

## ANNUAL HIGHLIGHTS IN CNAP

Provoking, probing, and modulating pain neuroplasticity is the CNAP approach that significantly impacts the understanding of fundamental mechanisms in human prolonged pain conditions. The highlights of 2023 were many, providing a vital translational link, connecting basic and human research of the pain system.





Significant progress has been established in understanding pain-related mechanisms following damage of small nerve fibres, a prevalent comorbidity of e.g. diabetes and some cancer treatments. A CNAP methodology was used to identified distinctive habituation patterns in small sensory nerve fibres, shedding light on their potential role in neuropathic pain chronification. This method, proven highly accurate in detecting diabetic neuropathy, addresses technical challenges, enhancing its reliability as a mechanistic diagnostic tool. The predictive capacity will be further assessed in the future large-scale "NeuroPredict" project.

In 2023, CNAP researchers curated a novel methodology to explore the way different brain areas communicate during pain. By coupling the recording of brain signals by electroencephalography (EEG) with transcranial magnetic brain stimulation, it was possible to record how the provocation of EEG activity in one brain area flows to other connected areas. For the first time, it was shown that provoked pain changes activity of brain areas according to few specific patterns, and that individuals tend to express only one of these patterns. Moreover, pain causes changes in the way brain waves are organised and distributed across different brain areas, and the intensity of these changes are correlated to a person's pain sensitivity.





Objective markers for pain neuroplasticity from intracortical neural signals in pigs is a key CNAP research area and therefore we established a chronic pig model of pain and cortical neuroplasticity. Event-related brain activity was analysed three weeks before and up to three weeks after applying a prolonged pain model. The results showed that the pig pain model resembles a similar human pain model with a comparable time profile of pain sensitisation/neuroplasticity. For the first time it was demonstrated in pigs that the degree of pain sensitisation correlated with the cortical signs of neuroplasticity.

To understand the complexity of pain conditions and its association with specific epigenetic fingerprints we analysed data from chronic knee pain patients using high-throughput Next Generation Sequencing and employed advanced statistical methods to assess the contributions to the pain reported by patients. This analysis integrated various datasets, including microRNAs, inflammatory markers, clinical outcomes, and quantitative sensory testing of pain mechanisms. The model highlighted variables across specific molecular, cognitive, and clinical components that could explain 75% of the pain. This finding underscores the multifactorial complexity of chronic pain and indicates that it should be approached as a network of interconnected factors rather than focusing on isolated parameters.



## Publications, Public Outreach, and Awards

CNAP's success hinges also on its commitment to disseminating knowledge and engaging the public. In 2023, CNAP researchers published a substantial number of peer-reviewed publications, many in high-impact journals. Through public lectures, educational efforts, media outreach, and partnerships with healthcare professionals and patient communities, CNAP shares research findings and strives to maximise its societal impact. In 2023 CNAP researchers successfully attracted several grants e.g. Inge Lehmann (DFF) and an ERC Consolidator Grant.

## Internationalisation, Interdisciplinarity, and Training

In 2023, CNAP comprised 33 researchers with diverse expertise in medicin and biomedical engineering, spanning neuroscience, psychology, and medicine, including neurology. The CNAP team nurtures rich interdisciplinary collaboration, achieving nearly equal gender representation. In 2023, 14 affiliated CNAP researchers are actively engaged in training as either PhD students or postdocs.