## The abstract

Chronic pain affects approximately 20% of people worldwide leading to enormous personal suffering and economic burden. A key factor contributing to chronic pain disability that thus far has been neglected is fear of painful touch – a core symptom in people with complex regional pain syndrome (CRPS). FABrIC (FeAr of painful touch in the Brain in Chronic pain) is a functional Magnetic Resonance Imaging (fMRI) study using a novel tactile fear conditioning paradigm that we developed. We will use this novel tactile fear conditioning paradigm to examine the neural correlates of the acquisition, generalization, and extinction of fear of painful touch and interrelationships with somatosensory neuroplasticity, and sensory impairments (i.e., abnormalities in processing of somatosensory stimuli) in individuals with CRPS (n = 20) compared to healthy controls (n = 20). This Marie Skłodowska-Curie Actions (MSCA) project is groundbreaking and can yield novel insights in hypothesized intertwined underlying neural mechanisms of pain-related fear (learning) and symptoms. We hypothesize impaired threat-safety learning, excessive fear generalization, and slower extinction in patients with CRPS compared to controls. This compromised fear learning will relate to changes in neural correlates of fear of touch in patients compared to controls. The intertwined neural mechanisms include a hypothesized relationship between changes in the representation of the fingers in the primary somatosensory cortex (S1) in individuals with CRPS (i.e., somatosensory neuroplasticity) and fear generalization. More specifically, we hypothesize that somatotopic imprecision (i.e., overlap) in finger representations in S1 will be related to reduced tactile acuity and excessive fear generalization (i.e., broader generalization gradients of fear of painful touch). In addition, we will investigate whether individual differences in vulnerability and resilience factors can modulate fear learning and whether they affect pain-related outcomes (e.g., pain severity).

Our project uniquely brings together pain researchers from physiotherapy, neuroscience, and psychology fields, offering potential of strong clinical relevance and translations and new avenues for improved treatment based on newly gained insights. We will go beyond the state-of-the-art to study this complex chronic pain condition and provide opportunities to alleviate CRPS stigma and increased recognition of the impact of fear of touch. Persons with CRPS endorsed the relevance of this project. We will perform for the first time the tactile fear conditioning paradigm in chronic pain patients in an fMRI environment and postulate that unique learning mechanisms play a role in fear of painful touch. By performing the paradigm on the non-affected hand in patients with unilateral symptoms, we can assess in a feasible way whether general fear of touch learning deficits are present.