Mechanisms and therapeutic implications of the placebo effect in neurological and psychiatric conditions

Danielle Murray, A. Jon Stoessl

Abstract

The power of a placebo to effect clinically meaningful neurobiological change comparable to pharmacological therapies has been demonstrated, although the mechanisms are not fully understood. Predicting placebo response has only recently received more attention, but psychological disposition, contextual and biological factors are now known to dramatically affect a person’s susceptibility to the placebo effect. The placebo effect depends upon expectancies that can be modified in a number of ways, including conditioning through explicit or implicit learned associations. Based on the dopaminergic response to anticipation of benefit in Parkinson’s disease, it was suggested that the placebo effect can be seen as analogous to the expectation of reward. Dopaminergic pathways have since been implicated in the placebo response in pain and depression. Additionally, endogenous opioid release is known to mediate many forms of placebo analgesia.

We provide an overview of the mechanisms and the therapeutic implications of the placebo effect in neurological and psychiatric conditions. We include evidence for detrimental effects arising from seemingly inert interventions, termed the ‘nocebo effect.’ Neuroimaging has critically advanced the study of the placebo effect and provides some of the strongest evidence for the mechanisms of this phenomenon prevalent across an array of human health-related circumstances. This review specifically focuses on mechanisms of the placebo effect in the three conditions that have most significantly demonstrated this effect and for which a plausible physiological basis can be identified: pain, PD and depression. Other neurological and psychiatric diseases reviewed include multiple sclerosis, Huntington’s disease, Alzheimer’s disease, schizophrenia and epilepsy.

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