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Slowing disease's mental ravages

Drug made for other ailments offers glimmer of promise in fighting Alzheimer's symptoms, researchers say

By Jeremy Manier

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Hope is often scarce in research on Alzheimer's disease, but a study released Tuesday at a Chicago medical conference offered tentative hope for a new way of slowing elderly patients' mental decline.

The preliminary study of 321 Alzheimer's patients from Singapore and Britain found that an old drug, previously used for urinary tract infections and other ailments, reduced the patients' rate of mental loss by 81 percent, based on a standard measure of cognitive performance and memory.

The results require further confirmation, but whatever the outcome, some experts are intrigued by the drug's novel way of attacking the disease.

Scientists say the medication, which goes by the commercial name rember, may work by dissolving tangles of a protein that collects in the brain cells of Alzheimer's patients.

If true, the therapy could be the first to stave off an underlying cause of Alzheimer's disease, unlike current treatments such as Aricept, which provide only temporary relief of symptoms through their effect on brain compounds that are important in cognition.

"The effect size is pretty large for drugs of this class," said Dr. Raj Shah, an Alzheimer's specialist and medical director of the memory clinic at Rush University Medical Center.

Researchers presented the findings Tuesday at the 2008 Alzheimer's Association International Conference on Alzheimer's Disease, being held this week in Chicago.

Other Alzheimer's treatments have shown early signs of promise but failed to deliver in clinical trials, making experts cautious about reading too much into Tuesday's findings.

For example, numerous drugs now in development attempt to take aim at the plaques of beta-amyloid protein that develop among the brain cells of many Alzheimer's patients, but some of the outcomes have



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been disappointing.

One such drug, tarenflurbil, which had promising results in an early-phase study, turned out to have no significant effect on the disease when tested in a larger clinical trial, researchers reported Tuesday.

"This field is in sore need of a success story," said Dr. Marsel Mesulam, director of the cognitive neurology and Alzheimer's disease center at Northwestern University.

Unlike drugs aimed at beta-amyloid, rember is meant to dissolve an abnormal protein called tau, which many experts had thought would be an elusive target for Alzheimer's treatments. Some theories suggest the tangles of tau protein that form in patients' brain cells could cause the symptoms of the disease by hampering chemical communication in the brain. It's also possible that the protein tangles are merely byproducts of a deeper problem that is the real source of cognitive decline.

Study leader Claude Wischik of Aberdeen University's Institute of Medical Sciences has spent two decades tracing the role of tau protein tangles in Alzheimer's disease. He said he agrees that further tests are needed to confirm the preliminary results, but he's encouraged by the findings so far.

"We've shown you can arrest disease development by targeting the protein tangle," said Wischik, who is also chairman of TauRx Therapeutics, which hopes to market the new treatment if it's successful.

The drug Wischik tested is a purified form of a substance commonly known as methylene blue, which has been in use for decades as a treatment for numerous conditions, including urinary tract infections and carbon monoxide poisoning. Many patients on the drug report that their urine turns blue, but Wischik said so far the drug appears safe.

Although in principle it would be possible for doctors to use the common version of the drug in patients before testing is complete, Wischik and other experts said that would be unwise. Among other problems, doctors who prescribed the drug on their own without proof that it works could be open to lawsuits if patients developed bad side effects, experts said.

Wischik said that if further tests of the compound show promise, the treatment could be available for general use by 2012 or 2013, depending on how quickly the drug moves through regulatory hurdles in the U.S. and overseas.

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