Depression and Alzheimer's disease share genetic roots

Depression may contribute to AD decline

Philadelphia, February 17, 2022 – Epidemiological data have long linked depression with Alzheimer's disease (AD), a neurodegenerative disease characterized by progressive dementia that affects nearly 6 million Americans. Now, a new study identifies common genetic factors in both depression and AD. Importantly, the researchers found that depression played a causal role in AD development, and those with worse depression experienced a faster decline in memory. The study appears in *Biological Psychiatry*, published by Elsevier.

Co-senior author Aliza Wingo, MD, of Emory University School of Medicine, Atlanta, USA, said of the work, "It raises the possibility that there are genes that contribute to both illnesses. While the shared genetic basis is small, the findings suggest a potential causal role of depression on dementia."

The authors performed a genome-wide association study (GWAS), a technique that scans the entire genome for areas of commonality associated with particular conditions. The GWAS identified 28 brain proteins and 75 transcripts – the messages that encode proteins – that were associated with depression. Among those, 46 transcripts and 7 proteins were also associated with symptoms of AD. The data suggest a shared genetic basis for the two diseases, which may drive the increased risk for AD associated with depression.

Although previous studies had examined AD and depression using GWAS, the current work was made more powerful by using larger, newly available data sets that revealed more detailed information.

"This study reveals a relationship between depression and Alzheimer's disease and related dementia at the genetic level," said co-senior author Thomas Wingo, MD. "This is important because it may explain, at least in part, the well-established epidemiologic association between depression and higher risk for dementia."

Dr. A. Wingo added, "This relationship raises the question of whether treatment of depression can mitigate the risk for dementia. We identified genes that may explain the relationship between depression and dementia here that merit further study. Such genes may be important treatment targets for both depression and reduction of dementia risk."

"The costs of ineffectively treated depression continue to mount. There has been increasing evidence that major depressive disorder increases the risk for Alzheimer's disease, but little insight into this relationship," John Krystal, MD, Editor of *Biological Psychiatry*, said. "This innovative study, which links genetic risk mechanisms to molecular changes in the brain, provides the clearest link to date supporting the hypothesis that depression plays a causal role in the biology of Alzheimer's disease."

This does not mean that if one has an episode of depression that dementia is an inevitable result. Instead, it suggests that ineffectively treated depression may aggravate the biology of Alzheimer's disease, potentially hastening the onset of symptoms and increasing the rate of functional decline."

Notes for editors
The article is "Genetic evidence supporting a causal role of depression on Alzheimer's disease," by Nadia Harerimana, Yue Liu, Ekaterina Gerasimov, Duc Duong, Thoomas Beach, Eric Reiman, Julie Schneider, Patricia Boyle, Adriana Lori, David Bennett, James Lah, Allan Levey, Nicolas Seyfried, Thomas Wingo, Aliza Wingo (https://doi.org/10.1016/j.biopsych.2021.11.025). It appears as an Article in Press in *Biological Psychiatry*, published by Elsevier.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at Biol.Psych@sobp.org or +1 254 522 9700. Journalists wishing to interview the authors may contact Aliza Wingo at aliza.wingo@emory.edu or Thomas Wingo at thomas.wingo@emory.edu.

The authors' affiliations and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, MD, is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available here.

About *Biological Psychiatry*
Biological Psychiatry is the official journal of the Society of Biological Psychiatry, whose purpose is to promote excellence in scientific research and education in fields that investigate the nature, causes, mechanisms, and treatments of disorders of thought, emotion, or behavior. In accord with this mission, this peer-reviewed, rapid-publication, international journal publishes both basic and clinical contributions from all disciplines and research areas relevant to the pathophysiology and treatment of major psychiatric disorders.

The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

Biological Psychiatry is one of the most selective and highly cited journals in the field of psychiatric neuroscience. It is ranked 7th out of 156 Psychiatry titles and 11th out of 273 Neurosciences titles in the Journal Citations Reports® published by Clarivate Analytics. The 2020 Impact Factor score for *Biological Psychiatry* is 13.382. www.sobp.org/journal

About Elsevier
As a global leader in information and analytics, Elsevier helps researchers and healthcare professionals advance science and improve health outcomes for the benefit of society. We do this by facilitating insights and critical decision-making for customers across the global research and health ecosystems.

In everything we publish, we uphold the highest standards of quality and integrity. We bring that same rigor to our information analytics solutions for researchers, health professionals, institutions and funders.

Elsevier employs 8,100 people worldwide. We have supported the work of our research and health partners for more than 140 years. Growing from our roots in publishing, we offer knowledge and valuable analytics that help our users make breakthroughs and drive societal progress. Digital solutions such as ScienceDirect, Scopus, SciVal, ClinicalKey and Sherpath support strategic research management, R&D performance, clinical decision support, and health education. Researchers and healthcare professionals rely on our 2,500+ digitized journals, including *The Lancet* and *Cell*; our 40,000 eBook titles; and our iconic reference works, such as *Gray's Anatomy*. With the Elsevier Foundation and our external Inclusion & Diversity Advisory Board, we work in partnership with diverse stakeholders to advance inclusion and diversity in science, research and healthcare in developing countries and around the world.

Elsevier is part of RELX, a global provider of information-based analytics and decision tools for professional and business customers. www.elsevier.com

Media contact
Rhiannon Bugno, Editorial Office
Biological Psychiatry
+1 254 522 9700
Biol.Psych@sobp.org