

# Cortical processing of pain

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# Valorisation

Below, the research presented in this thesis is placed in the context of social relevance, in other words valorisation. Valorisation is defined as “the process of creating value from knowledge, by making knowledge suitable and/or available for social and/or economic use and by making knowledge suitable for translation into competitive products, services, processes and new commercial activities.” In the next paragraphs, the relevance of the topic, possible target groups and future directions will be addressed.

## Relevance of the topic

Many individuals suffer from chronic pain. According to a large European study, almost 20% of adults experience moderate to severe chronic pain, and in approximately 50% of individuals pain was managed inadequately.<sup>1</sup> Another important issue is acute postoperative pain. Forty to 75% of patients suffer from moderate to severe pain during the first couple of days after surgery, many of whom develop chronic pain.<sup>2</sup> Remarkably, recent research suggests that patients who experience severe pain during the acute postoperative phase are at risk of developing chronic pain.<sup>3</sup> So, despite the availability of sophisticated pain management options, physicians fail to reduce pain to acceptable levels in a substantial number of patients. In the Netherlands, on average 13 workdays are lost annually due to chronic pain, decreasing productivity and costing billions of euros. Thus, chronic pain is a major health care problem and places a great burden on society and economy.

One of the difficulties in the treatment of (chronic) pain is its multidimensionality. Pain is a subjective experience, and many factors, such as genetic, psychological, and contextual factors, are involved in the pain experience. This explains why a large variability exists between individuals.

Because of its subjective nature, objective measurement of pain is a challenge. Compared to questionnaires, pain Event-Related Potentials (pain-ERPs) is considered to be a more objective way to measure pain. Pain-ERPs are time-locked EEG responses to painful stimuli. After receiving several pain stimuli, the corresponding brain potentials usually decrease, due to a phenomenon called habituation. In pain research, habituation is viewed as one of the key top-down processes that may prevent the chronification of pain. Several experimental studies have demonstrated an impaired habituation to painful stimuli in various chronic pain populations.<sup>4-6</sup> More knowledge about these factors and mechanisms, which explain the wide variability in pain experiences, will aid the

development of new diagnostic and tailored therapeutic options that predict and prevent the transition from acute to chronic pain.

In this thesis, an analysis method was developed, called Event-Related Fixed-Interval Area (ERFIA) multilevel method, enabling an in-depth investigation of the phenomenon of habituation to pain. Not only did the ERFIA multilevel method show similar results compared to conventional peak-based analysis, it also demonstrated that influences of stimulus intensity and habituation could be found in a much broader range of the pain-ERP. Furthermore, this thesis replicated earlier findings that habituation is impaired in chronic pain and again, that habituation was not limited to peak regions in the pain-ERP. In addition, it was demonstrated that pain hypervigilance, a psychological variable, independently of chronic pain, influenced the cortical processing of pain and habituation.

## **Target groups**

A logical target group is the surgical population. More insight in the chronification of postoperative pain will aid in reducing suffering from chronic pain. First, with more knowledge, prediction models to assess the risk of chronic postsurgical pain can be improved. Good prediction models aid physicians and their patients in decision-making concerning surgery. Next, insight in the chronification process will provide new targets for treatment and prevention. Besides surgical patients, patients with chronic pain will also benefit in several ways from more knowledge about factors and mechanisms, such as habituation, involved in chronic pain. For example, this knowledge could be used in the development of new treatment options and tools to measure the effectiveness of treatments.

## **Future directions**

This thesis provides evidence that habituation plays a role in chronic pain and that the psychological factor pain hypervigilance may modify habituation. Future research is of importance in several ways. First, longitudinal studies are undoubtedly needed to establish whether the degree of habituation to pain can (partially) predict chronification of pain. Based on such knowledge prediction models can be developed for the assessment of risk of developing chronic pain. Currently, these prediction models contain variables such as patient demographics, perioperative data, and psychological factors. Adding a neurophysiological measure such as cortical habituation to pain, may help to improve these prediction models. Good prediction models will aid in decision making regarding surgery. Second, research into the identification of factors that influence habituation,

positively or negatively, is also of great importance. Understanding the factors that affect habituation and simultaneously identifying the component in the pain-ERP is essential in guiding the development of interventions that target habituation. This thesis suggests that cognitions such as pain hypervigilance might be a target in the prevention of chronification of pain. Third, the identification of important components of the pain-ERP might lead to the development of an objective tool to assess whether treatments are effective.

In conclusion, this thesis, provides further evidence that habituation to pain and factors related to habituation may be fruitful targets for further development in prediction tools for chronification of pain and management of pain. If we could reduce suffering from chronic pain it will decrease the burden on society and economy, through increase in work participation, social participation and a decreased health care demand.