

Glutamatergic agents show promise for mood and anxiety disorders

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Glutamatergic agents may one day be used as a novel treatment for mood and anxiety disorders, new research presented at the 26th ECNP Congress suggests.

"Our results suggest the glutamatergic system is a truly viable target for antidepressant development," says Professor Gerard Sanacora, from the Yale School of Medicine, Connecticut, US.

In his talk, Professor Sanacora detailed how he and his team have used animal models to help understand how stress and other mechanisms that can disrupt glutamatergic function can lead to molecular, cellular and behavioural changes in the brain that are characteristic of depression.

He also presented results from a completed phase II trial with a unique non-selective NMDA receptor antagonist.

"We found that drugs that can target glutamate transmission, either by altering release, uptake or receptor activation can prevent or attenuate the cellular and behavioural changes seen in [mood disorders](#)," he explains.

In humans, the NMDA receptor antagonist showed a surprisingly rapid antidepressant effect. Importantly, the trial demonstrated the potential ability to dissociate the perceptual and cognitive effects of the NMDA receptor antagonists from the antidepressant effects.

His results also suggest the antidepressant effects can be extended for several weeks with repeated infusions.

In rodent models, the team demonstrated that stress has a major impact on the function of glutamate neurotransmission – especially glutamate clearance through glial cells – that appears to be related to behavioural changes.

Professor Sanacora presented a series of preclinical and clinical studies indicating that a novel class of drugs that target components of the glutamatergic neurotransmitter system may produce rapid and robust antidepressant effects.

"There is a rapidly expanding literature suggesting the glutamatergic neurotransmitter system is altered in the brains of individuals suffering with mood disorders," explains Professor Sanacora.

There is also increasing evidence suggesting stress may disrupt normal glutamatergic function in the brain and may be a mechanism contributing to the pathogenesis of several stress-related neuropsychiatric disorders," he adds.

Their research, due to be published in the journal *Molecular Psychiatry* adds to this body of evidence.

"First and foremost, our findings suggest the glutamatergic system is a truly viable target for antidepressant drug development," concludes Professor Sanacora.

Provided by European College of Neuropsychopharmacology

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