Can a Brief Relaxation Exercise Modulate Placebo or Nocebo Effects in a Visceral Pain Model?

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Introduction:

• This experimental study tested effects of a brief progressive muscle relaxation exercise, designed to alter psychobiological stress parameters on the magnitude of placebo (when the placebo makes you feel better) and nocebo (when the placebo makes you feel worse) effects in a standardized psychosocial treatment context.
• Previous trials have supported the efficacy of placebo interventions in patients with chronic low back pain and chronic visceral pain.
• Various aspects of the psychosocial treatment context shape treatment expectations along with the magnitude of placebo effects
  o Setting
  o Nature of intervention
  o Quality of patient-provider interactions
  o Quantity of patient-provider interactions

Methods:

• 120 people randomized into 2 groups (relaxation or control task)
  o The study was conducted as part of a larger trial which also included an additional 60 volunteers who were randomized to a psychosocial stress protocol
• The study recruited a tightly-screened, healthy population of young individuals with comparatively low levels of chronic stress or stress-related symptoms
• All 180 participants underwent training in progressive muscle relaxation to achieve proper blinding and randomization the day of the study
• Healthy volunteers were randomized to a brief muscle relaxation exercise or a control task just prior to randomly receiving deceptive positive, deceptive negative or truthful neutral treatment suggestions regarding an IV infusion that was in reality saline in all groups
• Rectal sensory and pain thresholds were determined with a pressure-controlled barostat system
  o During a baseline, each participant received a series of painful rectal distensions titrated individually to rectal threshold
  o Participants then randomized to relaxation or control
  o After the relaxation or control activity, participants were randomized to positive (pain relief), negative (opioid antagonist) or neutral (saline) treatment suggestions (when in reality everyone received IV saline)
In order to achieve proper blinding and randomization, all volunteers received deceptive information about ALL possible drug treatments during informed consent.

- Series of rectal distensions using the same systems was then repeated

- To verify the efficacy of the intervention and to gain insight into possible mechanisms, several relevant stress markers reflecting different biopsychological aspects of stress were assessed.
  - Pain expectation
  - Pain intensity
  - Pain unpleasantness in response to individually-calibrated rectal distensions
  - State anxiety
  - Salivary cortisol
  - Heart rate
  - Blood pressure

Results:

- Systolic BP and heart rate decreased significantly in the relaxation group but not the control group
- Salivary cortisol and state anxiety showed significant decreases over time
- Expected pain intensity was reduced by positive treatment suggestions and increased by negative treatment suggestions
  - Pain expectation was not affected by relaxation
- Significantly reduced perceived pain intensity at testing due to positive compared to neutral suggestions noted in the relaxation groups while similar placebo effect was not observed in the control group
- Significantly reduced unpleasantness at testing in response to positive suggestions when compared with neutral suggestions in relaxation groups but not in control
- Pain expectation was significantly associated with both perceived pain intensity and pain unpleasantness
- Pain expectation correlated with state anxiety but not other stress markers
- Within the placebo groups, pain expectation was positively correlated with perceived pain intensity and unpleasantness
- Within nocebo groups, pain expectation was significantly associated with pain intensity but not with unpleasantness

Discussion:

- This is the first study testing whether a behavioral intervention aimed at reducing acute stress parameters affects the response to positive and/or negative treatment suggestions in a clinically-relevant model of visceral pain.
  - Brief relaxation exercise may facilitate the induction of placebo analgesia by positive when compared to neutral treatment suggestions
  - Reduced pain expectation noted in groups receiving positive suggestions of pain relief
Increased pain expectation in groups receiving negative suggestions of enhanced pain sensitivity
Relaxation had no discernable effect on pain expectation but relaxation significantly interacted with positive treatment suggestions
Significantly reduced pain intensity and lower pain unpleasantness after positive compared to neutral treatment suggestions is noted only in the relaxation group
Relaxation had no discernable effect on groups receiving negative suggestions

- The ANS is increasingly appreciated in the context of pain modulation, especially in acute and chronic visceral pain
- Pain expectation was the only mediator they could identify to explain the association between treatment suggestions and pain-related outcomes
- Lack of a control group without prior relaxation training limits this study

Conclusion:
- Findings suggest that a brief relaxation exercise may facilitate the induction of placebo analgesia by positive when compared to neutral treatment suggestions
- Placebo research has demonstrated the clinical potential offered by psychological interventions
- Implementation of successful treatment requires effective communication skills to improve patient acceptance, adherence, treatment expectations and to optimize the patient provider relationship
- Optimizing the psychosocial treatment context has the potential to improve the efficacy of placebo treatment, and to maximize the benefits of placebo-elements that are an inherent part of therapeutic interventions

Discussion questions:
1) How do our words/description of treatment affect outcomes?
2) Are there placebo treatment techniques we can use in pelvic physical therapy?
3) What is the benefit of relaxation exercises prior to treatment for pelvic physical therapy patients?