Exploiting video tracking data to dissect watermaze learning and strategy choice of mutant mice

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Place navigation in the water maze is a popular procedure used to investigate spatial learning and cognitive abilities in rodents, including genetically modified mice. Using extramaze cues, subjects must learn to find an escape platform that is hidden at a constant position in cloudy water. A probe trial without platform serves to verify the learned spatial preference. Hippocampal lesions and manipulations of NMDA receptor dependent synaptic plasticity disrupt learning of this task, both in rats and in mice.

Learning the place navigation task is a multistage process that requires complex adaptive responses and involves multiple memory systems. Mice explore many different strategies as they gradually learn to master the task. Initially, they swim along the wall (thigmotaxis) and try to escape there. This is followed by random exploration of the pool surface permitting to hit the platform for the first time by chance. By scanning the interior of the pool more systematically, mice then rapidly increase their chance of hitting the platform. After a while, they realize that the platform is placed at a constant distance from the wall and adopt a circular swim pattern (chaining) which dramatically shortens escape latencies. Eventually, the animals realize that the goal has a fixed position in space. Using the extramaze cues, they begin to focus their search on successively smaller areas of the pool, until precise navigation leads them directly to the platform from any release point. Experimental manipulations can interfere with any of theses learning stages and do not necessarily disrupt spatial navigation per se. In order to draw conclusions in terms of spatial memory if an animal fails to reach the final stage, it is necessary to verify that learning progressed normally up to the stage where processing of spatial information becomes limiting.

Video tracking systems sample swim paths at high frequency and spatial resolution. Specialized software calculates a multitude of variables that can be used to describe the animal’s behavior. Given this computing power, one would expect to be able to quantify each learning stage by its own set of specific variables. However, when we ran principal component analysis on more than 120’000 individual watermaze tracks which we collected in our laboratory during the past fifteen years, we found that many of the variables that were designed to describe different aspects of spatial navigation are highly redundant and are correlated with very early rather than advanced learning stages. This prompted us to implement an automatic software algorithm that combines newly designed and previously published variables with empirically determined thresholds in order to classify swim tracks according to the predominant strategy. When applied to our database of watermaze experiments, the algorithm revealed characteristic differences of strategy choice between commonly used mouse strains. Furthermore, it showed that many targeted mutations interfere with very early stages of watermaze learning that are largely independent of the processing of spatial information. In some models, by contrast, the algorithm allowed us to show that the mutation specifically affects spatial navigation during advanced learning stages.

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