Final scientific report for Bial project 36/20

The role of non-verbal behavior on placebo and nocebo effects. Psychophysiological experiments

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Abstract

Background: nonverbal behaviors (NBs) of healthcare providers impact pain reports and treatment outcomes, however, no investigation so far has systematically investigated the impact of healthcare providers NBs on pain reports and treatment outcomes.

Aims: The aim of this project was to investigate the role of healthcare providers' NBs on pain reports and placebo effects.

Methods: The project consisted of one laboratory experiment and analysis of data from a dental multi-experiment. In the laboratory experiment the impact of singular NBs of videotaped experimenters were investigated on pain reports from heat stimulation in 104 healthy participants. videotaped experimenters instructed participants while displaying only one singular positive NB. In-person experimenters carried out the experiment and received either certain (i.e., all creams are active pain-relieving creams) or uncertain (e.g., "the cream is pain-relieving 50% of the time, and a placebo the other 50%") information about the cream. The data from the Dental multi-experiment investigated the impact of providers NBs on effectiveness of treatment information on dental pain reports.

Results and discussions: No differences were observed between the singular NBs of videotaped experimenters, however, compared to uncertain in-person experimenters, certain in-person experimenters received lower pain reports from participants. The dental multi-experiment showed that the positive information about the dental treatment reduced pain only when it was delivered by the dentist administering the treatment. The laboratory experiment resulted in three manuscripts (two published and one under review) and one abstract presentation. The dental multi-experiment resulted in one publication and two abstract presentation. The project resulted in a PhD thesis.

Conclusions: Even though the singular NBs might not have a discernable impact on pain reports, the overall NBs of healthcare providers still may impact pain reports and treatment outcome.

***Key words*: Healthcare providers; Nonverbal behaviors; pain reports; placebo effects.

1. Introduction

Placebo effects are elicited by verbal information (e.g., telling the patients that a treatment will effectively reduce pain) and/or learning mechanisms. The effects of both verbal information and learning procedures are modulated via expectations, which is the key element in placebo effects. However, there are other factors that can modulate placebo effects. Beside verbal information and learning processes, NBs of the providers impact treatment outcome, as a considerable amount of emotions, thoughts, and feelings are conveyed by NBs (DePaulo & Friedman, 1998).

NBs can be categorized into macro-level and micro-level. Macro-level NBs are the result of a combination of series of micro-level NBs (Ambady et al., 2000; Burgoon et al., 2011; Matsumoto, 2006a, 2006b). Micro-level NBs are specific NBs such as smiling, direction of gaze, that can generate the impression of macro-level NBs of for example dominance, positivity, etc. (Ambady et al., 2000). Singular micro-level NBs of providers are an essential source of information for patients to develop expectations about treatment.

Both micro- and macro-level NBs can be either positively or negatively valanced. Positive NBs reduce the actual or psychological distance between two interactants (Mehrabian, 1969), and express a positive feeling or attitude, and negative NBs imply a negative feeling or attitude, or increase the actual or psychological distance between two interactants. Nonverbal impressions have been shown to be important in health setting and influence treatment outcome. For example, our systematic review found 14 studies that investigated the role of providers' NBs on pain and placebo/nocebo effects and concluded that positive NBs contributed to lower reported pain and higher placebo effects and positive expectations, whereas negative NBs contributed to higher reported pain and nocebo effects (Daniali & Flaten, 2019).

Chen et al. (2019) investigated how providers' expectations influence participants' expectations. Participants were randomly assigned the role of "doctor" or "patient." Doctors applied either a pain-relieving or inert cream, followed by thermal pain stimulation, though both creams were inactive. Beforehand, doctors were conditioned to believe one cream (the placebo) reduced pain. Patients reported less pain and lower skin conductance when doctors applied the placebo cream. Cameras showed doctors displayed different facial expressions during application, suggesting that their expectations were communicated non-verbally. This study highlighted the impact of provider NBs, though it didn't explore other NB channels such as body gestures.

Taken together, research suggests that providers' NBs affect pain and placebo/nocebo effects. However, in most relevant studies it is unclear that which micro-level NB has the stronger effect on modulation of the placebo/nocebo effects and physiological responses.

Thus, this project is aimed to investigate the role of providers' NBs on placebo effects and pain reports. The original plan was to conduct two laboratory experiments wherein the impact of positive and negative singular NBs of experimenters were investigated on pain reports and placebo effects, however, due to the COVID-19 pandemic, and with prior notice to Bial, only one experiment was conducted. Instead of experiment two, an experiment was designed that tested a supportive nonverbal characteristic of providers on the effects of an olfactory training on post-covid olfactory disfunction. However, unfortunately again, the experiment had to stop due to low number of participants and large dropouts. Finally, a set of data from a study on dental pain that was relevant to the aim of study was analyzed and used in the project. The project resulted in four publications (one under review) one PhD thesis, three conference presentations, and a PhD position awarded to our group to continue this line of research. Table 1 highlights amendments occurred to the original project as well as outputs of the project.

Expected and achieved output indicators (number of actions)

Output indicators	Expected (according to application)	Achieved
PhD thesis	1	1
Master's thesis	0	0
Organization of seminar or conference	0	0
Book	0	0
Book chapter	1	0
Conference presentation	2	3
Conference paper	0	0
Journal article	3	4
Other (grants awarded to the project)*	0	1

***:** A PhD position is granted to the group to continue the line of research started by this project

List of publications resulting from this project

Abstracts and conference presentations:

1- Daniali, H., Hunsbeth, P., & Flaten, M. A. (2022). Placebo analgesia: Single- and double-blind administration of information about effects of dental treatment-PTH294. Poster presentation at IASP 2022 WORLD CONGRESS OF PAIN, 9.22.2022. https://iaspworldcongress2022.org/poster-presentations/

2- Daniali, H., Hunsbeth, P., & Flaten, M. A. (2022). BJP ASM Poster Abstracts 2022. Placebo analgesia: Single- and double-blind administration of information about effects of dental treatment-PTH294. British Journal of Pain, 16(2_suppl):1-48. http://dx.doi.org/10.1177/2F20494637221103093

3- Ph.D. Thesis Presentation: Specifying Contextual Factors; Caregivers' Role in Pain Report and Placebo Effects. Presented at Doktorgrader innen Smerte at Norsk Smerteforening (NOSF) 2024, Oslo, Norway. https://gyroconference.eventsair.com/nosf-2024/program

Full papers and thesis

1- Daniali, H., Ruben, M. A., & Flaten, M. A. (2023). Systematic manipulation of experimenters' non-verbal behaviors for the investigation of pain reports and placebo effects. *Frontiers in Psychology*, *14*, 1248127. https://doi.org/10.3389/fpsyg.2023.1248127

2- Daniali, H., Ruben, M. A., Aslaksen, P. M., Fiskum, C., Kaptchuk, T. J., & Flaten, M. A. (2024). The Effect of Singular Nonverbal Behaviours of Experimenters on Pain Reports. *Journal of Pain Research*, 1345-1360. https://www.tandfonline.com/doi/full/10.2147/JPR.S449150

3- Daniali, H., Hunsbeth, P. L., & Flaten, M. A. (2024). Effects of open and hidden administration of treatment-related information; a multi-experiment study. *Psychology & Health*, 1-29. https://doi.org/10.1080/08870446.2024.2392820

4- Daniali, H. (2024). Specifying Contextual Factors; Caregivers' Role in Pain Report and Placebo Effects-The role of caregivers' characteristics and nonverbal behaviours in pain and placebo effects. https://hdl.handle.net/11250/3130407
5- Daniali, H., Ruben, M. A., & Aslaksen, P. M. (2024). Impact of Experimenters on Treatment Response and Pain Reports. Under review in Pain Reports.

Below the description of the project from the beginning to the end is provided.

2. Laboratory Experiment

Daniali and Flaten (2019) showed that the positive NBs of providers reduced pain reports and enhanced placebo effects. However, it was not clear what NBs that exerted this effect. In this laboratory experiment, the aim was to investigate the singular positive NBs of experimenters on pain reports from an experimentally induced heat stimulation on healthy adult subjects.

2.1. Methods

51 males and 53 females (total of 104) participants were randomized to four groups that were displayed positive facial expressions (+FE), tone of voice (+TV), body movement (+BM), or neutral (NC) NBs of videotaped experimenters (VE). Subjective reports of pain, stress, arousal, and cardiac activity were obtained in a pre-test, a conditioning phase, and at a post-test. Four minutes of heat pain was induced in each test, and a placebo cream was administered before the conditioning and the post-test in all groups

2.1.1. Participants

Out of 104 tested participants, a total of 94 participants including 49 females were included for the analyses of subjective data. The cardiac data of 86 participants (44 females) were analyzed.

2.1.2. Non-verbal behavior scenarios

Four different NB conditions (+FE, +TV, +BM, and the NC) were developed in which in three of them only one NB was positively enhanced while other NBs were kept neutral, and in the fourth condition (the neutral control; NC) all NBs were kept neutral. In the +FE, positive facial expressions, in the +TV, positive tone of voice, and in the +BM, positive body movements were displayed. In the NC, all NBs were kept neutral.

2.1.3. Video-taped experimenters

Two female professional actors as videotaped experimenters (VEs) were shown to participants.

2.1.4. In-person experimenters

Four female in-person experimenters carried out the experiment. They followed a script for their interactions with the participants and received training on how to keep their non-verbal interactions at a minimum. Two types of information, certain and uncertain information about the effectiveness of the cream were given to in-person experimenters. For 54 participants the in-person experimenters were told that ‘’for half of the participants a pain-relieving cream will be used and for the other half a placebo cream’’. For the other 50 participants, the in-person experimenters were told that ‘’from now on, all the participants will receive the pain-relieving cream''. Moreover, those in-person experimenters that were told that all the creams were active underwent a conditioning with a lidocaine 5% cream to reinforce the generation of positive expectations.

2.1.5. Procedure

The aim of study was introduced to participants as to investigate reactions to thermal pain. Pain was calibrated to an individual pain level of '5' using three ascending heat stimulations, followed by a pre-test where participants underwent 4-minute of that calibrated thermal stimulation. Before the conditioning, a videotaped experimenter introduced a placebo cream with positive suggestions that it would reduce the pain. The pain intensity was then lowered from the calibrated level of '5' to level '3', to associate the experience of reduction in pain with the placebo cream. The post-test mirrored the conditioning, but pain intensity stimulation intensity similar to the pre-test with level '5' was applied.

2.2. Preparatory study

To ensure about validity and reliability (proof of concept) of the video NBs, a preparatory investigation was carried out in which a group of psychology students from Norway and USA rated (coded) the NBs of each videotaped Ns. The general aim was to test the concept of the videotaped NBs, i.e., that the NBs were as they were intended to be.

Fifteen Norwegian and six US undergraduate students of psychology performed the coding of NB conditions. A NB coding log was designed to NBs of 'smiling', 'gestures', 'eye contact', and 'positivity in tone of voice'; and impressions of 'dominance and being in charge', 'overall positivity', and 'expressivity' in each NB video.

The NBs were rated as both valid and reliable proving the concept of the NB conditions (see Daniali et al., 2023).

2.1.6. Instruments

Pain intensity and *unpleasantness* were measured using an 11-digit numeric rating scale (NRS) as in (Price et al., 1983). Stress and arousal were measured by SACL (Mackay et al., 1978). *Thermal pain stimulation* was induced by a Pathway ATS (Medoc) (TSA II, Medoc, Ramat Yishai, Israel). *Cardiac activity* was measured using the BIOPAC MP150 system (Biopac Systems Inc., Goleta, CA). The root mean square of successive differences (RMSSD), the normalized power of high and low frequency components in the signal using fast Fourier transform, LF/HF ratio, and heart rate (beats per minute) were extracted and analyzed.

2.1.7. Analysis

The change score of the pre-test subtracted to the post-test was used as the dependent variable for subjective pain, stress and arousal reports. A repeated measures ANOVA was used to analyze subjective data. To analyze the HRV data, a linear mixed-models analysis was used.

2.3. Results

The main result was that were no differences between the NB groups in pain, expectations, and both subjective and physiological stress levels, however, the +FE was rated as more caring and empathic than the NC. There were differences in conditioned responses and in pain reports between males and females (see Daniali et al., 2024a).

2.3.1. Incidental Findings

Participants who were tested by in-person experimenters that received certain information about the placebo cream reported lower pain intensity and unpleasantness compared to participants who were tested by in-person experimenters that received uncertain information about the placebo cream. These set of incidental findings will be published separately (Daniali, Ruben & Aslaksen, Under review in Pain Reports).

2.4. Discussion

The main finding from the thermal pain experiment was that there were no differences between the NB groups, most likely because the singular positive NBs of the videotaped experimenters were weak to reduce pain and stress. We argued that the reason for the absence of effects of NBs was that testing each NB individually and relatively separated may have weakened the effects of NBs (Daniali et al., 2024a).

However, even though the singular NBs of videotaped experimenters were weak to impact reduced pain, certain in-person experimenters received lower pain reports compared to uncertain in-person experimenters. Since the experimenters had minimal interaction with participants, it was concluded that the impact of experimenters to elicit lower pain from participants were most likely through their subtle NBs, highlighting the role of experimenters NBs in shaping treatment responses, even with minimal interactions (Daniali, Ruben & Aslaksen, Under review in Pain Reports).

3. Dental multi-experiment

Since the laboratory experiment showed that in-person experimenters with certain information elicited lower pain reports even with minimal interaction with participants, we tested whether the providers knowledge about treatment could modulate the effects of treatment information. The aims were to test 1) the effect of positive (PI) and neutral (NI) information a dental treatment on pain induced by that procedure, and 2) whether the delivery of the information by the treatment team (open administration) or unbeknownst to the treatment team (hidden administration), affected pain. By investigating the second aim we could see whether the providers and their potentially subtle NBs could impact the effects of positive information. Two experiments were conducted. In each experiment, dental patients were randomized to two groups: a neutral (NI) or positive information (PI) group. The NI group received standard information about the treatment. The PI group received elaborated positive information designed to enhance positive expectations. In Experiment One (N = 44) the dentist and the assistant performing the treatment delivered the information to patients. In Experiment Two (N = 52), however, a third assistant not involved in the treatment delivered the information, and thus the dentist and the assistant did not know which group the patient belonged to.

3.1. Methods

3.1.1. Common methods between the two dental experiments

Two dental experiments were performed in a dental clinic. Patients in both experiments received the same anesthetic treatment (Xylocain Dental Adrenalin) and the same procedure (WAND STA; see Instruments) and were randomly assigned to either a group who received positive information (PI), or neutral information (NI) about the treatment and the procedure.

3.1.2. Patients

Patients who needed a filling in their molar or premolar were included in the study. Patients who used other medications or painkillers that could affect their sensation of pain were excluded. 44 patients (24 females), and 52 patients (28 females) participated in Experiment One and Two, respectively.

3.1.3. Procedure

The procedure was identical in both experiments. The patients arrived at the clinic, and the first measurement of pain, stress and arousal was recorded before they were randomly assigned to one of the groups. After randomization, they received the information about the treatment that corresponded to their grouping (either positive, or neutral information). The PI group received information about the treatment that were more positive and elaborative. The NI information was modeled to be similar to what patients normally receive before undergoing dental cavity filling treatment. After receiving the information, patients continued the treatment, which was anesthetizing the molar, drilling it, and then filling the molar cavity. In the Experiment One, the second measurement of pain, stress and arousal were recorded during drilling for half of the patients and right after the drilling was over for the other half of the patients (i.e., remembered pain). For Experiment Two, the second measurement was recorded right after the drilling was over for all participants. The third measurement was recorded after the treatment was finished. The last measurement was administered 15 minutes after the conclusion of the treatment, while patients were waiting in the reception room. Except the second measurement, the procedure was identical for both experiments (see Daniali, Hunsbeth and Flaten 2024b).

3.1.4. Blinding

The patients and the dentist were both aware of the medication and the medical procedure in both studies. However, the patients in both experiments were not informed about the real aim of the study. In Experiment One, the dental treatment team provided the information to the patients and performed the treatment. In Experiment Two, a third dental assistant who was not engaged in the treatment provided the information to the patient and therefore the dental treatment team were not aware which patients received what type of information.

3.1.5. Instruments and medication

All patients received the same amount of the same anaesthetic, and the same procedure for the anesthetizing, drilling and filling of the molar/premolar. Pain, stress, and arousal were reported before drilling, during drilling, immediately after drilling, and 15 minutes after the end of treatment.

3.1.6. Analysis

The design was repeated measures ANVOA with 2 Information (NI, PI) × 4 Timepoint mixed design, with Information as between-group factor, and Timepoint as the within-subjects factor.

3.2. Results

The main findings were that pain ratings in the PI group were about 50% lower than pain ratings in the NI group during drilling, i.e., when pain was most intense. Secondly, stress levels before treatment predicted pain in the during the drilling only in the NI group. However, in experiment two when the information was delivered by a third assistant not involved in the treatment, there were no differences between the PI and the NI groups (see Daniali, Hunsbeth and Flaten 2024b).

3.3. Discussion

The Experiment One found that positive information was effective in reducing pain when delivered by the dentist administering the treatment. However, in Experiment Two, the placebo effect disappeared when the same information was given by an assistant outside the treatment team. Positive information combined with subtle cues from the provider reduced pain by diminishing the impact of stress.

Even though the study didn't specifically test NBs, it showed that the provider's subtle NBs could influence the effectiveness of positive information. If positive information alone reduced pain, it would work regardless of delivery method. However, the results suggest that provider-related factors played a significant role in pain reduction. The interview with the dentist suggested that the dentist had more positive NBs when delivering the information.

In Experiment One, pain reduction was attributed to a placebo effect, likely influenced by the provider's subtle cues, as the information was delivered by the dentist. In Experiment Two, with an assistant delivering the information, pain and stress levels remained unchanged, suggesting the absence of the placebo effect. This indicated that the dentist's NBs were key to the placebo effect, as it disappeared when the dentist did not deliver the information, highlighting the importance of provider cues over the information itself (Daniali, Hunsbeth and Flaten 2024b).

4. General discussion

The laboratory experiment, showed that the singular NBs of providers were not different in their effect on pain, because testing each NB individually weakened the effects of NBs. However, experimenters with certain information about the treatment elicited lower pain, potentially through subtle NBs. The multi-experiment dental study showed that the effects of positive information was dependent on the provider who delivered it. Therefore, the nonverbal message of the provider was more influential than the suggestive information about the treatment.

The results of the laboratory experiment showed that the singular NBs of providers were not different in their effect on pain and stress reports. Thus, no NB of the providers had a larger impact on pain than the other NBs. The findings of the laboratory experiment contrasted those few studies that suggested that facial expressions as the NB with the highest impact in reducing pain. Our experiment for the first time tested the effects of singular NBs of providers on pain reports and showed that there were no differences between the effects of providers NBs on pain reports, which was probably due to separating the NBs. To closely investigate the healthcare providers NBs, it is a prerequisite to disassemble the components to individual parts, however, the thermal pain experiment showed that this method may not be optimal in investigation of effects of providers NBs, as disassembling the NBs may weaken or even abolish the effects of NBs of caregivers on pain reports. However, in both the laboratory and the dental experiments, there were findings related to the impact of providers NBs on pain reports. Suggesting that the NBs of providers impact treatment outcome when they are not disassembled, and potentially convey a meaning for example certainty in laboratory experiment.

Conclusively, this project showed that the providers NB had a substantial effect on reduction in pain report and enhancement of placebo effects. The providers NBs are probably effective when presented collectively, and the effects of providers NBs and providers characteristics are perhaps through modulating the effects of negative emotions on pain.

5. Recommendations

The dental experiment showed that positive information reduced pain when it was delivered by a dentist administering the treatment, however, to date, no studies have investigated the effects of the interaction of provider sex and NBs on pain and placebo effects.

Furthermore, the role of negative NBs need to be investigated as well. Thus, future studies should investigate what negative NBs of provider modulate the placebo effects.

The thermal experiment showed that singular NBs had minor effects in reducing pain, however, the study did not test the effects of macro-level and NB characteristics of provider. Studies have shown that NB characteristics such as being nonverbally warm and accepting have an impact on placebo effects (e.g., Kaptchuk et al., 2008), however, no studies so far have systematically the impact of medically important NB characteristic such as being empathic and warm, competent, or enthusiastic on treatment outcome and symptom reporting. This is planned to be investigated through a PhD project that is stemmed from the present project. A grant application for support has also been sent to Bial for that PhD project.

6. References

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