ALZHEIMER DISEASE

A virtual Morris maze to assess cognitive impairment in Alzheimer disease

The Morris water maze is a well-established test of spatial learning and memory in rodents, and a team in San Francisco, led by Kate Possin and Pascal Sanchez, has recently developed a virtual counterpart that can detect cognitive impairment in humans. The researchers hope that the virtual maze can eventually be incorporated into Alzheimer disease (AD) clinical trials.

“AD has been cured many times in mouse models, but these successes in the laboratory have not translated to successful trials in humans,” explains Possin. “One of the reasons for the difficulty in translating discoveries is the major difference in methods to test for memory deficits,” adds Sanchez.

In the Morris water maze, animals are required to learn the position of a platform that is submerged under opaque water. The animals have to swim through the water, using visual cues to navigate to the platform. The virtual maze, which was developed

in collaboration with Microsoft Research, simulated driving around a field to locate buried treasure.

“In the human version, there are mountains, trees and a sun that the participant can use to help them learn where the treasure is located, similar to how you might orient yourself in San Francisco relative to major landmarks like the Ferry Building, the Bay Bridge and downtown,” says Possin. “We know that this type of navigation learning relies on the hippocampus — a brain region affected in the earliest stages of AD.”

To test the virtual maze, Possin, Sanchez and colleagues recruited 28 patients with mild cognitive impairment due to AD (MCI-AD) and 89 neurologically healthy controls. For comparison, 53 hAPP transgenic mice (a model of early AD) and 53 control mice were subjected to the conventional Morris water maze task.

The patients with MCI-AD and the hAPP mice exhibited comparable

impairments in hidden-target learning, in which the location of the target had to be memorized in relation to the cues provided, and in a probe trial, where the target was removed and performance was measured in terms of time spent at its former location.

“We were amazed to find that mouse models of AD and patients affected by the early stage of the condition show very similar learning and memory deficits in this task,” says Sanchez. “These findings are consistent with the hippocampal dysfunction that has been described in both mouse models and patients with AD.”

The researchers are now planning to further develop the virtual maze task for use in the clinic, as well as in trials of new therapies for AD.

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