

The relation of mind to body. Psychophysiological studies of the placebo effect

Results:

Placebo analgesia is the reduction in pain after administration of a placebo with information that it will reduce pain. We have shown that placebo analgesia can be objectively recorded by physiological measures (electromyography, heart rate variability, and event-related potentials (ERP)). Reduced ERPs indicate that placebos activate descending pain inhibitory pathways. The placebo response, or more precisely, the expectation of drug effects, can add to the effect of the drug. There is some evidence that placebo effects are strongest when expectations are reinforced by administration of an active drug. Of special importance to the present project was the investigation of the role of stress and negative emotions in placebo analgesia. Our hypothesis was that the placebo reduced stress and nervousness, and thereby reduced pain. Fear of pain was positively related to stress both during pain and in the anticipation of pain, and negatively related to placebo analgesia. However, other factors also contribute to the placebo analgesia. The present findings suggest that decreased stress may strengthen the placebo response. This may have important clinical consequences, as stress reduction could aid in treatment of pain. Furthermore, male subjects responded with lower stress after placebo medication, and larger placebo responses. These findings suggest that males respond differently to verbal placebo information compared to females. It is not known whether this is due to more effective pain inhibitory mechanisms in males, or to cognitive factors. In sum, there is a contribution of reduced stress to placebo analgesia, and for reasons unknown this effect is larger in males.

Published work:

Proceedings and meetings:

2007

- Aslaksen, P.M. & Flaten, M.A. Expectancy of pain relief reduces stress that mediates placebo analgesia. Meeting of the American Psychosomatic Society, Budapest, 7-10/3.
- Flaten, M.A. The role of gender in pain and placebo analgesia. Meeting of the American Psychosomatic Society, Budapest, 7-10/3.
- Aslaksen, P.M. & Flaten, M.A. Stress and placebo analgesia. Meeting of the American Pain Society, Washington DC, 2-5/5.
- Flaten, M.A. Placebo effekten – finnes den? Lecture, Department of Anaesthesiology, University Hospital of North Norway, 1/6.
- Flaten, M.A. The role of gender in experimental placebo research. Invited symposium, the 10th European Congress of Psychology, Praha, Checkia, 3-5/7.
- Flaten, M.A. Placebo analgesia and gender. Invited lecture, Charité Universitätsmedizin Berlin, Berlin, Germany, 6/7.
- Flaten, M.A., Aslaksen, P., Bjørkedal, E., & Lyby, P.S. The DNIC procedure reduces pain and cold sensation. World Institute of Pain Meeting, Budapest, 25-28/9.

- Aslaksen, P. & Flaten, M.A. Heart rate variability and placebo analgesia. World Institute of Pain Meeting, Budapest, 25-28/9.
- Bjørkedal, E. & Flaten, M.A. A review of active placebo. World Institute of Pain Meeting, Budapest, 25-28/9.
- Lyby, P.S., Aslaksen, P. & Flaten, M.A. The relation of fear of pain to placebo analgesia. World Institute of Pain Meeting, Budapest, 25-28/9.
- Aslaksen, P. & Flaten, M.A. Placebo analgesia related to reduced negative emotions. Meeting of the Society for Psychophysiological Research, Savannah, GA, USA, 17-21/10.
- Flaten, M.A. Doping og placebo i idretten. [Doping and placebo in sports]. Verdt å vite, NRK, [The Norwegian Broadcasting Corporation], 8/11.
- Aslaksen, P. & Flaten, M.A. The effect of subject and experimenter gender on pain and placebo analgesia. Symposium on Mechanisms of Placebo/Nocebo Responses, München, 28-30/11.
- Flaten, M.A. & Aslaksen, P. Emotional factors in placebo analgesia. Symposium on Mechanisms of Placebo/Nocebo Responses, München, 28-30/11.

2008

- Flaten, M.A. Om placebo-analgesi: Introduksjon og forskning ved UiT. Neurology Dept., University Hospital of North Norway (UNN), 3/1.
- Flaten, M.A. Betydinga av placebo analgesi. Norwegian Association for the study of Pain, Rikshospitalet, Oslo, 10/1.
- Flaten, M.A. Om placebo-effekten og korleis den kan studerast. Institutt for Biologisk og Medisinsk Psykologi, University of Bergen, 23.1.
- Flaten, M.A. Smerte og placebo analgesi. The Pain Clinic, St. Olavs Sykehus, Trondheim, 25/1.
- Flaten, M.A. Smerte og kjønn. Schrødingers Katt, Norwegian Broadcasting Cooperation, 14/2.
- Aslaksen, P.M. & Flaten, M.A. The relation of stress and heart rate variability to placebo analgesia. *American Pain Society* meeting, Tampa, FL, USA, 7-10/5.
- Flaten, M.A. The placebo effect exists, but does it have any consequences for health? Invited lecture at Tulsa University, Tulsa, OK, USA, 13/5.
- Aslaksen, P.M., Lyby, P.S., Bjørkedal, E. & Flaten, M.A. The effect of gender on placebo analgesia after classical conditioning. Meeting of the *International Association for the Study of Pain*, Glasgow, 17-22/8.
- Bjørkedal, E. & Flaten, M.A. A review of the effect of active placebo compared to placebo. Meeting of the *International Association for the Study of Pain*, Glasgow, 17-22/8.
- Lyby, P.S., Bjørkedal, E., Aslaksen, P.M., & Flaten, M.A. Is there a placebo responder? Meeting of the *International Association for the Study of Pain*, Glasgow, 17-22/8.
- Flaten, M.A. The role of gender in placebo analgesia. Meeting of the *International College of Behavioral Medicine*, Tokyo, Japan, 27-30/8.
- Flaten, M.A. Kva er placebo-effekten? *Norsk Psykiatrisk Forening*, Oslo, 17/9.
- Aslaksen, P.M. & Flaten, M.A. An ERP study of placebo analgesia. Meeting of the *Society for Psychophysiological Research*, Austin, TX, USA, 1-5/10.
- Åsli, O. & Flaten, M.A. Fear potentiated startle after delay and trace aversive classical conditioning. Meeting of the *Society for Psychophysiological Research*, Austin, TX, USA, 1-5/10.
- Flaten, M.A. The psychology of pain. Invitert foredrag ved Institutt for Klinisk Odontologi, UiT, 15/10.
- Flaten, M.A. Om placebo- og nocebo-effektane. Fagdag ved *Klinisk Forskningsenter*, UNN, Tromsø, 5/12.

2009

- Flaten, M.A. Neurobiology of placebo analgesia. Annual meeting of *the Norwegian Association for the Study of Pain*, Rikshospitalet, Oslo, 8-9/1.
- Aslaksen, P.M. & Flaten, M.A. Event-related potentials to painful stimuli are reduced during placebo analgesia. Meeting of *the American Psychosomatic Society*, Chicago, IL, USA, 4-7/3.
- Flaten, M.A. The role of experimenter gender in placebo analgesia. Meeting of *Deutsche Psychosomatische Gesellschaft*, Mainz, Germany, 18-21/3.
- Aslaksen, P.M., & Flaten, M.A. A methodological problem in pain research and how to deal with it. *11th European Congress of Psychology*, Oslo, 7-10/7.
- Flaten, M.A. & Enck, P. Symposium on the placebo effect across different response systems. *11th European Congress of Psychology*, Oslo, 7-10/7.
- Flaten, M.A. Truth and deception in the study of pain. University on Saturday, Tromsø, 19/9.
- Flaten, M.A. How do we know that the placebo effect exists? Invited lecture at Wake Forest University, Winston-Salem, NC, USA, 14/10.
- Bjørkedal, E. & Flaten, M.A. Does placebo analgesia modulate diffuse noxious inhibitory control. Meeting of *the Society for Neuroscience*, Chicago, IL, USA, 17-21/10.
- Lyby, P.S., Aslaksen, P.M., Vambheim, S.M., Bystad, M., Thorvaldsen, J., Solbakken, L., Nermo, T., & Flaten, M.A. Placebo analgesia: Reduced event-related potentials to painful stimulation related to decrease in stress. Meeting of *the Society for Neuroscience*, Chicago, IL, USA, 17-21/10.
- Aslaksen, P.M., Lyby, P.S., Vambheim, S.M., Bystad, M., Thorvaldsen, J., Solbakken, L., & Flaten, M.A. Objective measurement of placebo analgesia by event-related potentials. Meeting of *the Society for Psychophysiological Research*, Berlin, 21-25/10.
- Bjørkedal, E. & Flaten, M.A. The role of diffuse noxious inhibitory control in placebo analgesia. Similar mechanisms? Meeting of *the Society for Psychophysiological Research*, Berlin, 21-25/10.
- Flaten, M.A. Is the placebo effect underestimated in health care? Invited lecture at the 30- years anniversary, *Sogn og Fjordane College*, Førde, 5-6/11.
- Flaten, M.A. Negative affect as a mediator of placebo analgesia. Placebo conference, München, Germany, 27-28/11.

2010

- Flaten, M.A. Kva er det som verkar i behandling? (What is the active ingredient in treatment?) *Academia Borealis*, Tromsø, 11/2.
- Flaten, M.A. Placebo analgesia. A central topic in psychosomatic medicine. Meeting of *the American Psychosomatic Society*, Portland, OR, 10-14/3.
- Flaten, M.A. Placebo analgesia. Psychophysiological Mechanisms. *8th Bial Symposium*, Porto, Portugal, 7-10/4.
- Flaten, M.A. Mechanisms in placebo analgesic responding. Meeting of *the American Pain Society*, Baltimore, MD, 6-8/5.

Full journal articles

- Aslaksen, P., & Flaten, M. (2008). The roles of physiological and subjective stress in the effectiveness of a placebo on experimentally induced pain. *Psychosomatic Medicine*, 70(7), 811-818. doi: 10.1097/PSY.0b013e31818105ed

- Flaten, M. A. (2009). Drug effects: agonistic and antagonistic processes. *Scandinavian Journal of Psychology*, 50(6), 652-659. doi: 10.1111/j.1467-9450.2009.00776.x
- Åsli, O., Kulvedrøsten, S., Solbakken, L., & Flaten, M. (2009). Fear potentiated startle at short intervals following conditioned stimulus onset during delay but not trace conditioning. *Psychophysiology*, 46(4), 880-888. doi: 10.1111/j.1469-8986.2009.00809.x
- Lyby, P., Aslaksen, P., & Flaten, M. (2010). Is fear of pain related to placebo analgesia? *Journal of Psychosomatic Research*, 68(4), 369-377. doi: 10.1016/j.jpsychores.2009.10.009
- Aslaksen, P., Vambheim, S., Bystad, M., & Flaten, M. (2011). Gender differences in placebo analgesia: event-related potentials and emotional modulation. *Psychosomatic Medicine*, 73(2), 193-199. doi: 10.1097/PSY.0b013e3182080d73
- Flaten, M., Aslaksen, P. M., Lyby, P. S., & Bjørkedal, E. (2011). The relation of emotions to placebo responses. *Philosophical Transactions of the Royal Society B*, 366, 1818–1827. doi:10.1098/rstb.2010.0407
- Bjørkedal, E., & Flaten, M. (2011). Interaction between expectancies and drug effects: an experimental investigation of placebo analgesia with caffeine as an active placebo. *Psychopharmacology*, 215(3), 537-548. doi: 10.1007/s00213-011-2233-4
- Lyby, P., Aslaksen, P., & Flaten, M. (2011). Variability in placebo analgesia and the role of fear of pain—an ERP study. *Pain*, 152(10), 2405-2412. doi: 10.1016/j.pain.2011.07.010
- Bjørkedal, E., & Flaten, M. (2012). Expectations of increased and decreased pain explain the effect of conditioned pain modulation in females. *Journal of Pain Research*, 5, 289-300. doi: 10.2147/JPR.S33559

Chapters in books

- Flaten, M. (2010). Expectations of pharmacological treatment and their role in adjustment. In D. A. Powell (Ed.), *CNS mechanisms involved in learned autonomic adjustments* (pp. 115-131). New York, NY: Research Signpost.

Areas of interest:

Placebo analgesia, psychopharmacology, pain, event related potentials.

Researchers' Contacts:

Magne Arve Flaten,
Department of Psychology,
Dragvoll, Norwegian University of Science and Technology,
N-7491 TRONDHEIM, Norway
Mail: magne.a.flaten@svt.ntnu.no
Phone: +47-41047378