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Chemical signature of manic depression discovered by scientists

February 5 2008

People with manic depression have a distinct chemical signature in their brains, according to a new study. The research, published today in the journal Molecular Psychiatry, may also indicate how the mood stabilisers used to treat the disorder counteract the changes in the brain that it appears to cause.

Manic depression, which is also known as bipolar disorder, is a debilitating psychiatric condition characterised by alternating mania and depression, affecting about one in every hundred people worldwide. Although it is known that the condition can be treated relatively effectively using the mood-stabilising drugs lithium and valproic acid, the reasons why these treatments work are poorly understood.

The authors of the new study, from Imperial College London, the University of Cambridge, and the National Institutes of Mental Health in the US, hope that their research will enable a better understanding of the condition and of how it can be treated.

The researchers compared postmortem brain tissue samples of people with manic depression with those of age and gender matched controls. The samples were taken from the dorsolateral prefrontal cortex, which controls the processes involved in higher cognitive functioning. The researchers analysed these samples using Nuclear Magnetic Resonance spectroscopy and found that people with manic depression had different concentrations of chemicals in this area of the brain than those without.

The researchers also used rat models to see the effects of lithium and valproic acid on the metabolite makeup of non-bipolar brain tissue. They found that these drugs caused the opposite chemical changes to those seen in the bipolar brain tissue samples. Chemicals that were increased in the bipolar brain tissue were decreased in rats given the mood stabilising drugs, and vice versa.

The researchers' findings lead them to believe that an upset in the balance of different neurotransmitters known as excitatory and inhibitory neurotransmitters, which are involved in sending signals in the brain, may be central to the disorder. The study also suggests that lithium and valproic acid work by restoring the balance of these neurotransmitters in the brain.

Levels of glutamate, an amino acid which acts as a neurotransmitter in the central nervous system, were increased in post mortem bipolar brain but glutamate / glutamine ratios were decreased following valproate treatment. Levels of another neurotransmitter, gamma-aminobutyric acid, were increased after lithium treatment and decreased in the bipolar brain. Both creatine and myo-inositol were increased in the post-mortem brain but depleted with the medications.

Dr Tsz Tsang, one of the authors of the study from the Department of Biomolecular Medicine at Imperial College London, said: "By identifying a distinct biochemical profile in patients with bipolar disorder, our new research provides a valuable insight into the origins and causes of the disease. Moreover, the changes we see in people's metabolic signatures may give a target for drug therapy, allowing us to see how effective a drug is at correcting these changes.

"In this instance, we have already shown that the biochemical changes which valproic acid and lithium bring about in mammalian models represent almost a mirror image of the perturbations in bipolar disorder.

This may provide a useful insight to the actions of these treatments and a basis for which to improve therapy in the future," added Dr Tsang.

Source: Imperial College London