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大腦記憶系統間之交互作用

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□期中進度報告

大腦記憶系統間之交互作用

計畫類別：■ 個別型計畫　□ 整合型計畫
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計畫主持人： 蔡欣志
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計畫參與人員： 林俊成、顏妙綺、黃惠雯、劉又寧、蔡依凜、賴孟姍。

成果報告類型(依經費核定清單規定繳交)：■精簡報告　□完整報告

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(二)中、英文摘要及關鍵詞(keywords)**。**

Abstract

In the present study, we investigate the involvement of the pre-exposure as well as fimbria-fornix (FF) and Anterior Cingulate Cortex (ACC) in the learning of the food conditioned cue preference (CCP) in both CCP box and radial maze. Effects on rats' ability to locate food on a radial maze and CCP apparatus in situations that provided different types of information was used to suggest principles of information processing by these neural systems. The cue configurations in both box and radial maze CCP learning were modified to examine both ambiguous (adjacent arms in the maze and clear partition in the box) and unambiguous (widely separated arms in the maze and opaque partition in the box) cue situations. When animals were confined to food-paired and food-unpaired areas on different training trials, the learned discrimination in different form of learning was mediated by different neural structures determining by cues in the environment. In addition, pre-exposure had different effects on ambiguous than for unambiguous discriminations.

Keywords: Conditioned Cue Preference, Fimbria-Fornix, Anterior Cingulate Cortex, Pre-exposure

中文摘要

本研究是在探討前暴露以及腦穹及前扣帶皮質破壞對制約性線索偏好學習的影響。大鼠分別在八角迷宮及制約性線索偏好學習箱二種行為儀器中進行，每一行為儀器將變化出二種不同的學習情境：模糊線索及非模糊線索。八角迷宮的學習包括了鄰近跑道(模糊線索)及分離跑道(非模糊線索)；而制約性線索偏好學習箱則包括透明間隔(模糊線索)及不透明間隔(非模糊線索)。不同的學習情境所含的外在刺激型態變異甚大，大鼠在各階段的學習，將由腦中不同的學習記憶系統來完成。而外在線索及刺激環境型態將左右了何種神經系統將處理相關的制約性線索偏好學習。再者，儀器的前暴露對爾後的制約性線索偏好學習的影響，亦會受到外在線索及刺激環境型態等因素的影響，其相關的神經機制亦被進一步的探討 。

關鍵詞：制約性線索偏好學習，腦穹，前扣帶皮質，前暴露

(三)報告內容：

Introduction

The present study utilizes the conditioned cue preference (CCP) task to examine the effect of unreinforced pre-exposure on subsequent reinforced learning. This paradigm was used as a model to examine the interaction among multiple parallel memory systems. The CCP task usually includes three phases (White & McDonald 1993). In the pre-exposure phase rats are allowed to explore the maze or the CCP box with no food presented (unreinforced pre-exposure)(McDonald & White 1995b). In the training phase the rats were confined on the ends of the arms so that they could not move between them. Food was provided on one arm (the paired arm). The other arm is empty (the unpaired arm). In the test phase the rats were allowed to explore the maze (or the box) freely with no food present. The time spent on the two arms (or compartments) during the test was compared. If the rats spent more time on the paired arm than on the unpaired arm it was concluded that they had acquired sufficient information to discriminate between the two arm locations.

There are two versions each of the radial maze and box CCP tasks. In one version of the maze CCP, the food and no-food arms are widely separated (by 135 or 180 degrees)(McDonald & White 1995a). This is an unambiguous separate arm discrimination (SAD) because very few of the same cues are visible from both arms. This version of the CCP is usually modeled as an instance of Pavlovian conditioning which is sensitive to lesions of the lateral amygdala. The second version of the CCP procedure uses two adjacent arms of the radial maze (separated by 45 degrees). Rats can acquire the information required for the adjacent arms discrimination (AAD) if they are given sufficient unreinforced pre-exposure (Chai & White 2004). The adjacent arms discrimination that is learned when the rats move around on the maze is impaired by lesions of the fimbria-fornix, or the hippocampus, but not by lesions of the amygdala. The lesion evidence is also consistent with the idea that the two forms of CCP learning are mediated by different memory systems. Two conditions of box CCP learning were examined. In the OOO condition, the opaque partition was used in all three phases of the CCP procedure: pre-exposure, training, and testing. The OOO condition is the "standard" CCP box apparatus used in many (but not all) laboratories. Three conditions of ambiguous cue CCP learning were examined. In the CCC condition, the clear partition was used in all 3 phases of the procedure. The CCC conditions were similar to the adjacent arm CCP condition on the radial maze (McDonald & White 1995a) because the rats could see the cues in both boxes during all phases of the procedure. In the

Previous studies have shown that acquisition of the SAD is retarded by unreinforced pre-exposure to the maze, and that this effect was not eliminated by fimbria-fornix (FF) lesions as we predicted. These findings suggest that a form of learning requiring an intact FF occurs during the pre-exposure phase of the SAD and interferes with the subsequent amygdala-based learning that produces the CCP. While the same learning occurs during the pre-exposure phase of AAD and facilitates the later hippocampus-based learning. The ACC is a part of the medial prefrontal cortical systems that has been implicated in cognitive and emotional aspects of information processing (Koyama et al 2001, Buchanan & Powell 1982). Behavioural and neurophysiological data showed that the ACC was involved in processing affective information. Lesions of the ACC blocked conditioned place aversions induced by formalin injections, but not by electrical footshock (Gao et al 2004). Other evidence showed that the ACC has played a role in modulating fear conditioning (Takenouchi, Nishijo, Uwano, Tamura, Takigawa, & Ono, 1999). The ACC is also reported to be involved in the processing of both the unconditioned information and in anticipation of the incoming affective stimulus. It is possible that the linking of unconditioned stimulus and anticipatory (conditioned stimulus) stimuli may occur in the ACC. The focus of the present research is to examine several questions relating to the neural mechanisms of independent memory system and their interacting processes: a) If a "pure" form of fimbria-fornix dependent stimulus-stimulus association learning occurs during exploration of a radial maze (box CCP) with no reinforcers present, it should be possible to measure this form of learning indirectly by its retarding effect of subsequent passive SAD or OOO learning and by its facilitating effect on subsequent active AAD or CCC learning. b) If FF and some other areas of the brain other than the

hippocampus (such as the anterior cingulate cortex and medial thalamus) are important for acquisition, storage, and expression of the learning that occurs during exploration, lesions to the same parts of the brain should impair the effect of this form of learning on both indirect measures, AAD (or CCC) and SAD (or OOO).

Methods and Procedures

Subjects. 200 male Long-Evans rats were used and randomly assigned to the following group before the beginning of behavioral treatments. These animals were purchased from National Animal Breeding Center, weighing 200-250 grams at the start of each experiment. The rats were housed in individual cages in a temperature-controlled room with the lights on from 7 a.m. to 7 p.m. They had free access to water and food, except as indicated in the procedure.

Apparatus

Radial Arm Maze

An eight-arm radial maze made of wood and painted flat gray was used (see Figure 1). The maze has an octagonal center platform 40 cm in diameter. Eight arms, 60 cm long and 9 cm wide, were attached to the platform. Rectangular wooden blocks (35 x 19 x 8.5 cm) were used to obstruct six of the eight arms. Two similar blocks had wooden panels (31 x 28.5 cm) attached to the end farthest away from the center of the maze. These blocks were used to restrict the rats to their assigned paired and unpaired arms on the training days of the CCP task. The maze was located in the center of a windowless 2.9 x 2.9 m room that contains a variety of distal cues. A TV camera was suspended from the ceiling above the center of the maze. The camera was connected to a monitor in a room near the testing room.

Conditioned Cue Preference Box

Two 3 compartment conditioned cue preference boxes were used (see Figure 2). The boxes were made of wood with Plexiglas front walls. Two of the compartments were identical in size (45x45x30cm). One of these compartments was painted gray, and the other was painted with vertical black and white stripes. Both compartments had wood chips on the floor, which were replaced before each trial for each rat. The gray compartment was on the left side of one of the two boxes used, and on the right side of the other box. The two compartments were divided by either a clear plexiglas partition or an opaque wooden partition. The partitions were interchangeable. The third compartment was an unpainted tunnel (36x18x20cm) protruding from the rear of the two large compartments connecting their entrances, which were located at the back of both compartments next to the partitions.

Electrodes

Nichrome electrodes (0.25 mm in diameter) with enamel insulation were used for electrolytic lesions. The insulation at the tips of the electrodes was removed with Strip X (GC Electronics).

Surgery

All lesions were stereotaxically placed, bilaterally, with coordinates based on Paxinos and Watson (1998) measured in relation to bregma and the skull surface, using standard stereotaxic techniques (Paxinos & Watson 1998).

Radiofrequency lesions. Groups of rats receive bilateral radio-frequency lesions at fimbria-fornix or only sham lesions or other brain areas according to the requirement of the experiment. At the beginning of the surgery, each rat was placed, flat head, in a sterile stereotaxic instrument under chloral hydrate anesthesia (450mg/kg). Then the skull was drilled, and the dura was torn and removed. The lesions was made with a Radionics Research RF Lesion Generator System, Model RFG-4A. For the FF lesions, the electrode tip was maintained at 80°C for 30 seconds at 1.5mm posterior to bregma, ±0.8 and ±2.2 mm lateral to midline, and 1.5mm ventral of dura. For the ACC lesion, the electrode tip was maintained at 80°C for 30 seconds at 1.5mm anterior to bregma,

±0.5mm lateral to midline, and 1.5mm ventral of dura; and 2.5mm anterior to bregma, ±0.5mm lateral to midline, and 2.5mm ventral of dura for the ACC lesions; and 2.5mm posterior to bregma, ±1mm lateral to midline, and 5mm ventral of dura. The incision was then closed, and a substantial amount of penicilin (0.2 ml) was given at the end of the surgery. Rats were kept warm until recovery from anaesthesia and then were returned to its home cage. The subjects in the sham condition underwent identical procedures, except that no heat was delivered while the electrode was lowered down on the target. After surgeries, the subjects were weighed daily, and the state of postsurgical recovery was monitored for a period of one week before the start of the behavioral testing.

Controls. Control animals will not receive any surgical procedures.

Histology

After the completion of behavioral testing, the rats were deeply anesthetized with an injection of 30 % chloral hydrate and perfused with 0.9% saline follow by 10% formol-saline solution. The brains were stored in 10% formol-saline for more than a week before sectioning. Following fixation, they were frozen and cut into 30 um sections, and every fifth section through the lesion site was mounted on glass slides and stained with formol thionin.

Behavioral procedure

Handling

Handling and food deprivation of the rats begin seven days after surgery. Food was removed from all home cages. All rats were handled for 4 days before starting the CCP task. During the handling sessions, 6-8 rats were put into a large wooden handling box. After about 10 minutes, each rat was picked up in turn 5 times and handled for 1 minute each time. The rats will then be returned to their home cages where they were given two to three food pellets plus 10 pieces of Kellogg's Froot Loops cereal. The animals are weighed daily to ensure that they maintain at least 80% of their free-feeding weights. Water is freely available in all home cages.

Maze Conditioned Cue Preference

All CCP procedures involved three phases: pre-exposure, training and testing. In each phase, the experimenter placed the rat on the maze, left the room, close the door and observe the animals on the TV monitor. The maze was cleaned with germicidal detergent and deodorant Quatricide PV before each trial for each rat.

Each rat in each experimental group was assigned a unique set of radial maze arms: a food paired arm and a no food arm, the two arms assigned to each rat was either adjacent, or separate by at least two arms, to each other. The first phase is a 3 day pre-exposure phase. All rats were placed on the maze with no food present. The food and no food arms assign to each rat was open; all other arms were obstructed with the wooden blocks. Animals were placed on the center platform of the radial maze and allowed to explore the open arms freely for 10 min. The number of pre-exposure trials and the context in which they are taken place varied according to the experiment.

The second phase is the training phase. In each session, the animals were confined to the end of an arm using a wooden block. On food paired sessions, 50 Kellogg's Froot Loops are placed at the end of the arm. The rats remain on the arm for 30 min. The procedure is the same for food unpaired sessions, except that no food is placed in the arm. Half of the animals in each group were placed on their food arms on the first session, the other half were placed on the no food arms on the first session. These placements were reversed on the second day of the training phase. The two days constitute a single training trial. The number of training trials vary according to of the experiment.

The third phase was the test phase. This session is identical to the pre-exposure session except that animals are placed on the maze for 20 minutes. Both the paired and unpaired arms assigned to each subject are open, while the other arms are blocked. The time at which each rat entered and exited each arm was recorded. A rat is considered to be in an arm if its front feet cross the threshold form the center platform.

Box Conditioned Cue Preference

The procedure for the box CCP was similar to the procedure used for the maze CCP. In each phase of the experiment the partition between the two large compartments was either Opaque or Clear, depending on the requirements of the experiment.

During the pre-exposure phase, the entrances to the tunnel from the large compartments remained open. The rats were placed in the tunnel and allowed to explore the three compartments for 10 min. Half of the rats received 5 day/pre-exposure trials and the other half did not receive pre-exposure.

During the training phase, the rats were confined to one of the large compartments. For food paired sessions, 50 Froot Loops were placed in the corner of the appropriate compartment and the animals remained there for 30 minutes. For unpaired sessions, they were placed in the other large compartment with no food for the same amount of time. These two sessions constituted a single trial, and their order was counterbalanced within all groups. The number of trials was determined by the requirements of each experiment.

For the test phase, the entrances to the connecting tunnel were open. Each animal was placed in the tunnel and the times at which the rat entered and exited each compartment were recorded.

Data Analysis

In each experiment the food and no-food means for all groups were entered into a two-way, repeated measure ANOVA. The first factor was Group, with the number of levels equal to the number of groups. The second factor was Time in the paired and unpaired arms, a repeated measure with two levels. For each group the significance of the difference in time spent in the paired and unpaired locations was tested using the following formula:

$$F_{(\text{paired-unpaired})} = [\, N*(x_{\text{paired}} - x_{\text{unpaired}})^2]/[MS_{\text{Interaction}}]$$

This analysis is based on the ratio of the difference between the mean times spent in the two locations to the mean square error of the interaction term from the ANOVA. The degrees of freedom associated with the F value is N - 2 where N is the number of rats in each group. Since the comparisons were pre-planned, this statistic is considered to provide adequate protection from errors associated with multiple comparisons.

Experiment One

In this experiment, effects of pre-exposure, as well as FF and ACC lesions, on both adjacent and separate arm CCP learning in the radial maze were examined. During the pre-exposure trials, the rats were allowed to move freely between the central platform and two assigned arms. During the training phase, the rats can see only one set of stimuli during the food-pairing and no-food sessions. Therefore, only one set of stimuli is consistently associated with food during the training sessions. The other set of stimuli is consistently paired with no food. However, the rat can see the sets of environmental stimuli visible from the two arms at essentially the same time during the pre-exposure and testing phases. The hypothesis to be tested in the present experiment is that: if a "pure" form of fimbria-fornix dependent spatial learning (cognitive mapping) occurs during exploration of a radial maze with no reinforcers present, it should be possible to measure this form of learning indirectly by its retarding effect of subsequent separate arm CCP as well as its facilitating effects on the AAD. The role of ACC was also examined in the present study.

Methods and procedures 32 Long Evans rats were randomly assigned to control, FF, and ACC lesion groups. 8 animals in the control group, 12 animals each in FF and ACC lesion groups. All groups of rats received three day of pre-exposure, and 4 training trials. The rats in the pre-training lesion groups were allowed to recover for 7 days after surgery before the start of behavioral testing.

Results and Discussion

The results for the CCP tests are shown in Figures 3. In the SAD condition, the control, and ACC, but not FF, lesion groups of rats displayed preferences for their food-paired compartments. The statistical analysis revealed that the mean time spent in the paired and unpaired compartments differed significantly for the rats in both the control [$F(1,24)=5.05$; $p<0.05$], and ACC lesion [$F(1,24)=10.42$; $p<0.05$] groups, but it was not significantly different for the rats in the FF lesion [$F(1,24)=0.11$] group.

In the AAD condition, only the control group exhibited preferences to the food paired arms, but the rats with either FF or ACC lesions displayed no preferences for their food-paired compartments. The statistical analysis revealed that the mean time spent in the paired and unpaired compartments differed significantly for the rats in both the control [$F(1,25)=4.25$; $p<0.05$], and FF lesion [$F(1,25)=0.33$] groups, but it was not significantly different for the rats in the ACC lesion [$F(1,25)=0.08$] group.

Experiment Two

In this experiment, effects of pre-exposure, as well as FF and ACC lesions, on both OOO and CCC CCP learning in the CCP box apparatus were examined. During the pre-exposure trials, the rats were allowed to move freely between the two large compartments and the small compartment. During the training phase, both groups of rats were placed in one of the compartments, and the OOO rats could see only one set of stimuli during the food-pairing and no-food sessions. Therefore, only one set of stimuli is consistently associated with food during the training sessions. The other set of stimuli is consistently paired with no food. However, the rat in the CCC groups could see the sets of environmental stimuli visible from the two compartments at essentially the same time during the pre-exposure, training and testing phases. The hypothesis to be tested in the present experiment is that: if the fimbria-fornix is involved in spatial learning with no reinforcers present, it should be possible to measure this form of learning indirectly by its effects of subsequent CCC and OOO CCP. Similarly, the role of ACC was also examined in the present study.

In the OOO condition, the opaque partition was used in all three phases of the CCP procedure: pre-exposure, training, and testing. The OOO condition is the "standard" CCP box apparatus used in many (but not all) laboratories.

In the CCC condition, the clear partition was used during pre-exposure, training and testing. The CCC condition is similar to the CCP on the radial maze with adjacent arm discrimination (AAD). In that maze condition, the rat can see the sets of environmental stimuli visible from the two arms at essentially the same time during the pre-exposure, training and testing phases, as is the case in the present CCC condition.

Methods and procedures

Sixty four male Long Evans rats were randomly assigned to CCC and OOO groups. CCC groups consisted of 8 animals each in the control group, 12 animals each in fimbria-fornix (FF) lesion groups, and anterior cingulated cortex (ACC) lesion groups. Rats with each type of lesion were assigned to the OOO (Opaque pre-exposure, Opaque training, and Opaque testing) or CCC (Clear pre-exposure, Opaque training, and Clear testing) conditions. All groups of rats received three day of pre-exposure, and 2 training trials.

The rats in the lesion groups were allowed to recover for 7 days after surgery before the start of behavioral testing.

Results and Discussion

The results for the CCP tests are shown in Figures 5 (OOO) and 6 (CCC). In the OOO condition, the control and the fimbria/fornix (FF) lesion groups exhibited robust CCPs, but the ACC lesion rats displayed no preferences for their food-paired compartments. The statistical analysis revealed that the mean time spent in the paired and unpaired compartments differed significantly for the rats in both the control [$F(1,25)=10.55$; $p<0.01$], and FF lesion [$F(1,25)=22.30$; $p<0.01$] groups, but it was not significantly different for the rats in the ACC lesion [$F(1,25)=3.30$] group.

In the CCC condition, the control and the fimbria/fornix (FF) lesion groups exhibited robust CCPs, but the ACC lesion rats displayed no preferences for their food-paired compartments. The statistical analysis revealed that the mean time spent in the paired and unpaired compartments differed significantly for the rats in both the control [$F(1,25)=8.87$; $p<0.01$], and FF lesion [$F(1,25)=20.78$; $p<0.01$] groups, but it was not significantly different for the rats in the ACC lesion [$F(1,25)=2.65$] group.

Experiment Three

In this experiment, the role ACC on the CCP in the box apparatus with an opaque partition were studied. In the NOO condition, the opaque partition was used in both training and testing phases of the CCP procedure: training, and testing. Animals in this experiment did not receive pre-exposure to the CCP box compartment. A group of animals with no pre-exposure and trained and tested with clear partition was also examined.

Methods and procedures

Forty Long Evans rats were randomly assigned to NOO and NCC groups. The NOO group consisted of 8 animals each in the control group, 12 animal in the Anterior Cingulate cortex lesion groups. The NCC condition only included an 8 animal control group.

Results and Discussion

The results for the CCP tests are shown in Figures 7 (NOO) and 8 (NCC). In the NCC condition, the control and the fimbria/fornix (FF) lesion groups exhibited robust CCPs, but the rats with ACC lesions displayed no preferences for their food-paired compartments.
The statistical analysis revealed that the mean time spent in the paired and unpaired compartments differed significantly for the rats in both the control [$F(1,14)=9.17$; $p<0.01$] groups, but it was not significantly different for the rats in the ACC lesion [$F(1,14)=1.60$] group.

Discussion

The present study shows that pre-exposure to the context have different effects on the later learning task. Pre-exposure to the maze retarded later SAD learning, but facilitate AAD learning. Similar retardation and facilitation effect of pre-exposure was also observed in the box CCP experiments. The OOO CCP learning was retarded by 3 day/trials pre-exposure to the compartments, in which animals with no pre-exposure show significant preferences to the food paired compartments during the testing phase. In contrast, the CCC CCP was facilitated by the pre-exposures, in which animals with no pre-exposure did not show preference to the food paired compartments during the testing phase.

Latent Inhibition and Latent Learning

According to our hypothesis, pre-exposure to the context will result in different effects on subsequent learning dependent on the type of reinforced learning involved. When the opaque partition was used during the food training and testing trials a CCP was observed in the normal control rats that were not pre-exposed to the apparatus (NOO), but there was no CCP in normal rats 5 pre-exposed with the opaque partition (OOO). This appears to be a form of latent inhibition (Lubow & Moore 1959). In contrast, pre-exposing the rats to clear condition from

that used during training (CCC) did not result in latent inhibition but a latent learning, a possible context effect. Animal with no pre-exposure did not learn the NCC CCP learning.

Role of ACC in CCP learning

In the present study, lesions of the ACC eliminated the retardation effect of pre-exposure in the SAD and blocked the latent learning in the SAD. However, the elimination of latent inhibition effect was not found in the OOO group, but the blocking of latent learning was found in the CCC group. In addition, lesions of the ACC blocked the CCP in the NOO group, since lesions of the ACC blocked all type of CCP learning in the CCP box, this suggests that the ACC could be a critical structure for the CCP learning trained in the CCP box apparatus but not the maze. It is possible that the ACC may play a role in making the right choice during the testing phase in a close compartment, but not an open environment, such as a radial maze..

Role of fimbria-fornix

The hippocampus–FF complex has been associated with spatial learning of this type (Becker et al 1980, Rawlins & Olton 1982). Lesions of the FF has been shown to eliminate retardation effect of the pre-exposure in the SAD (White & McDonald 1993) and latent learning of in the AAD task (Chai & White 2004). However, lesions of FF had no effect on the latent leanring in the CCC condition. This finding suggests two possible conclusions: 1) The FF is not involved in ambiguous cue CCP learning. Although this suggestion is inconsistent with previous suggestions concerning ambiguous cue learning on the radial maze. It is consistent with another previous finding (McDonald et al 1997) that FF lesions failed to block 3 different types of non-spatial relational learning, although some of these tasks were impaired by hippocampus lesions; or 2) The ambiguous cue CCP is learned in parallel by two (or more) neural systems. If one of these systems includes FF, lesioning it alone would have no effect because the behaviour would be maintained by the other system. Only lesioning both systems simultaneously would eliminate the CCP in this situation.

Determination of Neural Substrate of Learning by Task Properties

The findings suggest that the involvement of neural systems in CCP learning is determined by the discriminability of the stimuli in the two environments. When the cues paired with food and not paired with food are clearly discriminable conditioned approach responses produce CCPs. When the food- and no food-paired cues are ambiguous the memory system fails to acquire information that discriminates among the ambiguous cues. This ambiguous cue CCP may be based on simultaneously acquired information about the spatial location of the food by an as yet unknown neural system.

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Figure Legends

Figure 1. Overhead view of radial arm maze illustrating two configurations of the maze used for Adjacent Arm and Separate Arm CCP learning.

Figure 2. (A) Front view of Conditioned Cue Preference (CCP) apparatus with a clear (left) or an opaque (right) partition inserted between the two large compartments. (B) Overhead view of a CCP apparatus. A smaller compartment connected to the two large compartments at the back of the apparatus. Entrances to the two big compartments is controlled by a guillotine door.

Figure 3. Effects of Pre-exposure and brain lesions on the separate arm discrimination (SAD) in radial maze in Experiment 1. Bars represent mean number of seconds spent in food-paired and no food-paired arms, error bars are standard errors of the mean.

Figure 4. Effects of Pre-exposure and brain lesions on the adjacent arm discrimination (AAD) in radial maze in Experiment 1. Bars represent mean number of seconds spent in food-paired and no food-paired arms, error bars are standard errors of the mean.

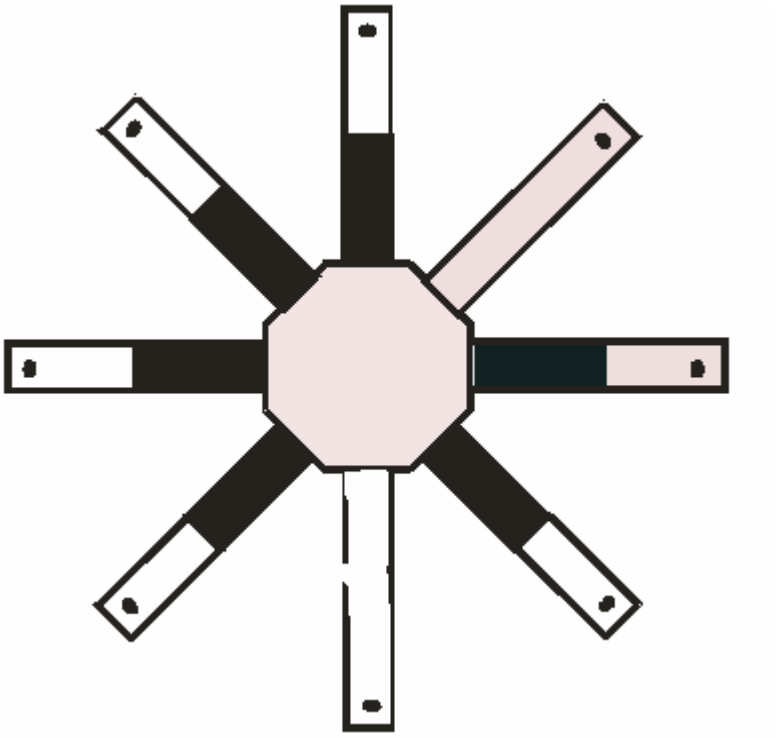
Figure 5. Effects of Pre-exposure and brain lesions on the unambiguous cue discrimination (OOO) in the CCP box in Experiment 2. Bars represent mean number of seconds spent in food-paired and no food-paired arms, error bars are standard errors of the mean.

Figure 6. Effects of Pre-exposure and brain lesions on the ambiguous cue discrimination (CCC) in the CCP box in Experiment 2. Bars represent mean number of seconds spent in food-paired and no food-paired arms, error bars are standard errors of the mean.

Figure 7. Effects of brain lesions on the CCP learning with no pre-exposure in the CCP box in Experiment 3. Bars represent mean number of seconds spent in food-paired and no food-paired arms, error bars are standard errors of the mean.

Figure 1

Separate Arm CCP



Adjacent Arm CCP

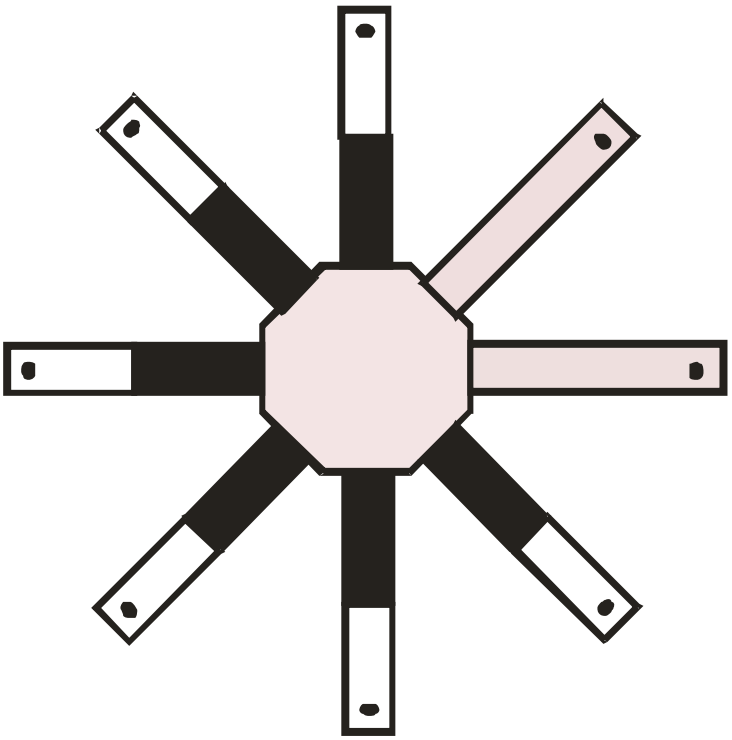
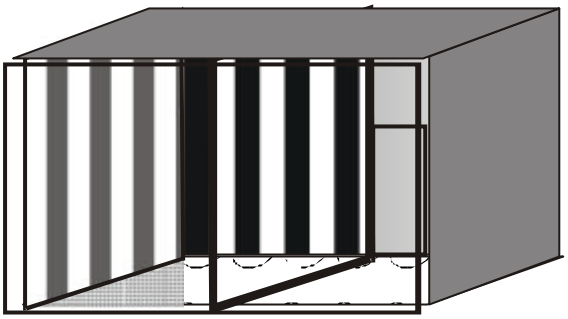


Figure 2

Clear Partition



Opaque partition

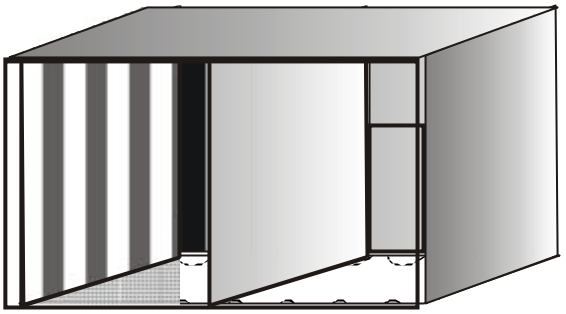


Figure 2A

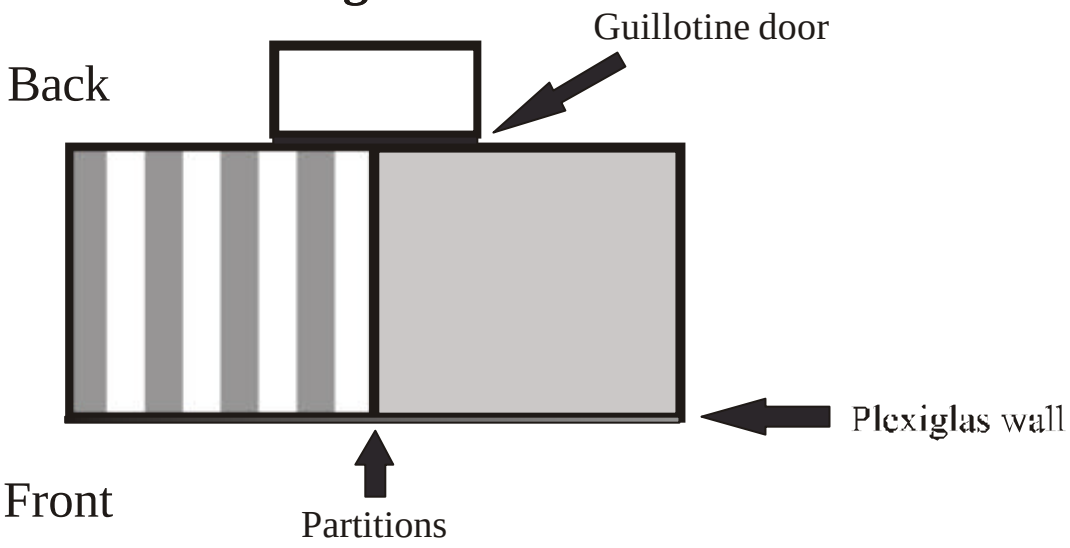


Figure 2B

Figure 3

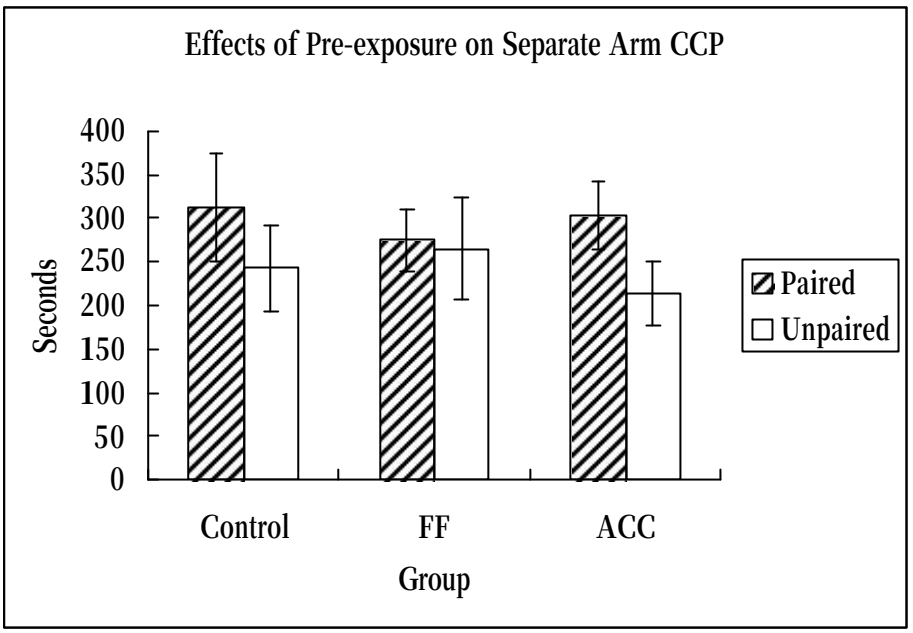


Figure 4

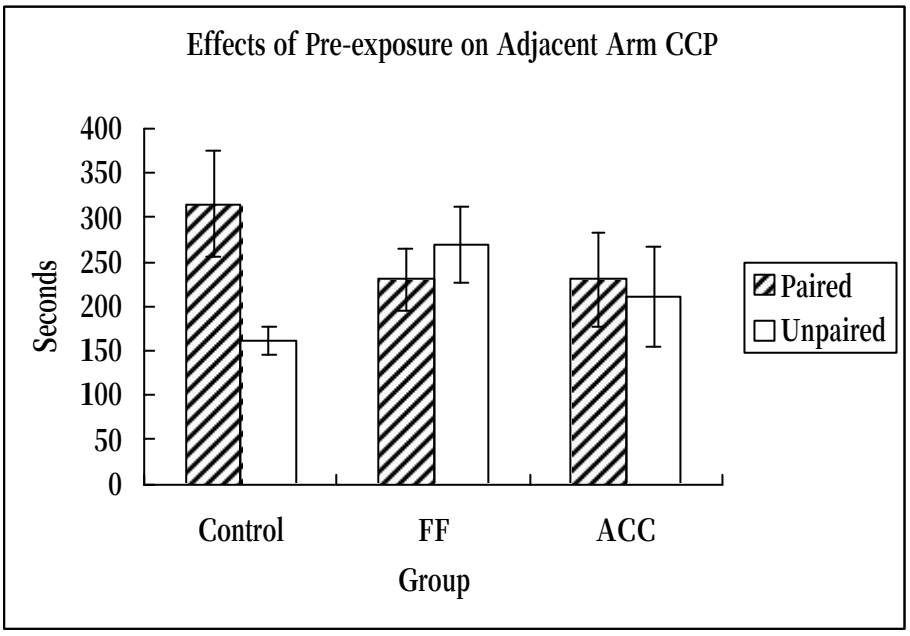


Figure 5

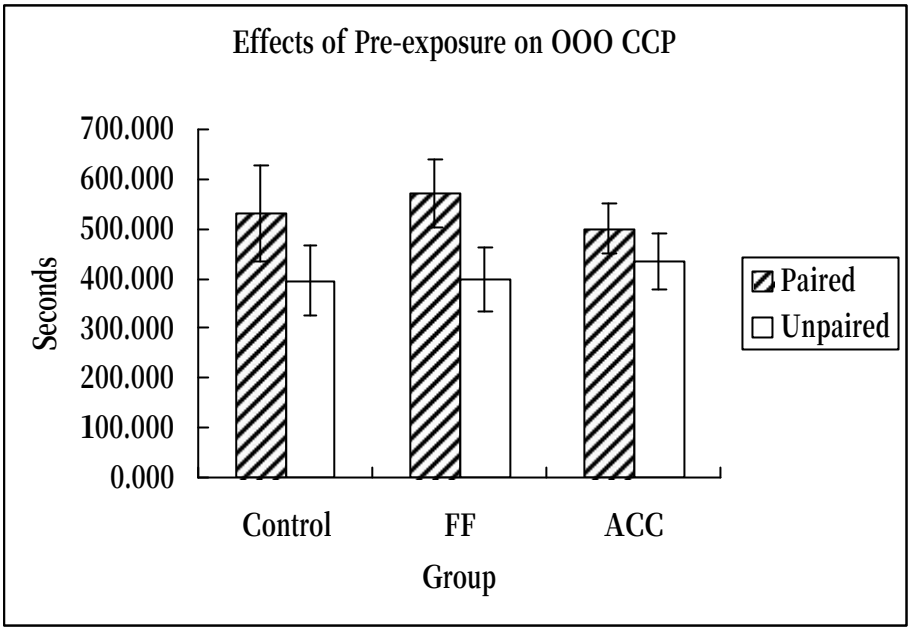


Figure 6

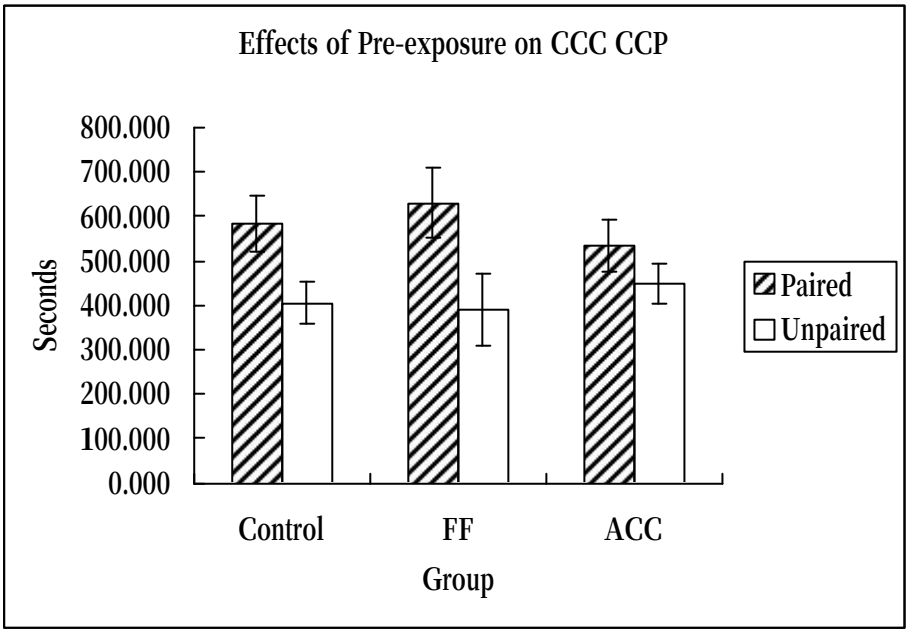
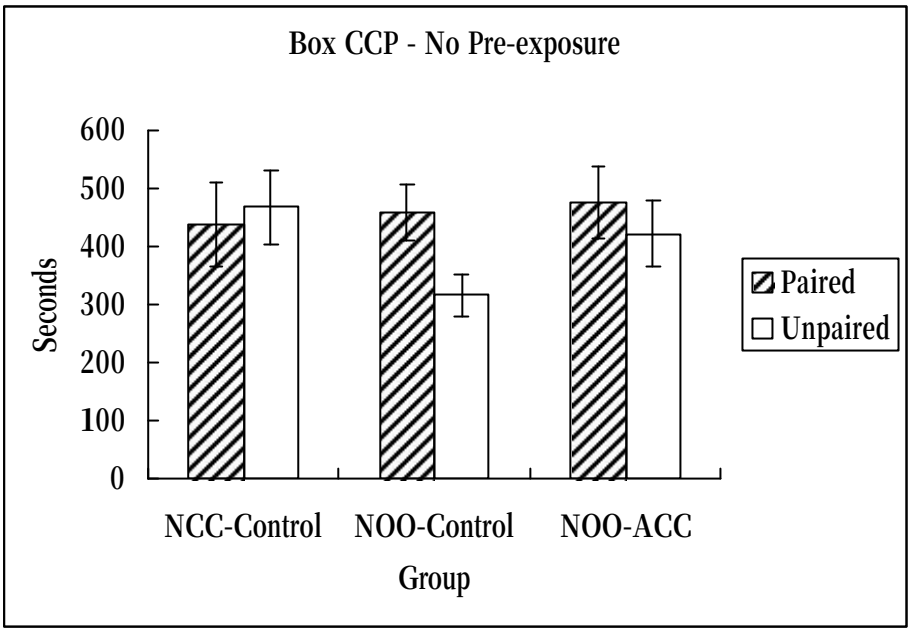


Figure 7


Box CCP - No Pre-exposure
600
500
400
300
200
100
0
Seconds
Paired
Unpaired
NCC-Control
NOO-Control
NOO-ACC
Group

(六)計畫成果自評部份，請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

本研究計劃原先是申請三年期研究計劃，最後核定一年期。原計劃一年期之進度為設立「八角迷宮」及「制約性線索偏好箱」制約性線索偏好學習行為的確立，以建立控制組之制約性線索偏好學習為初步目標。進而再研究前暴露對制約性線索偏好學習的影響，同時進行腦區域的破壞，了解不同腦區域在前暴露和制約性線索偏好學習各自扮演的角色。因為人力的問題，本實驗由原來計劃的「八角迷宮」加入「制約性線索偏好箱」的學習，試圖探討同樣問題。因為本系無研究所設立，國科會計劃核定只有大學生兼任助理。「八角迷宮」的實驗因為食物剝奪, 及學習成果的穩定考量，這部份需要持續在每天同一時段，進行約三至四小時實驗，每一組受試的行為訓練需花費約 20 天才能完成，因此在執行上有很大的難度，「八角迷宮制約性線索偏好」的實驗只能在暑假進行。故希望國科會在之後的行為實驗，能核定一專任助理，讓實驗能順利進行。本結果已達成原先計劃第一年期研究目標之百分之 80，因為不同天數的前暴露對「八角迷宮制約性線索偏好」的影響，每一實驗所需的實驗天數超過二十天，每天 3-4 小時，因為計劃的大學生助理人力，及考量顧用多名實驗者操弄對實驗動物帶來的影響，及成果穩定的傷害性，故以目前人力編製無法以完成此部份。

本實驗結果顯示：（一）可以了解同樣無酬賞前暴露對「制約性線索偏好」學習的不同影響及其原因；（二）前扣帶皮質在「制約性線索偏好」學習的角色。此二發現有助於了解前暴露學習及前扣帶皮質在學習記憶的角色。

□ 可申請專利　□ 可技術移轉　　日期：__年__月__日

國科會補助計畫	計畫名稱： 計畫主持人： 計畫編號：　　學門領域：
技術/創作名稱	
發明人/創作人	
技術說明	中文： （100~500 字） 英文：
可利用之產業及可開發之產品	
技術特點	
推廣及運用的價值	

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※ 2.本項研發成果若尚未申請專利，請勿揭露可申請專利之主要內容。

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