Medical Xpress

# Critical brain chemical shown to play role in severe depression

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The next advance in treating major depression may relate to a group of brain chemicals that are involved in virtually all our brain activity, according to a study published today in *Biological Psychiatry*. The study is co-authored by Drs. Andrea J. Levinson and Zafiris J. Daskalakis of the Centre for Addiction and Mental Health (CAMH).

This study shows that compared to healthy individuals, people who have major depressive disorder have altered functions of the neurotransmitter GABA (gamma-aminobutyric acid). In the study, individuals with the most treatment-resistant forms of illness demonstrated the greatest reductions of GABA levels in the brain.

This points to the possibility that medications which correct a GABA imbalance could advance the treatment of major depressive disorder. Approximately 4% of Canadians experience major depressive disorder each year.

Several current medications for mood disorders correct imbalances in neurotransmitters such as serotonin and dopamine. However, many patients do not benefit from these medications. "Our findings build on the idea that some current medications do not help many patients because those drugs don't affect the GABA-related brain chemistry," says study author Dr. Andrea Levinson.

## Applying the brakes

The GABA neurotransmitter and its receptors are involved in many different brain functions. Imbalances in GABA also are relevant to bipolar disorder, schizophrenia, and anxiety disorder.

The GABA neurotransmitter and its receptors are critical to how humans think and act, Dr. Levinson adds. "We apply so many conscious and unconscious perceptions and judgments to our actions at every second, without even realizing that we are doing so," she says. "GABA is part of the brain system that allows us to fine-tune our moods, thoughts, and actions with an incredible level of detail."

"It's a little like driving a car. You need the accelerator, but at every stage you need the brakes to work. Some of our neurotransmitters apply the spark and the gas to the engine, and GABA supplies the brakes," she says. "GABA provides the necessary inhibitory effect that we need in order to block out excessive brain activity that in depression may lead to excessive negative thinking."

In addition, today's study points to the reason why electroconvulsive therapy is still the most efficacious therapy for major depressive disorder, Dr. Levinson adds. "Electroconvulsive therapy may act on GABA brain chemicals in a way that can reset the balance," she says.

## Largest study to date

This study of 85 people is the largest such research effort on GABA and major depressive disorder to date. It compared four groups: 25 individuals with treatment-resistant depression, 16 with major depression who were unmedicated, 19 individuals with major depression who were successfully treated with medication and had normal mood, and a control group of 25 healthy individuals.

In all groups, a thumb twitch response to transcranial magnetic (brain)

stimulation (TMS) was used to measure how GABA acts physiologically in the brain. GABA receptors were found to be dysfunctional in the three groups with major depressive disorder when compared to healthy subjects. In people who were the least responsive (treatment-resistant) to medications, the physiological effect of GABA in the brain was at its lowest.

## Personalized medicine

"We are advancing the goal of a truly personalized medicine," says study co-author Dr. Daskalakis. "It is intriguing to think that we may soon be able to apply simple brain stimulation to identify which treatments are most likely to help the individual person, eliminating the guesswork. That is, through these findings we may be able to one day determine who is and who is not going to respond to traditional pharmacological approaches to depression."

The journal published a separate editorial to highlight the potential for an individualized approach to diagnosing depression, one that would include brain stimulation to identify low levels of the GABA neurotransmitters.

Dr. Daskalakis has international expertise in the electrophysiology of psychiatric disorders, particularly related to GABA.

Provided by Centre for Addiction and Mental Health