Brain structural deficits may contribute to increased functional connections between brain regions implicated in depress

July 8 2013

Major depressive disorder is associated with a dysregulation of brain regions including the prefrontal cortex and limbic system. The relationship between structural and functional abnormalities in these brain regions in depressed patients is far from clear. However, both types of changes are assumed to underlie the symptoms of this disorder..

This lack of understanding prompted Dr. Bart de Kwaasteniet at the Academic Medical Center in Amsterdam and his colleagues to use a multimodal neuroimaging approach to further investigate this relationship.

The researchers, led by Professor Damiaan Denys, recruited 18 patients with major depressive disorder and 24 healthy individuals, all of whom underwent multiple neuroimaging scans. They specifically focused on the structural and functional connectivity between the subgenual anterior cingulate cortex (ACC) and the medial temporal lobe, two regions that are connected by a white matter tract called the uncinate fasciculus. These regions are known to be involved in the regulation of emotion and memory.

de Kwaasteniet explained their findings: "We identified decreased structural integrity of the uncinate fasciculus connecting the medial temporal lobe and the subgenual ACC. Furthermore, we identified an increased functional connection between these regions in major

depression relative to controls. Importantly, we identified a negative correlation between the integrity of this white matter tract and the functional connection between the subgenual ACC and bilateral hippocampus in major depression."

These results suggest that structural disturbances in the uncinate fasciculus contribute to abnormally high functional interactions among brain circuits associated with the symptoms of depression. "This leads to the hypothesis that abnormalities in brain structure lead to differences in connectivity between brain areas in depressive disorder," added de Kwaasteniet.

However, they also hypothesized that the reverse may be true as well. In other words, that the increased functional connectivity among these brain regions leads to structural changes in the brain's white matter fibers by means of an abnormally increased signal transduction. This hypothesis is supported by recent studies in schizophrenia which suggest that circuit hyperactivity may be a predictor of subsequent cortical atrophy.

"This interesting study suggests that abnormalities in the structural connections between brain regions, the white matter, are associated with abnormal activity within a brain circuit implicated in the symptoms of depression. This observation raises an important question about the implications of treating the circuit functional abnormalities without fixing the underlying brain structure," commented Dr. John Krystal, Editor of Biological Psychiatry. "Perhaps the structural abnormalities contribute to the risk for the relapse of depression among individuals whose brain circuit activity has responded to antidepressant medications."

More research will be necessary to test the theories generated from the findings of this study.

More information: The article is "Relation Between Structural and Functional Connectivity in Major Depressive Disorder" by Bart de Kwaasteniet, Eric Ruhe, Matthan Caan, Maaike Rive, Silvia Olabarriaga, Martine Groefsema, Lieke Heesink, Guido van Wingen, and Damiaan Denys (doi: 10.1016/j.biopsych.2012.12.024). The article appears in *Biological Psychiatry*, Volume 74, Issue 1 (July 1, 2013)