# Selecting an appropriate placebo for a trial of spinal manipulative therapy

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Selecting an appropriate control group or placebo for randomised controlled trials of spinal manipulative therapy is essential to the final interpretation and usefulness of these studies. Prior to starting a randomised controlled trial of spinal manipulative therapy for acute low back pain we wanted to ensure that the placebo selected would be considered appropriate by experts in the field thereby making the results more likely to be accepted and more likely to influence clinical practice. We developed ten placebo techniques that aimed to mimic spinal manipulative therapy as closely as possible which, while not including the active component of spinal manipulative therapy, were still credible. This list of placebo techniques with detailed descriptions was sent to 25 experts in the field from Australia and New Zealand including both clinicians and academics. We asked the experts to rate whether they believed each technique was appropriate for use as a placebo in a trial of spinal manipulative therapy. Sixteen (64%) of the experts responded. There were extremely low levels of agreement between the experts on which placebos were appropriate (kappa = 0.05, 95% CI 0.01 to 0.10). For nine of the ten placebos at least one expert considered the placebo to include the active component of spinal manipulative therapy while at least one other expert believed the same placebo was not only not active but also not credible. The results of this study demonstrate the different views of experts on what constitutes an appropriate placebo for trials of spinal manipulative therapy. Different beliefs about what is the active component of spinal manipulative therapy appear to be responsible for much of the disagreement. **[Hancock MJ, Maher CG, Latimer J and McAuley JH (2006): Selecting an appropriate placebo for a trial of spinal manipulative therapy. Australian Journal of Physiotherapy 52: 135–138]**

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## Introduction

Randomised controlled trials investigating the effectiveness of spinal manipulative therapy must by definition include a control group. The options for the control group include a no treatment group, an alternate treatment group, or a placebo group. All three have been used in trials of spinal manipulative therapy (Bronfort et al 2004, Ferreira et al 2003) and each has methodological and practical advantages and disadvantages.

The use of a no treatment group is potentially simpler and cheaper and seems appropriate when the research question is to determine the effectiveness of spinal manipulative therapy including the specific and non-specific effects. A limitation of using a no treatment control group is that the specific effects due to spinal manipulative therapy cannot be differentiated from placebo effects (Vickers and de Craen 2000). Withholding treatment may also be an ethical and practical consideration when using a no treatment control group.

The use of an alternate treatment group (eg exercise) as the control group potentially overcomes the difficulties associated with withholding treatment. Any additional benefit of spinal manipulative therapy over an alternate treatment is more likely due to the specific effects of spinal manipulative therapy than non-specific effects, including placebo, which should be similar between groups (Jones et al 1996). The most obvious disadvantage of using an alternate treatment control group is that if both treatments have similar effects interpretation of the results is very difficult. In this case it may not be possible to determine if both treatments are equally effective or if neither treatment is effective (Tramer et al 1998). Sample sizes needed for this design may also be larger as the smallest effects that are of interest when treatments are compared will typically be smaller than when the treatment is compared to a no treatment control (Jones et al 1996).

The use of a placebo group as a control group potentially allows for the specific effects of spinal manipulative therapy to be separated from the non-specific effects. This design is therefore preferred if the study question is to investigate the effectiveness of the specific effects of spinal manipulative therapy over the non-specific effects. One difficulty with this design is that controversy exists as to the mechanism by which spinal manipulative therapy works (Bogduk and Mercer 2004) and therefore developing a placebo that contains the non-specific components but not the specific components is potentially problematic. Developing credible placebos for spinal manipulative therapy is also potentially difficult (Koes 2004).

As part of developing the protocol for a randomised controlled trial investigating the effectiveness of spinal manipulative therapy in acute low back pain we hoped to develop a placebo that was as close as possible to the active spinal manipulative therapy, but did not include the specific active component. In addition, the placebo needed to appear credible. In our trial, active spinal manipulative therapy is defined as mobilisation or manipulation procedures whereby a physiotherapist applies external forces to the patient which aim to produce motion at the intervertebral segments of the

**Table 1.** Experts' opinions of proposed placebo techniques (n = 16).

| Placebo technique | Considered appropriate | Considered active | Considered not credible |
|---|---|---|---|
| Spine glider thoracic spine | 5 | 4 | 7 |
| Spine glider lumbar spine | 8 | 7 | 1 |
| Rib glider | 8 | 2 | 6 |
| Log roll | 8 | 5 | 3 |
| Sham neural mobilisation | 0 | 10 | 6 |
| Hip twister | 3 | 6 | 7 |
| Hip glider | 7 | 4 | 5 |
| Hip compression | 2 | 7 | 7 |
| Skin twist thoracic spine | 8 | 4 | 4 |
| Skin twist lumbar spine | 7 | 9 | 0 |

lumbar and thoracic spine, the sacroiliac joint, the pelvis, and hip. The physiotherapist would adjust the treatment according to the clinical presentation of the patient. The active spinal manipulative therapy and placebo treatments would be delivered two to three times per week for up to four weeks. To test if we had been successful in developing an appropriate placebo for our trial we asked experts their opinion of a variety of potential placebo techniques.

## Method

Techniques which may be useful as placebos for spinal manipulative therapy were trialled and developed by three physiotherapists on colleagues and physiotherapy students. The recipients were asked for feedback on whether they believed the techniques were active or not and whether they would be believable to patients. This feedback was used to modify or exclude techniques. Generally the placebo techniques involved a therapist placing their hands on the patient and producing low forces in directions where producing lumbar intervertebral motion appeared unlikely. A final list of 10 techniques was developed and written descriptions for each technique generated. Four of the techniques were called 'gliders' and were designed to simulate passive accessory movements of the lumbar spine, thoracic spine, ilium, and ribs (Maitland 1986). The physiotherapist moved the skin sideways across the underlying bone rather than producing a downwards force. The starting position for the techniques was the same as that commonly used, however in the lumbar spine the technique was to be performed at least two joints from the most symptomatic level. Two of the techniques were called 'twisters' and involved placing the hands on either side of the lumbar spine or thoracic spine in the manner commonly used to perform a screw manipulation (Maitland 1986). From this starting point the hands were moved past each other stretching the skin without any downwards pressure. The placebo version of rotation mobilisation (Maitland 1986) was the 'log roll' technique which involved placing the patient in side lying and positioning the physiotherapist's hands over the lower ribs and ilium. The pelvis and trunk were then rolled together so no or minimal lumbar intervertebral motion would occur. A 'hip twister' technique involved the patient lying supine with the involved leg held at 90 degrees of hip and knee flexion by the therapist. The hip was then moved passively into internal and external rotation but only to half the available range. The final technique, 'sham neural mobilisation' (Butler 1991) involved a straight leg raise to approximately 45 degrees or lower if symptoms were elicited. From this point the knee was moved passively from 10 to 40 degrees flexion with the ankle relaxed in plantarflexion.

The list of ten techniques with descriptions was sent to 25 experts in the areas of spinal manipulative therapy and design of clinical trials from across Australia and New Zealand. Both academics and clinicians were included. The experts were asked to state whether they considered each of the ten techniques to be an appropriate or inappropriate placebo for a clinical trial of spinal manipulative therapy. A reminder was sent out to those who had not responded after two weeks.

Two assessors independently scored all responses as yes or no for all techniques. As nearly all respondents who felt a technique was not appropriate indicated that they believed the technique either contained the active component of spinal manipulative therapy or was not credible, the no responses were further divided into these two categories. Those respondents who did not provide this information were emailed for clarification. Therefore for each of the 10 techniques each expert's response was scored as appropriate placebo, not appropriate (active) or not appropriate (not credible). Where the ratings of the two assessors differed a third assessor made the final decision or the respondent was recontacted for clarification of the response. Agreement between raters was assessed using multi-rater kappa.

## Results

Sixteen (64%) of the 25 experts responded and their responses are shown in Table 1. Multi-rater kappa values demonstrated extremely low levels of agreement across the experts on all ten possible techniques (kappa = 0.05, 95% CI 0.01 to 0.10). The overall agreement between the experts was only 37% (chance agreement was 34%). Agreement between the experts was also low for the individual techniques. For nine of the ten placebos at least one expert considered the placebo to include the active component of spinal manipulative therapy while at least one other expert believed the same placebo was not only not active, but also not credible (Table 1). There was no technique that was considered an appropriate placebo by more than 50% of the respondents (Table 1).

## Discussion

The results of this study demonstrate the difficulty in developing an appropriate placebo for trials of spinal manipulative therapy. Even among experts in the field, beliefs about what constitutes an appropriate placebo are very different. The importance of this finding lies in the interpretation of results from placebo-controlled trials of spinal manipulative therapy and more particularly the change or lack of change in clinical practice as a result of trials of spinal manipulative therapy. A recent review of spinal manipulative therapy (Assendelft et al 2003) identified six placebo-controlled trials of spinal manipulative therapy. Of these six trials three used placebos designed to simulate spinal manipulative therapy (Ongley et al 1987, Triano et al 1995, Waagen et al 1986). Ongley et al (1987) used a placebo similar to the sham log roll we described (Ongley et al 1987). Based on our results, five (31%) of our experts would consider this placebo active, while three (19%) would consider it not credible.

Where readers of trials of spinal manipulative therapy do not accept the validity of a placebo it is our belief that they will tend to ignore the results and no change in clinical practice will result. One example of this is when readers believe that the placebo contains part or all of the specific active components of spinal manipulative therapy (Harman 2000). In this case negative results will potentially be ignored as the reader perceives that both groups contained the specific active component and therefore no significant difference should be expected between treatments (Paterson and Dieppe 2005). If, however, the results of a trial of spinal manipulative therapy find a significant difference between the placebo and intervention group then this is not such a problem. However the reader who believes the placebo is active will feel that the effect size underestimates the true value.

If the reader of a trial of spinal manipulative therapy believes the placebo is not credible then this will also impact on his or her interpretation of the results. In this case it is more of a problem when the results find a significant difference between the placebo and spinal manipulative therapy groups. Readers who believe the placebo is not credible will be concerned that the improvement found is due to placebo and not the active components of spinal manipulative therapy. This problem should be easier to deal with as studies can, and should, assess the credibility of the placebo using scales such as the treatment credibility scale (Borkovec and Nau 1972).

It is clear from the results of this study that readers of trials of spinal manipulative therapy do not agree on what constitutes an appropriate placebo. While this situation continues, the usefulness of placebo-controlled clinical trials of spinal manipulative therapy is diminished and their ability to guide and change clinical practice is compromised.

The results of this study beg the question: why do experts in the field have such poor agreement on what constitutes an appropriate placebo for a trial of spinal manipulative therapy? The experts' comments make it clear that much of the lack of agreement is due to different beliefs about what are the specific active components of spinal manipulative therapy. As an example, one expert who responded stated that he believed 'sensory input' to be an active constituent of spinal manipulative therapy and therefore any placebo that involves sensory input to the involved area is potentially active and not an appropriate placebo. On the other hand another expert felt that 'reproduction of the patient's symptoms was essential' for credibility and therefore many of our proposed placebos were deemed not believable. While the biological basis for spinal manipulative therapy remains unclear it appears that controversy will continue in interpreting clinical trials of spinal manipulative therapy that include a placebo.

A suggested way forward at this point is that studies investigating spinal manipulative therapy be very clear about the specific aim of the study and use a placebo that matches the aim. If the aim is to investigate the overall effectiveness in clinical practice of spinal manipulative therapy a non treatment group should be employed. If the aim is to investigate a specific component of spinal manipulative therapy (eg treating the correct level) then a placebo which includes all of the other components should be used so the only difference is the specific component to be investigated (Chiradejnant et al 2002, 2003). If the aim is to investigate some specific components of the treatment (eg intervertebral motion) but remove some more general components of care (eg interaction with a therapist and expectation) then a placebo that includes the general components but not the specific components of interest should be used. If the aim is to evaluate the specific and non-specific effects of treatment then a design including both a no treatment control and a placebo control will be needed. Following this model there should be less disagreement when interpreting the results of trials of spinal manipulative therapy. However, disagreement over what is the right question to investigate may still remain.

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