

# Studies on itch and sensitization for itch in humans

by

**Hjalte Holm Andersen**

Chronic itch, like chronic pain, is a common clinical problem that is associated with a markedly reduced quality of life for the affected patients. Itch is major symptom in several of the most prevalent dermatologic diseases (e.g., atopic eczema, psoriasis and urticaria) but it also occurs in a variety of non-cutaneous conditions (e.g., neuropathic and cholestatic itch). Chronic itch is often difficult to treat, has a detrimental impact on sleep quality as well as attention, and is consistently linked to increased rates of anxiety and depression.

Mechanistically, itch and pain are complexly entwined. While analgesic opioids facilitate itch, scratch-induced pain can abolish itch, thus suggesting an antagonistic relationship between the two sensations. At the same time, however, there is substantial overlap between pruritic and algogenic peripheral mediators as well as receptors, and strikingly similar patterns of neuronal sensitization for itch and pain have been documented. Recent evidence suggests that itch arise from at least two distinct peripheral cutaneous prurceptive subpopulations, which are subsets of a larger population of neurons that also respond to various noxious stimuli (nociceptors). Thus much of the psychophysical research methodology developed in the pain field can be converted and used to increase our understanding itch – and in particular to explore the sensory neuronal features that are unique to itch.

Within this context, the aim of this PhD-project was to explore itch as a somatosensory modality using histaminergic and non-histaminergic models of itch and itch sensitization in humans for three purposes: 1) to assess itch topography and itch sensitization in healthy controls (first study), 2) to evaluate the antipruritic effect of capsaicin-induced epidermal nerve-ablation in a mechanistic proof-of-concept study (second study), 3) To explore potential pathway-specific itch and cutaneous pain sensitization in patients with chronic itch due to atopic dermatitis (third study).

Results from the first study suggested that von Frey filaments above the tactile detection range and below the pain threshold can be used to assess itch sensitization (hyperknesis) and that there is considerable heterogeneity in chemical and mechanically evoked itch sensitivity between spinal versus trigeminal innervated areas. Results from the second study demonstrated profound antipruritic and anti-hyperknetic effects of high-concentration capsaicin pretreatment and suggested that the two most commonly applied models of itch in humans rely on TRPV1-positive cutaneous fibers. Finally, the third study revealed pathway-specific non-histaminergic itch sensitization as well as mechano-nociceptive sensitization occurring both intra- and extra-lesionally in patients with atopic dermatitis.

In conclusion, histaminergic and non-histaminergic models of itch and itch sensitization are useful tools in both human experimental and clinical itch research towards improved understanding of the mechanisms behind acute and chronic itch.

# Studies on itch and sensitization for itch in humans

**Ph.D. lecture**

by

**Hjalte Holm Andersen**

**Friday 15 December 2017**



**DEPARTMENT OF HEALTH SCIENCE AND TECHNOLOGY**  
AALBORG UNIVERSITY

This thesis is based on Hjalte Holm Andersen's research work at:



**SMI**  
**Department of Health Science and Technology**  
**Aalborg University**  
**Denmark**

To fulfill the requirements for the Ph.D. degree, Hjalte Holm Andersen has submitted the thesis: Studies on itch and sensitization for itch 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 Earl Carstens**  
**University of California**  
**USA**

**Professor Martin Metz**  
**Berlin University of Medicine**  
**Germany**

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

**Moderator:**  
**Professor Lars Arendt-Nielsen**  
**Aalborg University**  
**Denmark**

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

**Friday 15 December 2017 at 13:00**  
**Aalborg University – Room D2-106**  
**Fredrik Bajers Vej 7 D2**  
**9220 Aalborg East**

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

**Friday 15 December 2017**

**by**

**Hjalte Holm Andersen**

Studies on itch and sensitization for itch in humans

Chairman: Associate Professor Anne Estrup Olesen

Moderator: Professor Lars Arendt-Nielsen

13.00 Opening by the Moderator

13.05 Ph.D. lecture by Hjalte Holm Andersen

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