MedicalXpress

Ever-changing moods may be toxic to the brain of bipolar patients

May 31 2016

Bipolar disorder (BD) is a severe and complex mental illness with a strong genetic component that affects 2% of the world population. The disorder is characterized by episodes of mania and depression that may alternate throughout life and usually first occur in the early 20s.

Most recently, physicians have started to group patients as early or late-stage. Early-stage BD patients are classified as those who have had fewer episodes of either mania or depression whereas late-stage patients have had more episodes with more severe effects and are less likely to respond to treatment.

This classification between early- and late-stage BD patients has more to do with episode recurrence and severity than the length of time the patient has had the disease. BD diagnosis may be difficult to establish and may take up to 10 years from the first episode. There is no cure for BD but psychotherapy and prescription medication such as antipsychotics, mood stabilizers and benzodiazepines may alleviate symptoms.

The brain of bipolar patients shows changes such as reduction in volume and neuroprogression. The latter is a pathological version of an otherwise normal mechanism by which the brain re-writes its neuronal connections, a process that is associated to learning, memory and even recovery from brain damage. In bipolar patients, the process is associated with loss of neuron connections and clinical and neurocognitive deterioration.

A previous study has shown that the blood levels of several markers related to inflammation, oxidative stress and neurotrophins (proteins that promote neuron growth and survival) in BD patients are associated to recurrent mood episodes. For instance, the brain-derived neurotrophic factor (BDNF), a protein that promotes neuron growth and survival and helps establishing neuron connections, is lower in BD patients, as is the early-growth response 3 (EGR3), a protein associated to helping the brain cope with environmental changes such as stressful stimuli. Besides these alterations, another study has shown that abnormally low levels of chemokines (which are proteins that send signals to other cell components) have also been observed in the blood of BD patients. If these blood markers can be associated to the severity and frequency of mood episodes in BD patients, is it possible that they are also associated to changes observed in the brain of BD patients?

To answer this intriguing question, a group led by Fabio Klamt at the Laboratory of Cellular Biochemistry at the Federal University of Rio Grande do Sul (UFRGS), and Flávio Kapczinski at the Laboratory of Molecular Psychiatry at Clinics Hospital of Porto Alegre (HCPA), in Brazil, exposed differentiated neurons to blood serum from either healthy normal individuals or bipolar patients. The group then observed that neurons exposed to serum from bipolar patients had a significant loss in the density of neurites, which is used to estimate the number of neuron connections, if compared to neurite density of neurons exposed to serum from healthy individuals. Interestingly, when serum from early-stage and late-stage BD patients was analyzed separately, no difference in neurite density was observed between neurons exposed to serum from early-stage patients and those exposed to healthy controls' serum. However, a significant difference remained in the neurite density between neurons exposed to serum from late-stage patients and from early-stage patients or healthy controls. The group also found that the number of neurons was not that different between samples, except for those exposed to serum from patients at very late stages of the disease.

"Our results indicate that the blood of BD patients is toxic to brain cells and affects the connectivity ability of neurons. Considering our previous knowledge on the association between mood episodes and blood toxicity, we believe that the more episodes a patient has, the more cellular components are produced that impair the brain's ability to deal with environmental changes, inflammation and stress," says Klamt.

This is the first study to show the toxic effects of BD serum on human neuronal cells and to present an in vitro study model for a disease for which no animal model has been yet developed. Future studies should focus on finding drugs that can protect BD brain cells from the toxic effects of their own blood.

More information: The first draft of the study entitled "Reduced Neurite Density in Neuronal Cell Cultures Exposed to Serum of Patients with Bipolar Disorder" is available at the link below at the website of the *International Journal of Neuropsychopharmacology*
ijnp.oxfordjournals.org/conten … ijnp.pyw051.full.pdf

Provided by Publicase Comunicação Científica