Depression associated with sustained brain signals

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Depression and schizophrenia can be triggered by environmental stimuli and often occur in response to stressful life events. However, some people have a higher predisposition to develop these diseases, which highlights a role for genetics in determining a person's disease risk. A high number of people with depression have a genetic change that alters a protein that cells use to talk to each other in the brain. Imaging of people with depression also shows that they have greater activity in some areas of their brain. Unfortunately, the techniques that are currently available have not been able to determine why stress induces pathological changes for some people and how their genetics contribute to disease.

A new mouse model may provide some clues about what makes some people more likely to develop depression after experiencing stress. A collaborative group of European researchers created a mouse that carries a genetic change associated with depression in people. "This model has good validity for understanding depression in the human, in particularly in cases of stress-induced depression, which is a fairly widespread phenomenon" says Dr. Alessandro Bartolomucci, the first author of the research published in the journal, Disease Models and Mechanisms (DMM).

The scientists made genetic changes in the transporter that moves a signaling protein, serotonin, out of the communication space between neurons in the brain. The changes they made are reminiscent of the genetic changes found in people who have a high risk of developing

depression.

"There is a clear relationship between a short form of the serotonin transporter and a very high vulnerability to develop clinical depression when people are exposed to increasing levels of stressful life events." says Dr. Bartolomucci, "This is one of the first studies performed in mice that only have about 50% of the normal activity of the transporter relative to normal mice, which is exactly the situation that is present in humans with high vulnerability to depression".

Mice with the genetic change were more likely to develop characteristics of depression and social anxiety, which researchers measure by their degree of activity and their response to meeting new mice. The work from this study now allows researchers to link the genetic changes that are present in humans with decreased serotonin turnover in the brain. It suggests that the genetic mutation impedes the removal of signaling protein from communication areas in the brain, which may result in an exaggerated response to stress.

Dr. Bartolomucci points out that many of the chemical changes they measured occurred in the areas of the brain that regulate memory formation, emotional responses to stimuli and social interactions, which might be expected. "What we were surprised by was the magnitude of vulnerability that we observed in mice with the genetic mutation and the selectivity of its effects".

More information: The study is published in Volume 3 issue 7/8 of the research journal, *Disease Models & Mechanisms (DMM)*, dmm.biologists.org/

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