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Genetic and environmental factors contribute to the overlap between depression and endocrine-metabolic disorders

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Depression is common in individuals with endocrine-metabolic disorders and vice versa. In a study involving 2.2 million people in the Swedish

population, researchers at Karolinska Institutet confirmed that individuals with endocrine-metabolic disorders have increased rates of depression and found that there are also higher rates of depression in their siblings. The study is published in the *American Journal of Psychiatry*.

Further analysis revealed the balance of genetic and environmental influences underlying the co-occurrence of depression for a range of endocrine-metabolic disorders. It is known that there is elevated co-occurrence between endocrine-metabolic disorders and depression, but the relationship between them is still not well understood.

"Whether the overlap between these conditions is predominantly genetic or environmental has implications for whether the development of pharmacological or behavioral interventions would be more effective for treatment or prevention efforts," says Sarah Bergen, principal researcher at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet, who led the study.

Familial aggregation

The authors identified 2.2 million individuals born in Sweden between 1973 and 1996, as well as their full and half siblings, and followed them up to age 40. A number of medical conditions were studied; depression and various endocrine-metabolic disorders, including three autoimmune diseases (autoimmune hypothyroidism, Graves' disease, and type 1 diabetes) and three non-autoimmune disorders (type 2 diabetes, obesity, and polycystic ovary syndrome).

Individuals with endocrine-metabolic disorders had 1.4 to 3.5 times the risk of depression compared to people without these diagnoses. Full and half siblings of these individuals also showed some elevated risk for depression, suggesting that genetic and/or environmental risk factors

shared between family members play a role in the co-occurrence of these mental and physical disorders.

Genetic and environmental contributions

By comparing pairs of full sibling (who share about half of their genes) to pairs of half siblings (who share about a quarter of their genes), it was possible to calculate the relative contribution of genetic and environmental factors to the co-occurrence of depression and various endocrine-metabolic disorders.

The results were a mix of these possibilities; the overlap between depression and non-autoimmune conditions was mainly explained by shared genetic influences, while environmental factors were predominantly involved in the association between depression and autoimmune disorders, particularly type 1 diabetes.

This indicates that the link between depression and different endocrine-metabolic disorders may be driven by different mechanisms. For example, shared biological mechanisms, such as immuno-inflammatory and metabolic dysregulations, may underlie the co-occurrence of depression and type 2 diabetes, obesity, and polycystic ovarian syndrome. In contrast, the absence of shared genetics in the association between type 1 diabetes and depression may reflect the existence of environmental factors influencing the risk of both conditions and/or a direct link between these conditions through mediating factors—e.g., biological and psychosocial mechanisms connected to type 1 diabetes, including inflammation, cerebral damage, as well as stress of this lifelong condition that is often diagnosed early in life and that requires a complex management regime for both patients and their families.

"Our results underscore that clinicians should be aware of increased risks of depression in individuals with endocrine-metabolic disorders, and

vice versa, and be vigilant for shared symptoms. This study also provides a useful foundation for future research aimed at identifying and targeting the biological mechanisms and modifiable risk factors underlying the co-presentation of endocrine-metabolic disorders and depression," says Marica Leone, first author for the study.

More information: Marica Leone et al, Genetic and Environmental Contribution to the Co-Occurrence of Endocrine-Metabolic Disorders and Depression: A Nationwide Swedish Study of Siblings, *American Journal of Psychiatry* (2022). DOI: 10.1176/appi.ajp.21090954

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