

STAT3 identified as important factor in emotional reactivity

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Numerous scientific studies indicate that inflammatory processes play a key role in the development of psychiatric disorders. One of the areas of particular interest is the interleukin 6/STAT3 signal transduction pathway, which is associated with depression, schizophrenia, and bipolar disorder. In a study published in *Molecular Psychiatry*, MedUni Vienna researchers led by Daniela Pollak from the Division of Neurophysiology and Neuropharmacology showed that STAT3 plays an important role in the serotonergic system as a molecular mediator for controlling emotional reactivity, thereby establishing a mechanistic link between the immune system, serotonergic transmission and affective disorders such as depression.

The STAT3 [signal transduction pathway](#) is activated in response to a series of immunogenic and non-immunogenic stimuli, i.e. those that can and those that cannot trigger an immune response. "It was found that STAT3 is involved in nervous system functions that are important for controlling behavior in physiological and pathological situations. In an earlier study, we had managed to

show that STAT3 also regulates the expression of the serotonin transporter gene (Note: SERT)," explains Pollak.

Changes in serotonergic transmission, that is to say the transmission of information from one neuron to another using serotonin as a messenger substance, correlate closely with pathological changes in depression or other affective [disorders](#). However, the interaction between the STAT3 signal transduction pathway and the neuronal information flow in the brain and its importance in regulating emotional behavior has not yet been explored.

STAT3 deficiency reduces emotional reactivity

The published work therefore specifically investigated the significance of the STAT3 signal transduction pathway in the serotonergic system of the midbrain—an emotional regulation center—by targeted inhibition of STAT3 in a [mouse model](#). Says Pollak: "Where STAT3 was selectively absent from the serotonergic system of the midbrain, the mice displayed reduced, negative emotional reactivity in their behavior and a diminished response to the effects of amphetamine in the brain. These effects could be detected in mice with reduced STAT3 expression both in a genetic and in a viral model, so that it was possible to rule out developmental changes and to show that an acute manipulation of STAT3 in the adult organism impacts on emotional behavior."

In animals lacking in STAT3, there was also found to be a change in the neuronal activity of serotonergic cells of the midbrain. Changes in molecular networks that are significant in neuropsychiatric illnesses were also found on the level of gene expression. "The results of our study indicate that STAT3 plays an important role as a molecular mediator in the serotonergic system for controlling emotional reactivity, thereby establishing a mechanistic link between the [immune system](#), serotonergic transmission and affective disorders."

More information: Sonali N. Reisinger et al.
STAT3 in the dorsal raphe gates behavioral reactivity and regulates gene networks associated with psychopathology, *Molecular Psychiatry* (2020).
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