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Our individual genetic make-up determines the effect that stress has on our emotional centres. These are the findings of a group of researchers from the MedUni Vienna. Not every individual reacts in the same way to life events that produce the same degree of stress. Some grow as a result of the crisis, whereas others break down and fall ill, for example with depression. The outcome is determined by a complex interaction between depression gene versions and environmental factors.

The Vienna research group, together with international cooperation partners, have demonstrated that there are interactions between stressful

life events and certain risk gene variants that subsequently change the volume of the hippocampus forever.

The hippocampus is a switching station in the processing of emotions and acts like a central interface when dealing with stress. It is known to react very sensitively to stress. In situations of stress that are interpreted as a physical danger ('distress'), it shrinks in size, which is a phenomenon observed commonly in patients with depression and one which is responsible for some of their clinical symptoms. By contrast, positive stress ('eustress'), of the kind that can occur in emotionally exciting social situations can actually cause the hippocampus to increase in size.

According to the results of the study, just how stressful life events impact on the size of the hippocampus depends on more than just environmental factors. There are genes that determine whether the same life event causes an increase or decrease in the volume of the hippocampus, and which therefore defines whether the stress is good or bad for our brain. The more risk genes an individual has, the more negative an impact the "life events" have on the size of the hippocampus. Where there are no or only a few risk genes, this life event can actually have a positive effect.

Examining life crises

As part of the study, carried out at the University Department of Psychiatry and Psychotherapy (led by Siegfried Kasper), the study team obtained quantitative information from healthy test subjects about stressful life events, such as deaths in the family, divorce, unemployment, financial losses, relocations, serious illnesses or accidents.

A high-resolution anatomical magnetic resonance scan was also carried out (at the High-Field MR Centre of Excellence, Department of MR

Physics, led by Ewald Moser). The University Department of Laboratory Medicine (Harald Esterbauer and colleagues) carried out the gene analyses (COMT Val158Met, BDNF Val66Met, 5-HTTLPR). At the University Department of Psychiatry and Psychotherapy, primary author Ulrich Rabl measured the volume of the test subjects' hippocampi using computer-assisted techniques and analysed the results in the context of the genetic and environmental data.

"People with the three gene versions believed to encourage depression had a smaller hippocampus than those with fewer or none of these gene versions, even though they had the same number of stressful life events," says study leader Lukas Pezawas, describing the results. People with only one or even none of the risk genes, on the other hand, had an enlarged hippocampus with similar life events.

The study highlights the importance of gene and environment interaction as a determining factor for the volume of the hippocampus. "These results are important for understanding neurobiological processes in stress-associated illnesses such as depression or post-traumatic stress disorder. It is ultimately our genes that determine whether stress makes us psychologically unwell or whether it encourages our mental health," explains Pezawas.

The study, published in the highly respected *Journal of Neuroscience*, was funded by a special research project of the FWF (Austrian Science Fund) (SFB-35, led by Harald Sitte) and presented as a highlight at the international conference on "Organization for Human Brain Mapping."

More information: "Additive Gene–Environment Effects on Hippocampal Structure in Healthy Humans" – Ulrich Rabl, Bernhard M. Meyer, Kersten Diers, Lucie Bartova, Andreas Berger, Dominik Mandorfer, Ana Popovic,Christian Scharinger, Julia Huemer, Klaudius Kalcher, Gerald Pail, Helmuth Haslacher, Thomas Perkmann, Christian

Windischberger, Burkhard Brocke, Harald H. Sitte, Daniela D. Pollak, Jean-Claude Dreher, Siegfried Kasper, Nicole Praschak-Rieder, Ewald Moser, Harald Esterbauer, and Lukas Pezawas. The *Journal of Neuroscience*. 2014 Jul 23;34(30):9917-26. DOI: 10.1523/JNEUROSCI.3113-13.2014.