Assessment of executive functions in mice with the Fixed-Ratio schedule of reinforcement

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BACKGROUND

The simplest operant schedule of reinforcement is the Fixed Ratio (FR). In this task, animals must provide a determined number of responses (i.e., a ratio of responses) to obtain each food reward. In FR1, a single response is required, 2 responses in a FR2, 5 in a FR5 and so on. The FR is often used only to shape the operant response before to go further with another task, but of course, it can be used with more interesting goals. Classically, measures such as inter-responses time (IRT), latency to collect the delivered food reward, response or reward rate, but also post reinforcement pause are collected[1,2]. Together, they allow to obtain information about motor ability, learning and motivation. However, there is a lack of interest in the executive aspect potentially implied by the FR[3], especially in situations where the ratio is held constant across multiple training sessions. Indeed, in such situations, as training progress the subject can learn that a certain quantity of responses is required before the reward is available. And hence, checking the food tray to see if the reward is available should be more probable as the animal progress in the ratio. With this operant procedure, it seems therefore possible to investigate the animal's executive function. In this study, we thus focused on the premature head entries into the empty food tray (PHE, i.e., when the reward was not delivered yet) and their evolution across sessions of FR30. The analysis of the distribution of PHE could offer a way to analyze the subject's ability to optimize its operant behavior. We also compared this aspect of the operant behavior between young and old mice as the age is factor affecting the executive function.

METHOD

Animals and housing conditions
39 2- to 6-month-old (YOUNG) and 22 16- to 18-month-old (OLD) C57/BL6 male mice were singly-housed under a standard light-dark cycle (lights on at 07.00 and off at 19.00). They were maintained around 85-90% of their reference bodyweight during the operant task, water was ad libitum. (Data of animals in three similar experiments were pooled)

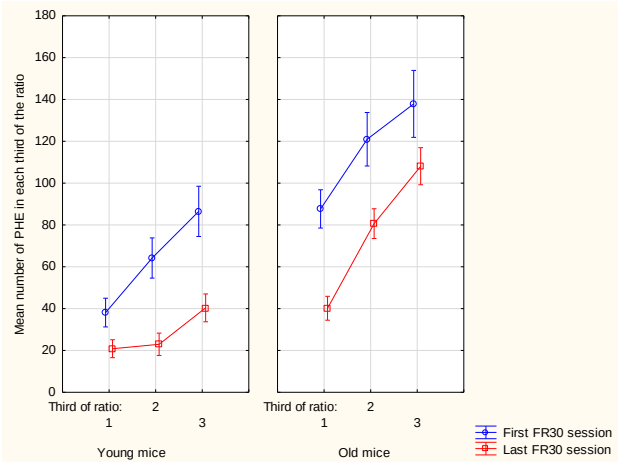
Apparatus
Behavioural training occurred in classic mouse modular operant chambers (MED Associates; St. Albans, VT) equipped with two levers for the operant response and the reward dispenser. The only sources of light were the visual stimuli above each lever. Reinforcers were 20mg pellets from Testdiet©.

Operant procedure
The mice were first trained to produce the operant response (lever press); they were then trained to produce more responses for each reward with 5 additional FR sessions (FR1, FR5, FR10, FR15 then FR20). We then analyzed the behavior produced in the 10 FR30 sessions that followed. There were 30 trials in each session. The Animal Care and Experimentation Committee gave its approval according to the Belgian implementation of the animal welfare guidelines laid down by the European Community.

Behavioural measures
For each mice, the total number of PHE after the 9 first responses of the ratio, after 9 responses in the middle of the ratio and finally after the 9 last responses of the ratio, in the first and in the tenth FR30 session.

Statistical analysis
A 3(Third of ratio: first, middle and last) X 2(Session: first and tenth) X 2(Age: Young vs old) with repeated measures on both first factors was realized. Tukey HSD test was used for post-hoc comparisons.

RESULTS



There was a main age effect : old mice produced significantly more premature head entries in the food tray than young ones ($F(1,59)=22.41$, $p<0.00002$). Mice also prematurely visited the food tray more and more as they pressed the lever (main third of ratio effect : $F(2,118)=122.34$, $p<0.000001$). Mice also produced less PHE because of training ($F(1,59)=36.62$, $p<0.000001$).
Post hoc also confirmed significant differences, essentially between age groups and, for each group, between the three part of the ratio.

CONCLUSIONS

We found that mice visited more the food tray as they got closer to the last response in the ratio. Doing this, animals exhibited a kind of estimation of the "right moment" to visit the food tray (the cognitive aspects underlying animals' behavior in fixed-ratio schedules of reinforcement have probably been less studied than those underlying it in fixed-interval ones.) Moreover, mice acquired this planification ability quickly (not represented here) and improved it across the training sessions. Old mice, although improving this aspect of their operant behavior, were less efficient than young mice. Finally, the analysis of the PHE could contribute to assess the executive functions of animals and could be used as a supplementary measure to obtain more information in various animal models where the executive functions are supposed to be negatively impacted.

REFERENCES

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