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# Is Depression an Inflammatory Disease?

Research is now frequently suggesting that people who have been diagnosed with clinical depression have a 30% increase in inflammation, a physical marker of many of the chronic conditions that are prevalent throughout the Western World today.

In this week article we look at the emerging research suggesting that the immune system and, in particular, inflammation in the brain is an important contributor to the pathophysiology of depression.

## Depression

The Mental Health Website give the following definition of Depression:

*is a common mental disorder that causes people to experience depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration.*

*Depression is different from feeling down or sad. Unhappiness is something which everyone feels at one time or another, usually due to a particular cause. A person experiencing depression will experience intense emotions of anxiety, hopelessness, negativity and helplessness, and the feelings stay with them instead of going away.”*

## Inflammation

Whenever the immune system is attacked by infections (viruses or bacteria), toxins, or even physical injury (such as a knee injury), it

creates an inflammatory response sending out messengers known as cytokines, which are either pro-inflammatory or anti-inflammatory.

## **Cytokines**

Cytokines are chemical messengers (ie similar to hormones) made by immune cells (and certain other cells) and are released in every single inflammatory process. When they are released into the blood, cytokines can affect the function of every tissue and organ in the body, including the brain.

Research indicates that during an infection, *brain cytokine activation coordinates a large number of behavioural changes including weakness, listlessness, malaise, low appetite, fatigue and transient mood changes collectively referred to as 'sickness behaviour'.*"

This so-called sickness behaviour has a useful purpose and usually resolves within a few days once the innate immune system is no longer activated. However, systemic immune activation and / or brain immune activation leads to significant and prolonged induction of brain cytokines. So while acute or short-term inflammation is a protective feature of the immune system, chronic or long-term inflammation, can cause simultaneous destruction and healing of the tissues, ultimately wreaking havoc on your body long-term.

## **Chronic Inflammation, Cytokines and Depression**

Microglia cells, the brain immune cells, make up 50% of the brain overall mass and are your central nervous system first and main line of defence.

They protect the brain and the spinal cord from pathogens and clear away debris such as beta amyloid plaques; a prominent feature in the pathology of Alzheimer's disease.

Once one of these cells is activated, it creates inflammation and can have a domino effect, causing other microglia cells to become active.

Extensive animal and human studies have clearly demonstrated that cytokines cause the symptoms and signs of disease and research suggests that there is also a clear biological link between the release of cytokines and depressive symptoms:

*in addition to producing all the symptoms and signs of physical illness, cytokines can provoke most, if not all, the symptoms of mental diseases, especially depression and schizophrenia.*

*Second, in addition to producing the mental symptoms of depression and schizophrenia, cytokines produce the physical signs commonly associated with depression or schizophrenia, such as, inflammation, hormone abnormalities, headache, and biochemical abnormalities.*

*Third, cytokines can pass from the blood to the brain. Also, they can be made by immune cells residing in the brain and there are receptors for cytokines throughout the brain.*

*Fourth, cytokines have powerful effects on neurotransmitter activities, including those linked with depression and schizophrenia, such as norepinephrine, serotonin and dopamine.”*

A recent article on ScienceDaily cited research highlighting the link between Cytokines and depression, stating that *patients suffering from clinical depression, concentrations of two inflammatory markers, CRP and IL-6, were elevated by up to 50 percent.”*

### **Mechanisms by which cytokines are thought to cause depression**

Cytokines are able to induce the synthesis of different enzymes in activated immune cells two in particular which are abbreviated to IDO and GTP-CH1.

The IDO enzyme results in tryptophan (the precursor to the brain

neurotransmitter serotonin) being broken down to kynurenine instead of being converted to serotonin, resulting in lower levels of serotonin (the happy brain chemical).

At the same time chronic inflammation also activates another enzyme called GTP-CH1 leading to the production of a product called neopterin at the expense of tetrahydrobiopterin (BH4).

BH4 plays a fundamental role in neurotransmitter synthesis including serotonin but particularly another neurotransmitter dopamine. Low levels of dopamine are also relevant in depression. The depression caused by poor dopamine activity is different to that caused by low serotonin.

People with low dopamine are reported as having a hard time getting motivated, they feel worthless and hopeless about their lives but if they can get motivated they enjoy themselves (whereas low serotonin is associated with a loss of ability to enjoy activities). Of course people can suffer from both low dopamine and low serotonin.

Long-term or chronic stress has actually been shown to change the gene activity of immune cells before they enter the bloodstream, priming them to fight infection when there is no infection. As a result, inflammation occurs unnecessarily but still wreaks havoc on tissues and body processes.

Chronic inflammation is often associated with cancer and other disorders such as heart disease and high cholesterol. Brain inflammation, meanwhile, has been linked to several disorders, including Alzheimer disease, Parkinson's disease, and multiple sclerosis.

The biggest problem in the Western World of today is that by virtue of several factors, including poor diet and lifestyle, most of us have higher readings of inflammation in our bodies than is considered to be healthy. This is something that clearly needs to be addressed.

Now research is suggesting that on top of inflammation being linked to

chronic conditions such as cancer and diabetes, it could also play a major role in the onset of depression. Indeed, many now consider depression to be a symptom of chronic inflammation.

## **We'd love your comments on this article**

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## **Triggers of inflammation**

It not only physical injury or infections that can trigger an immune response and brain inflammation, many other factors can as well, for example:

- High carbohydrate diet
- Lack of exercise
- Stress and emotional trauma
- Head trauma
- Gluten
- Exposure to environmental toxins/chemicals
- Obesity, diabetes, asthma
- Diet

## **Anti-inflammatory diet**

There are numerous problems with the modern diet that the majority of people living in the Western world adopt; It is high in foods that provoke inflammation, such as refined flour, excess sugar, inflammatory fats (eg rancid, trans and certain omega-6 fats). It is also very low in foods that reduce inflammation, such as vegetables , long-chain omega-3 fats and fermented foods. Numerous studies have associated the Western diet with major depressive disorder.

Inflammation is however something that can be controlled by making certain changes to your diet and lifestyle. Indeed, research from 2014 has found that providing patients with anti-inflammatory treatment can reduce depressive symptoms.

Adopting an anti-inflammatory diet and lifestyle means eating a nutrient-dense, whole foods diet, getting enough sleep, managing stress and engaging in appropriate (not too little or too much) physical activity.

We have written several blogs on the topic of the anti-inflammatory Paleo diet. You can find links to these at the bottom of this article.

## **Conclusion**

Clearly inflammation is a significant factor in depression. So identifying possible causes, such as chronic infections, food intolerances, heavy metals, toxins and gluten, and removing them should be a key focus along with anti-inflammatory diet and lifestyle measures.

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