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Onsdagen den 20:e maj kl. 14:30 – 16:00 konferensrummet, Intensiv- och perioperativ vård, arbetsavdelningen, Centralblocket, hisshall B, plan 6, Skånes universitetssjukhus, Lund

Main supervisor: Professor Mikael Bodelsson

Co-supervisors: Docent Niklas Mattsson, Docent Agneta Montgomery

Reviewers: Professor Eva Kosek (Karolinska institutet), Docent Gunnar Skagerberg (Lunds universitet)
Title: Neuroimmune signaling in persistent pain and the sleep-pain interface

Background: Pain and sleep interact bidirectionally; pain may lead to disturbed sleep, and sleep disturbance can cause pain and hyperalgesia. Preoperative sleep disturbance appears to be associated with poorer acute and long-term postoperative pain control. Given the salient links between sleep and pain, treatments that target sleep may have salutary effects not only on sleep itself, but also on pain perception.

Neuroinflammation is implicated in the development and maintenance of persistent pain states, but there is limited data linking cerebrospinal fluid (CSF) inflammatory mediators with neurophysiological pain processes in humans.

Aims and methods: I) To evaluate whether perioperative addition of a sleep-promoting medication would be associated with self-reported pain and analgesic consumption during the immediate postoperative period, we conducted a systematic review. Fourteen studies were included (9 melatonin, 5 zolpidem; 921 patients).

II) To examine whether there are coherent changes in CSF inflammation associated with clinically relevant objective measures of persistent pain we performed a prospective observational study. CSF inflammatory mediators were compared between patients with osteoarthritis (OA) who were undergoing total hip arthroplasty due to disabling pain symptoms (n=52) and pain-free controls (n=30). In OA patients detailed quantitative sensory testing was conducted.

Results: Our first study suggests that addition of a sleep-promoting pharmacological agent in the perioperative period may confer improved pain control during the immediate postoperative period. However, evidence is weak, results from both melatonin and zolpidem trials are mixed, and the quality of included studies varies considerably.

In the second study, compared to controls, OA patients had higher CSF levels of interleukin 8 (P=0.002), intercellular adhesion molecule 1 (P=0.007) and vascular cell adhesion molecule (P=0.006). Multiple logistic regression models showed that increased CSF Flt-1 was associated with central sensitization, assessed by remote site pressure pain detection threshold and peripheral venous cannulation pain, and MCP-1 with temporal summation in the area of maximum pain.
**Significance:** Our results mandate the need for increased research focus on the perioperative sleep-pain interface.

Pain phenotype may be influenced by specific CSF neuroinflammatory profiles. Targeting of mediators and pathways underlying neuroinflammation might provide improved pain control for patients suffering from persistent pain.

**Articles:**
