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## Preface

A recent meeting on placebo and nocebo responses, sponsored by the Volkswagen Foundation, and held in Tuebingen (Germany) in January 2013, represented the starting point for inviting many scientists involved in experimental placebo and nocebo research to contribute to this volume by describing their work. Therefore, this volume presents the main lines of placebo research which are in progress and which will represent a challenge in the near future. Although this is not a comprehensive book on placebo and nocebo effects, we believe that a general overview of the ongoing studies may be useful to experimental pharmacologists, hopefully stimulating new avenues of debate and research.

Placebo is one of the most widespread words in the field of biomedical sciences. Until two decades ago, physicians and clinical scientists referred to this word when designing and interpreting clinical trials. In fact, placebo has always represented a comparator in the clinical trials setting, whereby the efficacy of a new treatment, be it pharmacological or not, has to be assessed. However, there still exists a semantic confusion within the scientific community in the use and meaning of the term placebo. On the one hand, placebo refers to an inert treatment, for example, a drug without any intrinsic pharmacological property. On the other hand, placebo effect, or response, refers to the therapeutic outcome following the administration of the inert treatment.

The still persisting confusion and misconception about the word placebo comes from the different meaning that this word has for the clinical trialist and the neuroscientist. In fact, the former is only interested in comparing the efficacy of a specific, e.g., pharmacological, intervention with a placebo treatment and to establish whether the drug is superior to the placebo. The clinical trialist is not interested in understanding whether the placebo-treated patients improve because of a spontaneous remission, a bias of the experimenter and/or patient, or different psychobiological factors. By contrast, the neuroscientist is interested in isolating the psychobiological components of the placebo response from the spontaneous fluctuations of the symptom, the patient's biased reports, and the experimenter's biased measurements. In this sense, the neuroscientist uses the placebo to probe several brain functions, ranging from endogenous pain modulation to anxiety mechanisms and from behavioral conditioning to social learning.

Nocebos and placebo effects, on the other hand, are less studied and less understood, mainly due to many ethical constraints. In fact, placebo is the evil twin of placebo, that is, a clinical worsening following placebo administration. In other words, expectations of adverse events or clinical worsening may lead to anticipatory anxiety which, in turn, may induce a real worsening.

Today placebo and placebo effects are approached by means of modern biological tools that range from pharmacology to brain imaging and from genetics to single-neuron recordings in awake patients. Therefore, placebo and placebo effects, or responses, are considered today psychobiological phenomena worthy of scientific inquiry, thus turning them from artifacts in clinical research into models for neuroscience. Besides these basic neurobiological insights, placebo research is also aimed both at exploring the possibility of exploiting placebo mechanisms in medical practice for the patient's benefit and at developing new clinical trial designs for the validation of new treatments.

Fabrizio Benedetti  
Paul Enck  
Elisa Frisaldi  
Manfred Schedlowski

Placebo

Benedetti, F.; Enck, P.; Frisaldi, E.; Schedlowski, M.

(Eds.)

2014, VIII, 311 p. 40 illus., 24 illus. in color., Hardcover

ISBN: 978-3-662-44518-1