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Children with gene show reduced cognitive function

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Children who possess a gene known to increase the risk of Alzheimer's disease already show signs of reduced cognitive function, an Oregon Health & Science University study has found.

Scientists in the OHSU School of Medicine discovered that 7- to 10-year-olds with a member of a family of genes implicated in development, nerve cell regeneration and neuroprotection display reduced spatial learning and memory, associated with later-life cognitive impairments.

Results of the study, presented today at Neuroscience 2007, the 37th annual meeting of the Society for Neuroscience in San Diego, suggest that changes predisposing a person to Alzheimer's and other forms of dementia might occur much sooner in the brain than previously thought.

"One of our questions has been is this a risk that only happens with age, or is it already - early on - the cause of differences in performance," said study co-author Jacob Raber, Ph.D., associate professor of behavioral neuroscience and neurology in the OHSU School of Medicine. "This study suggests there already are cognitive differences very early on in life."

The results also mean therapeutic interventions that delay the effects of cognitive decline may be possible at a much younger age, Raber says.

Previous studies have shown that a member of the apolipoprotein E gene family, apoE4, increases a person's risk of age-related cognitive decline

and cognitive injury from such "environmental" challenges as brain trauma. Mice expressing human apoE4 developed progressive, age-dependent impairments in spatial learning and memory.

Half of all people with Alzheimer's disease carry apoE4, Raber said.

"When we looked at non-demented healthy elderly, we saw the clear effect of apoE4," he said. "So it's not just Alzheimer's disease. ApoE4 carriers generally do worse in our tests. Among the nondemented oldest old, where the mean age is 82, those who have apoE4 do less well" on cognitive tests.

In their study on children, Raber and colleagues - lead author Summer Acevedo, Ph.D., OHSU postdoctoral fellow, and Byung Park, Ph.D., senior biostatistics associate in the OHSU Biostatistics & Bioinformatics Shared Resource - examined 55 healthy boys and girls ages 7 to 10. Among them were eight girls and six boys who carried the apoE4 gene, and 17 girls and 24 boys who didn't.

The children were assessed using a combination of paper- and computer-based tests, including a 3-dimensional, virtual reality program called "Memory Island" that assesses spatial learning and memory. "Memory Island" immerses participants in a simulated world in which they must navigate to a location marked with a flag that's adjacent to the target in each of four quadrants. The participants are given several tries to navigate back to the targets based on memory.

The computer program mimics the Morris water maze, a standard scientific tool for testing memory in rodents by training them to swim to a platform based on visual cues.

Raber, Acevedo and Park found that apoE4 carriers scored lower in location recognition tests, and non-apoE4 carriers outperformed apoE4

carriers in the "Memory Island" test by navigating closer to the visible target location. Also, non-apoE4 carriers showed spatial memory retention when a target wasn't present and searched more frequently for the targets in the appropriate quadrants while apoE4 carriers did not.

In all, 75.6 percent non-apoE4 carriers showed target preference compared with only 43 percent of apoE4 carriers.

Source: Oregon Health & Science University