The effect of oxytocin administration on eye contact and trust between patient and physician – a preliminary analysis

Authors
Chiara Jongerius (AmsterdamUMC - Netherlands), Marij Hillen (AmsterdamUMC - Netherlands), Hans Romijn (AmsterdamUMC - Netherlands), Ellen Smets (AmsterdamUMC - Netherlands), Daniel Quintana (Oslo University Hospital - Norway)

Presenting author
Chiara Jongerius

Oxytocin is a hormone thought to be involved in eye contact and trust between humans. Oxytocin administration has shown to increase the levels of eye contact and trust. Both eye contact and trust are important for relationship building between patient and physician, which is essential for quality of care. However, methodological shortcomings, such as underpowered studies, have led to inconclusive evidence about the effects of oxytocin administration on trust and eye contact. We aimed to examine how oxytocin affects the patient-physician level of eye contact and trust. We conducted a randomized crossover design, with oxytocin administered intranasally. During the experiment, participants looked at a video of a physician giving information in a Skype-setting. The setting created the illusion of a real online consultation. Participants’ gaze towards the physician's eyes was measured using eye-tracking and trust was measured using a questionnaire. We analysed a sub-sample of 40 male patients. These unblinded results revealed that participants gazed at the physician's eyes 35% of the time, compared to other regions of the face, but the level of eye contact was not significantly associated to their trust in the physician (P=.667). Our findings provide a better understanding regarding the mechanisms of relationship building between patient and physician. The results support future studies on a more trusting relation between patient and physician, ultimately improving the quality of care.
A neurophysiological characterization of nocebo-augmented pain: An EEG study

Authors
Joseph Blythe (Leiden University - Netherlands), Mia Thomaidou (Leiden University - Netherlands), Simon Houtman (Vrije Universiteit Amsterdam - Netherlands), Dieuwke Veldhuijzen (Leiden University - Netherlands), Antoinette van Laarhoven (Leiden University - Netherlands), Andrea Evers (Leiden University - Netherlands)

Presenting author
Joseph Blythe

Nocebo hyperalgesia refers to increases in perceived pain, resulting from negative treatment expectations. We aimed to identify electrophysiological biomarkers of nocebo-augmented pain. Nocebo hyperalgesia was induced in 36 healthy humans of either sex through a combination of classical conditioning and negative suggestions. In a baseline phase, participants received high thermal pain stimulations. In an acquisition phase, participants learned to associate an inert gel applied to their forearm with high pain, relative to a moderate intensity control stimulus administered without gel. In the evocation phase, nocebo and control stimuli were paired with moderate pain to measure nocebo responses. Electroencephalography was recorded during rest pre- and post-nocebo acquisition and during baseline, acquisition, and evocation. Our primary hypothesis of pre- to post-acquisition decreases in alpha power was not confirmed. Nevertheless, conditioned nocebo hyperalgesia led to widespread pre- to post-acquisition increases in long-range temporal correlations, with changes in the gamma-band being negatively associated with nocebo magnitudes. Individuals with strong resting-state long-range temporal correlations showed larger nocebo responses than those with weaker long-range temporal correlations. Compared to baseline, alpha power was higher during nocebo-augmented pain. Nocebo acquisition trials were characterized by reduced alpha power. These findings support nocebo learning theories relating to the complexity of brain activity and highlight a role of nocebo-induced cognitive processing at the electrophysiological level. This study provides novel insights into neural underpinnings of nocebo hyperalgesia, a phenomenon able to greatly impact the experience of pain.
**Induction of nocebo effects on cowhage-evoked itch and generalization to mechanical stimulation**

**Authors**
Weng, L.L (Health, Medical and Neuropsychology Unit, Faculty of Social and Behavioral Sciences, Leiden University - Netherlands), van Laarhoven, A.I.M. (Health, Medical and Neuropsychology Unit, Faculty of Social and Behavioral Sciences, Leiden University - Netherlands), Peerdeman, K.J. (Health, Medical and Neuropsychology Unit, Faculty of Social and Behavioral Sciences, Leiden University - Netherlands), Evers, A.W.M. (Health, Medical and Neuropsychology Unit, Faculty of Social and Behavioral Sciences, Leiden University - Netherlands)

**Presenting author**
Weng, L.L

Introduction: Nocebo effects can increase itch caused by negative expectations and can generalize from one itch stimulus to another itch stimulus. The aims of the current study are to investigate whether nocebo effects on itch evoked by cowhage (itchy particles from a plant) can be induced by verbal suggestion and can generalize to mechanical itch and mechanical touch (induced by von Frey monofilaments) in healthy participants. Methods: Forty-four participants were included in this within-subject design. Participants received a verbal suggestion that an experimental solution will increase cowhage-evoked itch and a control solution will not affect itch. Subsequently, cowhage spicules, mechanical itch, and mechanical touch were applied on the skin twice, once after the experimental condition and once after the control condition. Itch ratings were compared between conditions. Results: Mean itch evoked by cowhage was significant higher in the experimental condition (mean (SD) = 2.13 (2.03)) compared to the control condition (mean (SD) = 1.35 (1.49)) (t(43) = 2.16, p < 0.05, d = 0.33). Mean itch evoked by mechanical itch and mechanical touch were significant higher in the experimental condition (median (IQR) = 0.11 (0.03-0.21), median (IQR) = 0.13 (0.05-0.32)) compared to the control condition (median (IQR) = 0.10 (0.02-0.16), median (IQR) = 0.10 (0.03-0.26)) (z = -2.03, p < 0.05, r = 0.30; z = -2.35, p < 0.05, r = 0.36, respectively). Conclusion: Nocebo effects on cowhage-evoked itch can be induced by verbal suggestion and can generalize to itch evoked by mechanical stimulation.
Fear as a facilitator of nocebo hyperalgesia: Higher pain predicts larger nocebo magnitudes.

Authors
Mia A Thomaidou (Leiden University - Netherlands), Dieuwke S Veldhuijzen (Leiden University - Netherlands), Ann Meulders (Leiden University - Netherlands), Andrea W M Evers (Leiden University - Netherlands)

Presenting author
Mia A Thomaidou

Introduction: Nocebo hyperalgesia refers to increases in perceived pain that putatively result from negative expectations (e.g., about an inert treatment). The precise cognitive-emotional factors contributing to the development of nocebo effects are poorly understood. Methods: We aimed to test the effects of experimentally induced fear on the acquisition and extinction of nocebo hyperalgesia in healthy participants (N=72). Acquisition and extinction of nocebo hyperalgesia were compared between a group receiving standard nocebo conditioning (Control group) and two groups receiving distinct fear inductions: high intensity of pain stimulations (High-pain group) or a threat manipulation (High-threat group). During nocebo acquisition, the Control and High-threat groups were administered moderate thermal-pain stimulations paired with sham electrical stimulation (nocebo trials), whereas high pain intensity was administered to the High-pain group. Throughout extinction, equivalent pain intensities were administered. Pain-related fear was measured by eyeblink startle electromyography and self-report. Results: Hyperalgesia occurred in all groups. Nocebo effects were significantly larger in the High-pain group compared to the Control group. This effect was mediated by fear, but not by fear-potentiated startle. Groups did not differ in extinction rate. However, only the High-pain group maintained significant nocebo responses at the end of extinction. Anticipatory pain-related fear induced via a threat manipulation did not amplify nocebo hyperalgesia. Conclusion: These findings suggest that fear of high pain may be a key contributor to the amplification of nocebo hyperalgesia, only when high pain is experienced and not when it is merely anticipated.