Immune cells from stressed mice found to lessen depression when injected into other mice

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Credit: Martha Sexton/public domain

(Medical Xpress)—A team of researchers working at the NIH–DHHS facility in Bethesda Maryland has found that injecting immune cells from mice that were stressed, caused lessened depression symptoms in other mice whose immune system had been compromised. In their paper published in *The Journal of Neuroscience*, the team describes their experiments with immune cell transfer in mice, and the implications of their results.

The immune system in humans, and mice, prior research has shown, has two major parts—the innate branch and the adaptive branch—the former is the branch that deals with actually fighting off diseases. The latter is the part that helps the body remember what occurred so that it can better fight of the same infections in the future. In this new study, the researchers sought to learn more about how the adaptive branch works by studying its impact on lab mice.

In one experiment, the team exposed one group of meek male mice to bullying mice, causing them to become withdrawn and sullen, which are symptomatic of depression. They then extracted adaptive branch immune cells from them and injected them into the bloodstream of another set of male mice which had been bred to develop without an adaptive immune system, restoring their immune system temporarily. The team notes that they fully expected the injected mice to become depressed, but were instead surprised to find that it appeared to have the opposite impact on them—they became more animated and more interested in pursuing females. The team also injected another group of mice that are known to be timid and shy, and found that the addition of adaptive cells reduced their reticent ways giving them more of an extroverted personality.

The research team does not know why the injected cells cause the changes they observed in other mice, but theorize that it has something to do with the role adaptive cells play in immunity—they may react to stress by building up a mood enhancing capability, for example. What is also unclear is whether the same experiment would offer the same result in humans. The team plans to continue their work and now have a goal of determining if they have found a possible tool for use in combating depression in people.

More information: Lymphocytes from Chronically Stressed Mice Confer Antidepressant-Like Effects to Naive Mice, *Journal of*

Neuroscience, www.jneurosci.org/content/35/4/1530.abstract

Abstract

We examined whether cells of the adaptive immune system retain the memory of psychosocial stress and thereby alter mood states and CNS function in the host. Lymphocytes from mice undergoing chronic social defeat stress or from unstressed control mice were isolated and adoptively transferred into naive lymphopenic Rag2−/− mice. Changes in affective behavior, hippocampal cell proliferation, microglial activation states, and blood cytokine levels were examined in reconstituted stress-naive mice. The mice receiving lymphocytes from defeated donors showed less anxiety, more social behavior, and increased hippocampal cell proliferation compared with those receiving no cells or cells from unstressed donors. Mice receiving stressed immune cells had reduced pro-inflammatory cytokine levels in the blood relative to the other groups, an effect opposite to the elevated donor pro-inflammatory cytokine profile. Furthermore, mice receiving stressed immune cells had microglia skewed toward an anti-inflammatory, neuroprotective M2-like phenotype, an effect opposite the stressed donors' M1-like pro-inflammatory profile. However, stress had no effect on lymphocyte surface marker profiles in both donor and recipient mice. The data suggest that chronic stress-induced changes in the adaptive immune system, contrary to conferring anxiety and depressive behavior, protect against the deleterious effects of stress. Improvement in affective behavior is potentially mediated by reduced peripheral pro-inflammatory cytokine load, protective microglial activity, and increased hippocampal cell proliferation. The data identify the peripheral adaptive immune system as putatively involved in the mechanisms underlying stress resilience and a potential basis for developing novel rapid-acting antidepressant therapies.