

Trial design in hypnotherapy - Does the RCT have a place?

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Abstract: Like many complementary or alternative therapies, hypnotherapy has been criticised by some for not having robust scientific evidence to back its claims. Studies aiming to determine the effectiveness of hypnotherapy are typically poorly designed or lack the patient numbers to achieve statistical power. Whilst it is acknowledged that more research is needed across a range of disease areas, few funding bodies are aware of the complexities of designing research which addresses the needs of both service providers, therapists and patients. The application of traditional clinical trial methods to hypnotherapy is not easy due to the differences in the underlying mechanism of therapy, however reliance on less rigorous methodologies does not address the need for high-grade evidence. This paper discusses some of the methodological issues which require consideration when undertaking research in hypnotherapy and concludes with a call for more well designed studies led by multi-disciplinary teams using multiple methods.

Keywords:

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Introduction

In 2000 the House of Lords Select Committee acknowledged that there was insufficient evidence upon which to base recommendations in most alternative or complementary therapies and stressed the need for therapists to substantiate claims of therapeutic effectiveness with scientific evidence.¹ For many this equates to data obtained from rigorously performed trials. However applying clinical trial methodology to evaluation of complementary or alternative medicine (CAM) or therapies is problematic. It has been argued that trial methods are inappropriate for use in CAM research as they remove fundamental aspects of the therapeutic relationship and adopt a reductionist approach, which is unable to fully evaluate benefits of holistic treatments. Whilst qualitative research has been used to provide much needed evidence about CAM, its mechanisms and benefits it is unable alone to address issues of effectiveness or cost-effectiveness which are essential pre-cursors to the adoption of CAM into more general usage or NHS provision.

This paper aims to explore the use of trials in hypnotherapy research. Very few trials of hypnotherapy

have been published in recent years, which suggests a decline in research activity, dominance of other research methodologies or difficulty publishing. It is important that evidence on effectiveness is more widely published and one of the key issues in facilitating this is improving awareness. The scientific community needs to be aware of the specific issues relating to trial methodology in CAM to ensure trials are evaluated using appropriate criteria and the research community need to design robust and rigorous trials, which withstand both methodological and therapeutic scrutiny. Compromises and methodological strategies for designing high quality research that addresses the needs and concerns of patients, therapists and health service providers will be proposed.

The Randomised Controlled Trial

The randomised controlled trial or RCT is generally accepted as the gold standard when trying to demonstrate the effectiveness of a medicine or treatment approach. One of the problems with cohort studies, whereby two groups are compared is that the groups are biased in some way and differences that exist may

be due to other factors (known as confounding factors) rather than the treatment itself. The RCT gets around this problem by randomly assigning patients to treatments and then treating both groups equally apart from the treatment under investigation. So patients in both groups of a drug trial, for example, will receive exactly the same package of care (investigations, treatment time etc) and only the drug prescribed will differ. As long as we have sufficient patients in our trial this enables us to say with some confidence that differences between groups are due to the treatment (or a chance finding) rather than other factors or biases. Even confounding factors that we aren't aware of should be controlled for by virtue of the fact that they are randomly split between the two groups, so in effect cancel each other out.

In clinical trials the RCT design is further improved upon by the use of placebos and blinding. Use of a placebo (such as an inert tablet in drug trials) allows us to determine whether the effect noted is due to the treatment itself or the placebo effect (patients experience benefit from the fact that they are being treated). The placebo response has been described as the therapeutic impact of incidental treatment ingredients. Such an effect, if noted, is not meaningless or worthless but in order to maximise benefit we need to feel the therapy we provide does indeed have an 'active ingredient' above and beyond this effect. The issue of the placebo effect is especially important in hypnotherapy research because many of the conditions which respond to hypnotherapy also demonstrate a large placebo effect. These will largely be conditions with a psychosomatic element, which responds in the short term to a placebo effect. It is these same conditions that hypnotherapy is particularly effective in treating by altering subconscious beliefs and patterns and imparting control to the patient. It is therefore important that trials are designed that try to control for the placebo effect in some way.

Blinding can be achieved on several levels – in a methodologically perfect trial, patients, therapists and researchers will all be blind – that is to say that they are unaware which treatment any patient is getting. This means that all patients are treated identically throughout the research and other factors such as the therapist treating patients differently or patients feeling better simply because of a placebo effect are all controlled for. It should be apparent that including placebos or blinding patients in hypnotherapy trials is either difficult or impossible and much more thought is therefore required to the design of such research.

Placebos

Can we design placebos for use in hypnotherapy trials? I put this question to a group of medical students earlier this year and generated a lively and creative discussion about ways of doing this, including using lay people to deliver hypnotherapy and getting patients to go through techniques used in a therapeutic consultation but without the induction of trace. Both have

obvious practical not to mention ethical problems. Previous studies have used alternative 'talking' therapies for their placebo or control group. Whorwell first evaluated hypnotherapy for Irritable Bowel Syndrome by comparing it to a 'psychotherapy' control group². This has the benefit of controlling for the amount of time, attention and empathy shown to patients but is not a placebo by any definition. The addition of a 'placebo' tablet to the control group whilst creative, somewhat muddies the waters in terms of treating groups equally and without understanding more about the mechanisms through which placebos work is perhaps a poor solution. Indeed the solution here seems again to be one of clarifying in our minds the specific question we are asking. It is becoming less and less likely that trials will be able to use true placebos as medical developments mean we are more often asking the question "is this new treatment better than the old one?" rather than the question "is it better than nothing?".

We therefore frequently see drug trials which are less Randomised Controlled Trials and more Randomised Comparison Trials – comparing treatments to determine which is most beneficial. Such an approach is ideally suited to the evaluation of hypnotherapy and other complex therapies – we have become too concerned with establishing which component of a therapy works when perhaps the important question, certainly from the patients perspective, is "is this going to be better for me than my current treatment". It therefore becomes acceptable (and sensible) to compare a drug with a complementary therapy. The argument that we haven't controlled for other factors, such as the time we spend with the hypnotherapy group is itself rather a futile argument when time, is a component of the treatment. Whilst with drug treatments it is sensible to ask what 'active' component of the medicine provides benefit to ensure cheap effective medication with minimal side effects, this argument holds little weight in CAM research where components of therapy are less likely to be additive but combine together in a holistic package of care.

Blinding

Blinding is a relatively redundant issue in the design of hypnotherapy trials as it is not truly possible to blind either the patient or therapist. Whilst it is still possible to blind the researcher collecting or analysing the data to some extent there is always the risk that blinding is broken by something the patient says or indicates on their outcome questionnaires. Trials of other CAMs have tried to introduce a degree of blinding by the use of placebos, sham acupuncture needles and other ingenious devices. The over-riding question however is whether the uncertainty caused by attempting to blind patients has a detrimental effect on the therapeutic relationship. If this is the case we will consistently underestimate the size of any benefit to the patient.

Randomisation and equipoise

The concept of randomisation, that is, allocating patients to a therapy on the basis of a coin toss has been argued to be in direct conflict with the nature of many complementary therapies whereby joint decision making and the patients choice and beliefs are fundamental. Ethical issues also come into play with the concept of randomisation. Typically it is argued that for a patient to enter a trial where they will be allocated to a treatment by chance, both the patient and doctor must be in a state of equipoise. By this we mean that they genuinely are uncertain about which treatment would be most efficacious. If either the doctor or patient believe one treatment option would suit them better than another, they should receive this treatment and should not be entered into a trial. This ethical requirement for trials conflicts with the belief systems implicated in treatments such as hypnotherapy, whereby optimal care can only be achieved when both the patient and treating therapist have belief in the treatment. This is not to say the treatment works only through faith but that the belief in benefit is a fundamental concept in the delivery of high quality effective treatment.

We could therefore aim to recruit patients who genuinely are in a state of equipoise. This patient group will be different from those who seek therapy and therefore results cannot be generalised to the patients hypnotherapists typically see. This is perhaps not an issue if our perspective is an NHS perspective i.e. we aim to answer the question "Would referring patients with IBS to a hypnotherapist be effective or cost-effective". If however we aim to determine "Is hypnotherapy effective for IBS management in patients who consult a hypnotherapist?" we risk underestimating the benefit by using a different and less engaged client group. It is therefore vital that we clearly define our question – both being equally valid – and ensure results are not interpreted out of context and the patients entered to the trial are indeed representative of the group we wish to generalise to.

Finding patients who would consult a hypnotherapist but are in a state of equipoise is however a near impossible task and their motivation to comply with treatment is questionable. Similarly we clearly are unable to find therapists who are in a genuine state of equipoise and if we did the quality of their treatment would perhaps be open to criticism. Possible methodological solutions to this are the use of partially randomised trials or preference trials. It is possible to recruit patients to a trial where they receive their choice of therapy where a preference exists but are randomly allocated where they do not express a treatment preference. This allows us to build into the study design the concept that choice and belief is a fundamental concept in treatment but will also allow us to look separately at the benefits accrued in groups who did and did not state a preference thus helping to unpick somewhat the difference in benefit experienced by those who would and would not choose the therapy themselves. There remains the risk that we end up with different groups and we lose some of the methodological benefits of

the RCT design but dependent on our question this may be an acceptable compromise.

Outcome measures

Clinical trials tend to favour the use of disease specific outcomes as these are sensitive to small changes in health, symptoms and disease-specific quality of life. However the selection of outcomes for CAM research is more complex. It is important that researchers have an understanding of the mechanisms through which the therapy works to ensure appropriate outcome data is collected and benefit not missed. A recent randomised controlled trial undertaken by myself and colleagues to determine the effect of gut directed hypnotherapy on primary care patients with Irritable Bowel Syndrome used disease specific outcome measures – a symptom measure and disease specific quality of life score³. Whilst initial differences between groups did not endure over time, the hypnotherapy group reported significant benefit from the treatment and the majority indicated they would recommend it to other sufferers and would be prepared to pay for treatment. The suggestion here is that benefit was accrued outside of the areas we were measuring, and with reflection given the holistic nature of treatment this is likely. For example it may be that the symptoms themselves have not reduced but the patient feels more empowered to manage their symptoms and have an increased sense of control. In illness which has a psychological component, such factors are vital and have the potential to improve quality of life almost as much as symptom removal.

This leaves a dilemma in terms of outcome selection as there is the risk we are comparing apples and pears. If we wish to compare hypnotherapy to usual (symptomatic) management to determine whether there would be benefit to patients from the wider introduction of this therapy, we need to ensure we have outcomes that are appropriate to both groups. Whilst disease specific measures may be good at identifying small differences between two drug treatments, it would seem that in trials where one or more treatment works holistically the most appropriate outcomes would be generic rather than specific. Trials of this nature should consider using broad measures of well-being and quality of life.

It has also been proposed that to ensure outcomes are patient-centred qualitative work is used both before a trial to establish the outcomes valued by patients and during or after the trial to complement quantitative data, provide insight into the mechanisms through which therapy worked and to indicate other benefits⁴. Such an approach is increasingly being adopted by researchers in CAM and multi-method studies a rapidly replacing traditional RCTs.

Standardisation

A further problem with the design of trials of hypno-

therapy is the concept of standardisation. Typically in clinical trials we aim to standardise our treatments and test very specific hypotheses. Drugs, doses, and treatment regimes are typically standardised. Attempts to do this in hypnotherapy would perhaps include the use of a standard script, in homeopathy the use of a set treatment for certain diseases. We know however that this is not the way these therapies are delivered and a 'one size fits all' approach is not appropriate. As with other issues we have discussed, adoption of such an approach will minimise the benefit of therapy and is not generalisable to real therapy situations. For results to be meaningful they should test the therapy in the environment and method in which it is used and pragmatic trials are therefore important. The hypnotherapy arm of any trial should deliver hypnotherapy to the patient in the way the therapist believes would be most efficacious for that individual.

The therapeutic relationship

Throughout I have highlighted the ways in which rigorous RCT methodology jeopardises the therapeutic relationship. It could be argued that any trial indicates uncertainty, which may damage faith and therefore reduce benefits of treatment and therefore RCTs are not appropriate tools in hypnotherapy research. Such an argument leaves us reliant on lower grades of evidence such as case series reports and means effectiveness of treatment will never unequivocally be demonstrated or cost-effectiveness be reported. Such an argument itself is self-limiting – if through appropriate RCT evaluation of a therapy we do demonstrate clear benefit, it suggests that the real benefit achieved for patients outside of the trial situation would be even greater than demonstrated and the fact that there is robust evidence of benefit should increase faith and confidence which in turn could lead to greater therapeutic return. The key however is defining the word 'appropriate'. To evaluate hypnotherapy outside of the usual mechanisms of delivery and treatment is inappropriate.

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To evaluate it in consultation with practitioners and in a pragmatic and realistic manner is useful and can be methodologically sound.

Summary

In summary, there are a range of methodological dilemmas one must face when designing, conducting or interpreting results from trial research in hypnotherapy. Whether reading papers or designing and conducting research the key is to be explicit about the question of interest. There is no correct way to design any research study – the fact that hypnotherapy research is difficult should not be a barrier to its conduction. Trials are the best way of demonstrating effectiveness and cost-effectiveness, but they must be designed in a way that allows for the mechanisms of the therapy to work as they would in practice and using outcomes that are sensitive not only to changes in the disease but also holistic changes which may be accrued by the therapy.

Trial design should therefore be something undertaken by teams with methodological expertise but also an understanding of hypnotherapy – its delivery and mechanics. Trial design should allow for the incorporation of multiple methods to address all aspects of therapy. In some ways adherence to current trial methodology gives strength and publication of a protocol with pre-specified aims is recommended, but in other areas methodological compromise is needed to ensure we keep as many benefits of trial methodology as possible without compromising the underlying delivery of the therapy. A study designed by a process of negotiation and information exchange should be robust methodologically but also have the generalisability needed to ensure its value to therapists and patients.

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A Commentary

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The House of Lords Inquiry recognised there is a growing demand for and benefit from what are still regarded as non-conventional therapies; including hypnotherapy.¹ Furthermore, they accepted that access to such therapies should increasingly be available through the NHS - so long as the efficacy of the treatments have been properly demonstrated. Assessing the value of hypnotherapy is, therefore, important if it is to become widely accepted as a part of routine health-care provision. Nevertheless, the research evidence for hypnotherapy is difficult to synthesise because of the small number of studies (particularly controlled studies); the small sizes of the studies; and, the considerable heterogeneity of participants, interventions and outcome measures.

Lesley Robert's paper "Trial design in hypnotherapy - Does the RCT have a place?" is a timely and useful discussion of the difficulties in applying biomedical reductionist approaches to the evaluation of hypnotherapy. However, randomised controlled trials (RCTs) are, and are likely to continue to be, widely accepted as the most reliable method of determining the effectiveness of treatments that are to be delivered within the NHS. Unlike trials of pharmaceutical products, most complementary or alternative therapies require the design and execution of research that addresses the additional problems resulting from evaluation of complex interventions. A trial of hypnotherapy may have to consider the expertise of the Hypnotherapist(s), the history taking, the actual hypnotherapy delivered and the number of hypnotherapy sessions, any additional counselling delivered and the follow-up provided. Individual Hypnotherapists may offer slightly different treatments and the active components of the stroke unit may be difficult to specify, making it difficult to replicate the intervention. However, an evaluation that is meaningful to the NHS, that is one that can conclude that referral to a Hypnotherapist is a useful management strategy, needs to be able to assess hypnotherapy "in general" rather than an individual practitioner in an individual setting. A further difficulty is that investigators need to include outcomes that not only are relevant to patients with the disease or condition being studied but also encompass measures of wider relevance to the health system, such as economic measures.

Michelle Campbell and colleagues have developed work undertaken by the Medical Research Council (MRC) to produce a framework for the design and evaluation of complex interventions to improve health.¹ They usefully describe the process of developing an evaluation of such complex interventions in a manner akin to the sequential phases of drug devel-

opment. Such a phased approach allows for the use of relevant research methods, both qualitative and quantitative, to address the different components of the overall research question. Phase 1 would enable the different components of successful hypnotherapy, and their interaction, to be described. Phase 2 would use the information gathered in Phase 1 to define the optimum intervention and develop the design of a trial (determining the acceptability of the intervention, feasibility of the trial, identifying a suitable control and relevant outcomes) to assess this intervention. Phase 3 would be the main RCT to establish the efficacy of the intervention. Whilst, Phase 4 would examine implementing the intervention into routine practice. This is a useful model; unfortunately much of existing research evidence seems to have stopped after Phase 1, or, has jumped straight in at Phase 3.

Comprehensive evaluations of hypnotherapy using the models described for the evaluation of complex interventions require the formation and retention of multi-disciplinary teams with experience of multi-method research; such teams are few and far between. Furthermore, such evaluations take several years to complete and, therefore, require a substantial amount of funding. Several of the major research funding bodies have frequently expressed a desire to support robust evaluations of complementary and alternative therapies. It is difficult to write a commentary on a paper written by someone I respect and work closely with, however, I'm afraid that I disagree with Lesley's conclusion that "methodological compromise is needed". I would encourage researchers to develop methodologically robust evaluations of this complex intervention and seek resources to undertake the comprehensive large-scale evaluations that will be taken notice of by the healthcare establishment.

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