Meta-analysis of strategy choice by 85 mutant mouse lines in a standardized place navigation task identifies behavioral flexibility as performance limiting factor

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When tested in procedures that were originally developed for rats, mice may use different strategies and may be affected by experimental manipulations in different ways than rats. Therefore, we have conducted a meta-analysis comparing hippocampally lesioned mice with 85 different mutant lines and find that performance of mice in a standardized watermaze place navigation task is limited by behavioral flexibility rather than by spatial memory.

Mice explore a variety of strategies while improving their efficiency to find the hidden platform. Whereas early learning stages depend on behavioral flexibility, processing and remembering spatial information becomes only important at advanced stages. We categorized training trials into six exclusive strategies according to the predominant swimming strategy: circling, floating, wall hugging, random swimming, scanning, chaining, focal searching, direct swims. Analysis of relative frequencies and strategy transitions between trials revealed that normal mice initially tend to perseverate on non-spatial strategies, giving up this tendency more or less rapidly in favor of a relatively unstable use of spatially focused strategies. Hippocampal lesions disrupt the flexibility to explore different strategies during early learning, essentially limiting the choice to wall hugging or floating and preventing progression to stages where processing of spatial information becomes relevant. Mutations that block plasticity-relevant signaling pathways or model human cognitive deficits produce either the same syndrome or a milder form in which progression to spatially directed strategies is only delayed. A selective spatial impairment in absence of behavioral inflexibility was observed only in Arg3.1/Arc null-mutants and in mice lacking glucocorticoid receptors in the brain.

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