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Neuroscience

Signals that strengthen the brain

Insights into an important signalling system for neural plasticity may enhance understanding of bipolar disorder and schizophrenia

The brain is capable of modifying itself over time by creating and strengthening synapses — the structures that carry electrical signals between neurons. This process, known as neural plasticity, enhances cognitive functions including learning and memory. Researchers at NAIST are at the forefront of investigations into the mechanisms surrounding cognitive functioning, and a major study in 2012 uncovered an important signalling system in neural plasticity involving an enzyme called neuropsin and a protein called NRG-1[1]. The dysfunction of the neuropsin-NRG-1 signalling system may be involved in psychiatric illnesses such as bipolar disorder and schizophrenia.

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"About 20-30 years ago, neural and synaptic structures were thought to be rigid and immovable, even in neural plasticity processes like memory acquisition," explains Sadao Shiosaka, of the NAIST Laboratory of Functional Neuroscience and one of the authors of the study. "We hypothesized that neural plasticity actually induces dynamic neural change, particularly in an area called the synaptic cleft, found between pre- and post-synaptic neurons."

The main problem with studying signalling systems in the synaptic cleft is that the specific enzyme-protein interactions happen very quickly and cannot easily be isolated and examined. Shiosaka and his team therefore pioneered a new method to uncover the protein substrates processed by neuropsin in the brains of mice.

"Neuropsin is thought to influence cognitive brain function, and has been implicated in working memory and bipolar disorders," explains Shiosaka. "We modified neuropsin so that it had a mutation which allowed binding to target proteins, but did not then release them. This allowed us to identify several of neuropsin's targets, including NRG-1."

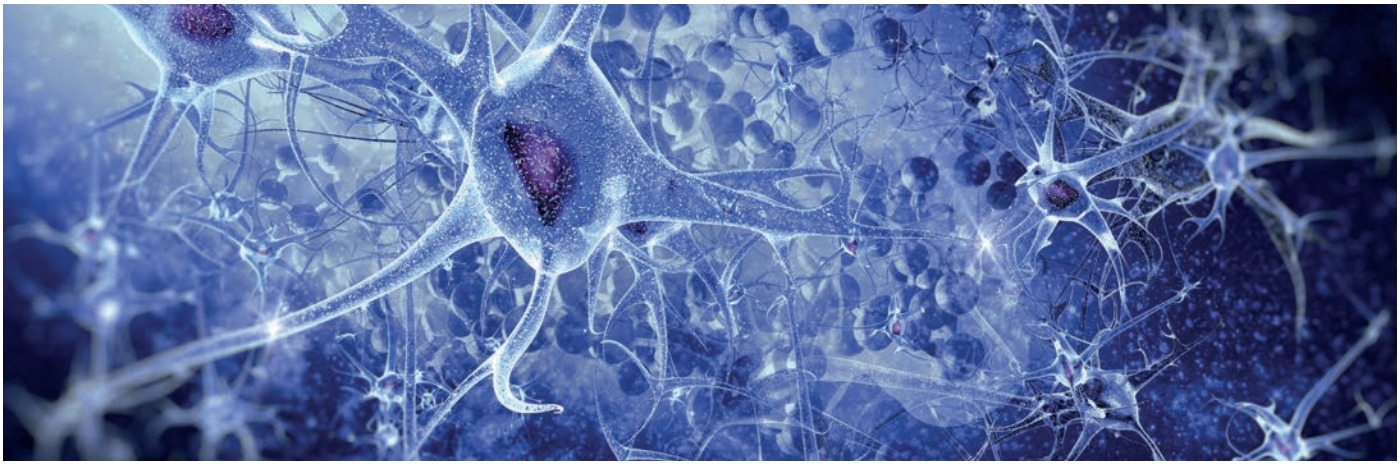
The team analysed samples taken from the hippocampus in the mice. They found that neuropsin processes NRG-1, which in turn activates the so-called ErbB4 receptor to stimulate a type of neuron called GABAergic neurons.

Signalling from ErbB4 allows for the strengthening of synapses between neurons, enhancing the brain's ability to learn from repeated activities, a process known as early long-term potentiation. When Shiosaka and his team created neuropsin-deficient mice, they found that the mice displayed both behavioural and neuronal hyperexcitability, as well as impairments in early long-term potentiation.

These results show that neuropsin-NRG-1 processing is a vital part of neural plasticity, and that functioning neuropsin pathways allow for the strengthening of synapses and normal cognitive function. Shiosaka and his team believe that their work could help further understanding of bipolar disorder and schizophrenia, and may one day provide a remedy for plasticity-related conditions such as hallucination and delusion.

Reference

1. Tamura, H., Kawata, M., Hamaguchi, S., Ishikawa, Y. & Shiosaka, S. Processing of neuregulin-1 by neuropsin regulates GABAergic neuron to control neural plasticity of the mouse hippocampus. *The Journal of Neuroscience* **32,** 12657–12672 (2012).



A major signalling pathway involved in strengthening synaptic connections between neurons in the brain has been identified. Its disruption may be connected with psychiatric disorders such as schizophrenia.

More information about the group's research can be found at the Functional Neuroscience webpage:
http://bsw3.naist.jp/eng/courses/courses205.html