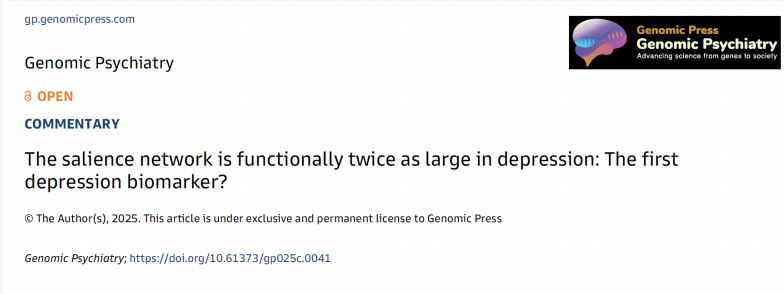
Enlarged salience network could be first reliable biomarker for depression risk

Individuals with depression have a brain salience network twice as large as non-depressed controls. This distinctive neural signature predates symptom onset.



The salience network is functionally twice as large in depression: The first depression biomarker?

OTTAWA, ONTARIO, CANADA, May 13, 2025 /EINPresswire.com/ -- In a comprehensive Genomic Press Commentary (review) published today, researchers have identified what could be the first reliable biomarker for depression risk, potentially transforming how this devastating condition is identified and treated. The commentary examines recent findings demonstrating that individuals with depression consistently exhibit a functionally enlarged salience network compared to non-depressed controls.

Distinctive Brain Connectivity Pattern Identified

The salience network, a neural system responsible for attention allocation and switching between different brain networks, appears to be functionally twice as large in people with depression as in those without the condition. This finding, highlighted in the commentary by researchers at the University of Ottawa and the University of California San Francisco, builds upon groundbreaking research published in Nature by Lynch et al. (https://doi.org/10.1038/s41586-024-07805-2).

"What makes this discovery so significant is that the expanded salience network predates the onset of depressive symptoms and remains stable regardless of symptom severity or treatment interventions," explained Dr. Nicholas Fabiano, co-author of the commentary from the University of Ottawa's Department of Psychiatry. "We're potentially looking at a distinctive neural signature that could identify individuals at risk for depression before they experience symptoms."
This characteristic brain connectivity pattern was observed consistently across individuals with depression, suggesting its potential as a depression biomarker. The salience network, comprising the fronto-insular cortex, dorsal anterior cingulate cortex, amygdala, and temporal poles, plays a crucial role in reward processing and regulating the switch between the default

mode network and frontoparietal network.

Potential for Early Identification and Intervention

Depression affects millions worldwide, yet remains poorly diagnosed and predicted despite significant advances in mental health awareness. The World Health Organization identifies depression as a leading cause of disability globally, with many cases going undiagnosed until symptoms become severe.
The commentary authors highlight how this biomarker could transform depression management. "By identifying those at risk before they experience the full impact of depression, we can intervene earlier, leading to lasting improvements in their quality of life," noted Katerina Palacek from the University of Ottawa's Faculty of Medicine.

Early detection has been proven to support remission in those with depressive symptoms and decrease the likelihood of progression to treatment resistance. This could ultimately lessen the chances of relapse, shorter periods of remission, and longer depressive episodes.

What factors might trigger an expanded salience network in those predisposed to depression? Does this pattern appear in other mental health conditions with overlapping symptoms? These questions represent important next steps for researchers in understanding the implications of this discovery.

Understanding Mechanisms Behind Network Expansion

The researchers propose three potential mechanisms underlying this salience network expansion:

1. Compensatory neural changes: The enlarged network could represent a compensatory response based on increased usage of this network in individuals predisposed to depression.

2. Genetic predisposition: There may be genetic factors contributing to the development of an enlarged salience network in those who later develop depression.

3. Relative expansion due to atrophy: The salience network might appear relatively enlarged as a consequence of atrophy in other brain regions that could predate depressive symptoms.

"While we observe similarities between regions implicated in depression-related brain atrophy and the salience network, including the insular cortex and anterior cingulate cortex, there are also notable differences," explained Dr. Robin Carhart-Harris, co-author from the University of California San Francisco's Weill Institute for Neurosciences. "This suggests complex interactions between various brain networks in depression that we're just beginning to understand."

Reconceptualizing Depression Treatment

The findings underscore the need to reconceptualize depression as a disorder of neural connectivity rather than isolated neurotransmitter imbalances, with potential implications for developing targeted therapeutic approaches.

"Depression is not a simple disease characterized by independently functioning brain areas or isolated neurotransmitter imbalances," noted the researchers. "By record, it is a multifaceted condition with altered brain-wide connectivity that cannot be comprehensively understood through fragmented lenses."

This suggests potential value in investigating how various established and novel depression treatments—including antidepressants, exercise, diet modifications, electroconvulsive therapy, ketamine, and psychedelics—might impact the salience network's functional connectivity. Emerging research has found these approaches implicated in central nervous system plasticity, potentially affecting brain network connectivity.

The commentary authors suggest longitudinal studies tracking how the size of the salience network evolves with different treatment modalities could provide transformative insights into whether external stimuli can modify this network and if these modifications improve depression symptoms.

The peer-reviewed Commentary (review) article in Genomic Psychiatry titled "The salience network is functionally twice as large in depression: The first depression biomarker?," is freely available available via Open Access on 13 May 2025 in Genomic Psychiatry at the following hyperlink: https://doi.org/10.61373/gp025c.0041

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