Lithium Builds Gray Matter in Bipolar Brains, Study Shows

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Neuroscientists at UCLA have shown that lithium, long the standard treatment for bipolar disorder, increases the amount of gray matter in the brains of patients with the illness.

The research is featured in the July issue of the journal *Biological Psychiatry*.

Carrie Bearden, a clinical neuropsychologist and assistant professor of psychiatry at UCLA, and Paul Thompson, associate professor of neurology at the UCLA Laboratory of NeuroImaging, used a novel method of three-dimensional magnetic resonance imaging (MRI) to map the entire surface of the brain in people diagnosed with bipolar disorder.

When the researchers compared the brains of bipolar patients on lithium with those of people without the disorder and those of bipolar patients not on lithium, they found that the volume of gray matter in the brains of those on lithium was as much as 15 percent higher in areas that are critical for attention and controlling emotions.

The neurobiological underpinnings of bipolar disorder — an illness marked by a roller coaster of emotions between mania and depression — are not well understood. Nor is it understood how lithium works in controlling these severe mood swings, even though it has been the standard treatment for some 50 years. These new findings suggest that lithium may work by increasing the amount of gray matter in particular brain areas, which in turn suggests that existing gray matter in these regions of bipolar brains may be underused or dysfunctional.

This is the first time researchers were able to look at specific regions of the brain that may be affected by lithium treatment in living human subjects, said Bearden.

"We used a novel method for brain imaging analysis that is exquisitely sensitive to subtle differences in brain structure," she said. "This type of imaging has not been used before to study bipolar patients. We also revealed how commonly used medications affect the bipolar brain."

Although other studies have measured increases in the overall volume of the brain, Bearden said, this imaging method allowed the researchers to see exactly which brain regions were affected by lithium.

"Bipolar patients who were taking lithium had a striking increase in gray matter in the cingulate and paralimbic regions of the brain," she said. "These regions regulate attention, motivation and emotion, which are profoundly affected in bipolar illness."

While conventional MRI studies have measured brain volume in total, this new image analysis allows researchers to examine differences in cortical anatomy at a much greater spatial resolution.

In this study, Bearden and colleagues at UCLA used computer analysis to analyze brain scans collected by collaborators at the University of Pittsburgh in order to determine whether bipolar patients showed changes in brain tissue and, if so, whether those changes were influenced by lithium treatment. Specifically, they employed high-resolution MRI and cortical pattern-matching methods to map gray matter differences in 28 adults with bipolar disorder — 70 percent of whom were lithium-treated — and 28 healthy control subjects. Detailed spatial analyses of gray matter distribution were conducted by measuring local volumes of gray matter at thousands of locations in the brain.

While the brains of lithium-treated bipolar patients did not differ from those of the control subjects in total white-matter volume, their overall gray-matter volume was significantly higher, sometimes by as

much as 15 percent.

Unfortunately, said Bearden, there is no evidence that the increase in gray matter persists if lithium treatment is discontinued. "But it does suggest that lithium can have dramatic effects on gray matter in the brain," she said. "This may be an important clue as to how and why it works."

Source: UCLA