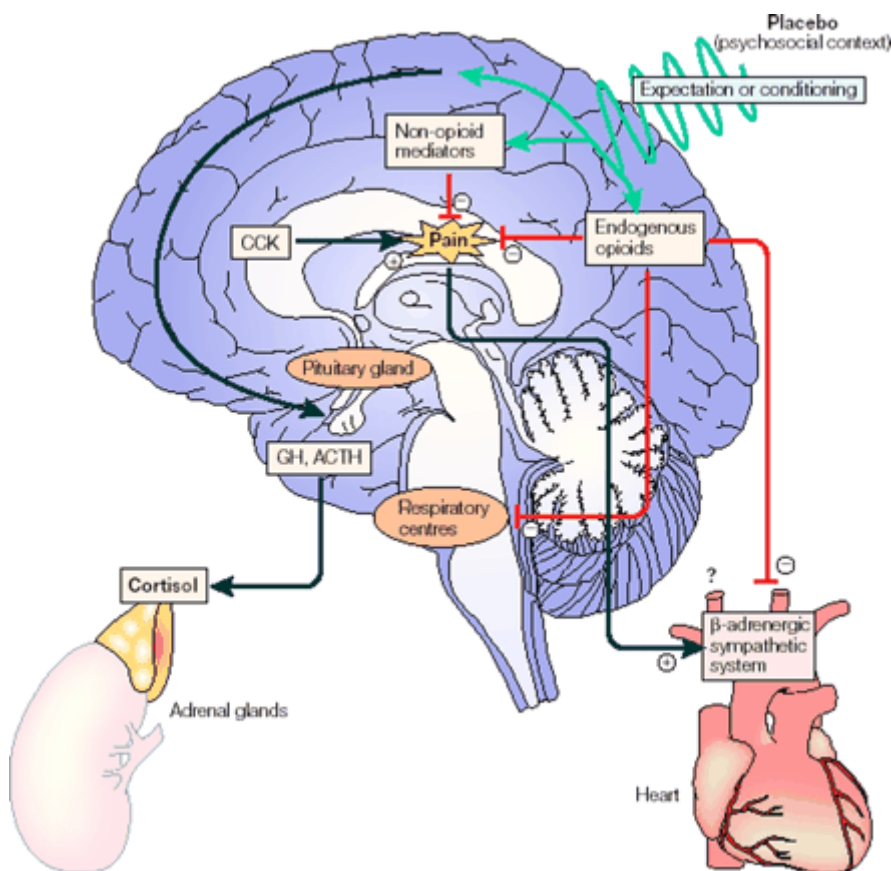


Placebo Induction

*"... the existence of placebo effects suggests that we must broaden our conception of the limits of endogenous human capability.... The study of placebo effect, at its core, is the study of how the context of beliefs and values shape brain processes related to perception and emotion and, ultimately, mental and physical health."*¹

A placebo response is often thought of as a faith-based response to a treatment modality that of itself has no proven therapeutic value. The belief, or belief system, causes what many now term a "meaning response."² It has also become apparent that both conscious expectation and unconscious conditioning, as reflected in types of learning, can serve to initiate a placebo response and do so via distinct biopathways.³ It is further evident that there is not one response but many, as evidenced by multiple areas of the body being influenced by different types of placebo responses.⁴ In addition, similar dynamics may produce negative results, "nocebo" responses, whereby patients develop pathological reactions rather than those of healing.⁵



Placebo Psychological Context

The various forms of meaning producing either response can result from the patient's confidence in the practitioner, the device, the procedure, the pill, the injection, or can be an effect of the patient's religiosity or other learning. Whatever the basis of a placebo response,

that agent triggers a cascade of biochemical or biophysical events that results in the desired clinical outcome in spite of the absence of proven utility of the regimen.

It cannot be denied that the placebo response is real and powerful. That it is without adverse side effects contributes, in part, to it representing the perfect medicine. Since it is not reproducible in any but the smallest population of patients, it presents a frustration. Learning how to selectively induce it in patients suffering from a range of maladies and regardless of belief systems is the goal.

Our question is whether we can trigger that same sequence of events leading to the same response using an artificial inducer in place of faith. We also ask as to the nature of the inducer. If effective, whether the inducer is a drug or other formulation, a thought, belief, or practitioner, as it has been developed to deliberately and independently stimulate an active response it is now a therapy and not a placebo. The ultimate aim of the project is to enhance the ability of responders and to induce a controlled response in non-responders.

The objectives of the project are therefore:

1. to determine the sequence of cellular and/or subcellular events initiated by a belief system plus a triggering agent (practitioner, device, technique, product) resulting in a healing response in the absence of a typical therapeutic substance;
2. to initiate the same sequence of events in the absence of, or in the place of, a belief system or learned behavior;
3. to study the effect of the successful completion of step 2 above on the patient's belief system; and
4. to determine if people can be taught to become responders or increase their ability to do so.

Contemporary placebo research has shifted from viewing the placebo response as a nuisance within clinical trials to recognizing it as a bona fide phenomenon in need of multi-disciplinary investigation. By accepting this challenge, we stand to reveal more of the intricacies of the human mind as well as "fundamental insights into human biology."⁶

PLACEBO INDUCTION PROJECT

Overview

Stemming from Institutional Review Board (IRB) and FDA-authorized clinical trials, review of the literature, and discussions with medical professionals, Institute investigators have experience with the placebo response. Our initial study targeting the physiological and psychological parameters of the placebo effect has two stages.

Using cortisol levels as a reflection of stress symptoms as the initial model, first-stage participants were screened to determine those suitable for further evaluation. During this time, measurements were taken relating to what is different with the placebo responders versus the non-responders as indicated by a variety of bio-markers. Analysis of these data is expected to provide a model for intentionally inducing the placebo response.

Among the instruments to measure the physiological basis of belief are cytokine and chemokine analysis, and real-time neuroimaging such as CAT scans, MRI, and EEG readings. Validated psychological questionnaires also provide information to determine one's relation to beliefs, faith, and religiosity before and after the study. Measurements also include Visual Analog Scales (VAS) and the global sense of well being questionnaire, SF-36.

This part of the study provides the placebo-responsive population which will undergo a subsequent series of experiments to determine whether we can artificially induce a placebo response. The response may not be initiated by a pill or injection but by something that has

been shown to trigger the change as noted in monitoring the subjects during the above mentioned study. Such an inducer could be sound, light, an energy impulse at a specific frequency.

The potential net effect of this preliminary study is immeasurable. The research itself may provide groundbreaking data in terms of physiological and psychological markers for a range of therapies. The long-term benefits may include increasing scientific knowledge in a variety of areas, enhancing the patient-physician relationship, and lowering the cost of treatment. The Institute's final objective is to develop a treatment, or combination of treatments, to evoke the placebo response. Again, at this stage of development the agent(s) evoking a placebo response is no longer a placebo but a bona fide therapy.

Project Location and Research

This project is being conducted at the University of Maine in Orono (UM). The Institute is supporting two full-time PhD candidates for three years each, with both focusing exclusively on this project. One student has a background in the medical laboratory fields of biochemistry and physiology, and is a nurse practitioner. She is currently conducting a study to identify modulators of deliberately induced psychosocial stress. Analysis of psychological and physiological variables is providing the means to correlate these data with pathological and resilient responses to stress elicited in the subjects. The second candidate has a master's degree in chemistry. He is developing a sophisticated technology that allows for the accurate measurement of extremely tiny amounts of a variety of potential biomarkers that may be useful in monitoring a placebo response. Their work is establishing a baseline for further studies.

Conferences

Early conferences formalized the protocols now being followed. Upon completion of the initial study, a conference will be held during which the PhD candidates will present their research to their advisors, Institute staff, and a group of experts in the field in order to critique the work done to date and develop protocols for continued studies. Additional conferences will depend on the outcomes of each round of the data generated by students.

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