

GUEST EDITORIAL

OUT OF HIPPOCRATES' SHADOW THE POWER OF THE 35% PLACEBO IN THE CITT STUDY

Leonard J. Press, O.D.

The Convergence Insufficiency Treatment Trial (CITT) is a multicenter, NEI-funded project that has significant implications for optometry in general and optometric vision therapy in particular. The project began in 1992 when a planning committee met for what was called CIRS, or the Convergence Insufficiency and Reading Study.

While it was apparent to clinicians engaged in vision therapy (VT) that convergence problems had some bearing on reading performance, there had not yet been a systematic study of the impact of VT on reading. At the time it seemed straightforward enough to design an appropriate study to investigate this. However, when the biostatisticians involved took a dispassionate look at the issues, they decided that other questions had to be answered first.

What is convergence insufficiency (CI)? It wouldn't have occurred to ophthalmic practitioners to pose this question as CI is a condition where there was seemingly universal agreement. Can CI be effectively treated? Take a look at any ophthalmic textbook on binocular vision or clinical practice guidelines, and you will find that treatment for this condition was already acknowledged to be effective.

This was not good enough according to the biostatisticians. Before begging the question of how effectively reading problems can be treated with therapy for CI, they insisted that the CIRS group rely on something beyond clinical consensus. The group first had to lay groundwork on the signs and symptoms that constituted CI. This begged specific questions that the group wasn't able to answer to the satisfaction of "gold standard" science. Were the clinical tests being used repeatable and reliable? Were the symptoms

commonly associated with the condition valid?

To be able to address these questions, CIRS was put on hold and the CITT group was formed. After a series of publications investigating the foundations of CI, the CITT group ultimately progressed to the question as to how the condition was best treated. No one involved with CIRS in 1992 envisioned that it would take 16 years to arrive at the point where we are now, with the publication of the first gold standard study on the treatment of CI.¹

Mitchell Scheiman, an optometric colleague and study chair of the CITT research published in the October 2008 issue of *Archives of Ophthalmology*, unveiled the findings of the study at the annual College of Optometrists in Vision Development's meeting in Palm Springs that same month.² It was, indeed, a monumental moment. The study had clearly shown that office based VT for CI combined with home VT was significantly superior to either home VT in isolation, or to placebo therapy.

Yet, there was another interesting outcome, one that wouldn't necessarily grab headlines or prompt editorial comment. *The results for the placebo group were indistinguishable from the results for the home-alone VT group.* Dr. Scheiman revealed how difficult it was to design appropriate placebo therapy so that the patient, or subject, would be convinced that the therapy was purposeful. The CITT group succeeded in designing a sufficiently powerful placebo paradigm and 35% of these subjects met the criteria for successful treatment. The seminal paper on the placebo effect most often cited in the literature was authored by Beecher, in 1955.³ The average effectiveness of the

placebo response rate in the 15 studies he examined was 35%.

David Newman is an emergency room physician who runs a clinical research program at Columbia University and St. Luke's – Roosevelt Hospital Center in New York City. Widely published in biomedical journals, Dr. Newman recently authored a thought-provoking book titled "Hippocrates' Shadow." In exploring the virtues and limitations of gold standard clinical trials, Dr. Newman made a prescient observation about the power of the placebo:

*Consider the accepted standard for interpreting the results of placebo-controlled trials: when a drug or intervention is 'equivalent to placebo' no one asks how good the placebo was. Even when the placebo was beneficial (as it often is), the intervention is considered a failure – despite being beneficial. When benefit is considered equivalent to no benefit, method has blatantly trumped outcome.*⁴ (pp.209-10)

Dr. Newman cautions us that it might be tempting to equate the placebo outcome with worthless therapy, but that would be trivializing the benefits of a well-designed placebo. Herein resides the power of the placebo effect in the CITT study outcome. A close look at this group reveals that they were engaged in a variety of activities that, on the surface, were unrelated to CI. It's worth taking a look at the placebo therapy activities used in the CITT study, available on line.⁵

The therapy design for the CITT study was based on the assumption that CI is primarily an eye muscle imbalance, and that only vergence or accommodative

Editorial continued on page 144

APPENDIX CITT Information

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PRESS continued

activities of substantive power done under binocular conditions would be credible therapy. However, many of the "placebo" activities are key ingredients of standard, office-based protocols for CI therapy. These include:

- 1) equalizing monocular skills through fixation training
- 2) equalizing monocular just noticeable differences with loose prism jumps
- 3) equalizing monocular pursuits

Many of the other placebo procedures involved sustained visual attention under binocular conditions, and several involve looking for changes in spatial localization with low power lateral yoked prisms.

It is not unreasonable to propose that CI is more than a primary eye muscle imbalance or a secondary accommodative problem, and is rooted in the inability to select an area of visual space for sustained visual attention at near. Then the 35% success rate of the placebo group in the CITT trial is not unusual. It opens up the possibility that roughly one third of the component of CI is not an eye muscle or

accommodative imbalance, but inability to sustain visual attention to a near target or task. This dovetails with observations that have been reported in the ophthalmic literature about the increased prevalence of CI in children with attention issues^{6,7} and the role of visual attention in vision therapy.^{8,9}

The power of the placebo effect in the CITT trial supports the notion that, in order to be successful, therapeutic intervention for CI should incorporate structured and monitored activities. These activities should then develop sustained visual attention to near space. These activities are necessary, but not sufficient to provide meaningful outcomes for VT. Office based visits that directly target vergence and accommodative interaction and optimization, with guidance by a knowledgeable doctor-therapist team, are needed to rise well above the 35% rate and attain the 73% success rate reported in the study.¹ The added power of non-placebo office-based therapy resides in the benefits of procedures that integrate binocular activities with accommodative, ocular motor, visual attention and other visual cognitive functions.¹⁰

The elegance of the placebo procedures and their effects in the CITT study is camouflaging "real" binocular procedures. They reinforced the scaffolding on which these procedures operate. To do anything less would result in a less "believable" placebo effect but, unlike drug trials, the procedures deliver benefits beyond endogenously released feel-good chemicals. In essence, the therapists who took part in the study were subliminally delivering a 35% baseline improvement one might anticipate from these types of procedures alone, and the "real" treatment group received significantly additional benefit. As is pointed out elsewhere in the editorial pages of this journal, we do not always give placebo effects the positive accord they are due.¹¹

Ciuffreda encapsulated these influences in his seminal paper on the scientific basis for and efficacy of optometric VT in non-strabismic accommodative and vergence disorders. His description is a fitting conclusion to these concepts:

Inclusion of related behavioral modification paradigms, such as general relaxation, visual imagery (e.g. think 'far' or 'near'), and attentional shaping may help one learn to initiate (i.e. provide a trigger mechanism) and/or enhance

the appropriate motor responses. However, the ultimate goal of optometric vision therapy is not simply to impact positively on various aspects of the oculomotor system per se, in isolation, but to attain clear and comfortable binocular vision at all times. It involves oculomotor integration with the head (i.e. eye-head coordination), neck (i.e. proprioceptive information), limbs, and overall body with information from the other sensory modalities, producing temporally efficient, coordinated behavior within a context of harmonious spatial sense under a variety of external and internal conditions and states.¹² (p.735)

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