PLACEBO ANALGESIA: THE INTERPLAY BETWEEN CLASSICAL CONDITIONING AND VERBAL SUGGESTIONS. RESULTS FROM A COMPREHENSIVE, MULTI-GROUP STUDY

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AIMS OF INVESTIGATION

This study aimed to:
- ✔ investigate the importance of classical conditioning and verbal suggestion in eliciting placebo analgesia
- ✔ control for the expectancies and their influence on placebo analgesia induced by classical conditioning and/or verbal suggestions

METHODS

Participants
- ✔ 419 healthy volunteers took part in the experiment; on this poster we present results from the part concerning placebo analgesia from 223 participants (124 women, 99 men; range of age: 18-35)
- ✔ 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 of alcohol, (7) presence or history of any neurological, respiratory, circulatory, musculoskeletal and/or psychiatric disorders

Stimuli
- ✔ Electrical stimuli: 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)
- ✔ 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 scales (NRS), ranged from 0 = 'no pain' to 10 = 'the most pain that is tolerable'

Design and procedures

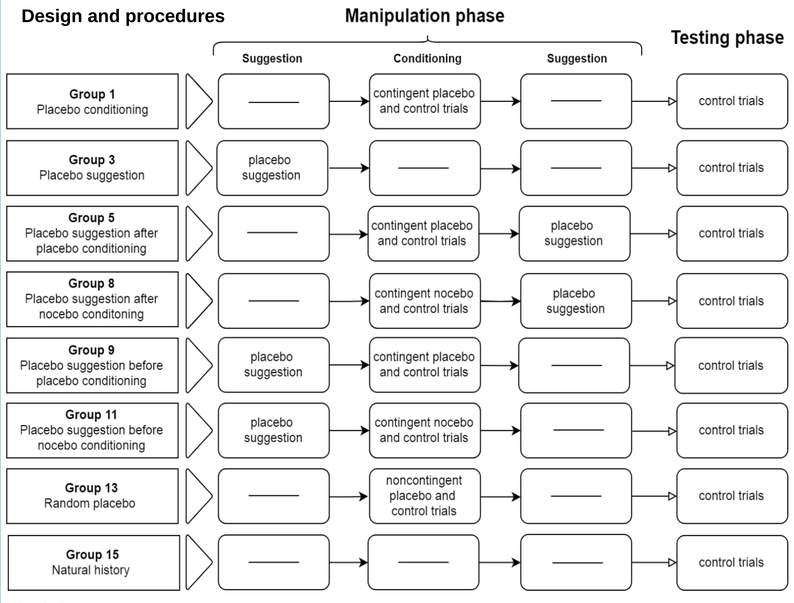

Fig. 1. Study design.

This experiment was a part of a multi-group study on placebo and nocebo effects comprising of 15 groups. For the part on nocebo hyperalgesia see poster entitled: 'Nocebo hyperalgesia: The interplay between classical conditioning and verbal suggestions. Results from a comprehensive, multi-group study'.

Pain intensity and pain expectancy trials:
- ✔ the NRS for expectancy ratings were shown during the presentation of the color stimuli, while the NRS for pain intensity rating was shown immediately after the electrical stimulus was applied (*Fig. 2*)
- ✔ 30 trials were preceded by expectancy ratings, 30 were followed by pain intensity ratings, and 36 were presented with no accompanying ratings.

Calibration phase
- ✔ Tactile sensation threshold (t) and pain threshold (T) were determined
- ✔ 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)

Manipulation phase
- ✔ In experimental groups classical conditioning and/or verbal suggestions (before or after the conditioning) were applied (Fig. 1)
- ✔ 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
- ✔ Placebo, nocebo and control trials were used in 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 group; colors and pain stimuli presented in a pseudorandom order)
- ✔ Verbal suggestion was either congruent or incongruent with preceding or following conditioning in groups with conditioning
- ✔ In natural history group no manipulations were used (testing phase only)

Testing phase
- ✔ In all groups only control trials were used

RESULTS

- ✔ Placebo analgesia was found in all experimental groups, in which both conditioning and suggestions were used, except the Group 11 (placebo suggestion applied before nocebo conditioning), in which nocebo hyperalgesia was found
- ✔ The significant effect was found for expected pain intensity in groups with placebo suggestion alone, after conditioning (both placebo and nocebo) in favour and before placebo conditioning in favour of the placebo effect and in group with placebo suggestion before nocebo conditioning in favour of the nocebo effect

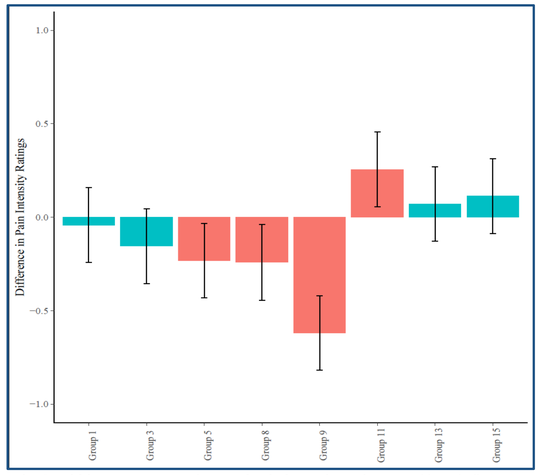

Fig. 2. Within-group comparisons of pain intensity ratings. Red bars indicate a significant effect ($p < 0.05$) within the group.

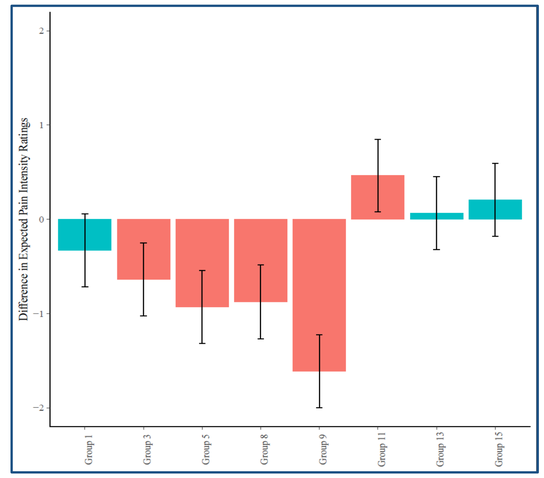

Fig. 3. Within-group comparisons of expected pain intensity ratings. Red bars indicate a significant effect ($p < 0.05$) within the group.

Group 1 - placebo conditioning
Group 3 - placebo suggestion
Group 5 - placebo suggestion after placebo conditioning
Group 8 - placebo suggestion after nocebo conditioning

Group 9 - placebo suggestion before placebo conditioning
Group 11 - placebo suggestion before nocebo conditioning
Group 13 - random placebo
Group 15 - natural history

Table 1. Between-group comparisons of pain intensity ratings

	Group 1	Group 3	Group 5	Group 8	Group 9	Group 11	Group 13
Group 15	0.283	0.069	**0.018**	**0.020**	**0.001**	0.326	0.789
Group 13	0.427	0.133	**0.039**	**0.030**	**0.001**	0.202	
Group 11	**0.040**	**0.005**	**0.001**	**0.001**	**0.001**		
Group 9	**0.001**	**0.001**	**0.007**	**0.012**			
Group 8	0.185	0.547	0.978				
Group 5	0.193	0.572					
Group 3	0.438						

Table 2. Between-group comparisons of expected pain intensity ratings

	Group 1	Group 3	Group 5	Group 8	Group 9	Group 11	Group 13
Group 15	0.059	**0.002**	**0.001**	**0.001**	**0.001**	0.380	0.602
Group 13	0.164	**0.016**	**0.001**	**0.002**	**0.001**	0.157	
Group 11	**0.005**	**0.001**	**0.001**	**0.001**	**0.001**		
Group 9	**0.001**	**0.001**	**0.013**	**0.008**			
Group 8	0.054	0.406	0.847				
Group 5	**0.033**	0.290					
Group 3	0.276						

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.

CONCLUSIONS

- ✔ Classical conditioning and verbal suggestion of placebo analgesia alone are insufficient to elicit placebo analgesia
- ✔ The obtained placebo or nocebo effect depends on the type of manipulation used last (e.g. placebo suggestion before placebo conditioning results in the placebo effect but placebo suggestion before nocebo conditioning results in the nocebo effect)
- ✔ The strongest placebo effect can be obtained by using placebo verbal suggestion before placebo conditioning
- ✔ Expectations mediate placebo analgesia induced by verbal suggestion and classical conditioning

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 of Jagiellonian University, Kraków, Poland.
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