The Circular Platform Task for Evaluation of Mci in the Grey Mouse Lemur (*Microcebus murinus*), a Non-human Primate Model

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The grey mouse lemur, a non-human primate model of aging

Mouse lemur (Microcebus murinus) is a nocturnal prosimian primate originating from Madagascar with a life expectancy of 8-10 years. The grey mouse lemur presents specific characteristics that make it a good primate model to study and evaluate behavioral and cognitive parameters. In particular they have a small size and weight (80 to 120 g) with an omnivorous dietary habits, and the possibility to assess their behavioral and cognitive performances with specific tasks which have been developed and adapted in our laboratory [1,2]. Some mouse lemurs spontaneously develop cognitive impairments after five years or older [3]. These cognitive impairments have been related in particular with age-related cerebral atrophy [1]. Among the cognitive task available to evaluate mouse lemurs cognitive performances, we use the circular platform task that evaluate spatial reference memory (hippocampus-dependent), and consists in a less stressful version of the Morris water maze.

The circular platform task

The circular platform task apparatus was an adaptation of the device described by Barnes [4] for mouse lemurs. It consisted of a white circular platform (diameter, 100 cm) with 12 equally spaced circular holes (each 5 cm in diameter) located 3 cm from the perimeter. The platform could be rotated. The maze platform was placed 60 cm above the floor, and a cardboard nest box (10 cm × 10 cm × 20 cm) could be inserted and removed beneath each hole and served as a refuge (goal box). To prevent the mouse lemur from escaping, the platform was entirely surrounded with a white wall 25 cm high and covered with a transparent Plexiglas® ceiling that permitted the mouse lemurs to see the extra-maze visual cues. The apparatus was surrounded by a black curtain hung from a square metallic frame (length of the side, 120 cm) located 110 cm above the floor. The roof of the frame was a one-way mirror to allow observation. Attached beneath the one-way mirror and along perimeter of the maze (about 50 cm above the platform), there are 24 evenly spaced 2-W lights, illuminating the maze. The maze center was also illuminated with a 60-W light. Between the one-way mirror and the upper edge of the wall, various objects were attached along the inner surface of the curtain to serve as visual cues. The starting box was an open-ended dark cylinder positioned in the center of the platform. Transparent radial Plexiglas partitions (25 cm high x 20 cm long) were placed between the holes to prevent the strategy used by some mouse lemurs to go directly to the periphery of the platform and then walk along the wall and inspect each hole one by one. Consequently, animals had to return to the center of the platform after each hole inspection.

Animals were given one session of habituation and training (day 1) and one session of testing (day 2). Each session included four trials, each of which began with placement of the animal inside the starting box. After 30 seconds, the box was lifted to release the animal. For the lemurs, the objective was to reach the goal box positioned beneath one of the 12 holes, kept constant relative to the cues for all trials. When the animal entered the goal box, the trial was stopped, and the animal was allowed to remain in its nest box for 2 minutes. After each trial, the platform was cleaned and randomly rotated on its central axis to avoid the use of intra-maze cues, although the position of the goal box was kept constant relative to the cues.

On day 1, trials 1 and 2 consisted of placing the animal in a four-walled chamber containing only the opened goal compartment (one-choice test). For trials 3 and 4, the platform comprised six evenly spaced open compartments (six-choices test). These two trials permitted the animal to explore the maze, observe the visual cues, and further learn the position of the goal box. On day 2 (testing day), 12 compartments were opened during the four trials. Performance was assessed based on the time required for the animal to reach the correct exit

(expressed in sec) and the number of errors (wrong quadrant visit) prior to reaching the goal box. Data were expressed as the mean time to reach the correct exit and mean number of errors during the 4 trials of day 2.

Results

The mean number of errors was 1.8 for the young adult group and 6.3 for the older group (see Figure 1). The difference between young and aged was significant (unpaired t-test, p=0.043 ; t=2.216 ; df=14). However, a large individual variability emerged within the older group, with some of the older animals performing as well as younger ones, whereas other older animals were severely impaired. A significant correlation between age and performance was identified (r = 0.67, p < 0.01).

Conclusions

The circular platform test seems to be adapted to observe significant age-related cognitive impairments in grey mouse lemurs.

Ethics statement

All experiments were performed in accordance with the Principles of Laboratory Animal Care (National Institutes of Health publication 86-23, revised 1985) and the European Communities Council Directive (86/609/EEC). The Research was conducted under the authorization n° 91–305 from the "Direction Départementale des Services Vétérinaires de l'Essonne" and the Internal Review Board of the UMR 7179. All the experiments were done under personal license (authorization number 91–460, issued 5 June, 2009) delivered by the Ministry of Education and Science.

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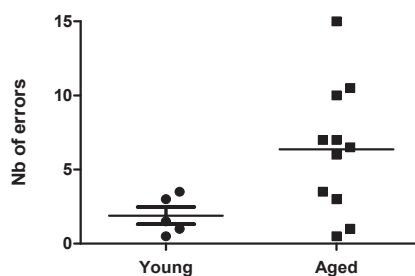
Figure 1. Performance. expressed as the number of errors before finding the correct exit of young and aged adult mouse lemurs in the circular platform task.