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Brain scans show distinctive patterns in people with generalized anxiety disorder

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Scrambled connections between the part of the brain that processes fear and emotion and other brain regions could be the hallmark of a common anxiety disorder, according to a new study from the Stanford University School of Medicine. The findings could help researchers identify biological differences between types of anxiety disorders as well as such disorders as depression.

The study, which will be published Dec. 7 in the *Archives of General Psychiatry,* examined the brains of people with generalized anxiety disorder, or GAD, a psychiatric condition in which patients spend their days in a haze of worry over everyday concerns. Researchers have known that the amygdala, a pair of almond-sized bundles of nerve fibers in the middle of the brain that help process emotion, memory and fear, are involved in anxiety disorders like GAD. But the Stanford study is the first to peer close enough to detect neural pathways going to and from subsections of this tiny brain region.

Such small-scale observations are important for understanding the brains of people with psychiatric disorders, said Duke University neuroscientist Kevin LaBar, PhD, who was not involved in the research. "If we want to distinguish GAD from other anxiety disorders, we might have to look at these subregions instead of the general signal from this area," he said. "It's methodologically really impressive."

To get close enough to discern one region of the amygdala from another, Stanford psychiatry resident Amit Etkin, MD, PhD, and his colleagues

focused on "regions of interest" defined by detailed anatomical studies of human brains. They recruited 16 people with GAD and 17 psychologically healthy participants and scanned their brains using functional magnetic resonance imaging, which measures blood-flow fluctuations caused by changes in activity in different regions of the brain. Each person spent eight minutes in the fMRI scanner, letting their minds wander.

The researchers analyzed the resulting data to determine which areas were connected — that is, which regions were likely to activate in tandem. They first looked at one subregion, the basolateral amygdala, which sits at the base of the amygdala. In healthy participants, they found that the subregion was linked to the occipital lobe at the rear of the brain, the temporal lobes beneath the ears and the prefrontal cortex just behind the forehead. These regions are associated with visual and auditory processing, as well as with memory and high-level emotional and cognitive functions.

The other subregion, known as the centromedial amygdala and found at the top of the amygdala, was associated with subcortical, or deeper, areas of the brain. These connections included the thalamus, which controls information flow throughout the brain and helps regulate alertness from its perch in the midbrain; the brain stem, which regulates heart rate, breathing and release of neurotransmitters like serotonin and dopamine; and the densely wrinkled cerebellum, which sits behind the brain stem and controls motor coordination. The associations corroborated what anatomical studies in animals have found, said Etkin, the lead author of the study. The team also analyzed resting fMRI data from 31 more healthy people and found similar results.

But in people with GAD, the scans revealed another pattern. The two regions still sent emissaries to their separate targets, but the lines of communication were muddled.

"The basolateral amygdala was less connected with all of its targets and more connected with centromedial targets," Etkin said. "And the centromedial was less connected with its normal targets and more connected with the basolateral targets."

The researchers also found that both amygdala regions had less connectivity to the region of the brain responsible for determining the importance of stimuli. This could mean that people with the disorder have a harder time discerning truly worrisome situations from mild annoyances. At the same time, the amygdala was more connected to a cortical executive-control network previously found to exert cognitive control over emotion.

The cognitive control connection might explain why GAD is characterized by obsessive worry, Etkin said. People with the disorder feel overwhelmed by emotion and don't believe they can feel sad or upset without coming completely undone. So, in an attempt to avoid facing their unpleasant feelings, they distract themselves by fretting. Such overthinking may work in the short term but becomes problematic over time.

Researchers can't say for sure whether the connectivity abnormalities came first or whether excessive worrying shaped the brain by reinforcing particular neural pathways. Still, the patterns uncovered by neurological scans could one day help psychiatrists diagnose and treat the disease.

"This is a nice example of neurology and psychiatry joining forces," said Michael Greicius, MD, assistant professor of neurology and neurological sciences at Stanford and senior author of the paper.

The next step, said Etkin, is to study patients with other anxiety disorders and with depression. That will allow researchers to see if patterns of amygdala connectivity differ between disorders. If they do, brain scans

could one day become additional diagnostic tools for disorders with symptoms that often overlap.

Source: Stanford University Medical Center (news : web)