



Cruising Review

placebo

Placebo: Publications and Research from SwissMixIt

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PDF Version of the webpage (first pages)

<https://cruisingreview.com/smx/placebo.html>

## Placebo Botanical Information

The field of placebo research has made considerable progress in the last years and it has become a major focus of interest. We know now that the placebo effect is a real neurobiological phenomenon and that the brain's inner pharmacy is a critical determinant for the occurrence of psychobiological and behavioural changes relevant to healing processes and well-being. However, harnessing the advantages of placebo effects in healthcare is still a challenge. First studies in patients suggest that conditioned immunosuppression may not only affect allergic responses but actually attenuate the course of disease of autoimmune illnesses. placebo, control group, clinical trials, nocebo, neurobiology, psychological mechanisms, randomized controlled trials, clinical practice, depression, antidepressants, effectiveness, serotonin

Keywords: placebo, control group, clinical trials, nocebo, neurobiology, psychological mechanisms, randomized controlled trials, clinical practice, depression, antidepressants, effectiveness, serotonin  
Description and Research Abstract: The field of placebo research has made considerable progress in the last years and it has become a major focus of interest. We know now that the placebo effect is a real neurobiological phenomenon and that the brain's 'inner pharmacy' is a critical determinant for the occurrence of psychobiological and behavioural changes relevant to healing processes and well-being. However, harnessing the advantages of placebo effects in healthcare is still a challenge. First studies in patients suggest that conditioned immunosuppression may not only affect allergic responses but actually attenuate the course of disease of autoimmune illnesses.

Recent research shows that placebo effects are genuine psychobiological events attributable to the overall therapeutic context, and that these effects can be robust in both laboratory and clinical settings. These psychosocially induced biochemical changes in a patient's brain and body may in turn affect the course of a disease and the response to a therapy. Placebo is derived from Latin and means I want to please, and originally placebo was conceptualized as a commonplace method or medicine prescribed in order to please the patient and not because of its efficiency. Traditionally, placebo agents have been used as controls for active treatments in randomized clinical trials. Over the last decades, however, studies have shown that many of the patients who receive placebo treatments in randomized clinical trials experience symptom reduction.

Recent research demonstrates that placebo effects are genuine psychobiological phenomenon attributable to the overall therapeutic context, and that placebo effects can be robust in both laboratory and clinical settings. Evidence has also emerged that placebo effects can exist in clinical practice, even if no placebo is given. Further promotion and integration of laboratory and clinical research will allow advances in the ethical harnessing of placebo mechanisms that are inherent in routine clinical care and the potential use of treatments to primarily promote placebo effects.

Such placebo research has established that the placebo response is more than patient report bias, regression to the mean, or spontaneous remission. As a result of these developments, placebo responses are emerging as a legitimate series of biological reactions that must be rigorously characterized to facilitate efficient pharmaceutical development and optimal clinical care.

The notion of something called placebo started with St. Jerome's incorrect rendering of the first word of the ninth line of the 116 psalm, where instead of translating the Hebrew I will walk before the Lord, he wrote I will please the Lord. By the thirteenth century, when hired mourners waited for Vespers for the Dead to begin, they often repetitively chanted the ninth line, and received the name of placebos to describe their fake behavior. Indeed, in the 14th century, in the Canterbury Tales, Chaucer named his sycophant, flattering courtier Placebo. Placebo controls, which entailed administering fake procedures to separate the effects of imagination from reality, began in the 16th century with progressive Catholic efforts to discredit right-wing exorcisms. Mainstream interest in placebo effects only began with the widespread adoption of the placebo controlled randomized controlled trial (RCT) after World War II, as it was quickly noticed that people improved; sometimes dramatically, in placebo control arms. Henry Beecher popularized this observation in his famous proto-meta-analysis which claimed that about 35 percent of patients responded positively to placebo treatment.

During the past decades the most impressive demonstrations of these effects have been presented in the field of pain and placebo analgesia. The effectiveness of analgesic placebo responses remains unchallenged and our knowledge about the underlying mechanisms that produce the placebo effect is expanding rapidly. From a neurobiological viewpoint, research findings have revealed the involvement of cortical, subcortical and recently spinal structures in the placebo-induced modulation of pain that cognitively triggers the release of endogenous opioid and non-opioid substances. For example, analgesic placebos activate the endorphin system, and placebos used as Parkinson Disease medication activate dopamine in the striatum and changes the activity of neurons in basal ganglia and thalamus. However, a specific mechanism is not always detectable. The underlining placebo mechanisms of antidepressant drugs seem to be somewhat dubious. In his provocative contribution of antidepressants and the placebo effect published in this issue, Kirsch shows that regardless of contradictory mechanisms of antidepressant medication, antidepressant placebos are almost as effective as antidepressants, yet eliciting far fewer side effects.

Placebo effects are beneficial effects that are attributable to the brain-mind responses to the context in which a treatment is delivered rather than to the specific actions of the drug. They are mediated by diverse processes — including learning, expectations and social cognition — and can influence various clinical and physiological outcomes related to health. Emerging neuroscience evidence implicates multiple brain systems and neurochemical mediators, including opioids and dopamine. We present an empirical review of the brain systems that are involved in placebo effects, focusing on placebo analgesia, and a conceptual framework linking these findings to the mind-brain processes that mediate them. This framework suggests that the neuropsychological processes that mediate placebo effects may be crucial for a wide array of therapeutic approaches, including many drugs. I would rather know the person who has the disease than the disease the person has. Hippocrates.

The analgesic placebo effect is well documented by numerous studies. Expectancies are shaped by processes of classical and social learning as well as verbal instructions and are strongly related to emotional factors. Expectancies trigger a cascade of endogenous opioids and nonopioids, which alter the experience of pain.

Patients given placebo had a statistically significant improvement in NAS (by 0.72 – 0.19), with a large amount of heterogeneity (I<sup>2</sup> [ 96 percent). Univariate and multivariate meta-regression showed that trials with a higher baseline NAS, those conducted in South America, and those in which patients had a decrease in body mass index, were associated with greater improvements in NAS among patients given placebo. Patients given placebo had significant reductions in intrahepatic triglyceride, measured by magnetic resonance spectroscopy (by 1.45 – 0.54) with moderate heterogeneity (I<sup>2</sup> [ 40), and in magnetic resonance proton density fat fraction (by 2.43 – 0.89), without heterogeneity (I<sup>2</sup> [ 0). Mean serum levels of alanine and aspartate aminotransferases decreased significantly (by 11.7 – 3.8 U/L and 5.9 – 2.1 U/L, respectively; P < .01 for both). In a meta-analysis of randomized controlled trials of NASH, patients given placebo have significant histologic, radiologic, and biochemical responses. The placebo response should be considered in designing trials of agents for treatment of NASH.

The placebo effect is defined as any improvement of symptoms or signs following a physically inert intervention. Its effects are especially profound in relieving subjective symptoms such as pain, fatigue, and depression.

The placebo effect is very well known, being replicated in many scientific studies. At the same time, its exact mechanisms still remain unknown. Quite a few hypothetical explanations for the placebo effect have been suggested, including faith, belief, hope, classical conditioning, conscious/subconscious expectation, endorphins, and the meaning response.

Antidepressants are supposed to work by fixing a chemical imbalance, specifically, a lack of serotonin in the brain. Indeed, their supposed effectiveness is the primary evidence for the chemical imbalance theory. But analyses of the published data and the unpublished data that were hidden by drug companies reveals that most (if not all) of the benefits are due to the placebo effect. Even the small statistical difference between antidepressants and placebos may be an enhanced placebo effect, due to the fact that most patients and doctors in clinical trials successfully break blind. The serotonin theory is as close as any theory in the history of science to having been proved wrong. Instead of curing depression, popular antidepressants may induce a biological vulnerability making people more likely to become depressed in the future.

Polyphenol-rich foods such as pomegranate, green tea, broccoli and turmeric have demonstrated anti-neoplastic effects in laboratory models involving angiogenesis, apoptosis and proliferation. Although some have been investigated in small, phase II studies, this combination has never been evaluated within an adequately powered randomised controlled trial.

Previous studies have found a positive effect of cosmetics on certain behavioral measures, such as the tip given to waitresses by male patrons. These studies have employed confederates who usually wear cosmetics.

In a series of experiments, Shiv, Carmon, and Ariely (2005) show that the price consumers pay for a beverage not only affects the perceived benefit from the product but also extends to actual performance on puzzle-solving tasks. Placebo effects that manifest as changes in subjective state (e.g., mood, aesthetic ratings) are one thing, but when the effect extends to behavior, the placebo passes out of the realm of being all in the head and into something real and measurable.

Marketing actions, such as pricing, can alter the actual efficacy of products to which they are applied. These placebo effects stem from activation of expectancies about the efficacy of the product. A

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