McGowan Institute for Regenerative Medicine
A program of the University of Pittsburgh and UPMC

Older Adults with Depression and Mild Cognitive Impairment Are More Vulnerable to Accelerated Brain Aging

People who develop depression and mild cognitive impairment (MCI) after age 65 are more likely to have biological and brain imaging markers that reflect a greater vulnerability for accelerated brain aging, according to a study conducted by McGowan Institute for Regenerative Medicine affiliated faculty member Michael Lotze, M.D. (Professor of Surgery and Bioengineering; Vice Chair of Research within the Department of Surgery; Assistant Vice Chancellor in the six schools of the Health Sciences at Pitt; and Director of Strategic Partnerships within the University of Pittsburgh Cancer Institute as well as the Catalyst Program within the recently funded Clinical and Translational Research Institute), and researchers at the University of Pittsburgh School of Medicine. The findings were published online in *Molecular Psychiatry*.

Older adults with major depression have double the risk of developing dementia in the future compared with those who have never had the mood disorder, said senior investigator Meryl A. Butters, Ph.D., associate professor of psychiatry, Pitt School of Medicine. But there's no clear explanation for why a treatable mood disorder like depression leads to increased risk for dementia, a progressive brain disease. Until now, most studies have examined only one or two biomarkers to get at this question.

"Our study represents a significant advance because it provides a more comprehensive and integrated view of the neurobiological changes related to mild cognitive impairment in late-life," she said. "Better understanding of the neurobiology of cognitive impairment in depression can provide new targets for developing more specific treatments, not only for its prevention and treatment, but also for its down-stream negative outcomes, including the development of dementia and related disorders."

The team collected blood samples from 80 older adults in remission after being treated for major depression, 36 of whom had MCI and 44 with normal cognitive function. Their blood was tested for 242 proteins involved in biologic pathways associated with cancer, cardiovascular diseases, and metabolic disorders as well as psychiatric and neurodegenerative disorders. The researchers also performed PET and MRI brain scans on the participants to look for indicators of cerebrovascular disease, brain atrophy or shrinkage, and beta-amyloid, which is the protein that makes up the brain plaques associated with Alzheimer's disease.

The MCI group was more likely to have differences in the biologic activity of 24 proteins that are involved in the regulation of immune and inflammatory pathways, intracellular signaling, cell survival, and protein and lipid balance.

Brain scans revealed a greater propensity for cerebrovascular disease – for example, small strokes – in the MCI group, but there was no difference in the amount of beta-amyloid deposition.

"If you take these results altogether, they suggest that people with depression and cognitive impairment may be more vulnerable to accelerated brain aging, which in turn puts them at risk for developing dementia," Dr. Butters said. "Ultimately, if we can understand what happens in the brain when people are depressed and suffer cognitive impairment, we can then develop strategies to slow or perhaps stop the impairment from progressing to dementia."

Next steps include assessing the protein panel in older people with normal cognitive function who have not experienced depression.

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Abstract (Plasma biosignature and brain pathology related to persistent cognitive impairment in late-life depression. B S Diniz, E Sibille, Y Ding, G Tseng, H J Aizenstein, F Lotrich, J T Becker, O L Lopez, M T Lotze, W E Klunk, C F Reynolds and M A Butters. Molecular Psychiatry , 5 August 2014.)

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