

## **Hippocampal lesions in mice: behavioral effects in the watermaze, naturalistic environment and Intelligence**

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Hippocampal lesions typically impair water-maze learning. Mutant mice with reduced hippocampal function were also unable to learn this task, but patrolled feeders in an outdoor pen without re-entry errors, yet failed to modify search behavior in presence of novel feeding sites.

Fifty-eight female C57BL/6 mice underwent complete bilateral hippocampal lesions by means of NMDA injections (HC), or received sham lesions (CTL). 14 HC and 10 CTL were then tested in a water maze. Excessive wall hugging and floating of HC mice entailed significant impairments in acquisition and platform reversal ( $p < 0.001$ ), but also in a cued swim test ( $p < 0.0001$ ). Forty mice (20 HC, 20 CTL) were transferred to our Russian field station, tagged with transponders, adapted to the outdoor feeder system and then released into an outdoor pen (10x10m). During daytime, food was available inside two large shelters. During the night, food was available in 8 computer-controlled feeder boxes, but only during the first visit.

Only two CTL mice were lost overall, but half of the HC mice did not survive the first 3 days. Further monitoring over 42 days showed CTL mice had learnt to visit each feeder only once a night, making few re-entry errors. The HC mice ( $n=8$ ) visited feeders frequently but showed stereotyped spatial preferences and many re-entry errors ( $p < 0.0001$ ). 8 CTL and 10 HC mice remaining in Zurich were tested in automated learning cages (INTELLICAGE). Adaptation and patrolling behavior to 4 corners giving access to water was monitored individually during 4 weeks. The HC mice developed a stereotyped preference for a given corner, while CTL mice also preferred a corner but visited the others regularly ( $p < 0.0001$ ).

Thus, hippocampal lesions in mice result in stereotyped spatial behavior in large and small terrestrial environments. How this relates to the water maze findings showing equally stereotyped escape strategies remains to be determined.

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