Brain imaging-based biomarker of depression identified

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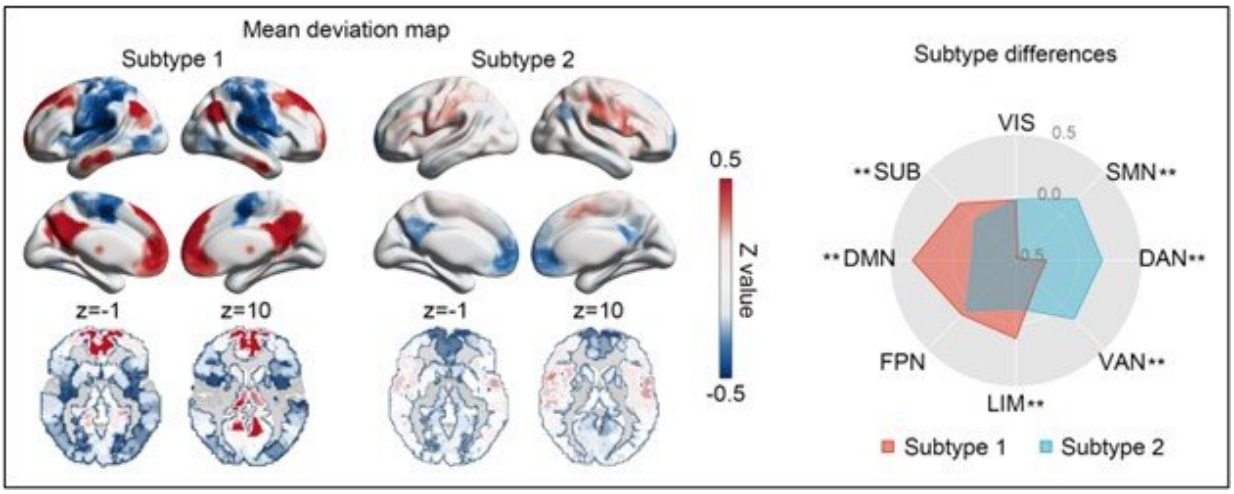

Brain imaging maps and a functional deviation map of the two depression subtypes across brain regions. Credit: *Biological Psychiatry*

Major depressive disorder (MDD) is not only among the most common mental illnesses, affecting more than 8% of Americans, but it is also extremely variable from one person to another. Researchers have recently begun making strides toward understanding the neurophysiology underlying different subtypes of depression, which could speed development of better treatments, but much remains to be discovered.

Now, a new study published in *Biological Psychiatry* identifies multiple subtypes of MDD using brain imaging.

John Krystal, MD, Editor of *Biological Psychiatry*, said of the work, "We have long known that disorders like major depressive disorder are highly heterogeneous. This study in a large sample of depressed patients provides leads that can be pursued in subtyping depression on the basis of functional magnetic resonance imaging (fMRI) tests that measure the degree of coordination across brain regions, also known as 'functional connectivity.'"

The researchers used resting-state fMRI collected at multiple clinical sites from a large cohort of more than 1,000 MDD patients and more than 1,000 healthy controls (HC). The study used the so-called normative model, which uses data from a large reference population to quantify individual deviations, much like the growth charts used by pediatricians. The researchers examined the functional connectivity among brain regions and mapped individual functional deviations in the MDD patients compared to this normative prediction across the lifespan.

Senior author Mingrui Xia, Ph.D., from Beijing Normal University, said, "This approach led to the identification of two reproducible neurophysiological subtypes exhibiting distinct deviation patterns, depressive item scores, and longitudinal treatment predictability."

One subtype of patients showed severe positive deviations—indicating increased brain connectivity—in the default mode network, limbic, and subcortical areas, and negative deviations in the sensorimotor and attention areas. The second subtype of patients featured a milder and opposite pattern of deviation, highlighting the heterogeneity of depression at the neurophysiological level. The authors speculate that the altered activity could be related to the tendency to ruminate in people with MDD.

The work is particularly exciting in that it moves the field toward finding biomarkers, or biological markers, of depression, which currently relies

on patient-reported clinical symptoms for diagnosis, treatment, and prognostics. Biomarkers could offer a way to improve all these aspects of treatment for MDD.

Dr. Xia went on to say, "These findings shed light on the diverse neurobiological mechanisms from a connectomics perspective underlying the complex clinical heterogeneity observed in individuals with depression. The implications of this research are far-reaching, providing valuable insights into the development of imaging-based candidate biomarkers. These biomarkers have the potential to guide future precise diagnostic and treatment strategies tailored to each patient's specific neurophysiological subtype."

Dr. Xia noted, "By embracing the concept of neurophysiological subtypes, we can potentially revolutionize the field of mental health by enabling clinicians to personalize treatments based on an individual's unique connectome characteristics. This approach opens up new avenues for precision medicine and holds the promise of improving therapeutic interventions for depression."

More information: Xiaoyi Sun et al, Mapping Neurophysiological Subtypes of Major Depressive Disorder Using Normative Models of the Functional Connectome, *Biological Psychiatry* (2023). DOI: 10.1016/j.biopsych.2023.05.021

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