

Over years, depression changes the brain, new study shows

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Is clinical depression always the same illness, or does it change over time?

New brain imaging research from the Centre for Addiction and Mental Health (CAMH) shows that the brain alters after years of [persistent depression](#), suggesting the need to change how we think about depression as it progresses.

The study, led by senior author Dr. Jeff Meyer of CAMH's Campbell Family Mental Health Research Institute, is published in *The Lancet Psychiatry*.

The research shows that people with longer periods of untreated depression, lasting more than a decade, had significantly more brain [inflammation](#) compared to those who had less than 10 years of untreated depression. In an earlier study, Dr. Meyer's team discovered the first definitive evidence of inflammation in the brain in [clinical depression](#).

This study provides the first biological evidence for large brain changes in long-lasting depression, suggesting that it is a different stage of illness that needs different therapeutics - the same perspective taken for early and later stages of Alzheimer's disease, he says.

"Greater inflammation in the brain is a common response with degenerative brain diseases as they progress, such as with Alzheimer's disease and Parkinson's disease," says Dr. Meyer, who also holds Canada Research Chair in the Neurochemistry of Major Depression. While depression is not considered a degenerative brain disease, the change in inflammation shows that, for those in whom depression persists, it may be progressive and not a static condition.

Yet currently, says Dr. Meyer, regardless of how long a person has been ill, major depressive disorder is mainly treated with the same approach. Some people may have a couple of episodes of

depression over a few years. Others may have persistent episodes over a decade with worsening symptoms, and increasing difficulty going to work or carrying out routine activities.

Treatment options for this later stage of illness, such as medications targeting inflammation, are being investigated by Dr. Meyer and others. This includes re-purposing current medications designed for inflammation in other illnesses to be used in [major depressive disorder](#).

In the study, [brain inflammation](#) was measured using a type of brain imaging called positron emission tomography (PET). The brain's immune cells, known as microglia, are involved in the brain's normal inflammatory response to trauma or injury, but too much inflammation is associated with other degenerative illnesses as well as depression. When microglia are activated, they make more translocator protein (TSPO), a marker of inflammation that can be seen using PET imaging.

The study involved 25 people with more than 10 years of depression, 25 with less than 10 years of illness, and 30 people with no depression as a comparison group. TSPO levels were about 30 per cent higher in different [brain](#) regions among those with long-lasting untreated depression, compared to those with shorter periods of untreated depression. The group with long-term depression also had higher TSPO levels than those with no depression.

Dr. Meyer also notes that in treatment studies, patients with serious, longstanding [depression](#) tend to be excluded, so there is a lack of evidence of how to treat this stage of [illness](#), which needs to be addressed.

More information: Elaine Setiawan et al, Association of translocator protein total distribution volume with duration of untreated major depressive disorder: a cross-sectional study, *The Lancet*

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