

## **Spatial and non-spatial deficits in the watermaze distinguished by automatic identification and classification of swimming strategies**

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Water-maze navigation is frequently used to assess spatial learning of mutant mice. However, learning the task is a multistage process that requires complex adaptive responses and involves multiple memory systems. During learning, mice explore many strategies. Initial wall hugging (thigmotaxis) is soon followed by random exploration of the pool. More systematic scanning of the pool then increases the chance of hitting the platform. After learning that the platform is at a constant distance from the wall, mice adopt a circular swim pattern (chaining). Eventually, they realize that the goal has a fixed position in space and focus their search on successively smaller areas, until precise navigation leads them directly to the platform from any release point.

Because manipulations can interfere with any learning stage and do not necessarily disrupt spatial navigation per se, it must be verified that learning progressed normally to a stage where processing of spatial information becomes limiting. We have implemented an automatic software algorithm that combines new and previously published variables with empirical thresholds in order to classify video-tracked trials according to the predominant swimming strategy. The algorithm revealed characteristic differences of strategy choice between commonly used mouse strains. Furthermore, it showed that pilocarpine induced hippocampal lesions and genetic ablation of forebrain TrkB receptors disrupt early stages of watermaze learning that are largely independent of the processing of spatial information. In *arg3.1*-null mice, by contrast, the algorithm revealed a selective impairment of spatial navigation during advanced learning stages.

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