Although the concept of active placebos is appealing, its application is limited to the study of active drugs the side effects of which can be mimicked by the active placebo.

Limitations of the Double-Blind Procedure. The use of the double-blind procedure decreases the possibility of an erroneous conclusion that a drug is effective when it is, in fact, ineffective. However, the double-blind procedure may result in incorrect conclusions about the effectiveness of drugs. This comes about for statistical reasons such as using too small a sample or inappropriate randomization or matching procedures, psychometric reasons such as using measures which do not adequately differentiate responses, and methodologic reasons such as staff bias in evaluating results.

Some investigators believe that objective experiments do not exist. This has prompted the suggestion that every experiment should be done by an enthusiast and a skeptic and that the investigator's bias about expected results be specified in the paper. Various suggestions have been offered concerning how to make methodology more sound and foolproof. Certainly, there is room for improvement.

Triple-Blind Procedure

The triple-blind procedure (a term more euphemistic than descriptive) has been used in two ways. Some investigators have attempted to exclude or minimize placebo effects by conducting a preliminary study with placebos. Subjects who respond to placebo are then excluded from the definitive study which follows. Unfortunately, because placebo responses are inconsistent, nonplacebo reactors in the preliminary study may develop placebo responses in the definitive study. A second use of the term refers to the "blindness" in the assessment of study results. An independent assessment team, unaware of study design and procedures, administers tests of therapeutic efficacy.

IMPLICATIONS

Therapy will be impaired if physicians are unaware of placebo effects. Therapeutic effects will be attributed to specific procedures, which, unknown to the physician, are caused by placebo effects. The therapist's credulity about the efficacy and specificity of the procedure will be incorrectly augmented, and the therapist may be encouraged to use one technique for all patients. Therapists who rely on one technique may be unable to treat many patients, some patients may be harmed because of inappropriate treatment, and specific indications for a therapeutic procedure will be confused. Awareness of placebo effects will enable physicians to better evaluate the effects of therapy, contribute to the development of more flexible and appropriate procedures, and make therapy more comprehensive, resourceful, and effective. The recognition that these factors will contribute to the treatment process will improve studies by investigators and may help clarify unsolved problems of specificity in many therapies.

It is important to remember that despite the massive evidence supporting the concept of placebogenesis and iatroplacebogenesis, the evidence is based primarily on retrospective data. Careful prospective studies will be necessary for clarification of the processes and the relevancy and validity of the concepts.

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