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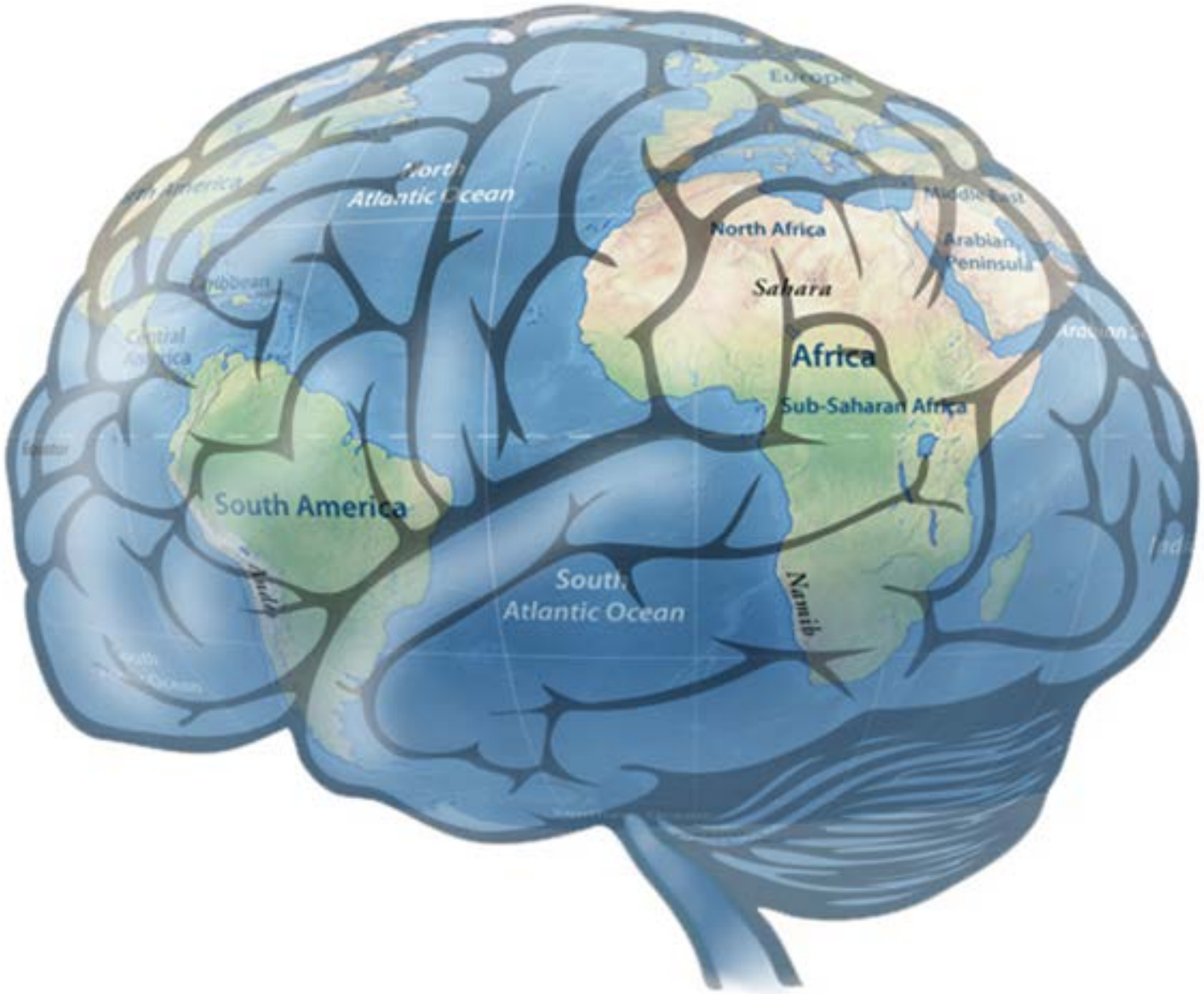
Новый Лабиринт-Трансформер для оценки различных видов пространственной навигации, памяти и обучения лабораторных животных

PhD Filatova E.V.

Laboratory of neurophysiology and pathology of behavior

GLP-PLANETIV, 28 - 30 июня 2023 г, Санкт-Петербург, Россия

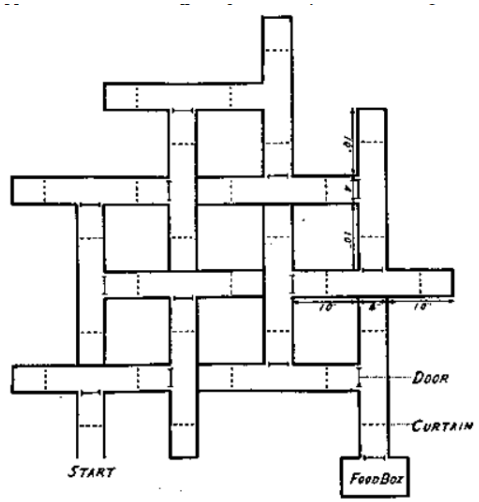
Spatial navigation



Spatial navigation and memory deficits

- Alzheimer's disease (AD)
- Parkinson’s disease (PD)
- Mild cognitive impairment (MCI)
- Autism
- Age-related deficits
- Over drinking

Alley maze



Plan of maze
14-Unit T-Alley Maze

FIG. 1

(From M. H. Elliott, The effect of change of reward on the maze performance of rats. *Univ. Calif. Publ. Psychol.*, 1928, 4, p. 20.)

Edward C. Tolman (1948)COGNITIVE MAPS IN RATS AND MEN.The Psychological Review, 55(4), 189-208.

Biel maze, and its more popular modification – Cincinati maze

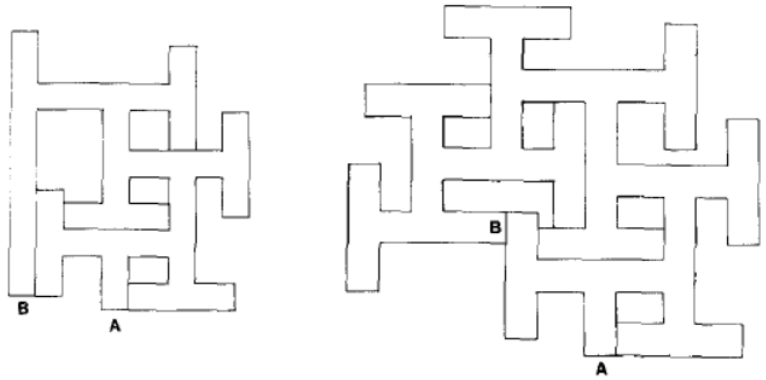


FIG. 1. Outline drawing of the Biel maze (left) and new or "Cincinnati" maze (right). Mazes are drawn in scale to one another. Channel width in the Biel maze is 12.7 cm (5 in) and 15.2 cm (6 in) in the new maze. Path A in the test refers to the start being at point A and exit at point B. Path B refers to the start being at point B and exit at point A.

the *Biel, W. C. Early age differences in the maze performance of the albino rat. J Genet Psychol 56: 439--453, 1940; Vorhees CV. Maze learning in rats: a comparison of performance in two water mazes in progeny prenatally exposed to different doses of phenytoin. Neurotoxicol Teratol. 1987;9:235–241.*

T-maze and Y-maze

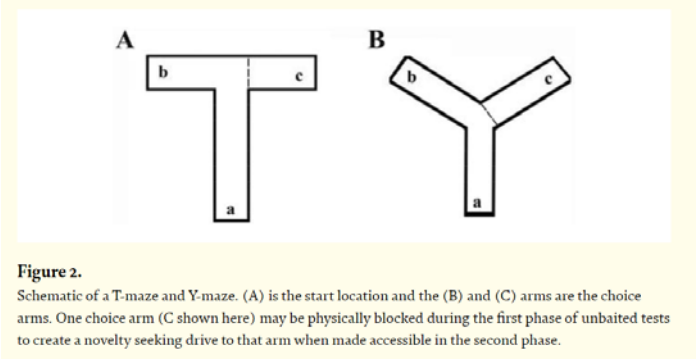
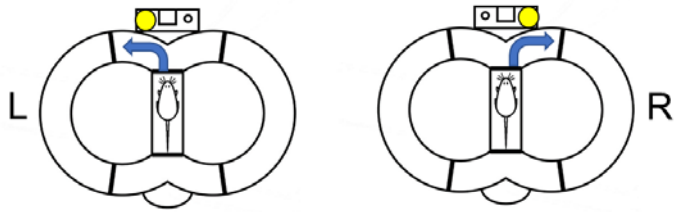


Figure 2.
Schematic of a T-maze and Y-maze. (A) is the start location and the (B) and (C) arms are the choice arms. One choice arm (C shown here) may be physically blocked during the first phase of unbaited tests to create a novelty seeking drive to that arm when made accessible in the second phase.

Grech, A. M., Nakamura, J. P., & Hill, R. A. (2018). The Importance of Distinguishing Allocentric and Egocentric Search Strategies in Rodent Hippocampal-Dependent Spatial Memory Paradigms: Getting More Out of Your Data. The Hippocampus - Plasticity and Functions.

Double-ring automatic maze



Filatova E.V., Orlov A.A., Afanas'ev S.V. A two-ring maze for studies of the behavior of laboratory animals. Neuroscience and Behavioral Physiology. 2015. T. 45. № 7. C. 765-770

Radial arm maze

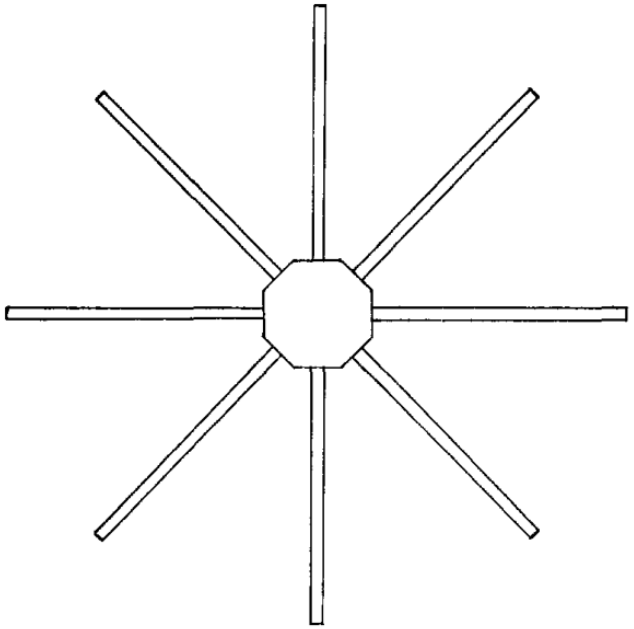


FIGURE 1. Diagram of a top view of the apparatus.

Olton, D. S., & Samuelson, R. J. (1976). Remembrance of places passed: Spatial memory in rats. Journal of Experimental Psychology: Animal Behavior Processes, 2(2), 97–116. doi:10.1037/0097-7403.2.2.97

Barnes maze

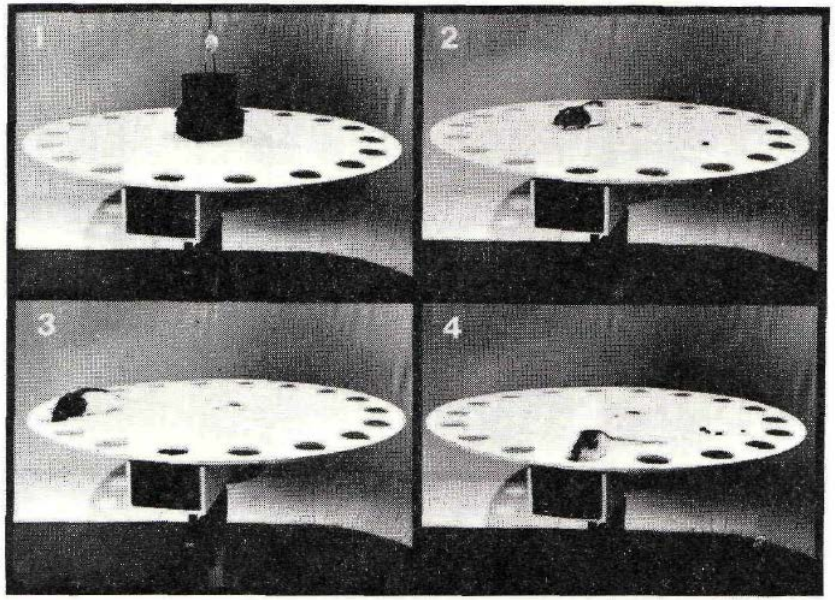
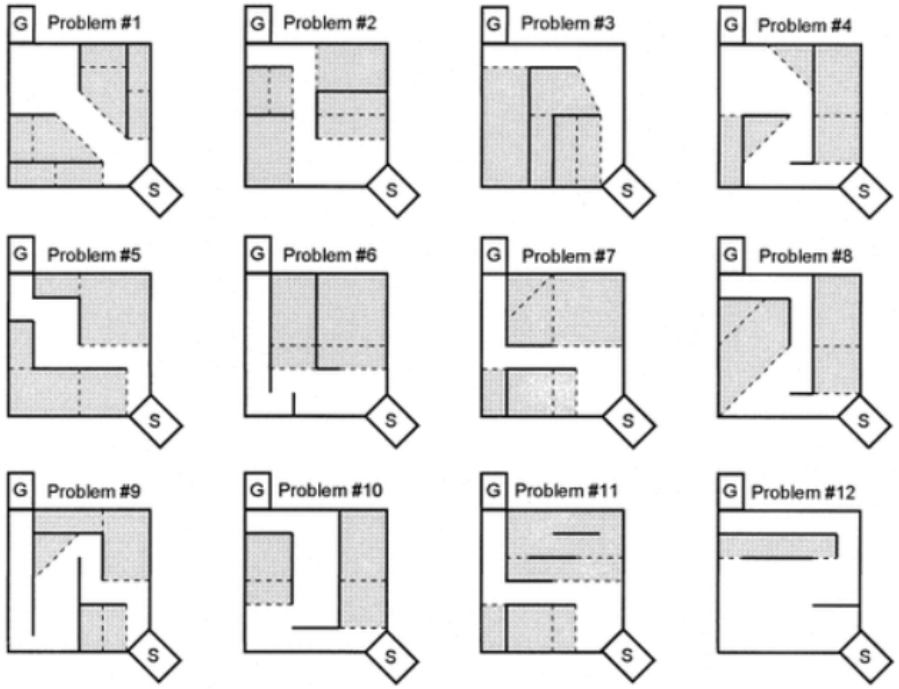


Figure 2. Examples of various stages in the performance of the circular platform task. (1: The rat was confined in the start box for 30 sec before the beginning of a trial. 2: The start box was raised after this period of time and the rat was allowed to move freely on the platform. 3: A nose-head-neck deflection into a hole that was not above the tunnel was considered an error. 4: The trial was terminated when the rat's four feet were no longer on the platform surface.)

Barnes, C. A. (1979). Memory deficits associated with senescence: A neurophysiological and behavioral study in the rat. Journal of Comparative and Physiological Psychology, 93(1), 74–104. doi:10.1037/h0077579

Hebb-Williams maze



Kobayashi S, Ohashi Y, Ando S. Effects of enriched environments with different durations and starting times on learning capacity during aging in rats assessed by a refined procedure of the Hebb-Williams maze task. J Neurosci Res. 2002 Nov 1;70(3):340-6.

Morris water maze

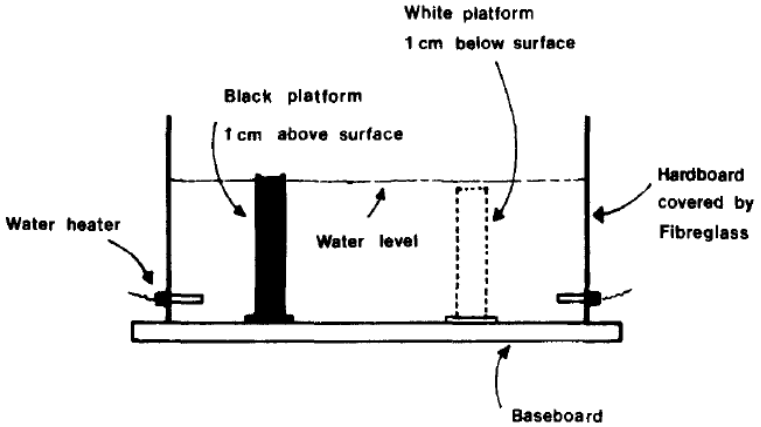


FIG. 1. A cross-sectional view of the apparatus showing both platforms in relation to the water level. Only one platform was present in any training condition. For a full description see text.

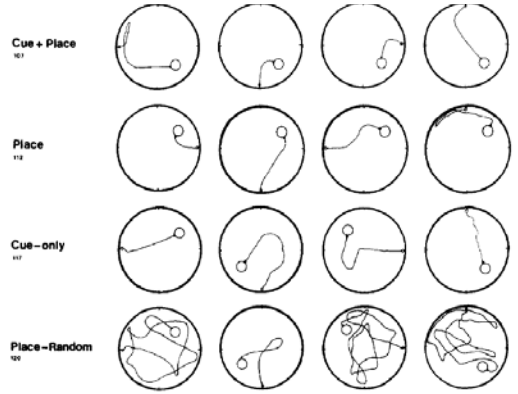
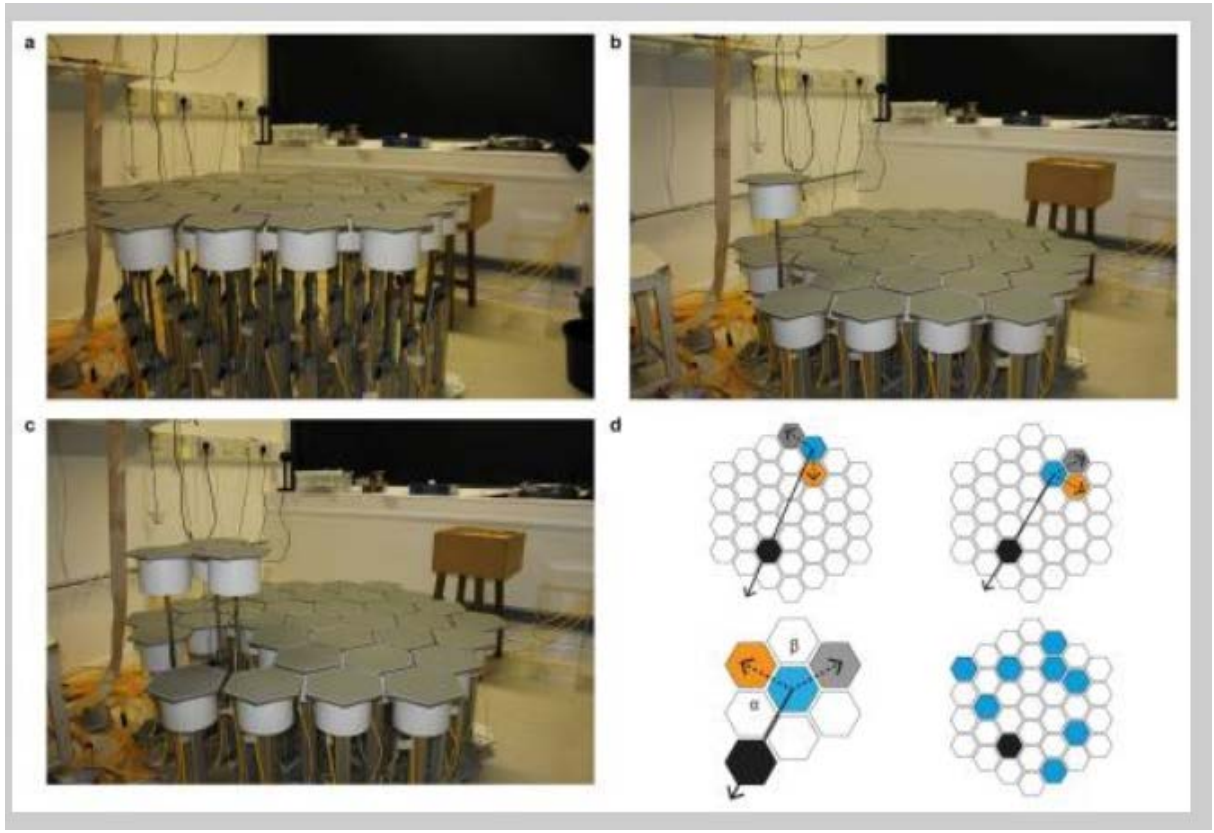


FIG. 5. A vertical view of the tracks taken by the rat in each group just poorer than the median (with respect to directionality). The paths are reasonably direct for Rats 107, 112, and 117, while Rat 120 of Group Place-Random swims all over the pool. Platform size is drawn larger than to scale for purposes of clarity.

Morris, R. G. M. (1981). Spatial Localization Does Not Require the Presence of Local Cues. Learning and Motivation, 12(2), 239–260. https://doi.org/10.1016/0023-9690(81)90020-5

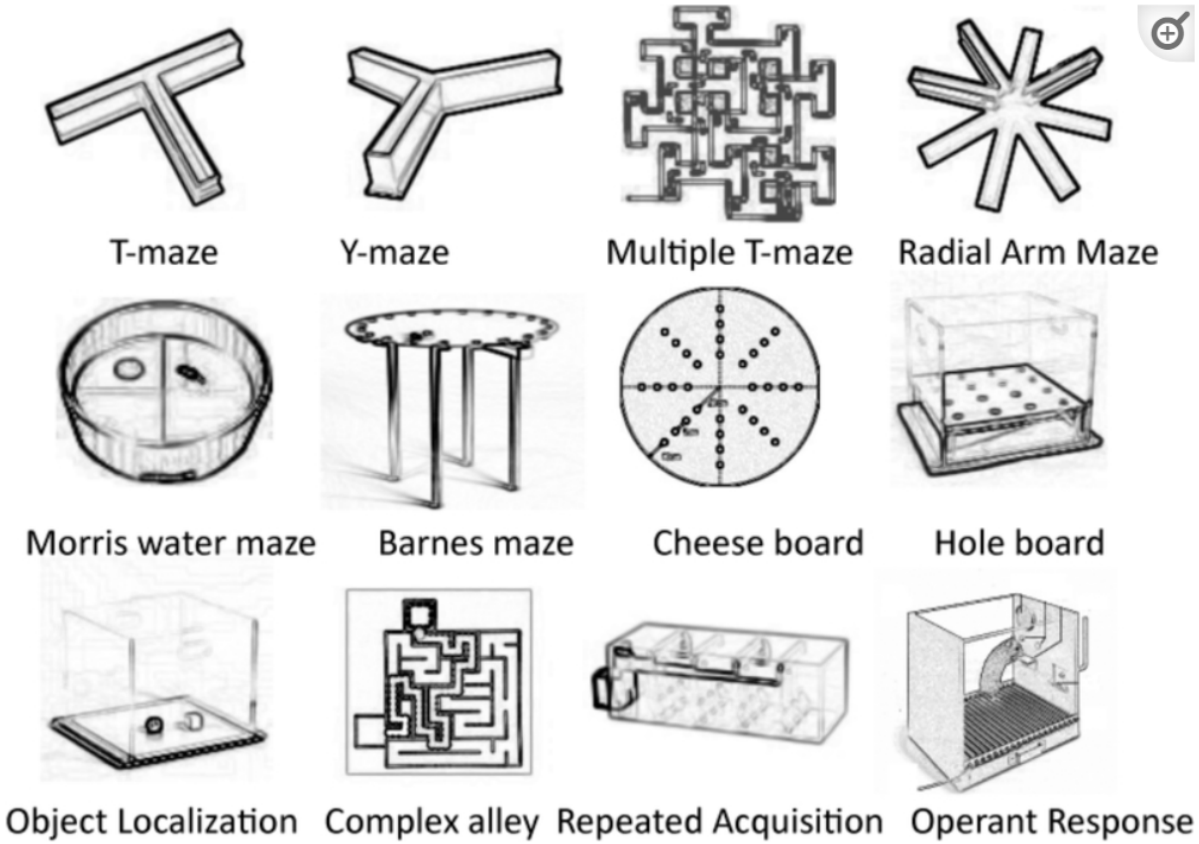
The Honeycomb Maze



Honeycomb Maze with all (a), one (b), and three platforms raised (c). (d) Schematic navigation paradigm: Upper left, at any given location (e.g. blue start platform) two choices are offered, correct (orange) having a smaller heading direction towards the goal (black) than the other (grey). Upper right, next choice: the platform previously chosen becomes the new “occupied” platform (blue). Lower left, each choice is described by two angles: α between correct choice and goal heading direction, and β between correct and incorrect choices. Lower right, eight different start platforms (blue).

from *Ormond J, O'Keefe J. Hippocampal place cells have goal-oriented vector fields during navigation. Nature. 2022 Jul;607(7920):741-746. doi: 10.1038/s41586-022-04913-9. Epub 2022 Jul 6. PMID: 35794477; PMCID: PMC9329099.*

Battery of tests



Sharma S, Rakoczy S, Brown-Borg H. Assessment of spatial memory in mice. Life Sci. 2010 Oct 23;87(17-18):521-36.

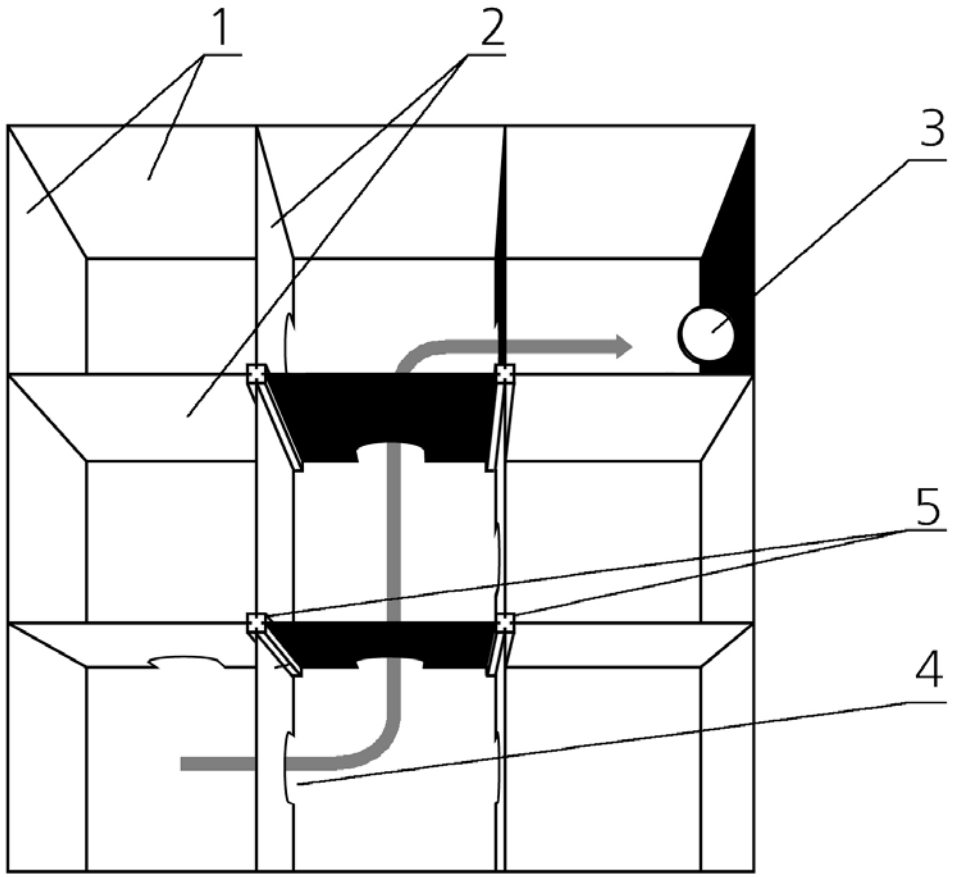
Transformer maze

- Modular design
- Different routes, comparable in difficulty level
- Different types of navigation
- The task can either include external cues or not

Filatova E. Transformer maze for the evaluation of the learning and memory in rodents. Heliyon. 2022 Oct 21;8(10):e11211. doi: 10.1016/j.heliyon.2022.e11211. PMID: 36325140; PMCID: PMC9619002.

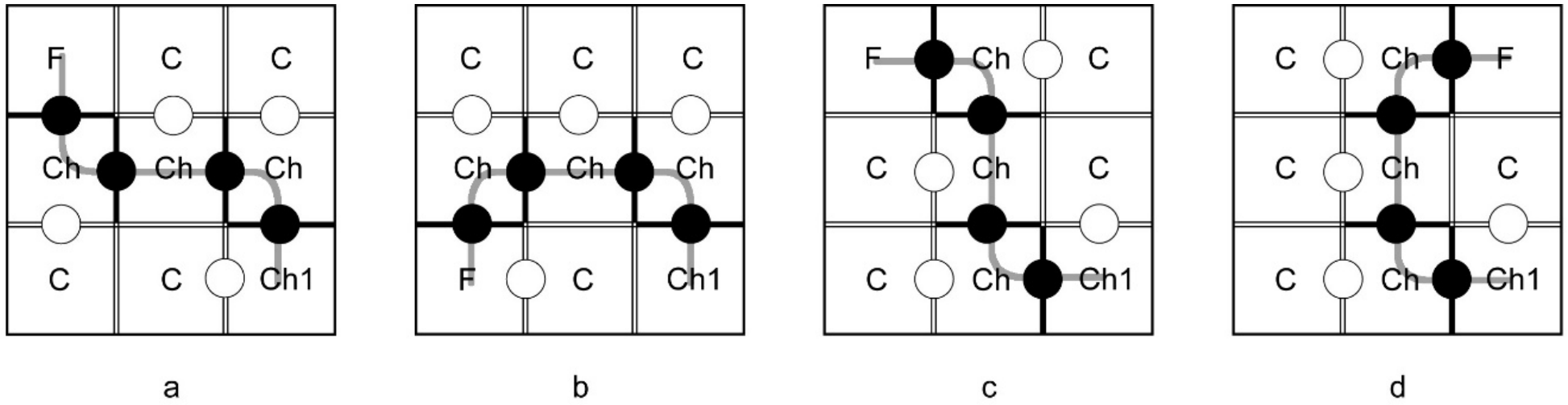
RF Patent No. 2789575 (Device for animal behavior testing and method of its using)

Transformer maze



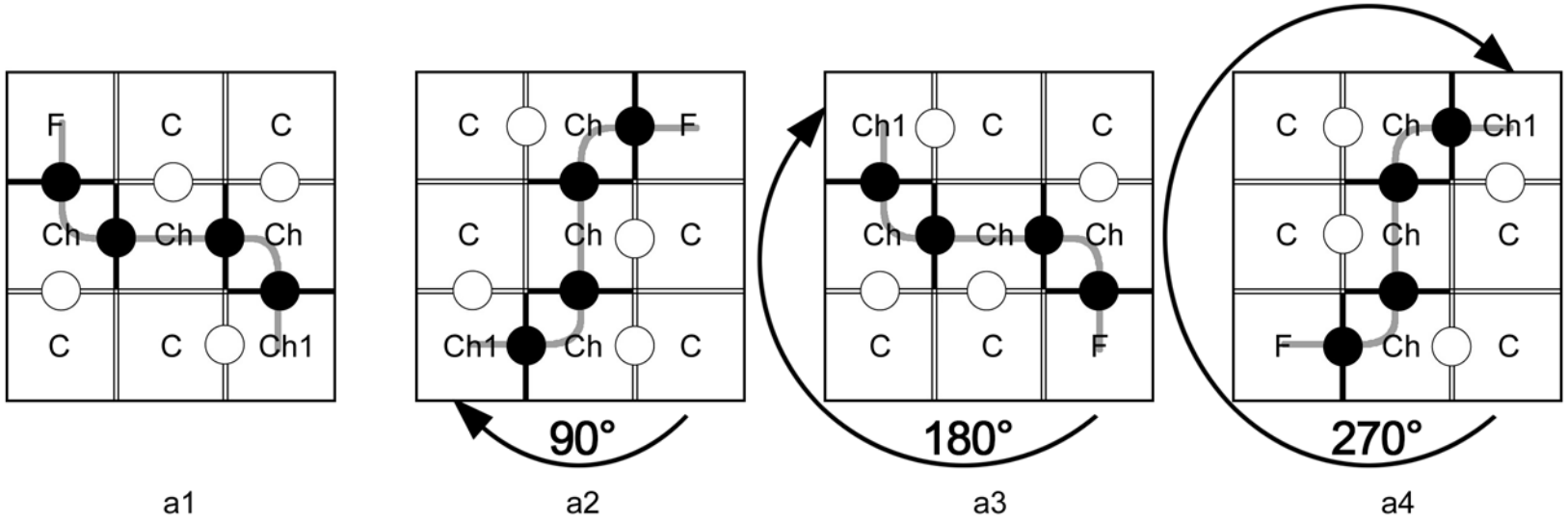
Maze schematic. Example of one possible route. 1 - external walls, 2 - interior walls, 3 - feeder, 4 – arch passage, 5- columns. The gray arrow shows the correct path to the finish compartment with positive reinforcement. The feeder is mounted on the black side of the barrier wall 10 cm above the floor.

Four different routes



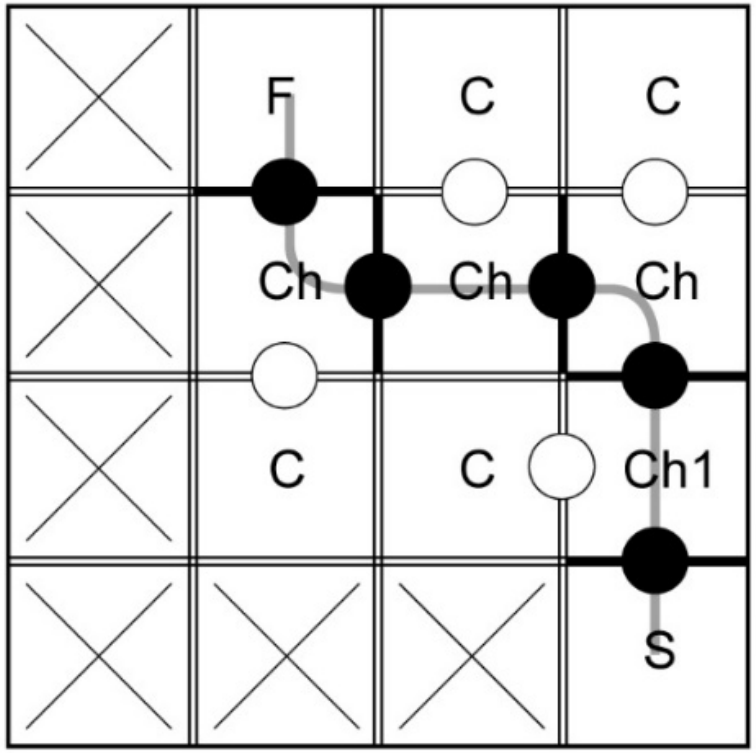
Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch- choice compartment. The white circle - passage through the white barriers, the black circle - passage through the black barriers. The grey line shows the correct route to the feeder.

Four options for one route after 90, 180 and 270 degrees rotation



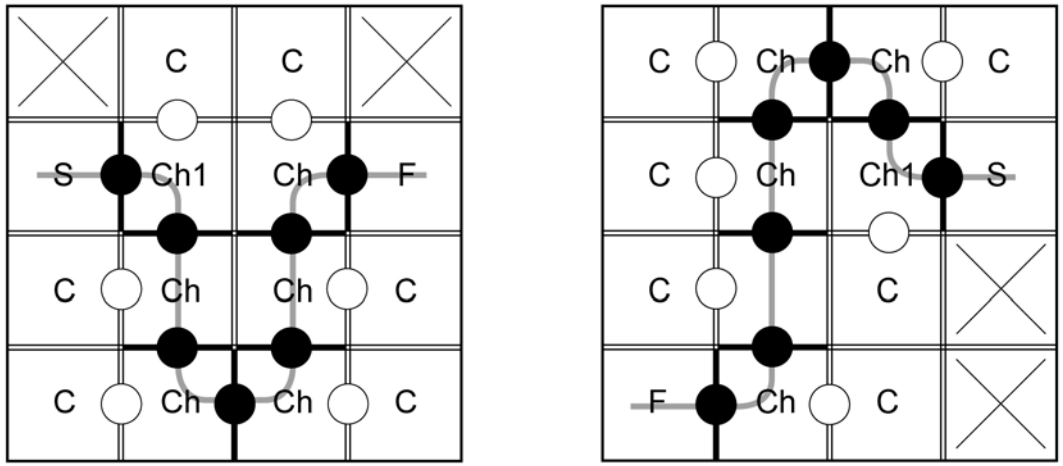
One route (a1) after a 90 (a2), 180 (a3) or 270 (a4) degrees rotation. Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch - choice compartment.

An example of a 3x3 maze with an additional start compartment built in a 4x4 maze



S-start compartment, Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch- choice compartment. Crosses indicate inaccessible compartments.

Examples of the test routes in a 4x4 maze



S-start compartment, Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch- choice compartment. Crosses indicate inaccessible compartments.

The protocol of successive trials

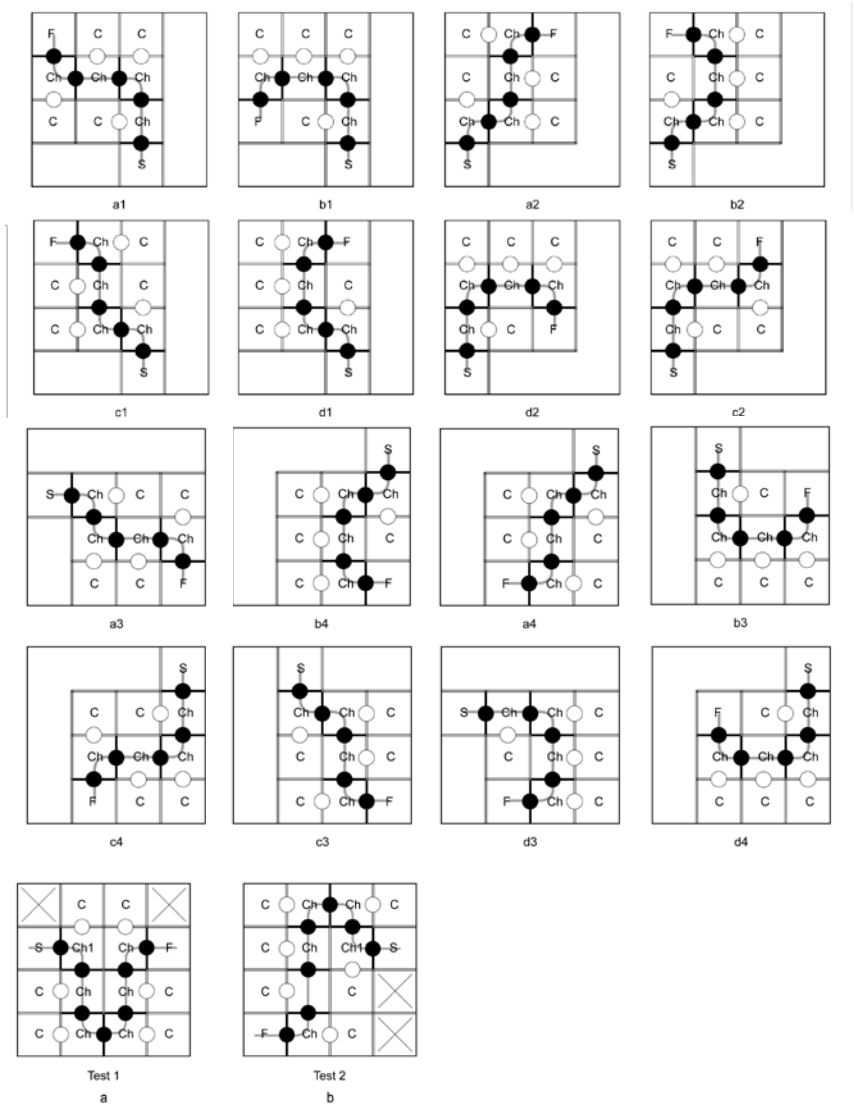
1 training session

2 training session

3 training session

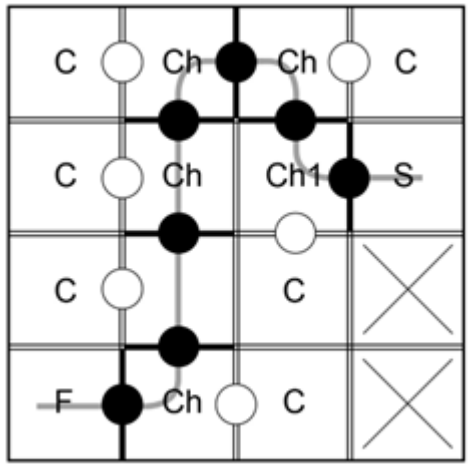
4 training session

Test session



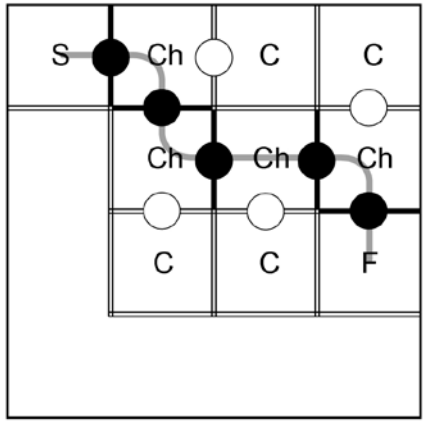
S-start compartment, Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch - choice compartment. Crosses indicate inaccessible compartments.

Assembling the test rout and execution



Video 1

The example of rat behavior at the beginning of the learning

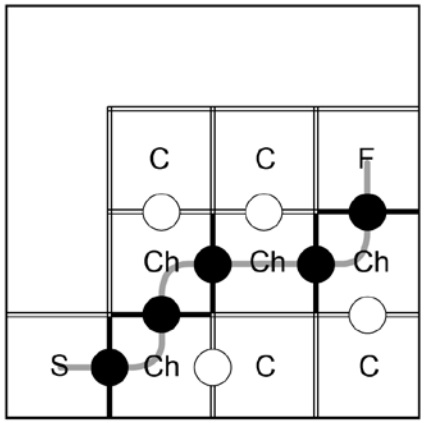


a3

Video 2

the rat has difficulty in finding the way

The example of rat behavior at the finish of the learning

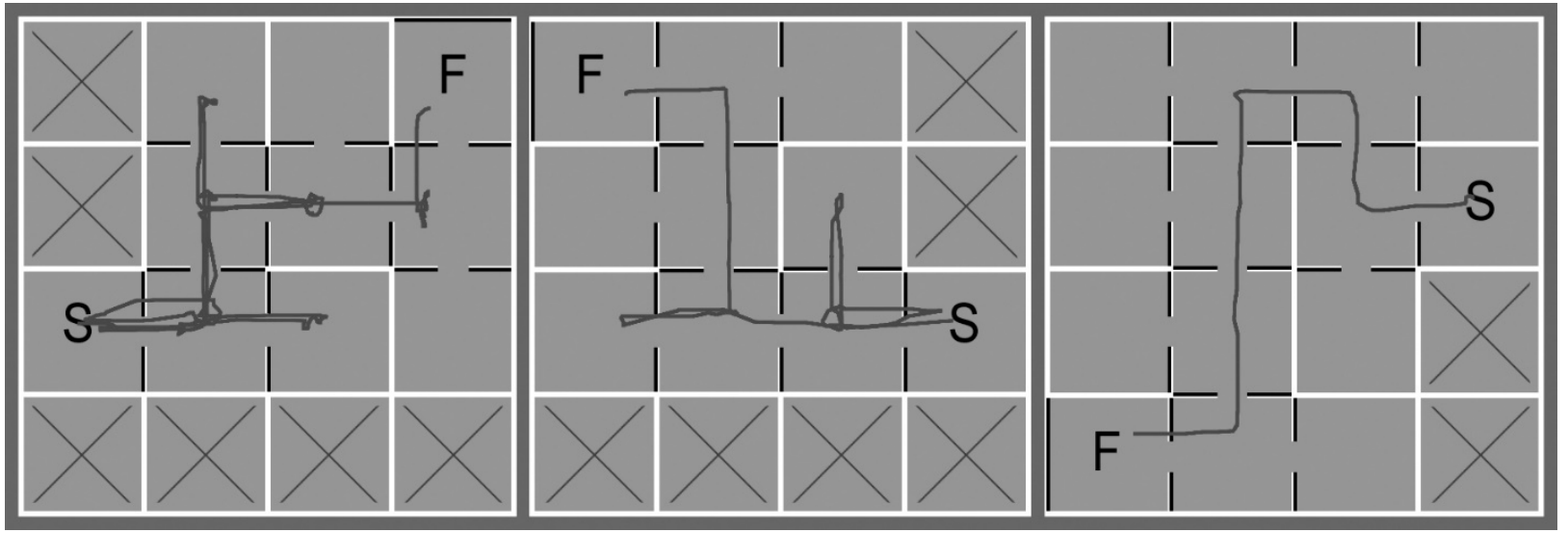


c2

Video 3

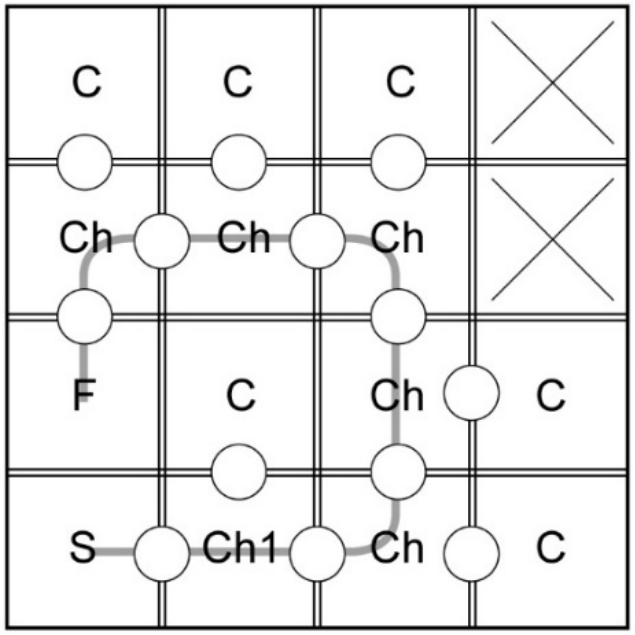
the rat fast finds the way

The samples of the rat tracks



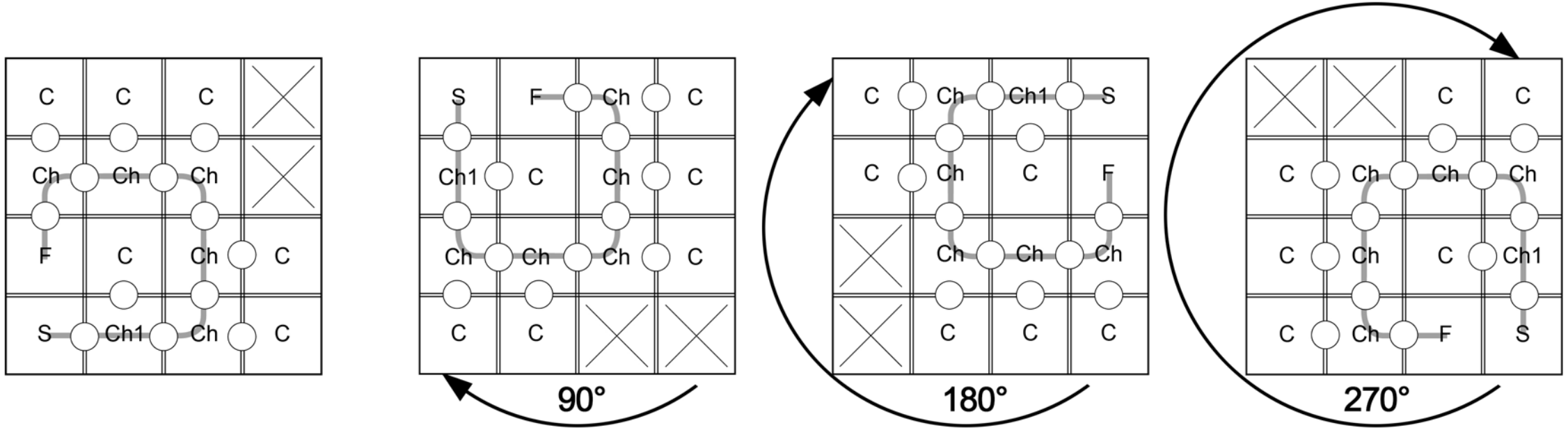
The superposition of the rat tracks and maze schemes. Samples of the same rat in different routes at the beginning, middle and the end of training. S - start compartment, F - finish compartment. Crosses indicate inaccessible compartments

Route-based navigation task



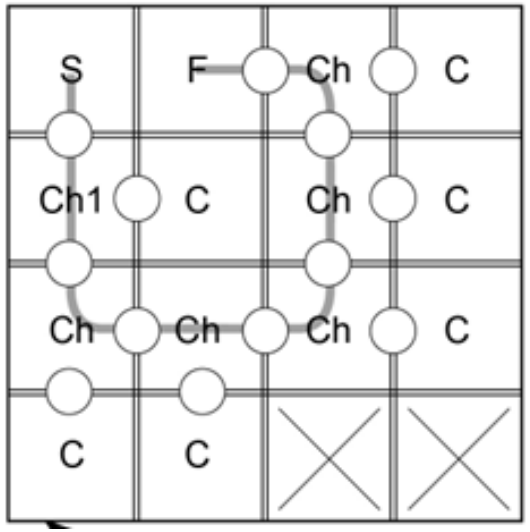
An example of the route without any cues built in a 4x4 maze that allows us to assess egocentric navigation. F - finish compartment with a feeder, C - cul-de-sac compartments, Ch - choice compartment; crosses indicate inaccessible compartments.

Four options for route after 90, 180 and 270 degrees rotation



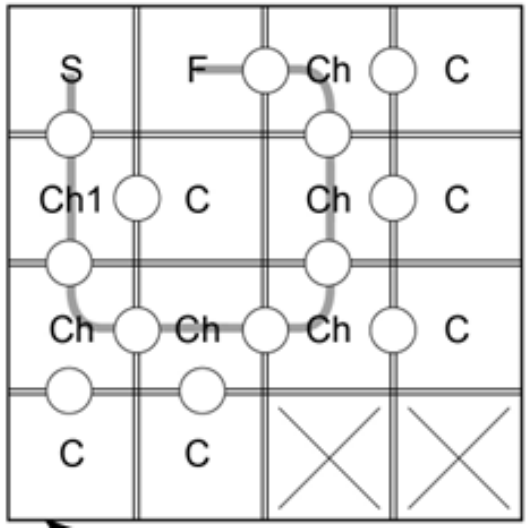
Route after a 90 , 180 or 270 degrees rotation. Ch1- first choice compartment, F- finish compartment with a feeder, C- cul-de-sac compartment, Ch - choice compartment.

Assembling the route-based navigation task and execution



Video 4

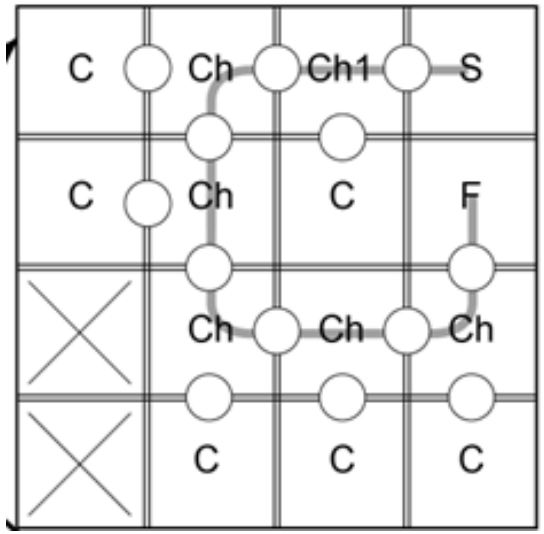
The example of rat behavior at the beginning of the learning



Video 5

the rat has difficulty in finding the way

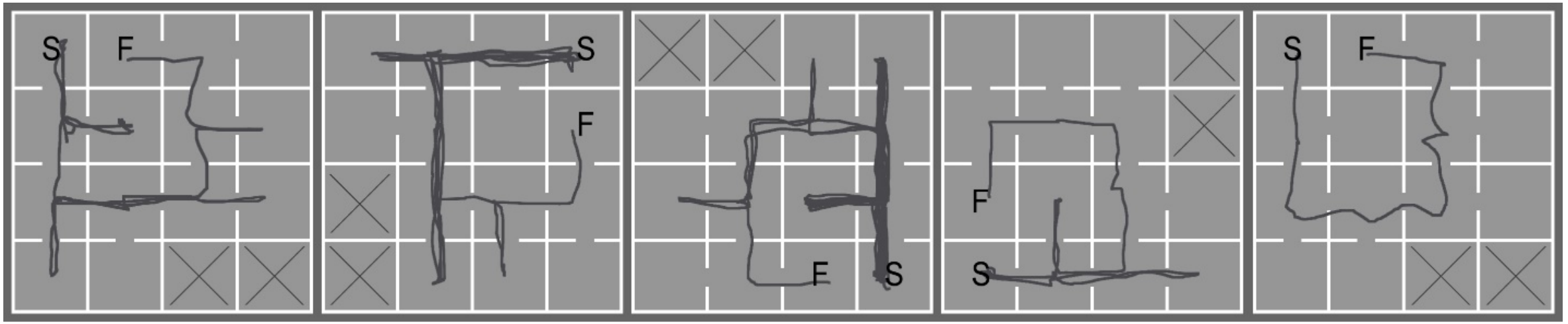
The example of rat behavior at the finish of the learning



Video 6

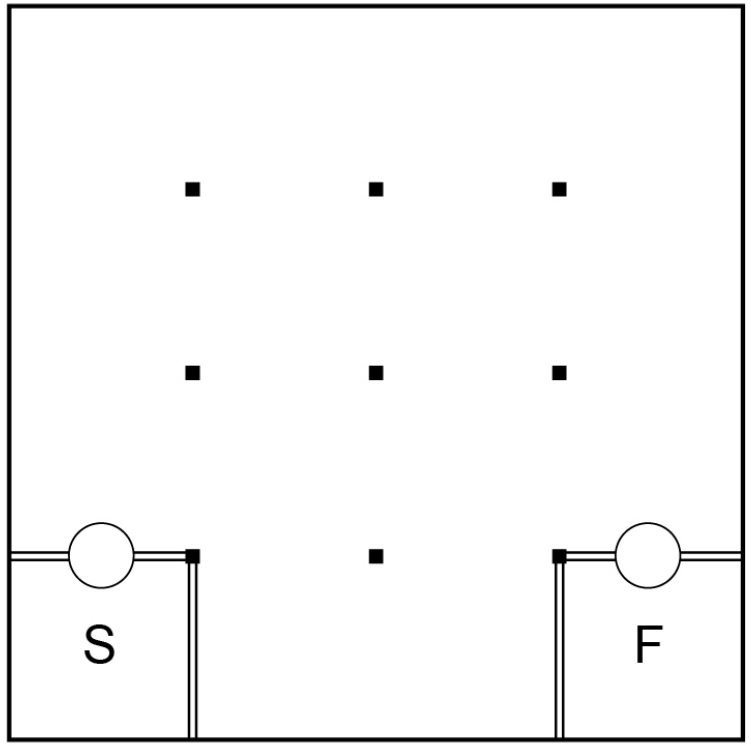
the rat fast finds the way

The samples of the rat tracks during the learning

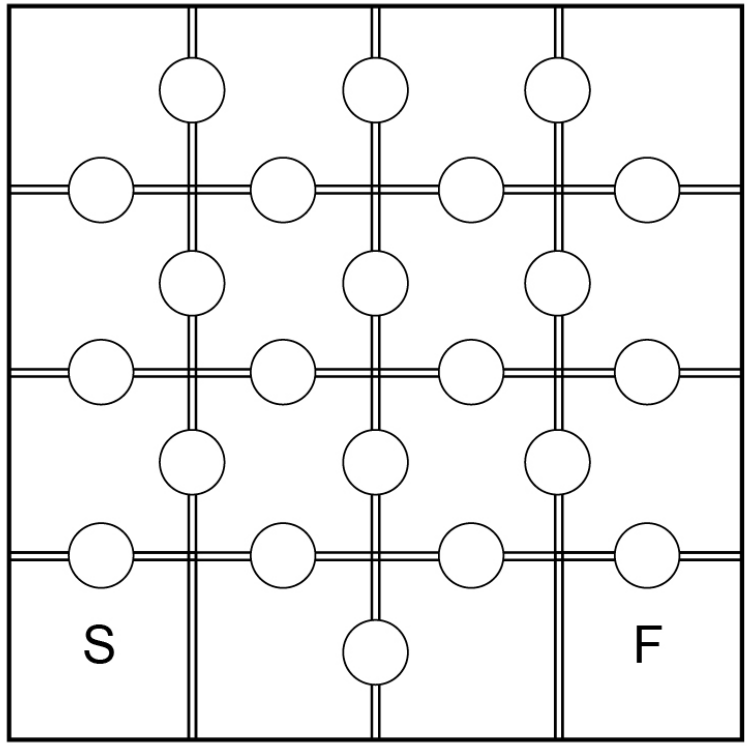


The superposition of the rat tracks in the route-based navigation task in the maze configuration without any cues. Samples of the same rat in different turns of the route at the beginning (var1), middle (var2, var3, var4) and the end of training (var1). Var.2, 3, 4 are route turns of 90, 180 and 270 degrees. S-start compartment, F- finish compartment. Crosses indicate inaccessible compartments.

Navigation task



a

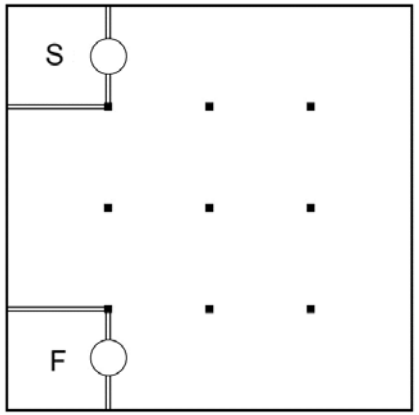


b

(a) Empty arena with start and finish compartments

(b) Arena with white barriers with holes

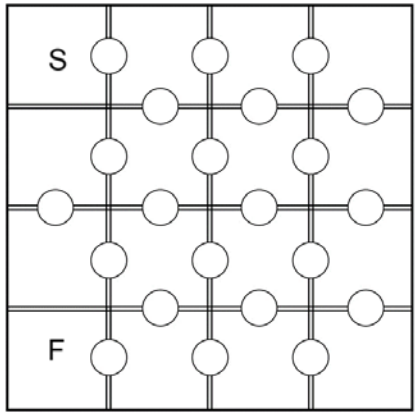
The example of rat behavior it the empty arena with visible finish compartment



Video 7

there are no any barriers, the landmarks are above the arena

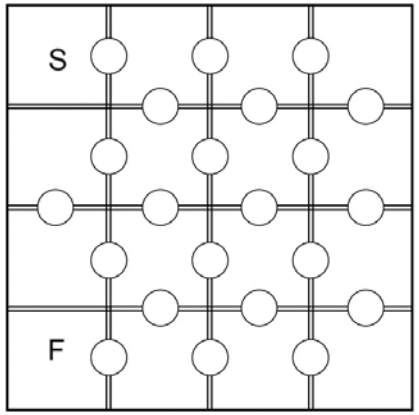
The example of rat behavior at the arena with invisible finish compartment



Video 8

the rat has difficulty in orientation

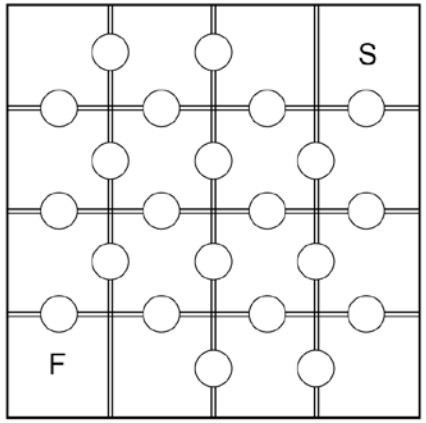
The example of rat behavior in the arena with an invisible finish compartment



Video 9

the rat chooses the shortest way

The example of rat behavior at the arena with invisible finish compartment and new start place



Video 10

the rat chooses the shortest way

Conclusion

The new transformer maze can be used in three different tasks:

- moving by signposts
- remembering the route
- the task using the arena with a visible and invisible feeder within one box

For mouse

Video 11

White maze option with black line

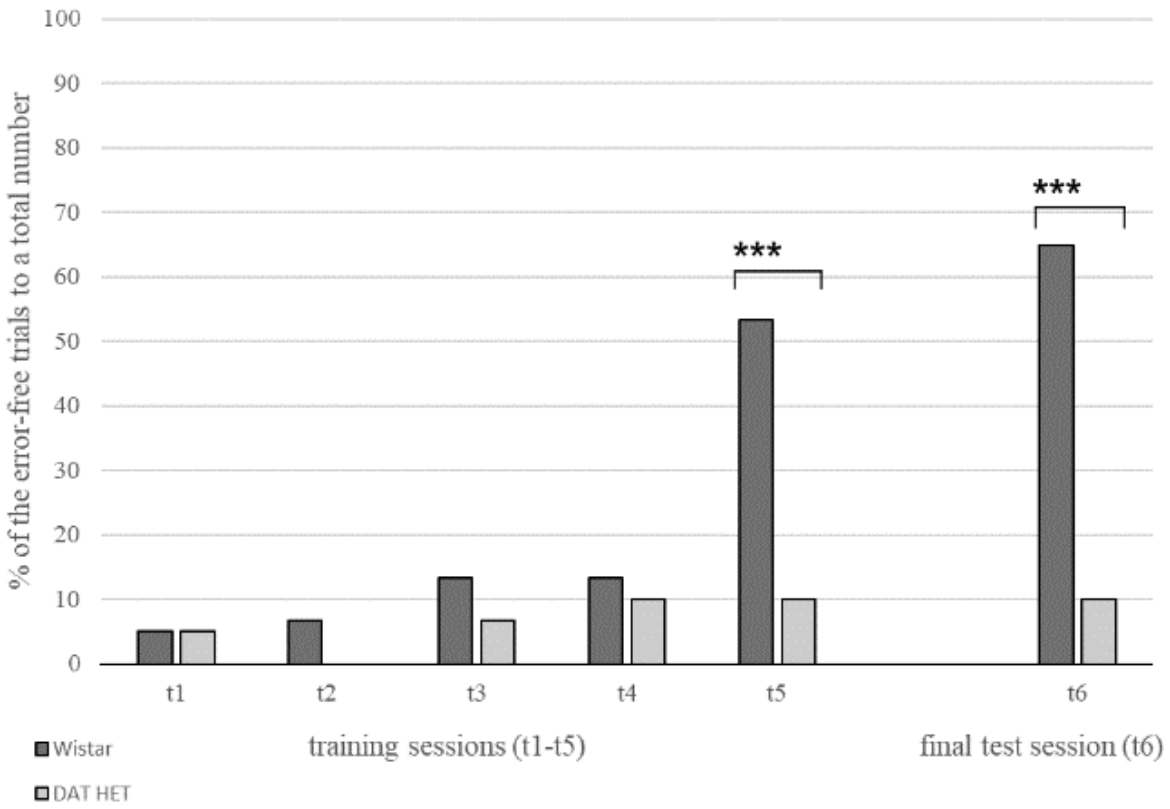
Thank you for your attention

Approbation of a new transformer maze in an animal model experiment

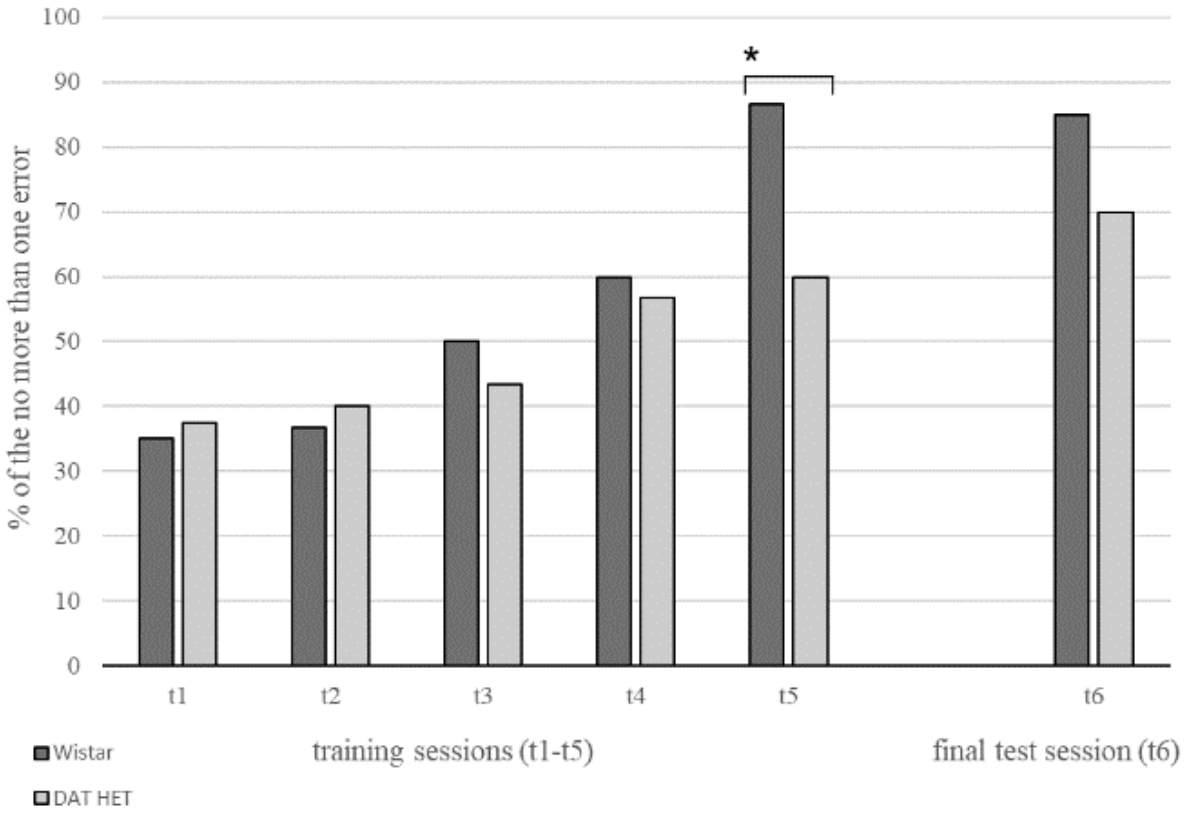
The aim was to compare cognitive and motor performance in the new transformer maze using the dopamine dysfunction model rats.

- Striatal dopamine (DA) dysfunction induces spatial information processing deficits.
- Neostriatal DA modulates, in both egocentric (route-based) and allocentric (spatial, map-based) learning.
- Manipulation of the dopamine transporter (DAT) gene in animal models results in delayed clearance of DA and leads to behavioral abnormalities.

The level of success in the task

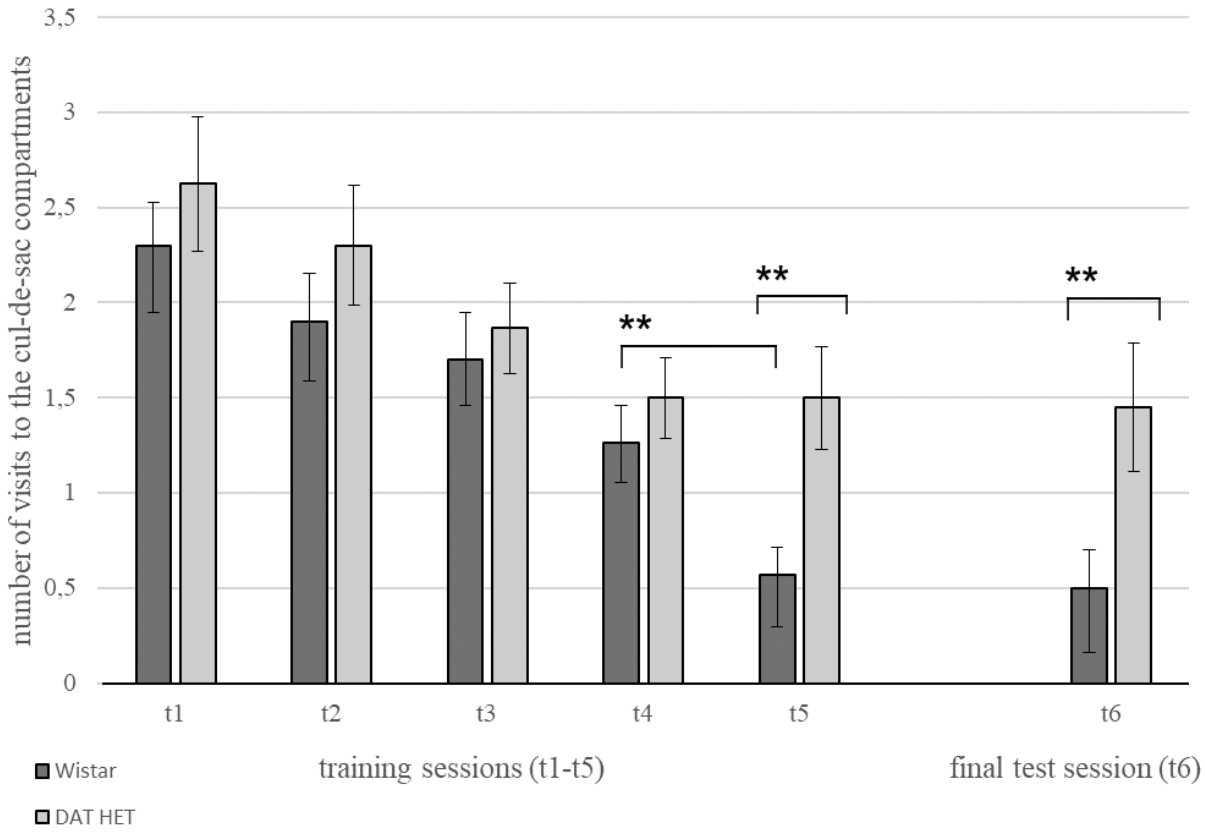


Error-free task execution. Ordinate - percentage of the error-free executions to a total number of the trials. Abscissa - experimental sessions (training sessions - t1-t5, final tests - t6). Statistical significance ***-p<0,0001(Chi-square test).



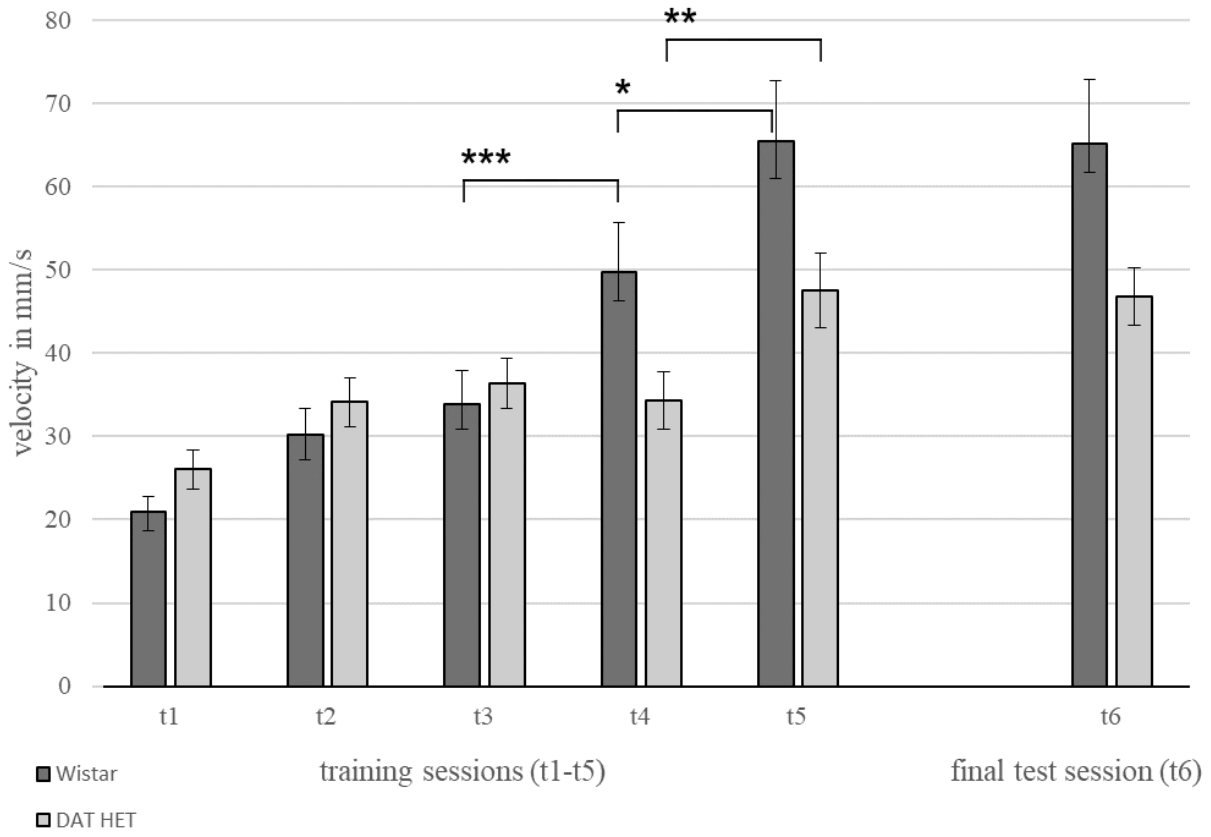
The task executed without mistakes or with one mistake. Ordinate - trials with ≤1 error, % to the total number of the trials. Abscissa - experimental sessions (training sessions - t1-t5, final tests - t6). Statistical significance *- $p < 0.05$ (Chi-square test).

Number of errors



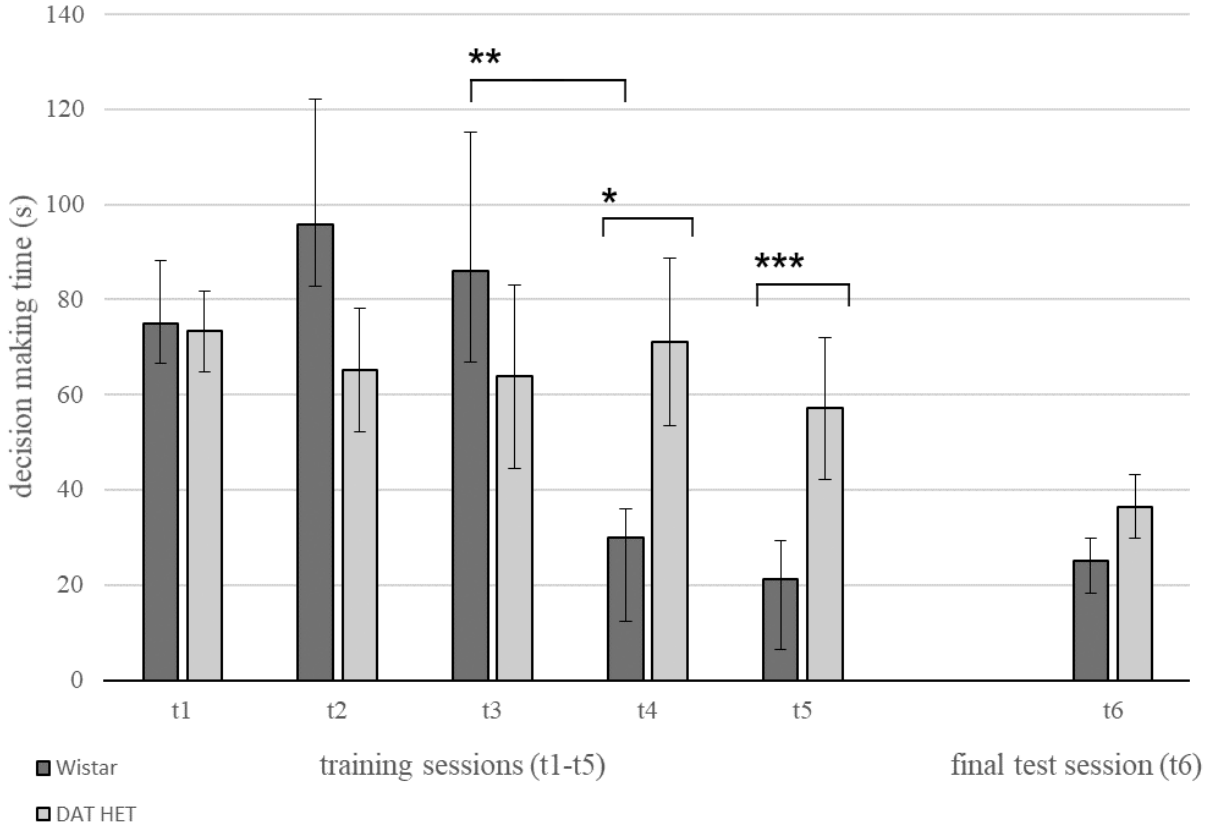
Number of visits to the cul-de-sac compartments. Ordinate - number of errors (mean ±SEM). Abscissa - experimental sessions (training sessions - t1-t5, final tests - t6). Statistical significance **- $p < 0.001$ (differences between groups -Mann-Whitney U test and between different sessions -Wilcoxon test).

The rat’s velocity



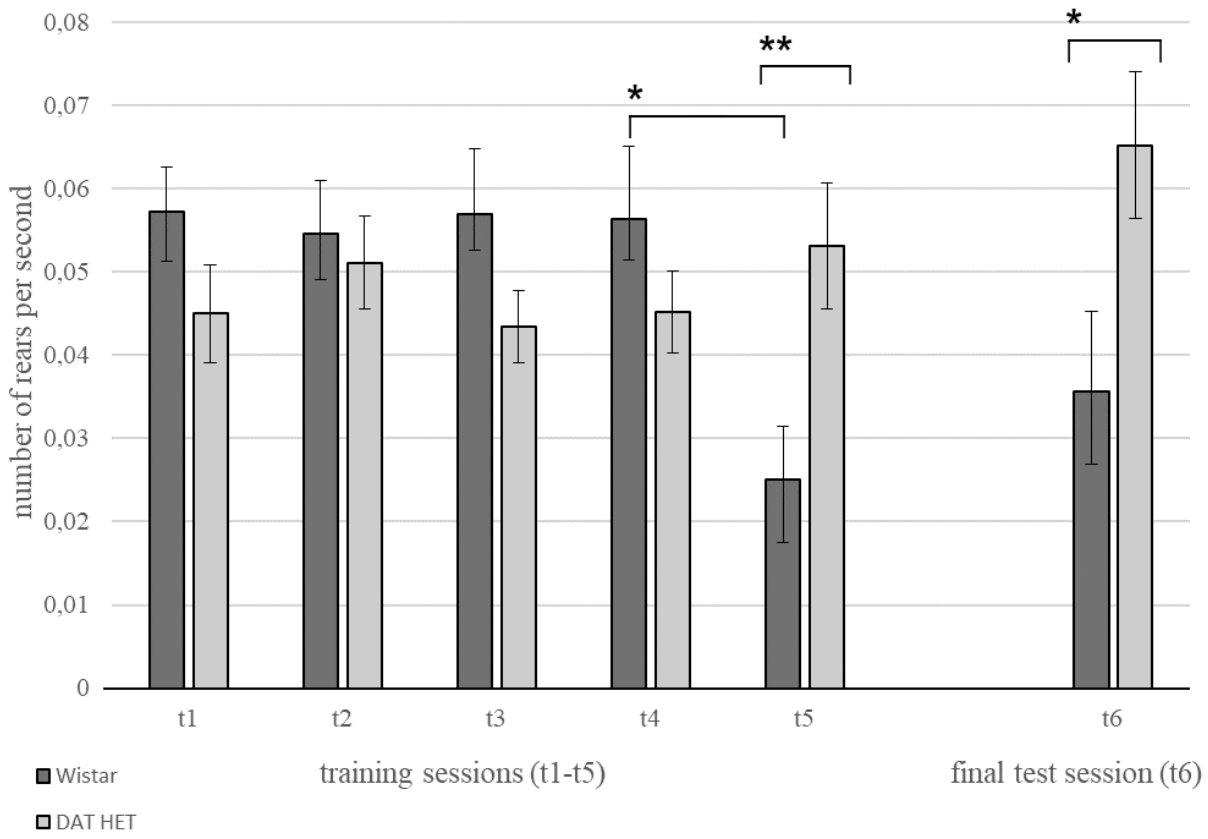
Velocity analysis results. Ordinate – average velocity (mm/s) (mean ±SEM). Abscissa - experimental sessions (training sessions - t1-t5, final tests - t6). Statistical significance *- $p < 0.05$; **- $p < 0.001$; ***- $p<0,0001$(differences between different sessions -Wilcoxon test).

Decision-making time



Decision-making time (s). Ordinate – average time, seconds (mean ±SEM). Abscissa - experimental sessions (training sessions - t1-t5, final tests - t6). Statistical significance *- $p < 0.05$; **- $p < 0.001$; ***-$p<0,0001$ (differences between groups -Mann-Whitney U test and between different sessions -Wilcoxon test).

The number of acts of standing upright



Rears. Ordinate – average number of rears per second (mean±SEM). Abscissa - experimental session (training sessions - t1-t5, final test day - t6). Statistical significance *- $p < 0.05$; **- $p < 0.001$(differences between groups -Mann-Whitney U test and between different sessions -Wilcoxon test).

Conclusion

- In Wistar rats, the observed learning behavior is closer to insightful learning, leading to successful cue-based performance. They showed sudden changes of behavior parameters while learning, and error-free trials in the final tests can be taken as a criterion of the animal using cues. In contrast to that, DAT-HET rats continue to use trial and error strategyes, and demonstrate gradually changing behavior parameters.

- Overall, the new transformer maze makes it possible to discover the differences in learning and performance patterns of these rats.