

This issue:

Frontiers in Placebo Effects

Devdutt Nayak, MD

Guest Editor



What if there was a healing technique that was time-tested, validated scientifically through demonstrable changes in the brain, produced minimal side effects that could be incorporated in your practice immediately, and that could improve your ability to help patients no matter what kind of treatment method you currently practice? I am sure you would be interested in learning everything you possibly could about it. But, what if the panacea described previously was simply the effects of placebo in modern medicine? Most likely, you would run my co-authors and me out of your office for trying to sell you snake oil.

For some, the word “placebo” may invoke images of a shaman shaking feathers or chanting incantations. However, until fairly recently, the giving of placebo was the practicing of medicine — whether it was the application of leeches for bloodletting to restore the humors, or the administration of colorful B-12 injections to help with fatigue. The definition of placebo, literally, “I shall please,” has undergone several paradigmatic shifts in last seven centuries and has had many definitions: the Latin vespers sung for the

dead;¹ a flatterer, a sycophant, or a toady;² a commonplace method or medicine;³ an epithet given to any medicine adopted to please rather than to benefit the patient;⁴ in clinical research, a nonspecific element of treatment; and finally, a way of studying the healing response and the art of healing in medicine.⁵⁻⁷

The articles in this issue explore the recent evolution of the new concept of placebo effects from the vantage points within biological, psychosocial, ethical, research, and clinical practice.

Pankaj Patel, MD, and I discuss the research that has given scientific underpinnings to the biological explanations of placebo effects. The prefrontal cortex is the primary site of placebo response via different mechanisms — conditioning, learning, and reward. It appears that drugs and placebos use similar biochemical pathways in the brain and act through both the conscious and the unconscious brain processes. Placebo responses can produce the release of different neurotransmitters, changes in the hypothalamic pituitary adrenal axis and endocrine systems, and alterations of immune response. Factors such as stress, motivation, mood, and cognition can influence the extent of placebo

response, and genetic variability may also play a role. Placebo responses begin as a product of our imagination but are by no means imaginary.

John Naliyath, MD, and I describe the psycho-social mediators of placebo effects. We discuss the role of expectancy, conditioning, “meaning effects,” and therapeutic relationship in the genesis of placebo responses. Studies suggest that the material aspects of pills influence patients’ perceptions and responses independent of their chemical ingredients. Early childhood experiences are very important in shaping the way we think about healing. Psychologists have proposed that early care givers are “hidden regulators” of an infant’s somatic activities and modulate the infant’s level of autonomic nervous system arousal and future emotional well-being. The therapeutic relationship rekindles the dormant soothing pattern of an early interaction with a caregiver, where the relationship is more important than any specific treatment given. Psychoanalysts have stressed the healing power of positive transference in promoting placebo response. Desire, belief, and expectations combine to produce hope, which is a po-

tent mediator of placebo response.⁸ We also discuss studies in which pharmacologically conditioned placebos are being used to decrease the dose and side effects of drugs in clinical practice. We conclude by emphasizing that therapeutic relationship remains the most important progenitor of placebo effect and point out that, in certain situations, increasing the “dose” of the doctor may be more beneficial than increased dose of medicine.

Noshin Chowdhury, MD, and I focus on thrashing out the lessons learned from randomized, placebo-controlled, double-blind design, which remain the best scientific method to evaluate efficacy of new therapeutic interventions. There has been a steady decline in the effectiveness of new agents during the last 25 years when compared with the placebo pill, the effect rates of which have risen 7% per decade during the same time. True placebo effects can only be separated from non-specific treatment effects if a no-treatment

control group is included. Such trials are rarely done in psychiatry for obvious ethical reasons. There is high, unpredictable, and uneven placebo responsiveness in many psychiatric conditions. Scouring the

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psychotherapy research literature, all bona fide psychotherapies appear to be efficacious compared to “inactive” therapies but are more or less equal when compared with one another. Furthermore, there are common “curative” features shared by all psychotherapies. We also discuss the difficulties of designing placebo-controlled psychotherapy studies.

With **Vicky Chodha, MD**, I explore the ethical conundrums associated with using placebos in clinical research as well as in everyday practice. Bioethical experts have taken issue with the idea of informed consent with the use of placebo in conducting research in psychiatric disorders, as the disorders themselves affect thinking, the ability to reason and make judgments, and the ability to act in one’s best interests. Even minor symptoms of mania, schizophrenia, and dementia can appreciably affect the decision-making capacity in giving informed consent. A significantly greater suicidal ideation can occur in depressed people taking placebo than in those who are taking antidepressant medication. We elaborate on the respective positions of the World Medical Association, the U.S. Food and Drug Administration, and the American Medical Association. The opposition to placebo use in clinical trials is based on the principles of biomedical ethics, namely those of be-

about the guest editor



Devdutt Nayak, MD, completed his medical and psychiatric training at King Edward Memorial Hospital/Bombay University in Bombay, India, prior to coming to the United States to begin psychiatric residency at Hillside Hospital in Long Island, New York. After graduation, he joined the research faculty at Hillside, during which time he developed interest in placebo effects while conducting placebo-controlled studies in schizophrenia and manic-depressive illness. His

professional experience includes 8 years as Staff Psychiatrist at Long Island Jewish-Hillside Medical Center, 23 years as Chairman of the Department of Psychiatry at New York Methodist Hospital in Brooklyn, and 4 years as the Director of Consultation Psychiatry at Richmond University Medical Center in Staten Island, New York. Dr. Nayak has also served as Clinical Associate Professor of Psychiatry at Cornell University Medical College in New York. His previous guest editorship for *Psychiatric Annals* was in 1998 for an issue focused on pharmacotherapy combination strategies for clinical practice.

neficence, non-maleficence, justice, and autonomy. It appears from international surveys that the practice of using placebos in clinical care is increasing for various reasons. We also discuss the inadvertent nocebo — literally, “I shall harm” — effects and how to minimize the catch-22 inherent in information disclosure to our patients.

In the article, “Enhancing Placebo Effects in Clinical Care,” Dr. Patel and I discuss the skillful use of placebo effect in everyday practice. Some practitioners are known to consistently elicit more positive responses via their communication and bedside manners. These placebo-enhancing practitioners are empathic listeners; participant prescribers; optimistic; and perceived as warm, friendly, and trustworthy. They are patient advocates and cheerleaders. These good doctors strive to restore the patient’s self-efficacy and enhance coping skills by boosting morale. In its current form, the practice of psychiatry is “low tech,” but it ought to be “high touch.”

Disturbing directions in psychiatry perpetuate the myth of mind-body difference. Like the Kiplingesque “East and West,” the biology and psychology are destined never to meet, and it is assumed that somehow the psychiatrists can treat the disorder without caring about the psyche while the therapists treat the mind divorced from the brain. By now, we have plenty of evidence that these two factors influence each other. The placebo effect (aka, the healing response) bridges the gap. It is a scientific revalidation of what we have known all along: that the therapeutic relationship is an important part of the healing process. The placebo response is a desired reaction in routine care and should be maximized. Health is not just an individual achievement, but rather is potentiated with the help of other individuals. It also refreshes our awareness of the indispensable human values of hope, faith, trust, and cooperative endeavors. Francis W. Peabody, MD, affirmed that the secret of the care of the patient is in

caring for the patient. The adage, “People don’t care how much you know until they know how much you care,” applies whether you are prescribing medications or providing therapy.

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