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The role of the dorsal CA1 and ventral CA1 in memory for the temporal order of a sequence of odors

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ABSTRACT

Memory for the temporal order of a sequence of odors was assessed in male rats. A sequence of five odors mixed in sand was presented in digging cups one at a time to each rat in a sequence that varied on each trial. A reward was buried in each cup. Following the fifth odor, two of the previous five odors were presented simultaneously and the rat needed to choose the odor that occurred earliest in the sequence to receive a reward. Temporal separations of 1, 2, or 3 were used which represented the number of odors that occurred between the two odors in the sequence. Once pre-operative criterion was reached, rats received a control, dorsal CA1 (dCA1), or ventral CA1 (vCA1) lesion and were retested on the task. On post-operative trials, only the vCA1 group was impaired relative to both control and dCA1 groups. All groups of rats could discriminate between the odors. The data suggest that the vCA1, but not dorsal CA1, is involved in separating sensory events (odors) in time so that one odor can be remembered separate from another odor.

1. Introduction

In the context of processing mnemonic information, it is thought that the development and maintenance of memory representations often require temporal processing. One feature of temporal processing of information is based on memory for the sequential occurrence of events as reflected by memory for relative recency or temporal order. One brain region that is assumed to play an important role in the processing of temporal order of events is the hippocampus (Eichenbaum, 2000; Kesner, 1998; Kesner, Lee, & Gilbert, 2004; Rawlins, 1985; Solomon, 1979). The hippocampus is well suited to process the temporal order of events, because almost all sensory information is processed by hippocampal neurons, to provide markers for time. It is, therefore, possible that newly processed sensory information is organized within the hippocampus in such a way to facilitate remembering and temporarily storing one event as separate from another event in time. Based on these ideas, researchers have examined the role of the hippocampus in tasks that may require the separation of temporally patterned information. For example, it has been shown that memory performance improves as the number of items in a sequence between the test items increases (Estes, 1985; Madsen & Kesner, 1995). This phenomenon is referred to as a temporal separation effect. It is assumed to occur because there is more interference for temporally proximal events than temporally distant events. Based on these findings, an experiment was designed to test memory for the temporal order of a sequence of items (spatial locations), when the number of items between the two choice items in the sequence varied (Chiba, Kesner, & Reynolds, 1994; Gilbert, Kesner, & Lee, 2001). The results of this study demonstrated a temporal separation effect for a sequence of spatial locations on a radial 8-arm maze, and following hippocampal or CA1 lesions, rats were significantly impaired. Similar findings have also been reported in humans with hippocampal damage (Hopkins, Kesner, & Goldstein, 1995). The results suggest that the hippocampus, and especially CA1, is involved in memory for spatial location as a function of temporal separation and that lesions of the hippocampus decrease efficiency in temporal pattern separation, and thus, the hippocampus may be involved in separating events in time (Chiba et al., 1994; Gilbert et al., 2001; Hopkins et al., 1995; Kesner et al., 2004). It should also be noted that in previous research, it was shown that the dorsal dentate gyrus plays an important role in spatial, but not temporal, pattern separation for spatial location information, suggesting that there is a double dissociation between the dorsal CA1 and dorsal dentate gyrus in processing spatial information (Gilbert et al., 2001).

Recently, it has been shown that the hippocampus also plays an important role in processing temporal order (temporal pattern separation) for odor information, in that lesions of the hippocampus produce in deficit in memory for temporal order for odors (Fortin,

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Agster, & Eichenbaum, 2002; Kesner, Gilbert, & Barua, 2002). With respect to a subregional analysis of CA1 function, previous research has determined that lesions of the dorsal CA1, but not the ventral CA1, subregion of the hippocampus disrupt temporal order for spatial information (Hunsaker, Fieldsted, Rosenberg, & Kesner, 2008). In contrast previous research has determined that lesions of the ventral CA1, but not the dorsal CA1, subregion of the hippocampus, disrupt temporal order for odor information (Hunsaker et al., 2008). It should be noted that in the Hunsaker et al. (2008) study, we were only able to provide data for temporal odor memory based on 1 trial, and furthermore we were not able to determine the presence or absence of a gradient based on temporal distance between the order of odor presentations. Thus, to determine more precisely whether odor information requires the operation of the dorsal and ventral hippocampus and more specifically the dorsal CA1 and the ventral CA1, the role of the dorsal CA1 and ventral CA1 in mediating temporal pattern separation based on odor cues was investigated using in this experiment the same paradigm described by Kesner et al. (2002) in which temporal pattern separation based on multiple trials can be more accurately assessed.

2. Materials and methods

2.1. Subjects

Eighteen male Long Evans rats (260–350 g) were singly housed in standard plastic rodent cages and maintained on a 12-h light/dark cycle. All testing was conducted in the light proportion of the light/dark cycle. Each rat was initially food-deprived to approximately 85–90% of their free-feeding weight, but was allowed free access to water throughout testing. All surgical and experimental protocols conformed to University of Utah IACUC and AAALAC protocols and regulations. The health of the animals was assessed weekly by an IACUC veterinarian.

2.2. Apparatus

The test apparatus (the same used by Kesner et al. (2002)) consisted of a box 84 cm long and 27 cm wide with four 30.5 cm high red Plexiglas walls. One removable guillotine door, also constructed of red Plexiglas, was placed 25 cm from one end of the box. The door divided the box into two separate compartments: a 27×25 cm start chamber and a 27×59 cm choice chamber. The floor of the maze consisted of wood that was painted black. On the back wall of the choice chamber, a spring was attached to the floor that secured one or two cup holders to the floor that were used to stabilize digging cups during testing.

2.3. Shaping

During the first week of training, each animal was handled for ~0.25 h daily and was then allowed to individually explore the test apparatus for 0.25 h. During the exploration period, ~10 pieces of Froot Loop cereal were spread out across the floor of the choice chamber and the guillotine door to the start chamber remained open. During the first week each rat was shaped in its home cage to dig in a small clear plastic cup (7 cm in diameter and 6 cm high) filled with sand to retrieve a food reward (Froot Loop cereal). Shaping continued by placing a reward on top of the sand and allowing the animal to find the reward. Across subsequent shaping trial presentations, the food reward was buried, partially at first and then deeper in the sand, until the rat dug in the sand even when the reward was not visible. Once an animal consistently dug in the sand, the rat was shaped to dig in a cup in the choice chamber of the test apparatus. The cup was placed in a cup holder that was mounted to the floor with a spring so that the rat could not spill the contents of the cup or displace the cup from its position. On each shaping trial, the rat was placed in the start chamber, the door was opened, and the rat was allowed to approach the cup and dig in the sand to retrieve the food reward. This procedure was followed 12 times each day. Once an animal consistently dug in the sand, the animal began pre-operative training.

2.4. Pre-operative training

Each subject was given four trials daily. Each trial consisted of a sample phase followed by a choice phase. During the sample phase, a rat was placed in the start chamber of the box with the door to the choice chamber closed. In the choice chamber a small plastic digging cup (6 cm high, 6 cm diameter) filled with sand mixed with one of 10 powdered odors was positioned centrally along the back edge of the choice chamber. A food reward (Froot Loops cereal) was buried 2.5 cm deep in the sand. The rats could not see the Froot Loop cereal. The door to the choice chamber was then opened and the animal was allowed to run to the cup, dig in the sand, and retrieve the reward. The rat then returned to the start chamber and the door to the choice chamber was closed. Following this same procedure for each trial, the rat was sequentially presented with five different odors in digging cups mixed with sand one at a time in a sequence which was randomly determined for each trial. The cups were presented to the subject with an approximate 10 s delay between each presentation. Following the presentation of the fifth odor cup, the subject returned to the start area of the apparatus to await the choice phase. Fifteen seconds later during the choice phase two of the previous five odors were presented simultaneously side by side and the animal was allowed to choose between the two odors. The rule to be learned in order to receive a food reward was to always choose the odor that occurred earliest in the sequence. No correction procedure was used. Temporal separations of 1, 2, or 3 were randomly selected for each choice phase and represented the number of odors that occurred between the choice odors in the sample phase. For example, a "3" separation would involve two odors in which three odors occurred between the two odors in the sequence. In a previous study, a few rats were tested using a "0" separation, however, these rats could not learn the task and showed difficulties learning the other separations. It is likely that there was too much temporal interference between any two odors that followed each other in the sequential presentation of odors during the study phase. Therefore, the "0" separation was dropped from the task. The position of the correct odor varied from trial to trial such that the correct odor was equally presented on the right and the left. Ten different odors were used in the study so that specific odors could be used on each consecutive trial to reduce interference. The odors used in the task were powdered odors including: cloves, cinnamon, cumin, garlic powder, coffee, baby powder, chicken base, curry, carob, and onion powder. Approximately 4–8 g of each odor, depending on the particular odor, was mixed in 160 g of sand (the odors were weakly discernable to the experimenter). The rats received 10 trials a day. Once an animal reached a criterion of 80–90% correct across all temporal separations based on 30 trials the animal was scheduled for surgery. Ten sample phases for each of the temporal separations were presented across the block of 30 trials. The inter-trial interval was 60 s.

2.5. Surgery

Rats were randomly assigned to control, dorsal CA1, and ventral CA1 surgery groups. Rats were anesthetized and maintained isoflurane (2–4% in 2 L/min medical air) and given atropine sulfate (0.2 mg/kg i.m.) as a prophylactic. Rats that received a lesion of

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the ventral CA1 subregion were given 0.75 ml of diazepam (2 mg/ml i.p.) 10 min prior to surgery to prevent any seizure activity that may result from the excitotoxic lesion. Rats that received a lesion of the dorsal CA1 subregion were not given a diazepam injection, because based on over one hundred dorsal CA1 lesions, seizures had not been observed. Each rat was placed in a stereotaxic apparatus (David Kopf Instruments, Tunjana, CA) with its head level. The scalp was incised and retracted to expose bregma and lambda which were adjusted into the same horizontal plane by moving the incisor bar dorso-ventrally. Dorsal CA1 lesions ($n = 6$) were made using ibotenic acid (Biosearch Technologies, Inc., San Rafael, CA, 8 mg/ml), infused using a micro infusion pump (Cole-Parmer; Vernon Hills, IL) and a 10 μl Hamilton syringe (Hamilton; Reno, NV) at a rate of 6 μL/h and a volume of 0.10 or 0.15 μl depending on the site, bilaterally into three sites. After infusion, the cannula remained in each site for one minute to allow diffusion of the injected excitotoxin. The coordinates for dorsal CA1 lesions ($n = 6$) based on the Paxinos and Watson atlas (1997) were 3.6 mm posterior to bregma, 1.0 mm lateral to the midline, 2.4 mm ventral to dura (0.1 μl of ibotenic acid injected); 3.6 mm posterior to bregma, 2.0 mm lateral to the midline, 2.1 mm ventral to dura (0.1 μl); 3.6 mm posterior to bregma, 3.0 mm lateral to the midline, 2.3 mm ventral to dura (0.15 μl). Ventral CA1 lesions ($n = 6$) were also made using ibotenic acid, infused following the same procedures as dorsal CA1 lesions, into three sites within the ventral hippocampus located 5.3 mm posterior to bregma, 3.0 mm lateral to the midline, 2.8 mm ventral to dura (0.1 μl); 5.3 mm posterior to bregma, 5.2 mm lateral to the midline, 4.0 mm ventral to dura (0.1 μl); 5.3 mm posterior to bregma, 5.8 mm lateral to the midline, 6.2 mm ventral to dura (0.15 μl). Vehicle control lesions (vCA1 vehicle $n = 3$ and dCA1 vehicle $n = 3$) were made using the same coordinates and procedures as the dCA1 group; however, physiological saline was infused. Following surgery, the incision was sutured, 1.5 ml of saline was injected into each hip subcutaneously to expel the anesthetic, and the rats were allowed to recover on a heating pad before returning to their home cage. In addition, rats received acetaminophen (Children's Tylenol; 200 mg/100 ml of water) as an analgesic and mashed food for 3 days following surgery. The behavior of all animals was monitored for epileptiform activity for 7 days post-surgery. There was no evidence of overt behavioral seizures. The animals were given a 7–10 day recovery period before testing.

2.6. Post-operative testing

Following recovery from surgery, each subject was again tested on the task following the same procedure used during pre-operative training for one block of 30 trials.

2.7. Discrimination task

Following post-operative testing, a discrimination task was conducted to assess the ability of dCA1 lesioned ($n = 6$), vCA1 lesioned ($n = 6$) and control ($n = 6$) rats to perceptually discriminate between two simultaneously presented odors. Each rat was given 10 trials each day. For the preference task, two odors similar to those used in the task were selected. One odor was designated as the rewarded odor and the other was designated as the nonrewarded odor. The rewarded odor varied across animals. The odors were again mixed in sand and placed in digging cups as described in the preceding section. On each trial, two digging cups were simultaneously presented to the rat. The cup containing sand mixed with the rewarded odor contained a reward but the cup with the nonrewarded odor contained no reward. Therefore, to receive a reward the rat must dig in the cup containing the rewarded odor. The position of the rewarded odor was randomly determined for each trial. Each animal was tested until a 90% correct criterion across 10 consecutive trials was achieved.

2.8. Histology

At the conclusion of all testing, each animal was deeply anesthetized with an intraperitoneal injection of 1.5 ml sodium pentobarbital (60 mg/kg), and perfused intracardially followed by a 10% formalin solution. The brain was removed from the skull and stored in a 10% formalin/30% sucrose solution for at least 72 h prior to sectioning. Each brain was frozen and cut at 24 μm sections starting at bregma and extending through the posterior region of the hippocampus. Every third section was mounted on a glass slide, stained with cresyl violet, and examined for histological verification of the lesion placement.

3. Results

3.1. Histology

Sections were photographed and the lesioned portion of the region of interest (either vCA1 or dCA1) was traced using the free-hand tool on Image J. The number of pixels contained within this region was compared to the number of pixels contained within a tracing of the entire region of interest (lesioned area + spared areas within the region of interest). This analysis was carried out upon all sections collected. In this way, the lesion extent was analyzed in multiple sections per animal as well as across multiple animals. Similar methods have been used in the past to quantify dorsal and ventral CA1 lesions (Hunsaker et al., 2008). The values obtained from Image J were averaged across all sections and all animals. No animals were excluded from statistical analysis due to inaccurate surgery. Fig. 1 shows control sections from different rats showing the ventral hippocampus in a horizontal section (A–B), representative ventral CA1 lesions from different rats showing selective ventral CA1 damage (C–D), representative sections from different rats showing selective dorsal CA1 damage in a coronal section(E–F), and representative section from a control animal in a coronal section (G). Dorsal CA1 lesioned animals had (mean ± standard error) 84 ± 5.2% damage to the pyramidal cell layers of CA1 with 4.5 ± 0.9% damage to the underlying medial blade of the dentate gyrus and 8.8 ± 2.1% damage to CA3 pyramids. Ventral CA1 lesioned animals had 72.4 ± 8.3% damage to the ventral CA1 pyramidal cell layer with 1.5 ± 0.25% damage to the ventral dentate gyrus and 12.5 ± 4.6% damage to the ventral CA3 pyramidal cell layer. Control lesions animals had no damage beyond that caused by the cannula track in both dorsal and ventral vehicle control lesioned animals.

3.2. Memory for temporal order for odors task

Pre-operative acquisition of the temporal order for odors task was analyzed by grouping the last 30 trials to reach criterion into three temporal separations with 10 observations for each distance. There were no significant differences between the two control groups and therefore they were combined into one group. Fig. 2 shows the mean percent correct performance of the control, and the to be lesioned dCA1 and vCA1 groups as a function of temporal separation (number of odors that occurred between the two choice phase odors) on pre-operative trials. The data indicate that the to be lesioned dCA1 and vCA1 lesioned groups matched the performance of control rats across all temporal separations on pre-operative trials. A repeated-measures 2-way analysis of variance with lesion (control, dCA1 and vCA1) as the between group factor and temporal separation (1, 2, 3) as the within group factors revealed

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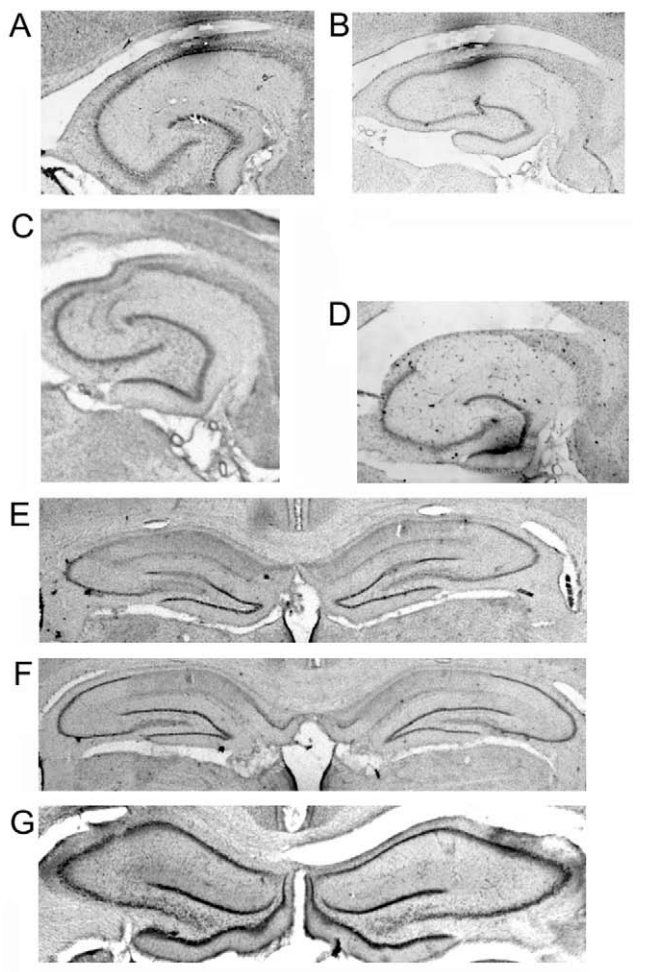

Fig. 1. Histology (A–B) control sections from different rats showing the ventral hippocampus in a horizontal section. (C–D) Representative ventral CA1 lesions from different rats showing selective ventral CA1 damage. (E–F) Representative sections from different rats showing selective dorsal CA1 damage in a coronal section. (G) Representative section from a control animal in a coronal section.

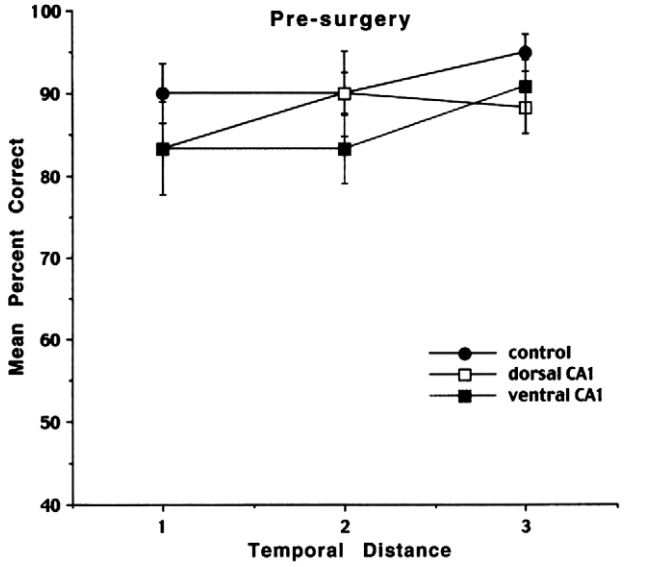

Fig. 2. Mean percent correct performance of control, dCA1 and vCA1 lesioned rats on pre-operative trials as a function of temporal separation. The temporal separation represents the number of odors that occurred between the choice odors in the sample phase. Note there are no differences between groups.

that there were no significant differences among the groups $F(2, 15) = .87$, $p = .44$, no significant differences across temporal separation $F(2, 30) = .077$, $p = .47$, and no significant interaction between groups and temporal separation $F(4, 30) = .70$, $p = .60$. Therefore, there were no differences in performance prior to surgery. The average number of trials required to reach the pre-operative criterion was 96 (range = 76–120) for the control group, 86 (range 65–110) for the dCA1 group, and 88 (range 65–130) for the vCA1 group. A one-way analysis of variance revealed that the number of trials required for each group to reach the pre-operative criterion was not significantly different $F(2, 15) = .75$, $p = .49$.

Similar to the pre-operative analysis, the post-operative analysis for the temporal order for odors task was analyzed by grouping the 30 trials into three temporal separations with 10 observations for each distance. There were no significant differences between the two control groups and therefore they were combined into one group. Fig. 3 shows the mean percent correct performance for the control, dCA1 and vCA1 lesioned groups as a function of temporal separation for the post-operative trials. vCA1, but not dCA1 lesioned, rats showed significant deficits postoperatively compared to controls. Furthermore, there appears to be a linear increasing function of correct performance across temporal distance for the vCA1 lesioned group. The deficit appears to be large for the first position, but decreases as one increases the distance from 1 to 3. At position 3, it appears that there is no deficit relative to controls. This pattern is indicative of a temporal pattern separation gradient. To evaluate this finding further, a repeated-measures 2-way analysis of variance with lesion (control, dCA1 and vCA1) as the between group factor and temporal separation (1, 2, 3) as the within group factors revealed that there was a significant effect for groups $F(2, 15) = 3.88$, $p = .04$, a significant temporal separation effect $F(2, 30) = 7.4$, $p = .0024$, and a significant interaction between groups and temporal separation effect $F(4, 30) = 3.5$, $p = .018$. A Newman-Keuls comparison test of the group $\times$ block interaction indicated that for the 1 distance, the vCA1 group was significantly impaired relative to the control and the dCA1 group ($p < .05$) and for the 2 distance the vCA1 group was significantly impaired relative to the control group ($p < .05$). Furthermore, for the vCA1 group

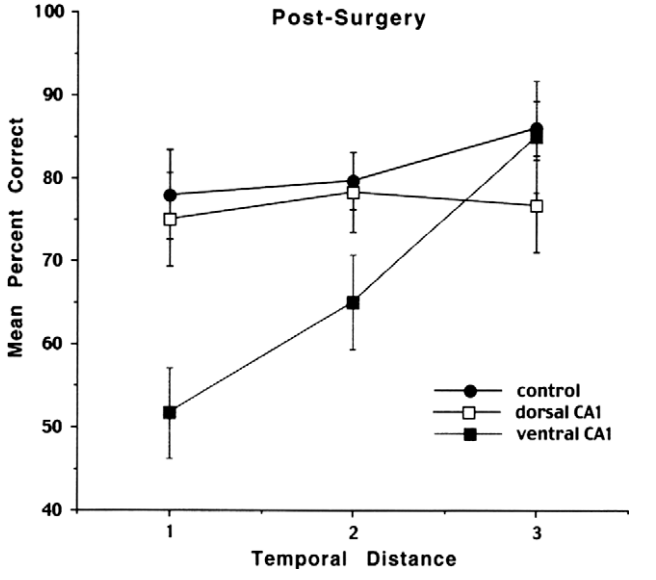

Fig. 3. Mean percent correct performance of control, dCA1 and vCA1 lesioned rats on post-operative trials as a function of temporal separation. The temporal separation represents the number of odors that occurred between the choice odors in the sample phase. Note that the vCA1 group is impaired relative to the control and dCA1 group for separations of 1 and 2, but not 3, suggesting impaired temporal ordering in vCA1 lesioned rats.

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performance for the 1 and 2 distance was significantly impaired relative to the 3 distance ($p < .05$). Thus, the data suggest that the vCA1, but not dCA1, is directly involved in processing temporal odor information. There do not appear to be any performance problems, since the vCA1 group did not have any difficulty in performing the task for a temporal distance of 3.

3.3. Discrimination task

Fig. 4 shows the number of trials required by control, dCA1 and vCA1 lesioned rats to reach a 90% correct criterion on the discrimination task based on 10 consecutive trials. The number of trials required to reach a 90% correct criterion based on 10 consecutive trials was recorded for each animal. A one-way analysis of variance revealed no significant difference in trials to criterion between the dCA1, vCA1 and the control groups $F(2, 15) = .61$, $p = .55$. Since there were no significant differences in trials to criterion between the control and hippocampal lesioned rats any deficit in performance of the temporal order olfactory task was not due to an inability to perceptually discriminate between odors.

4. Discussion

In previous research, it has been suggested that the ventral hippocampus may also be involved in supporting anxiety, hyponeophagia, and fear conditioning (Bannerman et al., 1999; Bannerman et al., 2002; Bannerman et al., 2004; Gray & McNaughton, 2001; Maren & Holt, 2004; Rogers, Hunsaker, & Kesner, 2006; Yoon & Holt, 2007) and that in some tasks both the dorsal and ventral hippocampus may participate in similar processing of information based on their respective inputs (Rudy & Matus-Amat, 2005). The purpose of the present study was to determine whether another contribution of the ventral hippocampus and more specifically the ventral CA1 subregion of the hippocampus would be to support the temporal processing of odor information. Furthermore, it was of interest to determine whether the dorsal CA1 could support temporal processing of odor information. Indeed, the present data showed that ventral CA1, but not dorsal CA1, lesions disrupt temporal order memory (temporal pattern separation) for odor information. These data provide important evidence to suggest that the ventral CA1, but not dorsal CA1, mediates temporal order for odors. The further implication of this finding is that the animals with control or dorsal CA1 lesions did not show deficits for temporal ordering for odors as a function of temporal separation. Not only did the ventral CA1 lesioned animals show deficits relative to the other two groups, the extent of the deficit was a linear function of the temporal distance between the odors presented—with the largest deficits at the more adjacent separations. These data quite strongly suggest that the ventral CA1 supports temporal pattern separation. When one compares the present study with the Gilbert et al. (2001) study, it is important to note that the shape of the graph for spatial and temporal distances are similar, suggesting that temporal distance may be analogous to spatial distance in that both are mediated by a pattern separation process.

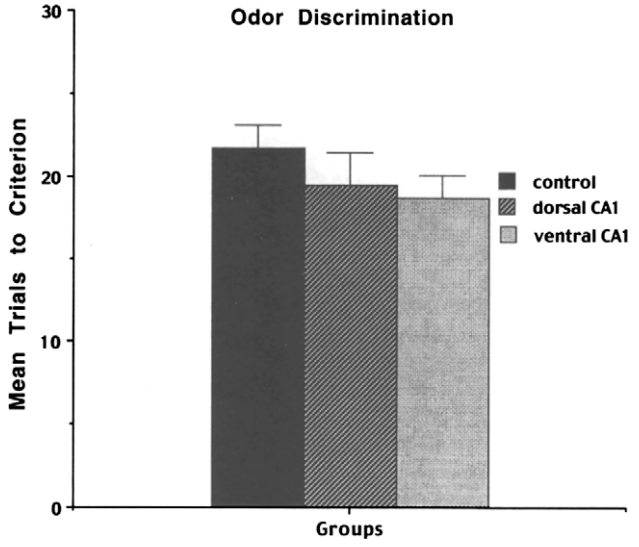

Fig. 4. Mean number of trials to criterion required by control, dCA1 and vCA1 lesioned rats to reach a 90% correct criterion on the discrimination task based on 10 consecutive trials. Note that there are no differences between groups, suggesting intact olfactory perception.

The ventral and dorsal CA1 lesioned rats showed normal odor discrimination suggesting that the deficit could not be due to a problem in odor information processing. Also, the observation that ventral CA1 lesioned rats could perform the temporal odor task with the longest lag suggests that the ventral CA1 lesioned rats do not have difficulty in using the temporal order rule and thus do not seem to have difficulties because of motivational problems.

Additional data supporting the idea that the ventral hippocampus and especially ventral CA1 may be critical for temporal processing of odor information comes from the findings of Hunsaker et al. (2008) who showed that when ventral and dorsal CA1 lesioned rats were tested on two temporal ordering paradigms based on exploratory behavior with olfactory stimuli or spatial locations, the rats with ventral CA1 lesions showed significant deficits for the temporal ordering of olfactory information relative to control and dorsal CA1 lesioned animals. In contrast, rats with dorsal CA1 lesions showed a significant deficit for the temporal ordering of spatial locations relative to control and ventral CA1 lesioned animals. These data suggest that both dorsal CA1 and ventral CA1 contribute to temporal ordering processes. These data also suggest that dorsal CA1 and ventral CA1 are dissociable for temporal ordering based upon the nature of the information that is processed and that ventral CA1 is capable of processing olfactory information into a temporal code that can be recalled, whereas dorsal CA1 is not critically involved for this processing (although dorsal CA1 does show some neural activity related to this temporal ordering; Manns, Howard, & Eichenbaum, 2007). This report supports previous anatomical models suggesting that the dorsolateral band of the entorhinal cortex, which carries olfactory information from olfactory and perirhinal cortices, projects to the ventral hippocampus more robustly than to the dorsal hippocampus (Kerr, Agster, Furtak, & Burwell, 2007; Steffenach, Witter, Moser, & Moser, 2005; Witter, Wouterlood, Naber, & van Haeften, 2000). Furthermore, the ventral CA1, but not the dorsal CA1, subregion of the hippocampus projects to the olfactory bulb (Gulyas, Toth, McBain, & Freund, 1998; Van Groen & Wyss, 1990). Additional data supporting a greater involvement of the ventral hippocampus compared to the dorsal hippocampus in processing odor information comes from the findings demonstrating that context conditioning to cat odor in rats resulted in decreased freezing following ventral, but not dorsal hippocampal lesions (Blanchard, Canteras, Markham, Pentkowski, & Blanchard, 2005; Pentkowski, Blanchard, Lever, Litvin, & Blanchard, 2006). As a control it was shown that exposure to a cat had no deleterious effects on freezing for either ventral or dorsal hippocampal lesioned rats (Pentkowski et al., 2006). Also, based on fMRI data for processing odor information, there was greater activation of the ventral compared to the dorsal hippocampus in mice and anterior compared to posterior hippocampus in humans (Cerf-Ducastel & Murphy, 2001; Kent, Hess, Tonegawa, & Small, 2007). Thus, there is a good possibility that the ventral hippocampus supports processing of odor information (Cerf-Ducastel & Murphy, 2001; Kent et al., 2007; Pentkowski

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et al., 2006), and especially for temporal processing of odor information (Hunsaker et al., 2008), whereas the dorsal hippocampus supports processing for spatial information (Moser & Moser, 1998; Rolls & Kesner, 2006) and especially for temporal processing of spatial information (Hunsaker et al., 2008).

Acknowledgments

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