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Some Conceptual and Methodological Issues Interfering with the Study of *Placebo* Effect

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S u m m a r y. The complete understanding of placebo effect is essential for the adequate design of clinical trials and holds central position in dominant biomedical theory. In this study we will try to inquire some major questions and inconsistencies that arise during the research about placebo effect.

INTRODUCTION

The term *placebo*, introduced into medicine in 1785, it was first defined in the 2nd edition of Motherby's New Medical Dictionary as *a commonplace method or medicine* (1). Stewart Wolf conducted the leading experimental studies of placebo effect (2) in the early 50's and the first summarized analysis of prior studies regarding the power of placebos, were carried out by Henry K Beecher in 1955 (3). During the same period of time the so-called *double blind procedure* gained wider acceptance within medical community. After 1960 randomized controlled trials (RCTs) were accepted as the only valid method to evaluate the efficacy and safety of new therapeutic methods or agents. Since then a lot of research has been conducted in different fields of biomedical sciences and many explanatory mechanisms of placebo effect have been recommended, attempting to specify the non-specific.

The aim of this study is to discuss the conceptual and methodological problems that appear while reviewing placebo effect and the relative literature.

RESULTS

Conceptual issues

The current definition of *placebo* effect was introduced by Arthur Shapiro in 1964, reviewed by the same author in 1997, and underlies every scientific work, which implicates this phenomenon. According to A. Shapiro, a *placebo* is any therapy (or that component of any therapy) that is intentionally or knowingly used for its nonspecific, psychological, or psychophysiological, therapeutic effect on a patient, symptom, or illness but is without specific activity for the condition being treated. A *placebo*, when used in experimental studies, is a substance or procedure that is without specific activity for the condition being treated. The *placebo* effect is the nonspecific, psychological, or psychophysiological, therapeutic effect produced by a *placebo* (4). This, by far concerted, definition conceals a simplistic sort of cause and effect. If we replace the word placebo in the third sentence with its definition from the first we get: The *placebo* effect is the therapeutic effect produced by (things) without specific activity for the condition being treated. *Placebos* are (a priori) inert and don't cause anything, but changes and treatment do occur, despite the use of inert substances. In other words, the definition mistakes cause for coincidence. Just because two things occur at the same time doesn't mean that one caused the other (5).

The fact of receiving medical treatment (rather than the content of this treatment) seems to initiate a healing process. This situation makes most physicians feel uncomfortable given their particular scientific background and education, who tend to deny even the existence of something called the placebo effect. The kind of science that physicians have to learn is the simpler sort of science, scientific fields that physicists worked out in 17th century, with obvious deterministic content like levers and plains (6). Thus, the understanding of social or meaning-related phe-

nomena, which is impossible to be described with positivistic terms, confuses them.

The interest for *placebos* and *placebo* effect was stimulated by the desire to design adequate double blind clinical trials. This interest has been increased during the last decade following the evolution in the field of Evidence Based Medicine. Hence, placebo effect is proved to be a fundamental factor, which has an impact on the roots of current biomedical theory. Taking into account these facts, we have to reconsider the question of what counts as an adequate explanation and how one establishes the truth of scientific theories.

Methodological issues

Early in the history of *placebo* there were only uncontrolled trials subjected to observational bias. After introduction of RCTs in medical methodology, tsands of experiments ap peared in medical literature that used a group of patients who are given inert medication and another group who are given the drug under study. The comparison between these groups might show something about the efficacy of the active drug but says nothing about placebo. To construct an argument about placebos we need three-arm experiments: one arm containing patients who receive active drug; one receiving *placebo*, and another one receiving no treatment at all. This kind of RCT is very rare in the literature due to ethical and financial reasons. Asbjorn Hrobjartsson and Peter Gotzsche in 2001 conducted a meta analysis of every three-arm experiment available at that time. They only found 114 articles eligible for their study, with this number being very small compared to the amount of the literature they searched. The ambiguous conclusion of this study was that there is inconsistent evidence of the existence of placebo effect for the majority of medical conditions (7). From this point of view, researchers are controlling their trials with something that, possibly, does not even exist.

The designation of clinical trials in order to study the *placebo* effect itself is very difficult and sometimes inhibited by ethical reasons. The use of *placebo* group in an experiment when there is an established treatment for a medical condition is unacceptable according to a valid interpretation of the 2000 Helsinki Declaration (8).

CONCLUSIONS

Current understanding of *placebo* effect seems to be inconsistent and fragmented. The main causes of the situation on hand are the ambiguous definition of *placebo* effect and the weak theoretical basis of the dominant biomedical theory.

Experiments that involve only *placebo* and no treatment groups appear to be not so simple to perform.

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