Study shows first evidence for independent working memory systems in animals

January 14 2016

A rat with several of the 100 common household spices used to test odor memory in the study. Credit: Indiana University

A new study from Indiana University could help ensure the hundreds of

millions of dollars spent each year to develop potential treatments for Alzheimer's disease aren't wasted on targeting the wrong types of memory.

The paper, published today in *Current Biology*, is the first to confirm that a key aspect of human memory impaired in memory disorders exists in the type of pre-clinical animal models that influence major decisions about drug development.

The study's results, which required over a year's worth of intensive data collection and analysis, could hold important insights for drug companies. That's because selecting less relevant data early in the research process can create costly errors later in the "translational pipeline" that connects basic science to new treatments and therapies.

"There is a huge history of translation failure in memory disorders caused by companies trying to develop compounds based on therapies that produce relief in pre-clinical animal models but later fail during early clinical trials," said Jonathon Crystal, professor in the IU Bloomington College of Arts and Sciences' Department of Psychological and Brain Sciences and director of the Program in Neuroscience, who led the study. "We're working to create stronger pre-clinical models of the types of memory systems that are impaired in human diseases."

The conclusions are notable in light of the federal government's recent 60 percent increase in Alzheimer's disease research funding, or $350 million in new spending. No treatment currently exists to halt or reverse the long-term effects of Alzheimer's disease, estimated to affect 5.3 million people in the United States alone.

The IU study, conducted in rats, shows for the first time that the animals possess two independent "working memory" resources, or the ability to remember more information across two categories versus a single

category. In humans, working memory consists of two memory resources: visual and auditory information. The average person, for example, cannot recall a phone number longer than seven characters despite easily remembering both the audio and video on a television show.

To test these forms of memory in animals, Crystal's team challenged rats to memorize odors and spatial information. To test rats' ability to remember spatial data, IU scientists had them find food pellets inside an eight-arm maze. To test their ability to remember new odors, they used pellets inside containers scented by up to 100 common household spices, with only new odors yielding food.

Across numerous trials, IU scientists consistently showed that the rats could recall significantly more details in combination—scents and spaces—compared to trying to remember a single type of information.

"We saw high-level performance because the animals were encoding information in two dedicated memory resources," Crystal said. "This is the defining quality of working memory in people; and for the first time, we've shown animals have this property of independent memory systems as well."

The results also suggest that this form of memory arose evolutionarily much earlier than previously thought.

Historically, Crystal said almost all investigations on the genetics of Alzheimer's disease depend upon spatial memory research because these studies are easier to carry out. Yet treatments based solely upon spatial memory data aren't likely to strike at the heart of what's so cruel about memory disorders. It's critical to also investigate more complex forms of memory, including working memory.

"What researchers are doing now is akin to coming up with a plan for developing a drug which, if successful after spending billions of dollars, helps your grandmother find her reading glasses or car keys," Crystal said. "Those symptoms aren't the most debilitating aspect of Alzheimer's disease. We need solutions that address the inability to remember significant things, like memories of the past or personal exchanges with friends and family, whose loss is so distressing to sufferers of the disease and their loved ones."

The IU study was made possible in part by student researchers from the College of Arts and Sciences whose work helped overcome the significant time investment required to perform complex memory trials in animals.

IU students who contributed to the project were first author Alexander Bratch, now a graduate student at the University of Minnesota, who wrote his undergraduate thesis on the work; Diana Arman, Austin Dunn, Shiloh Cooper, Hannah Corbin, Stefan Dalecki and Spencer Kann, all undergraduates, and Alexandra Smith, a graduate student.

Provided by Indiana University