LPS increases pain sensitivity by decreasing pain inhibition and enhancing interoceptive processing

B. Karshikoff, K.B. Jensen, M. Ingvar, E. Kosek, G. Kalpouzos, A. Soop, C. Olgart Höglund, M. Lekander, J. Axelsson

Conclusion

Our results support a connection between an experimentally induced sickness response and decreased capacity to regulate pain.

This effect was more pronounced in women.

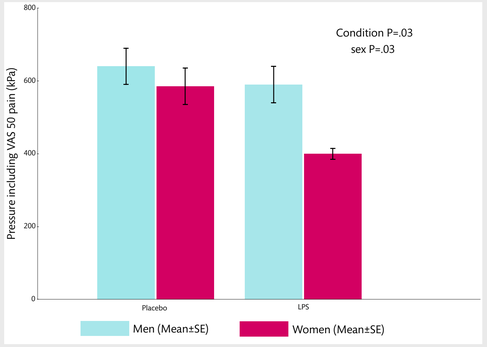
Our findings may provide a better understanding of how experimental sickness research relates to neural disturbances in chronic pain patients.

Aim

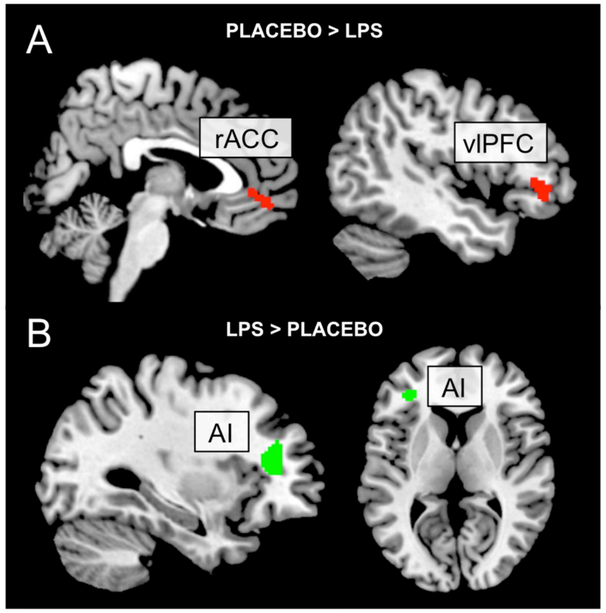
We have previously shown that lipopolysaccharide (LPS)-stimulation increases pain sensitivity in humans. Here we investigated the neural substrates underlying these effects, using an fMRI paradigm previously employed in a clinical population.

Method

Fifty-one participants (29 women) were injected with 0.6 ng/kg LPS (30, 18 women) or saline (21, 11 women). The subjects were tested with a pressure pain fMRI paradigm on the right thumb two hours after injection. The pressure was individually calibrated for 50 on a visual analogue scale (VAS 1-100mm).



The LPS group was significantly more sensitive to pressure pain than the placebo group, and women were more pain sensitive than men. There was no significant interaction effect between sex and condition.



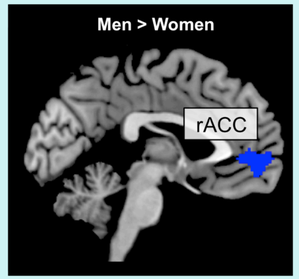
A) Sagittal representation of lower activity in the rACC and vlPFC, key areas for descending pain regulation, in LPS-treated subjects compared to placebo. B) Sagittal and axial representation of left (contralateral to pain stimulus) anterior insula, where LPS-treated subjects had higher activity compared to placebo. *RED indicates decreased activity, GREEN increased activity.*

Main findings

The LPS group became more pain sensitive during immune activation, and the increased pain sensitivity was paralleled by decreased activity in the ventrolateral prefrontal cortex (vlPFC) and the rostral anterior cingulate cortex (rACC), areas involved in endogenous pain inhibition. The LPS group also had higher activity in the anterior insular cortex, an area underpinning affective pain processing and interoception.

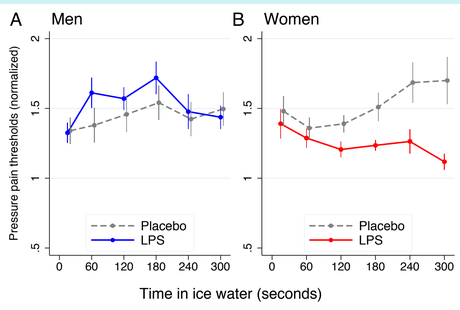
Sex differences:

Women displayed an overall reduced rACC activity compared to men, which may have rendered women less resilient to immune provocation. This may explain previously demonstrated sex differences in LPS-induced pain sensitivity and descending pain modulation in behavioral measures.



Male subjects had a significantly greater activation of the rACC compared to women during evoked pain (men > women), across both the LPS and placebo groups. The rACC is believed to be a key node of the descending pain inhibitory network.

In a previous study by our group*, women showed impaired descending pain inhibition in the LPS condition compared to the female placebo group, as measured with conditioned pain modulation. This effect was not seen in men.



I am currently studying the neural substrates of sickness behavior, and individual differences in the vulnerability to inflammatory effects.

The study was supported by: The Osher Center for Integrative Medicine, The Center for Allergy Research, Swedish Heart-Lung Foundation, Swedish Council for Working Life and Social Research, Hedlunds Stiftelse, The Swedish Society for Medicine, The National board of Health and Welfare and Stockholm Stress Center.

Modality and sex differences in pain sensitivity during human endotoxemia. Karshikoff B, Lekander M, Soop A, Lindstedt F, Ingvar M, Kosek E, Olgart Höglund C, Axelsson J. Brain Behav Immun. 2014 Dec 5. pii: S0889- 1591(14)00558-3.

Karolinska Institutet
Bianka Karshikoff, PhD
Dept. of Clinical Neuroscience
Div. of Psychology
Email: bianka.karshikoff@ki.se
Web: *www.ki.se/psychology*

Karolinska Institutet