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PRESS-RELEASE
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How the interaction of genetics and environmental factors can interfere with memory and attention in psychiatric diseases

A genetic predisposition and an activated immune system of the mother with an infection is a combination that can cause problems with memory and attention in the offspring that are part of the complex symptoms of psychiatric diseases, as experiments with mice show.

A team of researchers at the University Hospital Hamburg-Eppendorf lead by Prof. Dr. Ileana Hanganu-Opatz described today (xxx) at the FENS Forum 2018 in Berlin how these disorders occur. In early brain development, inherited factors and the exposure to an infection before they are born primarily disturb the activity of a certain group of neurons and thus the maturing interconnection between brain areas that are responsible for memory and attention.

"Cognitive deficits such as memory and learning problems are components of many mental illnesses," explained Mr Sebastian Bitzenhofer, PhD-Student in the group. Those affected have problems remembering things and are unable to concentrate. They seem distracted and their emotional life is also disturbed. The cause is a disrupted interaction between two brain areas, the prefrontal cortex (which is involved in cognitive control) and the hippocampus (involved in memory). This has already been shown by previous studies on human patients.

The Hamburg researchers have investigated how this happens using a mouse model, a so-called double-hit model. The animals have two risk factors: first, a gene (DSC1) in which a mutation increases the risk of schizophrenia in humans. Risk factor number two is an infection of the female mouse during pregnancy that activates the immune system. The offspring of these mice show a behaviour in adulthood that points to cognitive deficits. "Only the combination of these two risk factors produces behaviour in adult animals that resembles symptoms of psychiatric diseases," said Prof. Dr. Ileana Hanganu-Opatz, head of the developmental neurophysiology research group.

What this double blow does to the maturing brain of young mice has been investigated by the scientists with different methods down to the level of individual groups of neurons. A group of neurons in a specific layer of the prefrontal cortex seems to play an important role. Under the influence of risk factors, the cells form fewer dendrites – extensions of the neuron that receive signals from other neurons – with which they can absorb stimuli. These structural changes cause functional disorders and impair the ability of these neurons to coordinate joint firing with other cell groups, as studies show.

These deficits are over-compensated in the adult brain. The joint activity of the cell groups is strengthened and accompanied by cognitive deficits.

The scientists were also able to show that the abnormal communication in the maturing brain can be prevented or reversed if the mother's infection is treated and activated immune cells in the brain of the offspring, so-called microglia cells, come to rest.

END

Symposium 51: *Resolving the cognitive function of prefrontal circuits: From neurons to behaviour*

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