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. Addition- ally, 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.

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Ph.D. lecture

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Monday 11 March 2019

DEPARTMENT OF HEALTH SCIENCE AND TECHNOLOGY
AALBORG UNIVERSITY

This thesis is based on Enrico De Martino's research work at:

CNAP
Center for Neuroplasticity and Pain

CNAP
Department of Health Science and Technology
Aalborg University, Denmark

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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

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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