

Sham acupuncture is not a placebo treatment – implications and problems in research

Stephen Birch PhD, LicAc, MBAC

Associate Professor, University College of Health Sciences - Campus Kristiania, Oslo, Norway.

Introduction

There is considerable confusion and disagreement about what the placebo treatments and placebo effects are [16, 20, 49]. Placebo treatments are supposed to be biologically inert [46], but some define placebos as a therapy thought not to include the active ingredients, thereby including components or aspects of a therapy that are not inert [43] while some paradoxically go so far as to define any untested therapy as a placebo [52]. Some authors claim placebo effects are small [21] some claim they are large [24], and some claim placebo does not exist [28]. Some make claims of placebo effects [43] citing studies that state the effects may not be [34] or cannot be placebo related [42]. Such opposing interpretations of the same evidence are not uncommon with regards understanding placebo effects. Placebo effects vary with different treatments [24, 29, 44]; placebo effects of a drug are said to be different than a device for the same condition [25], though evidence now contradicts that [11]; different-colored placebo pills can change the placebo effect [12, 24, 44]; how treatment and placebo are explained (informed consent) in the study changes the placebo effect [24, 29, 33] and can trigger its opposite, the nocebo effect [15]. Placebo effects are assumed to be additive [24], but evidence exists showing that they are not [14]. When placebo effects are not additive but interact with other treatment effects [10, 29, 30], it makes it difficult if not impossible to control for them [24]. Some argue that placebo controlled trials may not be possible in complex interventions because they cannot separate placebo from other treatment effects [41, 48]. How should this bewildering array of opinions, claims, counterclaims, and contradictory findings be understood? When something supposedly so ubiquitous as the placebo effect is not really understood, what does it mean for clinical research?

Placebo and Sham studies

In pharmaceutical trials, the placebo pill is supposed to be inert, but trials have sometimes used substances that were not inert and had specific effects for the condition for which the drug was being tested thereby resulting in false negative trials and creating bias against the tested

therapy [13]. Surgical trials that have attempted to use sham surgical comparisons have made the same mistakes since the sham surgical procedures are, by definition, not inert and appear to produce many clinically active effects, creating false negative studies of surgical procedures [5, 47].

Sham acupuncture is used in clinical trials of acupuncture as a common tool for testing the efficacy of acupuncture. In principle it is used in order to control for placebo effects. However, it has been known for almost thirty years that ‘sham acupuncture’ is not inert like a placebo pill in a drug trial, thereby creating the need for large sample sizes when sham acupuncture trials are used, and thus many false negative studies due to inadequate sample size [32]. Since the identification of this problem, many publications have appeared on this problem [3, 4, 5, 6, 7, 8, 17, 37, 39, 56, 58] and some have attempted to design studies that in principle could lead to control of these non-placebo effects so that the study can be said to have controlled for placebo effects [4, 9, 39, 40]. The primary problem is that there are no sham acupuncture techniques that are inert [8, 35, 36, 57, 58, 59]. For the most part researchers have simply ignored this, some either accidentally or intentionally have treated the additional non-placebo effects of the sham as attenuated placebo effects [26, 27, 43] thereby creating bias against acupuncture.

Various forms of sham acupuncture have been tried mostly based on an understanding of modern Chinese needling methods, where the needles are inserted into specific acupoints to the required depth and then manipulated until sensations called ‘deqi’ are obtained. Sham acupuncture has varied two primary factors: the location of the stimulation and the nature of the stimulation. Unfortunately poorly informed research teams have routinely used sham acupuncture methods inappropriately. Shallow needling cannot be considered to be inert, and is in fact routinely used in countries like Japan instead of the typical modern Chinese needling methods. But because it is not typically used in China and the many countries that follow the Chinese deeper needling

	Technique	Acupoints	Potential Uses*
'Real' acupuncture	Real (RT)	Real (RP)	The test treatment
Sham acupuncture -1	Sham (ST)	Sham (non) (SP)	The sham treatment
Sham acupuncture -2	Same as real (RT)	Sham (SP)	Tests relative effects of point location **
Sham acupuncture -3	Sham (ST)	Same as real (RP)	Tests relative effects of needle techniques **

* I say 'potential' since there have also been serious problems with choice of the 'real' acupuncture [2, 55] and serious misunderstanding about the nature of what is tested in the so-called sham interventions.

** These two sham models are NOT tests of acupuncture per se, rather tests of the relative effects of the places of needling or the techniques of needling. Yet they are routinely used as though they were sham acupuncture -1 type studies, as valid tests of acupuncture and then confused further when said to be placebo treatments. These studies by their nature cannot control for placebo effects, they are similar to studies of acupuncture compared to another therapy, except here the other therapy is a variant form of acupuncture.

methods, superficial needling has been and continues to be used as a sham needling technique by many Western researchers' [34, 42, 51, 60]. Many still continue to interpret shallow needling as producing only placebo effects [43]. Curiously a recent Japanese trial that tested a shallow needling technique with 0.6mm depth press-tack needles compared to a non-penetrating sham on athletes demonstrated a clear difference between treatments in favor of the 0.6mm depth needles [23]. For those that interpret shallow needling as a placebo acupuncture treatment, this study is very difficult to interpret – how can a placebo treatment outperform an identical looking placebo treatment? This study reveals flaws in the interpretation of what constitutes a placebo treatment.

Sham testing in acupuncture trials

Since two primary variables are tested in sham acupuncture studies, we should look more carefully at this. In the 'real' or 'test' acupuncture the 'real' technique (RT) is applied to the 'real' acupoints (RP). Thus three variations of sham acupuncture are possible:

The following is an example of wrong methods used as 'sham acupuncture' and confused with placebo effects. So and colleagues in Hong Kong attempted to test the use of acupuncture as an adjunctive therapy with IVF procedure [53]. Unfortunately they applied a non-penetrating sham acupuncture treatment to the same acupoints as needled in the test treatment. Which means that this study makes a comparison of the relative effects of two treatment techniques, it is not and could never be an 'explanatory trial' nor is it able to control for placebo effects. When the sham treatment, which they call placebo treatment was significantly more effective than their test treatment, they concluded that placebo is more effective than real acupuncture and that the treatment does not help women become pregnant while undergoing IVF procedures.ⁱⁱ This study cannot draw such conclusions, nor is such a conclusion correct. The study demonstrated, contrary to the expectation of the researchers, that gentle stimulation (using the non-penetrating sham needle) is significantly more effective

than the heavier stimulation needling for women undergoing IVF procedures. This study is important also because the sham intervention that was used was the Streitberger non-penetrating needle [54]. Given the accidental design of this study as a comparison of the relative effectiveness of two techniques, the study thus shows that the non-penetrating sham is a highly active treatment that cannot be reduced to or labelled as placebo effects. Not only did the researchers misunderstand what they had done but readers and recently reviewers have also misunderstood the study [50], creating false negative conclusions and through the systematic review, bias against the use of acupuncture.

Unknown mechanisms

Researchers recently figured out that despite decades of research on the mechanisms of acupuncture, it is still unclear how it works. At best we have established correlations between the needling and measured effects, but we don't know what the mechanisms are inside the body [18, 19]. This has led leading researchers to call for a moratorium on sham acupuncture studies since if we don't know what the mechanisms of acupuncture are, we don't know how to choose an appropriate sham acupuncture therapy to test acupuncture in the 'explanatory trial' model of the placebo controlled clinical trial [31 see also 1]. The position paper of Langevin et al. advocates the use of pragmatic trials to test acupuncture clinically with renewed efforts in the laboratory to test its mechanisms. This is similar to the recommendations of UK professor, Hyland [22].

Conclusions

Sham acupuncture is still demanded in many trials of acupuncture despite the developing evidence base that it is a much misused and misunderstood technique. Its misuse is compounded by its incorrect association with placebo. As more researchers realize the difficult if not impossible challenges that sham acupuncture trials create, it should gradually become less utilized. It may be helpful to use sham acupuncture type controls in physiological studies rather than clinical studies [45], but these should not be confused with placebo. It makes more

sense to concentrate on investigating the mechanisms of acupuncture in laboratory studies and testing its effectiveness in pragmatic clinical trials.

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ⁱ Despite evidence of effectiveness from one of the first trials to use this method as a control treatment in an acupuncture trial [38].

ⁱⁱ Although they did acknowledge that their sham treatment may not have been inert [53].