The Effects of Cortisol.

Neuroscientists have discovered how chronic stress and cortisol can damage the brain. A new study reconfirms the importance of maintaining healthy brain structure and connectivity by reducing chronic stress.

Neuroscientists at the University of California, Berkeley, have found that chronic stress triggers long-term changes in brain structure and function. Their findings might explain why young people who are exposed to chronic stress early in life are prone to mental problems such as anxiety and mood disorders later in life, as well as learning difficulties

It has long been established that stress-related illnesses, such as post-traumatic stress disorder (PTSD) trigger changes in brain structure, including differences in the volume of gray matter versus white matter, as well as the and size and connectivity of the amygdala. However, researchers are just beginning to understand exactly how chronic stress creates long-lasting changes in brain structure which affect how the brain functions.

In a series of revolutionary experiments, Daniela Kaufer, UC Berkeley associate professor of integrative biology, and her colleagues, discovered that chronic stress and elevated levels of cortisol can generate more overproduction of myelin-producing cells and fewer neurons than normal. Kaufer et al published their findings in the February 11, 2014 issue of the journal *Molecular Psychiatry.*

Chronic Stress Changes Neural Networks

The "gray matter" of the brain is densely packed with nerve cell bodies and is responsible for the brain's higher functions, such as thinking, computing, and decision-making. But gray matter is only half of the brain matter inside our heads—the other half of brain volume is called white matter.

White matter is comprised of axons, which create a network of fibres that interconnect neurons and creates a communications network between brain regions. White matter gets its name from the white, fatty myelin sheath that surrounds the axons and speeds the flow of electrical signals between neurons and brain regions.

"We studied only one part of the brain, the hippocampus, but our findings could provide insight into how white matter is changing in conditions such as schizophrenia, autism, depression, suicide, ADHD and PTSD," Kaufer said. The hippocampus regulates memory and emotions, and plays a role in various emotional disorders and has been known to shrink under extended periods of acute stress.

The researchers found that hardening wires, may be at the heart of the hyper-connected circuits associated with prolonged stress. This results in an excess of myelin—and too much white matter—in some areas of the brain. Ideally, the brain likes to trim the fat of excess wiring through neural pruning in order to maintain efficiency and streamlined communication within the brain.

Cortisol Can Trigger Stem Cells to Malfunction

The 'stress hormone' cortisol is believed to create a domino effect that hard-wires pathways between the hippocampus and amygdala in a way that might create a vicious cycle by creating a brain that becomes predisposed to be in a constant state of fight-or-flight.

Chronic stress has the ability to flip a switch in stem cells that turns them into a type of cell that inhibits connections to the prefrontal cortex, which would improve learning and memory, but lays down durable scaffolding linked to anxiety, depression, and post-traumatic stress disorder.

Kaufer's lab focused on neural stem cells in the hippocampus of the brains of adult rats under acute or chronic stress. These stem cells were previously thought to mature only into neurons, or a type of glial cell called an **astrocyte**.

However, the researchers found that chronic stress made stem cells in the hippocampus mature into another type of glial cell called an **oligodendrocyte**, which produces the myelin that sheaths nerve cells.

The finding suggests a key role for oligodendrocytes in long-term and perhaps permanent changes in the brain that could set the stage for later mental problems. Chronic stress decreases the number of stem cells that mature into neurons and might provide an

explanation for how chronic stress also affects learning and memory, according to the researchers.

“Usually the brain doesn’t make much oligodendrocytes in adulthood from those neural stem cells,” according to Kaufer. In fact, a recent study suggested these cells were incapable of producing oligodendrocytes, which are somewhat like a vine spreading out and wrapping around axons, both insulating and supporting them.

Rats who have high levels of cortisol and chronic stress had fewer neurons overall but a big increase in oligodendrocytes. By blocking the equivalent of cortisol receptors, the researchers discovered the process was tied to the stress hormone. “This was absolutely not what we were expecting to find,” Kaufer said. “But those are always the best discoveries.”

Although this sheath is vital to human brains—myelin formation can be good or bad, depending on time or place, according to Kaufer. This excessive sheathing may have evolved to bolster the connection between the amygdala and hippocampus, which would improve fight-or-flight responses during extended periods of threat or attack… Unfortunately, in a modern world, chronic stress can hijack the fight-or-flight system and backfire in a daily life in which you are not in physical danger.

Conclusion: Plasticity Makes it Possible to “Sculpt” Your Brain Throughout a Lifespan

Regular physical activity and mindfulness meditation are two effective ways to reduce stress and lower cortisol. Although this study doesn’t focus on the benefits of reducing cortisol, other research suggests that making lifestyle choices that reduce stress and lower cortisol can improve brain structure and connectivity.

Daniela Kaufer is now conducting experiments to determine how stress in infancy affects the brain’s white matter, and whether chronic early-life stress decreases resilience later in life. She also is looking at the effects of therapies, ranging from exercise to antidepressant drugs, that reduce the impact of stress and stress hormones.

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