

*Media release*

**May 9, 2021**

**Endometriosis:**

## **Pain modulation by body's own cannabinoids**

**In a study recently published in the journal PAIN, researchers from the University of Bern and Inselspital, Bern University Hospital, report new findings on the genesis of pain in endometriosis. For the first time, the role of endogenous, pain modulating endocannabinoids (ECs) was examined in detail in groups of patients with precise descriptions of pain. It was shown that the pain results from a complex interaction between pain and inflammation modulation.**

Endometriosis is a chronic, inflammatory, hormone-dependent disease that results in infertility and severe discomfort due to cyclical abdominal pain. It is estimated that 10-15% of women in reproductive age suffer from endometriosis. Over 170 million patients are thought to be affected worldwide. In Switzerland between 190 000 and 280 000 women suffer from symptoms attributed to endometriosis. Despite these high numbers, the etiology of endometriosis is still surprisingly unclear. In particular, the modulation mechanisms of the pain that occurs are poorly understood.

### **Endocannabinoids modulate pain...**

The endocannabinoid 2-AG (2-arachidonoylglycerol) is of importance here. It binds to specific receptors on the nerve cell membrane and thus modulates the sensation of pain. If a high concentration of 2-AG is measured, pain should be reduced. According to this expectation, therefore, 2-AG would be absent in the group of patients with very severe pain.

However, the research group led by Prof. Dr. Michael D. Mueller found that precisely in this group of patients the levels of 2-AG locally in the abdominal cavity were elevated. First author Dr. Thomas Andrieu explains: "For the first time we measured the local concentration of ECs in the abdominal cavity – and not just in the (peripheral) blood, as previous authors had done. In addition, we kept a precise record of pain and were thus able to perfectly demonstrate a correlation between severe pain in the abdominal region and high EC concentrations."

### **...but quite different than assumed!**

The key to understanding the observations was found in a second area of the study design: the analysis of tissue inflammation associated with endometriosis. That is to say, the researchers in Bern examined not only the ECs in their study but also various inflammatory markers. EC 2-AGs are

known to have both analgesic and anti-inflammatory effects. In patients with severe pain, the inflammatory markers were also significantly elevated. The study authors conclude that ECs activate certain cells of the immune system and lead to inflammatory pain. This means ECs both are analgesic and, by activation of the immune system, pain stimulating (illustration in appendix).

### **Better understanding of endocannabinoids**

The study conducted by the research group in Bern has demonstrated a plausible link between ECs and their role in modulating pain and tissue inflammation. This finding was made possible in part thanks to the emulative research environment created at the sitem-insel. First author Andrieu comments: "Our research hypothesis arose from the collaboration between two laboratories: one specializing in endometriosis and the other a leader in the study of the endocannabinoid system. I had the opportunity to discuss with a leading EC researcher and that's how the idea was born to study the role of ECs in modulating endometriosis pain."

### **High motivation. Still a long way to go.**

The study has demonstrated a clear link between pain in the abdominal region and elevated EC levels, as well as elevated levels of inflammatory markers. The head of the study, Prof. Michael Mueller, adds: "It is possible that with ECs, a group has been found that could one day be of therapeutic importance. We are highly motivated to gain an even better understanding of the complex interplay of processes involved in the regulation of pain and modulation of inflammation. It is high time that we can more easily diagnose and treat endometriosis."

### **Experts:**

- Prof. Dr. med. Michael D. Mueller, Co-Chairman and Chief Physician, Gynecology and Gynecologic Oncology, University Women's Hospital, Inselspital, Bern University Hospital
- Dr. Thomas Andrieu, Team Leader, Department for BioMedical Research (DBMR), University of Bern

### **Links:**

- Original publication: DOI: [10.1097/j.pain.0000000000002333](https://doi.org/10.1097/j.pain.0000000000002333)
- [University Department for Gynecology, Inselspital, University Hospital Bern](#)
- [Department for BioMedical Research \(DBMR\), Endometriosis and gynecological oncology, Universität Bern](#)
- [Institute of Biochemistry and Molecular Medicine \(IBMM\), NCCR TransCure, University of Bern](#)

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