

New biomarker for dementia improves risk prediction

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Identifying individuals who are at risk for developing dementia, including Alzheimer's disease, is critical for the development of new therapies and interventions to slow or reverse cognitive symptoms. But current strategies are limited, both in terms of accuracy and the ability to incorporate them into routine practice. Unlike cerebrospinal fluid biomarkers that require a spinal tap, plasma biomarkers can be extracted from the blood, making their collection much less invasive and much more appealing. In a new study led by investigators from Brigham and Women's Hospital, researchers have measured circulating levels of insulin-like growth factor binding protein 2 (IGFBP-2), a potential biomarker for dementia. In a paper published in *Annals of Clinical and Translational Neurology*, the team reports that IGFBP-2 levels were associated with an increased risk of both all-cause dementia and Alzheimer's disease dementia. When added to a model of traditional risk factors for dementia, IGFBP-2 significantly improved dementia risk classification, suggesting that it may be a useful biomarker for predicting dementia risk.

"Identifying biomarkers for dementia could improve our ability to predict a person's risk of dementia and his or her future outcomes," said corresponding author Emer McGrath, MD, Ph.D., an associate neurologist in the Brigham's Neurology Department and an investigator with the Framingham Heart Study. "Novel biomarkers could also inform our understanding of complex biological pathways underlying the development of dementia, help to more accurately define disease subgroups and inform future clinical trials."

Recently, researchers have begun to focus on the role of metabolic dysfunction and [insulin resistance](#) in the brain in the development of dementia. The insulin-like growth factor (IGF) signaling system is known to play a role in neuroregeneration, neuronal survival and proliferation. IGFBP-2 is thought to impair IGF signaling, thereby inhibiting

the neuroprotection and proliferation.

In the current study, investigators measured levels of IGFBP-2 in plasma samples from almost 1,600 participants from the Framingham Offspring cohort. The team analyzed risk of dementia, cognitive performance and structural MRI brain measures predictive of dementia.

They found that elevated circulating IGFBP-2 levels were associated with an increased risk of both all-cause dementia and Alzheimer's disease dementia, as well as poorer performance on tests of abstract reasoning. Addition of IGFBP2 plasma levels to a model of traditional risk factors significantly improved dementia risk classification: based on the net reclassification improvement (NRI) index, 32 percent of individuals with dementia were correctly assigned a higher predicted risk, while 8 percent of individuals without dementia were correctly assigned a lower predicted risk.

The authors note that the Framingham Offspring cohort is predominantly Caucasian, potentially limiting the generalizability of the findings to more diverse populations. They were also unable to explore the association between cerebrospinal fluid levels of IGFBP-2 or Tau levels with IGFBP-2 plasma levels and cognitive outcomes.

"There is increasing interest in manipulating insulin sensitivity and IGF signaling in the brain to help target cognitive decline and dementia," said McGrath. "Our work suggests that manipulating IGF-signaling pathways via IGFBP-2 may be a promising therapeutic target for [dementia](#) prevention."

More information: Emer R. McGrath et al, Circulating IGFBP-2: a novel biomarker for incident dementia, *Annals of Clinical and Translational Neurology* (2019). [DOI: 10.1002/acn3.50854](https://doi.org/10.1002/acn3.50854)

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