The findings of a comprehensive review of the placebo phenomenon and its consequences for clinical medicine are contained in a new article, "Placebo and the New Physiology of the Doctor-Patient Relationship," published in *Physiological Reviews*. The effort, undertaken by physician-researcher Fabrizio Benedetti of the Department of Neuroscience, University of Turin Medical School, and National Institute of Neuroscience, Turin, Italy, provides an in-depth biological and evolutionary approach to examining the placebo effect in relationship to the doctor-patient relationship.

Placebo, in Latin, means "I shall please," and its role in research and medicine is a fascinating story. One of the first recorded use of placebos involved Benjamin Franklin who was commissioned by the French king Louis XVI to test the effectiveness of mesmerism, a kind of healing practice which was supposed to act through a healing fluid released from the healer. Franklin’s team utilized blind assessments and placebo interventions to women patients and determined that their improvements were spurred on by the imagination. Over time there was awareness to both researchers and physicians that clinical trials were susceptible to imagination and biases. This led to the use of the double-blind design, in which neither the investigator nor the patient knew the nature of the tested therapy (it could be either real or fake).

For many years placebos have been used for the validation of therapies, but they have also traditionally taken as an example of the powerful interaction between mind and body with associated commentary research appearing in psychology literature. Dr. Benedetti’s research is aligned with the current state of placebo research, a complex field of investigation which ranges from psychology to psychophysiology, from pharmacology to neurophysiology, and from cellular/molecular analysis to modern neuroimaging techniques.

Dr. Benedetti’s research methodology employed in this article transcends the traditional division between psychology, the study of the mind and how it works, and biology, the study of all living things. This article clarifies the research conducted to identify the relationship between pharmacological treatments administered to the patient and the role of the mind in the overall patient health. In addition, it clarifies the interaction between psychological processes and the many physiological functions of the human body.

This new discipline acknowledges that placebos and placebo responses with their wide range of physiological responses involving numerous mechanisms across a number of conditions, systems, and interventions represent an active field of neurobiological research. With that, Dr. Benedetti, using biochemical, cellular and physiological tools, aptly summarizes research new findings on describing the placebo effect on psychology and biology and their impact on the doctor-patient relationship. Among the issues discussed in detail are:

- There is no one "the placebo effect." There are different mechanisms in play across a variety of medical conditions and therapeutic interventions. For example, a placebo effect takes place because there is expectation. The patient expects a therapeutic benefit, and this kind of expectation actually has an effect on the brain and the body.
- The connection between expectation and real improvement that may occur is due at least to two mechanisms. The first may be a reduction of anxiety. The second is between expectation and the activation of a reward mechanism by the region of the brain known as the nucleus accumbens (which also governs pleasure, reinforcement learning, laughter, addiction, aggression, fear, impulsivity and the placebo effect.)

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- When a treatment is given to a patient, be it a placebo or real, it is administered in a complex set of psychological states that vary from patient to patient and from situation to situation. For example, when a placebo is given to relieve pain, it is administered along with stimuli which tell the patient that a clinical improvement should be occurring shortly. These stimuli can include the color and shape of the pill, patient and provider characteristics and the healthcare setting.
- Recent research has revealed a reduced efficacy of drugs when they are administered covertly to the patient. In fact, if the placebo/expectation component of a treatment is eliminated by means of a hidden administration (unbeknownst to the patient), the psychological component of the therapy is absent as well.

For physicians, psychologists, and health professionals these and other recent findings found in Dr. Benedetti's article can foster enhanced understanding of how their words, attitudes, and behaviors impact on the physiological profile of their patients' brains. This "direct vision" of the patient's brain will hopefully boost health professionals' empathic, humane, and compassionate behavior further. Moreover, understanding the physiological underpinnings of the doctor-patient relationship will lead to better medical practice as well as to better social/communication skills and health policy.


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