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Novel fMRI technique identifies HIV-associated cognitive decline before symptoms occur

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A five-minute functional MRI (fMRI) test can pick up neuronal dysfunction in HIV-positive individuals who don't yet exhibit cognitive decline, say neuroscientists and clinicians at Georgetown University Medical Center.

Their study in *Neuroimaging: Clinical* provides proof-of-concept that imaging can help track neural functioning in this population, known to be affected by the virus and potentially by the treatments meant to keep HIV at bay.

The issue of neural dysfunction in the HIV-positive population is significant, says Georgetown neuroscientist Xiong Jiang, PhD, the study's senior investigator.

"About half of people living with HIV are affected by HIV-associated neurocognitive disorders, or HAND, and we expect this condition will escalate as the current HIV-positive generation ages," he says.

But testing for cognitive decline that is not yet obvious is difficult. "There is no one clinical screening tool that has been found to be appropriately sensitive or specific for HAND yet," says co-author Mary Young, MD, director of Georgetown University Medical Center's HIV Women's Program. "Therefore, there has been great interest in developing biomarkers of overall brain health and disease in HIV to

streamline diagnosis and monitoring."

Young collaborated with Jiang on a potential biomarker based on fMRI techniques Jiang and his collaborators had developed, which have been shown to be sensitive to subtle behavioral changes.

To test whether these fMRI techniques might be capable of detecting and assessing neural injury due to HIV before symptoms occur, Jiang and Young studied 28 women (15 who were HIV-positive, with an average age of 50) from the National Institutes of Health-funded Washington, DC Metropolitan Interagency Women's HIV Study (WIHS) cohort. WIHS at Georgetown, led by Young since 1993, includes 300 participants and is one of nine national sites designed to follow HIV infected women along with a control population.

In this proof-of-concept study, the researchers used face processing and its associated brain region, fusiform face area, or FFA, as the mean to probe neural injury in HIV. They found that the neural specificity in the FFA - estimated via fMRI-adaptation, an established technique, and local regional heterogeneity analysis, or Hcorr, a novel technique - is reduced in the HIV-positive participants. "FFA neurons were not as finely tuned in this group, compared to uninfected participants," Jiang says.

"We are very excited about this finding because Hcorr, which can estimate neural specificity rapidly, holds the promise to serve as a research tool to examine neural injury and a clinical tool to assess and monitor HAND progression. It could also be useful for drug development as it is safe and non-invasive," says Jiang.

Currently, there are no ways to treat HAND other than to control HIV replication, Young says "Developing defined treatments guided by biomarkers would be the next step. Imaging techniques like Hcorr could

help identify dysfunction before deficits are in place," she says. "Based on the nature of those deficits, we could then try treatments used in other conditions and or begin to develop specific compounds to study. In the meantime imaging could help identify a group that might need additional psychosocial supports to successfully navigate older age."

The researchers say their findings also support the hypothesis that HIV-positive individuals are aging faster compared with a non-infected population.

"Our data, demonstrating the decrease in neural specificity before the onset of behavioral symptoms, is in line with reports from aging studies and provides supports to the accelerated aging theory," Jiang says.

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