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BIPOLAR DISORDERS Factsheet

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What are lipids?

Lipids, as fundamental membrane constituents, make up as much as 50-60% of the human brain's weight. The main lipid compounds present in the brain are essential fatty acids (EFAs), which bind largely to glycerophospholipids (GPLs). Due to the unique chemical structure of GPLs, they have a tendency to form bilayers, and consequently cellular membranes are comprised of a phospholipid bilayer structure. The fluidity of this membrane is determined by the EFA and cholesterol content. Different membranes have different requirements for ion channels, receptor activity and neurotransmitter release and so have different EFA concentration, for example excitable membranes, such as synapses, have a particularly high concentration of EFA.

There are several types of GPL, which each have distinct EFA composition. In the adult human brain these include phosphomonoesters (PME), such as phosphatidylethanolamine (PtdEtn), phosphatidylcholine (PtdCh, also lecithin), as well as phosphatidylserine (PtdSer) and phosphatidylinositol (PI). Phosphodiester (PDE) compounds include glycerophosphatidylcholine (GPCh) and mobile phospholipids (MP). Phosphomonoesters are precursors in phospholipid membrane synthesis, while phosphodiesters are phospholipid membrane breakdown products.

The two primary essential fatty acid series are n-3 (omega-3) and n-6 (omega-6). Linoleic acid (LA, 18:2n-6) and alphalinolenic acid (α-LA, 18:3n-3) are the parent compounds of these two EFA series, and both have 18 carbon atoms. Metabolites of LA and α-LA are referred to as 'derived EFAs', and include arachidonic acid (AA, 20:5n-6), docosahexaenoic acid (DHA, 22:6n-3) or eicosapentaenoic acid (EPA, 20:5n-3) and their products (eicosanoids) such as prostaglandins, thromboxanes, prostacyclins and leukotrienes. Derived EFAs are also known as 'bioactive lipids', and regulate the structure and function of membrane receptors, ion channels and enzymes, as well as influencing synaptic plasticity, processes such as neuronal migration, and signal transduction (via second messengers) which may be disrupted in bipolar disorders.

The metabolism of the LA and α-LA compounds into bioactive lipids (derived EFAs) is catalysed by the phospholipases A2 (PLA2), which are an enzyme superfamily defined by an ability to catalyse the hydrolysis of the middle ester bond of a GPL substrate, usually releasing a free fatty acid and a lysophospholipid. Early systems categorised PLA2s into calcium (Ca2+) -dependent and -independent subgroups, however more recent gene profiling has identified eleven subgroups of PLA2s. PLA2 activity is a key determinant of cell membrane composition, as well as modulating regulatory processes and second messenger pathways.

What is the evidence for changes in lipid levels in people with bipolar disorder?

Moderate quality evidence suggests a large effect of reduced erythrocyte polyunsaturated fatty acid docosahexaenoic acid in people with bipolar disorder, with lower quality evidence finding no differences in polyunsaturated fatty acids eicosapentaenoic acid, linolenic acid or arachidonic acid. High quality evidence suggests no differences in cholesterol or triglycerides comparing people with bipolar disorder with or without a history of attempted suicide. We found no reviews assessing levels of other lipids.

For more information see the technical table

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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.

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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