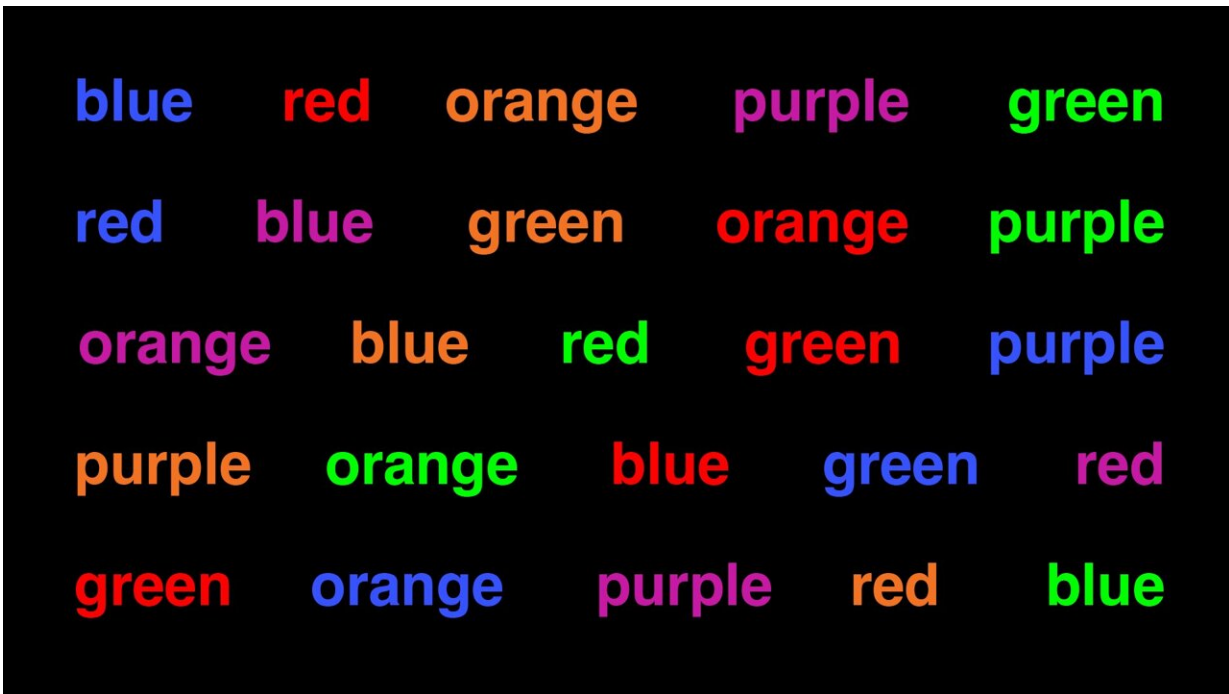


Team develops behavioral test to detect early risk of Alzheimer's

September 26 2022, by Lori Dajose



An example of a Stroop Paradigm test. It takes a bit of extra mental effort to name the color of a word when it doesn't match the word itself. Credit: Caltech

Alzheimer's disease is a neurodegenerative condition that damages a person's ability to think, remember, and perform basic functions. According to the National Institutes of Health, Alzheimer's affects more than 6 million Americans, mostly ages 65 and older. Though the neurological damage from the disease is irreversible, early detection and

intervention has been shown to slow its progression.

Before the onset of Alzheimer's physical symptoms, the most commonly used method to measure an individual's risk of developing the disease is through measuring levels of certain proteins, such as amyloid beta and tau proteins, in spinal fluid. This test is invasive, painful, and expensive.

Now, a team from Caltech and the Huntington Medical Research Institutes has made progress toward developing a simple behavioral test to measure an individual's risk of developing Alzheimer's before any symptoms arise. A paper describing the team's findings appears in the journal *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* on September 20.

The research was conducted in the laboratory of Shinsuke Shimojo, Gertrude Baltimore Professor of Experimental Psychology. Shimojo is an affiliated faculty member with the Tianqiao and Chrissy Chen Institute for Neuroscience at Caltech.

"Early detection of Alzheimer's disease is important in order to take interventions that can slow the progression of the disease," says the study's first author Shao-Min Sean Hung, formerly a postdoctoral scholar in the Shimojo laboratory and now an assistant professor at Waseda University in Japan. "Before the onset of the disease, by definition, cognitively healthy people do not have behavioral symptoms—and thus it's not possible to do traditional behavioral assessments for the disease because there are no behavioral symptoms yet. What we're trying to do is develop a test to detect behavioral abnormalities long before any onset of symptoms and in a less invasive way than measuring spinal fluid."



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While this gif is not the actual test used in the study, it illustrates the task participants were asked to carry out. A rapid "invisible" word is flashed before the actual word, to unconsciously distract the task participant. In this way, the team could measure if impaired implicit cognition correlated with biological factors for a high-risk of developing Alzheimer's disease. The word "ready" indicates that the task is about to begin. Credit: Courtesy of S. Hung

The study involved 40 people with an average age of 75 and all cognitively healthy, who underwent myriad tests related to Alzheimer's risk: magnetic resonance imaging (MRI) of the brain, genome sequencing, and the aforementioned invasive spinal fluid measurements. From these biological markers, individuals could be categorized as high risk or low risk. The researchers aimed to develop a behavioral test whose results would correlate with these biological measurements.

The team developed a task in which a participant undergoes a so-called Stroop Paradigm test. In this common test, a person is shown a word—the name of a color—displayed in colored ink. However, the word itself does not necessarily match the color of the printed word—for example, the word "RED" is printed in the color green. In each iteration of the task, the participant is asked to name either the color of the word or the word itself. Compared to naming the word itself, naming the color of the text is considered "high effort"—it is more challenging than it might seem.

In this study, the researchers also added a hidden element to the Stroop Paradigm. Right before the actual target is shown, a colorless word is flashed rapidly on the screen—so rapidly that a participant cannot detect it consciously.

The colorless word is intended to unconsciously distract the participant and measure "implicit cognition." In addition to conscious and intentional information gathering or "explicit cognition," our brains have a separate system in which sensory information is digested without conscious awareness—this is known as implicit cognition.



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Another gif demonstration of a typical trial. "Ready" signals the beginning of the trial. Participants are asked to name the color of an underlined word, or name the word itself if it is not underlined. Each trial contains two words, and an ultra-fast noise-masked prime is presented before the second word. "Masking" is one of the ways researchers make things "invisible"—the meaningless symbols occupy the same location as the "invisible" word and flash right before and after the word. The brain focuses on the bright noisy stimulus and only subconsciously processes the hidden word. Credit: Courtesy of S. Hung

"The participants in our study are cognitively healthy at the explicit level, and we measure this through a battery of neuropsychological tests," says Hung. "But this study's central question is: How about their implicit cognition? Could it be possible that their implicit cognition is more sensitive to show Alzheimer's-related cognitive decline? The study tested the hypothesis that high-risk and low-risk cognitive healthy participants would be distracted by an unseen word differently."

The study was double-blinded, so neither the participants nor the researchers knew anything about the participants' biological data prior to the data analysis.

The test showed that the individuals with high-risk biological factors slowed down by about 4 percent on the Stroop test when an unconscious and inconsistent word was flashed. This suggests, Hung says, that the conditions that lead to Alzheimer's may affect implicit cognition far before conscious cognition, and thus a test to measure implicit cognitive performance may be able to detect a high risk of developing Alzheimer's disease without the need for invasive physical measurements.

The researchers emphasize that this test is not diagnostic yet—that is, this particular test cannot measure an individual's risk for Alzheimer's, but simply shows a correlation between the group of high-risk individuals and worse performance on the test when an unconscious distracting word is present. The next steps are to combine the test with other noninvasive physical measurements, such as heart rate and other neurophysiological markers, with the goal of making it more predictive.

Additional Caltech co-authors are Shimojo and senior scientist Daw-An Wu, Ph.D. Professor Xianghong Arakaki of the Huntington Medical Research Institutes is an additional co-corresponding author.

More information: Shao-Min Hung et al, Stronger implicit interference in cognitively healthy older participants with higher risk of Alzheimer's disease, *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* (2022). [DOI: 10.1002/dad2.12340](https://doi.org/10.1002/dad2.12340)

Provided by California Institute of Technology

Citation: Team develops behavioral test to detect early risk of Alzheimer's (2022, September 26) retrieved 27 April 2024 from

<https://medicalxpress.com/news/2022-09-team-behavioral-early-alzheimer.html>

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