Dopamine-Targeting Treatments Show Only Modest Benefits for Anhedonia, Prompting Call for New Research Approaches

Experts call for a broader approach to understanding and treating one of the most debilitating symptoms of mental illness

Dopamine has long been considered central to understanding anhedonia – the loss of pleasure, interest and motivation that is a common feature of depression and other mental health conditions. However, a new international expert report published in BMJ Mental Health suggests that dopamine alone cannot explain the condition and that future research must look beyond a single biological pathway.

The report was developed following a meeting organised by the Wellcome-funded GALENOS project and the European College of Neuropsychopharmacology (ECNP), bringing together researchers, clinicians, industry partners and people with lived experience to identify priorities for future anhedonia research.

Anhedonia affects many people living with depression, schizophrenia, bipolar disorder, Parkinson's disease and other neurological and psychiatric conditions. It is associated with poorer quality of life, impaired daily functioning and poorer treatment outcomes. Despite its impact, current treatments often fail to adequately address the symptom.

Lead co-author Professor Brenda Penninx explains "anhedonia identifies someone who experiences less pleasure, interest, or motivation. It can mean that you enjoy something less that is normally pleasant, but also that you look forward to something less or feel less motivated to make an effort for something. This distinction is precisely what matters: anhedonia is likely not a single phenomenon, but consists of different processes surrounding reward and motivation."

The discussion was prompted by recent findings from a GALENOS living systematic review examining drugs that increase dopamine activity. While these treatments produced some improvements in anhedonia symptoms, the effects were relatively small. Unexpectedly, some antidepressants with a non-dopaminergic mechanism of action were associated with a bigger reduction of anhedonia symptoms than pro-dopaminergic drugs, showing that the 'anti-anhedonia' effect was potentially independent of the improvement in mood symptoms.

Lead co-author Professor Andrea Cipriani said: "Based on our findings, the neurobiology of anhedonia in depression likely involves systems that include, but are not limited to, dopaminergic pathways. A better understanding of the different biological mechanisms could ultimately help us identify more targeted approaches for people experiencing this often debilitating and neglected symptom."

The authors argue that anhedonia should no longer be viewed as a single symptom with a single cause. Instead, it encompasses several distinct but related processes, including reward anticipation, motivation, reward learning and the experience of pleasure itself. Different aspects may involve different biological systems, including dopaminergic, glutamatergic, opioid, inflammatory and metabolic pathways.

To accelerate progress, the report calls for the development of more precise definitions and measurement tools, greater use of biological markers, and clinical trials that specifically target anhedonia as a primary outcome rather than treating it as a secondary symptom of depression. Researchers also highlight the need for studies spanning different disorders and stages of life to better understand how anhedonia develops and responds to treatment.

The authors conclude that a more nuanced understanding of anhedonia could help drive the development of more effective and personalised treatments, moving the field closer to the goals of precision psychiatry.

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Notes to editors:

The paper, "Research agenda to advance anhedonia assessment, understanding and treatment: an ECNP-GALENOS expert meeting report", is published in BMJ Mental Health.

Anhedonia refers to a reduced ability to experience pleasure, interest or motivation.

GALENOS (Global Alliance for Living Evidence on Anxiety, Depression and Psychosis) is a Wellcome-funded initiative based at the University of Oxford that provides continuously updated evidence syntheses to inform mental health research, policy and practice.

ECNP is Europe's leading independent forum for the science of CNS treatments. The ECNP Congress showcases the world's best disease-oriented brain research, annually attracting some 6,000 psychiatrists, neuroscientists, neurologists and psychologists from around the world. The College's wide range of scientific and educational activities, programmes and events make it one of the largest non-institutional supporters of applied and translational neuroscience research and education in Europe.

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