Cortical neuroplasticity induced by muscle pain and non-invasive modulation of pain-induced neuroplasticity by

Enrico De Martino

Chronic musculoskeletal pain is the main cause of living with disability worldwide. Yet, one of the major problems in planning new therapeutic strategies is that the underlying mechanisms driving pain are not completely understood. Recently, pain researches have highlighted the role of central nervous system in maintaining pain chronicity, due to maladaptive pain-related neuroplasticity. However, it is still unknown how maladaptive pain-related neuroplasticity is altered during the transition from acute to chronic pain and at what time-point changes develop.

Therefore, the first aim of the present Ph.D. project was to investigate the nature and time-course of pain-related neuroplasticity provoked by experimental long-lasting muscle pain in healthy volunteers. In addition, neuromodulatory interventions have been recently proposed to treat chronic musculoskeletal pain. Consequently, the second aim of this project was to modulate the cortical excitability changes and the clinical manifestations provoked by experimental long-lasting muscle pain applying multiple sessions of repetitive transcranial magnetic stimulation (rTMS) to the left dorsolateral prefrontal cortex (DLPFC).

The results of the first two studies suggested that muscle pain induced by delayed-onset muscles soreness (DOMS), intramuscular injections nerve growth factor (NGF) and the two models combined are able to provoke long-lasting muscle pain up to 20 days, muscle hyperalgesia and functional disability. Moreover, temporary cortical excitability changes have been probed: While DOMS inhibited the corticomotor excitability, intramuscular injections of NGF facilitated it. Additionally, intramuscular injections of NGF modified both frontal and centro-parietal sensory cortical excitability while DOMS modified only centro-parietal sensory cortical excitability. In conclusion, these findings suggest that DOMS and muscle pain induced by NGF provoked different cortical sensorimotor adaptations.

The results from the third study showed that multiple sessions of 10 Hz rTMS to the left DLPFC were able to modulate the corticomotor and sensory cortical adaptations during muscle pain induced by intramuscular injections NGF, as well as reduced hyperalgesia, pain intensity and functional disability.

In conclusion, the results of this Ph.D. project showed promising findings regarding the opportunity to modulate pain-induced neuroplasticity as well as analgesic effects of 10 Hz rTMS to the left DLPFC.
To fulfill the requirements for the Ph.D. degree, Enrico De Martino has submitted the thesis: Cortical neuroplasticity induced by muscle pain and non-invasive modulation of pain-induced neuroplasticity, to the Faculty Council of Medicine at Aalborg University.

The Faculty Council has appointed the following adjudication committee to evaluate the thesis and the associated lecture:

**Professor Didier Bouhassira**  
University Paris-Saclay  
France

**Professor Massimilano Valeriani**  
Ospedale Bambino Gesù  
Italy

**Chairman:**  
Associate Professor Anne Estrup Olesen  
Aalborg University  
Denmark

**Moderator:**  
Professor Thomas Graven-Nielsen  
Aalborg University  
Denmark

The Ph.D. lecture is public and will take place on:

**Monday 11 March 2019 at 13:00**  
Aalborg University – Room D2-106  
Fredrik Bajers Vej 7 D2  
9220 Aalborg East

**Program for Ph.D. lecture on**

**Monday 11 March 2019**

**by**

**Enrico De Martino**

Cortical neuroplasticity induced by muscle pain and non-invasive modulation of pain-induced neuroplasticity

**Chairman:** Associate Professor Anne Estrup Olesen

**Moderator:** Professor Thomas Graven-Nielsen

13.00 Opening by the Moderator

13.05 Ph.D. lecture by Enrico De Martino

13.50 Break

14.00 Questions and comments from the Committee  
Questions and comments from the audience at the Moderator’s discretion

16.00 (No later than)  
Conclusion of the session by the Moderator

After the session a reception will be arranged