

New understanding of mental health

Mental health issues could show up in the physiology of the brain, according to a study published recently in *Science*. Examining the brain cortex of a large number of deceased patients, the researchers found, for the first time, molecular signatures of mental illnesses. They studied five major problems — autism, schizophrenia, bipolar disorder, depression and alcoholism — and discovered that these conditions go in parallel with specific gene activity and manifest in the genes' expression in the cerebral cortex, or the outermost layer of the brain. The study throws up overlaps in some of conditions and surprisingly counter-intuitive results in other cases.

In a scenario where diagnosis of psychiatric disorders is largely based on symptoms and signs, and treatment of these is primarily by targeting symptoms, this study has come as a milestone. It took up five common, major, disabling and chronic psychiatric conditions and looked for genetic expressions in the brain cortex. "This is a step toward an objective method of diagnosis as well as developing treatment methods that are disease modifying," said Dr. M. Suresh Kumar, consultant psychiatrist, Psymed Hospital, Chennai.

An international team of researchers, led by Dr. Daniel H. Geschwind, neurologist and neuroscientist at University of California, Los Angeles (UCLA), U.S., analysed 700 cerebral cortex samples from the brains of deceased individuals with one of the five disorders mentioned earlier.

The team also studied 293 controls and 197 samples from patients who had inflammatory bowel disease for comparison with a non-neural disease. "The novel aspect of this study was using the gene expression patterns as a basis for directly comparing these different psychiatric conditions together across a large number of samples. Based on the different causes and behaviours present in each disorder, it was quite surprising that they ended up showing many of the same gene expression changes," Dr. Geschwind said in an email to *The Hindu*.

Analysis revealed an overlap between bipolar disorder and schizophrenia. This was surprising because the former is usually viewed as a mood disorder and hence closer to depression. Also, despite the prevailing tendency to associate alcoholism with depression or bipolar disorder, the study showed no correlation between alcoholism and the four other disorders.

"It is interesting that the study finds a close overlap in genetic and molecular level brain changes between bipolar disorder and schizophrenia," said Dr. Suresh Kumar. Bipolar disorder and schizophrenia are completely distinct for the clinician. While the former is treated with mood stabilisers, the latter is treated with antipsychotic drugs. Perhaps the two may be similar in several ways as the study has shown. "Clinicians change the diagnosis from one to another over the course of time. In addition, currently second generation antipsychotic drugs are used as first-line drugs in both schizophrenia and acute stages of bipolar disorder," he added.

The study showed that while some genes were active in both schizophrenia and autism, they were much more active in the latter. There were also signs that brain cell communication was affected in three diseases, autism, depression and bipolar disorder. "We also identified unique disease signatures, such as an activation of microglial cells [a set of brain immune cells that protect the brain from inflammation] in autism, not seen in the others, and some changes in hormone regulation in major depression," Dr. Geschwind said.

While the study cannot immediately translate into therapeutics, as it was performed on the brains of deceased persons only, it could certainly pave the way for further research that would enable precision medicine approaches.

Based on the findings, Dr. Michael Gandal of UCLA is running a clinical trial using a drug predicted to reduce neuroinflammation in autistic individuals. "We are now planning to look at patterns across many different brain regions to see how widespread the results are. Finally, we also intend to look at these disorders with single cell resolution using new sequencing technology," Dr. Geschwind said.

The National Mental Health Survey of India 2015-2016 estimated that nearly 150 million people in India were in need of mental health interventions and care. Given this pointer, it becomes important to get a better grip on both diagnosis and treatment of mental disorders. This study should change the way psychiatric medicine works.

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