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News in brief

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Treating depressive symptoms from their roots

A wide range of compounds is on the market to ameliorate depressive symptoms, however their efficiency is achieved only after long periods of treatment and not in 100% of patients. Inserm researchers identified early cellular changes in the brain for the emergence of depressive symptoms, and a novel promising drug target.

These results are published in the journal *Nature Medicine* on Janaury 25th, 2016.

The aim of Manuel Mameli, Inserm researcher and Dr. Salvatore Lecca in his team, at Inserm Unit 839 the "Institut du Fer a Moulin (IFM)" (Inserm/UPMC), was to understand the initial cellular modifications occurring after a stressful aversive experience. Protracted stress and aversive experiences are indeed a trigger to engage depressive behaviors in animals and humans.

Using electrophysiological, viral-based and pharmacological approaches researchers found that the activity of neurons located in the lateral habenula - a cerebral nucleus for aversion and disappointment – increased after a stressful experience due to a reduced function of two proteins controlling neuronal function (GABAB and GIRK).

Inserm scientists designed a rescue strategy that reversed the cellular modifications and ameliorated depressive symptoms after aversive experience by targeting a specific phosphatase (PP2A). By employing a rodent model of mood disorders (Learned Helplessness), that recapitulates a number of behavioral phenotypes typical of human depression, they have shown that the inhibition of PP2A was efficient to rapidly ameliorate the behavioral phenotype of mice.

“Our study unravels unknown early cellular mechanisms able to trigger complex behavioral responses. Our study further highlights the role of the lateral habenula in the aetiology of depression. Our results provide insights on a novel potential pharmacological target that could be studied for a therapy of mood disorders” explain Manuel Mameli, Inserm researcher.

Sources

Rescue of GABAB and GIRK function in the lateral habenula by protein phosphatase 2A inhibition ameliorates depression-like phenotypes in mice
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