CAN VERBAL SUGGESTION ABOLISH THE EFFECT OF CLASSICAL CONDITIONING ON PLACEBO ANALGESIA AND NOCEBO HYPERALGESIA?

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AIMS OF INVESTIGATION

The results of the previous studies showed that classical conditioning followed by a verbal suggestion congruent with conditioning could effectively induce both placebo analgesia and nocebo hyperalgesia. This study aimed to investigate:

- ✔ how a combination of classical conditioning and a verbal suggestion incongruent with that conditioning would influence the placebo and nocebo effects,
- ✔ whether pain expectancy would be involved in shaping placebo and nocebo effects induced this way.

METHODS

Participants

- ✔ 419 healthy volunteers (55% females), age range: 18-35 took part in the experiment; on this poster we present results from 195 participants.
- ✔ Exclusion criteria: (1) age below 18 and over 35, (2) previous participation in a pain study, (3) pain complaints, (4) taking painkillers, (5) using drugs, (6) overusing alcohol, (7) presence or history of any neurological, respiratory, circulatory, musculoskeletal and/or psychiatric disorders.

Stimuli

- ✔ Pain stimuli: electrical square pulses with a duration of 200 μs, delivered to the volar surface of the nondominant forearm. Apparatus: Constant Current High Voltage Stimulator (Digitimer, Welwyn Garden City, England, model DS7AH). The intensity of the stimuli was set up individually for each participant according to a calibration procedure, in which the level of nonpainful tactile sensation (t) and the pain threshold (T) were determined. The intensity of the electrocutaneous stimuli paired with the nocebo stimuli was set at 2.2 x T - 0.2 x t, paired with placebo stimuli was set at 0.8 x T - 0.2 x t mA and the intensity for the control stimuli was set at 1.5T mA.
- ✔ Color stimuli: blue and orange colors presented in full-screen mode on a computer screen (17″, resolution 1280 x 1024) facing the participant at a distance of approximately 50 cm.

Measures

- ✔ Pain intensity and pain expectancy measured on an 11-point numeric rating scale (NRS), ranged from 0 = ‘no pain’ to 10 = ‘the most pain that is tolerable’.

Design and procedures

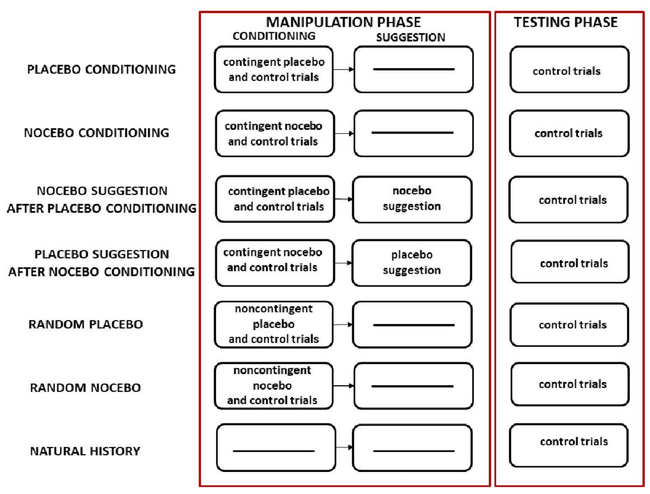

Fig. 1. Study design.

Manipulation phase

- ✔ Participants were randomly assigned to either one of experimental or one of control groups (random placebo, random nocebo, natural history). In the experimental groups, classical conditioning or classical conditioning followed by verbal suggestions were applied. Verbal suggestions were provided after classical conditioning and were incongruent with conditioning.
- ✔ During conditioning one of the two presented colors (e.g. blue) was paired with either a low intensity pain stimulus (placebo conditioning) or a high intensity pain stimulus (nocebo conditioning) and the other color (e.g. orange) was paired with a moderate intensity pain stimulus; the pairing of the colors was counterbalanced.
- ✔ Low intensity pain stimuli were set at 0.8 x T-0.2 x t (placebo trials), high intensity pain stimuli were set at 2.2 x T-0.2 x t (nocebo trials) and moderate pain stimuli were set at 1.5 x T (control trials).
- ✔ Placebo, nocebo and control trials were used in a contingent manner (experimental groups with conditioning, e.g. orange stimuli always paired with low intensity stimulus and blue with moderate intensity stimulus) or noncontingent manner (random control groups; colors and pain stimuli presented in a pseudorandom order).
- ✔ In the natural history group, no manipulations were used (testing phase only).

Testing phase

- ✔ In all groups only control trials were used.

RESULTS

- ✔ Placebo analgesia and nocebo hyperalgesia were found when placebo suggestion was applied after nocebo contitioning and when nocebo suggestion was applied after placebo conditioning, respectively.
- ✔ There was neither a placebo nor a nocebo effect in groups with classical conditioning alone.
- ✔ A significant effect was found for expected pain intensity in all experimental groups (both placebo and nocebo).
- ✔ Moreover, the obtained nocebo effect in the group where the nocebo suggestion followed the placebo conditioning went extinct over time.

We have fitted linear mixed model to pain ratings to see if the effects observed for pain ratings could be explained by expected pain. In this model expected pain was nested in the group factor. When expected pain was statistically controlled in this way all the effects observed for pain ratings were no longer significant.

We combined random placebo, random nocebo and natural history control groups into one control group due to the lack of differences between those three groups.

Group 1 - placebo conditioning
Group 2 - nocebo conditioning
Group7 - nocebo suggestion after placebo conditioning
Group 8 - placebo suggestion after nocebo conditioning
Group Ctrl – combined control groups (random placebo, random nocebo, natural history)

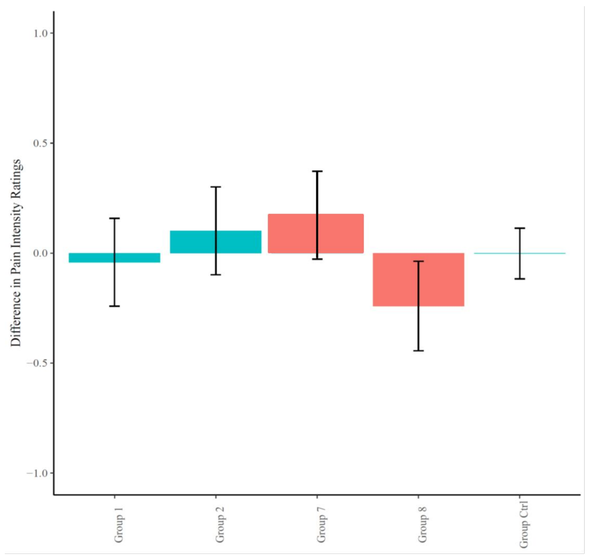

Fig. 2. Within-group comparisons of pain intensity ratings. Red bars indicate a significant effect ($p < 0.05$) within the group.

CONCLUSIONS

- ✔ Classical conditioning alone did not induce placebo analgesia or nocebo hyperalgesia
- ✔ Procedures combining two incongruent methods of inducing placebo effects created pain-related expectancies. The obtained expectancies depended on the type of manipulation used last (e. g. placebo suggestion after nocebo conditioning resulted in expectancy of decreased pain and nocebo suggestion after placebo conditioning resulted in the expectancy of increased pain)
- ✔ Expectations mediated both obtained placebo analgesia and nocebo hyperalgesia effects

ADDITIONAL INFORMATION

- ✔ The study was funded by the National Science Centre in Poland (grant no. 2014/14/E/HS6/00415).
- ✔ The study protocol was approved by the Research Ethics Committee at the Institute of Psychology, Jagiellonian University, Kraków, Poland.
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