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Repeated aggressions trigger social aversion in mice

One of the mechanisms involved in the onset of stress-induced depression has been highlighted in mice by researchers from CNRS, Inserm and UPMC[1]. They have determined the role of the corticosterone (stress hormone) receptor, in the long-term behavioral change triggered by chronic stress. In mice subject to repeated aggressions, this receptor participates in the development of social aversion by controlling the release of dopamine[2], a key chemical messenger. If this receptor is blocked, the animals become "resilient": although anxious, they overcome the trauma and no longer avoid contact with their fellow creatures. This work is published in *Science* on 18 January 2013.

In vertebrates, stress triggers a rapid release of glucocorticoid hormones, corticosterone in rodents and cortisol in humans. This hormone modifies the expression of numerous genes in such a way that the individual can best respond to the cause of stress. However, chronic or excessive stress can lead to depression, anxiety and social behavioral difficulties. Understanding the mechanisms involved is an important challenge in the treatment of stress-related psychiatric illnesses.

The researchers already suspected that the emergence of depressive symptoms caused by stress brought into play not only the stress hormone but also the dopamine neurons releasing this neurotransmitter, which is vital in controlling mood. To better understand this interdependence, the researchers subjected a group of mice to repeated attacks by stronger, aggressive congeners. After about ten days, the mice showed signs of anxiety and strong social aversion. In fact, when faced with a new congener, the aggressed mice preferred to avoid any contact. This social aversion is considered as a marker of depression.

The researchers repeated the experiment, but this time with various mouse strains in which the corticosterone receptor was absent in certain populations of neurons. In this way, they discovered that mice without this receptor in dopamine-sensitive neurons did not develop social aversion. Although anxious following repeated attacks, they did not however avoid contact with their fellow creatures. These rodents were thus more "resilient", in other words more resistant to stress, than "wild" mice.

In response to an aggression, a release of dopamine is always observed. However, scientists have noticed that, in mice without the corticosterone receptor in dopamine-sensitive neurons, this release is considerably reduced. In normal mice, dopamine-sensitive neurons thus control the release of this neurotransmitter through a feedback mechanism. In order to show that this release of dopamine triggers the development of social aversion, the researchers blocked the activity of dopamine-producing neurons. As a result, interest in

[1] More precisely, this work was conducted by a team from the laboratory "Physiopathologie des Maladies du Système Nerveux Central" (CNRS/Inserm/UPMC), in collaboration with the laboratory "Neurobiologie des Processus Adaptatifs" (CNRS/UPMC).
[2] Dopamine is a neurotransmitter, in other words a substance that modulates the activity of neurons in the brain.

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congeners was restored in mice subject to aggression. Dopaminergic activity is therefore crucial for the appearance of social aversion.

This study shows the important role of the stress hormone in the onset of social aversion induced by repeated traumas. More generally, it partially reveals the neurobiological mechanisms and the cascade of reactions that underlie the onset of depression. These results could lead to new therapeutic prospects for treating depression by revealing alternative targets for medicines, particularly with regard to the dopaminergic system.

Bibliography

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