

Source	DF	MS	F	P
Treatment	5	45.36	1.53	.18308
Age-of-Treatment	1	994.68	33.62	.00001
Treatment X Age-of-Treatment	5	14.57	.49	.78319
Error 1	126	29.58		
Trials	3	8.45	1.67	.16985
Treatment X Trials	15	2.53	.50	.93869
Age-of-Treatment X Trials	3	.92	.18	.90742
Treatment X Age-of-Treatment X Trials	15	2.02	.40	.97811
Error 2	378	5.03		

APPENDIX 26

Analysis of Variance for Activity Wheel Scores for All Groups.

Source	DF	MS	F	P
Treatment	5	209054.12	2.35	.04235
Age-of-Treatment	1	16546.88	.18	.67025
Treatment X Age-of-Treatment	5	144669.43	1.63	.15390
Error 1	147	88598.25		
Cycles	1	68551.31	1.67	.19515
Treatment X Cycles	5	132820.87	3.23	.00506
Age-of-Treatment X Cycles	1	38090.89	.92	.66156
Treatment X Age-of-Treatment X Cycles	5	47267.00	1.15	.33524
Error 2	147	41020.82		

APPENDIX 27

Treatment by Cycle Interaction for Number of Revolutions in the Activity Wheel for Animals in the Adult Conditions.

APPENDIX 28

Treatment by Cycle Interaction for Number of Revolutions in the Activity Wheel for Animals in the Infant Conditions.

APPENDIX 29

Mean Activity Wheel, Open-Field Activity, and Open-Field Exploration Scores for All Groups,

Group	N	Activity Wheel*		Open-Field**	Open-Field***
		Day	Night	Activity	Exploration
EA	14	586.1	371.0	98.4	.69
ES	14	184.7	303.9	67.1	.64
EPH	14	340.7	226.1	93.1	.75
EAH	14	311.2	253.7	110.5	.81
EF	14	374.2	282.5	105.1	.73
EAC	10	193.5	221.1	84.4	.69
ENC	10	273.0	324.9	86.8	.67
LA	8	380.7	175.6	153.5	.84
LS	10	108.5	192.0	68.0	.59
LPH	10	359.6	349.2	116.4	.73
LAH	10	271.0	372.8	107.1	.79
LF	10	346.2	432.3	90.8	.74
LAC	10	296.3	256.0	89.9	.72
LNC	10	375.0	218.4	76.9	.72

* Number of revolutions.

** Number of Squares Crossed.

*** Percentage of Squares Crossed.

APPENDIX 30

Analysis of Variance for the Open-Field Activity Scores for All Groups.

Source	DF	MS	F	P
Treatment	5	10158.38	3.80	.00321
Age-of-Treatment	1	3682.78	1.37	.24049
Treatment X Age-of-Treatment	5	3910.44	1.46	.20414
Error	147	2671.27		

APPENDIX 31

Treatment by Age-of-Treatment Interaction for Number of Squares Crossed (Activity Index) by All Groups During Testing for Social Interaction.

APPENDIX 32

Analysis of Variance for the Open-Field Exploration Scores for All Groups.

Source	DF	MS	F	P
Treatment	5	.10	2.53	.03093
Age-of-Treatment	1	.01	.32	.57695
Treatment X Age-of-Treatment	5	.03	.74	.59387
Error	147	.04		

APPENDIX 33

Treatment by Age-of-Treatment Interaction for Percentage of Squares Crossed (Exploration Index) by All Groups During Testing for Social Interaction.

APPENDIX 34

Analysis of Variance for Latency to First Contact (LFC) Scores
Obtained by All Groups During Testing for Social Interaction.

Source	DF	MS	F	P
Treatment	5	2218.09	1.60	.17107
Ane-of-Treatment	1	383.56	.27	.60688
Treatment X Ane-of-Treatment	5	754.54	.54	.74410
Error	67	1385.44		

APPENDIX 35

Treatment by Age-of-Treatment Interaction for Latency to First Contact (LFC) Scores for All Groups, During Testing for Social Interaction.

APPENDIX 36

Analysis of Variance for Total Time Spent in Physical Contact by
All Groups During Testing for Social Interaction.

Source	DF	MS	F	p
Treatment	5	2403.08	1.61	.16693
Age-of-Treatment	1	7989.55	5.37	.02214
Treatment X Age-of-Treatment	5	3806.11	2.56	.03473
Error	67	1486.73		

APPENDIX 37

Analysis of Variance for the Number of Contacts by All Groups During Testing for Social Interaction.

Source	DF	MS	F	P
Treatment	5	7.82	.26	.93065
Age-of-Treatment	1	372.50	12.52	.00107
Treatment X Age-of-Treatment	5	34.60	1.16	.33604
Error	67	29.74		

APPENDIX 38

Treatment by Age-of-Treatment Interaction for Number of Contacts
by Each Group During Testing for Social Interaction.

APPENDIX 39

Mean Glandular Weights for All Groups (In Grams).

Group	Tested Animals				Non-Tested Animals			
	N	Adrenals	Thyroid	Testes	N	Adrenals	Thyroid	Testes
EA	14	.0323	.0293	3.1871	8	.0320	.0236	3.3474
ES	14	.0288	.0265	3.1633	8	.0312	.0232	3.1296
EPH	14	.0317	.0315	3.4223	8	.0326	.0307	3.4481
EAH	14	.0305	.0276	3.0788	7	.0345	.0256	3.5516
EF	14	.0315	.0275	3.4361	7	.0351	.0293	3.4864
EAC	10	.0327	.0365	3.2533	10	.0350	.0281	3.4290
ENC	10	.0335	.0373	3.2443	9	.0342	.0279	3.4320
LA	8	.0332	.0312	2.9856	8	.0354	.0296	3.3788
LS	10	.0305	.0238	3.0437	9	.0329	.0262	3.4068
LPH	10	.0297	.0281	3.4903	9	.0376	.0311	3.3315
LAH	10	.0339	.0298	3.2383	8	.0342	.0354	3.7009
LF	10	.0367	.0318	3.4274	9	.0349	.0377	3.4806
LAC	10	.0358	.0342	3.514	9	.0397	.0351	3.6279
LNC	10	.0348	.0338	3.500	7	.0406	.0347	3.6277

APPENDIX 40

Analysis of Variance for Adrenal Weights for Animals in the Adult Conditions.

Source	DF	MS	F	P
Treatment	5	.0001	2.26	.05218
Age-of-Treatment	1	.0003	6.20	.10357
Treatment X Age-of-Treatment	5	.0000	.62	.68414
Error	116	.0001		

APPENDIX 41

Analysis of Variance for Adrenal Weights for Animals Which Had Not
Been Tested.

Source	DF	MS	F	P
Treatment	5	.0001	2.49	.03514
Age-of-Treatment	1	.0003	9.05	.00355
Treatment X Age-of-Treatment	5	.0000	.70	.61971
Error	104	.0000		

APPENDIX 42

Analysis of Variance for Thyroid Weights for Animals in the Infant Conditions.

Source	DF	MS	F	P
Treatment	5	.0002	3.55	.00507
Age-of-Treatment	1	.0003	5.76	.01602
Treatment X Age-of-Treatment	5	.0001	1.35	.24379
Error	134	.0001		

APPENDIX 43

Analysis of Variance for Thyroid Weights for Animals in the Adult Conditions.

Source	DF	MS	F	P
Treatment	5	.0003	5.27	.00039
Age-of-Treatment	1	.0002	4.35	.03669
Treatment X Age-of-Treatment	5	.0000	.81	.54390
Error	116	.0001		

APPENDIX 44

Analysis of Variance for Thyroid Weights for Animals Which Had
Been Tested.

Source	DF	MS	F	P
Treatment	5	.0002	3.46	.00637
Age-of-Treatment	1	.0002	3.41	.06403
Treatment X Age-of-Treatment	5	.0001	2.29	.05014
Error	104	.0001		

APPENDIX 45

Analysis of Variance for Thyroid Weights for Animals Which Had Not
Been Tested.

Source	DF	MS	F	P
Treatment	5	.0002	3.61	.00444
Age-of-Treatment	1	.0003	6.28	.01276
Treatment X Age-of-Treatment	5	.0001	1.59	.16518
Error	146	.0001		

APPENDIX 46

Analysis of Variance for Testes Weights for Animals in the Infant Conditions.

Source	DF	MS	F	P
Treatment	5	.28	2.32	.04598
Age-of-Treatment	1	.66	5.43	.02000
Treatment X Age-of-Treatment	5	.17	1.43	.21400
Error	134	.12		

APPENDIX 47

Analysis of Variance for Testes Weights for Animals in the Adult Conditions.

Source	DF	MS	F	p
Treatment	5	.35	1.37	.23693
Age-of-Treatment	1	1.54	5.94	.01549
Treatment X Age-of-Treatment	5	.27	1.06	.38162
Error	116	.25		

APPENDIX 48

Analysis of Variance for Testes Heights for Animals Which Had Been Tested.

Source	DF	MS	F	p
Treatment	5	.6567	2.9507	.01437
Age-of-Treatment	1	.0009	.0042	.94702
Treatment X Age-of-Treatment	5	.1175	.5281	.75706
Error	146	.2226		

APPENDIX 49

Representative Lesions

- a. Early amygdala lesion, immediately postoperative.
- b. Early amygdala lesion at sacrifice at approximately 130 days.
- c. Late amygdala and anterodorsal hippocampal lesions, immediately postoperative.
- d. Late amygdala lesion at sacrifice at approximately 180 days.

APPENDIX 49

Representative Lesions

- a. Early amygdala lesion, immediately postoperative.
- b. Early amygdala lesion at sacrifice at approximately 130 days.
- c. Late amygdala and anterodorsal hippocampal lesions, immediately postoperative.
- d. Late amygdala lesion at sacrifice at approximately 180 days.

Representative Lesions

- e. Early septal lesion, immediately postoperative.
- f. Early septal lesion at sacrifice at approximately 130 days.
- g. Late septal lesion, immediately postoperative.
- h. Late septal lesion at sacrifice at approximately 180 days.

Representative Lesions

- e. Early septal lesion, immediately postoperative.
- f. Early septal lesion at sacrifice at approximately 130 days.
- g. Late septal lesion, immediately postoperative.
- h. Late septal lesion at sacrifice at approximately 180 days.

Representative Lesions

- i. Early posteroventral hippocampal lesion (unilateral), immediately postoperative.
- j. Early posteroventral hippocampal lesion at sacrifice at approximately 130 days.
- k. Late posteroventral hippocampal lesion (unilateral), immediately postoperative.
- l. Late posteroventral hippocampal lesion at sacrifice at approximately 180 days.

Representative Lesions

- i. Early posteroventral hippocampal lesion (unilateral), immediately postoperative.
- j. Early posteroventral hippocampal lesion at sacrifice at approximately 130 days.
- k. Late posteroventral hippocampal lesion (unilateral), immediately postoperative.
- l. Late posteroventral hippocampal lesion at sacrifice at approximately 180 days.

Representative Lesions

- m. Early anterodorsal hippocampal lesion, immediately postoperative.
- n. Early anterodorsal hippocampal lesion at sacrifice at approximately 130 days.
- o. Late anterodorsal hippocampal lesion at sacrifice at approximately 180 days.

Representative Lesions

m

n

o

- m. Early anterodorsal hippocampal lesion, immediately postoperative.
- n. Early anterodorsal hippocampal lesion at sacrifice at approximately 130 days.
- o. Late anterodorsal hippocampal lesion at sacrifice at approximately 180 days.

Representative Lesions

p

q

- p. Early frontal cortical lesion at sacrifice at approximately 130 days.
- q. Late frontal cortical lesion at sacrifice at approximately 180 days.

Representative Lesions

p

q

- p. Early frontal cortical lesion at sacrifice at approximately 130 days.
- q. Late frontal cortical lesion at sacrifice at approximately 180 days.

APPENDIX 50

Some Effects on Physical Development of Early Amygdalectomy.

Both pictures are of the same two littermates who were sacrificed at 17 days of age. The larger animal had received bilateral anterodorsal hippocampal lesions at 10 days, and the smaller animal had received bilateral amygdala lesions at the same time. Notice how scalp wound is not yet properly healed in the amygdala infant, and how its eyes have not yet opened.