Indian J Physiol Pharmacol 2017; 61(3) : 237–245

Original Article

Differing Pellet Size During Reach to Grasp Task Modulates Skilled Forelimb Movements

Sibin Mathew Nesin[1], Vikash Prasad[2], Anupam Gupta[3] and T.R. Laxmi[1]*

[1]Department of Neurophysiology, NIMHANS, Bengaluru – 560 029

[2]Indian Institute of Science Education and Research, Kolkata

[3]Department of Neurological Rehabilitation, NIMHANS, Bengaluru – 560 029

Abstract

Neurodegenerative diseases such as ischemic stroke leads to severe changes in the pattern by which limb movements are completed during skilled forelimb movements. Assessments of such movements in animal models are carried out using tests like reach to grasp task. Rats acquire the reach to grasp task through training and the skill is retained over long period. Learning of a skill is affected by various factors like attention, knowledge of the results, prediction etc. Current study investigates the role of prediction in the improvement of performance in reach to grasp task in rats. Providing a challenging environment with the randomized pellet size has reduced the prediction ability of the rats in execution of movements.Current study shows that the prediction of pellet size has a critical role in reach to grasp performance and the rats are not able to form a unified movement strategy to accommodate any of given size of pellets.

Introduction

The dual visuomotor channel theory describes the distinct evolutionary origins of the movements- Reach and Grasp, involved in the reach to grasp task (1). Reach helps to direct the forearm towards the target whereas Grasp helps to pre-shape the paw and acquire the target for manipulation. Reach is driven mainly by the extrinsic properties of the target like location, whereas grasp is driven mainly by the intrinsic properties like shape or size (2). Following Peterson's (1932) studies on prehension, Reach to grasp task has been studied extensively to understand skilled movement behaviour in both animals and human beings (3). In the classical reach to grasp task the rat is trained to withdraw a pellet through a slit in front. Rats learn the task quickly, approximately in two weeks time with two sessions of training daily. Once the rat learns the task, it successfully withdraws the pellet in a single attempt (4, 5). Reach to grasp task is a skill which is retained over long periods (6, 7). Excellence in the task

***Corresponding author :**
T.R. Laxmi, Department of Neurophysiology, NIMHANS, Bengaluru – 560 029, Tel: +91-80-2699-5178 (office), Fax No. +91-80-2656-2121; Email : laxmir@gmail.com / trlaxmi.nimhans@nic.in

(Received on March 12, 2017)

requires the acquisition of the skill and skill is always learned (8, 9).

Skill learning involves acquisition and consolidation (10). Consolidation helps in stabilizing the memory and studies have shown that sleep helps in off-line skill improvement (11, 12). Motor acquisition requires repeated exposure to the task (13) and various factors like attention, knowledge of results (9, 14) and motor prediction helps in achieving it (15-17). Motor prediction improves with experience and learning from error in prediction helps in improving the prediction in forthcoming tasks (18). Repeated exposure is essential for accurate predictions. In the reach to grasp task, predicting the pellet size and position plays an important role in pre-shaping the paw to grasp the pellet thus improving the outcome (19).

Prediction helps in developing movement schemas and updating them based on feedback and feedforward information (15, 16). Human studies show the formation of multiple movement plans for a competing target (20-22). It is not clearly known whether similar multiple movement plans are made in the rat brain before choosing the best movement. Here we design a task in which the rat faces a challenge in predicting the pellet size. By providing three different sized pellets randomly in the current study, we are able to delineate movement prediction with execution.

Methods

Subjects

All experimental procedures were approved by the Institutional animal ethics committee, NIMHANS, Bengaluru (IAEC number: AEC/48/298/N.P.). The study was conducted in the at NIMHANS, Bengaluru. We assessed the performance of 18 Sprague Dawley male rats of 3 to 4 months old in reach to grasp task. One rat was eliminated as it was ambidextrous. The animals were food deprived to maintain 90% of their initial body weight throughout the study. They received water ad libitum and were housed in polypropylene cages with a 12-h light/dark schedule.

Pellets

Baseline training was accomplished with normal sized pellet (rice crispies, Bakery Machinery and Co., Bengaluru). We used pellets of three different dimensions as follows. The small sized rice crispies were 3 mm in diameter and weighed approximately 25 mg. For experiment, three different size sugar pellets (Bakery Machinery and Co., Bengaluru) were used. Small size pellet was having a diameter 3.5 mm and weighed approximately 35 mg. Medium sized pellets were having a diameter of 5 mm and weighed about 80 mg. Large size pellet was 7 mm in diameter and weighed 200 mg approximately (Fig. 1).

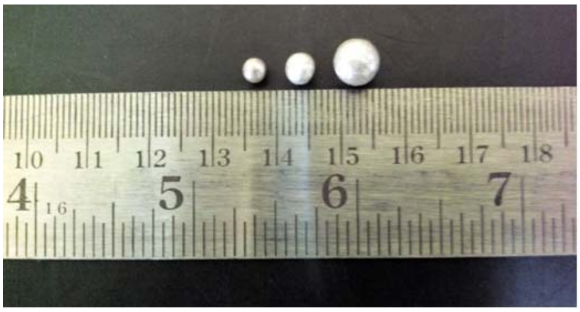


Fig. 1 : Sugar pellet used in the study.

Apparatus and video recording

The reach to grasp chamber was made of Plexiglass. It was a square shaped chamber with the following dimensions, length 300 mm, width 180 mm, height 250 mm, with a slit in front and a tray mounted on the exterior to hold the pellets. The slit was 55 mm above the ground and two wells of 1.5 mm depth were made in the food tray plate at 1.5 cm distance from outer side of the slit, for placement of the food pellets. Clean paper covered the floor of the chamber. Video records were made with a Cineplex camera (30 fps) operated using the Cineplex Capture software (Plexon Inc., USA). The camera was placed facing the slit and wells, to capture a frontal view.

Pre-training

The animals were given two sessions of training daily until they learned to perform the task with three successful consecutive reaches. 30 rice crispies were given during each session and paw preference was noted.

Training

After the animals learned to retrieve food pellets through the slot they were grouped into three. For all three groups, the training was continued for six days with 2 sessions daily. During each session 15 pellets were provided one after the other in the well, contralateral to the preferred paw. The first group - Constant size group (n=6), continued to receive the normal sized pellet (rice crispies). The second group - Concordant size group (n=5), received sugar pellets of all sizes uniformly beginning with small sized pellets and progressing to medium and then large sized pellets each for 2 days consecutively. The third group- Random size group (n=6), received 15 pellets per session in random order of pellet size. The random orders for 15 pellets were generated using a Python based algorithm (Ver. Python 3.4.0) for small, medium and large sized pellets which were presented each five times in random order. Each session differed by having a new random order, but same order was followed for all rats within the group.

Testing

A gap of one day was given following the training for the testing session. This was followed by two consecutive days of testing with two sessions each. For the constant size group, 15 normal sized pellets were given and for the other two groups the sugar pellets of small, medium and large size were given in a random order.

Behaviour Analysis

The captured video was analysed frame to frame using the Cineplex Markup software (Plexon Inc., USA). The following metrics were estimated.

Percentage of success in reach to grasp task

The percentage of success was scored using the formula given below, for 15 pellets.

$$\% \text{ of Success} = \frac{\text{number of successful reaches}}{\text{number of reaches}} \times 100$$

First attempt success scoring

The first attempt success was calculated for 15 pellets. If a pellet was successfully withdrawn at a single attempt it was considered as a successful attempt and each successful event was scored 1.

Movement component scoring

The movement components scoring was described previously in our earlier study and briefly eight movement components including orient, limb lift, digit close, pronation, digit open, grasp, supination and release were scored for all 15 pellets (23). Each movement was given a score based on the following conditions a) present and normal- scored 1, (b) present and abnormal- scored 0.5 and (c) absent- scored 0. In addition the grasp was marked separately, if the pellet was obtained abnormally using two digits.

Reach trajectory and velocity

To study reach trajectory and velocity, the first three reaches were excluded and succeeding three successful reaches at first attempt were taken into consideration. The trajectory was estimated from a frontal view for five movements, namely (1) digit close, (2) advance, (3) Pronation and digit open over the pellet, (4) grasp and (5) withdrawal of pellet near slit at supinated position. Using the Cineplex Markup software (Plexon Inc., USA) the Cartesian coordinates of each movement was marked frame by frame. The tip of the 3rd digit was marked for digit close gesture. For all other gestures the mid of the third digit was marked. Velocity was calculated for each trajectory and the average trajectory and average velocity of each day from two sessions, was used for statistical analysis.

Statistical Analysis

Statistical analysis was carried out by Two-way

Analysis of variance (ANOVA) followed by Bonferroni post tests. Data is represented as mean±SEM and p value less than 0.05 was considered as significant.

Results

In the current study male Sprague Dawley rats were used to study the skilled movement through reach to grasp task when different sized pellets were administrated. Endpoint measures like percentage of success, detailed movement component analysis and movement kinematics and dynamics were being explored in the study.

Percentage of success in reach to grasp task

Random size group has not shown increment in percentage of success when compared to both constant size group and concordant size group. Two-way ANOVA followed by Bonferroni post tests has shown significant improvement in percentage of reach success (Fig. 2A) for the Constant size group, as the day's progress. There was a significant effect of day ($F(7,98)=4.69$, $p<0.0001$) and significant effect of day × groups interaction ($F(14,98) = 2.69$, $p=0.0023$). When one type of pellet was given for two consecutive days, the reach success percentage has slightly improved in concordant group. Maximum success was attained on day 5 and day 6 were large sized pellet was given. Decrease in percentage of success was observed in the concordant size group when compared to constant size but significant difference was found only on test day 2 ($p<0.01$). Random size group has not shown any improvement in success percentage throughout the study. Significant difference in percentage of reach success was observed on day 6 when compared to concordant size and on all day starting from day 4, when compared with the constant size group. There was no significant difference observed between random size group and concordant group on both test days. Note that small, medium and large size pellets were given in random order on test days for both concordant size group and random size group.

First attempt success score - reach to grasp task

First attempt score for reach to grasp task has bettered for constant size group during the study (Fig. 2B). Two-way ANOVA followed by Bonferroni post tests has shown significant effect of day ($F(7,98) = 5.65$, $p<0.0001$) and significant effect of groups ($F(2,98) = 19.69$, $p<0.0001$). The improvement in performance of concordant size groups from day 1 to day 6 in first attempt success is similar to that

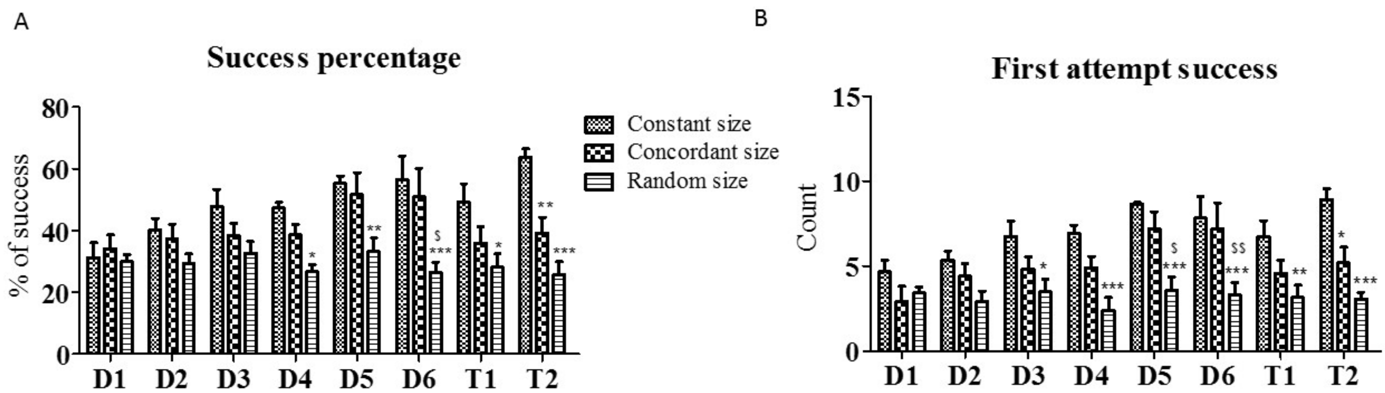


Fig. 2 : Reach to grasp task – (A) Percentage of success of Constant size group (n=6), Concordant size group (n=5) and Random size group (n=6), Two-way ANOVA followed by Bonferroni post tests has shown significant reduction in percentage of reach success in Random size group in comparison to Constant size group on day 4, 5, 6 and on test day 1 and test day. 2. Significant difference was found on day 6, for random group when compared to Concordant group. On test day 2 for the Concordant group in comparison to the Constant size group, a significant decrease in percentage of success was observed (B) First attempt success: Two-way ANOVA followed by Bonferroni post tests has shown significant reduction in first attempt success in Random size group in comparison to the Constant size group on day 3, 4, 5, 6 and on test day 1 and test day 2. Significant difference was found on day 5 and day 6, for random group when compared to Concordant group. On test day 2 for the Concordant group in comparison to the Constant size group, a significant decrease first attempt success was observed (*p<0.05, **p<0.01, ***p<0.001 in comparison with the Constant size group; $p<0.05, $$p<0.01 in comparison with Concordant group).

found in the Constant size group. There were significant differences in first attempt success in Random size groups compared to the Constant size group on day 3 ($p<0.05$), day 4 ($p<0.001$), day 5 ($p<0.001$), day 6 ($p<0.001$), test day 1 ($p<0.01$), test day 2 ($p<0.001$) and compared to the Concordant size group on day 5 ($p<0.05$) and day 6 ($p<0.01$). There was no significant difference between Concordant size group and Random size group on both test days were randomisation was administrated for both the groups.

Movement component Score of reach to grasp task

As the days progress, there was significant improvement in the quality of reach to grasp task in the Constant size group (Fig. 3A). Statistical analysis was carried out by Two-way ANOVA followed by Bonferroni post tests. Even though all eight components of movement were scored there were no significant differences was observed for the orient, limb lift and digit close gestures. Thus, they were omitted from the graphical representation. For Concordant size group, all the movement components have scored less when pellet size increased. Random size group has not shown any significant change throughout the study for all the movement components.

To test the performance across the groups, day 1, day 6 and test day 2 are considered for statistical analysis by Two-way ANOVA followed by Bonferroni post tests (Fig. 3B). On day 1 the Concordant size group had better score compared to constant size group and significant difference found between the two on grasp ($p<0.05$) and supination ($p<0.05$) ($F(2,112) = 4.39$, $p=0.0146$). But by day 6 the score for all the movement score has improved for the constant size group. There was a significant effect of groups ($F(2,112) = 25.42$, $p<0.0001$) and significant effect of components × groups interaction ($F(14,112) = 4.01$,) $p<0.0001$). Significant difference

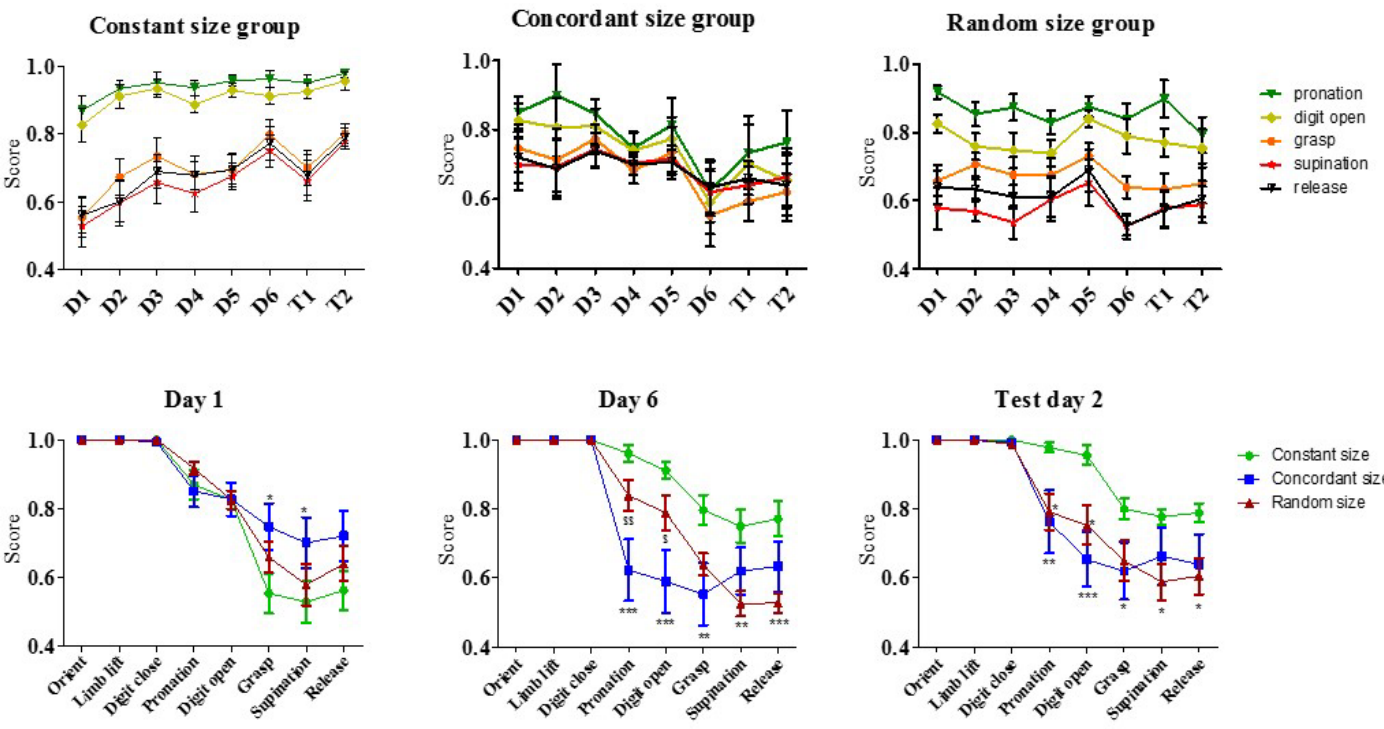


Fig. 3 : Movement component score; A) Reach movement Score of all time points across the groups and B) Reach movement Score of all groups across different time points. Two-way ANOVA followed by Bonferroni post tests has shown significant improvement in movement score by test day 2 for constant size group where no significant improvement for random size group. There was significant difference in different movement components for both concordant group and Random size group when compared to the constant size group on day 6 and test day 2 (*$p<0.05$; **$p<0.01$; ***$p<0.001$). A significant decline in movement score of pronation and digit open was found for concordant on day 6 when compared to random size group($ $p<0.05$, $$ $p<0.01$).

was found on day 6 for Pronation ($p<0.001$), digit open ($p<0.001$), and grasp ($p<0.01$) of concordant size group and for supination ($p<0.01$) and release ($p<0.001$) of random size group when compared to constant size group. Significant difference in pronation ($p<0.01$) and digit open ($p<0.05$) was found on day 6 for the random size group when compared to the concordant size group. A similar pattern was found on test day 2, where significant decrease in movement component score was observed for the concordant size group on pronation ($p<0.01$), digit open ($p<0.001$) and grasp ($p<0.05$) when compared to constant size and decrease in movement score was found on pronation ($p<0.05$), digit open ($p<0.05$), grasp ($p<0.05$), supination ($p<0.05$) and release ($p<0.05$) for the random size group when compared to the constant size group. There was a significant effect of groups ($F(2,112) = 19.11$, $p<0.0001$) and significant effect of components × groups interaction ($F(14,112) = 2.01$,) $p=0.0231$). It has to be noted that no significant difference in quality of reach was observed between concordant size group and random size group on test day where both groups has received all three sizes of pellets in random order.

Grasp

Extended Data Fig. 1 (Appendix 1: supplementary information) shows the doughnut pie chart of the percentage of grasp of day 1, day 6 and test day 2 of all the study groups. This represents the abnormal grasp used for successful retrieval of pellet compared to normal grasp. On day 1 all the groups had high abnormal grasp and by test day 2 the constant size group had least abnormal grasps.

Movement Trajectory and velocity

It was interesting to observe that there was no significant difference (Two-way ANOVA followed by Bonferroni post tests) in the trajectory (Fig. 4A) between all the three groups ($F(2,98) = 1.12$, $p=0.3564$). The velocity (Fig. 4B) has also shown no significant difference across the groups except for Concordant group, an increase in velocity on day 2 ($p<0.05$) and day 3 ($p<0.05$) when compared to Constant group. There was a significant effect of days × groups interaction ($F(14,91) = 1.96$, $p<0.0300$). Overall, trajectory and velocity of reach to grasp task didn't vary significantly across the days for all the three groups.

Qualitative observation of alternative reaching strategy

Except for the pellets which were successfully retrieved with the first attempt (Fig. 5A), the animals were able to withdraw the pellets successfully with two or three attempts. In case of an unsuccessful attempt (Fig. 5C), the paw was withdrawn to a digit close aim position and make another advance towards the pellet until successful reach is made (a hit) or till the pellet knocked off the platform (a miss). But rarely an unusual strategy was observed where the movement was altered soon after the paw came in contact with the pellet (Fig. 5B). In this case the paw was not withdrawn to a digit close aim position,

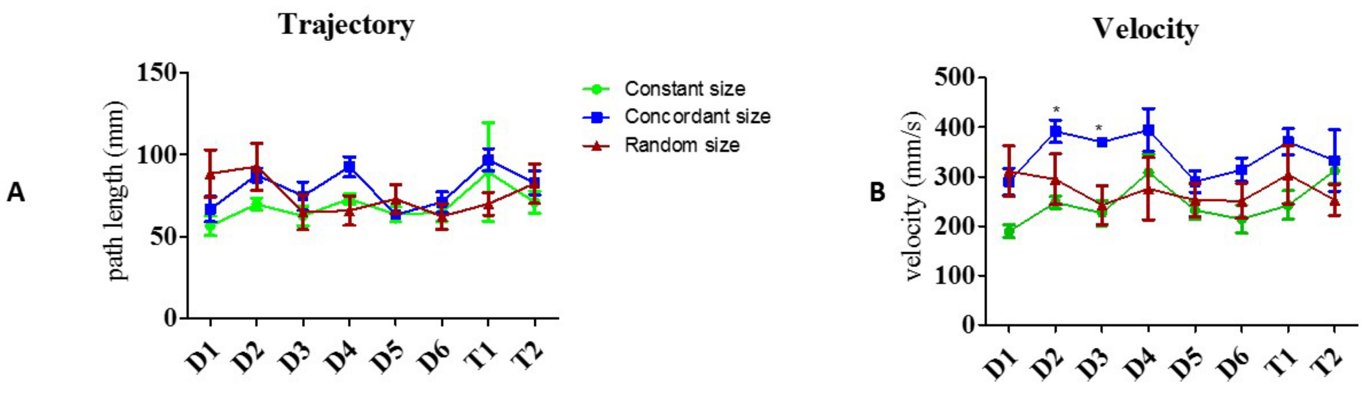
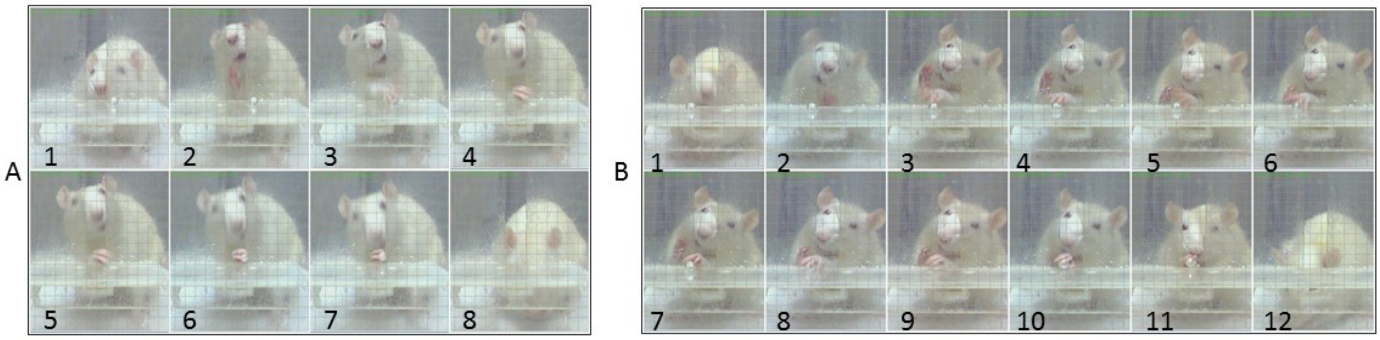


Fig. 4: A) Movement Trajectory of paw has not shown any significant variation between the groups across the time. B) Velocity of the paw movement also didn't show much variation across the days for all groups except on day 2 and day 3 for concordant group had a high velocity in comparison with the constant size group (*$p<0.05$).



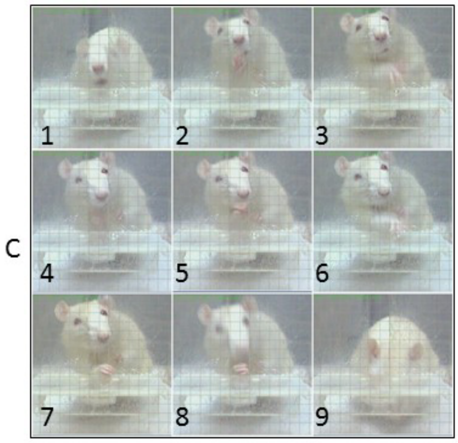
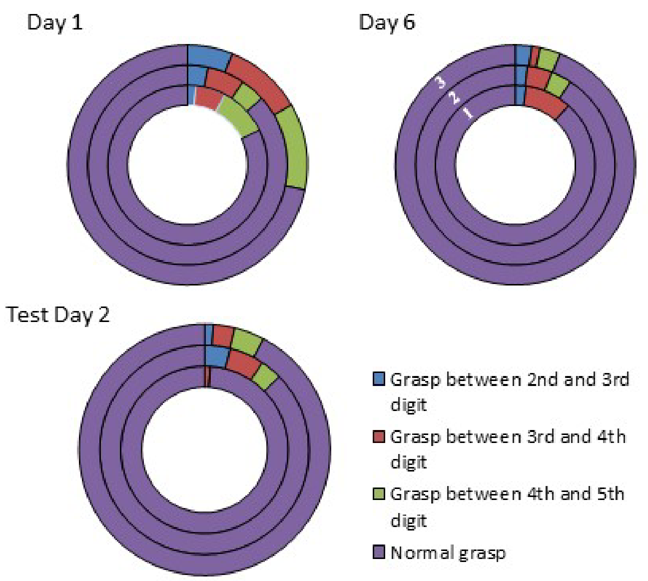


Fig. 5 : Reach to grasp movement of A) first attempt success, B) alternative movement strategy and C) multiple attempt success.



Appendix I: Supplementary information.

Extended Data Fig. 1 : Representative pie chart of the percentage of the grasp of day 1, day6 and test day2 of all the study groups (1: Constant size group, 2: Concordant size group, 3: random size group). This represents the abnormal grasp used for successful retrieval of pellet compared to normal grasp (purple)

but soon after the paw comes in contact with the pellet the paw was lifted up and the digits and paw was adjusted in an order to grasp a larger or smaller pellet than what was expected. This kind of movement strategy was observed mostly when random administration of pellet was given to concordant size group on test days and random size group on most of the days. Since the occurrence of such movement pattern was rare we could not quantify this. Also these reaches were excluded while analysing the trajectory and velocity.

Discussion

Motor skill studies have started over a hundred years (9) and reach to grasp task is being used as a wonderful paradigm to explore skilled movement in both rodents and primates since many decades. The task is comparatively easy to train and the learning is retained over long periods. Since the reach to grasp task help to model neurological conditions, it is being widely used in studies that involve rodents and primates as a model for disease conditions that affect movement (24).

In this study, we compared the performance of rats in reach to grasp task with a regular exposure of same size pellet versus a random exposure to different size pellets. Constant exposure to same size pellet throughout the task bestowed the learning of the skilled movement task and improved the outcome. To test whether pellet size affects the leaning, same size pellet was administrated for two days with two sessions each and a gradual improvement in performance was observed. The two day training for each size pellet might have helped in the consolidation of memory during sleep and thus improving the learning probably through off-line improvement (25). It is to be noted that the size of pellet used in the study was not too small or not too large, but in a range feasible manner for the rat paw to handle it effortlessly. However, this previous exposure didn't help in improvising the outcome when three different size pellets (small, medium and large) were given in random order. Random administration of different size of pellet helps to delineate the movement prediction and movement planning in reach to grasp task to certain extend. As already mentioned by Ian Q Whishaw et. al. (2000), skilled reaching in rodents has a nature of action pattern which is mostly fixed (4, 26). When a particular size pellet was given the animal learns to withdraw the pellet successfully by predicting the size and position of the pellet. The learning is through constant exposure and when this repeated exposure is disturbed, the learning hampers (27, 28).

This leads to a question whether the rats are able to form a movement plan to accommodate an unexpected size of pellet if random administration of various size pellets were given for a longer time. The poor performance even after 6 days of training with 2 sessions each indicate that rat is unable to form a unified/distinct movement plan to accommodate different size pellets. The study help to show that, only a continuous and repeated exposure to particular size pellet will help the rats to form a strategy to predict the expected target and to form a movement plan to reach to grasp the pellet. If there was a unified movement plan (though averaging of movement plans) to accommodate any size pellet then the rats would have succeeded in grasping the different pellets when administrated randomly. This would have improved the outcome. The result is similar to the findings in human studies where a distinct movement plan was made for the target of different orientation and no averaging of movement plan was observed (22). Unlike rodents, human, where vision help to predict the target properties, was able to prepare multiple potential actions parallel. The intrinsic property of the target (e.g., size) can be determined mainly from somatosensory information in rodents. By altering the intrinsic property of the target, the grasp part was found to be affected than the reach part in reach to grasp task which is similar to the previous findings (29).

Closer analysis of the task revealed a distinct movement made by the rats as they paw came in contact with the target. This helped in a faster withdrawal of pellet compared to the normal strategy where the paw has returned to aim posture and a new advance has been made. This alternative movement strategy where the paw was lifted and pre-shape of paw was modified soon after it came in contact with the pellet was unusual and not prevalent. It can be compared to the touch-then-grasp strategy used in human studies (1, 19). Further studies are required to figure out more about such variations. Except for the unusual movement made by rats during random administration of pellets, the reach to grasp trajectory didn't show significant variation among different study groups. Also, it is to be observed that the velocity didn't vary significantly across the different test groups.

Random administration has given a challenge to the animals to adjust their paw in such a way to accommodate the pellet in a successful manner. Random administration of different sized pellets helps to differentiate the movement prediction and movement planning from execution. The performance was increased since the rats were able to predict the expected size of the pellet when constant size pellet were given in the same session. But when the pellets were given in random order the rats were not able to predict the size of the pellet and also were not able to form a unified movement plan to withdraw any size pellet. This leads to the poor outcome and also formed a rare and unusual movement strategy. Our study also suggests exploiting the reach to grasp task to study the skilled movement in rodents in more divergent manner and random administration of different size pellets is one such way to do the same.

Acknowledgements

We thank University Grant Commission (UGC) India, for funding the study and National Institute of Mental Health and Neuro Sciences (NIMHANS) Bengaluru, for providing the infrastructure facilities for the study.

Conflicts of Interest

Authors do not have any conflicts of interests.

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