Stress disrupts human thinking, but the brain can bounce back

January 27 2009

(PhysOrg.com) -- A new neuroimaging study on stressed-out students suggests that male humans, like male rats, don't do their most agile thinking under stress. The findings, published this month in the *Proceedings of the National Academy of Sciences*, show that 20 male M.D. candidates in the middle of preparing for their board exams had a harder time shifting their attention from one task to another than other healthy young men who were not under the gun.

Previous experiments had found that stressed rats foraging for food had similar impairments and that those problems resulted from stress-induced changes in their brain anatomy. The new study, using functional magnetic resonance imaging (fMRI) to scan the stressed students' brains, is a robust example of how basic research in an animal model can lead to high-tech investigations of the human brain.

"It's a great translational story," says Bruce S. McEwen, head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology at The Rockefeller University, who worked on the project with colleagues at Weill Cornell Medical College. "The research in the rats led to the imaging work on people, and the results matched up remarkably well."

The work holds good news too, for both rats and humans: Their brains recuperate quickly. Less than a month after the stress goes away, they are back to normal. "The message is that healthy brains are remarkably resilient and plastic," McEwen says.

To probe the effects of stress, the researchers scanned the brains of volunteers, some stressed and others relatively relaxed, performing two subtly different kinds of mental tasks, either an attention-shift or a response-reversal. Lying inside the scanner, the subjects looked at two discs: one red and one green, with one moving up and the other down. In a series of trials, they were prompted to choose a disc according to motion or color. By ordering when the subjects did which tasks, they challenged their volunteers' brains to either switch focus from color to motion, or to suddenly reverse their choice of a disc in the same category.

"It's like the old story about the American crossing the road in England," says Conor Liston, an M.D.-Ph.D. student at Rockefeller and Cornell, who led the research. A response-reversal requires the brain to override the habitual impulse to first look left instead of right for oncoming cars. An American in Venice might require an attention-shift, by contrast, to seek out boats instead of evading cars.

In earlier research on rats, neuroscientists found that these two tasks place demands on different circuits in the brain, and the circuits are affected in different ways by stress. In particular, collaborative work by McEwen and John Morrison at Mount Sinai Medical Center have shown that repeated stress on rats shriveled nerve cells of the medial prefrontal cortex, and that a shrunken prefrontal cortex is linked to slower performance on attention-shifting tasks.

In those experiments, rats learned to dig through a certain texture, like sawdust, in the presence of an irrelevant odor to find food; then the researchers made odor, rather than texture, the clue for finding the food and measured how long it took the rats to switch their foraging strategies. But while the restricted prefrontal cortex — a larger version of which is thought to play a role in the "executive function" in humans — slowed the rats' performance on attention-shifts, it did not change their performance on response-reversal tasks. In fact, neurons in a different part of the brain thought to be involved in response-reversals, the orbital frontal cortex, actually grew larger from the stress.

The new research suggests that something very similar may happen to distressed humans. Liston, working with B.J. Casey at the Sackler Institute at Weill Cornell, used fMRI to explore his hunch that the brains of rats and men have some basic processes in common — that stress would also impair performance on attention-shifting tasks and diminish activity in the medial prefrontal cortex.

He found that male med students who said they were stressed out one month before they were to take their boards fared much worse on attention-shifting tasks than similar healthy adults who claimed to be taking it easy. The high stress levels, gauged by an established measure called the perceived stress scale, were also tightly associated with diminished activity in the prefrontal cortex. But their performance on response-reversals was unimpaired. Finally, as was found in the rats, when Liston scanned the students again one month after the test, he discovered that their attention-shifting performance had returned to normal along with their brains.

The uncanny similarities surprised even the researchers. “I certainly don’t want to say that rat brains are just like human brains,” Liston says. “But it does show that you can use research in animal models to help interpret human neuroimaging results.”

Liston plans to next explore how stress impacts the rest of the brain. He also wants to investigate whether or not there are differences in how the brains of men and women respond to stress. “Stress is doing a whole lot of things in your brain that we don’t understand yet, but we know that it is intimately involved in a wide range of neuropsychiatric disorders,” Liston says. A mechanistic understanding of stress could lead to insights into associated psychiatric problems, he says.

Reference: *Proceedings of the National Academy of Sciences* online: January 12, 2009, www.pnas.org/content/106/3/912.abstract

Provided by Rockefeller University