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이 논문을 이학석사 학위논문으로 제출함

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이 지 현

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Hippocampal functions in contextual disambiguation of choice behavior

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Advisor

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A Thesis for M.S. Degree in Sciences in BCS

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Abstract

Hippocampal functions in contextual disambiguation of choice behavior

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The role of hippocampus is well established in contextual information processing. The term ‘context’ has been broadly used and it has been difficult to specify the role of the hippocampus in context. In the current study, defining context as ‘visual background’ we have examined the hippocampal role specifically in context using 2D image patterns. We designed a novel task by using an array of monitors, presenting the context on the center touchscreen monitor. Rats learned to resolve the ambiguity of the choice behavior. In another words, rats learned to choose between the two identical response boxes and the context made it clear for the rats to touch which one was the correct choice in the trial (e.g. zebra pattern- touching the left response box; pebble pattern- touching the right

response box). Inactivation of dorsal hippocampus severely impaired the performance of the rats. When the same rats were trained to discriminate the 2D patterns on the T-maze using the same apparatus, hippocampal inactivation showed no significant deficit. The results suggest that hippocampus is important for using visual patterns as a cue but not as a direct target. This new design of task showed for the first time that 2D image patterns can serve as a background but not as a target stimuli and influence on choice behavior in rats. Hopefully the current behavioral paradigm will leave the door open to investigate the contextual information processing in the hippocampus further.

Keywords:

Context-cued response selection, hippocampus, context, 2D image, pattern discrimination

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Contents

Background

In behavioral tasks, when an animal is trained, the animal learns the appropriate behavior with its associated environment. While doing so, visual processing is an inevitable process. Place cells are a good example of showing that rat's visual perception of the environment can influence the hippocampus. Muller and Kubie (1987) discovered changes in the activation of place cells induced by changing cue card on the wall of the recording chamber. Similar examples were found showing that by changing the sensory stimuli provided the hippocampal activity was modified as well. Lee et al. (2004) recorded CA1 and CA3, the subfields of the hippocampus, cell firings by rotating the local cues and distal cues. Even in the virtual environment, hippocampus can still perceive the visual information. Robust cell firings were examined by the intracellular recording in a head-strained mice running on the spherical ball in a virtual linear track made of different textures on the wall (Harvey et al., 2009; Dombeck et al, 2010). These cell activities were comparable to those patterns seen in reality.

It seems the hippocampus can perceive the visual information but how it is processed in the hippocampus is not clear yet. A novel behavioral paradigm has been developed by Kim and Lee (2011). The role of the hippocampus in processing contextual cue information was done in a more controlled manner. Specifically, rats learned to associate the spatial configurations of distal cues with a correct food well on a center arm of the radial arm maze. When the hippocampus was lesioned, rats failed to retrieve the

association. In other similar studies (Lee et al., 2004; Anderson and Jeffery, 2003), rats were required to alter their responses according to the contextual cues provided per trial. Prusky et al. (2004) tested the hippocampal lesioned rats' ability to discriminate 2D visual stimuli presented on a monitor screen. Rats were reinforced to choose the correct stimuli by swimming towards a submerged platform located in front of the correct 2D stimuli. In human studies, six patients with medial temporal lobe lesions (four patients limited to hippocampal lesions) were assessed with a difficult visual perceptual discrimination task (Shrager et al., 2006). Across the experiments they conducted, the patients performed as well as healthy controls. These findings demonstrate that the hippocampus is important for contextual information processing but does not play a major role in visual discrimination.

It was originally proposed by Hirsh (1974) that 'contextual retrieval' is dependent on the hippocampus. By 'contextual retrieval', when a cue occurs, the stimulus-response (S-R) association is regained. However, the cue itself does not share any component with S-R association. As described in Hirsh's paper, the internal status (i.e. hunger or thirst) can also act as a cue for retrieving the pre-learned behavior resulting in obtaining the food or water. Since then, contextual retrieval hypothesis has been investigated thoroughly and it appears that hippocampus processes various types of context. The term 'context' was used spatially (Kim and Fanselow, 1992; Maren et al., 1997; Anderson et al., 2006; Rajji et al., 2006), and temporally (Manns et al., 2007; Ginther et al., 2011). Also the term context was used to mean task demand or motivation states (e.g. hunger, thirst) rather than spatial environments (Kennedy and Shapiro, 2004; Smith and Mizumori 2006).

It is evident that the hippocampus processes contextual information. However, the manipulations of traditional contextual studies have few components to be clarified. For example, when the environment consists of multiple sensory cues (Anderson and Jeffery, 2003; Cressant et al., 2002; Honey and Good, 1993; Ji and Maren, 2008), it is hard to clarify which cue in the environment will be picked up by the hippocampus as contextual information. Also, it is practically impossible to switch the contexts (odors, cue cards, extra-maze cues, different rooms, etc) flexibly trial-by-trial while maintaining the other environments the same. Furthermore, hippocampus is known for discriminating or generalizing similar contexts but with traditional manipulation using unspecified mixture of cues, it is difficult to control the level of ambiguity of the context accurately.

For these reasons, in the previous studies, we have designed a novel task, periphery visual context-cued response selection (pVCRS) task. In this study, context was defined specifically as a 'visual background' that helps disambiguating the animal's choice behavior. By delimiting the term context, it will allow us to clarify the hippocampus' role in those situations, because only the visual patterns presented on the screen served as a contextual cue. First, the context should not be a direct target of the response. This concept is in line with Hirsh (1974)'s proposal that the 'context' should provide the conditional cue to retrieve the goal-directed response. Second, the context should remain as a background. Finally, the context should be relatively large in size. In another words, the context should not be treated as an object. In the pVCRS task (Fig. 1A), one of the patterns (zebra, pebble patterns) presented on the periphery LCD monitors was associated one side of the response box that was presented on the center touchscreen monitor (e.g. zebra-left response box, pebble-right response box). When the correct

response was made, the reward was given. When hippocampus was inactivated with muscimol (MUS) the performance was severely impaired compared to the control (saline)(Fig. 1B). The response latency showed no significant differences between the SAL and MUS conditions showing no motor deficits (Fig. 1C).

In the pVCRS task, since the context and the response boxes were apart, there was a possibility of a small delay between the identifying the pattern and the response. First, the rat identifies the context when it comes out of the startbox. Then it needs to hold the memory of the context until it touches the touch screen because the response boxes and the periphery contexts are apart. This delay could serve as a critical factor contributing to the impairments in pVCRS task when the hippocampus was inactivated. It has been known that hippocampal impairments are sensitive to non-overlapping events (Rawlins et al., 1985). In order to eliminate the possibility of holding the memory 'on-line' from identification of the context to the response, the center visual context-cued response selection (cVCRS) task was designed. The context was moved to the center monitor behind the response boxes and the response according to the context remained the same as in the previous task. Nonetheless, rats failed to respond correctly based on the presented context when the hippocampus was inactivated. Since the performances of the rats in VCRS tasks were impaired, we tested if the deficiencies were due to the impairments in discriminating between the two patterns. By using T-maze, we trained the rats to learn to discriminate between the two patterns. The performance was not disrupted with hippocampal inactivation.

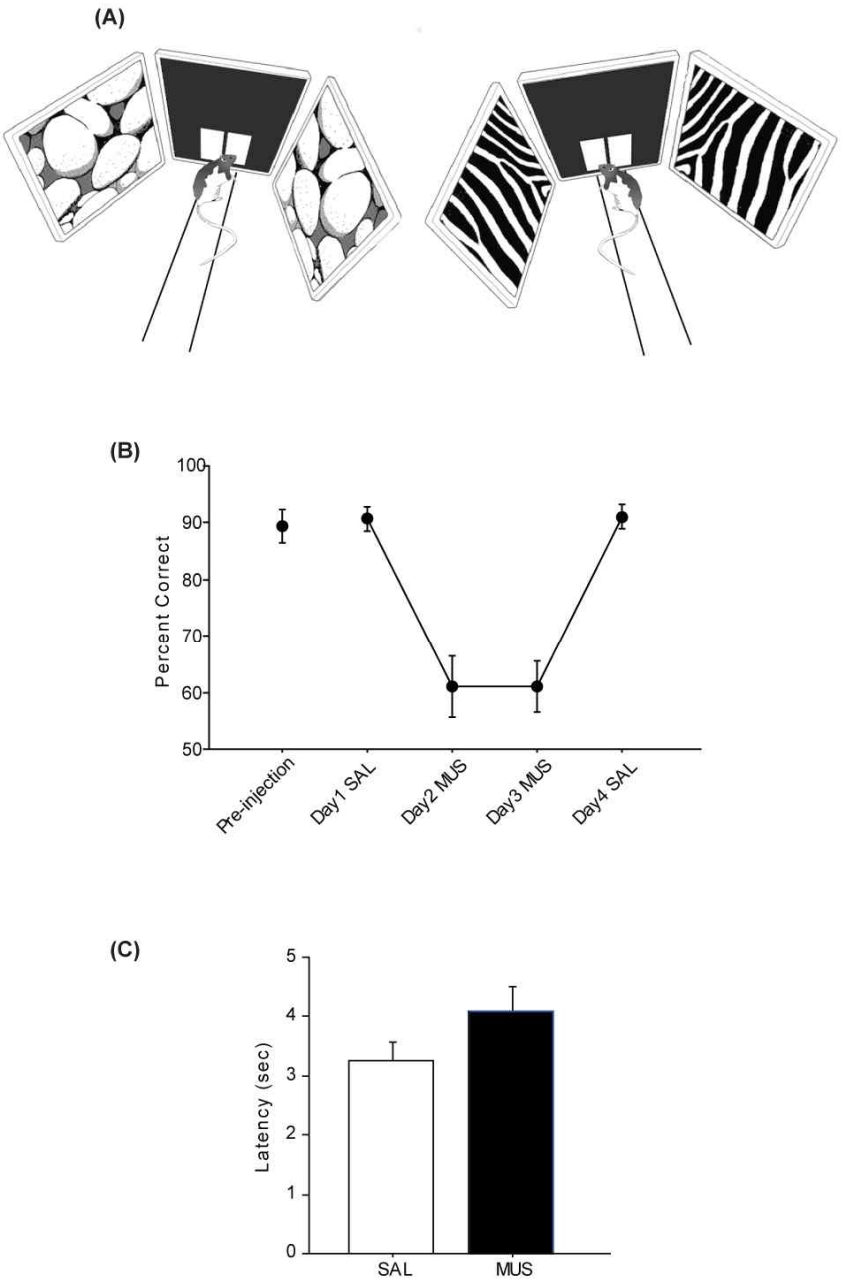

Figure 1. Peripheral visual context-cued response selection (pVCRS) task. (A) As a trial begun, the rat exited the start box (not shown) and traversed along the linear track. The track was surrounded by an array of LCD monitors. Periphery monitors were used to present a visual context and center touchscreen presented two response boxes. The rats were required to touch one of the response boxes (right-pebble pattern, left- zebra pattern) which was associated with visual context presented. (B) A percentage correct performance in pVCRS task. Before the injection (pre-injection), the rats were retrained to the criterion and showend no significant difference with SAL condition. The

performance dropped with MUS injection. (C) The latency from exit of the startbox to the touch response. There was no significant difference between SAL & MUS conditions. All graphs show means ± SEM.

Materials and Methods

Subjects

Six rats (Long-Evans, male, 250-400 g) were used. Upon arrival, rats were housed individually in Plexiglas cages in a temperature and humidity-controlled environment. All animals were maintained on a 12h light/dark cycle. Each rat was allowed to access to water ad libitum and food-deprived to 80% of its free-feeding weight for behavioral testing. Before handling, rats were given 2 weeks to acclimate to the environment. All protocols conformed to the NIH guide for the Care and Use of Laboratory Animals and the Institutional Animal Care and Use Committee of the Seoul National University.

Behavioral apparatus

Rats were trained on an elevated linear track (43×8 cm; 84 cm above the floor) with a rectangular start box (15×22×39 cm) at one end and an array of LCD monitors (elevated 13 cm from the linear track surface) at the other end (Fig.1). A 15-inch LCD monitor (AccuSync L154F0 TFT model, NEC; maximum viewing angle = 120° horizontally and 90° vertically) in the center and two 17-inch LCD monitors (Syncmaster MC17PS model, Samsung; maximum viewing angle = 160° horizontally and 90° vertically) on both sides were installed as an array with the midline of the center monitor aligned with the midline

of the track. The angle made by the lateral edges of the center monitor and it's adjacent peripheral monitor's was 98°. The center monitor's bottom was tilted upward at 13° angle and each peripheral monitor's bottom was tilted downward at 10° for providing best viewing angles for visual stimuli to the rats. The center monitor was equipped with a touchscreen panel (Elo TouchSystems, Menlo Park, CA) to register a touch response using infrared beams. All monitor's refresh rates were set at 60Hz. A transparent Plexiglas panel (35.4×27.3×0.15 cm) with two rectangular openings (each 6×10 cm) each serving as a response window was attached to the touchscreen panel. During the task, two white rectangular images ('response box' hereafter, each 4.6×8.6 cm, RGB value 255-255-255; 0.2 cd/m^2) were presented on black background (RGB value 30-30-30) in alignment with the response windows in the center monitor (Fig.1) and the rats touched either response box to indicate their choices. A food tray was installed below the center monitor and the rats retrieved a ball-shaped cereal reward from the tray during the task. There were three optic fiber sensors (Autonics, Busan, Korea) installed along the track (at both ends and in the middle of the track). Breakage of each sensor beam was registered via a data acquisition board (SCB-68, National Instruments, TX) interfaced with a PC. The PC was equipped with a high-performance multi-view graphic card (Firepro MIV 2450, ATI). Custom-written software using Psychtoolbox (Brainard, 1997; Pelli, 1997) in Matlab (Mathworks, Natick, MA) controlled stimuli and registered touch responses as wells as sensor times. The apparatus was located in a sound-attenuating room and a digital CCD camera was positioned above the apparatus for recording behavioral sessions. A halogen light was installed immediately adjacent to the CCD camera for illuminating the room at 0.2 lux. Two loud speakers were placed in the behavioral testing room for providing white

noise (80 dB) during behavioral testing.

Handling, familiarization and shaping

Naïve rats (250~400g) were handled approximately a week before shaping procedures began. On the first day of handling, rats were handled for 20 min to become acquainted to the experimenter. From the next day, the rats were handled 10 min and freely foraged for cereal for 20 min to become familiar with the food reward. That is, the rat was placed on a laboratory cart (outside the behavioral testing room) and several pieces of cereal were scattered randomly on the cart (78×44×83 cm). When the rat readily consumed multiple pieces of cereal, a shaping period began. During the shaping period, the rat was first familiarized to the apparatus and the testing room by letting the rat freely eat cereals scattered along the track. Afterwards, the animal was trained to touch one of the response boxes on the touch screen panel to obtain a reward with a sound feedback (2 kHz, 3 s, 83 dB). When rats failed to touch a response box, an error sound (0.2 kHz, 3 s, 83 dB) was given and the animal was guided back to the start box without any reward. Each shaping period ended after either 50 trials or 30 min, whichever came first, and the whole shaping procedure lasted for 5 days.

Behavioral Pre-training

Six rats were used in central visual context-cued response selection (cVCRS) task and

visual pattern discrimination (VPD) task. A within-subjects design was used in each group throughout the study.

Central visual context-cued response selection (cVCRS) task

In the cVCRS task, rats (n=6) were required to touch one of the response boxes in association with the visual patterns presented on the center screen (Fig.2). Unlike the pVCRS task, visual stimuli were not presented in the peripheral LCD monitors. The same visual contexts (i.e., zebra and pebbles patterns) that were used in the pVCRS task were presented in a pseudo-random order. Each trial began by presenting one of the visual contexts overlaid with response boxes on the center screen and then by opening the start box. Three rats were assigned to touch the left response box when the zebra pattern appeared and the right response box for the pebbles pattern for obtaining reward. The other three rats followed the opposite stimulus-response contingency. A correct response resulted an immediate sound feedback (2 kHz, 3 sec, 83 dB) followed by a reward in the food tray, while a wrong response initiated an error sound (0.2 kHz, 3 sec, 83 dB) with no reward. No correction was allowed once an incorrect response was made. An intertrial interval of 4 sec was given after a correct trial but a longer intertrial interval (15 sec) was imposed after an incorrect response before the next trial began. Fifty trials were given within a session. Each visual context appeared an equal numbers of times within a session and the presentation sequence of the contexts was pseudo-randomized. When the rat showed ≥75% correct performances for both scenes for two consecutive days, it was considered ready for implantation surgery for bilateral cannulae in the hippocampus. It

took 11 to 20 days (mean =16.5) for the rats to reach performance criterion. In addition, the latency from the presentation of the visual context until the rat touched the touchscreen was measured via fiber optic sensors.

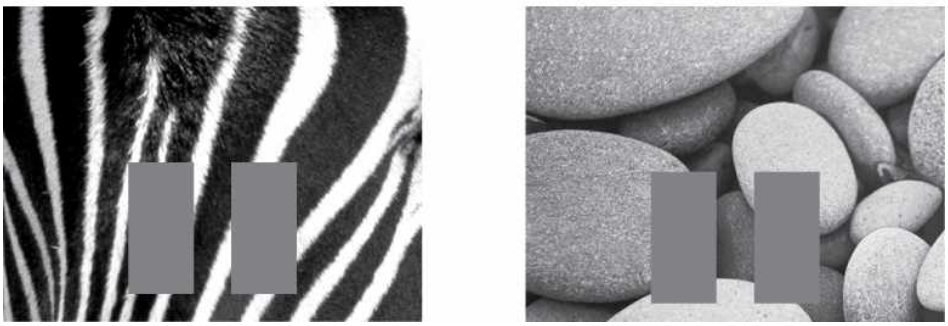

Figure 2. Patterns presented on the center monitor in the visual context-cued response (cVCRS) task. In the same apparatus that was used in Fig.1, the patterns were presented on the center monitor instead of the periphery monitors.

Surgery

Each rat was deeply anesthetized with isoflurane (4% mix with oxygen at a flow rate of 1 L/m) in an induction chamber, followed by an injection of Nembutal (70 mg/kg). The animal was placed in a stereotaxic instrument. The anesthesia was maintained by isoflurane (1-3%) throughout surgery. The skull was exposed and adjusted to place bregma and lambda on the same horizontal plane. After small burr holes were drilled, two sets of 26G guide cannulae (Plastics One, Roanoke, VA) were implanted bilaterally

into the dorsal hippocampus (3.9 mm anterior to bregma, 2.6 mm lateral to midline, 3.0 mm ventral from the skull surface). The cannulae were secured in place with anchoring screws and dental cement. A 32G dummy cannula was inserted into each guide cannula to prevent clogging. Rats were allowed to recover for 7 days.

Intracranial microinjection

After backfilling 10 μL syringe (Hamilton, Reno, NY) with mineral oil, 33G injection cannula was connected via polyethylene tubing (PE-20; Becton Dickinson). Either MUS or SAL was injected at the rate of 10 μL /h using a micro-infusion pump (KD Scientific, Holliston, MA). For injection, after dummy cannulae were moved, an injection cannula extending 1mm below the tip of the guide cannula was inserted. Sterile saline (SAL) was used for control conditions. A GABA-A receptor agonist, muscimol (MUS, 0.5 μg /0.5 μL) was bilaterally injected to temporally inactivate the dorsal hippocampus. The injection cannulae were left in place for an additional 1min to ensure a proper diffusion. The rat was returned to its home cage and was examined for any abnormal movement for 20 min before the actual task began.

Post-surgical behavioral paradigm

Testing performance in cVCRS task

After a week of recovery period, the rats were retrained to criterion (≥75% correct

performance for both scenes) in the cVCRS task. Then, the drug injection schedule of SAL-MUS-MUS-SAL began with a within-subject design for 4 consecutive days.

Testing performance in VPD task

After the rats finished postsurgical testing in the cVCRS task, the same rats were trained in the visual pattern discrimination (VPD) task. The rats discriminated between the two visual patterns which were used in the pVCRS and cVCRS task. The VPD task was conducted on a T-maze (35x35x7 cm) made of black Plexiglas. The T-maze was placed in the middle of the LCD monitor array of the same behavioral apparatus used in the VCRS tasks. A food well (2.5 cm in diameter and 0.5cm in depth) was located at the end of each arm of the T-maze and the food wells were always covered with small metal discs (each 3.5 cm in diameter). The food well of each arm of the T-maze was positioned in front of the peripheral LCD monitors (distance between the food well and the peripheral screen = 16.5 cm) and the rat could retrieve a piece of cereal (Froot-Loops, Kellogg's) by displacing the disc over the food well. On the first day of acquisition, the food wells were intentionally left half-open to show the food reward to the rats and the animals quickly learned to displace the overlying disc to retrieve the rewards. On the second day, the rat was forced to turn to a certain arm on each trial because access to a randomly chosen arm was blocked with a heavy plastic block (4.9×4.8×7.9, 477g). From the third day onwards, rats were trained in the VPD task. Specifically, the visual patterns were presented in both peripheral monitors (i.e., the zebra pattern for one of the monitors and the pebbles pattern for the other monitor). The task for the rat was, once released from the start box and

entering the stem of the T-maze, to simply enter the arm associated with the peripheral monitor showing the visual pattern that was associated with reward (Fig. 4A). The center monitor was not used and only showed dark gray screen (RGB values 30-30-30). In a given behavioral session (50 trials), each visual pattern appeared an equal number of times with equal probabilities of appearance in both monitors. The rewarding visual pattern was counterbalanced among rats. Latency was measured from the start box to the moment the rat displaced the disc by a stop-watch. Once the rat acquired the task to criterion (≥75% correct performances for both arms over two consecutive days), the same drug injection schedule (SAL-MUS-MUS-SAL) started for 4 consecutive days.

Histology

After the completion of all behavioral experiments, cannula positions were histologically verified. For this purpose, the rat was killed by the inhalation of a lethal dose of CO_2 followed by a transcardial infusion of 0.9% saline and a 4% formaldehyde solution. The brain was then extracted and stored in a 4% formalin-30% sucrose solution at 4°C for 48h. The brain was frozen and cut in coronal sections (40 μm) on a sliding microtome (Thermo Fisher Scientific, Waltham, MA). The sections were then Nissl-stained with thionin (Sigma, St. Louis, MO), and examined under the light microscope. Only the rats with cannula tips located bilaterally within the dorsal hippocampus were included in the final data analysis.

Results

Histological verifications of cannula positions

A representative photomicrograph showing cannula tracks through the dorsal hippocampus is shown in Figure 3. The cannula-tip positions of all rats were identified within the dorsal hippocampi.

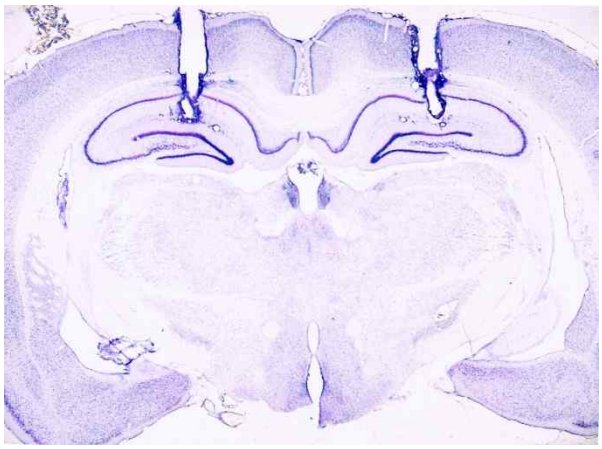

Figure 3. A representative photomicrograph showing the tracks of bilateral cannulae in the dorsal medial hippocampus

Inactivation of the dorsal hippocampus impairs visual contex-cued response

When SAL was injected rats (n=6) on average performed over 85% (Fig.4A). However, when MUS was injected for two consecutive days the rats were severely impaired. When SAL was injected on the last day of injection schedule, impaired performance recovered to the previous SAL condition performance. The repeated measures of ANOVA showed that the drug condition had a significant effect ($F_{(3,15)}$ =54.663, $p<0.0001$). Post-hoc comparisons (Tukey-Kramer) showed all SAL injection showed significant differences with all MUS injections ($p<0.010$). However, there was no significant difference between pre- and post- MUS injection. Also there was no significant difference on the first day and the last day of SAL injection as well. To see whether there was a mobility disorder when MUS was injected, the response latency during SAL and MUS injection showed no significant differences in performance ($F_{(3,15)}$ = 1.018, n.s.) (Fig.4B). We also calculated the bias by | # of left choice trials – # of right choice trials | / total trials. So if the rat chose only one side during the task the bias would be 1 and both sides evenly, the bias would be 0. The bias in SAL conditions stayed below 0.15 but the MUS conditions stayed over 0.5. By using repeated measures of ANOVA, there was a significant effect of drug-injected condition ($F_{(3,15)}$ = 12.644, $p<0.001$). The post-hoc comparison (Tukey-Kramer) showed significant differences between all SAL and MUS conditions ($p<0.050$). However, there was no significant difference between first day of SAL and the last day of SAL. Also the pre- and post-condition of MUS had no significant difference. The results strongly suggest that hippocampus is critical for visual context-cued response.

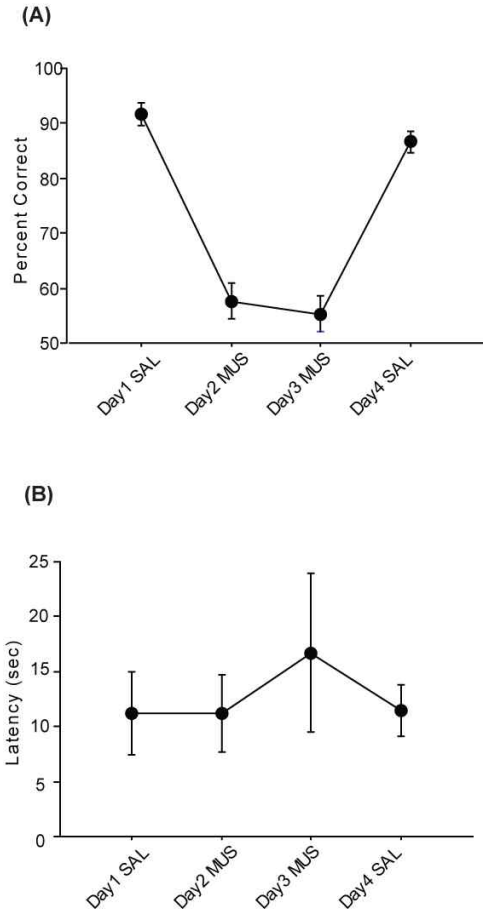

Figure 4. Effects of drug injection in the cVCRS task. (A) The drug injection showed a significant effect on the performance. The performance dropped when MUS was injected. (B) Latecy from the presentation of the context to touch response. There was no significant effect of drug conditions. All graphs show means ± SEM.

Hippocampus is not necessary for discriminating visual patterns

In the VPD task, the visual cues in cVCRS task were modified as a background image of

the responses reducing the distance between the response location and the context. In the VPD task, we examined if the MUS condition impaired discrimination ability by using a T-maze (Fig 5A). The average performance of rats during the injection schedule all stayed above 80% (Fig 5B). Concretely, rats showed over 95% average performances when SAL was injected. Due to this high performance of SAL, there was a significant effect of drug condition ($F_{(3,15)}$ =3.590, $p<0.050$). However, post-hoc comparisons (Tukey-Kramer) showed SAL and MUS had no significant differences ($p>0.050$). As in VCRS task, the response latencies were not significantly different between SAL and MUS conditions (Fig.5C). When the bias in VPD task was checked by repeated measures of ANOVA, it showed that drug-injection had significant differences ($F_{(3,15)}$ = 3.968, $p<0.050$). However, the post-hoc comparison (Tukey-Kramer) showed significance only for the last day of SAL and the second day of MUS. However, overall bias throughout the injection schedule stayed below 0.15. Considering in VPD task, the bias for SAL condition was below 0.15 and MUS being over 0.5, bias in VPD task was minimal. Overall, these results suggest that hippocampus is not required for discriminating visual patterns but might be involved in associating the context (background) and the response.

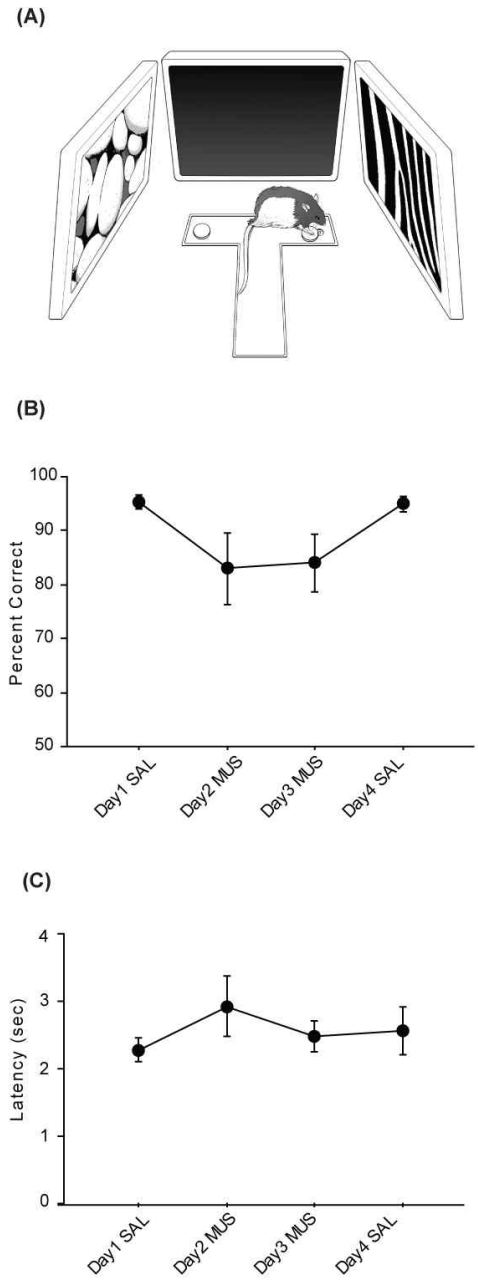

Figure 5. Effects of hippocampal inactivation in visual pattern discrimination (VPD) task. (A) Two different 2D images (i.e. zebra and pebble) were presented on each periphery monitors. On the T-maze, rats removed the disc covering the food well. In this figure, only zebra pattern was rewarded. (B) The mean performance during the injection schedule stayed above 80%. (C) There was no significant effect of drug injection on latency. All graphs show means ± SEM.

Discussion

In this paper, context is defined as the 'visual background' but not the stimulus itself. In the cVCRS task, we used 2D visual patterns as contextual cues for rats to choose one of two response boxes. Since the context was presented on the center monitor as a background to the response boxes, there was no spatial discontiguity between the context and response boxes as it was in the pVCRS task. However, the results of cVCRS task show that the location of the context wasn't the main cause for impairing the performance. Overall, the results show that hippocampus is indispensible in selecting the correct response based on the context.

The results from the control task, the VPD task, suggested that the rats were able to discriminate visual patterns from one another without any associations involved in the task. The results (Fig. 5B) showed that drug injection had a significant effect. However, this is due to the high performance of the rats in the SAL injection trials. Considering the minimum performance criterion of learned tasks is 75%, over 95% correct performance of VPD task suggest that VPD task was simpler compared to VCRS task. In MUS injection trials, the mean performance stayed above 80%, which is above the criterion for high correct performance. Furthermore, compared with cVCRS task results, it is difficult to conclude that performance was impaired. It can be concluded that the impairment was specifically involved in the associating the response and the context rather than discriminating the visual patterns.

It has been previously demonstrated that rats can visually discriminate visual patterns (Lashley, 1930; Tolman, 1948) and even 2D pictures of objects and patterns (Prusky et al., 2004; Forwood et al., 2007; Bussey et al., 2008). However, to our knowledge, Prusky and colleagues were only the group that tested visual discrimination of 2D images by the hippocampus. In their delayed, matching-to-sample (DMTS) task, black-and-white pictures were displayed on the monitor and rats swam toward the monitor in a modified water maze. Hipocampal lesioned rats showed significant impairments compared to control although the performance stayed around 80% correct with minimal delays and began to fall to 70% from 1min. In their DMTS task, 2D image served as a direct target as it was in our VPD task and the results as well support our results as well.

The overall results were in line with the results from Kim and Lee (2011) that dorsal hippocampal lesions severely impaired the selecting of the correct response based on the context. The difference between the two studies was the definition of context and how it was manipulated in the experiment. The concept and definition of 'context' has been used very broadly used (Hirsh, 1974; Kim and Fanselow , 1992; Maren et al., 1997; Anderson et al., 2006; Rajji et al., 2006; Manns et al., 2007; Ginther et al., 2011; Kennedy and Shapiro, 2004; Smith and Mizumori 2006). However, in this study the definition of context will be limited to 'visual stimuli'. For example, among the studies discussed in the introduction, the cue card that has been used in the Muller and Kubie study (Muller and Kubie 1987) will not be considered as a context for the purpose of this study. The cue itself can be considered as a foreground cue instead of background cue depending on rats' position. In addition, the 2D visual stimuli that was used in delay match-to-sample

(DMTS) task (Prusky, 2004) is unlikely to be called context as well because it is used as a direct stimulus which the rat was required to swim towards to in the task. In order to be fit the definition of context as defined here, it will be needed to work as a background and convey information that would act as a cue to solve the goal directed task.

Also in the previous study (Kim and Lee, 2011), the context was manipulated by varying the angular distances between the distal cues. However, in our study the context was manipulated as 2D image. To our knowledge, this is for the first time to demonstrate 2D images as a visual background removing the critical ambiguity of the target. The advantage in these virtual testing environments as opposed to the previous contextual studies is that the experimenter can limit the stimulus which subjects receive. Also by using a virtual testing environment, the onset and offset of the stimuli can be precisely controlled and the stimulus features can be parametrically manipulate. Comprehensively, our study demonstrated that hippocampus is critical in associating the response with the context and no significant role in simple visual pattern discrimination which is in line with prior studies (Prusky et al., 2004; Kim and Lee, 2011).

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국문초록

선택적 행동에서의 맥락적 모호함을 해결하는 해마의 역할

(Hippocampal functions in contextual disambiguation of choice behavior)

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맥락적 정보 처리(contextual information processing)에서의 해마의 역할을 잘 알려져있다. 하지만 '맥락(context)'의 정의는 매우 폭 넓게 사용되고 있으며, 이것은 맥락에서의 해마의 역할을 구체화하는 것을 어렵게 하고 있다. 따라서 현 연구에서는 맥락을 '시각적 배경'이라고 정의하고, 2D 이미지를 이용하여 맥락에서의 해마의 역할을 조사하였다. 중앙에 위치하고 있는 터치 스크린 모니터에 두 개의 동일한 반응 타깃 뒤에 시각적 배경을 띄운 뒤, 쥐들은 시각적 배경(e.g. 얼룩말 무늬, 조약돌 무늬)에 따라 두 개의 동일한 반응 타

깃을 골랐다. 즉, 맥락은 선택적 행동의 모호함을 해결한다. 예를 들자면, 얼룩말 무늬가 중앙의 모니터에 나타날 경우 왼쪽을 찍음으로써, 조약돌 무늬가 나오면 오른쪽을 찍는 것으로 쥐들은 보상을 받을 수 있다. 본 연구에서, 뮤시몰(muscimol)을 투여하여 해마를 일시적으로 불활성화 시켰을 때, 쥐들의 실험 수행 능력은 현저하게 떨어졌다. 하지만 똑같은 쥐들을 티-메이즈(T-maze)에서 2D 이미지를 구별하도록 훈련 시키고 해마를 불활성화 하였을 때에는 아무런 영향이 없었다. 이러한 결과는 해마가 시각적 이미지를 단서로 사용하였을 때에는 매우 중요하지만, 직접적인 타깃으로 작용하였을 때는 중요하지 않다는 것을 제안한다. 이러한 새로운 실험 디자인은 처음으로 2D 이미지가 타깃 자극이 아닌 배경으로 작용하였을 때 쥐들의 선택 행동에 영향을 줄 수 있는 것을 보여주었다. 또한 이러한 행동 패러다임은 훗날 맥락적 정보처리에 관한 해마의 역할을 연구할 때 더 기여할 것으로 기대된다.

주요어 : 시각적 배경, 맥락, 2D 이미지, 해마, 선택적 행동
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