Probing and modulating pain-induced corticomotor excitability reduction by engaging premotor cortex activity in humans

by

Dennis Boye Larsen

Chronic musculoskeletal pain is a major societal problem due to the impact on quality of life and the large financial burden. Arguably, a main reason why chronic musculoskeletal pain management is still suboptimal is that the underlying mechanisms remain undecided.

Over the last three decades our understanding of the influence of sensorimotor changes in response to acute and chronic muscle pain has improved. Nonetheless, technological limitations, controversial findings, and knowledge gaps contribute to no overwhelmingly successful rehabilitation regimes for individuals living with chronic musculoskeletal pain.

In this respect, the aim of this PhD project was to apply and test novel approaches for modulating the well-known phenomenon of a reduced motor cortical response following a painful episode. This PhD project utilized a well-established pain model for inducing localized transient pain and aimed to modulate the ensuing reduced motor cortical response by engaging the prefrontal and premotor areas of the brain. Premotor cortex activation has been shown able to facilitate primary motor cortex (M1) excitability. Therefore, the objectives of the PhD project were to (1) establish a robust model for inducing a reduction in corticomotor excitability and (2) modulate pain-induced reduction in corticomotor excitability by engaging premotor cortex activity.

The first study demonstrated and characterized a robust hypertonic saline pain-induced reduction in corticomotor excitability in the small hand, but not forearm musculature, indicating that despite shared corticomotor representation, differential responses can be elicited. The second study showed that performance of a two-back task was ineffective, possibly due to influences related to prefrontal, subcortical, and/or intracortical mechanisms, in modulating the pain-induced reduction in corticomotor excitability, but enhanced pain perception. Finally, the third study provided the first evidence that action observation combined with motor imagery successfully modulated pain-induced reduction in corticomotor excitability, possibly through premotor cortex activation facilitating M1 excitability.

In conclusion, the current PhD thesis provides novel evidence on how to modulate pain-induced reduction in corticomotor excitability in the acute phase of muscle pain by action observation and motor imagery. This contributes to our understanding of the malleability of the motor system, and that an easily delivered task such as action observation combined with motor imagery is warranted in future research in managing musculoskeletal pain.

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Ph.D. lecture by Dennis Boye Larsen Friday 16 August 2019



This thesis is based on Dennis Boye Larsen's research work at:



To fulfill the requirements for the Ph.D. degree, Dennis Boye Larsen has submitted the thesis: Probing and modulating pain-induced corticomotor excitability reduction by engaging premotor cortex activity in humans, 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 Catherine Mercier
University Laval
Canada

Reader Michael J. Grey University of East Anglia UK

Chairman:
Associate Professor Andrew J. T. Stevenson
Aalborg University
Denmark

Moderator:
Associate Professor Shellie Boudreau
Aalborg University
Denmark

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

Friday 16 August 2019 at 13:00 Aalborg University – Room D2-106 Fredrik Bajers Vej 7 D2 9220 Aalborg East

Program for Ph.D. lecture on

Friday 16 August 2019 by

Dennis Boye Larsen

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| Chairman: Moderator: | Associate Professor Andrew J. T. Stevenson Associate Professor Shellie Boudreau |
|----------------------|--|
| 13.00 | Opening by the Moderator |
| 13.05 | Ph.D. lecture by Dennis Boye Larsen |
| 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