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BIPOLAR DISORDERS Factsheet

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What is inflammation and the immune system?

Inflammation is caused by the immune system's response to pathogens or tissue damage. The immune system is the body's first line of defence and predominantly uses proteins called cytokines that are secreted by immune cells and act to allow cell-to-cell communication. Cytokines include interleukins (IL), interferons (IFN), tumor necrosis factors (TNF), transforming growth factors (TGF), adipokines, and chemokines. C-reactive protein (CRP) is released by the body during inflammation, with increased CRP suggestive of infection and chronic inflammatory conditions such as cardiovascular disease, diabetes, and metabolic dysfunction.

What is the evidence for inflammation and immune system anomalies in bipolar disorder?

Moderate to high quality evidence found medium to large increases in CRP levels in people with bipolar disorder during a manic phase, and medium-sized increases during a depressive phase, when compared to controls. These effects were increased slightly in studies that matched controls for age and body mass index (in depression only), in studies of drug-free patients (in depression only) and in studies using serum rather than plasma measures (in mania only). These effects were not related to symptom severity but were decreased slightly after resolution of the index mood episode.

Moderate quality evidence found IL-8, monocyte-chemoattractant protein-1 (MCP-1), eotaxin-1, and interferon-γ-induced protein 10 (IP-10) were elevated in people with bipolar disorder compared to controls. The elevated levels of IL-8 and MCP-1 appeared only during the depressive phase, while the elevated levels of IP-10 were present only during euthymia. The analysis of eotaxin-1 levels was mainly based on studies of euthymic patients. Small to medium-sized increases were also found in IL-4, IL-6, IL-10. sIL-2R, sIL-6R, TNF-a and sTNFR1 in serum or plasma of people with bipolar disorder. No differences were found in IL-2, IFN-γ, C-C motif ligand 2, or IL-1β in serum or plasma. However, small increases were found in IL-1β in cerebrospinal fluid of patients. In separate assessment of acutely ill patients, there were medium to large increases in blood IL-1RA, sIL-2R, IL-6, and TNF-α, with no increases in sIL-6R or IL-10. In chronic patients during euthymia, there were small to medium-sized increases in sIL-2R, sIL-6R, IL-4, sTNF-R1, IL-1β, IL-6, and IL-10, with no increases in IL-2, TNF-α, or IFN-γ.

Moderate to high quality evidence found medium-sized increases in neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) levels in people with bipolar disorder, particularly during a manic phase. Increasing age and male gender were associated with larger effect sizes for NLR but not for PLR. There were small to medium-sized reductions in tryptophan, kynurenine, xanthurenic acid, and kynurenic acid. However, increased kynurenic acid was found in cerebrospinal fluid. The kynurenic acid to kynurenine ratio and the kynurenic acid to quinolinic acid ratio were reduced in bipolar disorder. People in a manic episode had the greatest reductions in tryptophan, while kynurenic acid levels were more reduced in a depressive phase. There were similar reductions in kynurenine in depression and mania phases. Finally, adiponectin levels were significantly higher in bipolar patients during euthymia but may be lower than controls during depression.

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NeuRA (Neuroscience Research Australia) is one of the largest independent medical and clinical research institutes in Australia and an international leader in neurological research.

Diseases of the brain and nervous system pose the greatest health, economic and social burden of any disease group because they are chronic, debilitating and have no known cures.

Medical research is the cornerstone of efforts to advance the health and wellbeing of families and the community. Our dedicated scientists are focussed on transforming their research into significant and practical benefits for all patients.

While we hope you find this information useful, it is always important to discuss any questions about bipolar disorder or its treatment with your doctor or other health care provider.

For more information see the technical table

HOW YOUR SUPPORT HELPS

We are able to make significant advances due to the generosity of countless people. Your donation allows us to continue to work towards transforming lives. For information on how you can support our research, phone **1300 888 019** or make a secure donation at **neura.edu.au**.

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