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SCHIZOPHRENIA Factsheet

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What are inflammatory and immunological changes?

Inflammation is caused by the immune system's response to pathogens or tissue damage. Key cells in the innate (immediate) immune response are known as cytokines, including interleukins (IL), interferons (IFN), tumor necrosis factors (TNF), transforming growth factors (TGF), and chemokines. C-reactive proteins, autoantibodies, and lymphocytes are also involved in the immune system response.

What is the evidence for inflammatory and immunological changes?

For cytokines levels in serum or plasma, moderate to high quality evidence found a large increase in IL-1β, a large decrease in IFN-γ, medium-sized increases in MCP-1, eotaxin-1, and IL-8, and small increases in MIP-1β, IL-6, TNF-α, and sIL-2r. There were no differences in IL-2, IL-4, IL-10, MIP-1α, fractalkine or IP-10. In cerebrospinal fluid, there were medium to large increases in IL-6 and IL-8, a large decrease in sIL-2r (from moderate to low quality evidence), and no differences in IL-1β, IL-1α, IL-2, IL-6R, MIP-1α, MCP-2, sTNFR2, TGF-β1 or TGF-β2. In patients with acute symptoms, moderate to high quality evidence found medium-sized increases in IL-6, IL-8, TGF-β, IL-1ra, and sIL-2r, and small increases in IFN-γ, IL-1β, and TNF-α. There were small to medium-sized decreases in IL-10 and IL-4, and no differences in IL-2. After treatment for acute symptoms, there were reductions in IL-1β, IL-6, sIL-6r, TNF-α and IFN-γ, and a small increase in sIL-2r. There were no differences post-treatment in IL-12, IL-2, IL-17, TGF-β, IL-10, or IL-4. In first-episode psychosis patients, moderate to high quality evidence found large increases in IL-1β, IL-6, and sIL-2r, medium-sized increases in TGF-β and MCP-1, and small increases in TNF-α, IL-1ra, IL-12, IFN-γ, and IL-10. There was a medium-sized decrease in IL-4, and no differences in IL-2, IL-8, IL-17 or IL-18. After treatment for first-episode psychosis, there were reductions in IL-1β, IL-6 and IL-4. In antipsychotic-naïve patients, moderate to high quality evidence found medium-sized increases in IFN-γ, IL-17, IL-6, sIL-2r, TGF-β, and TNF-α. There were no differences in IL-10, IL-1β, IL-2, IL-4, or IL-8. After treatment, moderate to low quality evidence found medium-sized reductions in IL-2 and IL-6; there may also be reductions in IL-1β, IFN-γ, and IL-17. In people at high-risk of psychosis (clinical or genetic) there was a small increase in IL-6 and a medium-sized decrease in IL-1β.

For autoantibodies in serum or plasma, moderate to high quality evidence found a medium-sized increase in cardiolipin IgM and a small increase in cardiolipin IgG. There were increases in N-methyl-D-aspartate, nerve growth factor, antinuclear antibodies, DNA, dopamine receptor, gliadin IgA, heat shock protein 60, lupus anticoagulant, rheumatoid factor, smith, thyroglobulin, thyroid microsomal, and tissue transglutaminase. Moderate to low quality evidence also finds increases in cold agglutinin, histone/anti-histone IgG, nucleoprotein, phospholipid, and serotonin. Moderate quality evidence found an increase in anti-gliadin IgG and IgA (medium-sized effects), anti-TTG2 IgA (large effects) and other wheat protein antibodies (small effects for anti-gluten, anti-wheat and non-specified anti-gliadin). In cerebrospinal fluid, moderate to low quality evidence found medium-sized increases in IgG ratio and a medium-sized decrease in IgG/albumin ratio, with no differences in CSF IgG or IgG index. In first-episode psychosis patients, moderate quality evidence found increases in cardiolipin IgG and N-methyl-D-aspartate.

For leukocytes levels in schizophrenia patients' serum or plasma, moderate to high quality evidence finds medium-sized increases in total white blood cell count, monocytes, and neutrophils in people with schizophrenia or first-episode psychosis compared to controls, and medium-sized increases in neutrophil-to-lymphocyte and monocyte-lymphocyte ratios. There was a medium-sized decrease in T-lymphocytes (CD3 percentage) in stable medicated patients. In antipsychotic-naïve patients, there was a medium-sized decrease in T-lymphocytes (CD3 percentage), a medium to large increase in T-lymphocytes (CD3), a large increase in T-helper lymphocytes (CD4), and a medium-sized increase in T-helper/suppressor lymphocyte ratio (CD4/CD8). In patients with acute symptoms, there was a medium-sized decreases in T-lymphocytes (CD3 percentage), increases in total white blood cell count, T-helper lymphocytes (CD4 percentage), natural killer cells (CD56 absolute), and an increase in T-helper / suppressor lymphocyte ratio (CD4/CD8) Moderate to low quality evidence also found a large increase in natural killer cells (CD56 percentage) and no differences in total lymphocyte count. After treatment, moderate to high quality evidence finds a medium-sized increase in T-suppressor/cytotoxic lymphocytes (CD8 percentage), natural killer cells (CD56 absolute), and T-lymphocytes (CD3 percentage), a small to medium effect of increased T-suppressor/cytotoxic lymphocytes (CD8 absolute), and a small effect of decreased T-helper/suppressor lymphocyte ratio (CD4/CD8).

For C-reactive protein levels in serum or plasma, moderate to high quality evidence finds a medium-sized increase in patients. This effect was largest in those who were drug-naïve or drug-free, in those on first than second generation antipsychotics, and in those with more severe positive symptoms. For tryptophan catabolites there was a medium-sized increase in kynurenic acid, particularly in cerebrospinal fluid, brain tissue, in older patients, in medicated patients, and in male patients. There was also a medium to large increase in kynurenine in the CSF of patients compared to controls.

For translocator protein levels in serum or plasma, moderate quality evidence found a small to medium-sized increase in people with schizophrenia when measured using binding potential, but not when measured using volume of distribution. There was also a large increase in homocysteine in first-episode patients.

For more information see the technical table

NeuRA
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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 schizophrenia or its treatment with your doctor or other health care provider.

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/donate/schizophrenia**.

NeuRA (Neuroscience Research Australia) Foundation
T 1300 888 019 **F** +61 2 9399 1082
ABN 57 008 429 961

Margarete Ainsworth Building
Barker Street, Randwick NSW 2031
PO Box 1165 Randwick Sydney NSW 2031 Australia

neura.edu.au