



Immune Dysfunction and Mental Health

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Optimal mental health does not only depend on a healthy brain and nervous system. Dysfunction of various other body systems may disrupt neurotransmission and other aspects of biochemical and structural mechanisms of the nervous system. One interconnecting link receiving attention recently is that of the immune system. The neuro-immune connection refers to the bidirectional interplay between the immune and nervous systems. Research has indicated that ongoing persistent activation of the hypothalamic pituitary adrenal axis and the sympathetic adrenal medullary axis seen in the chronic stress response and in depression, impairs the immune response and may even contribute to the development and progression of some types of cancer.¹ There are also indications that, in the other direction, immune dysfunction may be an underlying pathophysiological mechanism contributing to mood disorders including schizophrenia and major depression.

The inflammatory response and mental health

Cytokines, which regulate immune function, may influence the central nervous system and play a key role in mediating depression-like neuro-behavioural changes.² It has been established that physiological concentrations of pro-inflammatory cytokines that occur after infection, act in the brain to induce common symptoms of sickness, such as loss of appetite, sleepiness, withdrawal from normal social activities, fever, aching joints and fatigue. This syndrome has been defined as sickness behaviour. The fact that cytokines act in the brain to induce physiological adaptations, leads to the hypothesis that inappropriate, prolonged activation of such cytokines through immune dysfunction may be involved in a number of pathological disturbances in the brain.³

Specifically, pro-inflammatory cytokines have been associated with alterations in neurotransmitter balance, and hence a number of psychological disorders. Interferon alpha has been associated with confusion, apathy, anxiety and depression. Long term, increased levels of interferon alpha may lead to down-regulation of dopamine and depletion of serotonin.⁴ Interferon gamma may specifically promote the degradation of tryptophan, leading to reduced synthesis of serotonin and hence may play a role in depression.^{5, 6}

Studies on specific psychological disorders have shown alterations in pro-inflammatory cytokine levels. A recent small scale study has shown that patients with bipolar depression have significantly higher production of the pro-inflammatory cytokines IL-8 and TNF-alpha compared to healthy subjects. Manic phases were also associated with increased production of these cytokines.⁷ Another study showed depressed patients to have significant nocturnal elevations of circulating IL-6 compared to controls.⁸ An overactivation of the Th1 and pro-inflammatory immune response may be seen in major depression.⁹ Significantly higher levels of IL-12 echo this finding, as IL-12 activates T-helper 1 cells and inhibits T-helper 2 cells. Depressed patients, shown to have increased IL-12, have also shown a significant decrease of these cytokines during recovery from depression.¹⁰ Similarly, a different immune state of overactive type 2 response can be seen in schizophrenia.

Table 1 – Nutrients which may help to down-regulate some cytokines associated with psychological disorders

Cytokine	Action	Nutrients to down-regulate
Interferon-gamma	Produced by T h1 cells Pro-inflammatory	Fish oil ^{11, 12}
TNF-alpha	Stimulates proliferation of B lymphocytes	Fish oil ^{13, 14} Zinc ¹⁵ Vitamin A, Vitamin E ¹⁶
IL-6	Stimulates production of CRP	Fish oil ¹⁷ Vitamin E ¹⁸
IL-12	Activates Th1 cells Facilitates production of IFN-gamma	Fish oil ^{11, 12}

Information indicates altered immune states to have a significant role in psychological conditions. It may therefore be pertinent to examine underlying immune disorders as well as the possibility of the involvement of cytokines in the pathophysiology of psychological disorders. Anti-inflammatory and immune modulating therapies may therefore also be beneficial for such conditions. While antidepressants and antipsychotics may directly influence particular neurotransmitters and their activity, anti-inflammatory and immune modulating therapies may act more basically on the pathophysiological mechanism.⁹

An example is seen in the adjunctive use of COX-2 inhibitors (anti-inflammatory drugs) with antipsychotic medications in schizophrenic patients. Small scale studies indicate anti-inflammatory therapy here may offer potential benefit.¹⁹

Nutritional anti-inflammatory and immune modulating therapies may also prove to be beneficial in such psychological conditions. Biochemical and nutritional imbalances may in fact be one factor contributing to altered cytokine levels.

Dr Bill Walsh of the Pfeiffer Treatment Centre and Health Research Institute has written on many other biochemical mechanisms involved in behavioural disorders. To read about such mechanisms and therapies relating to violent behaviour click on the link below.

Reduced violent behavior following biochemical therapy

<http://www.bioconcepts.com.au/download.php?id=148>

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