CONTRIBUTION OF BRAIN WITH OR WITHOUT VISUAL CORTEX LESION TO EXPLORATORY LOCOMOTION IN THE RAT

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Dedication

To my family

Abstract

Over the past five decades spatial behavior has been a subject of research interest in psychology and neuroscience, in part based on philosophical theories of mental spatial representations. In order to continue uncovering the facts regarding spatial behavior, the focus of this thesis was on the contribution of entry point and visual inputs to the organization of exploratory locomotion and spatial representation in the rat. Despite the contribution of the hippocampus to spatial abilities, the exploratory locomotion is still visually organized in rats with damage to the hippocampus. On the other hand, recent studies have demonstrated a contribution of visual areas to the spatial ability of the rat. Nevertheless, the contribution of visual cortex to the organization of exploratory locomotion has not been studied in an open field. The experiments in this thesis were designed to characterize the organization of exploratory locomotion to the point of entry and/or visual cues. Rats were started from the edge or center of an open table near or on which a salient object could be placed. The main findings were that rats organized their exploratory locomotion to their point of entry and modified their behavior as they encountered objects. Also, rats with damage to visual cortex displayed an extra-attachment to the visual objects and in contrast to controls did not expand their exploratory locomotion with time. The results are discussed with respect to the centrality of the entry point in the organization of exploratory locomotion and the neural network that control visual exploration in the rat.

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General Introduction

Over the past fifty years there has been a concentrated effort to describe how the brain mediates spatial behavior. The present thesis is a continuation of this effort. The objective of the thesis is to examine the contribution made by visual cortex to the organized exploratory locomotion of the laboratory rat. Before describing the experiments, I will first give an introduction to spatial behavior.

Spatial behavior is a broad range of animal activity that includes behaviors such as migration at one extreme of the spatial dimension to exploratory locomotion in small laboratory open fields at the other extreme. The main focus of this thesis is on exploratory locomotion of rats in an open field. The organization of general introduction in this thesis will be as follows: Because the concept of space is the common element of all spatial behaviors including exploratory locomotion, I will first describe the main philosophical theories regarding the nature of space that inspired some of the most influential current psychological and neurological theories on spatial navigation. I will then describe some of main theories of spatial behavior that originate from experimental studies in behavioral science and neuroscience. This will be followed by an overview of brain substrates of spatial behavior, including anatomical and lesion studies. Ethological approaches to space and exploratory behavior will then be described. I will conclude with a description of the theoretical background for the proposed research in the thesis.

Philosophical theories of space

Although philosophers and scientists have played an essential role in the history of science, their most influential theories on the relationships between the mind and the world were developed after the *Renaissance*. Among many phenomena, the nature of space was one of their concerns. The focus of this section will be on a brief description of Newton and Leibniz's notions of space, and their influence on Kant's theory. Kant's theory of space formed the philosophical basis of the first theory on neural basis of spatial representations, "cognitive mapping theory", which will be described further along in this introduction.

According to the Newtonian view, space was a real entity, but independent of both mind and matter. In contrast, in the Leibnizian view, space was an idea extracted from the relationships between objects. In other words, Leibniz believed that Newtonian space as an entity independent of mind and matter was difficult to picture. Thus, while the existence of objects did not play any role in the creation of the space based on the Newtonian point of view, the Leibnizian conception of space postulated nothing but a relation between existing objects.

These two approaches formed the philosophical background for Kant's position regarding space [Alexander, 1956; Jammer, 1969]. In 1781, Kant wrote "*Critique of pure reason"* and outlined his theory regarding the relations between the mind and objective world. Kant proposed that an experience is a "property of being mine", which distinguishes the "I" from "something else", which is nothing but the objective world. Although Kant agreed with the importance of sensations

[experience] in human's knowledge, he believed that the mind does exist as an independent entity. Kant [1781] developed a model of the mind in which the objective world is perceived through the cooperation of two preexisting mental faculties: the faculty of understanding and the faculty of sensibility. Understanding makes sense of the raw data by organizing sensibility's intuitions. Consequently, Kant identified the categories of qualities and quantities such as color, space, and time, and considered them as *a priori,* meaning that they require no experiential proof. Space was *a priori* in his view. According to his view, the notion of space originates in the mind but has nothing to do with relations between objects in a given moment. It is a real entity but based on a schema that is already built in the mind.

In "*Critique of pure reason",* Kant [1781] stated:

> 1] Space is not a conception, which has been derived from outward experiences…
>
> 2] Space then is a necessary representation, *a priori*, which serves for the foundation of all external intuitions…
>
> 3] Space is not a discursive or as we say, general conception of the relations of things, but a pure intuition…
>
> 4] Space is represented as an infinitive given quantity… *"Critique of pure reason",* [translated by *T. K. Abbott, 1952; page* 24].

Although the concept of space was the convergent point of British empiricism and German rationalism in the Kant's philosophy of mind, these two strands of thought on phenomena such as learning, memory, and spatial

representation continued to be in conflict in the twentieth century. Then, new research paradigms in psychology and other behavioral sciences emerged.

Experimental approaches to spatial behavior

The objective of this section is to describe theories that have used behavioral methods in research that are relevant to spatial behavior, including spatial learning, spatial memory, and innate spatial behaviors. First I will describe some of the theories in "behavioral science" that attempt to explain spatial behavior as learned [Lehrman, 1970]. These theories form the foundations of theories formulated in "behavioral neuroscience" that attempt to describe the neural basis of spatial behavior. One of the subjects of speculation in the mid-twentieth century was related to claims made by ethologists that behavior was innate [Lorenz, 1950]. That ethologists have proposed that spatial behavior is innate will also be discussed.

The development of behavioral sciences led to the formal investigation and analysis of human and non-human animal behavior. Laboratory-based studies of behavior favored the laboratory rat and tested its ability in a variety of "mazes" that had spatial components [Hodges, 1996]. Maze is used as a generic term for an apparatus in which an animal was required to find its way from a start to reach a goal, where it usually received a food reward [Jeffery, 2003; Hodges, 1996]. Hull and Tolman's use of somewhat similar experimental approaches originated two opposing theories of spatial learning.

Theories that proposed that behavior could be described as a series of learned movements to various relevant stimuli were often referred to as stimulus-

response [S-R] theories. Hull [1943] exemplified such an approach and emphasized that behavior could be envisioned as a series of S-R responses that eventually led to a goal. The motivation for an animal to engage in behavior was hypothesized to be a drive, such as hunger, that was reduced when an animal reached a goal and found a reward, such as a small quantity of food. Hull tested this hypothesis in mazes and estimated the strength of learned responses or "habits" in terms of number of reinforcements, quantity of food obtained at the goal object, etc. [Spence, 1951].

Although behavioral theories were not specifically directed toward describing spatial behavior, they did assume that explanations derived from their more formal studies would be able to account for most behavior, including spatial behavior. For example, S-R theory would predict that a hungry animal placed in a large empty box would likely walk around in an attempt to find food. If it did, it would be likely to engage in exactly the same behavior when it was again placed in such a situation. Thus, exploration was activated by drive, and the stimuli to which an animal directed its exploration would form a number of linked stimulus-response conjunctions that were eventually reinforced by finding food. The stimulus-response couplets that were reinforced would be used to guide behavior when an animal was again introduced to the situation.

In a sharp contrast to S-R theory, Tolman and his colleagues [1946a,b] obtained evidence that the behavior of rats is goal-directed and flexible, and so not easily explained by S-R learning. They trained rats to turn right in a T-maze [a maze with a start alley at the end of which two arms projected at right angles,

so forming a T] to reach food. Once an animal had acquired the response, the T-maze was rotated by 180°. If a rat had acquired a response [R] of turning right when it came to the stimulus of the maze junction [S], it should turn right. But in fact, the rat turned left and went to the place or location in the room where it had previously found food. This unexpected finding clearly did not support an S-R explanation of behavior, but the behavior was nevertheless adaptive. Tolman [1948] thus proposed a new theory to explain this spatial flexibility, the cognitive map theory. He envisioned that as the rats were performing the “right-turn” during initial training they were forming a cognitive map, or brain representation, of the room and were learning to go to a place in the room. When the maze was rotated, the rat responded not to the stimulus of maze but to room stimuli that indicated the former location of food. That the rat was responding to room cues, or distal cues, indicated that it had learned and was now using a central representation of the room. This central representation could be envisioned as a map of the room.

Tolman designed a maze, known as “Sunburst maze” [Fig. 1.1], to test his theory. He predicted that if a cognitive map existed, animals would be able to take a short cut when the original path by which they reach the goal is removed. In the first stage of his experiment, animals took the only possible path [Shaded path in Fig. 1.1] to reach the goal box. Thus, at this stage of training, rats followed this single path from the start point to the goal a number of times. In the next phase of training, the original path was blocked and some other arms were added to the maze. One of these arms actually provided a shorter route to the

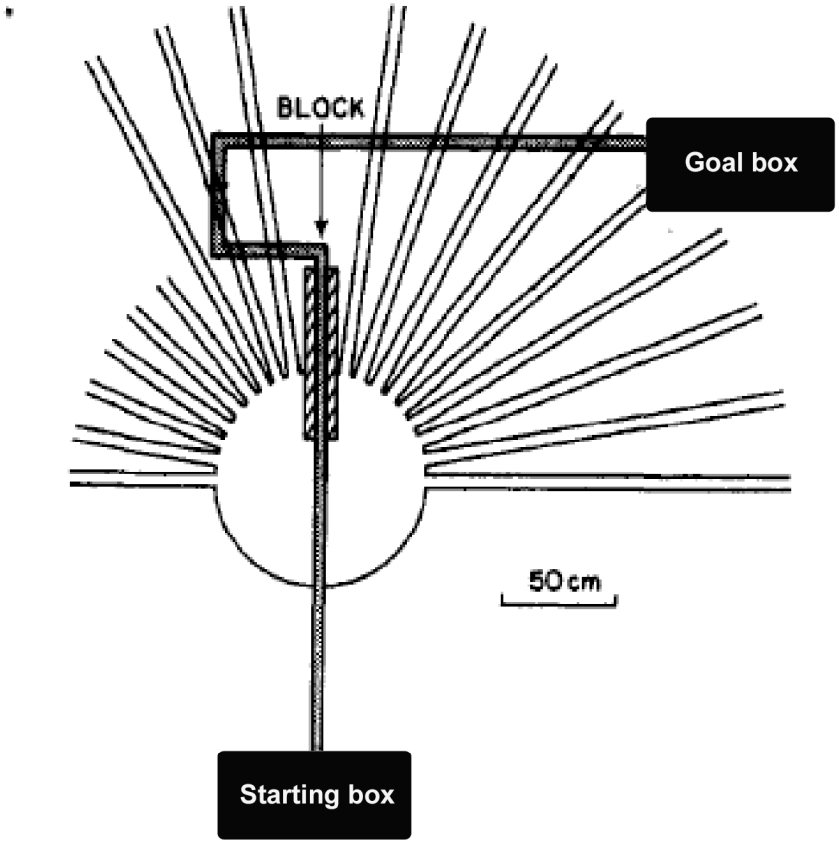

Fig. 1.1. Tolman's sunburst maze. Rats placed in the center of the maze learned to reach the goal through the shaded path. After the blockade of the path, rats chose the arms that were oriented toward the goal [Adopted from Tolman, 1948].

goal than the route provided during first stage training. If rats were aware of the spatial relations between the start point and the goal, they could take this short cut. Most of the rats did so. Because taking a short cut requires the formation of at least a general picture of the environment containing the box baited with food, Tolman assumed that the rats had formed a “cognitive map”. They then used this map to navigate through the environment, even to the point of adopting a more efficient route than that provided during original training.

Although the contribution that Tolman made to understanding spatial behavior was new, the fact that no brain mechanisms were introduced as the foundation of cognitive map was a limitation of his theory. The first theory of the neural basis of spatial representations stemmed from the discovery of place cells in the hippocampus. O’Keefe and Dostrovsky [1971] recorded the activity of hippocampal pyramidal cells in the CA1 field of the anterior dorsal hippocampus in exploring rats [Fig. 1.2]. They noticed that the cells fire when rats are in certain locations, which they called places, and do not respond simply to a specific stimulus in the animal’s sensory environment. They proposed that each cell represents a place or has a place field of the environment and that the cell is able to designate this place by encoding the relationship between at least two distal stimuli. That cells in the hippocampus are able to respond to the position of an animal in space gave raise to the suggestion that the hippocampus is the site of Tolman’s cognitive map [O’Keefe and Nadel, 1978].

The theory that the hippocampus is the site of Tolman’s cognitive map was more formally proposed in O’Keefe and Nadel’s [1978] book, “The hippocampus

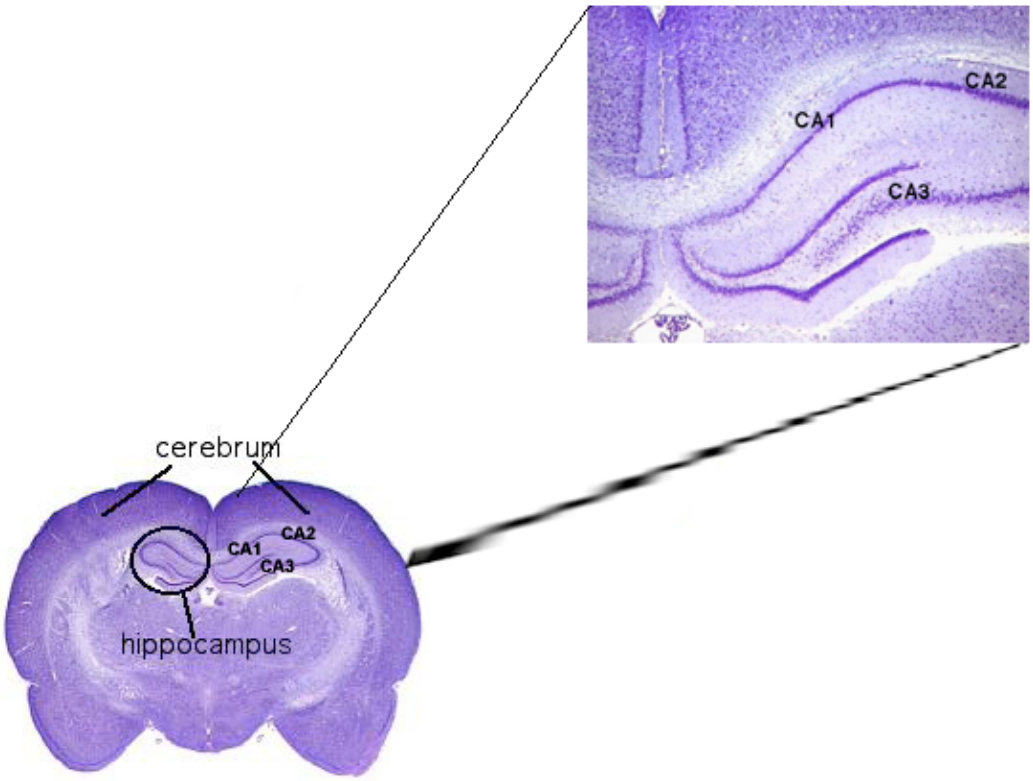

Fig. 1.2. Nissl staining of rat's brain frontal section. A. The hippocampus is located underneath the cerebrum [shown in the circle]. B. Three areas in the hippocampus proper [CA1, CA2, and CA3] are illustrated in the figure. [The figures are adopted from www.bio.davidson.edu/.../method/Brainparts.html].

as a cognitive map". Here the theory was linked both to Kant's theory that the mind has a representation of space and Tolman's theory that locomoting rats form cognitive maps of their environment. In support of the theory, they summarized a wide array of supporting information; including electroencephalographic evidence that the hippocampus was active when animals moved and lesion evidence that demonstrated that rats that had suffered damage to the hippocampus were impaired in spatial learning.

The initial observation that there are place cells in the hippocampus was confirmed by many subsequent studies [O'Keefe & Nadel 1978; O' Keefe, 1991]. Rotating cues in the environment caused a rotation in firing field of place cells, suggesting that place fields are influenced by distal cues [O'Keefe, 1976]. Further studies confirmed the involvement of visual cues in formation of place fields [Hill & Best, 1981; Muller et al., 1987; O'Keefe & Speakman, 1987]. Place cells also become disorganized when the majority of cues in the environment are removed. These finding suggests that it is a constellation of cues that contributes to the stability of place fields [O' Keefe & Conway, 1978]. Also, proximal and distal cues play controlling roles in the orientation of place fields in an exploratory context [Knierim, 2002]. For example, some place fields follow the rotation of distal cues, and some others rotate with proximal cues.

Further examination of hippocampal place cells indicated that their activity was not simply correlated with visual cues. In the absence of visual cues in total darkness [Muller et al., 1987; O'Keefe, 1976; O'Keefe & Speakman, 1987; Quirk et al., 1990] or using blindfolded rats [Hill & Best, 1981] place fields remained

stable. This is consistent with the finding that place fields can still be formed in blind rats [Hill & Best, 1981; Save et al., 1998]. These findings led to the notion that cues from an animal's own movements can be involved in updating the firing pattern of place fields [O'Keefe, 1976; McNaughton, et al., 1989].

Other studies have shown that the firing fields of place cells in rats is influenced by the location of their refuge [Gothard et al., 1996], their point of entry into an environment [Sharp et al., 1990], and their destination during navigation [Hok et al., 2007]. The contribution of tactile inputs to the organization of behavior and firing fields of their place cells was shown in a study in which peripherally blind rats made a greater number of contacts with the object inside the cylinder as they were exploring the open environment, and the firing fields of their place cells were stable as that of control rats [Save et al., 1998].

The activity of cells in other portions of the hippocampal formation also appears to contribute to spatial orientation. Head direction cells are the cells that discharge as a function of rat's head direction in a horizontal plane [Rank, 1984; Taube, 1995a,b]. They are found in the postsubiculum [Rank, 1984], the anterior dorsal nucleus of the thalamus [Taube, 1995a], the dorsal sector of lateral dorsal thalamic nucleus [Mizumori & Williams, 1993], both agranular and granular areas of retrosplenial cortex [area 29, posterior cingulate], and portions of extrastriate cortex [areas V2M and V2L] [Chen et al., 1994a,b], lateral mammillary nuclei [Leonhard et al., 1996], and the dorsal striatum [Wiener, 1993]. An animal's directional heading modulates place cell discharge in tasks that require linear

motion such as radial arm maze task [McNaughton et al., 1983; Breese et al., 1989; Wiener, 1993].

Environmental manipulations influence the activity of head direction cells. The rotation of a card in a cylinder, when animals do not see the displacement of the cue, causes changes in the preferred directions of discharges of head direction cells in the postsubiculum [Taube et al., 1990b], lateral mammillary nuclei [Leonhard et al., 1996] and retrosplenial cortex [Chen et al., 1994a], that shifted back when returning the cue card to the initial position. The preferred direction of discharge rotated more than 30° after the removal of the cue card in the absence of the rats [Taube et al., 1990a] and returned to its first condition when the cue was repositioned in the presence of the rats [Goodridge & Taube, 1995]. Finally, when rats move from a familiar cylinder, in to a novel rectangular apparatus [Taube & Burton, 1995], or when they are transported from a familiar cylinder into the novel rectangle apparatus passively [Taube et al., 1996]; the firing fields of head direction cells remain stable.

The effect of environmental manipulations on the activity of head direction cells might depend on the locus of the cells in the brain and experimental conditions. Head direction cells also maintain their directional firing in either anterior dorsal thalamic nucleus or in postsubiculum when animals were blindfolded while their preferred direction shifted in a non-blindfolded session [Goodridge et al., 1998; Taube, 1998]. Head direction cells in the lateral dorsal thalamus did not discharge in a directional fashion when placing rats onto the apparatus in the dark [Mizumori & Williams, 1993; Taube, 1998]. Taube [1998]

concluded that the stable discharge of head direction cells in the lateral dorsal thalamus depends on visual inputs. Also, removal of the cue did not change the preferred direction of discharge in cells in retrosplenial cortex [Chen et al., 1994b]. The activity of head direction cells in postsubiculum was not sensitive to lack of visual stimuli when the lights were turned off in the testing room [Taube, 1998]. Chen et al., [1994a] reported a similar finding in which directional firing of head direction cells did not change in retrosplenial and secondary visual cortex when placing rats in the room with light off.

The fact that hippocampal place cells respond to visual and non-visual cues in the environment [Save et al., 2000] raises the question of where the information about the position of animal independent of environmental context is computed in the brain [Hafting et al., 2005]. Such computation would provide a representation of space that is functional in any context. The cells in the superficial layers of dorsocaudal region of the medial entorhinal cortex appear to be essential for this computation. In contrast to place cells with a single firing field, cells in this region have multiple fields forming a topographically organized grid of triangles [Hafting et al., 2005]. The triangular firing structure and the spacing of the grid cells remains the same when external cues are displaced or removed and remains after visual deprivation. It has been speculated that entorhinal cortex may provide maps of environment that guide navigation using outputs coming from hippocampus or other brain areas. O'Keefe & Burgess [2005] suggest that grid cells may serve to reflect the distance traveled by the animal in a given direction. They propose that this is based on cooperation

between grid cells, head direction cells, and a kind of integrator cell, found in layer V of the entorhinal cortex [that can integrate over a long timescale]. They also proposed that two integrator cells could mark the start and end of the animals' movement. In order to compare the geometric structure of grids in different layers and to determine the interaction of grid cells with other cell types in MEC, Sargolini et al., [2006] recorded the activity of single cells from the most dorsal part of MEC. They also demonstrated that grid structure was apparent in a sinusoidal form with peaks recurring at multiples of 60º in all principal layers of medial entorhinal cortex. The degree of 'gridness' was defined as the difference between the correlations at the expected peaks [60º and 120º] and the expected troughs [30º, 90°, and 150º]. The proportion of cells with strong sinusoidal firing was layer-dependent, with less frequency in the deeper layers. Beneath layer II, grid cells and head direction cells were found in the same location. Firing rate changes whenever the rat's head faced a certain range of direction. The proportion of grid cells with conjunctive properties is layer dependent [Largest populations in layers III & V]. Cells with different degrees of gridness and directionality responded as a coherent ensemble during environmental manipulation. Grid structure and directional tuning can be maintained during brief stops along the rat's trajectory.

In a review of such evidence in 2006, McNaughton states that the combined finding of place cells, head direction cells, and grid cells in the hippocampus or structures closely related to it, support the idea that the hippocampal formation is involved in spatial functions.

A second line of evidence that supported the cognitive mapping theory is evidence obtained from rats that had a damaged hippocampus produced by experimentally induced lesions [O'Keefe & Nadel, 1978]. An exemplary demonstration comes from studies using the place task in the swimming pool. Morris and coworkers originally proposed that if a refuge platform was located just below the surface of the water where it is not visible, it could only be found efficiently by a swimming rat using distal room cues. A typical swimming pool is a circular tank filled with water to a height of 25cm with a temperature from 21 to 22 °C. Powdered milk is added to water to make it opaque. A number of cues may be present in the room, including counters, cupboards, posters, etc. An invisible platform can be placed in the pool so that the top of the platform on which rats climb is 1cm below the water [Fig. 1.3]. In a typical procedure of water place learning task, rats are released at one of the cardinal compass points of a pool, and must find a submerged platform located in one of four quadrants of a swimming pool [Morris, 1981]. Rats with hippocampal lesion are impaired in the place learning task [Morris et al., 1982; Aggleton et al., 1986, Jarrard et al., 1984, Morris et al., 1982, Sutherland et al., 1982]. Control rats trained to swim to a submerged platform quickly learned to swim directly to the hidden platform, whereas rats with hippocampal lesion were not able to do so. Nevertheless, hippocampal rats are still able to learn the place task [Whishaw & Tomie, 1997]. It is important to note that the cognitive mapping theory did not attempt to link all spatial behavior to the hippocampus. The theory proposes that there are at least three ways that animals can find their way around in their environment, cue

Fig. 1.3. Swimming pool. In a typical water task, swimming pool is placed in an ordinary room with various cues such as posters on the wall, desk, chair …etc. Immediately after rats are released in the water, it starts swimming to find a way [e.g. submerged platform] to escape the water.

guidance, route guidance, and place guidance. Cue guidance consists of approaching or moving away from a prominent landmark. A moth that orients to a light is displaying cue guidance. Route guidance consists of following a pathway, such as a road or an odor trail. A salmon that migrates from the ocean to its spawning grounds in a river by following an odor trail is displaying route guidance. Thus, an animal without a hippocampus can display spatial behavior and spatial learning but it does so using cue and route guidance and not cognitive mapping. Furthermore, brain regions other than the hippocampus would mediate these spatial guidance strategies.

One interesting study uncovers the role of various sensory informations in spatial navigation, and indicates that place learning in a swimming pool is at least partially dependent on visual cues, although different visual strategies might be used to learn the location of a hidden platform [Sutherland & Dyck, 1984].

The theory that the hippocampal formation including the hippocampus related areas and pathways represents the space as a cognitive map is not without its critics. Olton and Sumuelson [1976] proposed that working memory might be the underlying process of spatial navigation [Also see: Olton et al, 1986]. They used a maze with eight-arms extending out radially from the center with food placed at the end of each arm to measure memory processes in rats [Olton, 1979; Fig. 1.4]. Rats were free to explore from the center and to find the food at the end of each arm. To be efficient in this task rats must visit each arm only once to eat all the food without wasting time and energy. Visiting each arm

Fig. 1.4. Olton's elevated radial-arm maze. Placed in the center of a maze, rats have to enter each arm [which can be marked by different pattern] to eat the food pallet that is placed at the end of each arm. Rats must remember the arms they have already entered to prevent entering again and wasting time.

more than once was scored as an error. Most rats were able to save time and enter each arm once, meaning that they remembered the arms they had visited.

Olton and Papas [1979] concluded that rats used a type of short-term [working] memory to keep track of arms they had entered. Olton and Feustle [1981] proposed that hippocampus serves as the site of working memory in this task.

Among other notions that suggest an alternative to cognitive mapping theory is configuration association theory [Rudy & Sutherland, 1995]. This theory can be traced to psychological learning theories in which individual events can be represented in an associative network [Wagner & Rescorla, 1972]. According to this theory, association systems combine a number of stimulus elements in to a unique configural representation, which retrieves a target memory. Consistent with configuration association theory, the contribution of hippocampus to spatial navigation is not a map, but episodic representations of configured cues.

Brain substrates of spatial behavior

That the hippocampal formation has a wide range of cell activity sensitive to visual cues has suggested that the hippocampus is part of the “visual system”, or more correctly part of an extended visual system. On anatomical evidence, Felleman and van Essen [1991] have made just such a proposal. They propose that there are as many as 32 visual areas of the brain and that the entorhinal cortex and hippocampus are the end points of these many connected regions. In a sense, according to their anatomy, vision begins at the retina and ends in the

hippocampus. Stated differently, “Vision is the process of discovering from images what is present in the world and where it is”, [Marr, 1982; Page 3].

The contribution of some cortical areas including visual cortex, posterior parietal cortex, cingulate cortex and also hippocampus that are in connection with visual cortex and are involved in spatial behavior will be described in the following sections. For each area I will first describe its anatomical feature and then will review the related lesion studies that have uncovered the contribution of the area to spatial behavior. Figure 1.5 illustrates a simplified diagram of visual pathways.

Originating in retina, which is a thin sheet of interconnected nerve cells, the optic tract ends at the other parts of the brain [visual cortex and other brain areas]. The retina has the same type of cells as the brain does, and projects via the optic tract formed by retinal ganglion cells to various brain areas. Retinal ganglion cells include two types of cells named magnocellular [M cells] and parvocellular [P cells]. M cells found especially in the periphery of retina are sensitive to movement, and P cells found mostly in the fovea are sensitive to color and fine details. The brain cells to which retinal ganglion cells connect retain the same distinctive features via their visual pathways, including the geniculostrate and tectopulvinar pathways.

The geniculostriate pathway originates in the retina and projects through the lateral geniculate nucleus [LGN] of thalamus to layer IV of striate visual cortex [also named as primary visual cortex, V1, or area 17] located in the occipital lobe. Striate visual cortex is the place from which the visual pathway

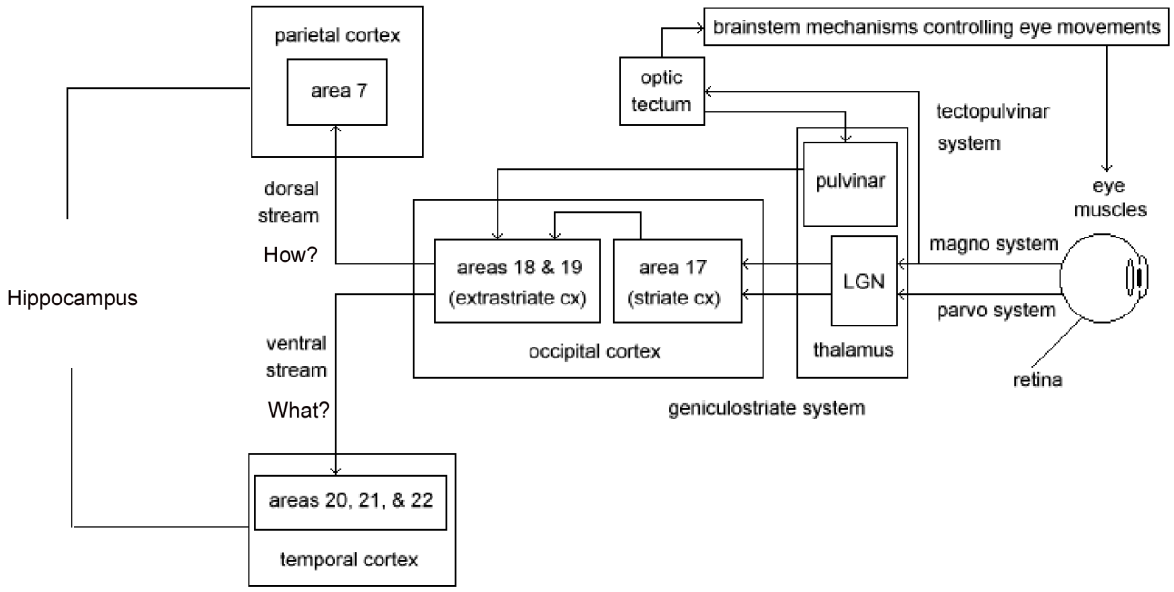

Fig. 1.5. A simplified schematic view of extended visual system. Ganglion cells [M & P cells] project from retina to the tectum and also to the thalamus. Projections from different parts of thalamus innervate extrastriate and striate visual cortex, and from there, cells project to the parietal and temporal cortex [ww2.coastal.edu/kingw/psyc450/visualpaths.html].

projects to the other vision-related areas including extrastriate visual cortex [V2, V3, V3A, V4, and V5]. The tectopulvinar system originates in the retina and projects to cells in the superior colliculus of the tectum, which in turn project to the pulvinar. The pulvinar is the place from which visual information transferred from superior colliculus is transmitted to the vision-related areas of the temporal and parietal lobes [Kolb & Whishaw, 2006]. The superior colliculus includes the superficial lamina to which retinas' fiber project, and also, receive projections from striate visual cortex, and in turn project to the deep laminae. The deep laminae receive diffuse projections from other visual and non-visual areas [Kolb & Whishaw, 2006; Foreman et al., 1978; Sprague, 1975]. The two visual pathways are similar in primates and rodents, but there are differences. Ninety percent of the rat's retinal ganglion cells project to the superior colliculus, and 20 to 50 percent of the cells innervate the dorsal lateral geniculate nucleus, whereas the retinal ganglion cells are almost reversely distributed in macaque monkeys. The recent type of distribution indicates the dominance of tectocortical projection [via the thalamus] in rat's visual system [Dean, 1993; Linden & Perry, 1983; Sefton & Dreher, 1985].

Consistent with differential neuroanatomical distribution of visual pathways, the effect of damage to geniculostriate system is sometimes described as mild in rats in comparison with monkeys [Humphrey & Weiskrantz, 1971; Keating & Dineen 1982], nevertheless when similar tasks are used primates and rodents display similar deficits.

Visual cortex includes striate and extrastriate cortex, which are interconnected. Malach [1989] identified the following patterns of connections in the rat's visual cortex: 1. The neighboring sites make more extensive connections than the distant ones. 2. Those extrastriate loci that receive common inputs from striate cortex [such as projections from rostral striate cortex] tend to be interconnected. 3. The projections from rostral and caudal as well as projections from medial and lateral striate cortex [opposite poles] tend to avoid each other. Visual acuity, the ability to detect visual stimuli and resolve objects separated in space, [Mcbueney & Collings, 1984], is reported to be from 1 to 1.5 cycles per degree [c/d] for rats [Keller et al 2000; Dean, 1981a; Prusky et al., 2000a; Seymour & Juarska, 1997; Silveira et al., 1987]. The ablation of striate visual cortex causes a small reduction of behaviorally measured visual acuity, from about 1.0 to 0.7 c/d. With larger lesions including both striate and prestriate cortex [V2L], the visual acuity of rats is reduced to 0.3 c/d [Dean, 1981a,b]. Preserved visual acuity in rats with damage to striate visual cortex may be mediated by either spared remnants of the geniculocortical pathway or by the pathway from superior colliculus to prestriate cortex via the lateral posterior nucleus. A further lesion given to the superior colliculus severely disrupted contrast detection in destriate rats suggesting that destriate rats can use spatial information conveyed by the tectocortical path. The remaining capability of pattern discrimination after the removal of all visuotopically organized regions may be related to perirhinal and/or retrosplenial areas.

Although, the role of visual cortex in spatial navigation has not been studied extensively, a number of studies imply such role for visual cortex in rats [Goodale & Dale, 1981; Hoh et al., 2003, Lashley, 1939; Whishaw, 2004]. Lashley [1939] demonstrated that visual cortex provides rats with a non-visual function by which a spatial problem can be solved. The peripherally blind rats, which he used in his experiment, lost their maze habit after they were given posterior visual cortex lesions. Goodale and Dale [1981] showed that in a radial-maze task, visual cortex plays a role in the spatial behavior of both sighted and blind rats. Hoh et al., [2003] suggest that striate visual cortex contributes to learning water task strategy, but is not crucially required for place learning per se. Whishaw [2004], however, has demonstrated that rats with damage to visual cortex were impaired in a matching-to-place water task learning [Whishaw, 1985].

Using a retrograde tracer, Kolb and Walkey [1987] showed that posterior parietal cortex in the rat is located between approximately 4 to 6 mm lateral to the midline, and markedly distinguished by decrease in cortical thickness. They argued that this area corresponds with Krieg's description of area 7 and multisensory association cortex described by Miller and Vogt [1984]. Posterior parietal cortex is connected to some other cortical and subcortical areas, located between the rostrally adjacent hindlimb sensorimotor area and caudally adjacent secondary visual areas [Reep et al., 1994]. Posterior parietal cortex receives afferents from the lateral dorsal [LD], the lateral posterior [LP], and posterior [Po] nuclei of thalamus, while it receives no projections from the ventrobasal complex [VB] or the dorsal lateral geniculate [DLG] nuclei. Posterior parietal cortex makes

cortical connections with some areas including secondary visual areas V2M and V2L, and retrosplenial cortex [Kolb & Walkey, 1987; Reep et al., 1994, see Fig. 1.5 & 1.6].

The contribution of posterior parietal cortex to spatial ability of rats has been shown in a number of studies [Chen et al., 1994a,b; Kolb & Walkey, 1987; Mizumori et al., 1992]. Kolb et al., [1983] demonstrated that rats with parietal cortex lesion showed some impairment in short-term spatial memory and adopted a looping strategy to find the submerged platform in the swimming pool. Bilateral lesions of area 7 in rats trained to move toward visual targets, caused less accurate navigation than control rats [Forman et al., 1992]. The deficits in homing behavior of rats with lesions in posterior parietal cortex increases with the complexity of their outward paths, suggesting that posterior parietal cortex plays a role in spatial behavior [Save et al., 2001]. Poucet and Benhamou [1997] proposed that parietal cortex maybe more involved in abstraction of spatial features and providing a metric representation of spatial information obtained in the course of locomotion [Save & Poucet, 2000; Thinus-Blanc et al., 1991]. These findings along with the proposal that an intact posterior parietal cortex is more involved in abstraction and integration of spatial features obtained in the course of locomotion [Poucet & Benhamou, 1997, Save & Poucet, 2000; Save et al., 2001] suggest that posterior parietal cortex of the rat may play a role in the formation of a representation of the environment.

A. B.

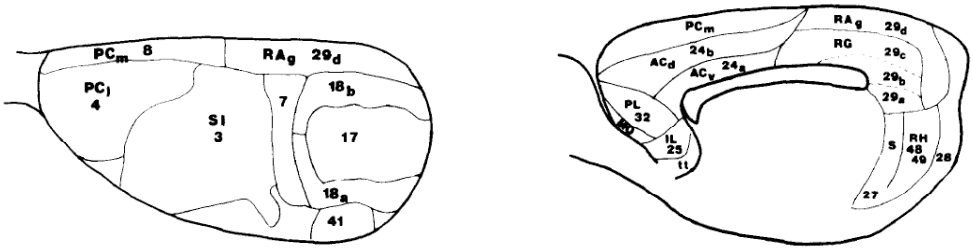

Fig. 1.6. Various cortical areas related to spatial navigation. Striate visual cortex [area 17] is surrounded by prestriate cortex [area 18a and 18b], posterior parietal cortex [PC], cingulate cortex including anterior cingulate cortex [AC-different areas] and retrosplenial cortex [R-different areas] [From Kolb & Walkey, 1987].

Cingulate cortex is a heterogeneous region structurally arched around the corpus calosum [Fig. 1.6]. The major subdivisions are: 1. Anterior cingulate cortex [area 24] 2. Posterior cingulate cortex [so called retrosplenial cortex “RS”, area 29]. Using antrograde and retrograde tracing, Vogt and Miller [1983] show that anterior cingulate cortex [area 24] receives projections from posterior cingulate cortex [Retrosplenial cortex], and visual cortex [area 18b & medial area 17].

Area 24b projects to retrosplenial cortex and through which to visual cortices. Posterior cingulate cortex [Retrosplenial cortex, area 29] has been described in a number of studies [For example, see Van Groen & Wyss, 1990, 1992, and 2003]. Three divisions of retrosplenial cortex were identified: 1] The retrosplenial a cortex [Rga]. 2] The retrosplenial dysgranular cortex [Rdg]. 3] The retrosplenial b cortex [Rgb] Retrosplenial a cortex [Rga] receives dense cortical projections from the ventral [temporal] subiculum, the posterior subiculum, and the contralateral Rga. It is also innervated by subcortical projections from the claustrum, the diagonal band of Broca, the thalamus, the midbrain raphe nuclei, and the locus coeruleus. Retrosplenial a cortex [Rga] projects to the postsubiculum, the rostral presubiculum, the parasubiculum, and the caudal medial parts of the entorhinal cortex. There are some reciprocal connections between retrosplenial dysgranular cortex [Rdg] and septal parts of CA1, postsubiculum, caudal parts of the entorhinal cortex, visual cortex [area 17 & 18b]. Retrosplenial b cortex [Rgb] is innervated by the hippocampus [CA1], the dorsal [septal] subiculum, the post-subiculum, and projects to the postsubiculum.

With respect to function, Van Groen and Wyss [1990] concluded that Rga integrates thalamic and limbic information, whereas integration of information from thalamus, hippocampus, and neocortex take place in Rdg cortex [see Van Groen & Wyss, 1992; Van Groen & Wyss 2003]. Movement-related inputs arrive in retrosplenial cortex via direct projections from posterior parietal cortex and anterior thalamic nuclei [ATN] [Van Groen & Wyss, 1990]. Visual projections from both geniculostriate and tectocortical pathways also converge to retrosplenial cortex [Cooper & Mizumori, 2001]. Vogt and Miller [1983] proposed that cingulate cortex has a role in feature extraction from environment and sensorimotor integration.

The function of cingulate cortex has been investigated in a number of studies that indicate that cingulate cortex [especially retrosplenial cortex] plays a role in spatial navigation. Sutherland et al., [1988] demonstrated that rats with complete removal of bilateral cingulate cortex and also with that of posterior cingulate cortex [retrospelenial] showed considerable deficits in place learning task, whereas rats with anterior cingulate cortex lesions showed less impairment and their function improved with more training. Sutherland et al., [1988] interpreted their results as suggesting a role for retrosplenial cortex in transmitting and elaborating topographical information between hippocampal formation and neocortical association areas. Retrosplenial cortex has also been considered as the site within which mnemonic associations of visual and nonvisual environment can be built to guide relatively accurate navigation in darkness [Cooper & Mizumori 2001; Maguire, 2001].

Six interrelated areas in the brain form a subcortical structure known as hippocampal formation [Amaral & Witter, 1989]. These areas are the hippocampus proper, the dendate gyrus, the presubiculum, the subiculum, the parasubiculum, and the entorhinal cortex. Fig. 1.7 illustrates the spatial position of hippocampus and its neural connections. The hippocampus proper consists of Ammon's horn and the dentate gyrus.

The entorhinal cortex projects to the dentate granule cells through the perforant path [Amaral & Witter, 1989]. The granual cells project to CA3 pyramidal neurons of Ammon's horn, which in turn project to CA1 pyramidal cells and the CA1 cells branch back to the entorhinal cortex via the subiculum. The collateral connections between CA1 and CA3 cells act as inhibitory modulations of information coming from both directions of the path [Kelso & Ganong, 1986]. That these regions of the visual brain contribute to spatial behavior has been reviewed above.

In order for visual information to be used in forming a spatial representation, it is assumed that it has to be transferred to the hippocampus. Ungerleider and Mishkin [1982] proposed that there are two visual streams, the dorsal stream and the ventral stream. The dorsal stream projects from visual cortex to parietal cortex and the ventral stream projects to temporal cortex and eventually end in the hippocampus. The ventral stream serves to identify objects, and dorsal stream mediates movement-related spatial vision [Goodale & Milner, 1992; Milner &

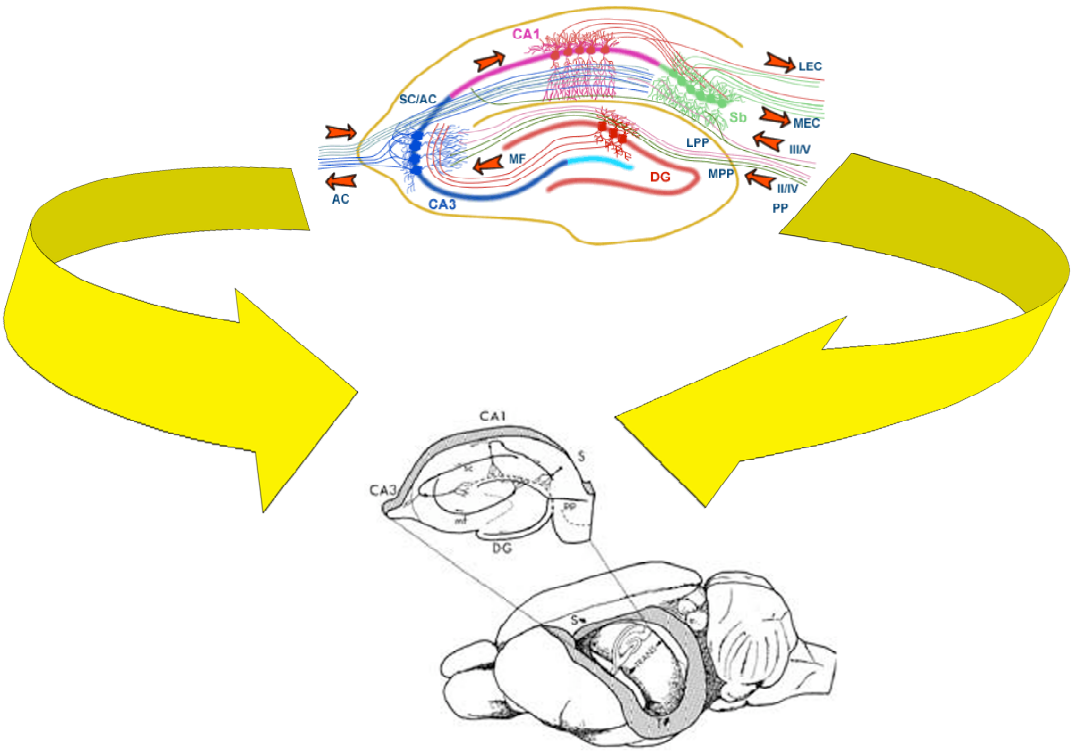

Fig. 1.7. A photograph of hippocampus inside the brain [bottom] and its saggital section [middle]. The hippocampus is a peanut-like structure located underneath neocortex, which is formed of various areas including the CA1-CA3, and dendate gyrus [The figure is adopted from www.duke.edu/.../hippocampalslice.jpg]. The figure on the top illustrates interrelated areas in the hippocampal formation. Hippocampus proper, Mossy fibers [MF], entorhinal cortex [EC], dendate gyrus [DG], profrant path [PP], subiculum [SC] [The figure is adopted from www.bristol.ac.uk/.../pathway/hippocampal.htm].

Goodale, 1995]. This well-documented distinction between dorsal and ventral streams, which serves for visual recognition and vision for action respectively in primates, is proposed to serve the same function in rats [Kolb et al., 1994].

A number of structures in the ventral stream are proposed to be associated with visual function. Aggleton et al., [2000] have reviewed the cortical inputs to the rat hippocampus that contribute to allocentric spatial navigation. Medial entorhinal cortex appears to receive visual information from the posterior rhinal cortex, subiculum, presubiculum, and parasubiculum. Posterior rhinal cortex receives numerous visual inputs from the occipital and parietal cortex [Burwell & Amaral., 1998]. Pre- and postsubiculum receive direct projections from occipital and cingulate cortex [Swanson et al., 1987; Witter et al., 1989]. Functionally, neurons in prerhinal cortex are responsive to the novelty/familiarity of visual stimuli [Brown, 1996]. Lateral entorhinal cortex receives inputs from retrosplenial cortex [Burwell & Amaral., 1998], which in turn receives direct inputs from visual areas 17 and 18 [Van Groen & Wyss, 1992], and anterior thalamic nuclei [Warburton et al., 1997]. Visual areas 17 and 18 project directly to presubiculum.

The entorhinal cortex is divided into subareas including the medial and lateral entorhinal cortex and is suggested to transfer visual information to the hippocampus. Inputs from cortical regions such as posterior rhinal, subiculum, presubiculum and parasubiculum enters medial entorhinal cortex. These connections implicate entorhinal cortex in vision. Inputs from posterior rhinal cortex especially are important because this area receives heavy projections

from occipital cortex. Additionally, retrosplenial cortex is assumed to be a crucial area in transferring visual information to the hippocampus because it receives visual inputs from areas 17 and 18, and it projects to entorhinal cortex [Pandya & Yeterian, 1981; Steward & Scoville, 1976]. Reep et al., [1994] speculated that the flow of visual inputs from visual cortex projects to the posterior parietal cortex, retrosplenial cortex, and then anterior dorsal thalamic nucleus in the rats. Taube [1998] postulated that the visual inputs then project to the postsubiculum, entorhinal cortex, and hippocampus, where they can be used to guide spatial behavior. Along with the contribution of visual system, Taube also summarized three possible pathways through which movement-related inputs required for self-movement-based navigation [called dead reckoning, see below] may provide the limbic system with a motor efferent copy of locomotion in the environment: 1. From the midbrain reticular formation to the laterodorsal tegmental nucleus, which projects to the lateral mammillary nuclei [Satoh & Fibiger, 1986]; 2. From striatum to the ventral tegmental nucleus, which projects to medial mammillary nuclei and then to the anterior dorsal thalamic nucleus [Shibata, 1989, 1992]; and 3. From motor cortex to area 29c of retrosplenial cortex that in turn projects to the anterior dorsal thalamic nucleus [Vogt & Miller, 1983; Van Groen & Wyss, 1990]. He proposes that the anterior dorsal thalamic nucleus might serve as a "convergent point" for idiothetic inputs projecting to the postsubiculum, entorhinal cortex and the hippocampus.

Consistent with the notion that striate visual cortex is important in spatial behavior, Paz-Villagran et al., [2002] recorded the activity of place cells while rats

foraged for food pallets in a cylindrical arena. They found that spatial coherence of firing by place cells was less organized in rats with lesions of striate visual cortex than control rats, and also the orientation of their place field was less controlled by three-dimensional objects. They suggested that visual cortex might contribute to the selection of cues to define the firing fields of place cells in space.

Additionally, Miller and Vogt [1984] speculated that the neocortex can be sufficient for spatial navigation. They showed that striate visual cortex [area 17] has reciprocal connections with each subdivision of visual cortex, and directly or indirectly through area 18a and 18b with other cortical areas such as area 8 [the frontal eye fields], 7 [posterior parietal cortex], 36 [temporal cortex], and area 11 [frontal cortex]. They suggest that cortical visuosensory and visuomotor integration is the result of these cortico-cortical connections that provide the rat with a spatial framework for visually guided behavior. The form of spatial behavior mediated by this dorsal stream route may be directly related to ongoing movement and thus might be distinct from spatial behavior mediated by the ventral stream.

Ethological approach to spatial behavior

Lorenz [1981] defined ethology as “the comparative study of behavior which applies to the behavior of animals and humans”. The notion that behavior can be explained entirely based on stimulus-response relationships, cognitive mapping and learning was opposed by ethologists who believed that behavior is innately organized. Additionally, behaviorists tend to reduce the effect of

environmental variables on behaviors in the laboratory, and study simplified behavior [For example, movement from a start box to a goal box] to minimize behavioral variability. Ethological studies are characterized by a different methodological approach, usually observation of animals in a natural habitant or laboratories that model a natural habitant [see: Brown, 1966; Shillito, 1963 for an example of exploratory behavior]. Ethologists focus on the study of patterns of movements and expect that they vary less between animals of the same species [Pfluger & Menzel, 1999] but distinguish animals of different but related species. For example, during his studies in the Berlin Zoo on waterfowl, Lorenz showed that waterfowl performed behaviors in the zoo that were similar to those displayed by birds in the wild. In addition, he demonstrated that birds of the same species displayed similar movements, which is termed "species-specific" behaviors [Marler, 2004]. This evidence suggested that the movements were unlikely to have been learned and were thus innate. Nevertheless, current notions in neuroscience can be traced to both aforementioned paradigms theoretically [Pfluger & Menzel, 1999].

With respect to spatial behavior, ethological studies suggest that there are two forms of spatial behavior, piloting and dead reckoning. Piloting is very similar to spatial learning in the sense that it employs environmental cues for guidance. It is primarily a strategy used by animals to move through familiar environments and to learn to find their way through novel environments. Dead reckoning [Wallace & Whishaw, 2003] is a process by which an animal calculates its current distance and direction relative to a starting point based on updated record of its

moment-to-moment movements [Whishaw et al., 2001; Wallace & Whishaw, 2005]. Because dead reckoning depends upon self movement cues, it is much more likely to be used for returning to a starting location. It has been shown that both piloting and dead reckoning contributes to the calibration of space and solving spatial problem in an open field [Whishaw & Brooks, 1999]. Just as piloting is proposed to be mediated by the hippocampus so too has dead reckoning [For an example see Wallace & Whishaw., 2003; also see; McNaughton et al., 1996; Wallace et al., 2002a; Whishaw & Masswinkel, 1998; Whishaw et al., 2001].

Because spatial navigation by animals in natural environments depends upon learning about the environment, exploration is central to understanding spatial behavior. Exploration includes a number of behaviors such as locomotion, rearing, sniffing etc. all of which are assumed to be used for gathering information about the environment [Renner & Seltzer, 1991]. Early studies of exploratory behavior were confounded by the complexity of the behavior. A rat placed in even the simplest of environments, [e.g., a box containing no objects], would traverse the box many times, all the while stopping frequently and rearing.

In observing spontaneous exploratory behavior, the pattern of activity was considered too complex to understand [Hall, 1934, Halliday, 1968]. It was not even clear whether the behavior was organized or random. Nevertheless, open field tests have proved useful in analyzing a host of behaviors in animals that are brain injured, treated with pharmacological agents, or suffering from disease. In

most of these studies the total activity, e.g., walking or rearing, displayed by an animal is the dependent measure.

The first finding that indicated that exploratory behavior is organized was made by Eilam and Golani [1989] in their article “Home base behavior of rats (*Rattus norvegicus*) exploring a novel environment”. Using a large table placed in a featureless testing room, they videotaped the rats’ behavior as they individually explored the table for 1 hour. In order to analyze the rats’ activity, they mapped the open arena in a way consistent with Eshkol-Wachman method of mapping topographical positions. The arena was divided into 25 sectors and the rats’ behavior in each sector was analyzed. The videotapes were time coded and displayed on the screen. The analysis distinguished between stops and progressions. A stop was defined as a lack of progression, and the length of time that rats were stopped was recorded. To record stopping time, a trained observer pressed a key when rats stopped and repressed that key when rats left that location.

Upon being placed on the open table in a novel environment, rats started making progressions interrupted by stops. Each rat stopped in many places but more frequently in one or two locations. Additionally, the preferred stopping locations for each rat were idiosyncratic. The researchers described the preferred stopping locations as “home bases”. They observed that the home bases were the only places in which the animals displayed behaviors of grooming, and rearing. Home bases were places that gave structure to other aspects of exploratory behavior; i.e., home bases were places from which rats make

excursions. Furthermore, the characteristics of outward and homeward portions of rats' excursions were different. The outward progressions were slower and interrupted whereas homeward progressions were direct.

Eilam and Golani [1989] argued that their results indicated that exploratory behavior of rats is innately organized. Because the testing room was featureless, and because each rat had a preferred location for its home bases, this seemed to be evidence for the idea that the rat imposes structure on its behavior and on the environment. This structure in turn determines where other activities will occur and how they will take place. Following these findings, Golani and his colleagues conducted a series of experiments to further examine other characteristics of home base behavior as an organized activity.

Golani et al., [1993] found that when a rat left a home base on an excursion, the number of stops that it made on the excursion is limited by an intrinsic upper bound of about 12 stops per excursion. The upper bound of stop number did not increase with the size of the explored environment. This observation suggested, in turn, that home base attraction increased as a function of the number of stops that a rat makes. Tchernichovski, et al., [1998] observed that the geometrical characteristic of exploratory locomotion and stopping was a function of time and repeated exposure to the same environment. Although the length of excursions was different between rats, the shape and size of excursions showed similar pattern of changes during exploratory bouts. At the beginning of exploratory session progressions were short and featured few stops whereas toward the end of the session outward progressions were longer and had more stops.

Nevertheless, as exposure time passed, or if rats repeatedly were exposed to the same environment, the global shape of excursion trajectory changed. Outward excursions became longer with time or exposure, the duration of an excursion increased with time, and the number of stops on an excursion increased with time or exposure. Again, these studies suggest that changes in the geometry of excursions follow an organized and predictable pattern, again suggesting that the rat was imposing structure on its behavior.

Drai et al., [2000] identified three modes of progressions during exploration, and termed each mode as a gear “G”, which included G1, G2, G3. Rats traveled distances of rarely more than one rat length around the home base, and with usually low speed [G1] and they cover more than one rat length on outward portions of their trips at a faster speed [G2]. The homeward portions of their trips took place at greater speed [G3]. Thus, this study demonstrated that the speed of locomotion is also spatially and intrinsically organized.

Whereas the Golani group emphasized the intrinsic origins of organized exploratory behavior, their work is useful in understanding how animals organize their behavior in more complex environments. More complex environments are those that contain many sensory cues or other surrounding objects. Whishaw and his colleagues provided evidence for the contribution of such salient cues to the organization of exploratory behavior [Leowen et al., 2005; Hines & Whishaw, 2005; Wallace et al., 2002a; Wallace & Whishaw, 2003].

Leowen et al., [2005] studied development of spatial behavior in rat pups. In their study, they made use of a small heat pad, as an artificial huddle, or a

huddle of pups as a possible home base. They found that the heat pad or the huddle served as the pups' home base. Pups made excursions from the huddle that had all of the features of excursions displayed by rats forming natural home bases in a featureless environment. The complexity of exploratory behavior also changed during development, as the length of excursion and the number of stops increased with age. When the rats reached 22 days of age, they began to respond to distal visual cues to form home bases and now relied less on other rats or the heat pad for a home base. The results can be taken as indicating that the intrinsic organization of spatial behavior incorporates external cues to demark home bases and organize other aspects of spatial behavior.

This conclusion was extended by Wallace et al., [2002a], who showed that when a cage is present on a large open table, adult rats use the cage as a home base for excursions, and the pattern of their outward and homeward trips is similar to those found in a relatively featureless environment in studies conducted by Golani and his colleagues. Additionally, Hines and Whishaw [2005] demonstrated that rats could organize their exploration to a large visual object presented near the open table. When the object moved, the rats accordingly moved their home base. Even if a salient object was not present the rats formed home bases near other visual features of the room, including pictures on the wall, the door, and event a paper towel dispenser or a light switch.

The pattern of organization displayed by rats in novel environments gives rise to the suggestion that they are using two different navigation strategies, each mediating a different aspect of their behavior. On outward excursions, it seems

likely that they are piloting and are learning about their environment. Thus, as they explore, they make longer and longer excursions that take them to different locations in the environment. The information that they gather on each trip can thus be usefully applied to the next trip. Because the homeward trips are direct and rapid, even when the home base is not marked by a landmark, it is likely that the rats are using dead reckoning. That is, they integrate movement cues from their outward movements, and then double integrate this information to generate a rapid direct homeward trip. The upper limit on the number of their outward stops likely indicates the limit on their capacity to integrate self movement cues. Wallace et al., [2002b] suggest that vestibular information provides the main self movement information used for dead reckoning.

Because exploratory behavior is intrinsically organized suggests that it should vary in different species. Using a large open arena, which was confined with walls, Zadicario et al., [2005] investigated exploratory locomotion of Tristram's jirid [a species of gerbil] in the dark and light condition. Each animal explored the environment in a dark room for a period of 10 min and in the next day the same animal was tested for the same period of time in the same room with the light on. The exploratory locomotion of jirids was organized when they explored the environment in the light. They formed a home base from which they explored the environment and returned to it following each excursion. Nevertheless, animals did not form a home base in the dark and adopted a looping strategy to return to their last stop. Characteristics of stops and progressions in the dark and light were also different. Animals stopped for a

shorter period of time in the dark compared to the light. Because the exploratory behavior of rats is organized in featureless environments and also in the dark [Hines & Whishaw, 2005] it demonstrates a species difference.

Some caution should be adopted in supporting this conclusion; however, as the test time used was quite short. Avni et al., [2006] conducted an experiment in which jirids were tasted in three conditions of Dark-Light group, Light-Dark group, and Dark-Dark group. Jirids were given a longer period of time for exploration [50 min] and showed a different organization of exploratory locomotion. Exploration was scattered in various zones of the arena at the beginning and after a while began to become organized to a corner of the arena from which they made excursions with increasing traveled distance as a function of time. The main finding of these experiments, a transition from looping and scattered to an organized exploratory locomotion, suggests that exploration continues to be organized in the dark if the testing time is longer.

Although an empirical analysis of exploratory behavior does not necessitate a causal explanation, a variety of theories have attempted to account for why rats explore. Among earlier theories of this type, exploration was first assumed to stem from curiosity derived by novel stimuli or to be a product of boredom resulting from exposure to an unchanged environment for a long period of time [See Russell, 1983].

Some other theories emphasized on the role of fear as a core element. In monophasic theories, there exists a motivational system whose function varies based on the testing environment. One theory proposes that “fear” is a

determinant of exploratory activity [Russell, 1973; 1983]. The concept of threshold defines the tendency to avoidance or explore. Various test factors determine whether the motivation for exploration is above or below the threshold. Arousal theory proposes that the amount of exploration depends on the magnitude of arousal [Russell, 1983]. Small changes in the environment lead to low level of arousal, and increase the exploratory behavior that is directed toward increasing arousal to an optimal level. From this point of view, large increases of arousal level leads to withdrawal. Fear has been considered one of the important factors that contribute to the level of arousal and exploration [Halliday, 1966; Brown et al., 1999].

Biphasic theories propose that fear and information gathering interact to produce exploration [Brown et al., 1999; Montgomery, 1955; Russell, 1973]. According to this biphasic theory, two separate motivational systems have resulted in a certain level of exploratory activity through their conflicting interactions [Russell, 1983]. A tendency to withdraw is motivated by fear, and a tendency to explore the environment is elicited by novelty. The behavioral outcome reflects the competition between these two motivational systems such that small environmental change is associated with exploration of the environment, and large changes in the environment is associated with fear and withdrawal [Montgomery, 1955].

Environmental modeling and discrepancy theories propose that exploration serves to gather information about novel items that leads to a neural model of the environment [a set of internal representations] and aims to eliminate the

discrepancy between the model and current environmental inputs [See Russell, 1983]. In this category, cognitive mapping theory argues that the objective of exploration is to gather information. O'Keefe and Nadel [1978] proposed that exploration is a response to novelty, and serves to gather information that leads to construction of cognitive maps of the environment. Novelty is a property of items or places that have not been experienced before and response to it depends on memory such that exploration decreases with repeated exposure or learning about a novel item. In this theoretical framework a novel item or place is not part of an existing cognitive map of the environment, but exploratory learning updates the map. O'Keefe and Nadel [1978] also distinguish between novel items that elicit exploration and noticeable but familiar stimuli that trigger either approach or avoidance.

Theoretical background and proposed research

In my review to this point, I have presented evidence that machinery for spatial representations involves the hippocampal formation and is at least partially visually dependent. I have also presented evidence that indicates that rats placed in novel environments, even relatively featureless novel environments, impose organization on their activity in that environment. Nevertheless, the availability of visual cues importantly influences their behavior, in that they form home bases near visual cues. At face value, this evidence suggests that the organization of spatial behavior depends in part on visual cortex. Indeed, Lashley [1943] suggests behavior depends upon primary visual cortex and a number of subsequent studies have reported spatial deficits in rats

subjected to visual cortex lesions. Additionally, organized spatial behavior must also depend upon the hippocampal formation.

Given this background, a series of reports examining the contribution of the hippocampus to organized exploratory behavior of rats is puzzling [Clark et al, 2005; Lehmann et al, 2007; Hines & Whishaw, 2005; Wallace et al., 2002a]. These studies show that many features of organized exploratory behavior are intact in rats with hippocampal damage, especially in tests given in the light. In short the rats form home bases, they make excursions from their home bases, and they stop on the outward portions of their trips and travel back to their home base relatively directly, etc. These results do not support the contention that all exploratory behavior will be abolished after hippocampal lesions [O'Keefe & Nadel, 1978] and they do not support the contention that all organized exploratory activity depends upon the hippocampal formation.

In view of the paradox that so much evidence supports a role for the hippocampal formation in spatial behavior while the organization of exploratory behavior remains largely intact after hippocampal formation damage, the present thesis was directed toward examining the contribution of other regions of the extended visual system to spatial behavior. It was expected that if not the hippocampus, then some other portion of the extended visual system must contribute to visually-organized spatial exploration. Parsimony suggested that this examination should begin with primary visual cortex. The main prediction was that if organized exploratory behavior related to visual cues was importantly dependent upon information from primary visual cortex, then after visual cortex

removal exploratory behavior should become impoverished or may even be absent.

The experimental portion of the thesis consists of two parts. In the first part of the thesis, a spontaneous exploratory paradigm was developed in which visual cues importantly influenced the organization of exploratory locomotion to the entry point. In the second part of the thesis rats with visual cortex lesions were tested on the task. The theory proposed is that the extended visual cortex contributes to organized exploratory spatial behavior dependent upon visual cues. The specific hypothesis tested was that removal of primary visual cortex would deprive the extended visual system of information essential to visually organized spatial exploration.

Experimental Paradigm

The point of entry and Cue saliency

Abstract

The exploratory behavior of rats on an open field is organized in that animals spend disproportionate amounts of time at certain locations, termed home bases, which serve as centers for excursions. Although home bases are preferentially formed near distinctive cues, including visual cues, animals also visit and pause and move slowly, or linger, at many other locations in a test environment. In order to further examine the organization of exploratory locomotion, the present study examined the influence of the point of entry on animals placed on an open field table that was illuminated either by room light or infrared light (a wave length in which they cannot see) and near which, or on which, distinctive cues were placed. The main findings were that in both room light and infrared light tests, rats visited and lingered at the point of entry significantly more often than comparative control locations. Although the rats also visited and lingered in the vicinity of salient visual cues, the point of entry still remained a focus of visits. Finally, the preference for the point of entry increased as a function of salience of the cues marking that location. That the point of entry influences the organization of exploratory locomotion is discussed in relation to the idea that the exploratory locomotion of the rat is directed toward optimizing security as well as forming a spatial representation of the environment.

1. Introduction

Open field tests are widely used to study locomotion and other activity that comprises “exploratory” behavior of the rat [Barnett & Cowan, 1976; Brown, 1966; Chance & Mead, 1955; Renner & Seltzer, 1991; Shillito, 1963; Whishaw & Brooks, 1999]. Exploratory tests are relatively simple procedurally in that they involve simply placing an experimental animal in a simple environment and observing its behavior. Nevertheless, the behavior first appeared to be haphazard or perhaps too complex to study in an open field [Hall, 1934; Halliday, 1968].

More recent work suggests that there is some organization to exploratory activity. Studies in which rats explore a relatively featureless environment report that rats spend long periods and move slowly or “linger” in one or only a few locations. These places have been termed “home bases” [Eilam & Golani, 1989], presumably suggesting that in natural habitats, the animals also adopt some location as “home”. Home bases appear to be central to organizing many other features of exploratory behavior. They are locations from which rats make excursions characterized by slow outward progressions with periodic stops and more rapid and direct homeward returns [Eilam & Golani, 1989; Tchernichovski et al., 1998; Wallace et al,. 2002a] and they are locations in which rats sometimes make slow turning movements and rearing and in which they groom [Eilam & Golani, 1989].

Subsequent work has shown that home bases are formed in relation to salient distal cues or near local cues, including objects on the room walls,

furniture, and cues placed near or on the open field [Hines & Whishaw, 2005; Wallace et al,. 2002a]. Exploratory locomotion can also be organized to two proximal visual objects in a novel environment [Clark et al., 2006; Lehmann et al., 2007]. That rats form home bases in relatively featureless environments, in the dark, and adjacent to salient visual or tactile cues [Hines & Whishaw, 2005; Wallace et al., 2002a; Whishaw & Brooks, 1999] and that a combination of cues contributes to spatial behavior [Collett et al., 1986; Etienne, 2003; Georgakopoulos & Etienne, 1994; Hughey & Koppenaal, 1987; Kimchi & Terkel, 2001; Morris et al., 1982; O'Keefe & Nadel, 1987; Poucet et al., 1986] suggest that rats may use a variety of spatial strategies for organizing their behavior. These may include piloting [moving in relation to allothetic or external cues] and dead reckoning [moving using self movement cues] [Gallistel, 1990; O'Keefe & Nadel, 1987] to form and locate home bases, or organizing their behavior.

Although there is substantial evidence that the exploratory locomotion of rats is organized, the point at which this organization begins is not known. There are at least three possibilities. First, a rat may carry a spatial frame of reference into the test environment. For example, Martin et al., [1997][see also, Huxter et al., 2001; Margules & Gallistel, 1988; Poucet, 1993; Taube & Burton, 1995] have demonstrated that rats can learn maze locations using an inertial reference located outside the maze. Second, a rat could use its point of entry as a reference point to solve a spatial problem [Hynes et al., 2000] or to guide its subsequent movements. For example, a rat placed in a novel environment displays "warm-up" a sequence of movement from which they initiate movement

from the point of entry [Eilam & Golani., 1989; Golani et al., 1981]. In warm-up, successive movements escalate in size from and return to the starting position. Warm-up may in part underlie progressions from and returns to a point of security in an open field [Sharp et al, 1987; Whishaw et al., 1992]. Third, it may be necessary that a rat make initial exploratory excursions through the environment before it can begin to organize its exploratory locomotion. Rats have been reported to "calibrate" a working space prior to using that space for other behaviors and after changes are made in their working space [Buzacki, 2005; Whishaw & Brooks, 1999]. In addition, in familiar environments, rats have been reported to return to a point of entry, possibly to recalibrate their spatial reference, when test demands are changed [Whishaw & Mittleman, 1986].

The purpose of the experiments was threefold. First, the study examined the organization of exploratory locomotion of rats to their entry point in a relatively featureless environment. The design of experiment was suitable for investigating whether organization of exploratory locomotion to the entry point is mediated only by distal and/or movement-related cues. Second, the effect of local object on exploratory locomotion [Hines & Whishaw, 2005, Wallace et al., 2002a] was studied as a function of cue saliency. Third, the effect of local object on exploratory locomotion when rats started from a location in the environment at which there was no local cue but a salient local cue was observed from the starting location.

For the study, rats were placed individually on a large circular table and their movements were recorded using a computer-based video tracking system. In

four experiments, rats were started from different locations in room light, in infrared light, adjacent to cues that varied in saliency, or from locations distant from a salient cue. Measures of organized exploration in relation to the segmentation of the table surface included travel distance, dwell time, durations of stops, returns to the point of entry, and stop dispersion.

2. Materials and Methods

2.1. Animals

Fifty six female Long-Evans rats used in the experiments were about three months old, and weighed approximately 250-300g. They were housed in groups of three in Plexiglas cages with sawdust bedding and *ad libitum* food and water. The colony room temperature was at 20-21º C and was illuminated on a 12/12 hr light/dark cycle. Experiment was conducted in accordance with guidelines from Canadian Council of Animal Care and the University of Lethbridge Animal Care Committee.

2.2. Open field

A 244 cm diameter white circular wooden table [Fig. 2.1], elevated 64 cm above the floor, was used as an open field [Hines & Whishaw, 2005]. The table was located in a large testing room and was surrounded by a number of cues including a paper towel dispenser, switches, and posters on the wall. Very large salient cues, including a bookcase, sink were covered with white sheets to make them less conspicuous. In order to minimize local olfactory cues, the table was cleaned with soap and water following each trial for each rat.

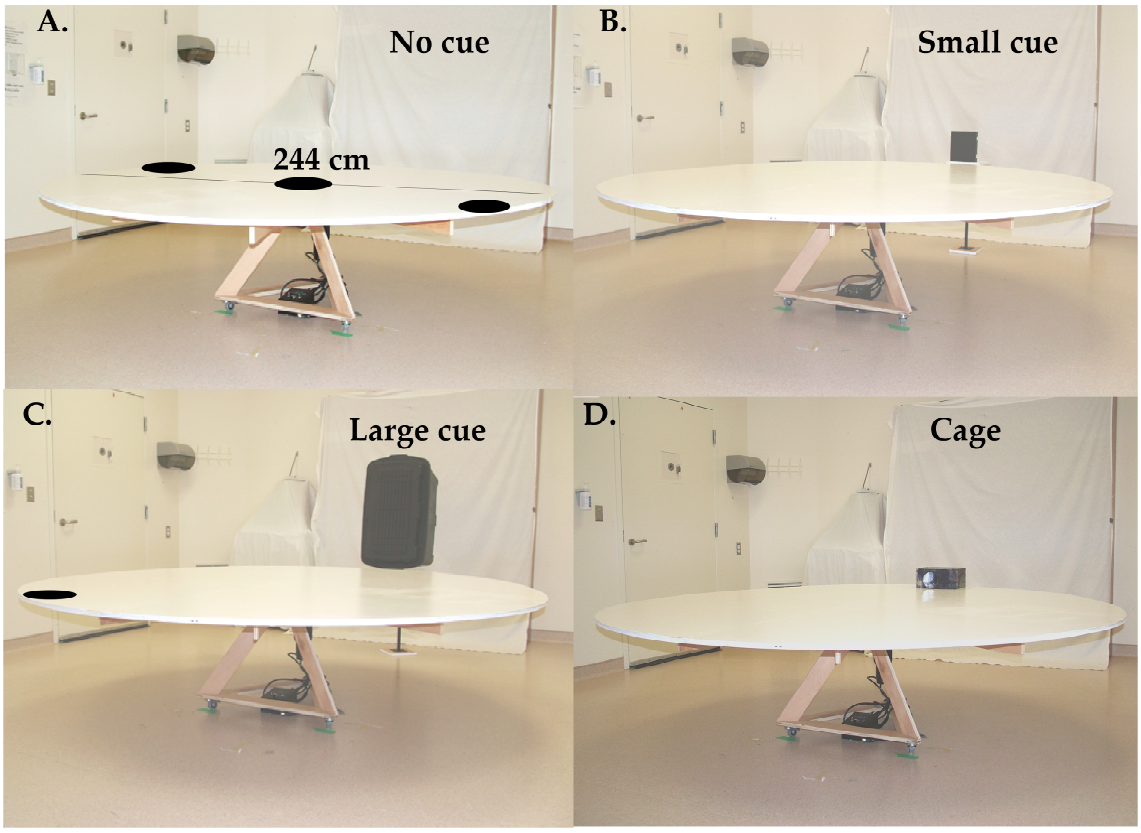

Fig. 2.1. Apparatus, the point of entry and cues. A. Open table. Black circles indicate locations where rats were placed to begin a session. B. Open table with small local cue. C. Open table with large local cue. D. Open table with a cage the rat can enter.

2.3. Movement tracking and analysis

An HI-8 Sony video camera sensitive to normal and infrared light was located in the ceiling of the test room to record the movements of rats. The video record was converted to x-y coordinates using a sampling rate of 30Hz using AccuTrack software [AccuScan Instruments, Inc. Columbus, OH, 43228, USA]. The AccuTrack system automatically tracks the midline of a rat's back at the level of the forelimbs by selecting one pixel per frame of digital computer file. The x-y coordinates were analyzed using programs written in C++.

2.4. Test conditions

Rats were tested in the following different proximal and distal cue conditions:

[1] No cue. Room lights were on and no cues were placed on or around the table [Fig. 2.1A].

[2] Small visual cue. A small visual cue [a 19 cm x 22 cm x 3 cm black box], oriented toward the table was placed 20 cm away from the edge of the table [Fig. 2.1B].

[3] Large visual cue. A large visual cue [a 48 cm x 48 cm x 52 cm black box], oriented toward the table was placed 20 cm away from the edge of the table [Fig. 2.1C].

[4] Cage. The cage was a black box [20 cm x 12 cm x 25 cm] with a 4 cm x 4 cm entrance, facing the center of the table, was placed on the edge of the table [Fig. 2.1D].

[5] Infrared light. Room lights were off and infrared light, a wavelength in which rats cannot see [Hines & Whishaw, 2005, Wallace & Whishaw 2005], was reflected from the room walls. The experimenter used infrared goggles to place the rat on the table.

2.5. Test procedure

Each rat was carried from the colony to the testing room [50 m distance with 3 turns] in a cage similar to the one that they were housed in. After a 2-3 min wait outside the test room, a rat was lifted by its shoulders and taken singly into the test room and gently placed on the table. Each rat was video recorded for the duration of its test. The experimenter left the room immediately after placing the rat on the table. Test durations lasted 20 min or 30 min, durations that have been described as sufficient for establishing home bases in previous research [Eilam & Golani, 1989].

2.6. Behavioral measures

To derive behavioral measures that quantified the rats' movements on the table, the table was divided into either 4 quadrants, 17 sectors, or into 2 annuli by the computer based programs. Each table division was defined as a zone, and with respect to the zones the following measures were made:

[1] *Time*. The total time was the time in seconds either moving or still.

[2] *Stop.* A stop was defined by a filter that placed x-y coordinates into bins of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec. From the program, both the total time spent stopped and the number of stops could be derived.

[3] *Stop dispersion.* The stop dispersion measure was calculated as a measure of the distribution of stops on the table. Thus, a dispersion value approaching '0' indicated that a rat was still only at one location during a test session, whereas a higher value indicated the extent to which a rat stopped at different locations of the table. In order to quantify dispersion of stops, a computer-based program computed the average distance between points where stops occurred based on the following formula:

$$D = \frac{1}{n^2 - n} \sum_{i=1}^{n} \sum_{j=1}^{n} \sqrt{(x_j - x_i)^2 + (y_j - y_i)^2}, \quad \text{where } i \neq j$$

.

In the formula "n" represents the number of stops and "X" and "Y" are values that represent each stop in a Cartesian coordinate system.

[4] *Distance*. The travel paths were measured for total length [cm] and length traveled in zones.

2.7. Statistical analysis

The results were analyzed using ANOVA of treatment groups and repeated measures, with Bonferroni, Student-Newman-Keuls post hoc tests, and unpaired t-tests [Winer et al., 1991].

3. Procedure

Four experiments were conducted in various cue conditions:

Experiment 1: Rats return to their entry quadrant on the edge of the table.

Two groups of rats were tested twice for 20 min tests in a counter balanced design. One group [n=6] was tested in room lighting condition. The second group [n=6] was tested in infrared light condition. For each testing condition, three rats

received a first test in which they were placed at the table's edge in the southwest [SW] quadrant of the table and a second test two days later in which they were started at the table's edge in the northeast [NE] quadrant of the table. For the other three rats in each group, the testing sequence was reversed. Thus, a comparison group consisted of six rats, 3 of which received their first test and 3 of which received their second test, from the same starting location.

Experiment 2: Rats return to their entry quadrant at the middle of the table.

Two groups of rats were tested for 20 min under normal light condition on the open table. One group [n=6] was started from the middle of the table. For the other group [n=6], starting locations were counterbalanced such that three rats started in the SW quadrant of the table and three rats started in the NE quadrant of the table.

Experiment 3: The salience of cues at an entry quadrant influences returns.

Four groups of rats [n=5 per group] were tested for 30 minutes in the light condition on the open table. All rats were started from the southeast [SE] quadrant of the table but for each group the cue at or near the entry point was different, as follows:

Group 1: no salient cue

Group 2: the small visual cue was located near the table

Group 3: the large visual cue was located near the table

Group 4: the rats were released into the small refuge

Experiment 4: Rats return to an entry quadrant in the presence of a salient visual cue.

Rats [n=12] were placed at the table's edge in the northeast [NE] quadrant of the table for a 20 min test. A large visual cue was located near the southeast [SE] quadrant of the table.

4. Results

Experiment 1: Rats return to their entry quadrant on the edge of the table.

With the point of entry counterbalanced for two separate trials, when the rats started in the SW quadrant of the table, they displayed a preference for that quadrant and when they started in the NE quadrant of the table they displayed a preference for that quadrant, in both room and infrared light conditions. Fig. 2.2 illustrates the preference for the entry quadrant by showing travel paths and stops for one rat tested in room light and one rat in infrared light condition. These general findings were confirmed by the formal analyses:

Total time. ANOVA indicated that there was no significant effect of trial order, $F[1,10]=0.02$, $p=0.88$, the rats displayed the same quadrant preference strength relative to the entry quadrant on both their first and second trials. There was a significant preference by both light and dark groups for the entry quadrant, $F[1,10]=21.7$, $p<0.001$, and an absence of a room light vs. infrared light test effect, $F[1,10]=0.82$, $p=0.38$, indicated that the preference for the entry quadrant occurred in both illumination conditions. There was no significant interaction of group by quadrants on the total time, $F[1,10]=3.5$, $p=0.09$. The main effects are illustrated in Fig. 2.3A.

Stop time. ANOVA indicated that there was no significant effect of trial order, $F[1,10]=0.009$, $p=0.92$, the rats displayed the same quadrant preference strength

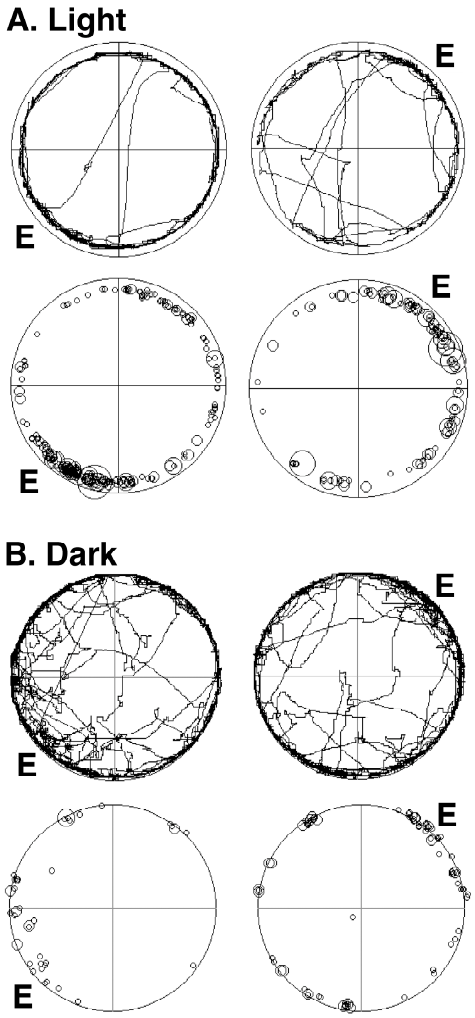

Fig. 2.2. The paths and stops made by representative rats placed in SW or in NE quadrants in the light [A] or in the dark [B] conditions. The large circle represents the table on which rats explored the environment, and their path [lines], and stops [circles] illustrate preference for the point of entry [E]. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

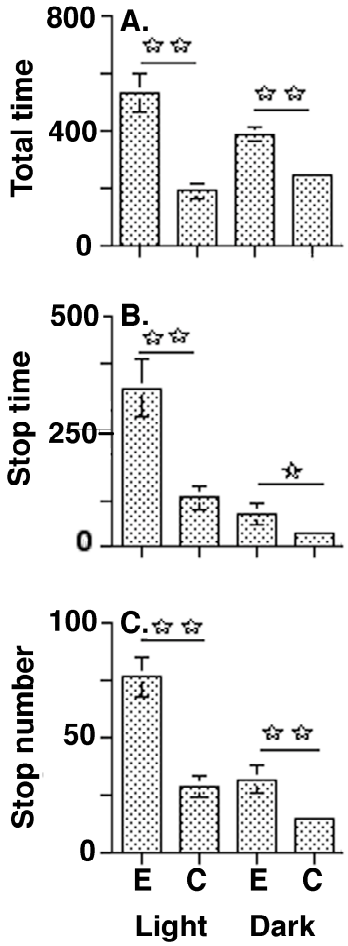

Fig. 2.3. The effect of point of entry on exploratory locomotion in room light and infrared light conditions [means and standard errors in seconds]. Rats spent greater length of time [A], and stopped longer [B] and more frequently [C] around the entry [E] than the control [C] quadrant. *=P<0.05; **=p<001.

relative to the entry quadrant on both their first and second trials. There was a significant preference by both light and dark groups for the entry quadrant, $F[1,10]=10.59$, $p<0.01$. There was also a significant group difference for rats tested in the light vs. dark, $F[1,10]=12.87$, $p<0.01$, as the rats tested in the light had longer stop times compared to rats tested in the dark. There was also a significant interaction of entry quadrant by group, $F[1,10]=4.99$, $p<0.05$, as the magnitude of the preference for entry quadrant of the rats tested in the light was greater than that for rats tested in the dark. The main effects are illustrated in Fig. 2.3B.

Number of stops. ANOVA indicated that there was no significant effect of trial order, $F[1,10]=1.4$, $p=0.26$, the rats displayed the same quadrant preference strengths relative to the point of entry on both their first and second trials. There was a significant preference by both light and dark groups for the entry quadrant, $F[1,10]=12.11$, $p<0.01$ [Fig. 2.3C]. There was also a significant group difference for the rats tested in the light vs. dark, $F[1,10]=25.23$, $p<0.001$, and a significant interaction of entry quadrant by group, $F[1, 10]=5.49$, $p<0.05$, as the magnitude of the preference for entry quadrant of the rats tested in the light was greater than that for rats tested in the dark. The main effects are illustrated in Fig. 2.3C.

Follow up t-test indicated the rats' preference for the entry quadrant vs. the diagonally opposite quadrant was significant [$p<0.05$] on measures of total time, time spent stopped, and numbers of stops in rats tested in room and infrared light conditions.

Distance. ANOVA indicated no significant effect of trial order $F[1,10]=0.01$, $p=0.92$, the rats displayed the same quadrant preference strengths relative to the point of entry on both their first and second trials.

There was significant preference by both light and dark groups for the entry quadrant, $F[1,10]=02.14$, $p<0.05$. There was a significant group difference for rats tested in the light vs. dark, $F[1,10]=23.57$, $p<0.001$, as the rats tested in the dark had longer travel path compared to rats tested in the light. There was also a significant interaction of entry point by groups, $F[1,10]=40.42$, $p<0.002$, as the magnitude of the preference for entry quadrant of the rats tested in the light was greater than that for rats tested in the dark.

Follow up t-test indicated the rats' preference for the entry quadrant vs. the diagonally opposite quadrant was significant [$p<0.05$] on measures of distance traveled in room light and infrared light conditions.

Temporal analysis of behavior. That the rats displayed a preference of the entry quadrant was not due to the fact that they simply remained in that quadrant when placed on the table. As is illustrated in Fig. 2.4 for a representative rat, when the rats' activity was represented in 2-min time blocks, the animals made a number of excursions from the entry quadrant. A measure of the time taken to first leave the entry quadrant indicated that as a group the rats left quite quickly in both the room light [mean=1.30±0.05 min] and infrared light [mean=0.47±0.13 min] conditions.

An analysis of the overall time spent in the entry quadrant as a function of 2-min time bins indicated that there was no significant group effect $F[1,10]=2.17$,

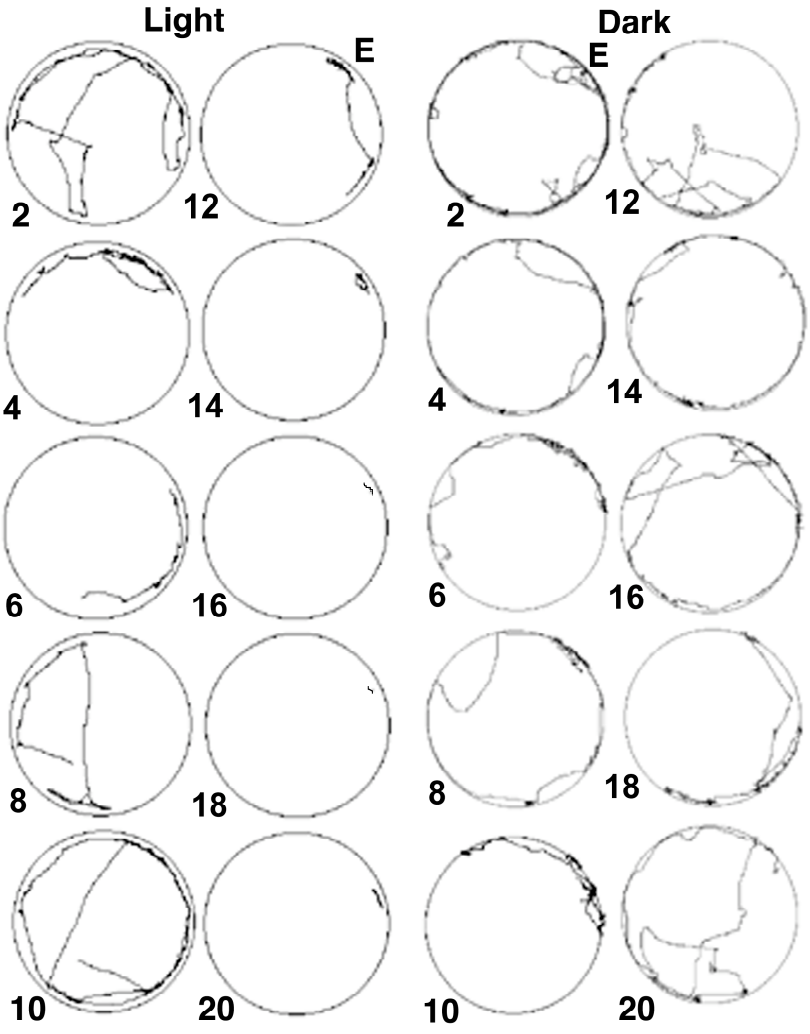

Fig. 2.4. The paths by representative rats tested in room and infrared light conditions as a function of 2-min time bins. Note: there were repeated visits to the entry location [E].

p=0.17 and no effect of time bins, under the normal F[1,9]=0.24, p=0.63 or infrared F[1,9]=0.08, p=0.77 light conditions. Thus, although the rats left the entry quadrant relatively quickly, they made return visits periodically throughout the test period [Fig. 2.5].

Experiment 2: Rats return to their point of entry in the middle of the table.

Two groups of rats were tested under room light condition, with one group started from the middle of the table and the other group started from the table edge. The rat's preference for the inner annulus was the dependent variable, and results indicated that only the rats that were started from the middle of the table displayed a relative preference for that annulus.

Fig. 2.6 illustrates travel paths, stops, and stop durations for the rats started at the NE quadrant edge vs. rats started in the middle of the table.

Preference for the center annulus of the table was confirmed by t-tests between the group started there vs. the group started at the edge of the table: there were significant differences between two groups for the total time, t=2.49, p<0.04 [Fig. 2.7A]; stop time t=2.43, p<0.04 [Fig. 2.7B]; and number of stops, t=2.39, p<0.04 [Fig. 7.2C].

Experiment 3: The salience of cues at an entry quadrant influences returns.

Four groups of rats were started in a quadrant near which there was no local cue and no salient distal cue, in a quadrant near which was a small visual cue, in a quadrant near which was a large visual cue, and in a quadrant on which there was a small refuge. The main findings were that all of the rats displayed a

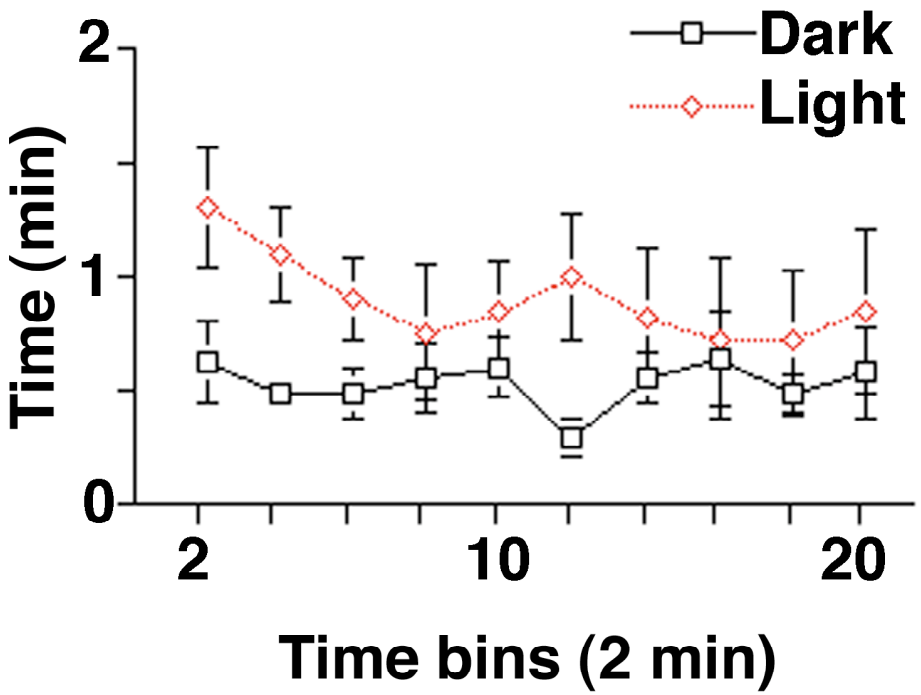

Fig. 2.5. Time spent around the point of entry in both room lights as a function of 2-min time bins [means and standard errors]. Note: rats were equally likely to be at the point of entry at each time bin.

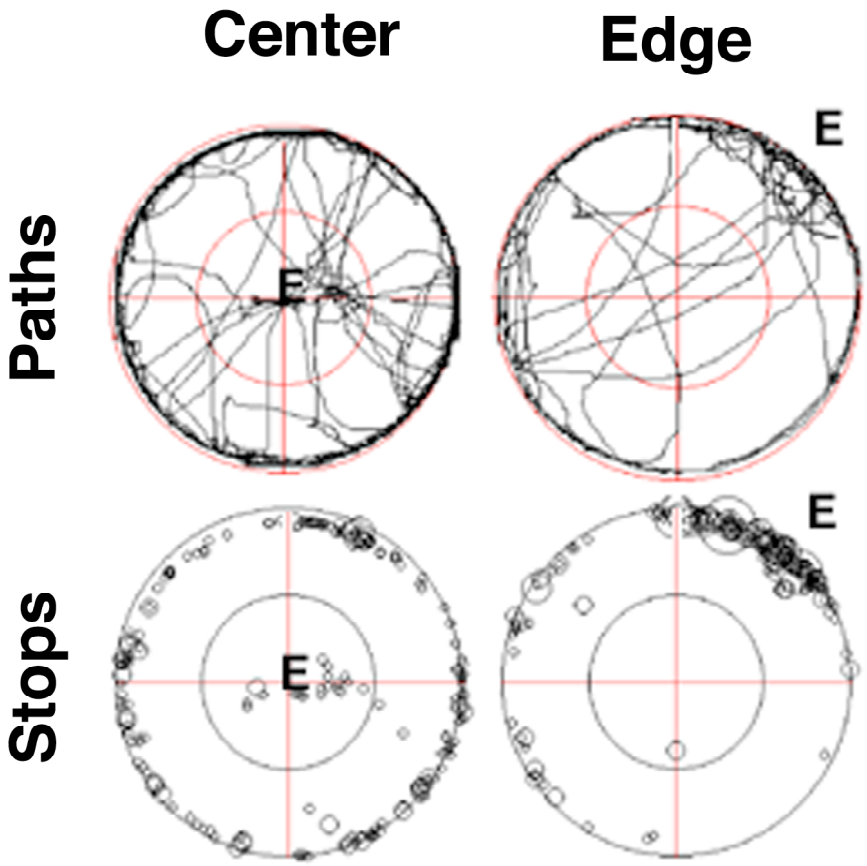

Fig. 2.6. The paths and stops made by representative rats that were started from the edge or from the middle of the table. The denser path [lines], and the greater number of stops [circles] made in the inner annulus by rats that had been placed in the middle of the table represents their preference for the middle of the table as the point of entry [E]. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30 > 60 sec, and > 60 sec.

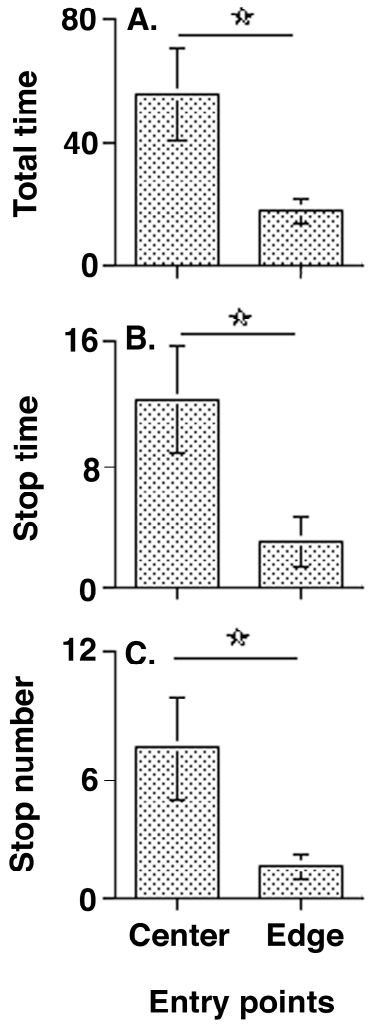

Fig. 2.7. Measures of inner annulus preference [means and standard errors in seconds] by rats started in the middle of the table or on the edge. Rats spent greater length of time [A], and stopped longer [B], and more frequently [C] in the inner annulus when they started from the middle of the table than when they started from the edge of the table.

preference for the point of entry but as the salience of the additional cues increased so did the preference for the point of entry [Fig. 2.8].

ANOVA of time spent in the different sectors gave no effect of group, a significant effect of sector, $F[16,256]=55.43$, $p<0.001$, and a significant group by sector interaction, $F[48,256]=8.83$, $p<0.001$. The preference of the entry sector increased with cue saliency [cage = large visual cue > small visual cue, no cue], as did the total time spent in that sector [Fig. 2.9]. The ANOVA of total time stopped gave very similar results of no group effect but significant effects of sector, $F[16,256]=13.45$, $p<0.001$, and group by sector, $F[48,256]=13.45$, $p<0.001$. Additionally, ANOVA on number of stops gave a significant group effect, $F[3,16]=4.39$, $p<0.01$, a significant effect of sector, $F[16,256]=16.08$, $p<0.001$, and group by sector interaction, $F[48,256]=2.89$, $p<0.001$. Finally, ANOVA on traveled distance gave no effect of group $F[3, 16]=1.75$, $p=0.19$, but a significant effect of sectors, $F[3,16]=40.04$, $p<0.001$, and group by sector, $F[3,45]=20.23$, $p<0.001$. Thus, on all of these measures, behavior was influenced by the salience of the cue [cage > large cue > small cue > no cue].

Fig. 2.10 illustrates the dispersion of stops on the table [a value of '0" would indicate that a rat stopped once in one location]. An ANOVA indicated that there was a significant group effect, $F[3,16]=5.15$, $p<0.01$. Dispersion decreased as a function of the salience of the cue at the starting location and follow-up t-tests [$\alpha=0.05$] indicated that no cue = small cue < large cue = cage. The significant group effect of stops was due to the greater activity of the rats in conditions with

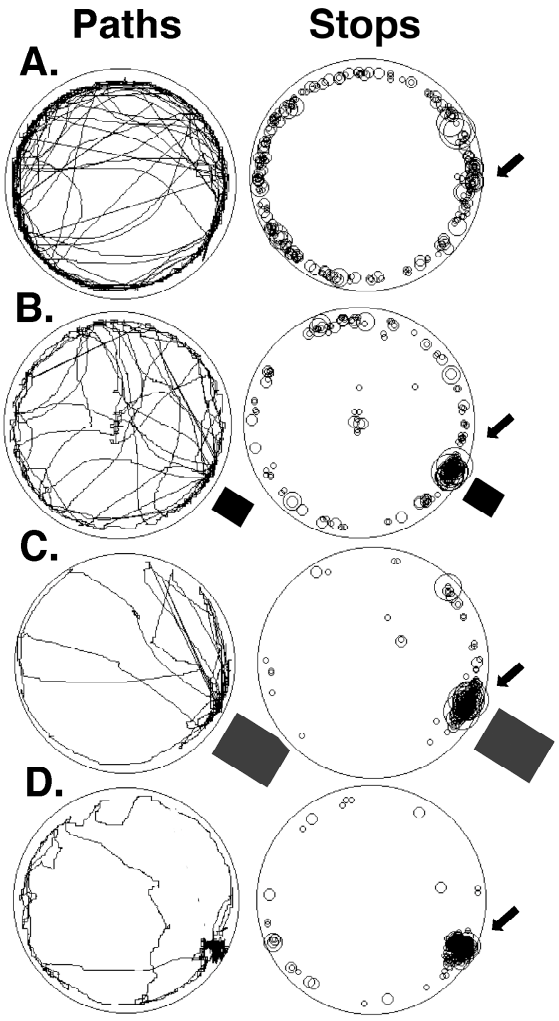

Fig. 2.8. Exploratory paths and stops made by representative rats as a function of cue salience. A. started at the edge only, B. started beside a small visual cue, C. started beside a large visual cue, D. started before a small refuge placed on the table. Lines represent paths, circles stops. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

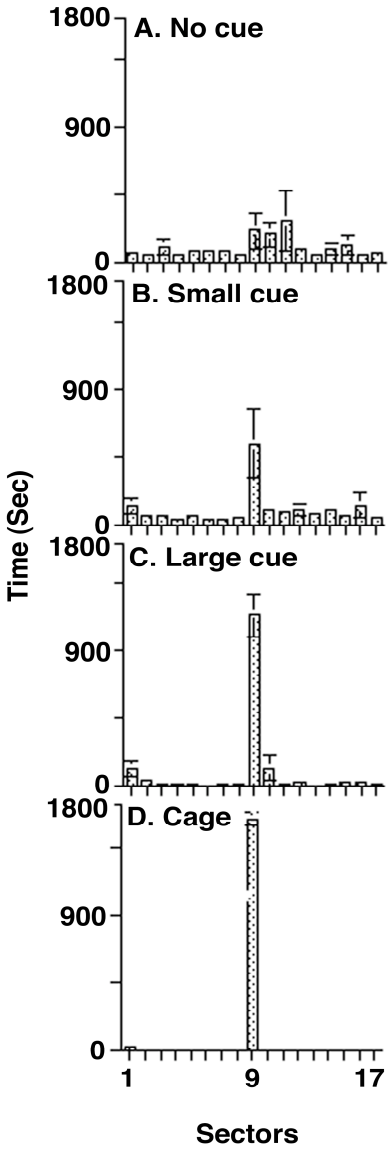

Fig. 2.9. The time [mean and standard errors in seconds] spent on different sectors of the table in one of four cue conditions [top to bottom]. The point of entry and cue location was sector 9. The time spent at the point of entry gave a preference relationship Cage=Large visual cue, Cage>Small visual cue, Cage>No cue.

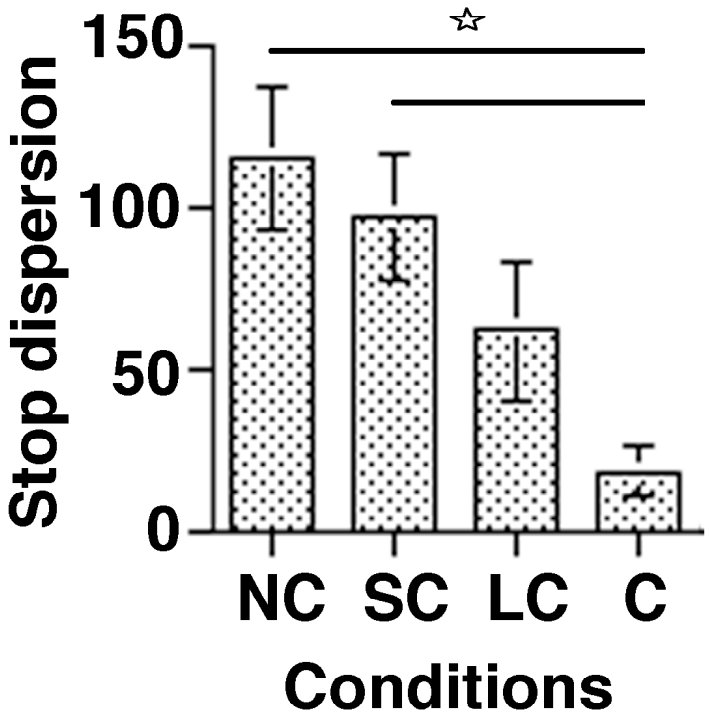

Fig. 2.10. Dispersion of stops [mean and standard error in seconds] in four conditions. Note: Stop dispersion decreased as a function of cue salience: Cage [C]=Large cue [LC]<Small cue [SC]=No cue [NC].

the least salient cue, such that rats made few long stops in impoverished cue conditions and more and longer stops in the presence of salient cues.

Experiment 4: Rats return to an entry quadrant in the presence of a salient visual cue.

The rats were tested by starting them from the NE quadrant of the table, with the large visual cue located near the SE quadrant of the table. As is illustrated in Fig. 2.11 for a representative rat, although the rats visited many portions of the table, on measure of time spent, stop time, and numbers of stops, they showed relative preferences for both the entry quadrant and the cued quadrant.

ANOVA yielded a significant effect of quadrants on the measures of total time, $F[3,33]=10.59$, $p<0.0002$; Fig. 2.12A; stop time $F[3,33]=7.27$, $p<0.0008$, Fig. 2.12B; and number of stops $F[3,33]=7.76$, $p<0.0006$, Fig. 12.2C. Follow-up t-tests indicated that on all three measures there were no differences in preference values for the point of entry and the cued location, which were the most preferred locations relative to the two remaining quadrants. The preference of these locations over the other two quadrants was significant except for the contrast between the cue quadrant and quadrant 2 and 3 on the measure of number of stops.

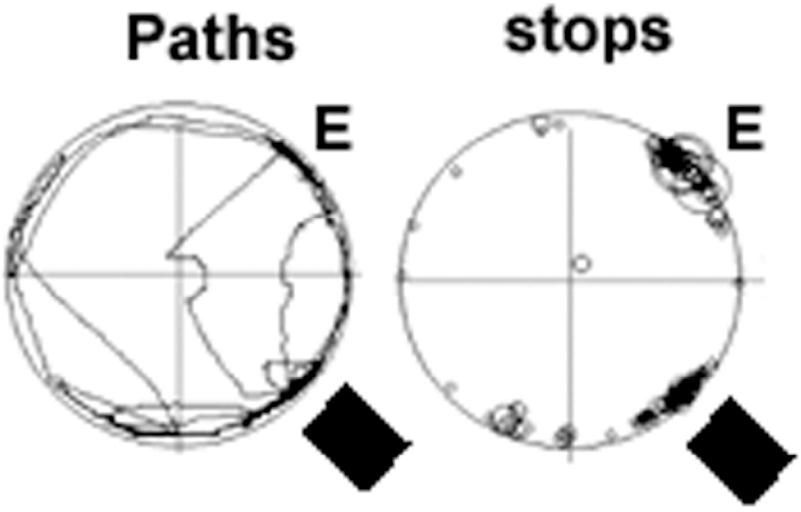

Fig. 2.11. The path and stops made by representative rats started in the quadrant adjacent of a visual cue. Note the preference for both the point of entry [E] quadrant and the cue quadrant [black square]. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

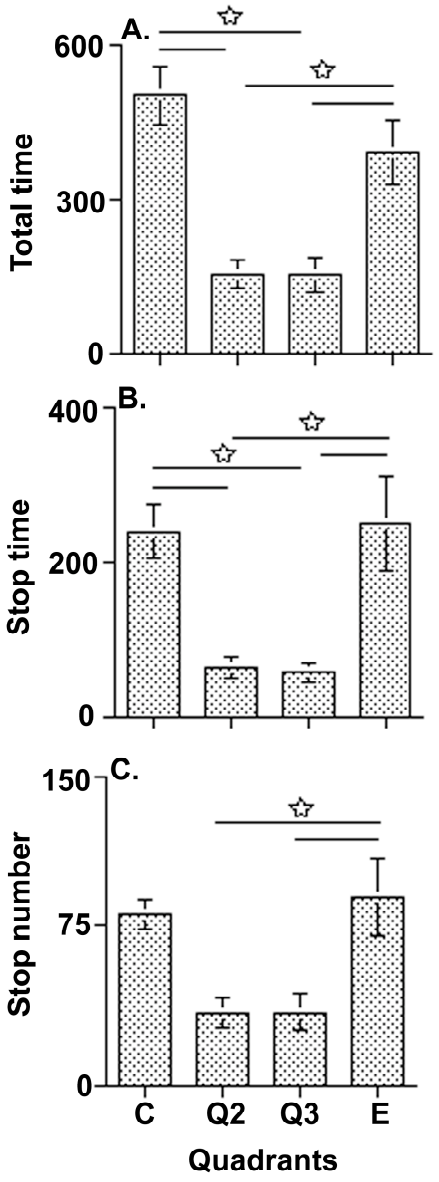

Fig. 2.12. The measures [mean and standard error in seconds] of point of entry preference. The point of entry [E] and cued [C] quadrants were both preferred over the two remaining quadrants [Q2 and Q3].

5. Discussion

The purpose of the present experiments was to examine when exploratory locomotion of rats placed on an open table first becomes organized and how the organization of exploratory locomotion is influenced by cue saliency. Rats were placed on a large circular table in a number of conditions in which no special cues were present, salient cues were placed near or on the table, or tests were given in infrared light, a wavelength in which rats cannot see.

The main findings were that under all conditions, rats note their point of entry by returning to it, stopping, and lingering there throughout a test session. Additionally, the strength of the attachment to point of entry was proportional to the salience of cues near or at the point of entry. Thus, the results indicate that organized exploratory activity begins immediately after placing a rat in a novel environment.

The centrality of the point of entry to exploratory behavior suggests that it serves as a reference point for an animal's spatial representation of a new environment. In addition, because the attachment to the point of entry increases in proportion to the saliency of its cues, the point of entry also represents a location of security.

The design of the present experiments was similar to that used in a number of previous studies of exploratory behavior in that rats were tested on an open table [Eilam & Golani, 1989; Hall, 1934], test durations lasted from 10 to 30 min [Clark et al., 2005; Drai et al., 2001; Wallace et al., 2002a], cues near or on the table were used to influence the animals' behavior [Clark et al., 2005; Hines & Whishaw, 2005],

and the animals' movements were tracked using a video-based tracking system [Drai et al., 2000, Drai & Golani, 2001]. The methods have been used to document the fact that rats will organize their exploratory behavior in terms of preferred stopping locations, and that these locations will occur near salient cues if they are available, findings that were confirmed in the present study. Elsewhere [Eilam & Golani, 1989], the term home base has been used to refer to preferred stopping locations, however, for the present study, test sessions were shorter than those used to document home base behavior, and adjunct behaviors of rearing and grooming, which sometimes occur at home bases, seldom occurred and so were not measured. Nevertheless, the measures used in the present study indicate that rat exploratory locomotion is not stochastic but organized.

The question addressed in the present study was when organized behavior begins and how it is influenced by sensory inputs. The main finding was that organization begins as soon as animals are placed on the table. When rats were placed on the table, whether on an edge or in the middle, they periodically returned to that location. If the rats were placed near a salient cue, a visual cue located near the table or a cage placed on the table, their preference for that location, as measured by dwell time or returns to that location was stronger still. Even when a rat was started from a location that lacked an obvious salient cue or was tested in a situation in which a salient cue was located at another location, it still returned to the point of entry. Although the numbers of animals used in each of the individual experiments were not large, all animals in the many varied

conditions in which they were tested displayed the behavior of returning to the point of entry. Additionally, although the table demarcations for fractionating behavior were quadrants and annuli, the more detailed measures of stopping location and sectors indicated that a rat's accuracy in identifying the point of entry was quite precise.

These findings are consistent with previous less detailed observations that rat uses the point of entry in a maze to aid problem solving [Hynes et al., 2000], that rats visit a point of entry when spatial learning problems are changed in a swimming pool place task [Whishaw & Mittleman, 1986], and that the point of entry contributes to the representation of the environment that is encoded by place cells in the hippocampus [Sharp et al., 1990]. The novel finding of the present study is that the point of entry has a constraining influence on exploratory locomotion even in a situation in which there are no obvious learning requirements. It is interesting that Tourestzky et al., [1996] in a preliminary report find that exploration is similarly influenced by the point of entry in the Mongolian gerbil [*Meriones unguiculatus*].

It is possible, however, that returns to the point of entry were influenced by local cues, especially odors left on the table by the rats themselves. This possibility was not specifically examined in the present study, but a number of observations suggest that odor cues do not exclusively guide the rats' behavior. Normal rats will ignore odor cues in order to take short cuts [Whishaw & Gorny, 1999], rats without olfactory bulbs still form home bases in open field exploratory tests [Hines & Whishaw, 2005] and in the present study on many trials, rats did

not obviously defecate or urinate at the point of entry. In addition, when they returned to a point of entry that they had left, they did so using quite different routes than that taken on the departure.

Gallistel [1990] has proposed that animals solve spatial problems using at least two navigation strategies, piloting, in which ambient cues are used for orienting, and dead reckoning, in which self-movement cues are used for orienting. That the rats displayed a preference for the point of entry in both room and infrared light conditions on the open table suggests both navigation strategies are used for organizing spatial behavior, as has been found in other spatial navigation studies [O'Keefe & Nadel, 1987; Whishaw & Brooks, 1999; Tchernichovski et al., 1998].

Another possibility was that return visits to the point of entry in the light condition may be due to the association between a local cue [such as tactile stimulation elicited by the edge of open table at the point of entry] and an immediate local view of the cues associated with the entry point. However, Organization of exploratory locomotion of rats started from the center of the open table suggested that their return visits were independent of the effect of an association between edge [a salient local cue] and local visual cues. This finding is consistent with the idea that spatial navigation can result from associating local views with dead reckoning coordinates [McNughton et al., 1996; Sharp, 1991; Redish, 1999].

The suppressing effect of salient local cues [such as a large visual object or a cage] on exploratory locomotion of rats has been shown in previous studies

[Hines & Whishaw, 2005; Wallace et al., 2002a; Wallace & Whishaw, 2003], and was confirmed more formally here. Differential response of rats to local cues of various saliencies in this study also suggests the important effect of cue saliency on the organization of exploratory locomotion. This finding is also confirmed by distribution of stop dispersion on the open table in various cue conditions. Proximal cues with less saliency exert less suppressing effect on exploratory locomotion, which leads to greater expansion of locomotion. Thus, the reference points with various degrees of saliency in this experiment provided a repulsive-attractive gradient for exploratory locomotion of rats [Golani et al., 1993]. It is interesting that local and distal cues have strong controlling effect on firing fields of place and head direction cells in the hippocampal formation [Knierim**,** 2002; Knierim et al., 1998; Yoganarasimha et al., 2006].

Among factors that influenced the organization of exploratory locomotion to the point of entry was the size of proximal visual cue, and tactile stimulation. Rats spent long periods of time near the large visual object, and when provided with a refuge, entered into it and displayed little subsequent exploratory activity. However, their response to a small visual cue and to their point of entry was not as strong. That the cage placed on the table was about the same size as the small visual cue located near the table, and rats spent longer time near the cage supports the idea that tactile cues influence selection of a home base. The present series of studies suggests two main factors that are associated with the salience of a cue; 1. The number of sensory modalities involved and 2. The magnitude of the stimulus. In the present experiment, time spent near a

reference point appeared to be related to the number of sensory modalities that could be activated by a certain cue. For example the refuge box involves a greater number of sensory modalities, e.g., visual system, tactile system. With regard to the comparative magnitude of the response, visual perception of the large visual cue vs. small visual cue for example can be considered as a function of object size, which is correlated with the visual angle.

That rats organize their exploratory locomotion to both local visual objects and their entry point is also consistent with the observation that rats may form one or two home bases usually close together [Eliam & Golani, 1989] or in relation to two salient visual cues near the open table [Clark et al., 2005; Lehmann et al., 2007]. This finding suggests that rats are able to organize their exploratory locomotion to more than one location. Also, it is interesting that presence of a salient object in the environment not only amplifies the preference for the point of entry when they are spatially adjacent, it does so when it is near the open table but not at the entry point.

It has variously been proposed that exploration is motivated by fear [Montgomery, 1955], is an interplay between the motivating forces of fear and curiosity [Halliday, 1968, Russell, 1973], optimizes security, or is simply directed toward information gathering [O'Keefe & Nadel, 1978]. The explanation favored here is that the exploratory behavior of rats in the open field is directed toward optimizing security [Whishaw et al., 2006].

Because foraging animals tend to maximize their security [Lima et al., 1985; Lima, 1985; Whishaw, 1991; Whishaw, 2005; Whishaw et al., 2006] through

various strategies such as carrying food to the refuge to eat [Lima et al., 1985; Whishaw & Tomie, 1987; 1989], the attachment of laboratory rats to their point of entry and the large visual object in an unstructured environment may render that environment more similar to their natural habitant. This suggests a security value by both a point of entry and a large cue.

Optimization theory suggests that a rat's behavior will be mediated by opposing influences of concern for safety and motivation for other gains. In order to optimize its safety, a rat may spend most of its time at a home base, while at the same time emerging with care only when necessary. Consistent with optimization theory [Whishaw, 1993], the point of entry may be a favored location because, as an entrance to the table, it also represents a possible exit. It is also a location at which the animal was once safe, at least momentarily. In this respect it is relevant that when rats are tested in environments with walls, they are much more likely to remain at a point of entry near a wall and to make excursion from that location [Leonard & McNaughton, 1990; Whishaw, 1992; Whishaw et al., 1983]. It is also relevant that even when on the open table, a rats' movement is constrained by the table edge, and so in any search for security they must make the best of available options. That is, since they cannot escape from the table, they are reduced to finding the safest place on it. One previous study has shown that when rats are not constrained by testing condition, they are much more likely to run away than to remain or return to a starting location, unless that location provides a refuge [Whishaw et al, 2006].

Nevertheless, exploration can also serve to develop a representation of the environment. That rats are able to remember their point of entry can be taken as an example of memory for place [O'Keefe & Nadel, 1978]. It may also represent a form of episodic memory for place [Babb & Crystal, 2005, Eacott & Norman, 2004, Ergorul & Eichenbaum, 2004]. Because, the rats' preference for a point of entry was greater when it was marked by a salient cue, including the edge of the table, a large local cue near the table, or a refuge on the table, it is likely that local cues, in addition to providing security, aid in forming a representation of the environment. It is interesting in this respect that Stopka & MacDonald [2003] report that the wood mouse [*Apodemas sylvaticus*] moves local objects in order that they can serve as landmarks to guide the animal's subsequent movements.

In conclusion, the main findings of the present study are that rats note their point of entry to an environment by returning to that location periodically during their subsequent exploratory locomotion. That they did so in both light and dark tests suggests that they use both piloting and dead reckoning navigation strategies to do so. In addition, when a salient object was at the point of entry, including the edge of the table, a visual cue near the table, or a cage on the table, the preference for that point of entry was amplified and the expansion of exploratory locomotion was decreased with cue saliency. These results suggest that the point of entry can represent a location of security as well as contributing to the formation of a spatial representation of the environment, and that rats modify their exploratory locomotion as they encounter the sensory features of the environment including visual cues.

Visual Cortex

and

Exploratory Locomotion

Abstract

Recent evidences have supported the notion that visual cortex play a role in spatial navigation. Because exploration is involved in learning the locations and significance of visual cues in navigation tasks, rats with damage to striate visual cortex and control rats were tested in a series of open field exploratory tests in which they were placed individually on an open field table that was illuminated either by room light or infrared light (a wave length in which they cannot see). Rats started exploring the environment when a large visual object was located near the table at a location distant from their point of entry, when the object was associated with their point of entry, or when no proximal object marked their entry point. Measures of exploratory locomotion demonstrated that both groups organized their exploratory locomotion to salient local objects and/or to their point of entry in both experimental and probe trials. Nevertheless, rats with damage to striate visual cortex displayed a stronger attachment to the salient visual object and did not expand their exploration across days. These findings provide evidences for the contribution of brain with visual cortex lesion to the organization of exploratory locomotion in the rat.

1. Introduction

There are at least three reasons to suppose the visual cortex plays a role in spatial behavior. First, most contemporary views of exploratory behavior posit that it is involved, at least in part, in learning the locations and significance of visual cues. Thus, a significant part of exploration consists of exploring visual cues using eye movements only or by using a combination of eye movements and locomotion. Second, Lashley [1939] demonstrated that visual cortex provides rats with a non-visual spatial function via which a spatial problem can be solved. The peripherally blind rats, which he used in his experiment, lost their maze habit after they were given posterior visual cortex lesions. Similarly, Goodale & Dale [1981] have shown that in a radial-maze task, visual cortex plays a role in the spatial behavior of both sighted and blind rats. Hoh et al., [2003] suggest that striate visual cortex contributes to learning a spatial problem in the Morris swimming pool and Whishaw [2004] has demonstrated that rats with damage to visual cortex were impaired in a matching-to-place water task [Whishaw, 1985]. Thus a number of studies have suggested a role for visual cortex in spatial behavior [Goodale & Dale, 1981; Hoh, et al., 2003, Lashley, 1939, 1943; Milner & Lines, 1983; Schneider 1969; Whishaw, 2004]. Third, a number of studies have demonstrated that exploratory locomotion of rats with hippocampal damage is still organized in room light condition [Clark et al., 2005; Hines & Whishaw, 2005]. Thus, this must mean that major features of exploratory behavior are dependent on structures earlier in the extended visual system of

Felleman and van Essen [1991] and primary visual cortex; the first cortical region in the visual system should be involved.

Perhaps one reason that the role of visual cortex in exploration has not been previously examined is that there have not been objective measures of exploratory behavior available. This is no longer true because rat exploratory behavior has been found to be organized and this organization can be objectively described. When placed in a novel environment, rats alternate between modes of locomotion of various speeds such as stops and progressions and organize their exploratory behavior to one or a few places termed “home base” [Eilam & Golani, 1989; Golani et al., 1993; Drai et al., 2000]. Home bases are places from which a rat sets out on round trips termed excursions and spend a disproportionate amount of time there. The characteristics of this organized behavior are subjects of changes with time and the level of visibility [Tchernichovsk et al., 1998; Zadicario et al., 2005; Avni et al., 2006]. Also, exploratory locomotion tends to expand with repeated exposure to the same environment [Tchernichovsk et al., 1998]. Rats also organize their exploratory locomotion to local objects such a cage or a large visual object on or near the open table respectively [Wallace et al., 2002a; Hines & Whishaw, 2005]. Exploratory locomotion can even be organized in relation to two visual objects [Lehmann et al., 2007, Clark et al., 2006]. Rats also displayed a pattern of excursions with respect to salient local objects similar to the pattern that they display in a featureless environment [Wallace et al., 2002a]. Previous experiments in this thesis also demonstrated a similar organization of exploratory locomotion to the point of entry. Rats organize

their exploratory locomotion to their point of entry [Experiment 1 & 2], to which they periodically return and near which they spend a disproportionate amount of time influenced by salience of cues marking that [Experiment 3] or other location of the environment near the open table [Experiment 1,2,3,4]. The organization of exploratory expansion was also influenced by cue saliency [Experiment 3].

The purpose of the present experiments was twofold. The first objective was to examine the role of visual cortex in organization of exploratory locomotion of rats to reference points [the point of entry and/or local salient objects]. The second objective was to examine the influence of distal cues on the expansion of exploratory locomotion in a relatively featureless environment. In order to test the organization of exploratory locomotion to reference points, rats with and without damage to visual cortex explored the environment starting from the edge of an open table with or without local cues near or on the open table. To examine exploratory expansion, rats with or without damage to visual cortex were tested under low and high level of visibility or explored the environment for several exploratory sessions under room light. The movements of rats were taped and the measures of total time, stop duration, number of stops, stop dispersion, and traveled distance were used to examine the organization of exploratory locomotion.

2. Materials and Methods

2.1. Animals

Thirty six female Long-Evans rats used in the experiments were about three months old, and weighed approximately 250-300g. Rats were randomly assigned

to two groups. One group received visual cortex lesion and the other group went through initial procedure of surgery but did not receive any lesion. Rats were housed in groups of three in Plexiglas cages with sawdust bedding and *ad libitum* food and water. The colony room temperature was at 20-21º C and was illuminated on a 12/12 hr light/dark cycle. Experiment was conducted in accordance with guidelines from Canadian Council of Animal Care and the University of Lethbridge Animal Care Committee.

2.2. Surgery

A mixture of isofluorane and oxygen [4% with 1 L/min of oxygen, and 2% after surgical level of anesthesia was established] was used to anesthetize the rats that were placed in a stereotaxic device. An incision was made in the scalp and the periosteum to expose the cranium. A dental burr was used to drill small holes in the skull at specific coordinates while rat's head was still in a fixed position in the stereotaxic device. Rats went through surgical operation in which either their visual neocortex was damaged by means of an aspiration method [Experiment 1] or their visual neocortex was damaged by injection of N-methyl-D-aspartate solution [Experiment 2, 3 & 4].

For aspiration, an incision was made in the scalp to expose the skull of each rat. Following removal of the skull, the neocortical tissue of visual area was removed by means of suction. For N-methyl-D-aspartate [NMDA] lesions, an incision was made in the scalp to expose the skull. A dental bar was used to drill small holes in the skull bilaterally at measurements relative to bragma and midsagittal suture. The lesions were made by infusions of N-methyl-D-aspartate

solution [NMDA: 0.2 μg/μl; Sigma Chemical, st. Louis, MO] at each of 6 sites [12 injection sites bilaterally] in each hemisphere. The infusions were done through a 30-gauge injection needle attached to a 10 μl Hamilton syringe via polyethylene tubing [PE-50]. Following injection was done in each site the needle was left in place for an additional 3 min to facilitate diffusion. Coordinates used to make lesions centered in striate visual cortex were: Posterior to bregma: 5.9 [Lateral from bregma: 3], 5.9 [Lateral from bregma: 5], 7.2 [Lateral from bregma: 3], 7.2 [Lateral from bregma: 3], 8.57 [Lateral from bregma: 3], 8.57 [Lateral from bregma: 5]. Ventral to the surface of the dura: 2.4, 2.8, 3 [Posterior to bregma]. Control animals did not undergo any surgical procedure. However, they went through anesthetic procedure and incision of skull. Animals were given at least two weeks recovery period before behavioral testing began.

2.3. Histology

Shortly after the experiments were completed, the rats were deeply anesthetized using sodium pentobarbital and perfused transcardially with saline. A saline formalin [10%] solution was transcardially used to fix the tissue. Each brain was removed from the skull and stored in 30% sucrose-formalin solution to cyro-protect the tissue. The brains were frozen and cut at 40 μm on a cryostat. Alternate sections were taken and stained with cresyl violet.

2.4. Open field

A 244 cm diameter white circular wooden table [Fig. 3.1], elevated 64 cm above the floor, was used as an open field [Hines & Whishaw, 2005]. The table was located in a large testing room and was surrounded by a number of cues

Fig. 3.1. Open arena. A circular table with no wall placed in an ordinary room provides freely moving rats with a motivating environment for exploration and locomotor behavior.

including a paper towel dispenser, switches, and posters on the wall. Very large salient cues, including a bookcase, and a sink were covered with white sheets to make them less conspicuous. In order to minimize local olfactory cues, the table was cleaned with soap and water following each trial for each rat.

2.5. Movement tracking and analysis

An HI-8 Sony video camera sensitive to normal and infrared light was located in the ceiling of the test room to record the movements of rats. The video record was converted to x-y coordinates using a sampling rate of 30Hz using AccuTrack software [AccuScan Instruments, Inc. Columbus, OH, 43228, USA]. The AccuTrack system automatically tracks the midline of a rat's back at the level of the forelimbs by selecting one pixel per frame of digital computer file. The x-y coordinates were analyzed using programs written in C++.

2.6. Test conditions

Rats were tested in the following different proximal and distal cue conditions:

[1] No cue. Room lights were on and no cues were placed on or around the table.

[2] Large visual cue. A large visual object [a 48 cm x 48 cm x 52 cm black box], oriented toward the table was placed 20 cm away from the edge of the table.

[3] Cage. The cage was a black box [20 cm x 12 cm x 25 cm] with a 4 cm x 4 cm entrance, facing the center of the table, was placed on the edge of the table.

[4] Infrared light. Room lights were off and infrared light, a wavelength in which rats cannot see [Hines & Whishaw, 2005, Wallace & Whishaw, 2005], was

reflected from the room walls. The experimenter used infrared goggles to place the rat on the table.

2.7. Test procedure

Each rat was carried from the colony to the testing room [50 m distance with 3 turns] in a cage similar to the one that they were housed in. After a 2-3 min wait outside the test room, a rat was lifted by its shoulders and taken singly into the test room and gently placed on the table. Each rat was video recorded for the duration of its test. The experimenter left the room immediately after placing the rat on the table. Test durations lasted 20 min or 30 min, durations that have been described as sufficient for establishing home bases in previous research [Eilam & Golani, 1989].

2.8. Behavioral measures

To derive behavioral measures that quantified the rats' movements on the table, the table was divided into either 4 quadrants, 16 sectors, or into 2 annuli by the computer based programs. Each table division was defined as a zone, and with respect to the zones the following measures were made:

[1] *Time*. The total time was the time in seconds either moving or still.

[2] *Stop.* A stop was defined by a filter that placed x-y coordinates into bins of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec. From the program, both the total time spent stopped and the number of stops could be derived.

[3] *Stop dispersion.* The stop dispersion measure was calculated as a measure of the distribution of stops on the table. Thus, a dispersion value approaching '0' indicated that a rat was still only at one location during a test session, whereas a

higher value indicated the extent to which a rat stopped at different locations of the table. In order to quantify the dispersion of stops, a computer-based program computed the average distance between points where stops occurred based on the following formula:

$$D = \frac{1}{n^2 - n} \sum_{i=1}^{n} \sum_{j=1}^{n} \sqrt{(x_j - x_i)^2 + (y_j - y_i)^2}, \quad \text{where } i \neq j$$

In the formula “n” represents the number of stops and “X” and “Y” are values that represent each stop on a Cartesian coordinate system.

[4] *Distance*. The travel paths were measured for total length [cm].

2.9. Statistical analysis

The results were analyzed using ANOVA of treatment groups and repeated measures, with Bonferroni, Student-Newman-Keuls post hoc tests [Winer et al., 1991].

3. Procedure

Four experiments were conducted in various cue conditions:

Experiment 1: Rats with visual cortex lesion use distal and proximal cues to organize their exploratory locomotion in the open field.

In an experimental trial, rats with visual cortex lesion [n=6] were placed on the edge in the northeast [NE] quadrant of the open circular table where they started to explore the environment for a 20 min test. Also, a large visual cue was located near the southeast [SE] quadrant of the table. After three days, rats were started from the center of the table where they explored the environment for a 20 min test, while the large visual object was removed.

Experiment 2: Rats with visual cortex lesion spend longer time near a large visual object than near a cage.

Rats with visual cortex lesion [n=5] and control rats [n=5] explored the environment on an open table for 30 min tests. Three rats of each group received a first test in which they were placed inside a cage in the southwest [SE] quadrant of the table and a second test on the next day in which they were started from the same place in the absence of the cage but in front of a large visual object near the open table. For the other groups of two rats, the testing sequence was reversed.

Experiment 3: Exploratory expansion of rats with visual cortex lesion is influenced by the level of visibility in the open field.

Rats with damage to visual cortex [n=5] and control rats [n=5] explored the environment starting from the center of a large circular table for 20 min tests. Each rat was tested under infrared light first and in the next day it was tested in room light.

Experiment 4: Rats with damage to visual cortex do not expand their exploratory locomotion in an open field.

Rats with visual cortex lesion [n=5] and control rats [n=5] were started from the same location on the edge of the table and explored the environment for five consecutive days. The exploratory trips were videotaped for 20 min in the first day of the experiment. Rats explored the environment for 10 min period in three consecutive days after the first day of the experiment. On the fifth day of the

experiment, both groups were videotaped again for a 20 min trial in which they were started from the same location on the edge of the open table.

4. Results

Experiment 1: Rats with visual cortex lesion use distal and proximal cues to organize their exploratory locomotion in the open field.

Histology

N-methyl-D-aspartate [NMDA] lesions were centered in area 17. The measures made from the cortical surface [dorsal view] of the removed tissue indicated that the sizes of damage to striate visual cortex [measured in square pixels] varied from the smallest [78%] to the largest [95%] in different rats. ANOVA indicated no significant difference between the lesion sizes in the right compared to the left hemisphere; $F[4, 1]=6.53$, $p=0.06$; [Left hemisphere: Mean=2685.2; SE=100.69; Right hemisphere: Mean=2432.6; SE=40.42]. From the frontal view, all layers of striate visual cortex and the convexity of corpus callusum, but not the underlying hippocampus were removed. Microscopic examination indicated bilateral degeneration of cells and some shrinkage in lateral geniculate nucleus [LGN]. However, some cells in this area remained normal. Figure 3.2 illustrates a representative lesion centered in striate visual cortex.

Behavior

Rats with visual cortex lesion were tested by starting them from the NE quadrant of the table, with a large visual cue located in the SE quadrant. Fig. 3.3 illustrates the experimental condition.

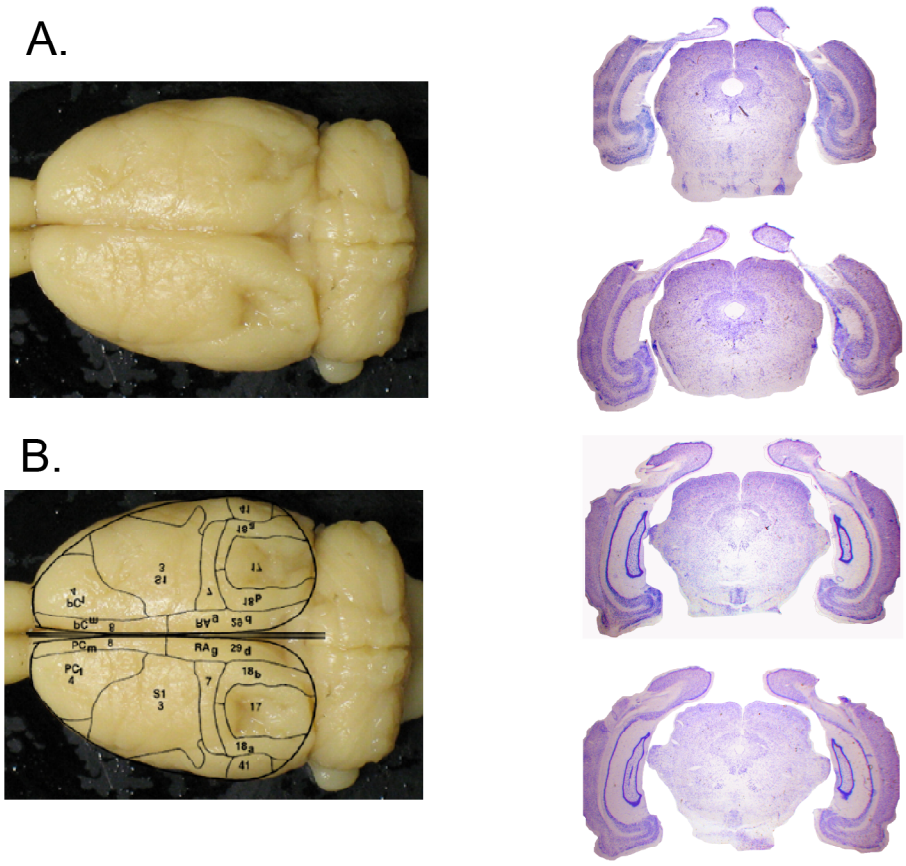

Fig. 3.2. Lesions centered in the striate visual cortex. The figure on the top left [A] illustrates damage to striate visual cortex on left and right side of the brain, and the figure on the bottom right [B] illustrates the position of the lesions to area 17 and other visual and non-visual areas. The lesion on the bottom illustrates the depth of the lesion from frontal view.

Fig. 3.3. Apparatus, point of entry and cues. A. Open table. B. The black circle indicates location where rats were placed to begin a session. C. A large black object was used as a local visual cue.

Fig. 3.4 illustrates a relative preference for both the entry and cued quadrant by a representative rat on measures of exploratory locomotion in both experimental and probe trial. ANOVA indicated a significant effect of quadrants on the measures of total time, $F[3,5]=17.75$, $p<0.0002$; stop time $F[3,5]=13.75$, $p<0.0002$, and number of stops $F[3,5]=9.16$, $p< 0.002$, Fig. 3.5A.

ANOVA on the measures of total time, $F[3,5]=10.61$, $p<0.0006$; stop time $F[3,5]=6.85$, $p<0.005$, and number of stops $F[3,5]=10.84$, $p< 0.0006$, in probe trial also indicated a significant effect of quadrants in which rats still displayed a preference for the previously cued and entry quadrant Fig. 3.5B.

Follow-up t-tests were set for [p=0.05] and indicated no significant difference in preference for the entry and cued quadrants in experimental trial on all measures. Entry quadrant was preferred relative to the two remaining quadrants [Q2, Q3] on all measures except for the contrast between the entry quadrant and quadrant 3 on the measure of total time and between entry quadrant and quadrant 2 & 3 on the measure of stop number. The cued quadrant was preferred over remaining quadrants, except quadrant 3 on the measure of stop number.

In probe trial, follow-up t-tests [p=0.05] indicated no significant difference in preference for the location that previously were assigned as entry and cued quadrants on all measures. The quadrant that was previously designated as the entry quadrant was preferred relative to the two remaining quadrants [Q2, Q3] on all measures except for the contrast between that

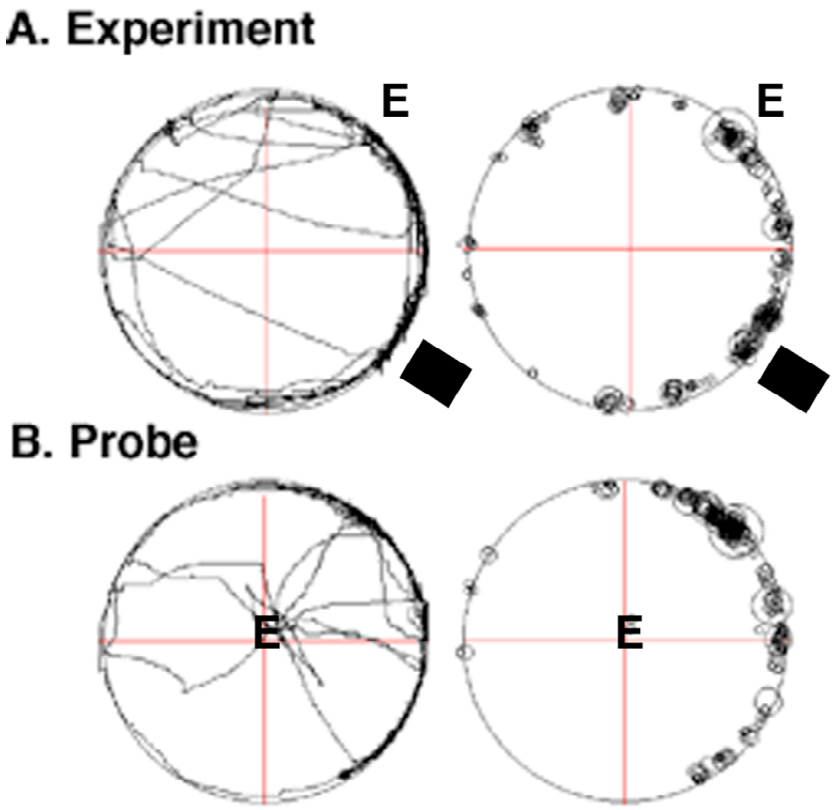

Fig. 3.4. A. The path and stops made by representative rats with damage to striate visual cortex started on the edge of the table in the quadrant adjacent of a visual cue. Note the preference for both the point of entry [E] quadrant and the cue quadrant [black square]. B. In a probe trial, although rats were started from the center of the table while the large visual cue had been removed exploratory locomotion was still organized to the point of entry [E] quadrant and the cue quadrant [black square]. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

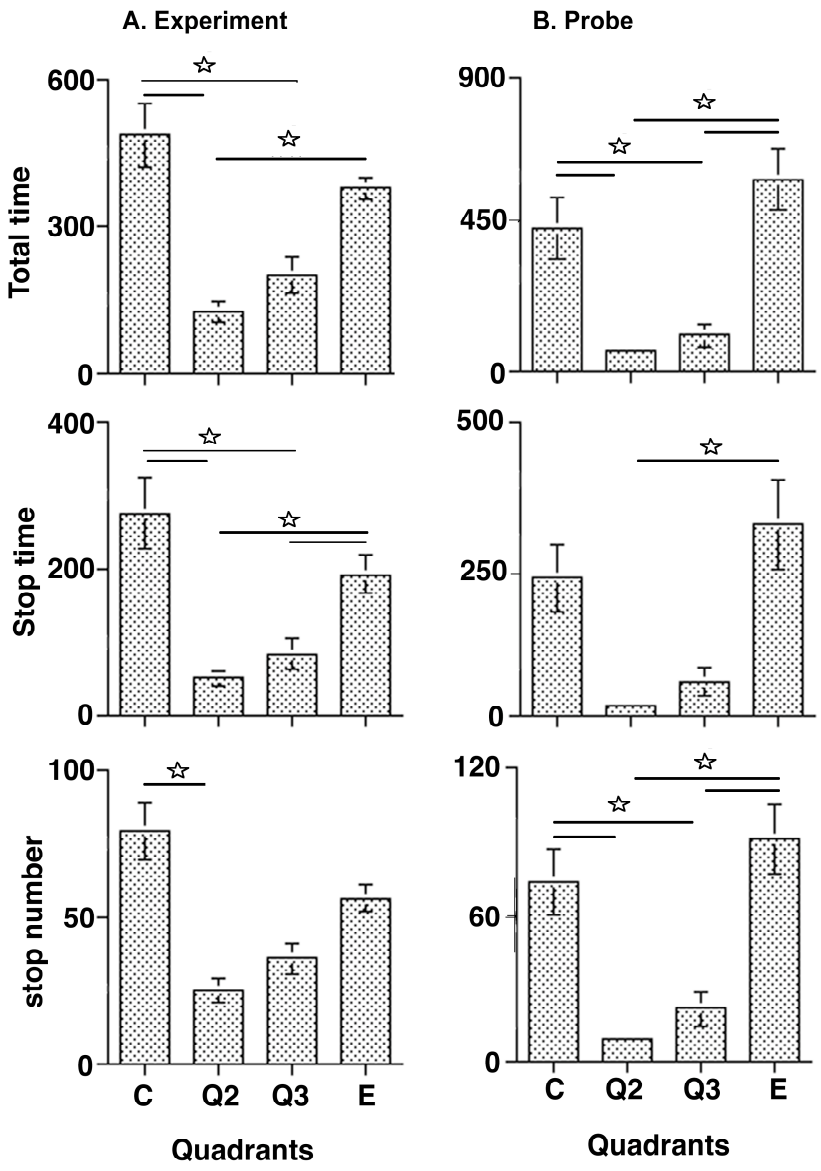

Fig. 3.5. The measures [mean and standard error in seconds] of preference for the point of entry and cued quadrants in experimental [A] and probe trial [B]. In experimental trial rats with damage to visual cortex preferred both the point of entry [E] and cued [C] quadrants over the two remaining quadrants [Q2 and Q3].

quadrant and quadrant 2 and 3 on the measure of stop time. The quadrant that was previously marked by a large visual object was preferred over remaining quadrant except quadrant 3 on the measure of stop time.

Experiment 2: Rats with visual cortex lesion spend longer time near a large visual object than cage.

Histology

Using aspiration technique the lesions were centered in area 17. The measures made from the cortical surface [dorsal view] of the removed tissue indicated that the sizes of damage to striate visual cortex [measured in square pixels] varied from the smallest [87%] to the largest [100%] damage in different rats.

ANOVA indicated no significant difference between the lesion sizes in the striate visual cortex $F[4, 1]=0.09$, $p=0.77$ in the right compared to the left hemisphere [Left hemisphere: Mean=909.4; SE=146.26; Right hemisphere: Mean=945.2; SE=49.05]. Area 18b was invaded slightly at least in one of the hemispheres of the brain in all rats. For verification, see Lashley's [1931] diagram of primary visual cortex boundaries, and Krieg's [1946] drawing of the size and position of visual areas. ANOVA indicated a significant difference between the lesion sizes of the V1 and V2; $F[4, 1]=3.27$, $p<0.0002$. The average of lesion sizes in V1 was considerably larger [V1: Mean=1993.80; SE=80.50; V2: Mean=269.80; SE=56.30]. From the frontal view of some sections, all layers of striate visual cortex and the underlying corpus callusum were removed in three rats and penetrated in others. Hippocampus was not damaged. The LGN

appeared to be shrunk with some bilateral degeneration of cells in this area. Nevertheless, there were cells with normal features in this area. Figure 3.6 illustrates a representative lesion centered in striate visual cortex of this group.

Behavior

With the groups counterbalanced with respect to experimental conditions [large visual cue vs. cage] rats explored the environment for a 20 min test. Fig. 3.7 illustrates the experimental condition of this experiment.

Rats in both groups displayed preference for the place near the visual object and cage as reference points however, rats with damage to visual cortex spent longer time near the large visual cue than control rats. Fig. 3.8 illustrates the preference for the cue sector by showing travel paths and stops for a representative rat tested in room light. These general findings were confirmed by the formal analyses:

Total time. ANOVA yielded no significant group effect $F[8, 1]=0.84$, $p=0.38$, no significant effect of cage vs. visual cue conditions $F[8, 1]=0.85$, $p=0.38$ or interaction of group by conditions $F[1, 1]=1.04$, $p=0.33$. There was a significant effect of zones $F[15, 1]=48.88$, $p<0.0002$. Also, there was a significant interaction of group by zones $F[15, 8]=10.45$, $p<0.0002$, and also a significant interaction of conditions [cage vs. visual object] by zones $F[15, 1]=25.01$, $p<0.0002$. The interaction of group by conditions [cage vs. large visual cue] and zones was also significant $F[15, 1]=8.79$, $p<0.0002$, Fig. 3.9A.

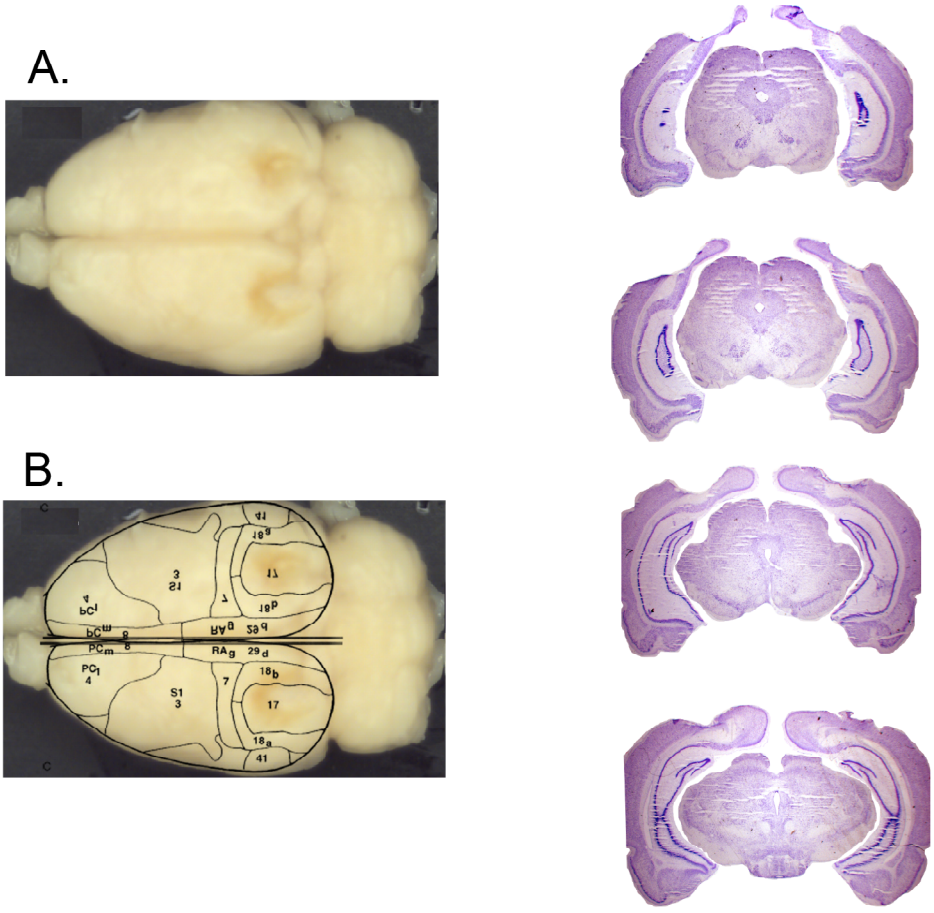

Fig. 3.6. Lesions centered in the striate visual cortex. The figure on the top left [A] illustrates damage to striate visual cortex on left and right side of the brain, and the figure on the bottom right [B] illustrates the position of the lesions to area 17 and other visual and non-visual areas. The lesion on the bottom illustrates the depth of the lesion from frontal view.

A. B.

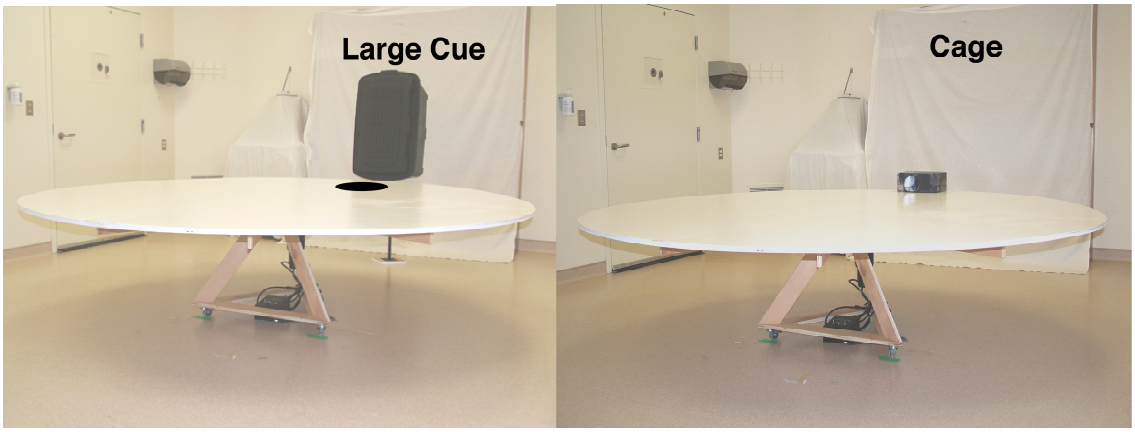

Fig. 3.7. Apparatus, the point of entry and cues. A. Open table with large local cue. B. Open table with a cage in which the rat can enter. Black circles indicate locations where rats were placed to begin a session.

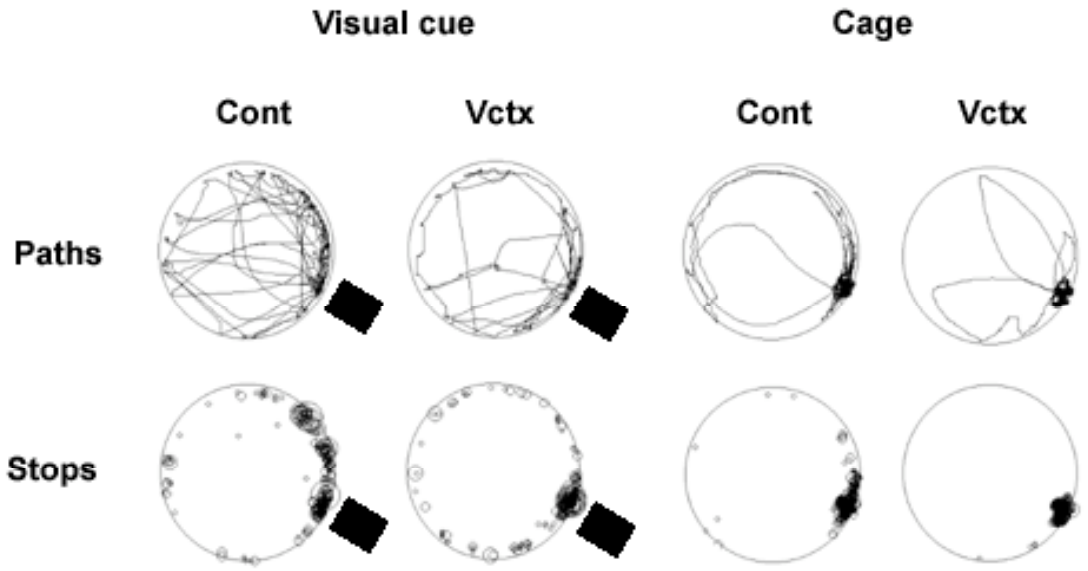

Fig. 3.8. Exploratory paths and stops made by representative rats as a function of cue saliency. Rats in either group were started at the edge inside the refuge box or beside a large visual cue. Lines represent paths, circles, and stops. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

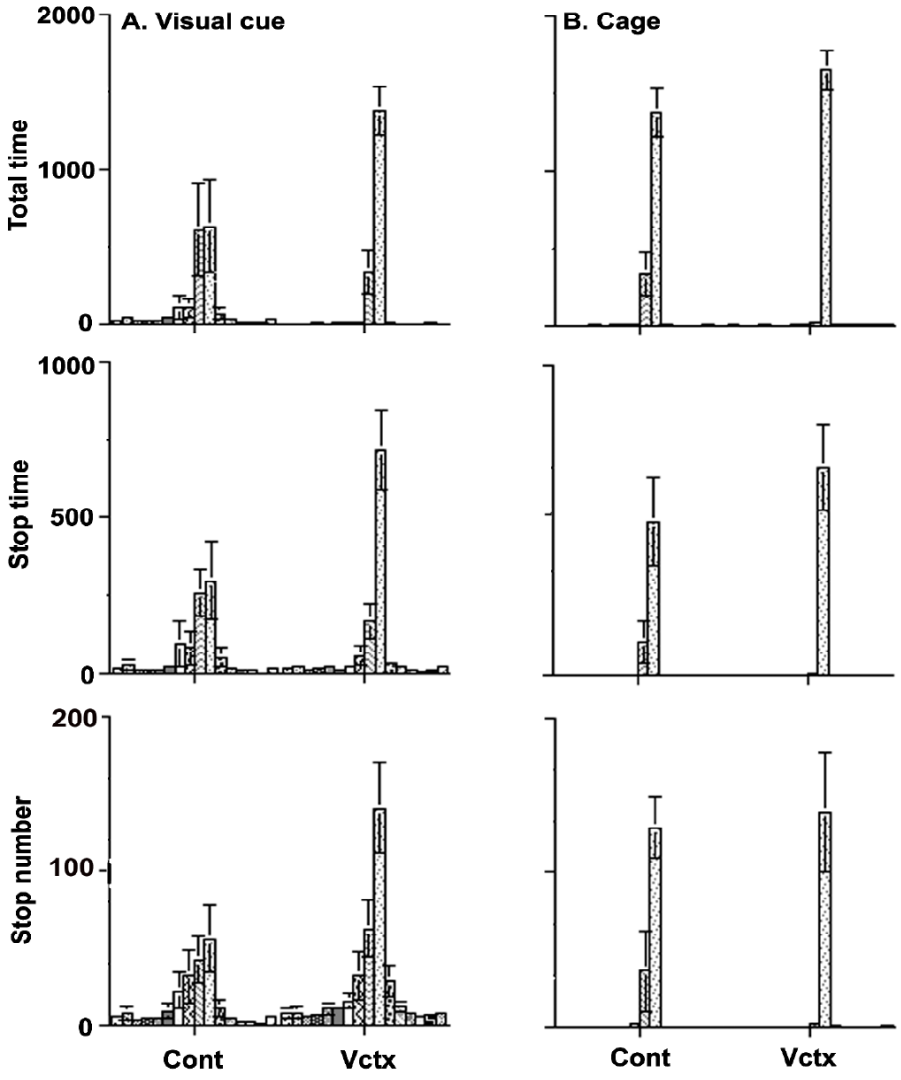

Fig. 3.9. The time [mean and standard errors in seconds] spent on different sectors of the table in each condition. Rats with damage to visual cortex spend longer time and make greater number of stopping visits near the large visual cue [A]. Rats in control and visual cortex groups were not different on the measures of total time, stop time, and stop numbers in the cage condition [B].

Stop time. ANOVA yielded no significant group effect F[8, 1]=0.54, p=0.48, no significant effect of cage vs. visual cue conditions F[8, 1]=0.15, p=0.70 or interaction of group by conditions F[8, 1]=0.16, p=0.69. There was a significant effect of zones F[15, 1]=41.41, p<0.0002. Also, there was a significant interaction of group by zones F[15, 1]=3.11, p<0.0004 and also a significant interaction of conditions by zones F[15, 1]=5.61, p<0.0002. The interaction of group by conditions [cage vs. large visual cue] and zones was not significant F[15, 1]=0.30, p<0.99, Fig. 3.9B.

Stop number. ANOVA yielded no significant group effect F[8, 1]=0.30, p=0.59, no significant effect of cage vs. visual cue conditions F[8, 1]=1.47, p=0.25 or interaction of group by conditions F[8, 1]=1.81, p=0.21. There was a significant effect of zones F[15, 1]=43.88, p<0.0002. Also, there was no significant interaction of group by zones F[15, 1]=1.06, p<0.39 and also a significant interaction of conditions by zones F[15, 1]=11.55, p<0.0002. The interaction of group by conditions [cage vs. large visual cue] and zones was not significant F[15, 1]=0.66, p<0.81, Fig. 3.9C.

Follow-up t-tests indicated that rats with visual cortex lesion spent significantly [p=0.05] longer period of time stopped near the large visual cue than control rats. Also follow-up t-tests indicated that rats with visual cortex lesion made significantly [p=0.05] greater number of stops near a large visual cue than control rats. The difference between two groups also was not significant in any of the measures for the zone associated with the cage.

Experiment 3: Exploratory locomotion of rats with damage striate visual cortex is influenced by the level of visibility in the environment.

Histology

The pictures taken from the brains are not available. Nevertheless, N-methyl-D-aspartate [NMDA] lesions were centered in area 17 and were almost of the same size, located at the same place in the brain. From the frontal view, all layers of striate visual cortex and dorsal part of corpus callusum, but not underlying hippocampus, were removed. Microscopic examination indicated bilateral degeneration of cells and some shrinkage in the LGN. Nevertheless, there were cells with normal features in this area. Fig 3.10 illustrates the frontal sections of the brain.

Behavior

Started from the center of the table, control rats and rats with damage to visual cortex explored the environment on the open table for 20 min either under room or infrared light. Fig. 3.11 illustrates experimental condition of the present experiment. Rats stopped more frequently and for a longer period of time on the open arena and their stops were more dispersed in the room light in comparison with infrared light condition.

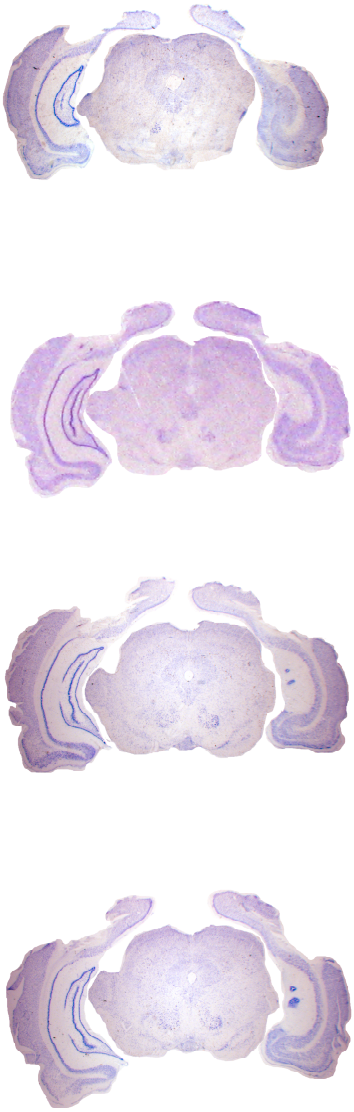

Fig. 3.10. Lesions centered in the striate visual cortex. The depth of the lesions is illustrated from frontal view.

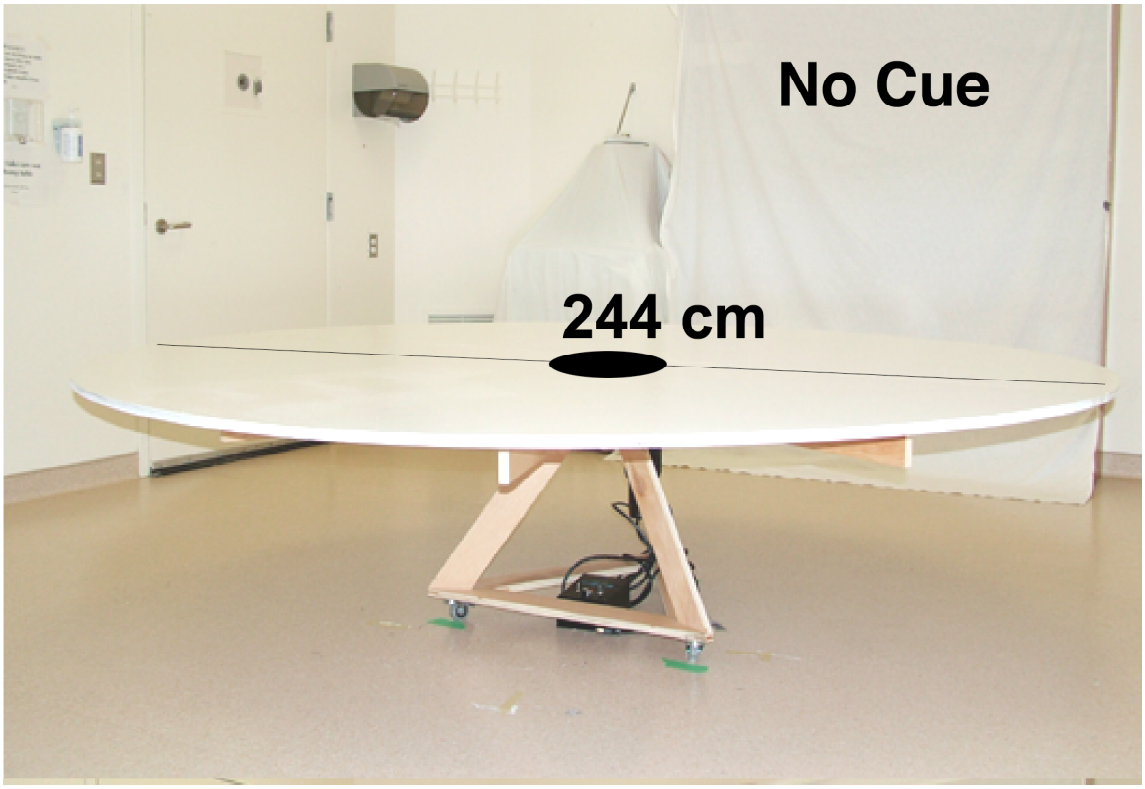

Fig. 3.11. The point of entry on the open table. The black circle in the center of the table indicates the entry point of rats.

Fig. 3.12 illustrates stopping behavior of a representative rat with longer [represented by circle size] and greater number [represented by the number of circles] and dispersion of stops in the room light in comparison with their stopping behavior under infrared light. These general findings were confirmed by following analyses:

Stop time. ANOVA indicated no significant effect of group $F[1, 12]=1.1$, $p=0.32$, and also no significant interaction of group by trial $F[2, 2]=2.74$, $p=0.13$. There was a significant effect of trials $F[2, 1]=47.47$, $p<0.0002$, suggesting that rats in both groups stopped longer under the room light condition, Fig. 3.13A.

Stop number. ANOVA indicated no significant effect of group $F[2, 12]=2.38$, $p=0.98$, and also no interaction of group by trial $F[2, 2]=0.23$, $p=0.63$.

There was a significant effect of trials $F[1, 2]=59.59$, $p=0.0002$, suggesting that rats in both groups made greater number of stops in the arena in room light, Fig. 3.13B.

Stop dispersion. ANOVA indicated no significant effect of group $F[1, 8]=2.16$, $p=0.17$, or interaction of group by trial $F[1, 8]=0.10$, $p=0.75$. There was a significant effect of trials $F[1, 2]=6.4$, $p=0.04$, suggesting that stops in both groups of rats were more dispersed in the light than in the dark condition, Fig 3.13C.

Distance. There was no significant effect of group $F[1,8]=1.82$, $p=0.21$, or interaction of light condition by group $F[1,8]=1.77$, $p=0.21$. The cumulative

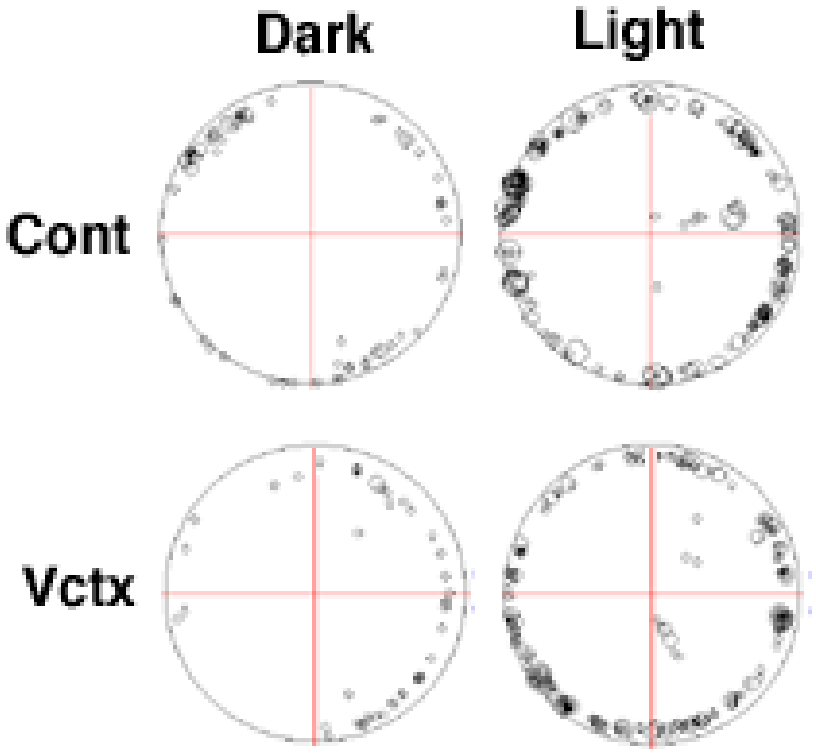

Fig. 3.12. The stops made by a representative rat that were started from the middle of the table. The stops [circles] made by rats under room light condition are longer in duration, greater in numbers, and more dispersed on the open table in comparison to those under infrared light condition. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

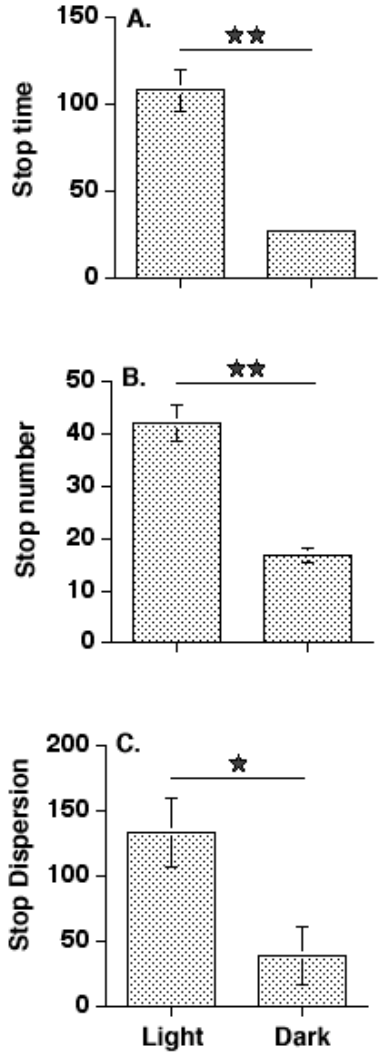

Fig. 3.13. Measures of stops [means and standard errors in seconds] by rats started in the middle of the table. Rats spent greater length of time stopped [A], and stopped more frequently [B] and their stops were more dispersed on the table [C] when they explored the environment under room light than when they did so under infrared light.

distance traveled in the dark was significantly longer $F[1,1]=29.35$, $p<0.0007$ than that in the room light condition.

Experiment 4*: *Rats with visual cortex lesion do not expand their exploration.

Histology

N-methyl-D-aspartate [NMDA] lesions were centered in area 17. The measures made from the cortical surface [dorsal view] of the removed tissue indicated that the sizes of damage to striate visual cortex [measured in square pixels] varied from 81% [smallest lesion] to 92% [largest lesion] in different rats. ANOVA indicated no significant difference between the lesion sizes in the striate visual cortex $F[4, 1]=0.09$, $p=0.77$ in the right compared to the left hemisphere [Left hemisphere: Mean=2175.40; SE=49.27; Right hemisphere: Mean=2147; SE=43.10]. From the frontal view, all layers of striate visual cortex and the convexity of corpus callusum were removed in some sections, but the underlying hippocampus was intact. The LGN appeared to be shrunk and microscopic examination indicated bilateral degeneration of cells in this area. Nevertheless, there were cells with normal features in this area. Figure 3.14 illustrates a representative lesion of visual cortex.

Behavior

Started from the edge of the table rats with visual cortex lesion and control rats were videotaped for 20 min in the first and the fifth day of the experiment [Fig. 3.15]. In between they were placed at the same location and explored the environment for 10 min in three consecutive days. As is illustrated in Fig. 3.16 for

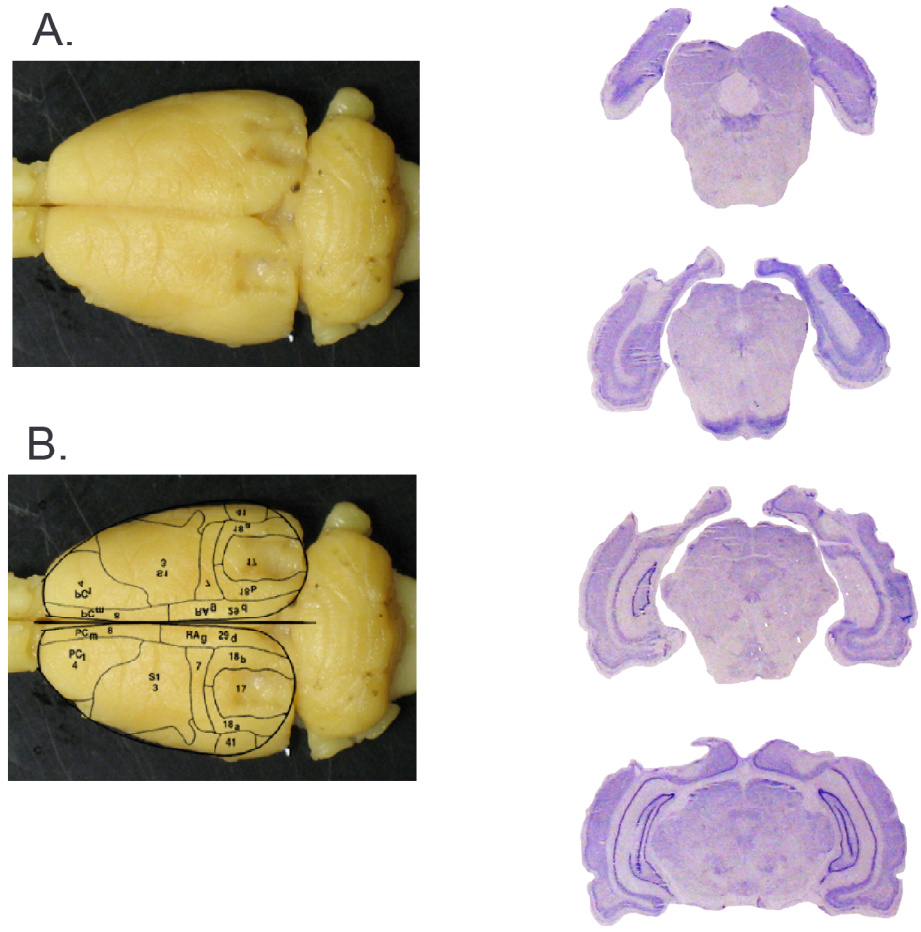

Fig. 3.14. Lesions centered in the striate visual cortex. The figure on the top left [A] illustrates damage to striate visual cortex on left and right side of the brain, and the figure on the bottom right [B] illustrates the position of the lesions to area 17 and other visual and non-visual areas. The lesion on the bottom illustrates the depth of the lesion from frontal view.

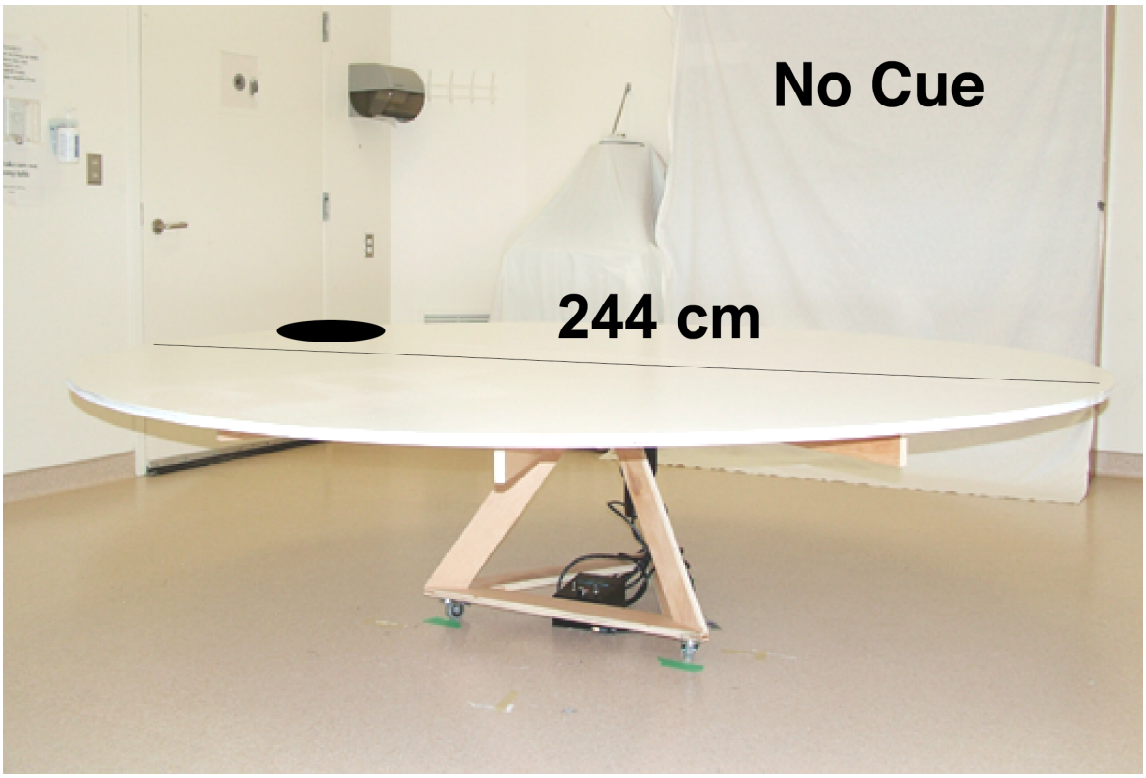

Fig. 3.15. The point of entry on the open table. The black circle on the edge of the open table indicates the rats' entry point.

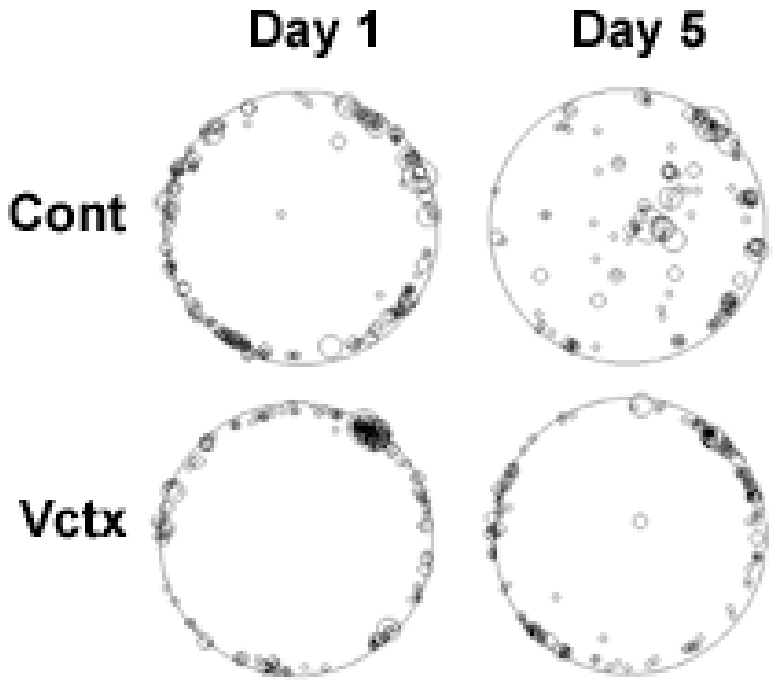

Fig. 3.16. The stops made by representative rats for control and lesion group in the first [day 1] and last day of the experiment [day 5]. The stops [circles] made by rats in the last day of exploratory test are greater in numbers in the inner annulus of the table, and are more dispersed on the table in comparison with control group. Circle sizes indicate stopping duration of 1-2 sec, 2-10 sec, 10-30 sec, 30-60 sec, and > 60 sec.

a representative rat, although control rats and rats with damage to the visual cortex made almost the same number of stops in the first day of the exploration, the stops made by control rats was considerably more dispersed and larger in number in the fifth day of exploration.

The following is a more formal analysis of these findings:

Stop number in the outer annulus of the open table. ANOVA yielded no significant group effect $F[1, 8]=0.02$, $p=0.88$, day effect $F[1, 8]=1.13$, $p=0.31$ or interaction of group by day $F[1, 8]=0.28$, $p=0.61$ on the measure of stop number made in the outer annulus [edge] of the table [Fig. 3.17A].

Stop number in the inner annulus of the open table. There was a significant effect of group $F[1,8]=14.79$, $p<.005$, day $F[1, 1]=13.85$, $p=0.006$, and interaction of group by day $F[1, 1]=7.32$, $p=0.03$, on the measure of stop number made in the inner annulus of the table [Fig. 3.17B], suggesting that control rats visited the inner annulus of the table more than rats with visual cortex lesion on the last day of exploratory sessions.

Stop dispersion. ANOVA yielded a significant effect of group $F[1,8]=6.12$, $p<0.03$, no significant effect of day $F[1,8]=0.44$, $p<0.52$ or significant interaction of group by day $F[1,1]=2.71$, $p<0.13$ [Fig. 3.18A].

Distance. There was no significant effect of group $F[1,8]=1.14$, $p<0.31$, day $F[1,8]=0.02$, $p<0.87$ or interaction of group by day $F[1,1]=0.08$, $p<0.78$ on the cumulative distance traveled by two groups of rats [Fig. 3.18b].

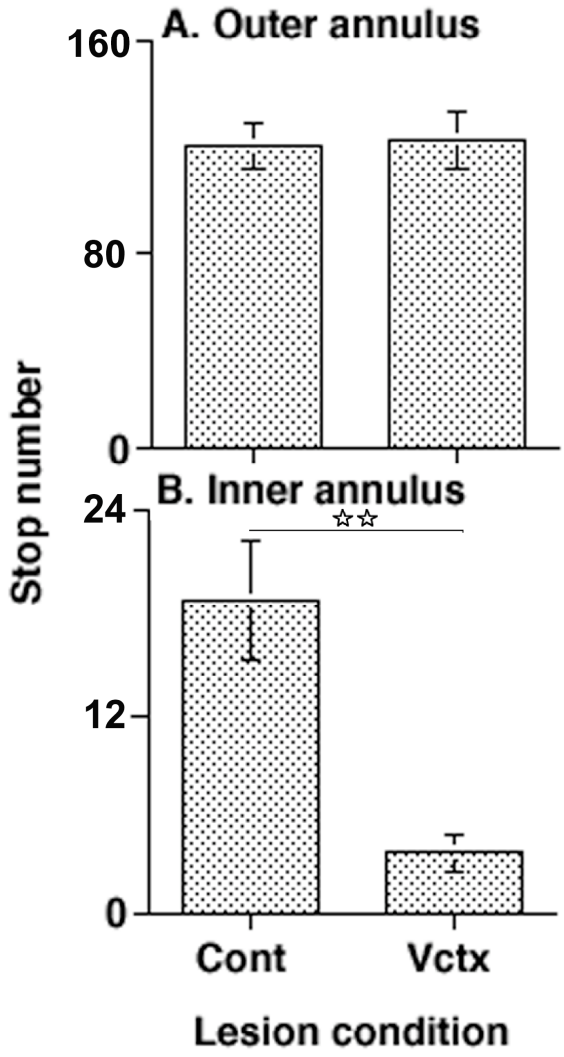

Fig. 3.17. Measures of stops [means and standard errors in seconds] by rats started in the middle of the table. Rats spent greater length of time stopped [A], and stopped more frequently [B] when they explored the environment under room light than when they did so under infrared light.

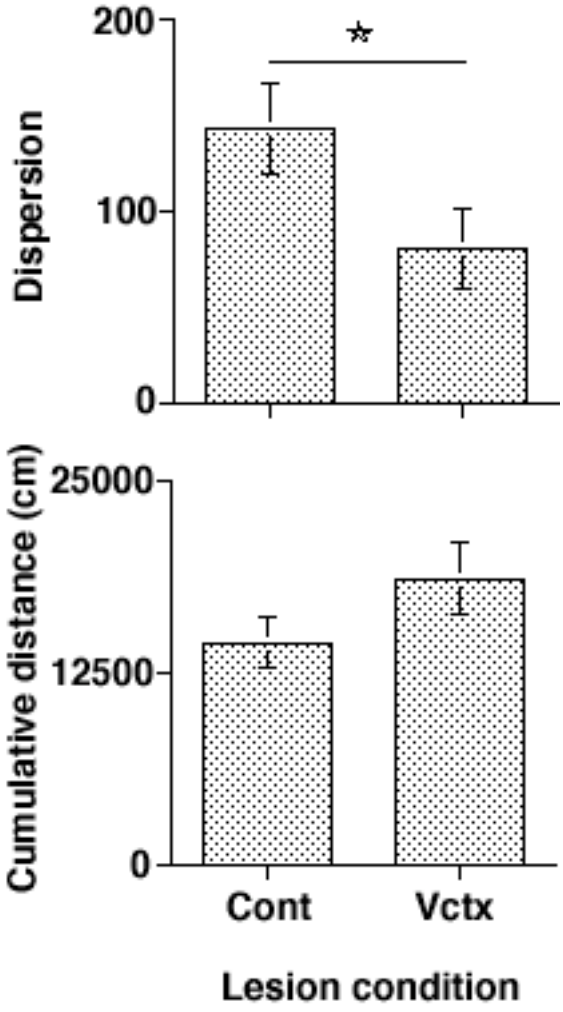

Fig. 3.18. Measures of stop dispersion and traveled distance [means and standard errors in seconds for stops and in cm for distance] by rats. The stops by control rats in the last day of the test were more dispersed [A] on the table than those by rats with damage to visual cortex. There was no considerable difference in traveled distance between groups [B].

5. Discussion

The purpose of present experiments was to investigate the effect of damage to visual cortex on exploratory organization of rats to their entry point, local objects, distal cues, and also investigation of this effect on expansion of exploratory locomotion in a series of open field tests. Rats were tested on a large circular table in conditions in which a salient object was located near or on the table, or in a relatively featureless environment in which they explored the environment under different level of visibility or several times under room light. The main findings were that rats with damage to visual cortex organized their exploratory locomotion to their point of entry or to local objects presented on or near the open table. However, they displayed a stronger attachment only to a large visual object near the open table. The exploratory expansion of rats with damage to visual cortex was influenced by visual cues, but it did not follow a temporal pattern that paralleled that of the control rats. This behavioral profile suggests that much, but not all, of exploratory behavior is not dependent upon visual neocortex.

Using the spatial paradigm developed in previous study in this thesis, the experiments conducted here attempt to document the possible difference between the organization of exploratory locomotion of rats with or without damage to visual cortex. The organization of exploratory locomotion to the point of entry, and local objects as places that offer similar cue background are highly predictable and also is influenced by cue saliency. These features provide a research paradigm to test visually guided behavior in rats with visual cortex

lesion. Similar to previous experiments in this thesis, the focus here is on exploratory locomotion of rats. Other exploratory behaviors such as rearing and grooming, which sometimes occur at home bases, were not measured.

The question was whether or not visual cortex of the rat contributes to the organization of exploratory locomotion. The main findings can be summarized as follows: 1. Upon placing rats on a circular open table, visual cortex rats organized their exploratory trips to their entry point or a local object as did control rats. 2. If started near a salient object all rats returned to them regularly, but rats with damage to visual cortex displayed more attachment to the large visual object near the table. 3. Both groups of rats stopped longer and more frequently and their stops were more dispersed in the light in comparison with their stopping behavior in the dark. 4. Rats with damage to visual cortex did not expand their exploratory locomotion with repeated exposure to the environment. Taken together, the results suggest that visual cortex makes a contribution to spatial behavior by recalling and building upon previous experience.

Organization of exploratory locomotion to reference points

The fact that rats with damage to visual cortex approached the large visual object with a considerable vigor in their first outward excursion from their point of entry suggests that rats could also orient their locomotion toward a visual object. The similarity between stopping behavior of control rats and rats with damage to visual cortex tested under room and infrared light also suggest that both groups of rats respond to visual information in the environment similarly. These findings

are consistent with previous finding that rats with visual cortex lesion are still able to see [Dean 1981b, Dean, 1993].

The finding that rats with damage to visual cortex probably could see the large visual cue and approach it also suggests that their ability for taxon navigation is probably intact. Taxon strategy is an approaching locomotion toward an orienting stimulus [such as a large visual cue] in the environment [Save & Poucet, 2005; Redish, 1999]. This finding is consistent with the fact that other brain structures such as superior colliculus contributes to goal-directed orientation movements [Milner & Lines, 1983]. The fact that both visual cortex and superior colliculus contribute to orienting locomotion to a target [Goodale et al., 1978] suggests that rats with either lesions may be capable of orienting their locomotion toward a cue in an experimental condition similar to this study. A number of previous studies have demonstrated that rats with visual cortex lesions can solve problems using visual flux cues [Bauer & Cooper, 1964]. Additionally, other studies suggest that visual pathways to the neocortex that project from the superior colliculus via the pulvinar can mediate pattern vision [Dean, 1981b]. In this respect, the present experiments, although excluding primary visual cortex from a fundamental role in visual exploratory behavior, do not exclude higher visual cortical areas.

Nevertheless, there is also a possibility that rats use both piloting and dead reckoning to reach the reference point after their first approach in an open field test. A previous observation in our laboratory suggests that rats might use idiothetic cues to reach a certain location even though visual cues are available.

In an open field test rats that had returned to a refuge box following several excursions, retuned to the same location when the box was removed after they left the refuge in one of their excursions. The pattern of their return trips suggested that they were using dead reckoning to reach their reference point [Wallace & Whishaw, 2005]. Other experiment indicated that rats established a home base near a place where a large visual object was located and in probe trial when the large visual object was removed the rats were able to identify and reestablish their home base there [Hines & Whishaw, 2005]. The authors concluded that rats had used piloting strategy to reach the location of their home base.

Because in the probe trial of experiment 1, rats were started from the center of the open table, only distal visual cues could be used to identify and reach the locations designated as the entry or the cued quadrant earlier in experimental trial. The fact that rats with damage to visual cortex organized their exploratory locomotion to these locations suggests that they are still able to use visual distal cues to navigate to these locations. Thus, piloting on the open table appears to be intact in rats with visual cortex lesion.

In an environment in which the entry point lacked a salient local cue and a large visual object was present in another location near the open table, the pattern of exploratory excursions indicated that rats with damage to visual cortex commuted frequently between their point of entry and the large visual object, although the excursions starting from one reference point and ending at the same one [the point of entry or large visual cue] also occurred. This finding

suggests that rats treated these two locations as reference points similar to home bases established near each other [Eliam & Golani, 1989; Golani et al., 1993].

Because rats with damage to visual cortex did not use tactile cues as the most dominant organizer of their exploratory locomotion, their visual processing appears to be functional. The normal preference of rats with damage to visual cortex to organize their exploration near the cage that conveys tactile stimulation [Study 1: experiment 3] suggests that probably spatial processing in these rats was different in nature from that of peripherally blind rats reported by Save et al., [1998]. It is interesting that in their study peripherally blind rats made a greater number of contacts with the object inside the cylinder as they were exploring the open environment, and the firing fields of their place cells were stable as that of control rats.

Nevertheless, the greater length of time spent near the large visual object by rats with damage to visual cortex suggests a spatial function for visual cortex. This is consistent with previous finding in which rats with damage to visual cortex displayed spatial impairments in matching-to-place learning task [Whishaw, 2004]. The present finding can be considered as a behavioral evidence for the contribution of visual cortex to hippocampal circuit [Paz-Villagran et al., 2002; Poucet et al., 2003; Whishaw, 2004].

One possible explanation for more frequent returns and the attachment of rats with visual cortex lesion to the large visual object is that this pattern of behavior is compensatory. Regular returns of rats to their home base has been proposed to serve as a compensatory behavior for correcting the associations

between local view of the home base and dead reckoning coordinates that tends to drift significantly as a function of the time that animals are involved in exploring the environment [Touretzky et al, 1996; Redish, 1999]. This notion can be generalized to the attachment of rats with visual cortex lesion to the large visual object in experiment 2. Because spatial coherence of place fields in hippocampus of rats with damage to visual cortex is lower in comparison with control rats and also because place cells in these rats use three dimensional objects as spatial anchors for firing field less efficiently than control rats [Paz-Villagran et al., 2002; Poucet et al., 2003], it is possible that these rats use their remaining visual capacity to recalibrate the environment around the salient visual object as a dominant reference point repeatedly and in an over compensatory manner to visually organize their exploration. This interpretation is also consistent with excessive use of visual cues by hippocampal rats to compensate the lack of spatial coding while taxon strategy is still functional [Foreman & Stevens, 1987, O'Keefe & Nadel, 1978].

It is also possible that damage to visual cortex and consequently its projection to posterior partial cortex have led to the above mentioned behavioral patterns observed in the experiment. This notion is supported by the findings that 1. Cells in posterior parietal cortex show directional correlates [Chen et al., 1994a,b] 2. Cells in lateral dorsal thalamic nuclei that project to posterior parietal cortex [Kolb & Walkey, 1987] show directional response but their responses are dependent on initial availability of light [Mizumori et al., 1992] and 3. Striate visual cortex projects to posterior parietal cortex [Kolb & Walkey, 1987]. These facts

along with the proposal that an intact posterior parietal cortex is more involved in abstraction and integration of spatial features obtained in the course of locomotion [Poucet & Benhamou, 1997, Save & Poucet, 2000; Save et al., 2001] suggest that this area may play a role in formation of spatial representation. The behavioral profile of rats with damage to posterior parietal cortex in which rats learn to navigate to a hidden platform in the swimming pool after a considerable amount of training but their trajectories follow a looping pattern [Kolb & Walkey 1987] provide a further evidence for the possible involvement of this area in tasks that demand dominant visual processing. Similar spatial impairment may occur following denervation of projections from visual cortex to posterior parietal cortex.

The notion of distinction between dorsal and ventral streams in primates [Ungerleider & Mishkin, 1982; Goodale et al., 1994] that also has been identified in rats [Kolb et al., 1994] provides an anatomical basis for the explanation of the finding in this experiment based on the process of vision for action. As an expansion of the theory, a defective dorsal stream due to damage to visual cortex may disrupt the proper visual feedback for action and result in the attachment to a salient visual object to compensate the disrupted visual feedback.

Expansion of exploratory locomotion

The effect of visual information on the expansion of exploratory locomotion is consistent with the notion that rats move to different locations and stop to gather visual information and incorporate it into their spatial representation during exploration [Drai et al., 2001; O'Keefe & Nadel, 1978; Tchernichovski et al.,

1998]. Consistent with the notion that stops are indirect measures of scanning that determine the amount of information that animals are gathering from their environment [Drai et al., 2001; Tchernichovski et al., 1998], is the finding that head scanning and locomotor initiation reflect reciprocal processes [Sinnamon et al., 1999]. Similar patterns of stopping behavior in rats with visual cortex lesion and control rats along with association of stops and scanning behavior provides a convincing rationale to suggest that rats with damage to visual cortex probably have the visual capacity to gather visual information necessary to form spatial representation of their environment. However, the lower coherence of place fields in rats with damage to visual cortex [Paz-Villagran et al., 2002] may result in lower efficiency in the formation of spatial representation based on gathered information.

In an exploratory context, the expansion of exploratory locomotion has been characterized by a gradual increase in the length of excursions as a function of time being exposed to a novel featureless environment and familiarity with the environment [Tchernicovski et al., 1998]. A straightforward rationale to explain the limited expansion of exploratory locomotion in rats with damage to visual cortex in the present thesis is that they do not become habituated to the explored part of the environment [open table] because of the aforementioned disruption in the formation of spatial representation. The process of information gathering through different sensory systems is assumed to lead to habituation, which is a gradual decrease of response to stimuli. Several authors have reported a disruption of habituation process in rats with hippocampal damage and attributed

this impairment to formation of spatial representations of the environment [Forman & Stevens, 1987; Gray & McNaughton, 1983; Mumby et al., 1995; Poucet, 1989; Save et al., 1992; Thinus-Blanc et al., 1991]. In this regard, environmental cues may remain novel for longer period of time. This resistant novelty can lead to a longer exploration of apparently explored part of the environment [Altman et al., 1973], and form the basis of habituation deficits. It is interesting that Kirkby et al., [1967] suggested that rats with hippocampal damage are slow in processing spatial information and consequently will not be habituated to the visited part of the maze, which will result in revisiting the same area repeatedly. Hence, the present finding is consistent with the notion that visual cortex contributes to spatial ability of rats [Lashley, 1943, 1939; Goodale& Dale, 1981; Goodale et al., 1978; Whishaw, 2004] and also provides a behavioral evidence for the possible contribution of visual cortex to formation of spatial representation and visual habituation.

As an alternative explanation, the possible visual control of dorsal stream over moment-to-moment displacements in space may be the underlying mechanism of the present finding. Identification of a similar dorsal pathway in rats [Kolb et al., 1994] provide an explanation of how a defective dorsal stream due to damage to visual cortex may disrupt the proper visual feedback for action and results in stronger attachment of rats to the most salient cue in the environment. The removal of proximal visual cues used in experiment 2 left the edge of the table as the only salient local cue. Especially because rats with damage to visual cortex appears to be capable of processing visual information

[Experimet 1, 3] the pattern of exploratory locomotion of these rats can again be due to their attachment to the edge [local salient object in experiment 4] to compensate the disrupted visual feedback.

In conclusion, the main finding of the present study is that although rats with damage to visual cortex are still able to use distal and proximal visual cues to navigate towards the reference points and expand their exploratory locomotion, damage to visual cortex disrupts their normal attachment to reference points and expansion of their exploratory locomotion. These findings suggest that exploratory locomotion is mediated by different subdivisions of visual system and damage to visual cortex is likely to disrupt the visual habituation and visomotor coordination.

General Discussion

The purpose of this thesis was to study the contribution of visual cortex to exploratory locomotion in rats. The visual cortex is the first cortical region in an "extended visual system" that includes a number of secondary visual areas, a number of cortical regions in the cingulate and temporal cortex and a number of limbic structures including its terminal destination, the hippocampus. Because the hippocampus is strongly implicated in spatial behavior, it is expected that the visual cortex will make a contribution to spatial behavior, including exploratory behavior. Two sets of experiments were conducted in an open field and the following results were obtained. In the first set of experiments procedures were developed for quantifying exploratory locomotion and in the second set of experiments rats with lesions to visual cortex were subjects to the same experimental tests. The main findings of the experiments are that the behavior of control rats and rats with visual cortex lesions is surprisingly similar. Both groups of rats remember the first location that they encounter on the table and return to it periodically, both groups of rats form home bases near prominent landmarks or cues when they are available, and patterns of behavior are similar for rats tested in room lighting or in infrared lighting. The behavior of rats with visual cortex lesions was different in a number of ways, however. They spent longer times near visual cues, and did not explore the center of the table. The similarities and differences between control and visual cortex rats suggest that most features of exploratory behavior in rats do not depend upon visual information provided by primary visual cortex. The following discussion will first consider the experimental

strategy and experimental design, it will then consider the main experimental findings, and finally it will consider the implications of the central results.

Ethologists emphasize on the importance of testing animals in a natural habitant or testing animals in a laboratory setting that resembles a natural habit [Pfluger & Menzel, 1999; Shillitio, 1963]. The systematic observation of rats in the open field, in which animals move freely and have their choice of determining their routes, has provided valuable information about exploratory behavior [Jeffery, 2003; Wallace & Whishaw., 2005]. Recent studies have combined the pure observational methods with experimental design to study brain mechanism underlying exploratory behavior. For example, such research has considered the role of the hippocampus, part of the brain considered to be a spatial brain, in mediating exploratory behavior. This approach has provided a potential to control independent variables of the experiments [See experiments conducted by Whishaw and his colleagues, [Whishaw et al., 1992; Whishaw et al., 1995a,b, Whishaw et al., 1997; Whishaw & Jarrard, 1996; Whishaw & Maaswinkel, 1998; Whishaw & Gorney, 1999].

Among various behavioral tests used to study exploratory behavior or locomotion [Cruze et al., 1994; Gharbawie et al., 2004; Ossenkopp et al., 1996; Renner & Seltzer., 1991] open field tests have proved popular [Eilam & Golani, 1989]. Despite their popularity, they have not always provided much in the way of insights into exploratory behavior. In initial studies, experimentalists only observed a complex series of actions in which animals traveled from one place to another in a seemingly random fashion. This activity could be quantified in order

to discriminate rats with brain lesions or rats under the influence of pharmacological agents, but it did not provide insight into motivation or cognitive disposition. The initial lack of information obtained from open field tests [such as Hall's table, 1934] was attributed to the limitations of methods for examining and analyzing exploration [Halliday, 1968]. The invention of computer programs and novel methods of behavioral analysis led a better understanding of exploratory behavior [Drai et al., 2000, Drai & Golani, 2001, Golani et al, 2004]. It is now recognized that the main characteristic of a rat's behavior on the open table is related to the ability of the animals to stop and move in any direction [Jeffery, 2003; Wallace & Whishaw, 2003]. This ability provides the possibility of studying exploratory behavior of rats in a laboratory setting adopting an ethological approach.

In comparison with other tests the open field test has a number of useful characteristics. In the swimming pool task, which is widely used to examine spatial behavior, an animal is not free to stop, the task is mainly a test of escape, the test is brief, and the animal is stressed by the cold water used to motivate swimming [Golani et al., 1993; Hodges, 1996; Jeffery, 2003; Morris, 1981]. In dry land mazes that have arms or cul de sacs, the movements of the animal are constrained, locomotion usually requires food or water deprivation for motivation, and the test must be repeated in order to determine what an animal may have learned [Save et al., 2000; Whishaw et al., 1995b]. Experimentalists have also used rather confined boxes to study exploration but these have drawbacks in

limiting locomotion, obscuring room cues, and favoring one form of behavior, such as rearing against a wall, over other behaviors.

The present study used a large open table located in a large room. The large size of open table, with no corners or walls attenuates tigmotaxic behavior and promotes the use of external cues in the environment [Hines & Whishaw, 2005]. These cues could be normal room cues, such as the door to the room, a bookcase, a sink, light switches on the wall, and wall posters. They could also include cues purposefully placed near the table or on the table. All visual cues could also be eliminated by turning off the room lights and filming the behavior of the animals under infrared light, a wavelength in which rats cannot see. Animals in open field tests need not be food deprived [Hodges, 1996]. Perhaps one of the most important features of an open field is that an animal is free to set its own agenda. Thus, if its behavior is organized, that organization will not only be revealed, the organization is more likely to be revealed in the less structured testing environment.

It is that latter argument that has been articulated by the original designers of the open table test [Eliam & Golani, 1989]. Their argument was that the more constrained the environment, the more likely that an animal's behavior will be constrained and biased. A less constrained environment is one in which an animal is likely to display species-specific actions that reveal a fundamental structure to is behavior. They also proposed that computerized techniques could be used to reduce the complex actions of an animal into meaningful units. For example, by measuring stopping durations and locations, they were able to show

that animals had preferred locations that they called “home bases”. The number of home bases developed by an animal was idiosyncratic as were their locations. This suggested that the animals imposed a structure on their environment that was not actually there. In other words, the animals revealed that their behavior was organized according to some central plan or schema.

The experimental designs in this thesis are characterized by a number of methodological strengths. These strengths were based on the development of analytical methods derived in the first study. One such analytical method was noting the importance of the point of entry to the organization of exploratory locomotion. The results of the first study revealed that immediately upon being placed on the table, exploratory locomotion became organized. The rats paused at the point of entry and then left only to return again and again. In other words, the point of entry became a home base. Even when cues signifying security, such as large black visual cues, were located elsewhere on the table and were used by the rats to develop a proximal home base, rats continued to return to the point of entry. Comparison of exploratory locomotion of rats on the edges of the table was based on the observation that rats spend most of their time on the edge of the table. If rats returned to their point of entry their returns were expected to occur more frequently on the edge of the table than the middle of the table. Formation of home bases at the point of entry was not limited to locations on the edge of the table. If rats were started in the center of the table they then returned to the center of the table, convincingly demonstrating the centrality of the point of entry. In some of the experiments, cues were placed on or near the

table and the saliency of the cues was varied. If cues importantly influenced behavior, it was expected that expressed behavior would be proportional to the saliency of the cues. It was found that if these cues coincided with the point of entry, time spent at the location increased. The experiments were also conducted in both room light and in infrared light. Because rats can use distal cues as well as self movement cues, it was expected that self movement cues would more likely to be used in the infrared light condition. Again, it was found that rats did use self movement cues because they returned to the point of entry in infrared light.

The exploratory locomotion of the rats was also shown to consist of two patterns, stops and progressions. The rats preferentially began progressions at idiosyncratically formed home bases to which they returned [Eliam & Golani, 1989]. Previous studies have shown that salient local cues are reliable reference points for rats [Wallace et al., 2002a; Wallace & Whishaw, 2003; Hines & Whishaw, 2005]. Local salient cues used in this thesis included a small visual object near the table, a large visual object near the table, and a cage as refuge on the table. The use of salient local cues in this thesis was to mark a specific area of the environment as important so that organization of behavior in relation to the cues could be analyzed.

The two proximal cues with different sensory salience used in this thesis were a large visual object placed near the table and a cage that was placed on the table. These cues provided evidence for the relative weight of visual and tactile information in the organization of exploratory locomotion. In addition, use

of more distal cues in the room could be contrasted with the use of these more proximally located cues. The use of tactile versus visual cues of the same saliency was necessary to measure the reliance of rats with damage to visual cortex on either cue. Documentation of entry point as a reference point independent of local cues and characterization of exploratory locomotion in relation to local cues provided a unique opportunity to use them as a measure to investigate the organization of exploratory locomotion of rats with damage to visual cortex.

Thus, the characteristics of the behavioral methods used in the present thesis can be summarized as follows. The point of entry provides a predictable place for the organization of exploratory locomotion to immediate distal and/or local cues. While the entry point is a predictable location for the organization of exploratory locomotion, it can be marked by a local cue or be identified by immediate distal cues. Thus, the point of entry can be considered the core of a useful paradigm to study spatial/temporal organization of exploratory locomotion. Local cues provide a predictable location for the initiation of the organization of exploratory locomotion. The main differential characteristics of home bases formed idiosyncratically and those formed to local cues is that the locations of the later reference point are predictable. Finally the cage [or refuge box] on the open table provides salient tactile cues. A cage can be used to test the dominance of a combination of cues including tactile and visual cues compared with proximal visual cue in the organization of exploratory behavior. The importance of local visual cues on the formation of place response and home base formation has

been shown in previous studies [Wallace & Whishaw, 2003; Hines & Whishaw 2005; Prusky et al., 2000b; Wallace et al., 2002a]. Using objects with various degrees of saliency in the present thesis, the effect of cue saliency on exploratory locomotion could be demonstrated.

The major finding of the second series of experiments was that rats with visual cortex lesions can organize their behavior in relation to visual cues. The rats with visual cortex lesion returned to the point of entry, as did control rats. They also formed home bases in both light and dark conditions. If a large visual cue was located near the table they formed home bases near that cue. Indeed, they spend more time near a visual cue than did the control rats. If a cage was present on the table, then they formed a home base near that. In some respects, the visual cortex rats were different, not only by spending more time near visual cues but also by exploring the center of the table less than did the control rats.

The presence of organized exploratory behavior in relation to visual cues in the rats with visual cortex lesions means that remaining portions of the visual system mediate the behavior. It is well known that the visual tectum is quite capable of sophisticated visual functions, especially functions related to orienting to visual cues [Dean 1981b, Dean, 1993; Goodale et al., 1978; Schneider 1969]. Indeed the visual tectum in fish, amphibians, and reptiles, and also other available evidences [Gallistel, 1990] suggest that most species in these orders display preferences related to differentially illuminated environments. If the visual tectum is sufficient for organized exploratory behavior, this may mean that

cortical visual pathways are in the main not engaged at all in organizing exploratory behavior.

There is also substantial evidence that animals with visual cortex lesions might use different features of visual cues for guidance than do animals with intact visual systems. For example, Bauer and Cooper [1964] demonstrate that rats with visual cortex lesions will fail a visual discrimination test that they have learned using pattern cues but will retain the discrimination if it was learned on the basis of light flux. The cues used in the present study likely provided sufficient contrast to permit a light flux discrimination on the part of the rats with visual cortex lesions. There is also evidence that some visual tectal projections that reach higher levels of visual cortex via the pulvinar can mediate pattern discrimination. Future experiments could examine the contribution of the visual tectum and the pulvinar projects to the organization of visual exploration.

It is well known that rats can use either piloting or dead reckoning to guide their spatial behavior [McNaughton et al., 1996; O'keefe & Nadel 1978; Redish 1999; Whishaw & Brooks, 1999; Wilson & McNaughton, 1993]. Piloting involves the use of ambient cues to guide behavior while dead reckoning involves the use of self movement cues to accomplish the same end. Animals exploring the environment to form a spatial representation of their working space [Okeefe & Nadel, 1978; Whishaw & Brooks, 1999] use both piloting and dead reckoning to navigate through their environment [Gallistel, 1990]. A number of studies have shown that dead reckoning system can function as the only source of information gathering at least for a limited period of time [Alyan & Jander, 1994; McNaughton

et al., 1996; Wilson & McNaughton, 1993]; nevertheless, resetting orientation using a cue could extend the usefulness of the strategy. The fact that all rats organize their exploratory locomotion to their point of entry suggest that at least for a short period of time after introducing animal to the environment, the organization of exploratory locomotion is probably mediated by a dead reckoning system. This finding is consistent with the recent finding that head direction cells maintain their firing fields in novel environments using self movement cues. When rats move from a familiar cylinder, in to a novel rectangular apparatus [Taube & Burton, 1995] or when they are transported from a familiar cylinder into the novel rectangle apparatus passively [Taube et al, 1996], the firing fields of head direction cells remain stable. This finding is consistent with the theories that emphasize on the role of dead reckoning as a underlying mechanism of navigation, which is active even when external cues are available [McNaughton et al., 1996; Wallace & Whishaw, 2005].

Cortical-hippocampal interactions have long been recognized to play important roles in spatial learning and memory [Burwell et al., 2004; Eichenbaum et al., 1996; McNaughton et al., 1989; Poucet et al, 2003; Teyler & DiScenna 1986; Wickelgren, 1979]. Also, disruption of a sensory system may even change the function of systems that are not directly related to sensory manipulation [Turkewitz & Kenny, 1982]. Recent studies on adult rats provide electrophysiological evidences for the interaction between cortex and hippocampus, for example, spatial coherence of place fields in rats with damage to visual cortex are lower than that of control rats [Paz-Villagran et al., 2002;

Poucet et al, 2003]. Such findings are consistent with the notion that hippocampus is part of the extended visual system [Felleman & van Essen, 1991]. Unfortunately, just as the present findings indicate a limited role for visual cortex in exploration, previous work has shown that exploratory behavior retains a good level of organization in rats with hippocampal damage [Hines & Whishaw, 2005]. Thus as interesting as the relations between neural activity and the spatial environment are, their biological significance is still uncertain.

Consistent with the contribution of neocortex and subcortical structures, mainly hippocampus, to spatial navigation, the present finding is also relevant to the contribution of visual cortex to the organization of exploratory locomotion that is known to be mainly mediated by hippocampus [O'Keefe & Nadel, 1987] and the hypothesis that the mapping system contains several maps of the explored environment [O'keefe & Nadel, 1978, Bures et al., 1997; Quirk et al., 1990]. Whishaw & Brooks [1999] conclude that: "*The finding that rats will explore the same space with equal vigor under lighted and infrared conditions could suggest that this exploration serves to create a separate reference-frame for that space for each form of navigation*" Page: 666. The notion that animals may form separate spatial representations of the environment [O'keefe & Nadel, 1978] in which they explore raises the question of whether or not damage to the brain areas that are related to each form of representations produces a unique pattern of the behavior. A large body of evidence suggests the hippocampus as the main neural structure involved in dead reckoning and the processing of movement-related cues. Also, visual cortex is one of the main sensory modalities to convey

visuospatial information recovered from the environment to other areas of the brain including the hippocampus [Aggleton et al., 2000]. In a recent study, Hines & Whishaw [2005] demonstrated that exploratory locomotion of rats with the hippocampus removed is still organized under room light condition in an open field test, but not under infrared light [using self-movement cues]. This finding suggests that the hippocampus contributes to the organization of idiothetic exploration.

There are a number of differences in the exploratory locomotion in rats with damage to visual cortex that is different from that in rats with hippocampal damage. It is worthwhile considering whether these differences provide any insight into exploratory behavior. As it is presented in table 4.1, rats with hippocampus removed are characterized by higher dispersion of stops under infrared light [in comparison with control rats] and normal range of stop dispersion under room light [in comparison with control group]. In an opposite direction, rats with damage to visual cortex are characterized by a normal range of stop dispersion under infrared light condition [in comparison with control group] and a lower dispersion of stops in room light. Although the testing time was not the same in these two series of studies, the results still are comparable, because when rats explore the environment under infrared light, their exploratory locomotion tends to get more organized with time [Zadicario et al., 2005; Avni et al., 2006]. Thus, despite the longer time spent exploring the environment, one can still consider the significance of Hines and Whishaw [2005] results and the results from experiment 4 in the second study of this thesis. In addition, the

Table 4.1. The pattern of stop dispersion. Rats with hippocampal damage displayed higher dispersion of stops under infrared light compared with control rats but normal dispersion of stops under room light [Hines & Whishaw, 2005]. Compared with control rats in experiment 8 of this thesis, rats with damage to visual cortex displayed lower dispersion of stops under room light but normal range of stop dispersion under infrared light.

	HPC	Vctx
Dark	High	Normal
Light	Normal	Low

behavior of rats with damage to visual cortex are characterized by lower dispersion of stops in room light. Nevertheless, as has been mentioned before this behavioral profile can be due to disintegration of posterior areas of cortex [Lashley, 1939; Miller & Vogt, 1984]. The fact that damage to visual cortex or hippocampus generates two different patterns of exploratory locomotion in that damage to hippocampus disrupts idiothetic, but not the allothetic mode of exploratory locomotion and damage to visual cortex generates an opposite pattern in which visual exploration is disrupted, raises the question of whether different idiothetic and allothetic representations of space may be formed independently and these representations are mediated by two different brain areas, hippocampus and visual cortex, respectively. In other words, it is possible that separate brain areas can mediate the two different strategies. Damage to visual cortex may impair allothetic representation of the space, but not the processing of idiothetic cues, whereas hippocampal damage may disrupt idiothetic representation of the space, but not visual representation. This possibility is consistent with the notion that idiothetic and visual exploration might be two separate calibrating strategies that each generates a separate representation of the environment [Whishaw & Brooks, 1999].

Investigation of this possibility would require the direct contrast of rats with visual cortex damage vs. rats with hippocampal damage. This is especially necessary because there are many differences between the methods used in the present study and methods used in previous studies using hippocampal rats. Nevertheless, this is a provocative contrast.

Conclusion

The objective of this thesis was to determine at what level of the extended visual system spatial behavior became organized. It was expected that damage to primary visual cortex should produce impairment in organized exploratory locomotion that should be severe. First, early studies have argued that visual cortex in addition to playing a role in visual functions also played a role in spatial functions. Second, it was expected that by virtue of having poor visual acuity, rats with visual cortex lesions would be less likely to respond to visual features of the environment and so be less able to organize their behavior in relation to visual cues. Visual cortex lesions were produced both by aspiration and by using a neurotoxic method and the histological analysis indicated that both types of lesion successfully ablated most, if not all, primary visual cortex in both groups of lesion rats. Surprisingly, the finding that most features of exploratory behavior were intact in rats with visual cortex lesions suggests that visual cortex is not essential for organized exploratory behavior and plays only a limited role in exploration. The rats with visual cortex lesions were more likely to spend time near prominent visual cues and less likely to explore the center of the table, but in other respects they were not different from the control rats. Even on a measure of episodic memory, memory for the point of entry, the visual cortex rats did not differ from the control rats. These results raise two questions. First, taken together with previous finding that the hippocampus is not essential for all aspects of organized exploratory behavior, the present results raise the question of what region(s) of the brain are responsible? Second, given that the rats with

visual cortex lesions did respond to visual cues in much the same way as control rats raises questions concerning the visual features of cues that are used and which portions of the remaining visual system mediate the behavior? These questions could be usefully addressed in future research.

References:

Aggleton JP, Vann SD, Oswald CJ, Good M [2000] Identifying cortical inputs to the rat hippocampus that subserve allocentric spatial processes: a simple problem with a complex answer. Hippocampus 10:466-474.

Aggleton JP, Hunt PR, Rawlins JNP [1986] the effects of hippocampal lesions upon spatial and non-spatial tests of working memory. Behav Brain Res 19:133-46.

Alexander HG [1956] The Leibniz-Clarke correspondence. University of Manchester Press, London.

Altman J, Brunner RL [1973] The hippocampus and behavioral maturation. Behav Biol 8:557-596.

Alyan SH, Jander RJ [1994] Short-range homing in the house mouse, Mus musculus: Stages in the learning of directions. Anim Behav 48:285-298.

Amaral DG, Witter MP [1989] The three dimentional organization of the hippocampal formation: a review of anatomical data. Neuroscience 31:571-591.

Avni R, Zadicario P, Eilam D [2006] Exploration in a dark open field: a shift from directional to positional progression and a proposed model of acquiring spatial information. Behav Brain Res 171:313-323.

Babb S, Crystal JD [2005] Discrimination of what, when, and where; Implications for episodic-like memory in rats. Learn and Motiv 35:177-189.

Barnett SA, Cowan PE [1976] Activity, exploration, curiosity and fear: an ethological study. Int Sci Rev 1:43-59.

Bauer JH, Cooper RM [1964] Effects of Posterior Cortical Lesions on performance of a Brightness-Discrimination Task. J Comp Physiol Psychol 58:84-92.

Breese CR, Hampson RE, Deadwyler SA [1989] Hippocampal place cells: stereotypy and plasticity. J Neurosci 9:1097–1111.

Brown MW [1996] Neuronal responses and recognition memory. Semin Neurosci 8:23–32.

Brown JS, Laundre JW, Gurung M [1999] The ecology of fear: Optimal foraging, Game theory, and trophic interactions. J Mammalogy 80:385-399.

Brown LE [1966] Home range and movement of small mammals, Symp Zool Soc Lond 18:111-142.

Bures J, Fenton AA, Kaminsky Y, Rossier J, Sacchetti B, Zinyuk L [1997] Dissociation of exteroceptive and idiothetic orientation cues: effect on hippocampal place cells and place navigation. Philos Trans R Soc Lond B Biol Sci 352:1515-1524.

Burwell RD, Amaral DG [1998] Cortical afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. J Comp Neurol 398:179-205.

Burwell RD, Saddoris MP, Bucci DJ, Wiig KA [2004] Corticohippocampal contributions to spatial and contextual learning. J Neurosci 24:3826-3836.

Buzsaki G [2005] Theta rhythm of navigation: link between path integration and landmark navigation, episodic and semantic memory. Hippocampus15: 827-840.

Chance MRA, Mead AP [1955] Competition between feeding and investigation in the rat. Behaviour 8:174-182.

Chen LL, Lin LH, Green EJ, Barnes CA, McNaughton BL [1994a] Head direction cells in the rat posterior cortex. I., Anatomical distribution and behavioral modulation. Exp Brain Res 101:8-23.

Chen LL, Lin LH, Green EJ, Barnes CA, McNaughton BL [1994b] Head direction cells in the rat posterior cortex. II., Contributions of visual and idiothetic information to the directional firing. Exp Brain Res 101:24-34.

Clark BJ, Hamilton DA, Whishaw IQ [2006] Motor activity [exploration] and formation of home bases in mice [C57BL/6] influenced by visual and tactile cues: modification of movement distribution, distance, location, and speed. Physiol Behav 87:805-816.

Clark BJ, Hines DJ, Hamilton DA, Whishaw IQ [2005] Movements of exploration intact in rats with hippocampal lesions. Behav Brain Res 163:91-99.

Collett TS, Cartwright BA, Smith BA [1986] Landmark learning and visuo-spatial memories in gerbils. J Comp Physiol [A] 158:835-851.

Cooper BG, Mizumori SJY. [2001] Temporary Inactivation of the Retrosplenial Cortex Causes a Transient Reorganization of Spatial Coding in the Hippocampus. J Neurosci 21:3986–4001.

Cruz AP, Frei F, Graeff FG [1994] Ethopharmacological analysis of rat behavior on the elevated plus-maze. Pharmacol Biochem Behav 49:171–6.

Dean P [1993] Sensory cortex: visual perceptual functions. In T.R.C. Kolb B. [ed] The Cerebral Cortex of the Rat. MIT Press, Cambridge [MA], pp.563-588.

Dean P [1981a] Grating detection and visual acuity after lesions of striate cortex in hooded rats. Exp Brain Res 43:145-153.

Dean P [1981b] Visual pathways and acuity hooded rats. Behav Brain Res 3:239-271.

Drai D, Golani I [2001] SEE: a tool for the visualization and analysis of rodent exploratory behavior. Neurosci Biobehav Rev 25:409-426.

Drai D, Kafkafi N, Benjamini Y, Elmer G, Golani I [2001] Rats and mice share common ethologically relevant parameters of exploratory behavior. Behav Brain Res125:133–140.

Drai D, Benjamini Y, Golani I [2000] Statistical discrimination of natural modes of motion in rat exploratory behavior. J Neurosci Method 96:119-131.

Eacott MJ, Norman G [2004] Integrated Memory for object, place, and contex in rats: A possible model of episodic-like memory? J Neurosci 24:1948-1953.

Eichenbaum H, Schoenbaum G, Young B, Bunsey M [1996] Functional organization of the hippocampal memory system. Proc Natl Acad Sci U S A 93:13500-13507.

Eilam D, Golani I [1989] Home base behaviour of rats [Rattus norvegicus] exploring a novel environment. Behav Brain Res 34:199-211.

Ergorul C, Eichenbaum H [2004] The Hippocampus and memory for “What,” “Where,” and “When”. Learning and Memory 11:397-405.

Etienne AS [2003] How does path integration interact with olfaction, vision, and the representation of space?. In: The neurobiology of spatial behaviour [Jeffery KJ, ed], pp 48-66. Oxford, UK: Oxford University Press.

Felleman DJ, Van Essen DC [1991] Distributed hierarchical processing in the primate cerebral cortex. Cereb Cortex 1:1-47.

Foreman NP, Save E, Thinus-Blanc C, Buhot MC [1992] Visually guided locomotion, distractibility, and the missing-stimulus effect in hooded rats with unilateral and bilateral lesions of parietal cortex. Behav Neurosci 106: 529-38.

Foreman N, Stevens R [1987] Relationships between the superior colliculus and hippocampus: Neural and Behavioral considerations. Behav Brain Sciences 10: 101-152.

Foreman NP, Goodale MA, Millner AD [1978] Nature of postoperative hyperactivity following lesions of the superior colliculus in the rat. Physiol & Behav 21:157-160.

Gallistel CR [1990] The organization of learning. Cambridge; MA: MIT.

Georgakopoulos J, Etienne AS [1994] Identifying location by dead reckoning and external cues. Behav Proc 31:57-74.

Gharbawie OA, Whishaw PA, Whishaw IQ [2004] The topography of threedimensional exploration: a new quantification of vertical and horizontal exploration, postural support, and exploratory bouts in the cylinder test. Behav Brain Res 151:125–35.

Golani I, Benjamini Y, Dvorkin A, Lipkind D, Kafkafi N [2004] Locomotor and Exploratory behaviour. In: Ian Q. Whishaw, Bryan Kolb, editors. The behavior of the laboratory rat: a handbook with tests. Oxfords: Oxford University Press.

Golani I, Benjamini y, Eilam D [1993] Stopping behaviour: constraints on exploration in rats [Rattus norvegicus]. Behav Brain Res 51:21-33.

Golani I, Bronchti G, Moualem D, Teitelbaum P [1981] Warm-up along dimensions of movement in the ontogeny of exploration in rats and other infant mammals. Proc Natl Acad sci 78:7226-7229.

Goodale MA, Meenan JP, Bulthoff HH, Nicolle DA, Murphy KJ, Racicot CI [1994] Separate neural pathways for the visual analysis of object shape in perception and prehension. Curr Biol 4:604-610.

Goodale MA, Milner AD [1992] Separate visual pathways for perception and action. Trends Neurosci 15:20-25.

Goodale MA, Dale RH [1981] Radial-maze performance in the rat following lesions of posterior neocortex. Behav Brain Res 3:273-288.

Goodale MA, Foreman NP, Milner AD [1978] Visual orientation in the rat: a dissociation of deficits following cortical and collicular lesions. Exp Brain Res 31:445-457.

Goodridge JP, Dudchenko PA, Worboys KA, Golob EJ, Taube JS [1998] Cue control and head direction cells. Beh Neurosci 112:749 –761.

Goodridge JP, Taube JS [1995] Preferential use of the landmark navigational system by head direction cells. Behav Neurosci 109:49–61.

Gothard KM, Skaggs WE, Moore KM, McNaughton BL [1996] Binding of hippocampal CA1 neural activity to multiple reference frames in a landmark-based navigation task. J Neurosci 16:823-835.

Gray JA, McNaughton N [1983] Comparison between the behavioural effects of septal and hippocampal lesions: a review. Neurosci Biobehav Rev 7:119–88.

Hafting T, Fyhn M, Molden S, Moser M, Moser EI [2005] Microstructure of a spatial map in the medial entorhinal cortex. Nature 10:801-762.

Hall CS [1934] Emotional behavior in the rat I Defecation and urination as measures of individual differences in emotionality. J Comp Psychol 18:385–403.

Halliday MS [1968] Exploratory behavior. In: Weiskrantz L, editor. Analysis of behavioral change. New York: Harper and Row, p:117.

Hill B, Best P [1981] Effects of deafness and blindness on the spatial correlates of hippocampal unit activity in the rat. Exp Neurol 74:204–217.

Hines DJ, Whishaw IQ [2005] Home bases formed to visual cues but not to self-movement [dead reckoning] cues in exploring hippocampectomized rats. Eur J Neurosci 22:2363-2375.

Hodges H [1996] Maze procedures: the radial-arm and water maze compared. Brain Res Cogn Brain Res 3:167-181.

Hoh TE, Kolb B, Eppel A, Vanderwolf CH, Cain DP [2003] Role of the neocortex in the water maze task in the rat: a detailed behavioral and Golgi-Cox analysis. Behav Brain Res 138:81-94.

Hok V, Lenck-Santini PP, Roux S, Save E, Muller RU, Poucet B [2007] Goal related activity in hippocampal place cells. J Neurosci 27:472-482.

Hughey DJ, Koppenaal RJ [1987] Hippocampal lesions in rats alter learning about intramaze cues. Behav Neurosci 101:634-643.

Hull CL [1943] Principles of behavior. New York: Appleton-Century-Crofts.

Humphrey NK, Weiskrantz L [1971] Vision in monkeys after removal of the striate cortex. Nature 215:595-597.

Huxter JR, Thorpe CM, Martin GM, Harley CW [2001] Spatial problem solving and hippocampal place cell firing in rats: control by an internal sense of direction carried across environments. Behav Brain Res 123:37-48.

Hynes CA, Martin GM, Harley CW, Huxter JR, Evans JH [2000] Multiple points of entry into a circular enclosure prevent place learning despite normal vestibular orientation and cue arrays: Evidence for map resetting. Journal of experimental psychology: Animal Behavior Processes 26:64-73.

Jammer M [1969] Concepts of Space: The history of theories of space in physics. Cambridge, Massachusetts: Harvard University press.

Jarrard LE, Okaichi H, Goldschmidt R, Steward O [1984] On the role of hippocampal connections in the performance of place and cue tasks: comparison with damage to the hippocampus, Behav Neurosci 98:854-946.

Jeffery KJ [2003] Introduction. In: Kathryn J. Jeffery editor. The Neurobiology of Spatial Behavior. Oxfords: Oxford University Press.

Kant I [1781] Critque of pure reason: and other ethical treatises transl. By Thomas Kingsmill Abbott, 1952 Encyclopedia Britannica, INC: London.

Keating EG, Dineen J [1982] Visuomotor transforms of the primate tectum. In D.J. Ingle, M.A. Goodale & R.J.W. Manfield [eds.] Analysis of Visual Behavior. Cambridge, Mass.: MIT Press, p:335-365.

Keller J, Strasburger H, Cerutti DT, Sabel BA [2000] Assessing spatial vision-automatated measurement of the contrast-sesitivity function in the hooded rat. J of Neurosci Meth 97:103-10.

Kelso SR, Ganong AH [1986] Hebian synapses in hippocampus. Proc Natl Acad Sci USA 86:1388-92.

Kimchi T, Terkel J [2001] Spatial learning and memory in the blind mole-rat in comparison with the laboratory rat and Levant vole. Anim Behav 61:171-180.

Kirkby RJ, Stein DG, Kimble RJ, Kimble DP [1967] Effects of hippocampal lesions and duration of sensory input on spontaneous alternation. J Comp Physiol Psychol 64:342-345.

Knierim JJ [2002] Dynamic interactions between local surface cues, distal landmarks, and intrinsic circuitry in hippocampal place cells. J Neurosci 22: 6254-6264.

Knierim JJ, Kudrimoti HS, McNaughton BL [1998] Interactions between idiothetic cues and external landmarks in the control of place cells and head direction cells. J Neurophysiol 80:425-46.

Kolb B, Buhrmann K, McDonald R, Sutherland RJ [1994] Dissociation of the medial prefrontal, posterior parietal, and posterior temporal cortex for spatial

navigation and recognition memory in the rat. Cereb Cortex 4:664-680.

Kolb B, Walkey J [1987] Behavioural and anatomical studies of the posterior parietal cortex in the rat. Behav Brain Res 23:127-145.

Kolb B, Sutherland RJ, Whishaw IQ [1983] A comparison of the contributions of the frontal and parietal association cortex to spatial localization in the rat. Behav Neurosci 97:13–27.

Kolb B, Whishaw IQ [2006] [2006] An introduction to brain and behavior [2th ed]. NY: Worth Publishers.

Krieg WJS [1946] Connections of the cerebral cortex. I. The albino rat. A. Topography of the cortical areas, J comp Neurol 84 p:221–275.

Lashley KS [1943] Studies of cerebral function in learning. XII.loss of the maze habit after occipital lesions in blind rats. J Comp Neurol 79:431-62.

Lashley KS [1939] The mechanism of vision. XVI. The functioning of small remnants of the visual cortex. J Comp Neurol 70:45-67.

Lashley KS [1931] The mechanism of vision. IV. The cerebral areas necessary for pattern vision in the rat. J comp Neurol. 53 p:419–478.

Lehmann H, Clark BJ, Whishaw IQ [2007] Similar development of cued and learned home bases in control and hippocampal-damaged rats in an open field exploratory task. Hippocampus 17:370-380.

Lehrman DS [1970] Semantic and Conceptual issues in the nature-narture problem. In Lester R. Anderson, Ethel Tobach, Daniel S. Lehrman, Jay S. Rosenblatt, editors. Development and evolution of behavior. Sanfrancisco: W. H. Freeman and Company.

Leonhard CM, Stakman RW, Taube JS [1996] Head direction cells recorded from the lateral mammallary nuclei in rats. Soc Neurosci Abstr 22:1873.

Leonard B, McNaughton BL [1990] Spatial representation in the rat: conceptual, behavioral, and neurophisiological perspectives. In: Kenser, RP and Olton DS, editors. Neurobiology of comparative cognition. Erlbaum, Hillsdale, NJ, p:363-422.

Lima SL [1985] Maximizing feeding efficiency and minimizing time exposed to predators: a trade-off in the black-capped chickadee. Oecologia 66:60-67.

Lima SL, Valone TJ, Caraco T [1985] Foraging-efficiency-prediction-risk trade-off in the grey squirrel. Anim Behav 33:155-156.

Linden R, Perry V [1983] Massive retinotectal projection in rats. Brain Res 272:145–149.

Loewen I, Wallace DG, Whishaw IQ [2005] The development of spatial capacity in piloting and dead reckoning by infant rats: use of the huddle as a home base for spatial navigation. Dev Psychobiol 46:350-361.

Lorenz KZ [1981] The foundations of ethology. Sppringer-Verlag, New York.

Lorenz, KZ [1950] The comparative method in studying innate behavior patterns. Sympos Soc Exp Biol 4:221-268.

Malach R [1989] Patterns of connections in rat visual cortex. J Neurosci 9:3741-3752.

Maguire EA [2001] The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. Scand J psychol 42:225-38.

Margules J, Gallistel CR [1988] Heading in the rat: determination by environmental shape. Anim learn behav 16:404-410.

Marler P [2004] Innateness and the instinct to learn. An Acad Bras Cienc 76:189-200.

Marr DC [1982] Vision. San Fransisco: Freeman.

Martin GM, Harley CW, Smith AR, Hoyles ES, Hynes CA [1997] Spatial disorientation blocks reliable goal location on a plus maze but does not prevent goal location in the Morris maze. J Exp Psychol [Anim Behav Process] 23:183-193.

McNaughton BL, Barnes CA, Gerard JL, Gothard K, Jung MW, Knierim JJ, Kudrimoti H, Qui Y, Skaggs WE, Suster M, Weaver KL [1996] Deciphering the hippocampal polyglot: The hippocampus as a path integration system. J Exp Biol 199:173-185.

McNaughton BL, Leonard B, Chen L [1989] Cortical–hippocampal interactions and cognitive mapping: A hypothesis based on reintegration of the parietal and inferotemporal pathways for visual processing. Psychobiol 17:230–235.

McNaughton BL, Barnes CA, O'Keefe J [1983] The contributions of position, direction and velocity to single unit activity in the hippocampus of freely-moving rats. Exp Brain Res 52:41-49.

Mcbueney DH, Collings VB [1984] Introduction to sensation and perception. NJ: Prentice-Hall, Inc.

Miller MW, Vogt BA [1984] Direct connections of rat visual cortex with sensory, motor, and association cortices. J Comp Neurol 226:184-202.

Milner AD, Goodale MA [1995] The Visual Brain in Action. Oxford: Oxford University Press.

Milner AD, Lines CR [1983] Stimulus sampling and the use of distal visual cues in rats with lesions of the superior colliculus. Behav Brain Res 8:387-401.

Mizumori SJ, Williams JD [1993] Directionally selective mnemonic properties of neurons in the lateral dorsal nucleus of the thalamus of rats. J Neurosci 13:4015-4028.

Mizumori SJ, Ward KE, Lavoie AM [1992] Medial septal modulation of entorhinal single unit activity in anesthetized and freely moving rats. Brain Res 570:188-197.

Montgomery KC [1955] The relation between fear induced by novel stimulation and exploratory behavior. J Comp Physiol Psychol 48:132–6.

Morris RGM [1981] Spatial localization does not require the presence of local cues. Learn Motiv 12:239-260.

Morris RGM, Garrud P, Rawlins JNP, O'Keefe J [1982] Place navigation impaired in rats with hippocampal lesions. Nature 297:681-683.

Muller RU, Kubie JL, JB Ranck Jr [1987] Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. J Neurosci 7:1935-1950.

Mumby DG, Pinel JPJ, Kornecook TJ, Shen MJ, Redila VA [1995] Memory deficits following lesions of hippocampus or amygdala in rat: assessment by an object-memory test battery. Psychobiol 23:26–36.

Olton DS [1979] Mazes, maps, and memory*, Amer Psychol* 34:588-596.

Olton DS, Wible CG, Shapiro ML [1986] Mnemonic theories of hippocampal function. Behav Neurosci 100:852-855.

Olton DS, Feustle WA [1981] Hippocampal function required for nonspatial working memory. Exp Brain Res 41:380-389.

Olton DS, Pappas BC [1979] Spatial memory and hippocampal function. Neuropsychol 17:669-682.

Olton DS, Samuelson RJ [1976] Remembrance of places passed: Spatial memory in rats. Journal of Experimental Psychology: Animal Behavior Processes

2:97-116.

O'Keefe J [1991] An allothetic spatial model for the hippocampal cognitive map. Hippocampus 1:230-235.

O'Keefe J [1976] Place units in the hippocampus of the freely moving rat. Exp Neurol 51:8-109.

O'Keefe J, Burgess N [2005] Dual phase and rate coding in hippocampal place cells: theoretical significance and relationship to entorhinal grid cells. Hippocampus 15:853-866.

O'Keefe J, Speakman A [1987] Single unit activity in the rat hippocampus during a spatial memory task. Exp Brain Res 68:1–27.

O'Keefe J, Conway DH [1978] Hippocamual place units in the freely moving rat: Why they fire where they fire. Exp Brain Res 31:573-90.

O'keefe J, Nadel L [1978] The Hippocampus as a Cognitive Map. Oxford: Oxford University press.

O'Keefe J, Dostrovsky J [1971] The hippocampus as a spatial map: preliminary evidence from unit activity in the freely-moving rat. Brain Res 34:171-175.

Ossenkopp PK, Kavaliers M, Sanberg PR [1996] Measuring movement and locomotion: From invertebrates to humans. New York: Springer.

Pandya DN, Yeterian EH [1984] Proposed neural circuitry for spatial memory in the primate brain. Neuropsychol 22:109-122.

Paz-Villagran V, Lenck-Santini PP, Save E, Poucet, B [2002] Properties of place cell firing after damage to the visual cortex, Eur J Neurosci. 16:771-776.

Pfluger HJ, Menzel R [1999] Neuroethology, its roots and future. J Comp Physiol A 185:389-392.

Poucet B [1993] Spatial and cognitive maps in animals: new hypotheses on their structure and neural mechanisms. Psychol Review 100:163-182.

Poucet B [1989] Object exploration, habituation, and response to a spatial change in rats following septal or medial frontal cortical damage. Behav Neurosci 103:1009-1016.

Poucet B, Lenck-Santini PP, Paz-Villagran V, Save E [2003] Place cells, neocortex and spatial navigation: a short review. J Physiol Paris 97:537-546.

Poucet B, Benhamou S [1997] The neuropsychology of spatial cognition in the rat. Crit Rev Neurobiol 11:101–120.

Poucet B, Chapuis N, Durup M, Thinus-Blanc C [1986] A Study of exploratory behavior as an index of spatial knowledge in hamsters. Animal Learning and Behavior 14:93-100.

Prusky GT, West PWR, Douglas RM [2000a] Behavioural assessment of visual acuity in rats and mice. Vision Res 40:2201-9.

Prusky GT, West PW, Douglas RM [2000b] Reduced visual acuity impairs place but not cued learning in the Morris water task. Behav Brain Res 116:135-140.

Quirk GJ, Muller RU, Kubie JL [1990] The firing of hippocampal place cells depends on the rat's recent experience. J Neurosci 10:2008-2017.

Rank JB [1984] Head direction cells in the deep layer of dorsal presubiculum in freely moving rats. Soc Neurosci Abstr 10:599.

Redish AD [1999] Beyond the cognitive map: From place cells to episodic memory. Cambridge, MA: MIT Press.

Reep RL, Chandler HCV, King, JV [1994] Rat posterior parietal cortex: topography of corticocortical and thalamic connections. Exp Brain Res 100:67-84.

Renner MJ, Seltzer CP [1991] Molar characteristics of exploratory and investigatory behavior in the rat [*Rattus norvegicus*]. J Comp Psychol 105:326-339.

Rudy JW, Sutherland RJ [1995] Configural theory and the Hippocampal formation: An appraisal and reconfiguration. Hippocampus 5:375-389.

Russell PA [1983] Psychological studies of exploration in animals: a reappraisal. In: John Archer, Lynda Birke, editors. Exploration: in animal and humans. England: Van Nostrand Reinhold [UK] Co. Ltd.

Russell PA [1973] Relationships between exploratory behavior and fear: a review. Br J Psychol 64:417-33.

Sargolini F, Fyhn M, Hafting T, McNaughton BL, Witter MP, Moser MB, Moser EI [2006] Conjunctive representation of position, direction, and velocity in entorhinal cortex. Science 312:758-762.

Satoh K, Fibiger HC [1986] Cholinergic neurons of laterodorsal tegmental nuclus: efferent and afferent connections. J Comp Neurol 253:277-302.

Save E, Poucet B [2005] Piloting. In: Whishaw IQ, Kolb B, editors. The behavior of the laboratory rat: a handbook with tests. Oxford: Oxford University Press, 392-400.

Save E, Guazzelli A, Poucet B [2001] Dissociation of the effects of bilateral lesions of the dorsal hippocampus and parietal cortex on path integration in the rat. Behav Neurosci 115:1212-23.

Save E, Nerad L, Poucet B [2000] Contribution of multiple sensory information to place field stability in hippocampal place cells. Hippocampus 10:64-76.

Save E, Poucet B [2000] Hippocampal-parietal cortical interactions in spatial cognition. Hippocampus 10:491-499.

Save E, Cressant A, Thinus-Blanc C, Poucet B [1998] Spatial firing of hippocampal place cells in blind rats. J Neurosci 18:1818-1826.

Save E, Poucet B, Foreman N, Buhot MC [1992] Object exploration and reactions to spatial and nonspatial changes in hooded rats following damage to parietal cortex or dorsal hippocampus. Behav Neurosci 106:447-456.

Schneider GE [1969] Two visual systems. Science 163:895-902.

Sefton AJ, Dreher B [1985] Visual system. In G. Paxios [ed.], The Rat nervous system, Vol. 1 Forbrain and Midbrain. Sydney: Academic press, 169-221.

Seymour P, Juarska JM [1997] Vernier and grating acuity in adult hooded rats: the influence of sex. Behav Neurosci 111:792-800.

Sharp PE [1991] Computer simulation of hippocampal place cells. Psychobiol 19:103-115.

Sharp PE, Kubie JL, Muller RU [1990] Firing properties of hippocampal neurons in a visually symmetrical environment: Contribution of multiple sensory cues and mnemonic processes. J Neurosci 10:3093-3105.

Sharp PE, Barnes CA, McNaughton BL [1987] Effects of aging on environmental modulation of hippocampal evoked responses. Behav Neurosci 101:170-178.

Shibata H [1992] Topographic organization of subcortical projections to the anterior thalamic nuclei in the rat. J Comp Neurol 323:117-127.

Shibata H [1989] Descending projections to the mammillary nuclei in the rat, as studied by retrograde and anterograde transport of wheat germ agglutinin–horseradish peroxidase. J Comp Neurol 285:436-452.

Shillito E [1963] Exploratory behaviour in the short-tailed Vole Microtus Agrestis. Behaviour 21:145-154.

Silveira LC, Heywood CA, Coway A [1987] Contrast sensitivity and visual acuity of the pigmented rat determined electrophisiologically. Vision Res 27:1719-31.

Sinnamon HM, Karvosky ME, Ilch CP [1999] Locomotion and head scanning initiated by hypothalamic stimulation are inversely related. Behav Brain Res 99:219-229.

Spence KW [1951] Theoretical interpretations of learning. In: SS Stevens, editor. Handbook of experimental psychology NY:John Wiley & Sons, Inc.

Sprague JM [1975] Mammalian tectum: Intrinsic organization, afferent inputs, and integrative mechanisms: Anatomical substrate. Neurosci Res Prog Bull 13: 204-213.

Steward O, Scoville SA [1976] Cells of origin of entorhinal cortical afferents to the hippocampus and fascia dentata of the rat. J Comp Neurol 169:347-370.

Stopka P, Macdonald DW [2003] Way-marking behavior: an aid to spatial navigation in the wood mouse (*Apodemus sylvaticus*). BMC Ecol 3:3.

Sutherland RJ, Whishaw IQ, Kolb B [1988] Contributions of cingulate cortex to two forms of spatial learning and memory. J Neurosci 8:1863-1872.

Sutherland RJ, Dyck RH [1984] Place navigation by rats in a swimming pool. Can J psychol 38:322-347.

Sutherland RJ, Kolb B, Whishaw IQ [1982] Spatial mapping: definitive disruption by hippocampal or medial frontal cortical damage in the rat. Neurosci Lett 31:271-276.

Swanson LW, Mogenson GJ, Simerly RB, Wu M [1987] Anatomical and electrophysiological evidence for a projection from the medial preoptic area to the 'mesencephalic and subthalamic locomotor regions' in the rat. Brain Res 405:108-122.

Taube JS [1998] Head direction cells and the neurophysiological basis for a sense of direction. Prog Neurobiol 55:225–256.

Taube JS [1995a] Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. J. Neurosci 15:70-86.

Taube JS [1995b] Place cells recorded in the parasubiculum of freely moving rats. 5:569-83.

Taube JS, Stackman RW, Dudchenko PA [1996] Head-direction cell activity monitored following passive transport in to a novel environment. Soc Neurosci Abstr 22:1873.

Taube JS, Burton HL [1995] Head direction cell activity monitored in a novel environment and during a cue conflict situation. J Neurophysiol 74:1953-1971.

Taube JS, Muller RU, Ranck JB [1990a] Head-direction cells recorded from the postsubiculum in freely moving rats. I, Description and quantitative analysis. J Neurosci 10:420–435.

Taube JS, Muller RU, Ranck JB [1990b] Head-direction cells recorded from the postsubiculum in freely moving rats. II., Effects of environmental manipulations. J Neurosci 10:436–447.

Tchernichovski O, Benjamini Y, Golani I [1998] The dynamics of long-term exploration in the rat. Part I. A phase-plane analysis of the relationship between location and velocity. Biological cybernetics 78:423-432.

Teyler TJ, DiScenna P [1986] The hippocampal memory indexing theory. Behav Neurosci 100:147-154.

Thinus-Blanc C, Save E, Buhot MC, Poucet B [1991] The hippocampus, exploratory activity and spatial memory. In J. Paillard [Ed.], Brain and space [pp. 334-352]. London: Oxford University Press.

Tolman EC [1948] Cognitive maps in rats and men. Psychol Rev 55:189-208.

Tolman EC, Ritchie BF, Kalish D [1946a] Studies in spatial learning.II. Place learning vs. response learning. J exp psychol 36:221-229.

Tolman EC, Ritchie BF, Kalish D [1946b] Studies in spatial learning.IV. Place learning vs. response learning. J exp psychol 36:221-229.

Tourestzky DS, Gaulin SJC, Redish AD [1996] Gerbils regularly return to their entry point when exploring a novel environment. Society for Neuroscience Abstracts 22:449.

Turkewitz G, Kenny PA [1982] Limitations on input as a basis for neural organization and perceptual development: a preliminary theoretical statement. Dev Psychobiol 15:357-368.

Ungerleider LG, Mishkin M [1982] Two cortical visual systems. In: DJ Ingle, MA Goodale and RJW Mansfield, Editors, *Analysis of Visual Behavior*, MIT Press, Cambridge, Massachusetts p:549–586.

Van Groen T, Wyss JM [2003] Connections of the retrosplenial granular b cortex in the rat. J Comp Neurol 463:249-263.

Van Groen T, Wyss JM [1992] Connections of the retrosplenial dysgranular cortex in the rat. J Comp Neurol 315:200-216.

Van Groen T, Wyss JM [1990] Connections of the retrosplenial granular a cortex in the rat. J Comp Neurol 300:593-606.

Vogt BA, Miller MW [1983] Cortical connection between cingulate cortex and visual, motor, and post-subicular cortices, J Comp Neurol 216:192-210.

Wagner AR, Rescorla RA [1972] Inhibition in Pavlovian conditioning: application of a theory. In Inhibition and learning, ed. RA Boakes, MS Halliday, p:301-36. New York:Academic.

Wallace DG, Whishaw IQ [2005] Dead reckoning. In: Ian Q. Whishaw, Bryan Kolb, editors. The behavior of the laboratory rat: a handbook with tests. Oxfords: Oxford University Press.

Wallace DG, Whishaw IQ [2003] NMDA lesions of Ammon's horn and the dentate gyrus disrupt the direct and temporally paced homing displayed by rats exploring a novel environment: evidence for a role of the hippocampus in dead reckoning. Eur J Neurosci 18:513–23.

Wallace DG, Hines DJ, Whishaw IQ [2002a] Quantification of a single exploratory trip reveals hippocampal formation mediated dead reckoning. J Neurosci Methods 113:131-145.

Wallace DG, Hines DJ, Pellis SM, Whishaw IQ [2002b] Vestibular information is required for dead reckoning in the rat. J Neurosci 22:10009-10017.

Warburton EC, Baird AL, Aggleton JP [1997] Assessing the magnitude of the allocentric spatial deficit associated with complete loss of the anterior thalamic nuclei in rats. Behav Brain Res 87:223-32.

Whishaw IQ [2005] Foraging. In: Ian Q. Whishaw, Bryan Kolb, editors. The behavior of the laboratory rat: a handbook with tests. Oxfords: Oxford University Press.

Whishaw IQ [2004] Posterior neocortical [visual cortex] lesions in the rat impair matching-to-place navigation in a swimming pool: a reevaluation of cortical contributions to spatial behavior using a new assessment of spatial versus non spatial behavior. Behav Brain Res 155:177-184.

Whishaw IQ [1993] Activation, travel distance, and environmental change influence food carrying in rats with hippocampal, medial thalamic and septal lesions: Implications for studies on hoarding and theories of hippocampal function. Hippocampus 3:373-385.

Whishaw IQ [1992] What are voluntary movements made of? Behavioural and Brain Sciences 15:290-291.

Whishaw IQ [1991] The defensive strategies of foraging rats: A review and synthesis. The psychological record 41:185-205.

Whishaw IQ [1985] Formation of a place learning-set by the rat: a new paradigm for neurobehavioral studies. Physiol Behav 35:139-143.

Whishaw IQ, Gharbawie OA, Benjamin JC, Lehmann H [2006] The exploratory behavior of rats in an open environment optimizes security. Behav Brain Res 171:230-239.

Whishaw IQ, Gorny B [1999] Path integration absent in scent-tracking fimbria-fornix rats: evidence for hippocampal involvement in “sense of direction” and “sense of distance” using self-movement cues. J Neurosci 19:4662-4673.

Whishaw IQ, Hines DG, Wallace DG [2001] Dead reckoning [path integration] requires the hippocampal formation: Evidence from spontaneous exploration and spatial learning task in light [allothetic] and dark [idiothetic] tests. Behav Brain Res 127:49-69.

Whishaw IQ, Brooks BL [1999] Calibrating space: exploration is important for allothetic and idiotheticnavigation. Hippocampus 9:659-667.

Whishaw IQ, Maaswinkel H [1998] Rats with fimbria–fornix lesions are impaired in path integration: a role for the hippocampus in “sense of direction. J Neurosci 18:3050-3058.

Whishaw IQ, McKenna JE, Maaswinkel H [1997] Hippocampal lesions and path integration. Curr Opin Neurobiol 7:228-234.

Whishaw IQ, Jarrard LE [1996] Evidence for extrahippocampal involvement in place learning and hippocampal involvement in path integration. Hippocampus 6:513-524.

Whishaw IQ, Cassel JC, Jarrad LE [1995a] Rats with fimbria-fornix lesions display a place response in a swimming pool: a dissociation between getting there and knowing where. J Neurosci 15:5779-5788.

Whishaw IQ, Coles BL, Bellerive CH [1995b] Food carrying: a new method for naturalistic studies of spontaneous and forced alternation. J Neurosci Methods 61:139-143.

Whishaw IQ, Dringenberg HC, Comery TA [1992] Rats [Rattus norvegicus] modulate eating speed and vigilance to optimize food consumption: Effects of cover, circadian rhythm, food deprevation, and individual differences. J Comp Psychol 4:441-419.

Whishaw IQ, Tomie JA [1997] Perseveration on place reversals in spatial swimming pool tasks: further evidence for place learning in hippocampal rats. Hippocampus 7:361 370.

Whishaw IQ, Tomie J [1989] Food-pallet size modifies the hording behavior of foraging rats. Psychobiol 17:83-101.

Whishaw IQ, Tomie J [1987] Food wresting and dodging: Strategies used by rats [Rattus norvegicus] for obtaining and protecting food from conspecifics. J Com Psychol 101:110-123.

Whishaw IQ, Mittleman G [1986] Visits to starts, routes, and places by rats [Rattus norvegicus] in swimming pool navigation tasks. J Comp Psychol 100:422-31.

Whishaw IQ, Kolb B, Sutherland RJ [1983] The analysis of behavior in the laboratory rat. In: Robinson TE, editor. Behavioral approaches to brain research. Oxford: Oxford University Press, p:141-211.

Wickelgren WA [1979] Chunking and consolidation: a theoretical synthesis of semantic networks, configuring in conditioning, S-R versus congenitive learning, normal forgetting, the amnesic syndrome, and the hippocampal arousal system. Psychol Rev 86:44-60.

Wilson MA, McNaughton BL [1993] Dynamics of the hippocampal ensemble code for space. Science 261:1055-1058.

Wiener SI [1993] Spatial and behavioral correlates of striatal neurons in rats performing a self-initiated navigation task. J Neurosci 13:3802-3817.

Winer BJ, Brown DR, Michels KM [1991] Statistical principles in experimental design. New York: McGraw-Hill.

Witter MP, Groenewegen HJ, Lopes da Silva FH, Lohman AH [1989] Functional organization of the extrinsic and intrinsic circuitry of the parahippocampal region. Prog Neurobiol 33:161-253.

Yoganarasimha D, Yu X, Knierim JJ [2006] Head direction cell representations maintain internal coherence during conflicting proximal and distal cue rotations: comparison with hippocampal place cells. J Neurosci 26:622-631.

Zadicario P, Avni R, Zadicario E, Eilam D [2005] 'Looping'-an exploration mechanism in a dark open field. Behav Brain Res 159:27-36.

Appendix

C++ program

A. Stop program

```
#include "allegro.h"

#include "adime.h"

#include "winalleg.h"

#include <stdlib.h>

#include <stdio.h>

#include <math.h>


#define X 0

#define Y 1

#define DSIZE 60000

#define PI 3.14159265

#define DEG 180/PI

#define ZONENUM 12

#define ANNULINUM 5


char text_file[1024]= "";

char bmp_file[100];

char BMP_filename[100];

char STOPBMP_filename[100];

char TXT_filename[100];
```

```
int  ZoneNum = 4;
int  AnnuliNum = 1;
int  DrawLine = 0, DrawBlack = 0;
int  VarTime = 0;
int       t1=2, t2=2, t3=10, t4=10, t5=30, t6=30, t7=60, t8=60;
float X0, Y0, dia;

//--------------------------------- User Input Dialog --------------------------------


void no_time_dialog[void]
{
adime_dialogf["No time range specified!",
                                    ADIME_ALIGN_CENTRE,
ADIME_ALIGN_CENTRE, 200,
                                    "You      must      enter      time      range
variable%nothing[]"];
//                                  "check 'Draw entire test'.%nothing[]"];
}
void main_dialog[void]

{
  if[ adime_dialogf["File Settings",
```

```
                                ADIME_ALIGN_CENTRE,
ADIME_ALIGN_CENTRE, 200,

                                "Input data file:%filename[1024, txt;txy,
Select a data file you want to draw]"
                                "Number of Zone [max.12]:%int[1,12]"
                                "Number of Annuli[max.5]:%int[1,5]"
                                "Time range variable[minute]:%int[0,30]"
                                "%line[]"
                                "Save BMP/TXT file as:%string[100]"
                                "Draw zone/annuli divided lines:%bool[]"

                                "Draw black circle only:%bool[]"
                                "%line[]"
                                "Stop <=[second]:%int[]"
                                "Stop >[second]:%int[]"

                                "    <=[second]:%int[]"
                                "Stop >[second]:%int[]"

                                "    <=[second]:%int[]"
                                "Stop >[second]:%int[]"
                                "    <=[second]:%int[]"
```

```
"Stop >[second]:%int[]"
"%line[]"

"Table diameter:%float[]"
"Table Centre point X0:%float[]"
"Table Centre point Y0:%float[]"
,
text_file,
&ZoneNum,
&AnnuliNum,
&VarTime,
bmp_file,
&DrawLine,
&DrawBlack,
&t1,
&t2,
&t3,
&t4,
&t5,
&t6,
&t7,
&t8,
&dia,
```

```
                                        &X0,
                                        &Y0
                                        ] == 2]
        exit[0];

         if[ VarTime == 0]          //if user doesn't specifiy time period , return
to main dialog

        {
                no_time_dialog[];
                main_dialog[];
        }
}

//---------------------------------- Read Data File [subroutines]-----------------------------
-
void readstr[FILE *f,char *string]
        //read in a string from a file
{
        do
{
                fgets[string, 255, f];
        // fgets is function to read one line from stream
```

```
        } while [[string[0] == '/'] || [string[0] == '\n']];  // to see first char is '/' or
empty line '\n'
        return;
}
// Calculate rat travel distance
float Distance[double x2, double y2, double x1, double y1]
{
          float distance;
          distance = [float] sqrt[pow[[x2-x1],2] + pow[[y2-y1],2]];
          return distance;
}

//********************************** MAIN ********************************

 int main[int argc, char **argv[]]

{
        BITMAP* buffer;
        FILE* filein;
        FILE* fileout;
        PALETTE pal;
        char   msgbuf[100];
```

```
        int             i, j, k, m, stopCount, Total_time, loop, TotNum = 0,
TotTim = 0;
        float   deg, radius;
        float   x, y;
        float   XMAX, XMIN, YMAX, YMIN;
        int             LineCount = 0;
        float   totalDistance = 0;
        char    oneline[255];

        int
        zCount1[ZONENUM][ANNULINUM],zCount2[ZONENUM][ANNULINUM
],zCount3[ZONENUM][ANNULINUM],zCount4[ZONENUM][ANNULINUM],zCo
unt5[ZONENUM][ANNULINUM];

        int             TotalStopTime[ZONENUM][ANNULINUM];

        float   DATA[DSIZE][2];
        float   deg_DATA[DSIZE/3];              //degree of each STOP point
        float   rad_DATA[DSIZE/3];              //radian of each STOP point
        int             stoprad[DSIZE/3];       //assume to hold STOP data
array as DSIZE/3=20000, typically, stopcount=5000

        float   STOPDATA[DSIZE/3][2];
```

```
        bool   Sflag;                          //set flag for STOP

        int          SCount1=0,    SCount2=0,    SCount3=0,    SCount4=0,
SCount5=0, SCount6=0;
// Install various parts of Allegro

        if[allegro_init[]]
                exit[1];
        if[install_keyboard[]]{
                allegro_message["Could not installed keyboard.\n"];
                exit[1];
        }
        install_timer[];
        if[install_mouse[]== -1]{
                allegro_message["Could not install mouse.\n"];
                exit[1];
        }
        show_mouse[screen];
        if[set_gfx_mode[GFX_AUTODETECT_FULLSCREEN,  1024,  768,  0,
0]]{
                allegro_message["Could not set graphics mode.\n"];
```

```
                exit[1];
}
buffer = create_bitmap[SCREEN_W, SCREEN_H];
set_palette[default_palette];
// Install Adime

        if[     adime_init[] !=0]{
                set_gfx_mode[GFX_TEXT, 0,0,0,0];
                allegro_message["Error initializing ADIME.\n"];
                exit[1];
        }

        clear_to_color[screen, makecol[0,0,0]];
        clear_to_color[buffer, makecol[0,0,0]];
// User Interface Dialog

        textout_centre[screen, font, "Rat's Stop Number & Time in Each Zone
and Annulus", SCREEN_W/2, 150, makecol[255,255,255]];

        main_dialog[];
        sprintf[TXT_filename, "%sstp.txt", bmp_file];
        sprintf[STOPBMP_filename, "%sstp.bmp", bmp_file];
        set_palette[desktop_palette];
```

```
//set white background
        clear_to_color[screen, makecol[255,255,255]];
        clear_to_color[buffer, makecol[255,255,255]];
//Read in whole data file to calculate total test time, and X, Y maximum, minimum
        if[![filein = fopen[text_file, "rt"]]]
        {
                sprintf[msgbuf, "Cannot open data file for reading"];
                allegro_message[msgbuf];
                allegro_exit[];
                exit[0];
        }
        while[!feof[filein]]
        {
                readstr[filein, oneline];
                sscanf[oneline, "%f %f", &x, &y];
                LineCount++;

                DATA[LineCount-1][X] = x;
                DATA[LineCount-1][Y] = y;
}
fclose[filein];
// Make a directory if it isn't existed and change dir path
```

```
        mkdir["Output"];
        chdir["Output"];
        Total_time = LineCount/1800;                    //minute

        loop = Total_time/VarTime;                      //determite      how
many loop to run

//Calculate X, Y maximum and minimum values

        XMAX = DATA[0][X];
        XMIN = DATA[0][X];
        YMAX = DATA[0][Y];
        YMIN = DATA[0][Y];
        for[i = 1; i < LineCount; i++]
        {
                if[XMAX < DATA[i][X]]           XMAX = DATA[i][X];
                if[XMIN > DATA[i][X]]           XMIN = DATA[i][X];
                if[YMAX < DATA[i][Y]]           YMAX = DATA[i][Y];
                if[YMIN > DATA[i][Y]]           YMIN = DATA[i][Y];
        }

/* // comment out -------For testing ONLY
```

```
        X0 = [XMAX + XMIN]/2;
        Y0 = [YMAX + YMIN]/2;

*/ // ----------End of testing
//Calculate the degree of each zone

        deg = 360/[float]ZoneNum;

//      ========================================      DRAW      STOP
========================================

        clear_to_color[screen, makecol[255,255,255]];
        clear_to_color[buffer, makecol[255,255,255]];
        //set white background

/* // Comment out********** for testing ONLY

        if[[XMAX-XMIN] >= [YMAX-YMIN]]

                radius = [XMAX - XMIN]/2;
        else
                radius = [YMAX - YMIN]/2;
```

```
        circle[buffer, X0, Y0, radius + 8, makecol[0,0,0]];

*/ //********************************* End of testing

        radius = dia/2;

        circle[buffer, X0, Y0, radius, makecol[0,0,0]];
        textout[buffer, font, "Note: Annulus number starts from inner centre.", 50, SCREEN_H/2-20, makecol[0,0,0]];

// If user wants to draw the zone and annuli divided lines

        if[DrawLine == -1]

        {
                hline[buffer, 80, Y0, XMAX+30, makecol[255, 0, 0]];
        //draw X axis in red
                textout[buffer, font, "X", XMAX+50, Y0, makecol[0,0,0]];
                textout[buffer, font, "Y", X0, YMAX+50, makecol[0,0,0]];
                if[ [ZoneNum/2] % 2 == 0 ]
                                vline[buffer, X0, 30, YMAX+30, makecol[255,0,0]];

                for[i = 1; i < ZoneNum/2; i++]
```

```
        {
            if[i == [float]ZoneNum/4]
                continue;
            else
                line[buffer, XMIN, tan[deg*i*PI/180]*[XMIN-X0]+Y0,
XMAX, tan[deg*i*PI/180]*[XMAX-X0]+Y0, makecol[255,0,0]
        }
        textout[buffer, font, "zone1", XMAX+20, Y0+10,
makecol[0,0,255]];
        sprintf[msgbuf, "zone%d", ZoneNum/2];
        textout[buffer, font, msgbuf, XMIN-70, Y0+10,
makecol[0,0,255]];
        sprintf[msgbuf, "zone%d", ZoneNum/2+1];
        textout[buffer, font, msgbuf, XMIN-70, Y0-20,
makecol[0,0,255]];

        sprintf[msgbuf, "zone%d", ZoneNum];
        textout[buffer, font, msgbuf, XMAX+20, Y0-20,
makecol[0,0,255]];
//Draw the annulus circles
        for[i=0; i < AnnuliNum-1; i++]
            circle[buffer, X0, Y0, radius*[i+1]/AnnuliNum,
makecol[0,0,0]];
```

```
        }
// Display Input data file at top / Display Output bmp file at bottom

        textout[buffer, font, text_file,      20, SCREEN_H-70, makecol[0,0,0]];


        textout[buffer, font, STOPBMP_filename , 100, SCREEN_H-50,
makecol[0,0,0]];

//      textout[buffer, font, "TEST RESULTS:", 500, 40, makecol[0,0,0]];

//=============================================================
==================

// Write the header of output txt file.


        if[![fileout = fopen[TXT_filename, "w"]]]
         {
                sprintf[msgbuf, "Cannot open text file for writing %s",
TXT_filename];
                allegro_message[msgbuf];
                allegro_exit[];
```

```
            exit[0];
        }
        fprintf[fileout, "Input data file: \n%s\n", text_file];
        fprintf[fileout, "\nTotal Test Time = %d minutes\n\n", Total_time];
        fprintf[fileout, "Time range = %d minutes\n\n", VarTime];
        fprintf[fileout, "\t\t\tRAT'S STOP NUMBER & TIME

DURITION\n\n"];

        fclose[fileout];
//************************************ Start BIG LOOP
**********************************

for [m = 0; m < loop; m++]

{

// Initialize all arrays
        for[i = 0 ; i < ZoneNum; i++]
        {
            for[j = 0; j < AnnuliNum; j++]
            {
                zCount1[i][j] = 0;
```

```
                zCount2[i][j] = 0;
                zCount3[i][j] = 0;
                zCount4[i][j] = 0;
                zCount5[i][j] = 0;

                TotalStopTime[i][j] = 0;
            }

        }
        SCount1=0;  SCount2=0;  SCount3=0;  SCount4=0;  SCount5=0;
SCount6=0;
        TotNum = 0, TotTim = 0;
        for[i = 0; i < DSIZE/3; i++]

            for [j = 0; j < 2; j++]
                STOPDATA[i][j] = 0;
// FIX this bug, get different results of STOP
        for[i = 0; i < DSIZE/3; i++]          //NOTE:  very  significant
change from DSIZE/20 to DSIZE/3!!! MAR-09-2007
            stoprad[i] = 0;
// End of bug.....
        stopCount = 0;
        Sflag = FALSE;
```

```
//Convert original data to relative coordinate x y
//      for[i = 0; i < LineCount; i++]
        for [i = m*VarTime*60*30;  i < [m+1]*VarTime*60*30; i++]
        {
                DATA[i][X] =  DATA[i][X] - X0;
                DATA[i][Y] =  DATA[i][Y] - Y0;
        }
//      for[i = 1; i < LineCount; i++]
                //original line
        for[i  =  [m*VarTime*60*30  +  1];  i  <  [m+1]*VarTime*60*30;  i++]
        //newline
        {

                if[Distance[DATA[i][X], DATA[i][Y], DATA[i-1][X], DATA[i-1][Y]]
== 0]
                        {
                                if[!Sflag]
                                        {
                                                STOPDATA[stopCount][X]          =
DATA[i][X];
                                                STOPDATA[stopCount][Y]          =
DATA[i][Y];
```

```
                                    stopCount++;
                                }

                                stoprad[stopCount]++;
                                Sflag = TRUE;
                        }
                else
                        {
                                Sflag = FALSE;                  //go to check next
stop point
                        }
        }
//Convert STOP point X, Y coordinate to degree and radian

        for[i = 0; i < stopCount; i++]
                {
                if[STOPDATA[i][Y] > 0]
                        deg_DATA[i]     =     [float]     atan2[STOPDATA[i][Y],
STOPDATA[i][X]] * DEG;
                if[STOPDATA[i][Y] < 0]
                        deg_DATA[i]     =     [float]     atan2[STOPDATA[i][Y],
STOPDATA[i][X]] * DEG + 360;
```

```
            rad_DATA[i] = [float] sqrt[STOPDATA[i][X]*STOPDATA[i][X] +
STOPDATA[i][Y]*STOPDATA[i][Y]];

            }

// Calculate numbers of STOP more than 1 second in each Zone then in
each Annuli ***********************************************************

//      for[i = 0; i < stopCount; i++]              //Original line, change to
next line

      for[i = 1; i <= stopCount; i++]
      for[j = 0; j < ZoneNum; j++]
            {

if[[stoprad[i]+1]/30 >= 1 && [stoprad[i]+1]/30 <= t1]
{
if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
                                          //which zone
                              for[k = 0; k < AnnuliNum; k++]
                              {
if[rad_DATA[i]    >=    k*radius/AnnuliNum    &&    rad_DATA[i]    <
[k+1]*radius/AnnuliNum ]      //which annulus
```

```
                                    {
                                     zCount1[j][k]++;
                                     TotalStopTime[j][k] += [stoprad[i]+1]/30;
                                                          //second
[1second=30data]
                                    }
                                     }
                          }
if[[stoprad[i]+1]/30 > t2 && [stoprad[i]+1]/30 <= t3]
                          {
if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
for[k = 0; k < AnnuliNum; k++]
{
if[rad_DATA[i]     >=     k*radius/AnnuliNum     &&     rad_DATA[i]     <
[k+1]*radius/AnnuliNum ]
 {
  zCount2[j][k]++;
 TotalStopTime[j][k] +
= [stoprad[i]+1]/30;
                            }
                            }
                            }
if[[stoprad[i]+1]/30 > t4 && [stoprad[i]+1]/30 <= t5]
```

```
                    {
if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
for[k = 0; k < AnnuliNum; k++]
{
if[rad_DATA[i] >= k*radius/AnnuliNum && rad_DATA[i] <
[k+1]*radius/AnnuliNum ]
                                {
zCount3[j][k]++;
TotalStopTime[j][k] +
= [stoprad[i]+1]/30;
                                }

                    }
                    }
if[[stoprad[i]+1]/30 > t6 && [stoprad[i]+1]/30 <= t7]
                    {
if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
for[k = 0; k < AnnuliNum; k++]
                                {
if[rad_DATA[i] >= k*radius/AnnuliNum && rad_DATA[i] <
[k+1]*radius/AnnuliNum]
                                {
                                 zCount4[j][k]++;
```

```
                                        TotalStopTime[j][k] += [stoprad[i]+1]/30;
                                    }
                                    }
                        }
if[[stoprad[i]+1]/30 > t8]
                        {
if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
for[k = 0; k < AnnuliNum; k++]
                                    {
if [rad_DATA[i] >= k*radius/AnnuliNum && rad_DATA[i] <
[k+1]*radius/AnnuliNum ]
                                    {
zCount5[j][k]++;
TotalStopTime[j][k] +
= [stoprad[i]+1]/30;
                                    }
                                    }
                        }
                }
// Draw stop circles
        if[DrawBlack == -1]                                         //draw
BLACK stop circle only
        {
```

```
for[i = 0; i < stopCount; i++]
{
    if[ [stoprad[i]+1]/30 >= 1 && [stoprad[i]+1]/30 <= t1
        {
        circle[buffer,  STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 3, makecol[0,0,0]];
        SCount1++;
    if[ [stoprad[i]+1]/30 > t2 && [stoprad[i]+1]/30 <= t3]
        {

        circle[buffer,  STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 6, makecol[0,0,0]];

        SCount2++;

        }

    if[ [stoprad[i]+1]/30 > t4 && [stoprad[i]+1]/30 <= t5]
        {

        circle[buffer,  STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 10, makecol[0,0,0]];
```

```
                    SCount3++;


                    }


                if[ [stoprad[i]+1]/30 > t6 && [stoprad[i]+1]/30 <= t7]
                    {
                    circle[buffer,                STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 15, makecol[0,0,0]];

                    SCount4++;
                    }

                if[ [stoprad[i]+1]/30 > t8]

                    {
                    circle[buffer,                STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 20, makecol[0,0,0]];

                    SCount5++;
                    }
/*  //do not display on the BMP file
                sprintf[msgbuf, "Stop 1-%d second = %d times", t1,
SCount1];
```

```
                    textout[buffer, font, msgbuf, 450,60, makecol[0,0,0]];
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t2, t3,
SCount2];
                    textout[buffer, font, msgbuf, 450,80, makecol[0,0,0]];
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t4, t5,
SCount3];
                    textout[buffer, font, msgbuf, 450,100, makecol[0,0,0]];
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t6, t7,
SCount4];
                    textout[buffer, font, msgbuf, 450,120, makecol[0,0,0]];
                    sprintf[msgbuf, "Stop more than %d second = %d
times", t8, SCount5];
                    textout[buffer, font, msgbuf, 450,140, makecol[0,0,0]];
 */
                    blit[buffer, screen, 0, 0, 0, 0, SCREEN_W, SCREEN_H];
               }
          }
          else
          {
               for[i = 0; i < stopCount; i++]
               {
                    if[ [stoprad[i]+1]/30 >= 1 && [stoprad[i]+1]/30 <= t1 ]
               //        [GREEN]
```

```
                    {
                    circle[buffer,                    STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 3, makecol[0,255,0]];
                    SCount1++;
                    }
                if[ [stoprad[i]+1]/30 > t2 && [stoprad[i]+1]/30 <= t3]
    //      [BLUE]

                    {

                    circle[buffer,                    STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 6, makecol[0,0,255]];
                    SCount2++;
                    }
                if[ [stoprad[i]+1]/30 > t4 && [stoprad[i]+1]/30 <= t5]
    //      [MAGENTA]
                    {
                    circle[buffer,                    STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 10, makecol[255,0,255]];

                    SCount3++;

                    }
```

```
                    if[ [stoprad[i]+1]/30 > t6 && [stoprad[i]+1]/30 <= t7]
        //  [GREY]
                                {
                                circle[buffer,                  STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 15, makecol[125,125,125]];
                                SCount4++;
                                }

if[ [stoprad[i]+1]/30 > t8]
         //       [RED]
                                {
                                circle[buffer,                  STOPDATA[i][X]+X0,
STOPDATA[i][Y]+Y0, 20, makecol[255,0,0]];
                                SCount5++;
                                }
/* //do not display on the BMP file
                    sprintf[msgbuf, "Stop 1-%d second = %d times", t1,
SCount1];
                    textout[buffer, font, msgbuf, 450,60, makecol[0,255,0]];
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t2, t3,
SCount2];
                    textout[buffer, font, msgbuf, 450,80, makecol[0,0,255]];
```

```
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t4, t5,
SCount3];

                    textout[buffer,  font,  msgbuf,  450,100,
makecol[255,0,255]];
                    sprintf[msgbuf, "Stop %d-%d second = %d times", t6, t7,
SCount4];
                    textout[buffer,  font,  msgbuf,  450,120,
makecol[125,125,125]];
                    sprintf[msgbuf,  "Stop  more  than  %d  second  =  %d
times", t8, SCount5];
                    textout[buffer, font, msgbuf, 450,140, makecol[255,0,0]];

*/
                    blit[buffer, screen, 0, 0, 0, 0, SCREEN_W, SCREEN_H];

               }
        }
// Save output data to text file

if[![fileout = fopen[TXT_filename, "a"]]]
         {
```

```
            sprintf[msgbuf, "Cannot open text file for writing %s",
TXT_filename];
            allegro_message[msgbuf];
            allegro_exit[];
            exit[0];
        }

   fprintf[fileout, "\n\nTime period from %d to %d minutes\n", m*VarTime,
[m+1]*VarTime];

        fprintf[fileout,                "ZONE\tS1-%d\tS%d-%d\tS%d-%d\tS%d-
%d\tS>%d\tTOTAL[number]\tTOTAL[second]\n", t1, t2, t3, t4, t5, t6, t7, t8];
        fprintf[fileout, "----------------------------------------------------------------------
--\n"];

        fclose[fileout];
        if[![fileout = fopen[TXT_filename, "a"]]]
        {
            sprintf[msgbuf, "Cannot open text file for writing %s",
TXT_filename];

            allegro_message[msgbuf];
            allegro_exit[];
```

```
            exit[0];
        }
        for[i = 0;  i < ZoneNum; i++]
        {
            fprintf[fileout, "%d\n", i+1];

            for[j = 0; j < AnnuliNum; j++]
                {
                    fprintf[fileout,                                    "
A%d\t%d\t%d\t%d\t%d\t%d\t%d\t\t%d\n",
                                        j+1,
                                        zCount1[i][j],
                                        zCount2[i][j],
                                        zCount3[i][j],
                                        zCount4[i][j],
                                        zCount5[i][j],
        zCount1[i][j]+zCount2[i][j]+zCount3[i][j]+zCount4[i][j]+zCount5[i][j],
TotalStopTime[i][j]
                                        ];
TotNum+
= zCount1[i][j]+zCount2[i][j]+zCount3[i][j]+zCount4[i][j]+zCount5[i][j];
TotTim +
= TotalStopTime[i][j];
```

```
                    }
        }
fprintf[fileout,"-------------------------------------------------------------------------------\n"];

//      fprintf[fileout,"TOTAL:\t%d\t%d\t%d\t%d\t%d              |\t%d\t\t%d\n",
SCount1, SCount2, SCount3, SCount4, SCount5, TotNum, TotTim];

        fprintf[fileout,"TOTAL:\t\t\t\t\t\t%d\t\t%d\n", TotNum, TotTim];
        fclose[fileout];

 }                      //************************      End      LOOP
*****************************************************************************
        get_palette[pal];
        save_bmp[STOPBMP_filename, buffer, pal];
        allegro_exit[];
        return 0;
}
END_OF_MAIN[];
```

B. Path Program

```
*/

#include "allegro.h"

#include "adime.h"

#include "winalleg.h"

#include <stdlib.h>

#include <stdio.h>

#include <math.h>


#define X 0

#define Y 1

#define DSIZE 60000


#define PI 3.14159265

#define DEG 180/PI

#define ZONENUM 12


#define ANNULINUM 5


char text_file[1024]= "";

char bmp_file[100];

char BMP_filename[100];
```

```
char TXT_filename[100];


int  ZoneNum = 4;

int  AnnuliNum = 1;

int  DrawLine = 0;

int  VarTime = 0;


float X0, Y0, dia;

//int  DrawTotal = 0;

//int  StartTime = 0;

//int  EndTime = 0;


//------------------------------- User Input Dialog -------------------------------


void no_time_dialog[void]

{

        adime_dialogf["No time range specified!",

                                ADIME_ALIGN_CENTRE,

ADIME_ALIGN_CENTRE, 200,

                                "You must enter time range

variable%nothing[]"];

//                              "check 'Draw entire test'.%nothing[]"];

}
```

```
void main_dialog[void]
{
  if[adime_dialogf["File Settings",
                                ADIME_ALIGN_CENTRE,
ADIME_ALIGN_CENTRE, 200,
                                "Input data file:%filename[1024, txt;txy,
Select a data file you want to draw]"
                                "Number of Zone [max.12]:%int[1,12]"
                                "Number of Annuli[max.5]:%int[1,5]"
                                "Time range variable[minute]:%int[0,30]"
                                "%line[]"
                                "Save BMP/TXT file as:%string[100]"
//                              "Time ranges from[minute]:%int[0,30]"
//                              "    to[minute]:%int[0,30]"
//                              "Draw entire test:%bool[]"
                                "Draw zone/annuli divided lines:%bool[]"
                                "Table diameter:%float[]"
                                "Table Centre point X0:%float[]"
                                "Table Centre point Y0:%float[]"
                                ,
                                text_file,
                                &ZoneNum,
                                &AnnuliNum,
```

```
                                &VarTime,
                                bmp_file,
//                              &StartTime,
//                              &EndTime,
//                              &DrawTotal,
                                &DrawLine,
                                &dia,
                                &X0,
                                &Y0
                                ] == 2]
        exit[0];

         if[ VarTime == 0]                          //if user no selection,
return to main dialog

//   if[DrawTotal == 0 && EndTime == 0]

        {

                no_time_dialog[];
                main_dialog[];
        }
}
```

```
//-------------------------------- Read Data File -----------------------------

void readstr[FILE *f,char *string]                                    //read
in a string from a file
{
        do
        {
                fgets[string, 255, f];
        // fgets is function to read one line from stream
        } while [[string[0] == '/'] || [string[0] == '\n']];  // to see first char is '/' or
empty line '\n'

        return;
}

float Distance[double x2, double y2, double x1, double y1]
{
          float distance;
          distance = [float] sqrt[pow[[x2-x1],2] + pow[[y2-y1],2]];
          return distance;
}
```

```
//********************************** MAIN ********************************
int main[int argc, char **argv[]]
{
        BITMAP* buffer;
        FILE* filein;
        FILE* fileout;
        PALETTE pal;

        char msgbuf[100];
        int i, j, k, m, Total_time, loop;

        float deg, radius;
        float x, y;
        float XMAX, XMIN, YMAX, YMIN, SMAX, SMIN;
        int LineCount = 0;
        float totalDistance = 0;
        char   oneline[255];
//      int             zCount[50];
//      float   zTime[50];
//      float   zDis[50];
        float   DATA[DSIZE][2];
        float   deg_DATA[DSIZE];
```

```
        float   rad_DATA[DSIZE];
        int             zCount[ZONENUM][ANNULINUM];

        float   zTime[ZONENUM][ANNULINUM];
        float   zDis[ZONENUM][ANNULINUM];
        float   Tot_Time, Tot_Dis;

// Install various parts of Allegro
        if[allegro_init[]]
                exit[1];
        if[install_keyboard[]]{
                allegro_message["Could not installed keyboard.\n"];
                exit[1];
        }
        install_timer[];
if[install_mouse[]== -1]{
                allegro_message["Could not install mouse.\n"];
                exit[1];

        }
show_mouse[screen];
```

```
        if[set_gfx_mode[GFX_AUTODETECT_FULLSCREEN,  1024,  768,  0,
0]]{
                allegro_message["Could not set graphics mode.\n"];

                exit[1];
  }
        buffer = create_bitmap[SCREEN_W, SCREEN_H];

        set_palette[default_palette];

// Install Adime
        if[     adime_init[] !=0]{

                set_gfx_mode[GFX_TEXT, 0,0,0,0];
                allegro_message["Error initializing ADIME.\n"];
                exit[1];
        }

// Clear screen and buffer to black
        clear_to_color[screen, makecol[0,0,0]];
        clear_to_color[buffer, makecol[0,0,0]];

// User Interface Dialog
```

```
        textout_centre[screen, font, "Rat Spent Time & Distance in Zone and
Annulus",SCREEN_W/2, SCREEN_H/2-150, makecol[255,255,255]];
        main_dialog[];
        sprintf[BMP_filename, "%spth.bmp", bmp_file];
        sprintf[TXT_filename, "%spth.txt", bmp_file];

        set_palette[desktop_palette];
//set white background
        clear_to_color[screen, makecol[255,255,255]];
        clear_to_color[buffer, makecol[255,255,255]];
// Read the txt/txy datafile
        if[![filein = fopen[text_file, "rt"]]]
        {
                sprintf[msgbuf, "Cannot open data file for reading"];
                allegro_message[msgbuf];
                allegro_exit[];
                exit[0];
        }
// Read all data to figure out X, Y max. min.
        while[!feof[filein]]
        {
                readstr[filein, oneline];
                sscanf[oneline, "%f %f", &x, &y];
```

```
            LineCount++;
            DATA[LineCount-1][X] = x;
            DATA[LineCount-1][Y] = y;
        }
        fclose[filein];

// Calculate total time of entire test and divide by how many periods

            Total_time = LineCount/1800;
            loop = Total_time/VarTime;
// Make a directory if it isn't existed and change dir path
        mkdir["Output"];
        chdir["Output"];

// Calculate X, Y maximum and minimum values
        XMAX = DATA[0][X];
        XMIN = DATA[0][X];

        YMAX = DATA[0][Y];
        YMIN = DATA[0][Y];
        for[i = 1; i < LineCount; i++]
        {
            if[XMAX < DATA[i][X]]          XMAX = DATA[i][X];
```

```
            if[XMIN > DATA[i][X]]           XMIN = DATA[i][X];
            if[YMAX < DATA[i][Y]]           YMAX = DATA[i][Y];
            if[YMIN > DATA[i][Y]]           YMIN = DATA[i][Y];
        }

        deg = 360/[float]ZoneNum;
/* for temp testing purpose ONLY
        X0 = [XMAX + XMIN]/2;
        Y0 = [YMAX + YMIN]/2;
*/

// AcuScan calibrating coordinate of the table center point
//      X0 = 213.30;            //just for testing, pls comment out this three
lines when go to production
//      Y0 = 144.90;
//      dia = 244.00;

//      ================================      Draw      circle
======================
        clear_to_color[screen, makecol[255,255,255]];

        clear_to_color[buffer, makecol[255,255,255]];
        //set white background
```

```
/*for temp testing purpose ONLY
                    //commented on Jan-08-2006

        if[[XMAX-XMIN] >= [YMAX-YMIN]]

                radius = [XMAX - XMIN]/2;
        else
                radius = [YMAX - YMIN]/2;

// Expand radius more 5 pixel to include all spots of rat's stops
        radius = radius + 5;
        circle[buffer, X0, Y0, radius, makecol[255,0,0]];

// end of temp

*/

        radius = dia/2;
        circle[buffer, X0, Y0, radius, makecol[255,0,0]];
        textout[buffer, font, "Note: Annulus number starts from inner centre.", 50, SCREEN_H/2-20, makecol[0,0,0]];
// If user check to draw the zone divided lines
        if[DrawLine == -1]
```

```
{
        hline[buffer, 80, Y0, XMAX+30, makecol[255, 0, 0]];
    //draw X axis in red
        textout[buffer, font, "X", XMAX+50, Y0, makecol[0,0,0]];
        textout[buffer, font, "Y", X0, YMAX+50, makecol[0,0,0]];

        if[ [ZoneNum/2] % 2 == 0 ]

            vline[buffer, X0, 30, YMAX+30, makecol[255,0,0]];

        for[i = 0; i < ZoneNum/2; i++]
            if[i == [float]ZoneNum/4]
                continue;

            else
                line[buffer, XMIN, tan[deg*i*PI/180]*[XMIN-X0]+Y0,
XMAX, tan[deg*i*PI/180]*[XMAX-X0]+Y0, makecol[255,0,0]];
    textout[buffer, font, "zone1", XMAX+20, Y0+10, makecol[0,0,255]];
        sprintf[msgbuf, "zone%d", ZoneNum/2];
        textout[buffer, font, msgbuf, XMIN-70, Y0+10,
makecol[0,0,255]];
        sprintf[msgbuf, "zone%d", ZoneNum/2+1];
```

```
            textout[buffer, font, msgbuf, XMIN-70, Y0-20,
makecol[0,0,255]];
            sprintf[msgbuf, "zone%d", ZoneNum];
            textout[buffer, font, msgbuf, XMAX+20, Y0-20,
makecol[0,0,255]];
            //Draw the annuli circles
            for[i = 0; i < AnnuliNum-1; i++]
circle[buffer, X0, Y0, radius*[i+1]/AnnuliNum, makecol[255,0,0]];
        }
// Display Input data file at top / Display Output bmp file at bottom
            textout[buffer, font, text_file, 20, SCREEN_H-70,
makecol[0,0,0]];
            textout[buffer, font, BMP_filename , 100, SCREEN_H-50,
makecol[0,0,0]];
// we want to show time variable on the bmp file
          textout[buffer, font, "TEST RESULTS:", 500, 40, makecol[0,0,0]];

            sprintf[msgbuf, "Total Time = %d minutes", Total_time ];
            textout[buffer, font, msgbuf, 450,70, makecol[255,0,0]];
// Write the head of output txt file.
        if[![fileout = fopen[TXT_filename, "w"]]]
         {
```

```
            sprintf[msgbuf, "Cannot open text file for writing %s",
TXT_filename];
            allegro_message[msgbuf];
            allegro_exit[];
            exit[0];
        }
        fprintf[fileout, "Input data file:\n%s\n\n", text_file];
        fprintf[fileout, "\tSPENT TIME & DISTANCE IN EACH ZONE AND
ANNULUS\n\n"];

//      fprintf[fileout, "ZONE/ANNULI\tTOTAL[second]\tDISTANCE[cm]\n"];

//      fprintf[fileout, "----------------------------------------\n"];

        fclose[fileout];
// NEW PROGRAM PART: ************************** BIG LOOP
**************************************
for [m = 0; m < loop ; m++]
 {
        LineCount = 0;                                          //reset      all
variable equal zero for each loop

        Total_time = 0;
```

```
if[![filein = fopen[text_file, "rt"]]]
        {
            sprintf[msgbuf, "Cannot open data file for reading"];

allegro_message[msgbuf];
allegro_exit[];
exit[0];
        }

// Skip the previous part section

        for[i = 0;  i< m*VarTime*60*30; i++]

            readstr[filein, oneline];
    // Read in the desired time selection data
        for [i = m*VarTime*60*30;  i < [m+1]*VarTime*60*30; i++]
        {
            readstr[filein, oneline];
            sscanf[oneline, "%f %f", &x, &y];
            LineCount++;

            DATA[LineCount-1][X] = x;
            DATA[LineCount-1][Y] = y;
```

```
            }
            fclose[filein];

        // Calculate total time of desired time range
        Total_time = LineCount/1800;
//--------------------------------------------------
//Convert original data to coordinate xy
        for[i = 0; i < LineCount; i++]
        {
            DATA[i][X] =  DATA[i][X] - X0;
            DATA[i][Y] =  DATA[i][Y] - Y0;
        }

//Convert X, Y coordinate to degree and radian
        for[i = 0; i < LineCount; i++]
            {
            if[DATA[i][Y] > 0]
                deg_DATA[i]  =  [float]  atan2[DATA[i][Y],  DATA[i][X]]  *
DEG;

            if[DATA[i][Y] < 0]
                deg_DATA[i]  =  [float]  atan2[DATA[i][Y],  DATA[i][X]]  *
DEG + 360;
```

```
        rad_DATA[i]      =      [float]      sqrt[DATA[i][X]*DATA[i][X]      +
DATA[i][Y]*DATA[i][Y]];
                }

//      deg = 360/[float]ZoneNum;

// Initialize all arrays

        for[i = 0 ; i < ZoneNum; i++]

                for[j = 0; j < AnnuliNum; j++]
                {
                        zCount[i][j] = 0;
                        zTime[i][j] = 0;
                        zDis[i][j] = 0;
                }
        Tot_Time = 0;
        Tot_Dis = 0;

//=======================================      DRAW      PATH
=======================================
// Calculate rat spent time, travel distance in each zone and each annuli
```

```
        for[i = 1; i < LineCount; i++]
        {
                line[buffer,  DATA[i-1][X]+X0,  DATA[i-1][Y]+Y0,  DATA[i][X]+X0,
DATA[i][Y]+Y0, makecol[0,0,0]];
                totalDistance += Distance[DATA[i][X], DATA[i][Y], DATA[i-1][X],
DATA[i-1][Y]];
// we want to show travel distance variable on the bmp file
                sprintf[msgbuf, "Total distance = %8.2f cm", totalDistance];
                textout[buffer, font, msgbuf, 450,90, makecol[255,0,0]];

                for[j = 0; j < ZoneNum; j++]
                {
         if[deg_DATA[i] >= j*deg && deg_DATA[i] < [j+1]*deg]
                                                        //which zone
                        {
                                for[k = 0; k < AnnuliNum; k++]
                                        {
                                 if[rad_DATA[i]    >=    k*radius/AnnuliNum    &&
rad_DATA[i] < [k+1]*radius/AnnuliNum]       //which annuli
                                        {
                                         zCount[j][k]++;
```

```
                                        zDis[j][k]                    +=
Distance[DATA[i][X], DATA[i][Y], DATA[i-1][X], DATA[i-1][Y]];
                                    }
                                }
                            }
                        }
                        blit[buffer, screen, 0, 0, 0, 0, SCREEN_W, SCREEN_H];
                }
// calculate spent time in each zone and annuli
for[j = 0; j < ZoneNum; j++]

                        for[k = 0; k < AnnuliNum; k++]
                            zTime[j][k] = [float] zCount[j][k]/30;          //second
//  Open output txt file for appending

                if[![fileout = fopen[TXT_filename, "a"]]]
                {
                        sprintf[msgbuf, "Cannot open text file for writing %s",
TXT_filename];
                        allegro_message[msgbuf];
                        allegro_exit[];
exit[0];
```

```
        }

fprintf[fileout, "\nTime period from %d to %d minutes\n", m*VarTime,
[m+1]*VarTime];
        fprintf[fileout,
"ZONE/ANNULUS\tTOTAL[second]\tDISTANCE[cm]\n"];
        fprintf[fileout, "-----------------------------------------\n"];
        for[i = 0;  i < ZoneNum; i++]
        {
                fprintf[fileout, "%d\n", i+1];
                for[j = 0; j < AnnuliNum; j++]
                        {
                                fprintf[fileout,                                "
A%d\t\t%5.1f\t\t%5.2f\n",j+1,zTime[i][j],zDis[i][j]];
                                Tot_Time = Tot_Time + zTime[i][j];
                                Tot_Dis = Tot_Dis + zDis[i][j];
                        }
        }
        fprintf[fileout,"-----------------------------------------\n"];
        fprintf[fileout,"TOTAL:\t\t%5.2fminute\t%5.2fcm\n",Tot_Time/60,Tot_
Dis];
        fclose[fileout];
```

```
 }                                  //End                 BIG                 LOOP
*****************************************************************************************
*******
// Save the bitmap
        get_palette[pal];
        save_bmp[BMP_filename, buffer, pal];
        allegro_exit[];
        return 0;
}
END_OF_MAIN[];
```