

Brain Mechanisms of Placebo Analgesia

Results:

Four studies investigated whether negative emotions (stress, anxiety, fear) reduced or abolished placebo analgesia. Several studies have shown less placebo analgesia in females compared to males, which could be due to more negative emotions in females. Study 1 showed that higher fear of pain reduced subjective and electrophysiological placebo analgesic responses. Sensation of pain can be inhibited by applying a second noxious stimulus elsewhere on the body. This procedure activates endogenous pain inhibitory mechanisms. Study 2 investigated whether expectations modulated this effect on tonic pain. Negative information about the effect of conditioning stimulation induced stress in females, and higher fear of pain was associated with increased stress during conditioning stimulation in females. In Study 3 fear was induced by the anticipation of electric shock to investigate whether fear reduced placebo analgesia. Induced fear abolished placebo analgesia, and this was strongest in subjects with high scores on measures of fear. Study 4 used functional resonance imaging (fMRI). It was hypothesized that differences in placebo responding between males and females should be correlated with larger placebo-related neural responses in the thalamus, the ACC and the insular cortex in males compared to females. During anticipation of pain, females had higher activation in the left cerebellum and the left hippocampus compared to males, areas that in previous research have been implicated in emotional processing. In sum, the four studies indicate that placebo analgesia is stronger in males than in females. This is due to more fear and anxiety in females in anticipation of the painful stimulation.

Published work:

Lyby, P.S., Aslaksen, P.M. & Flaten, M.A. (2011). Variability in placebo analgesia and the role of fear of pain - an ERP study. *Pain*, 152(10), 2405-2412.

doi.org/10.1016/j.pain.2011.07.010

Meissner, K., Colloca, L., Bingel, U., Wager, T.D., Watson, A. & Flaten, M.A. (2011). The placebo effect: advances from different methodological approaches. *Journal of Neuroscience*, 31(45), 16117-16124. DOI:10.1523/JNEUROSCI.4099-11.2011

Bjørkedal, E. & Flaten, M.A. (2012). Expectations of increased or decreased pain explain the effect of conditioned pain modulation in females. *Journal of Pain Research*, 5, 289-300.

Lyby, P.S., Åsli, O., Forsberg, J.T., & Flaten, M.A. (2012). Induced fear reduces the effectiveness of a placebo intervention on pain. *Pain*, 153(5), 1114-1121.

dx.doi.org/10.1016/j.pain.2012.02.042

Submitted

Vambheim, S.M. & Flaten, M.A. Sex differences in the placebo effect.

Aslaksen, P.M., Vambheim, S.M., Vangberg, T.R. (submitted). Imaging sex differences in placebo analgesia

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Books

Colloca, L., Flaten, M.A., & Meissner, K. (2013). *Placebo and Pain. From Bench to Bedside*. Elsevier (27 ch., 312 p). ISBN: 9780123979285.

In preparation

Flaten, M.A. & Al'Absi, M. (in prep.). *The Neuroscience of Pain, Stress, and Emotion: Psychological and Clinical Implications*. Elsevier.

Chapters in books

Flaten, M.A. (2011). Placeboeffekten. In F. Svartdal (Ed.), *Psykologi: I Praksis*. Oslo: AdNotam/Gyldendal, s. 45-49.

Flaten, M.A. & Al'Absi, M. (2012). Placebo and placebo effect. *Encyclopedia of Behavioral Medicine*. New York: Springer. 1497-1499.

Flaten, M.A. (2012). Nocebo and nocebo effect. *Encyclopedia of Behavioral Medicine*. New York: Springer. 1340-1341.

Flaten, M.A., Meissner, K., & Colloca, L. (2013). Methodological issues in research on placebo analgesia. Colloca, L., Flaten, M.A., & Meissner, K. *Placebo and Pain*. Elsevier, p. 149-157.

Flaten, M.A., Aslaksen, P.M., & Lyby, P.S. (2013). The role of positive and negative emotions in placebo analgesia. In Colloca, L., Flaten, M.A., & Meissner, K. *Placebo and Pain*. Elsevier, p. 73-81.

Flaten, M.A. (2013). Antagonistic responses, homeostasis, and the placebo effect. In Colloca, L., Flaten, M.A., & Meissner, K. *Placebo and Pain*. Elsevier, p. 103-113.

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Flaten, M.A. Pain related negative emotions and placebo analgesia. In *Handbook of Experimental Pharmacology*. Springer: New York.

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