

Exploration of long-term potentiation (LTP)-like pain amplification and conditioned pain modulation (CPM) on pain-LTP in humans

by

Weiwei Xia

Chronic pain is a worldwide health problem. It involves an imbalance of pain inhibition and pain facilitation systems. Spinal nociceptive long-term potentiation (LTP) induced by high frequency conditioning electrical stimulation (CES) has been considered to be a potential mechanism underlying central sensitization demonstrated as hyperalgesia and allodynia in clinical patients. However, it is still questionable on the biological significance of high frequency CES paradigm as actually the low frequency discharging of nociceptors plays a critical role inducing central sensitization. Conditioned pain modulation (CPM) is a kind of endogenous pain inhibitory modulation. The study of the counteraction between CPM and pain facilitation are crucial to understand the role of endogenous pain inhibition in preventing LTP-like pain amplification in humans.

The aims of the present Ph.D. project were to: investigate the different CES paradigms to induce pain LTP in healthy humans in order to find a paradigm more like inflammatory/neuropathic pain conditions (study I); show the reliability of the corresponding measurements indicating LTP-like pain amplification and inflammation responses, and calculate sample sizes for potential drug testing studies (study II); assess the pain inhibitory effect of CPM on the development of pain LTP (study III).

In study I, 10 Hz CES induced heterotopic pain amplification like the high frequency (100, 200 Hz) CES but associated a less pain experience during the CES process, however, homotopic pain amplification were absent in all paradigms. In study II, the test-retest reliability results for 10 Hz CES paradigm showed that superficial blood flow is reliable indicator for neurogenic inflammation response; painful pinprick and light stroking stimuli are reliable indicators for measuring heterotopic perception amplification. In study III, CPM induced by cold pressor conditioning stimulus inhibited the development of heterotopic perception amplification to non painful mechanical stimuli but no effect was observed to heterotopic pinprick painful stimulus, homotopic electrical stimuli and peripheral inflammation responses.

In conclusion, the present work has provided more information on pain LTP induction in healthy human models and recommends 10 Hz CES paradigm in potential analgesic studies because of the biological significance. The endogenous pain inhibition effect of CPM may play a role in modulating LTP-like pain amplificatory process.

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Ph.D. lecture

by

Weiwei Xia

Wednesday 5 October 2016



DEPARTMENT OF HEALTH SCIENCE AND TECHNOLOGY
AALBORG UNIVERSITY

This thesis is based on Weiwei Xia's research work at:



SMT
Department of Health Science and Technology
Aalborg University
Denmark

Program for Ph.D. lecture on

Wednesday 5 October 2016

by

Weiwei Xia

To fulfill the requirements for the Ph.D. degree, Weiwei Xia has submitted the thesis: Exploration of long-term potentiation (LTP)-like pain amplification and conditioned pain modulation (CPM) on pain-LTP 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:

Dr. Thomas Klein
Pharmacological and Translational Science
Mundipharma Research GmbH & Co. KG
Germany

Professor Nanna Brix Finnerup
Danish Pain Research Center, Aarhus University
Denmark

Chairman:
Associate Professor Laura Petrini
SMI, Aalborg University
Denmark

Moderator:
Professor Ole Kæseler Andersen
SMI, Aalborg University
Denmark

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

Wednesday 5 October 2016 at 13:00
Aalborg University – Room D2-106
Fredrik Bajers Vej 7 D2
9220 Aalborg East

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Chairman: Associate Professor Laura Petrini
Moderator: Professor Ole Kæseler Andersen

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| 13.00 | Opening by the Moderator |
| 13.05 | PhD lecture by Weiwei Xia |
| 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