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Can Oxytocin influence Placebo and Nocebo effects in Pain?

A.Skvortsova^{1,2}, D.S.Veldhuijzen^{1,2}, H. van Middendorp^{1,2}, O.van den Bergh³,
L.Colloca⁴, A.M.W.Evers^{1,2,5}

¹Department of Health, Medical and Neuropsychology, Leiden University, the Netherlands, ²Leiden Institute for Brain and Cognition, the Netherlands, ³KU Leuven – University of Leuven, Belgium, ⁴University of Maryland Leiden, School of Nursing, ⁵Psychiatry Department, Leiden University Medical Center, the Netherlands

Background

Placebo effects are favorable treatment outcomes not due to the treatment mechanism itself while **nocebo effects** are unfavorable treatment outcomes, e.g., side effects of medicines.

Two mechanisms can induce placebo/nocebo effects:

- Expectations (e.g., of improvement)
- Classical conditioning¹

Placebo effects were found for pain², itch³, but size of the effects varies across the studies

Study aim: Investigate whether oxytocin enhances placebo effects and decreases nocebo effects for pain and itch.

Oxytocin is a hypothalamic hormone that might influence placebo effect through its positive effects⁴

Study 1:

Research question: Does oxytocin enhance placebo effects for pain and itch in healthy females?

RCT double blind, 4 groups:

- Oxytocin (24IU) with suggestions
- Oxytocin without suggestions
- Control with suggestions
- Control without suggestions

108 healthy females, 18-35 y.o.

Outcomes:

Subjective pain ratings (0-10 VAS)

Subjective itch ratings (0-10 VAS)

Cold water +4 °C
1 minute
Outcome: pain ratings every 15 seconds

2,5 minutes itch stimulation
Outcome: itch rating every 30 seconds

Positive suggestions: “This spray contains oxytocin. It has been demonstrated in previous studies that oxytocin decreases pain and itch sensitivity. We expect that after receiving oxytocin, you will also experience less pain during the CPT and less itch during the histamine test”.

Study 2:

Research question: Does oxytocin enhance placebo effect and decrease nocebo effect for pain in healthy males?

RCT double blind, 2 groups:

- Oxytocin (40 IU)
- Control

80 healthy males, 18-35 y.o.

Outcomes:

Subjective pain ratings (0-10 VAS)

Suggestions: “Before each stimulus you will see a color on the screen. Green color will indicate that the TENS is in the pain-relieving mode and will decrease your pain levels. Yellow color will indicate that the TENS is off and will not modify your pain levels. Red color will indicate that the TENS is in the pain enhancing mode and will enhance your pain sensitivity”.

Results

Conclusions

- Oxytocin does not influence placebo and nocebo effects neither in females nor in males and with various dosages;
- Positive verbal suggestions induce placebo effect for pain and decrease pain sensitivity;
- Positive verbal suggestion with conditioning induce placebo and nocebo effect and decrease and increase pain sensitivity.

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