Scientists identify brain abnormalities underlying key element of borderline personality disorder

December 21 2007

Using new approaches, an interdisciplinary team of scientists at NewYork-Presbyterian Hospital/Weill Cornell Medical Center in New York City has gained a view of activity in key brain areas associated with a core difficulty in patients with borderline personality disorder -- shedding new light on this serious psychiatric condition.

"It's early days yet, but the work is pinpointing functional differences in the neurobiology of healthy people versus individuals with the disorder as they attempt to control their behavior in a negative emotional context. Such initial insights can help provide a foundation for better, more targeted therapies down the line," explains lead researcher Dr. David A. Silbersweig, the Stephen P. Tobin and Dr. Arnold M. Cooper Professor of Psychiatry and Professor of Neurology at Weill Cornell Medical College, and attending psychiatrist and neurologist at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

The findings are featured in this month's issue of the *American Journal of Psychiatry*.

Borderline personality disorder is a devastating mental illness that affects between 1 to 2 percent of Americans, causing untold disruption of patients' lives and relationships. Nevertheless, its underlying biology is not very well understood. Hallmarks of the illness include impulsivity, emotional instability, interpersonal difficulties, and a preponderance of

negative emotions such as anger -- all of which may encourage or be associated with substance abuse, self-destructive behaviors and even suicide.

"In this study, our collaborative team looked specifically at the nexus between negative emotions and impulsivity -- the tendency of people with borderline personality disorder to 'act out' destructively in the presence of anger," Dr. Silbersweig explains. "Other studies have looked at either negative emotional states or this type of behavioral disinhibition. The two are closely connected, and we wanted to find out why. We therefore focused our experiments on the interaction between negative emotional states and behavioral inhibition."

Advanced brain-scanning technologies developed by the research team made it possible to detect the brain areas of interest with greater sensitivity.

"Previous work by our group and others had suggested that an area at the base of the brain within the ventromedial prefrontal cortex was key to people's ability to restrain behaviors in the presence of emotion," Dr. Silbersweig explains.

Unfortunately, tracking activity in this brain region has been extremely difficult using functional MRI (fMRI). "Due to its particular location, you get a lot of signal loss," the researcher explains.

However, the Weill Cornell team used a special fMRI activation probe that they developed to eliminate much of that interference. This paved the way for the study, which included 16 patients with borderline personality disorder and 14 healthy controls.

The team also used a tailored fMRI neuropsychological approach to observe activity in the subjects' ventromedial prefrontal cortex as they

performed what behavioral neuroscience researchers call "go/no go" tests.

These rapid-fire tests require participants to press or withhold from pressing a button whenever they receive particular visual cues. In a twist from the usual approach, the performance of the task with negative words (related to borderline psychology) was contrasted with the performance of the task when using neutral words, to reveal how negative emotions affect the participants' ability to perform the task.

As expected, negative emotional words caused participants with borderline personality disorder to have more difficulty with the task at hand and act more impulsively -- ignoring visual cues to stop as they repeatedly pressed the button.

But what was really interesting was what showed up on fMRI.

"We confirmed that discrete parts of the ventromedial prefrontal cortex -- the subgenual anterior cingulate cortex and the medial orbitofrontal cortex areas -- were relatively less active in patients versus controls," Dr. Silbersweig says. "These areas are thought to be key to facilitating behavioral inhibition under emotional circumstances, so if they are underperforming that could contribute to the disinhibition one so often sees with borderline personality disorder."

At the same time, the research team observed heightened levels of activation during the tests in other areas of the patients' brains, including the amygdala, a locus for emotions such as anger and fear, and some of the brain's other limbic regions, which are linked to emotional processing.

"In the frontal region and the amygdala, the degree to which the brain aberrations occurred was closely correlated to the degree with which

patients with borderline personality disorder had clinical difficulty controlling their behavior, or had difficulty with negative emotion, respectively," Dr. Silbersweig notes.

The study sheds light not only on borderline personality disorder, but on the mechanisms healthy individuals rely on to curb their tempers in the face of strong emotion.

Still, patients struggling with borderline personality disorder stand to benefit most from this groundbreaking research. An accompanying journal commentary labels the study "rigorous" and "systematic," and one of the first to validate with neuroimaging what scientists had only been able to guess at before.

"The more that this type of work gets done, the more people will understand that mental illness is not the patient's fault -- that there are circuits in the brain that control these functions in humans and that these disorders are tied to fundamental disruptions in these circuits," Dr. Silbersweig says. "Our hope is that such insights will help erode the stigma surrounding psychiatric illness."

The research could even help lead to better treatment.

As pointed out in the commentary, the research may help explain how specific biological or psychological therapies could ease symptoms of borderline personality disorder for some patients, by addressing the underlying biology of impulsivity in the context of overwhelming negative emotion. The more scientists understand the neurological aberrations that give rise to the disorder, the greater the hope for new, highly targeted drugs or other therapeutic interventions.

"Going forward, we plan to test hypotheses about changes in these brain regions associated with various types of treatment," Dr. Silberswieg says.

"Such work by ourselves and others could help confirm these initial findings and point the way to better therapies."

Source: New York- Presbyterian Hospital