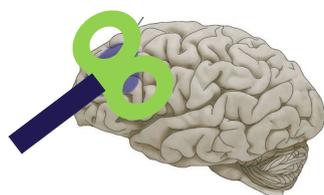


ANNUAL HIGHLIGHTS IN CNAP

CNAP aims to be the leading research center conducting cutting-edge research on pain neuroplasticity. Our research approach is based on the concepts of provoking, probing and modulating pain neuroplasticity, and a research environment that is dynamic, international, supportive, and cross-disciplinary.

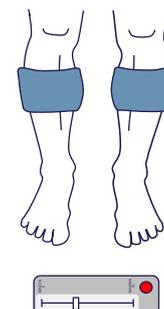
Research Highlights: The skin is densely innervated by sensory nerve fibres allowing us to perceive our surroundings and pain when the nociceptors are activated by potential harmful stimuli. Increased excitability of the nociceptors leads to increased pain perception and possibly neuroplastic neural changes. Using computational modelling a single-use electrode has been developed that can selectively activate the nociceptors and it has been validated in healthy human subjects. The electrode will be used to assess the possible excitability changes in persons at risk of developing diabetes neuropathy. This will lead to a deeper understanding of the pathophysiological processes leading to neuropathic pain.

Self-regulating processes are essential to avoid extreme conditions of the central nervous system (homeostatic plasticity) and may be important for pain neuroplasticity. For instance, when a brain response is high, the homeostatic response will be a regulation towards dampened activity if a new condition appears which would normally cause a facilitation. In some chronic pain conditions, the homeostatic regulation has been found to be less efficient in brain regions controlling movements and this may contribute to the maladaptive neuroplasticity often accompanying persistent pain conditions. Based on CNAP research, a



reliable protocol to probe the degree of the homeostatic plasticity has been devised. Using this protocol, twenty-four hours of prolonged experimentally-provoked pain impaired the homeostatic response when compared to a pain-free condition and interestingly this was not restored by immediate pain relief, suggesting that ongoing pain progressively impairs the homeostatic response even for a while after the pain is gone.

Prior CNAP research has resulted in advanced psychophysical protocols for provoking and probing neuroplastic properties in the pain system in e.g. chronic pain patients. Understanding the normative characteristics of the pain system a highly standardised protocol was performed in a collaborative study assessing a cohort of more than 15,000 participants. Ongoing analysis shows a progressive increase in pain sensitivity with age in both genders, but women are more pain sensitive than men. Moreover, participants with self-reported chronic pain are hypersensitive. Such findings in large populations are highly important for understanding changes and variability in the pain system and vulnerability towards neuroplastic changes in persistent pain conditions.



To study details not available in our human studies, a goal for CNAP is to establish a preclinical pig model to probe manifestations of pain neuroplasticity over time by invasive brain electrodes. This initiative is highly novel and expected to provide important translational findings. Major steps have been taken to develop and validate the methodology used to record brain signals during an acute condition of pain neuroplasticity. Next step is to study these brain signals over weeks during pain provocation.

Publications and Public Outreach: CNAP researchers published 84 peer-reviewed papers in 2021, many of them in high-impact journals for the field. CNAP researchers contribute actively to public debates on pain research and management, outreach events aiming to informing the public about pain, and teaching at Aalborg University.

Congresses and Events: Events in 2021 continued to be partially affected by the Covid-19 pandemic, but CNAP researchers were strongly represented at and involved in the organisation of numerous events, both online, physical and hybrid (e.g. the *IASP World Congress on Pain* held online, and the annual meeting of the *Danish Society for Neuroscience* with physical appearance). Five CNAP PhD fellows successfully defended their PhDs in 2021.

Internationalisation, Interdisciplinarity, and Training: In 2021, 35 researchers of very diverse backgrounds, e.g. biomedical engineering, medicine, psychology, and physiotherapy were affiliated to CNAP. They came from 14 different countries, made up an almost equal gender balance, and 19 of them were early career researchers.