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Place vs Response Learning Strategies of Rats: A deeper look inside the Plus Maze

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Abstract: Rat exhibits two types of learning strategies on Plus Maze: Place Learning and Response Learning strategies which are coded by medial temporal lobe (e.g. hippocampus) and dorsal striatum (caudate-putamen) respectively. In this study, we investigated the 'Place vs Response' learning strategies of 12 young (4 months of age) male wistar rats. 5 rats out of 12 rats exhibited Place Learning strategy while 7 rats out of 12 rats exhibited Response Learning strategy. They were divided into two groups: one group with fixed reward location and other group with alternate reward location. On extended training during repeated trials with fixed reward location, rats exhibited more pronounced Response Learning behaviour. Moreover, previously Place Learners started to shift into Response Learning strategy. In other group with alternate reward location, rats became more dependent on the Place Learning strategy. Even, the previous Response Learner started to exhibit Place Learning strategy. We conclude that Place and Response Learning strategies of rat are quite flexible and rat quickly adopts the best learning strategy for the adequate solution. On fixed reward paradigm in the Plus Maze, rat forms a Stimulus-Response Habit of turning the body on the same side again and again on repeated trials very successfully. But with alternating reward paradigm, rat follows the general principle of the task adopting Place Learning strategies. This concept of learning strategies can also be applied in cognitive fields like education and training programme as well as understanding pathophysiologic basis of learning disorders.
Keywords: Plus Maze, Place vs Response Learning.

INTRODUCTION

Throughout the history of cognitive study, exploring animal learning strategies were very popular and were closely observed to theorize multiple memory systems of mammals [1, 2]. Neurobiologists have identified different forms of memory systems which can work in unitary independent fashion or simultaneously activated in parallel or can work together [3]. For instance, we humans have 'Declarative Memory' for the memory of past events and facts which can be recalled consciously (explicit in nature) and 'Non-Declarative or Procedural Memory' for the memory of motor skills which does not require conscious recall (implicit in nature) [4, 5].

Rat also uses different types of strategies to explore the world and remember the places where it finds rewards. Two types of memory systems are identified in rats while training on the maze. One form closely related to 'Declarative memory' relies on medial temporal lobe (e.g. hippocampus) and is characterized by accessible memory of past events or places [1, 6, 7]. The other form of memory is derived from 'Stimulus-Response Habit' involving basal ganglia (e.g. caudate-putamen) motor responses [8, 9].

Early experimenters like Tolman [7] used double T maze, more commonly known as 'Plus Maze' or 'Cross Maze' to explore this two types of learning strategies. In this Plus Maze task [10], rat obtains food in a particular arm of T approaching from the same starting box or arm during the training period. After training, probe trials are given placing the rats in the opposite arm of the previous starting box. On probe trial, if the rat enters on the same arm (the spatial location where food reward was given during training) it is designated as 'Place Learner' and if the rat enters the opposite arm making the same body turn response which was reinforced during the training it is designated as 'Response Learner' [10]. This 'Place versus Response' strategies has led to a historical debate

between cognitive and 'Stimulus-Response' theorists with conflicting results [6-11].

Aims and Objectives

In this study, we investigated the 'Place vs Response' learning strategies of young (4 months of age) male wistar rats in Plus Maze with extended training with fixed reward location and alternate reward location.

MATERIALS AND METHODS

Subjects

12 young (4 months of age) male Wistar rats were selected for this study. The animals were housed in standard polypropylene cages (max. three to four rats per cage) and maintained in 24±2°C and relatively low humidity with 12:12 hours day and night cycle. All rats were provided with commercially available rat pellet diet (Animal diet, Provimi) and water ad-libitum. The guidelines of committee for the purpose of control and supervision of experiments on animals (CPCSEA), Govt. of India were followed and prior permission was sought from the institutional animal ethics committee, IPGME&R, Kolkata, India for conducting the study.

Materials

Plus Maze (Fig. 1)

This Plus Maze is made up of wooden material. It has four arms designated as East, West, North and South. Each arm has a length of 24 inch, width of 4 inch and height of 4 inch. All four arms are connected to an octagonal central arena. Each arm is provided with a gate at the junction with central arena to control the movements of the rats. Extra-maze cues are provided in between the areas of the arms. Other objects in the testing room including direction of light through the windows and fixed position of the examiners also provide the extra-maze cues for navigation in the maze as well.

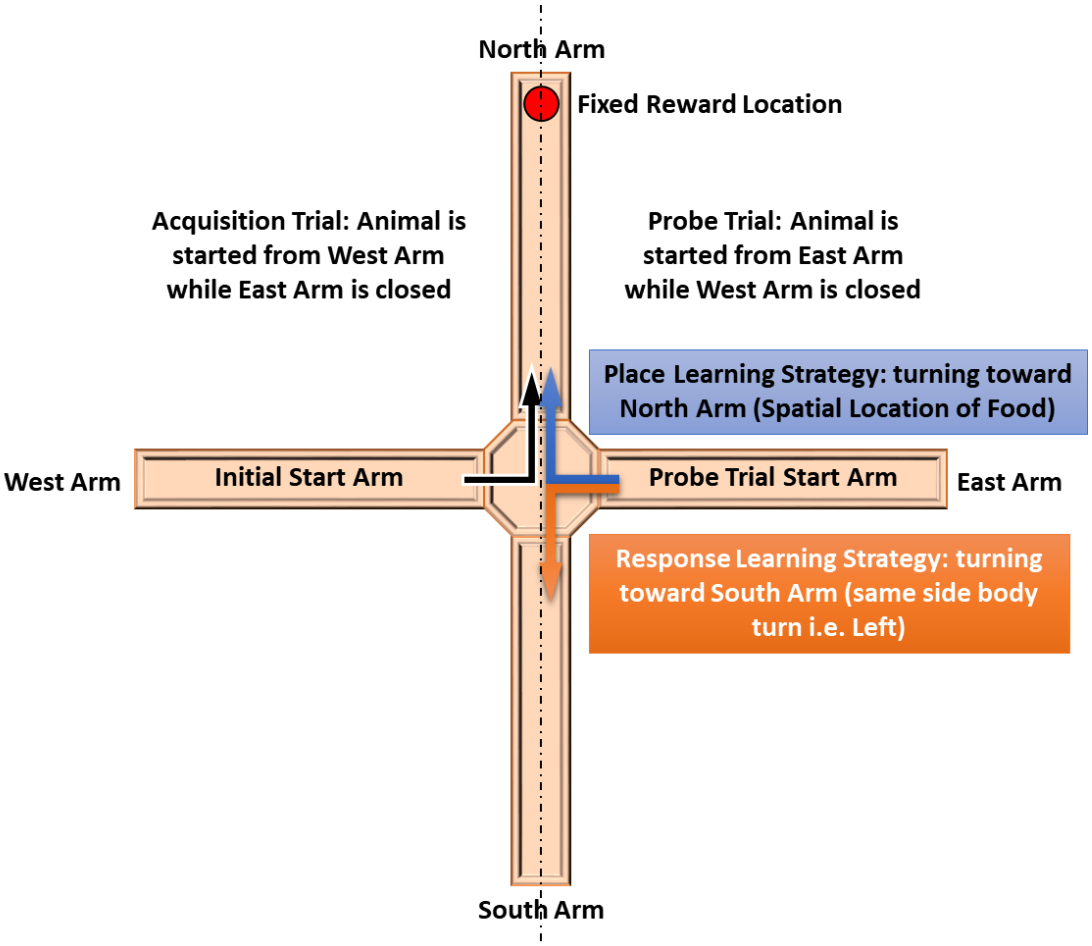

Fig-1: Schematic diagram of Plus Maze

Food Rewards

Sprouted grams are placed over a circular food tray at the end of Reward Arm. For each trial, one sprouted gram is placed on the food tray to maintain optimum appetite for the next successive trials.

Methods [7]

Rats were kept on fast overnight (for 6-8 hours) to maintain adequate appetite taking pre-cautions not to lose the weight more than 20% of ad-libitum body weight.

Acclimation: Rats in home cage were placed in the testing room for at least 1 hr before trials to minimize effects of stress.

Habituation: Rats were first habituated in the Plus maze for 3 consecutive days and were allowed open access to all arms of Plus Maze.

Trials (Fig. 2)

Each Trial was divided into two phase:

(i) Acquisition Phase: Initially rat was placed on the West Arm (Initial Start Arm) while the opposite East Arm was closed. Food reward was placed at the end of North Arm (left side of the start arm). Gates were opened and rat was allowed to visit both the arms (Rewarded North Arm as well as Non-rewarded South Arm). After that, rat was guided to enter the Initial Start Arm (East Arm), then collected and returned to the home cage to stay for a delay period of 2 minutes during which rat significantly lost its working memory of previous trial [11] but retained the general principle of the maze task (reference memory).

(ii) Probe Trial Phase: After 2 minutes delay, rat was placed on the East Arm opposite to the Initial Start Arm which was closed now. Food rewards were placed at the end of both North as well as South Arms. Gates were opened and when all four paws of rat entered one arm, that sided arm gate was closed and arm entry was recorded. If the rat entered the previously visited North Arm, it remembered the spatial location of the reward and it was recorded as Place Learning Score of 'P'. If the rat entered the South Arm, it remembered the previous body turn movement (i.e. left turn) and it was recorded as Response Learning Score of 'R'.

Group Division

- Initially for each rat, 4 Probe Trials were given per day for 4 days (total 16 Probe Trials). Their Strategy Learning Scores (either 'P' or 'R') were calculated. On the basis of predominant 'P' or 'R' score, they were designated as Place Learner or Response Learner.
- They were divided into two groups (each group 6 rats) randomly for the successive trials:
  - Group A with Fixed Reward Location: The reward location was fixed as it had been before (North Arm) during the acquisition phase for the next trials.
  - Group B with Alternate Reward Location: The reward location was alternated between North and South Arm during the acquisition phase for the next trials.
- After group division for each rat, 4 Probe Trials were given per day for 4 days (17^{th} to 32^{nd} Trials). Their Strategy Learning Scores (either 'P' or 'R') were calculated again.

Parameters

- Strategy Learning Score (either 'P' or 'R') of 1^{st} to 16^{th} Trials: Total no. of 'P' vs total no. of 'R' (Max Score = 16).
- Strategy Learning Score (either 'P' or 'R') of Last 8 Trials (25^{th} to 32^{nd} Trials): Total no. of 'P' vs total no. of 'R' (Max Score = 8).
- Strategy Learning Score (either 'P' or 'R') of 9^{th} to 16^{th} Trials: Total no. of 'P' vs total no. of 'R' (Max Score = 8).
- Strategy Learning Score of Moving Sum of 8 Trials (Max Score = 8).

Statistical Analysis: Analysis of the data was performed in Graph Pad Prism v 5.03.

RESULTS

Strategy Learning Score per individual rat after initial 16 trials **(Fig. 2)** shows that 5 rats (Rat 1, Rat 4, Rat 6, Rat 7 and Rat 9) out of 12 rats preferred Place Learning Strategy over Response Learning Strategy. Unpaired T test between their Place vs Response Learning Score shows the p value <0.0001 and t = 17.89. Whereas remaining 7 rats favoured Response Learning Strategy with the p value <0.0001 and t = 16.04 by unpaired T test between their Place vs Response Learning Score.

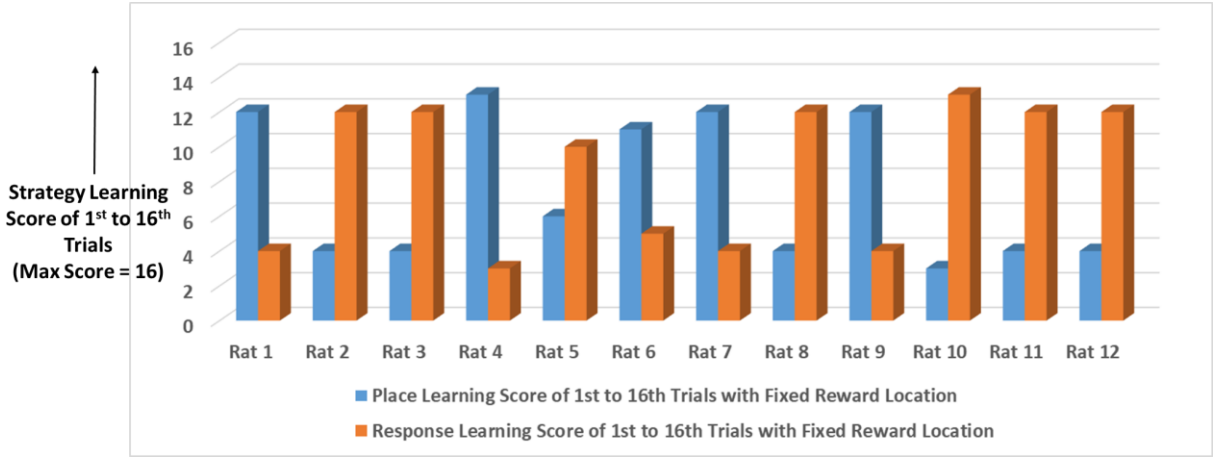

Fig-2: Strategy Learning Score of 1st to 16th Trials of individual rat

Strategy Learning Score per individual rat during last 8 trials (25th to 32nd) **(Fig. 2)** shows that all Group A rats with fixed reward location have adopted Response Learning Strategy (p value <0.0001 and t = 8.257 by unpaired T test between their Place vs Response Learning Score). Whereas all Group B rats with alternate reward location have adopted Place Learning Strategy (p value 0.4205 and t = 0.8341 by unpaired T test between their Place vs Response Learning Score).

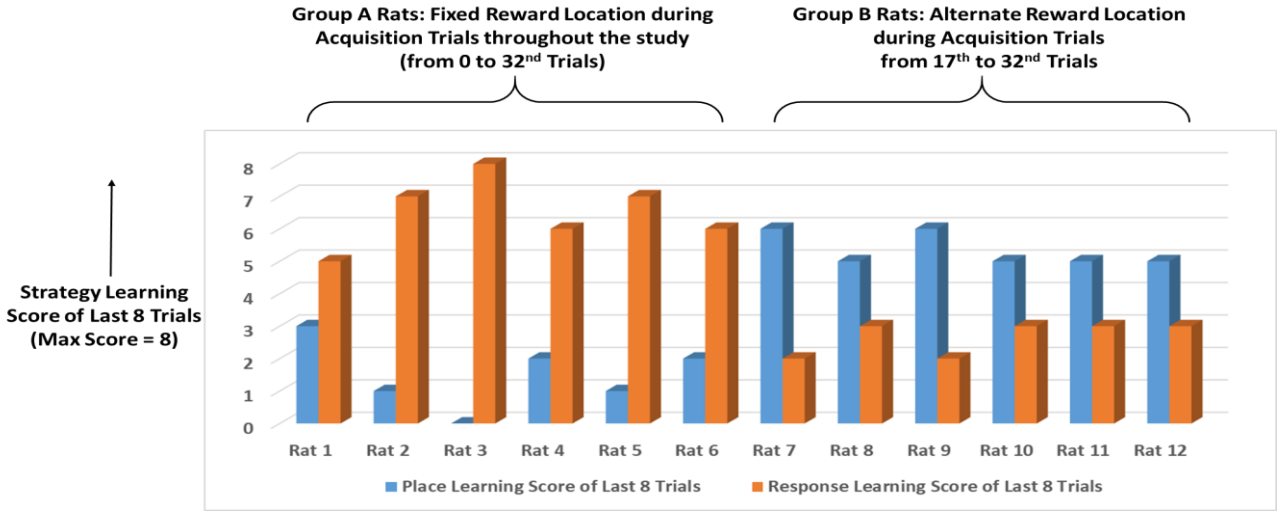

Fig-3: Strategy Learning Score of Last 8 Trials (25th to 32nd) of individual rat

Inside the Group A (with fixed reward location throughout the study) Strategy Learning Score of Moving Sum of 8 Trials (Fig. 4) shows that, three previously Place Learner Rats shifted their strategy to Response Learning Strategy on repeated trials with fixed reward location, whereas the Response Learner Rats of Group A retained their Response Learning Strategy.

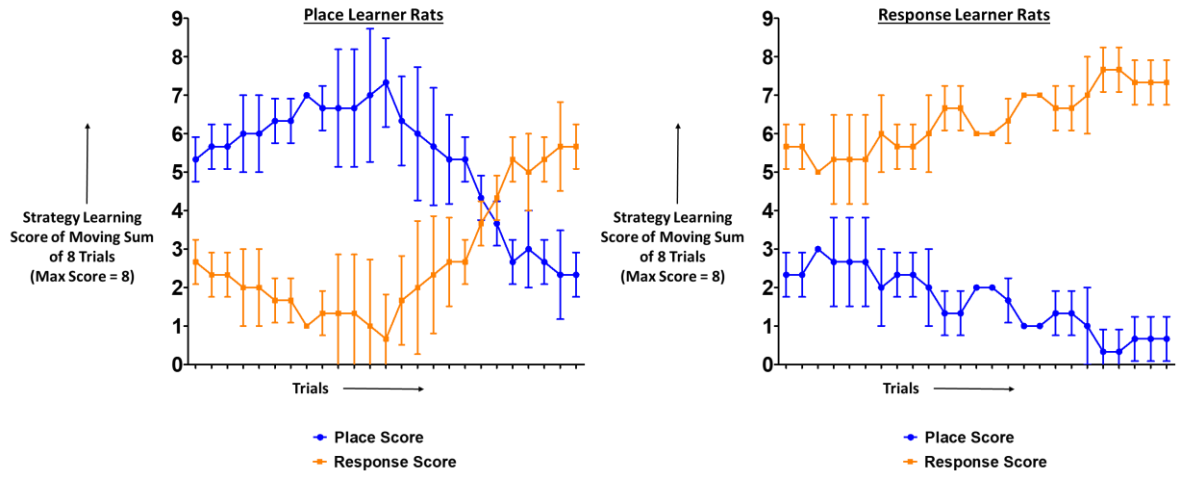

Fig-4: Group A Rats (With Fixed Reward Location): Strategy Learning Score of Moving Sum of 8 Trials

Inside the Group B (with alternate reward location from 17th to 32nd trials) Strategy Learning Score of Moving Sum of 8 Trials (Fig. 5) shows that, the Place Learner Rats retained their Place Learning Strategy but four previously Response Learner Rats shifted their strategy to Place Learning Strategy during trials with alternate reward location.

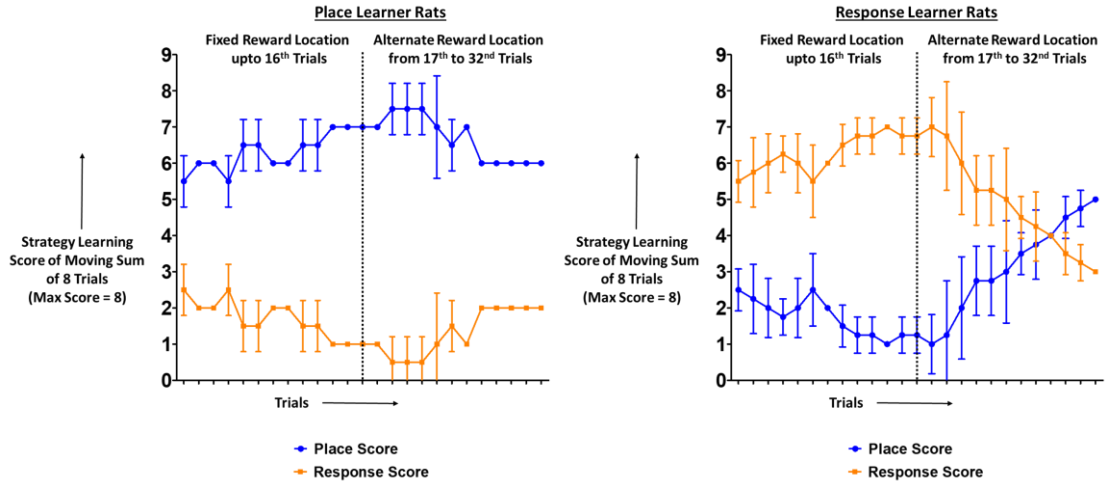

Fig-5: Group B Rats (With Alternate Reward Location): Strategy Learning Score of Moving Sum of 8 Trials

Inter-group analysis of previously Place Learner Rats by two way ANOVA (Fig. 6 and Table 1) between their Place Learning Score of 9th -16th trials vs Place Learning Score of Last 8 trials (25th – 32nd trials) shows the p value 0.0034 for Place Learning Score variable, p value 0.0246 for Reward Location variable and p value 0.0067 for group interaction which are significant. Bonferroni post-tests shows the group difference of Place Learning Score of Last 8 trials is very significant ($p < 0.001$ and $t = 7.266$). This analysis reveals that on repeated trials with fixed reward location the shifting of strategy of Place Learner Rats from Place Learning to Response Learning strategy is highly significant.

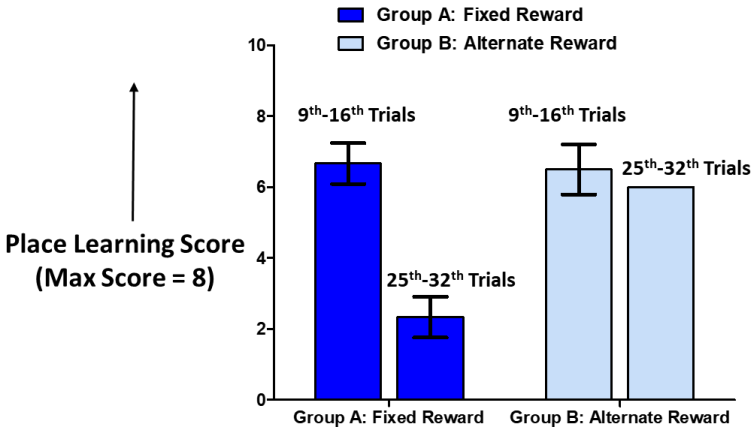

Fig-6: Inter-group Analysis of Place Learner Rats by Two way ANOVA

Inter-group analysis of previously Response Learner Rats by two way ANOVA (Fig. 7 and Table 1) between their Response Learning Score of 9th -16th trials vs Response Learning Score of Last 8 trials (25th – 32nd trials) shows the p value 0.0037 for Response Learning Score variable, p value 0.0023 for Reward Location variable and p value 0.2421 for group interaction which are significant. Bonferroni post-tests shows the group difference of Response Learning Score of Last 8 trials is very significant ($p < 0.001$ and $t = 12.43$). This analysis reveals that on alternate reward location the shifting of strategy of Response Learner Rats from Response Learning to Place Learning strategy is highly significant.

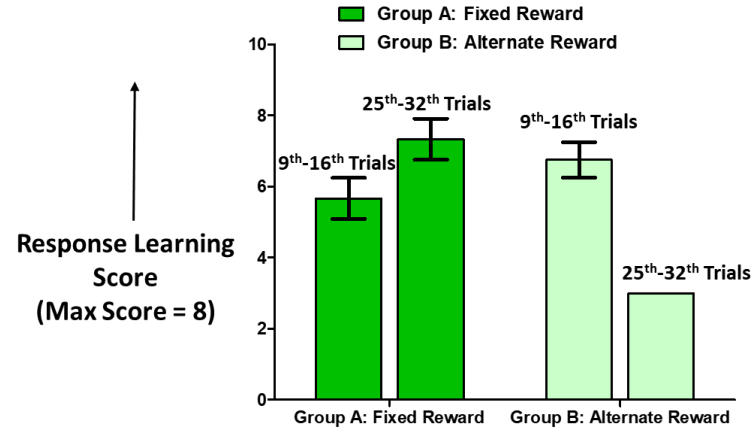

Fig-7: Inter-group Analysis of Response Learner Rats by Two way ANOVA

Table-1: Two way ANOVA Group Analysis

	Place Learner Rats								Response Learner Rats							
	Group A: Fixed Reward Location				Group B: Alternate Reward Location				Group A: Fixed Reward Location				Group B: Alternate Reward Location			
	9th to 16th Trials		25th to 32nd Trials		9th to 16th Trials		25th to 32nd Trials		9th to 16th Trials		25th to 32nd Trials		9th to 16th Trials		25th to 32nd Trials	
	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score	Place Score	Response Score
Number of values	3	3	3	3	2	2	2	2	3	3	3	3	4	4	4	4
Mean	6.667	1.333	2.333	5.667	6.5	1.5	6	2	2.333	5.667	1	7	1.25	6.75	5	3
Std. Deviation	0.5774	0.5774	0.5774	0.5774	0.7071	0.7071	0	0	0.5774	0.5774	1	1	0.5	0.5	0	0
Std. Error	0.3333	0.3333	0.3333	0.3333	0.5	0.5	0	0	0.3333	0.3333	0.5774	0.5774	0.25	0.25	0	0

DISCUSSION

In our study, we found that rats exhibited two types of learning strategies to solve the reward locating task in Plus Maze. 5 rats out of 12 rats exhibited Place Learning strategy while 7 rats out of 12 rats exhibited Response Learning strategy **(Fig. 1)**. According to Kesner *et al.*, Response Learning strategy which is an ego-centric approach within an expectancy based memory is more common than Place Learning strategy which is an allocentric behaviour within a data based memory system [17].

Both place and response learning can be acquired in a plus or cross maze task by separate

memory systems that include the hippocampus and caudate-putamen, respectively [6-10]. In a study of cross or plus maze, Packard *et al*. showed that post-training glutamate infusion into hippocampus and caudate-putamen selectively strengthened place and response learning strategies of rat respectively in the plus maze [12].

In some tasks where both systems can provide adequate learned solutions, simultaneous activation of hippocampus and dorsal striatum (caudate-putamen) occurs and this two memory systems can work co-operatively and in parallel fashion [14]. More evidences were found from the work of previous experimenters, that early learning is mediated by the hippocampal system, and with extended training the dorsal striatum comes to guide learned behaviour [12, 13]. Under different conditions animal exhibits different types of learning strategies [15].

On extended training during repeated trials with fixed reward location (Group A), rats exhibited more pronounced Response Learning behaviour. Moreover, previously Place Learners started to shift into different kind of learning strategy i.e. Response Learning strategy **(Fig. 4)**. This result is consistent with the previous findings that on extended training dorsal striatum (memory system of Response Learning) takes the upper hand [12, 13]. On the other hand, when the reward location was alternated during the acquisition phase (Group B), rats became more dependent on the Place Learning strategy **(Fig. 5)**. Even, the previous Response Learner started to exhibit Place Learning strategy.

This shifting of behaviour not only proves that memory is flexible in nature but also to the fact that animals quickly adopt the best learning strategy for the adequate solution [2]. On fixed reward paradigm, rat forms a Stimulus-Response Habit of turning the body on the same side again and again on repeated trials very successfully. However, if the reward location is not fixed i.e. either random or alternating, remembering the last body turn movements will be less reliable memory system. Also, it will fall on the working memory system which is a short term memory of remembering a previously visited area or body turn which lasts for a single trial [11]. In our previous study, we have shown that the limit of working memory of rat is in between 45-75 seconds and after 2 minutes it significantly declined to a very lower level [11]. In our study, there was a delay of at least 2 minutes between the acquisition phase and probe trial phase (see methods), which can significantly decay working memory. So, rat starts to shift to the Place Learning strategy which is a kind of reference memory, a memory system for remembering the general rule or principle of the maze task [18].

This result will help to conduct and design different maze tasks which involves place learning and response learning strategies. The concept of learning strategies can also be applied in cognitive fields like education and training programme. Understanding the underlying memory systems (e.g. hippocampus and dorsal striatum) will also help us to know the pathophysiologic basis of cognitive impairment in many diseases.

CONCLUSION

We conclude that Place and Response Learning strategies of rat are quite flexible and rat quickly adopt the best learning strategy for the adequate solution. On fixed reward paradigm in the Plus Maze, rat forms a Stimulus-Response Habit of turning the body on the same side again and again on repeated trials very successfully. But with alternating reward paradigm, rat follows the general principle of the task (reference memory) adopting Place Learning strategies which becomes more reliable memory system.

Conflict of Interest: None.

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