# Scientists develop new strategy that may improve cognition

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For the first time, scientists have linked a brain compound called kynurenic acid to cognition, possibly opening doors for new ways to enhance memory function and treat catastrophic brain diseases, according to a new study from the University of Maryland School of Medicine. When researchers decreased the levels of kynurenic acid in the brains of mice, their cognition was shown to improve markedly, according to the study, which was published in the July issue of the journal *Neuropsychopharmacology*. The study is the result of decades of pioneering research in the lab of Robert Schwarcz, Ph.D., a professor of psychiatry, pediatrics and pharmacology and experimental therapeutics at the University of Maryland School of Medicine.

"We believe that interventions aimed specifically at reducing the level of kynurenic acid in the brain are a promising strategy for cognitive improvement in both healthy patients and in those suffering from a variety of brain diseases ranging from schizophrenia to Alzheimer's disease," says Dr. Schwarcz.

Kynurenic acid is a substance with unique biological properties and is produced when the brain metabolizes the amino acid L-tryptophan. The compound is related to another breakdown product of tryptophan known as quinolinic acid. In 1983, Dr. Schwarz published a paper in the journal Science identifying the critical role excessive quinolinic acid plays in the neurodegenerative disorder Huntington's disease. He has since designed a therapeutic strategy targeting quinolinic acid for the treatment of Huntington's disease. Dr. Schwarcz also is involved in a company called

VistaGen, which pursues the development of neuroprotective drugs based on this concept.

In the study published this month, Dr. Schwarcz and his colleagues at the Maryland Psychiatric Research Center — a world-renowned clinical and basic science research center at the University of Maryland School of Medicine — examined mice that had been genetically engineered to have more than 70 percent lower kynurenic acid levels than ordinary mice. These mice were found to perform significantly better than their normal peers on several widely used tests that specifically measure function in the hippocampus. The hippocampus is a critical area of the brain for memory and spatial navigation. The mice were clearly superior in their ability to explore and recognize objects, to remember unpleasant experiences and to navigate a maze. The engineered animals also showed increased hippocampal plasticity, meaning they had a greatly improved ability to convert electrical stimuli into long-lasting memories.

"These results are very exciting, because they open up an entirely new way of thinking about the formation and retrieval of memories," says Dr. Schwarcz. "Kynurenic acid has been known for more than 150 years, but only now do we recognize it as a major player in one of the fundamental functions of the brain. Our most recent work, still unpublished, shows that new chemicals that specifically influence the production of kynurenic acid in the brain predictably affect cognition. We are now in the process of developing such compounds for cognitive enhancement in humans."

"I feel confident Dr. Schwarcz's determined pursuit of answers for the desperate patients suffering from devastating neurodegenerative disorders such as Alzheimer's disease and Huntington's disease, and psychotic disorders such as schizophrenia, will pay off," says E. Albert Reece, M.D., Ph.D., M.B.A., vice president for medical affairs, University of Maryland, and John Z. and Akiko K. Bowers Distinguished

Professor and dean, University of Maryland School of Medicine. "His work creates hope for these patients and their families, and his findings are making a significant impact on the field of neuroscience and psychiatric medicine."

Provided by University of Maryland Medical Center