MedicalXpress

A new approach to combatting anxiety states, pain and inflammation

June 6 2017

Endogenous cannabinoids (endocannabinoids) play an important role in the brain and immune system. Bern researchers from the National Centre of Competence in Research (NCCR) "TransCure" have now found a new way to influence the endocannabinoid system. Anti-inflammatory, analgesic as well as anxiolytic effects could be achieved in an animal model.

Endocannabinoids are substances similar to fatty acids which are produced by the body. They activate specific cannabinoid receptors and among other things can exert anti-inflammatory or analgesic effects. Cannabis or tetrahydrocannabinol (THC) exhibit similar therapeutic effects in clinical use, but they are fraught with adverse effects. In contrast, endogenous cannabinoids are only produced in the cells when the body needs them, and therefore cannot be overdosed. The endocannabinoid system is considered promising as it uncovers new therapeutic options, for instance for disorders of the nervous system. For years, the research team led by Jürg Gertsch from the Institute of Biochemistry and Molecular Medicine at the University of Bern has been exploring the possibility to selectively activate endocannabinoids in the brain in order to treat neuropsychiatric disorders – for example, anxiety states – within the scope of the NCCR "TransCure" financed by the Swiss National Science Foundation (SNSF).

In cooperation with an international research team, the Bern research group led by Gertsch has now succeeded in blocking the transport route or endocannabinoids in the brain of mice for the first time by means of

innovative inhibitors. This led to positive effects on the stress behaviour and immune system of mice. Anti-inflammatory, analgesic as well as anxiolytic effects have been observed. Although for several years it has been assumed that there is an endocannabinoid transport system in nerve cells and immune cells, this could now be shown for the first time. "I am convinced that in addition to the administration of exogenous cannabinoids, the endocannabinoid system will be specifically activated for therapeutic purposes in the future," says Gertsch. The study was published in the journal *Proceedings of the National Academy of Sciences* (*PNAS*).

Endocannabinoid Transport blocked

In cooperation with chemists from the Swiss Federal Institute of Technology/ETH Zurich (research group led by Prof. Karl-Heinz Altmann) and the industry, hundreds of endocannabinoid transport inhibitors were synthesised in order to develop ideal pharmacological properties. The researchers were inspired for these inhibitors by a natural substance from the purple coneflower (Echinacea purpurea), a medicinal plant which is frequently utilised for colds and partially has an effect on the endocannabinoid system. The newly developed inhibitors block the uptake of endocannabinoids through the membrane of cells. As a result, cannabinoid receptors on nerve and immune cells are activated, which leads to a "brake" in the brain and in the immune system upon stress and in inflammatory disorders, restoring the physiological equilibrium.

New perspectives for new medicines

Andrea Chicca, lead author of the study from the group led by Prof. Gertsch, is confident that the molecular mechanism of endocannabinoid transporter can be elucidated in the coming years: "Then nothing stands

in the way for the development of new medicines." Thanks to the new findings from the study, already now substances can be made which differ from previous drugs as they specifically activate the endogenous cannabinoids in the brain. The researchers see great potential in the field of stress-related disorders, because endocannabinoids regulate important stress hormones and restore the equilibrium in the brain.

More information: Andrea Chicca et al. Chemical probes to potently and selectively inhibit endocannabinoid cellular reuptake, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1704065114

Provided by University of Bern