How stress can cause depression

It is well known that chronic stress can provoke a depression. Through studies with rats and humans, researchers have now discovered a possible explanation for the phenomenon.

The rat studies showed that stress reduces the brain’s innate ability to keep itself healthy. As a result, the hippocampus – a vital part of the brain – shrinks, impacting negatively on both our short-term memory function and our learning abilities.

“This gives us a good model for explaining why depression is so widespread in our modern, stressed society,” says Ove Wiborg, an associate professor at the Department of Clinical Medicine, Centre for Psychiatric Research, at Aarhus University Hospital, who led the study.

Unpredictability is stressful

The researchers were allowed to use rats in their research because they could document that rats react to stress in the same way as humans.

A large number of the animals actually develop a depression-like condition when they are subjected to stressful situations over extended periods.

The researchers tested whether this was the case by exposing the rats to dramatic changes in their environments over a period of eight weeks.

These dramatic changes included:

- Suddenly filling the rats’ cages with water, so the rats had difficulty in maintaining their foothold.
- After a long period in the water, the cages were emptied and tipped through 45 degrees, so it was again difficult for the rats to maintain their foothold and not slide to the end of the cage.
- The cage was then tipped back to normal, but the soft lighting in the laboratory was replaced by harsh light from a stroboscope, which prevented the rats from orientating themselves in their cages.

“Rats are normally good at adapting to new living conditions, but not in this case,” says Wiborg. “The stress factors were changed in a way that was completely lacking in transparency for the rats, completely unpredictably, and that was something many of the animals had difficulties dealing with.”

Rats showed depression symptoms

After the study, many of the rats showed the same symptoms of depression as humans:

- Inability to feel joy
- Poorer sleep patterns
• Lower pain threshold
• Poorer learning ability
• Reduced working memory

The researchers concluded that stress can trigger a depression-like condition in rats.

Then the researchers studied the rats’ brain tissue to find traces of physical changes in the brain caused by stress. They used a chemical process that stains young fresh cells, enabling them to count the number of new cells in the rats’ brains after the stress studies.

Comparing the brains of stressed rats and healthy rats, the researchers found that the stressed rats produced fewer new brain cells – 20 percent fewer than the healthy rats.

The area worst affected was the dentate gyrus, an important part of the hippocampus, which is associated with short-term memory and other functions.

“We now regard the reduction in the formation of new cells as an important cause of depression,” says Wiborg. “The hippocampus shrinks in connection with chronic depression. A healthy brain is able to rebuild healthy brain tissue using a process called neurogenesis. The smaller hippocampus in depressed rats appears to be caused by reduced neurogenesis.”

Genes and environment play a role

Wiborg and his colleagues have yet to find out why some people get stressed and then depressed, while others are less affected by what happens around them. With the answer to this question, we might be able to give preventive treatment.

This subject is being studied by other Danish groups, including one at Cimbi – the Centre for Integrated Molecular Brain Imaging at the Copenhagen University Hospital’s Neurobiology Research Unit.

The Cimbi group’s studies show that people who through their family connections are susceptible to developing depression and who at the same time are easily stressed have a strongly increased risk of being hit by depression.

“Depression doesn’t have just one cause – it seems to arise as a consequence of several different factors, one of which is stress,” says Vibe Frøkjær, a PhD and doctor of medicine affiliated with Cimbi. “Adverse combinations of genetics, stress, disturbances during the early development of the brain, and the brain’s uptake of serotonin appear to enhance one another.”

Sensitive serotonin system

Frøkjær and her colleagues have also studied whether there is a connection between the serotonin system and a special personality trait called neuroticism.

Individuals who score high on neuroticism are more likely than average to experience negative feelings such as anxiety, anger, guilt and depressed moods; at the same time they are also easily stressed.

The Cimbi study, which was based on brain scans of 83 healthy people, whose personality was also tested, showed that people with high neuroticism scores had a more sensitive serotonin system.

In a follow-up study that compared healthy twins who had a high risk of developing a depression with healthy twins who had a low risk of developing a depression, the researchers also found this connection
between neuroticism and the serotonin system; they could also show that the connection was stronger in the high-risk group.

**Therapy against stress**

“Being easily stressed and having a familial susceptibility towards depression, which gives an imbalance in the serotonin system and thus a greater risk of developing a depression, may be an added disadvantage,” says Frøkjær. “But as soon as we know who actually gets a depression we will be able to talk about this risk.”

People who are easily stressed can probably benefit from cognitive therapy, where a psychologist works with the person’s thought processes.

“Stress is a reflex that is closely connected with the individual patient’s personality,” says Frøkjær. “But it may be possible for patients to change their ways through therapy, analysis and training, so they learn some tricks for dealing with the stress.”

Read the article in Danish at Videnskab.dk [7]

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**Fact box**

People with depression that is treated using antidepressant medicine, which increases the amount of serotonin in their brains, are more likely to suffer relapses if the medication is discontinued.

By giving them a drink that sharply reduces their serotonin level, researchers have been able to provoke a negative change in their mood – thus showing that depression is related to the level of serotonin in the brain.

**Fact box**

Depression is a common disease. At least 15 percent of people will develop a depression during their lifetime. Twice as many women as men get depressions.

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Ove Wiborg

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High familial risk for mood disorder is associated with low dorsolateral prefrontal cortex serotonin transporter binding. Neuroimage, doi: 10.1016/j.neuroimage.3009.02.008

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