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Scientific tools, fake treatments, or triggers for psychological healing: How clinical trial participants conceptualise placebos

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ABSTRACT

Placebos are an essential tool in randomised clinical trials, where they are used to control for bias and contextual healing effects. Placebos and their effects are also studied from multiple diverse perspectives, but the perspectives of placebo recipients are seldom considered. Research shows that people form cognitive and affective representations of active treatments such as medicines, and that they use these representations to guide their behaviour; it seems reasonable to suggest that people might also think about and develop representations of placebos. We adopted a qualitative approach to examine in detail how participants in one RCT, conducted in the USA, conceptualised placebos. 12 people were interviewed 3 times each, at the start, middle, and end of a trial of placebo effects and acupuncture for Irritable Bowel Syndrome (IBS). The interview data were analysed inductively and we identified four ways in which the participants conceptualised placebos: placebos are necessary for research; placebo effects are fake; placebo acupuncture is not real acupuncture; placebos have real effects mediated by psychological mechanisms. Participants' conceptualisations of placebos were dynamic and situated in a broader psychological and socio-cultural context. Seeing placebo effects as legitimate seemed to be facilitated by having more holistic models of healing, viewing IBS as psychological, and seeing treatment as multi-factorial. However, some participants maintained a negative view of placebo effects (e.g. as illusions) that was apparently inconsistent with their other beliefs (e.g. in mind-body healing mechanisms). This may indicate a dominance of negative discourses around placebos at a socio-cultural level. Negative views of placebos are inconsistent with evidence that placebo treatments can have positive effects on symptoms. RCT participants should be informed about potential benefits of placebo treatments to avoid misunderstandings and unease. Future work should improve methods of providing participants with full accurate information about placebos and their effects.

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Introduction

In their broadest sense, placebo effects are healing outcomes derived from the ritual of medicine, the patient–provider relationship and the power of the therapeutic imagination (Kaptchuk, 2011). Placebos are both the tools and subjects of scientific research. Administering placebos to patients can elicit beneficial effects including the reduction of symptoms such as chronic pain (Finniss, Kaptchuk, Miller, & Benedetti, 2010), insomnia (Bélanger et al., 2007) and depression (Kirsch et al., 2008). For neuroscientists, psychologists and anthropologists, placebos constitute a means to examine how contextual factors contribute to healing

processes and to test theories about how the administration of placebos triggers various salutary effects. For clinical researchers, placebos are essential tools in randomised clinical trials (RCTs), used to control for bias and contextual and psychological components of healing and thus isolate the specific effect of a new drug or treatment. From the perspective of biomedical trialists then, placebos are research tools and their effects must be controlled for. But what about those people who volunteer to take part in clinical research, those who can experience placebo effects at first hand: what do placebos mean to their recipients? This paper explores how participants in one RCT conceptualised placebos and the implications of this for both practical applications and theoretical understandings of placebos.

According to the Common-Sense Model of illness cognition, people construct cognitive and emotional representations of symptoms which they use to guide their selection and evaluation of coping

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procedures (Leventhal, Diefenbach, & Leventhal, 1992). According to the extended version of the model, people also construct representations of different coping procedures including medicines, and these representations influence uptake of and adherence to treatment (Horne & Weinman, 2002). Thus we might reasonably expect people to construct representations of placebos, and for these representations to guide their actions. The few (mostly survey and focus group) studies that have been published in this area do indeed suggest that people develop (often limited) ideas about placebos and that these ideas can shape their behaviour, particularly in relation to participation in RCTs. To our knowledge, such studies are scarce.

Existing research suggests that lay people have somewhat limited understandings of placebos and their effects. Focus group participants in Australia and Japan were described as confused by and unfamiliar with the use of placebos in medical research (Asai et al., 2004; Ellis & Butow, 1998). In surveys, rheumatology patients (and nurses) as well as general practice patients have been described as underestimating the size of the placebo effect and having little knowledge about it (Berthelot, Maugars, Abgrall, & Prost, 2001; Chen & Johnson, 2009). While there is a paucity of evidence in this area, it seems that people may have limited knowledge about placebos and yet be willing to accept their use in medical research: A public consultation in Canada concluded that participants viewed placebo-controlled trials as valuable research tools and accepted their use (with informed consent) depending on the severity of the condition and the availability of alternative control treatments (Huston, 2007). Furthermore, potential trial participants' attitudes towards placebos may influence their willingness to take part in placebo-controlled RCTs (Hummer et al., 2003; Welton, Vickers, Cooper, Meade, & Marteau, 1999). For example, in an interview study with people with schizophrenia, some respondents reported being encouraged to take part by the chance of getting a placebo (rather than active medication) while others reported being put off by not knowing whether or not they were taking placebo (Hummer et al., 2003). This suggests the need to adopt a broader perspective that goes beyond documenting the accuracy (or absence) of knowledge about placebos and instead focuses on how RCT participants conceptualise placebos and their effects.

How RCT participants conceptualise placebos also has implications for ethical research conduct. If a participant does not understand that the benefits of treatment and placebo might be equal, then they cannot be said to have given informed consent to take part in a placebo-controlled trial. Disparities between medical and lay understandings of technical RCT processes such as randomisation and clinical equipoise have been documented in many settings (Featherstone & Donovan, 1998; Robinson et al., 2005) and are often attributed to the therapeutic misconception, whereby RCT participants mistakenly attribute therapeutic motives to trial physicians and investigators (Appelbaum, Roth, Lidz, Benson, & Winslade, 1987). There is some evidence that trial participants also hold beliefs about placebos that are incorrect and/or at odds with researchers' beliefs (Criscione, Sugarman, Sanders, Pissetsky, & St Clair, 2003; Pope et al., 2003). For example, in a placebo-controlled trial in arthritis, 87% of participants understood that some people in the trial would receive a placebo but only 50% correctly disagreed with a statement that they would definitely receive an active treatment (Criscione et al., 2003). Quantitative work can establish the existence and prevalence of participants' misunderstandings about placebos in RCTs. However, qualitative work with RCT participants is needed to explore how their views of placebos differ from researchers' views and to suggest reasons for and consequences of any such differences. We therefore analysed qualitative data from one RCT that investigated both placebo effects and acupuncture and aimed 1) to identify the ways in which participants conceptualised placebos and 2) to suggest reasons for and possible consequences of different ways of thinking about placebos.

Methods

This analysis is part of a larger qualitative study which was nested within an RCT investigating placebo effects and acupuncture for irritable bowel syndrome (IBS). The RCT was conducted in the USA between December 2004 and April 2006. Participants were informed that the study was an efficacy study comparing acupuncture to sham acupuncture and they gave written informed consent. After completing the study participants were debriefed that the study also examined the effectiveness of the patient–practitioner relationship and placebo effects. The research was approved by the IRB of the Beth Israel Deaconess Medical Center and Harvard Medical School. The design and main findings of the trial and nested qualitative study are summarised below and described in full elsewhere (Kaptchuk et al., 2008, 2009).

The trial

The aim of the trial was to investigate three components of the placebo effect: assessment and observation, therapeutic ritual (placebo acupuncture), therapeutic relationship (between acupuncturist and patient). Participants were 262 adults diagnosed with IBS according to Rome II criteria. They were randomly assigned to one of three treatment arms: waiting list (assessment and observation), placebo acupuncture with minimal (“limited”) interaction (assessment, observation, and therapeutic ritual) or placebo acupuncture with interaction (assessment, observation, therapeutic ritual, plus “augmented” supportive patient–practitioner relationship). After three weeks, participants in the placebo acupuncture groups were then re-randomised to continue with placebo acupuncture or to receive real acupuncture. The trial continued for a further three weeks (six weeks total). Participants but not acupuncturists were blinded to treatment allocation during the trial. As hypothesised, patients receiving placebo acupuncture with augmented interaction experienced greater improvement than those who received placebo acupuncture with limited interaction, who in turn experienced greater improvement than those on the waiting list (Kaptchuk et al., 2008).

The nested qualitative study

The primary aim of the qualitative study was to investigate the experiences of patients receiving placebo acupuncture in the context of the parent trial. A random selection of nine participants from each trial arm was invited to take part in semi-structured open-ended interviews at baseline, three weeks and six weeks. Interviews were conducted in 2004–5 by EEJ (not otherwise known to participants), took place in the large teaching hospital in the USA that hosted the trial, lasted 15–45 min, were recorded and transcribed verbatim. Topic guides differed slightly for the three interviews, were employed flexibly, covered broad topics such as what it was like to be in the trial, and included questions designed to elicit narrative accounts and explanatory models. We conducted two separate analyses, the second of which forms the basis of this article. The first analysis (Kaptchuk et al., 2009) focused on participants' experiences of placebos. Of the 18 participants invited to interviews who had been allocated to one of the two placebo arms, 13 completed the trial but one declined to take part in the qualitative study. Therefore, the first qualitative analysis was based on interviews conducted with 12 participants. The dataset consisted of baseline and mid-point interviews with six participants (who received placebo acupuncture for the first three weeks and real acupuncture for the final three weeks) and baseline, mid-point and end-point interviews with a further six participants (who received placebo acupuncture throughout). Six of the participants

had received limited interactions with their acupuncturist and six had received augmented interactions. Analysis identified and explored the following themes: thinking about placebo, discourses of anticipating and joining the trial, accounts of change, idioms of doubt, idioms of certainty, dramatic behavioural and psychosocial changes, and rhetoric of alliance. Of particular interest here is that this first analysis highlighted how participants oriented to the possibility that they might be receiving placebo acupuncture, expressed opinions about the nature of the treatment they were receiving and were often keen to discover whether they had received placebo or real acupuncture (Kaptchuk et al., 2009). Our second analysis, presented below, expanded on these insights by using a systematic and rigorous approach to examine how participants think about placebos and their effects.

Participants for this analysis

In the analysis presented here, we included baseline, mid-point and end-point interviews with all 12 participants in the qualitative study who were initially allocated to placebo acupuncture. Compared to the first qualitative analysis (Kaptchuk et al., 2009) we used an expanded dataset that included the end-point interviews conducted with the six participants who had been switched from placebo acupuncture to real acupuncture at the trial mid-point. This is consistent with our aim to examine how trial participants conceptualise placebos and their effects. Of the 12 participants, 7 were women and 5 were men. They were aged between 23 and 65 years (mean = 43 years, standard deviation = 17 years).

Analytic approach

Based on observations from the original broad analysis of the entire qualitative data corpus, we approached this analysis believing that participants had some ideas about placebos and that they had expressed these ideas in a particular context (during research interviews conducted as part of the trial of acupuncture for IBS as described above). Following existing psychological theory, we assume that people construct mental models of their experiences and that these models guide their actions. However, we do not see such models solely in cognitivist or phenomenological terms, as fixed or static entities that are independent of the particular situation a person finds themselves in. Rather, we assume people actively construct models and use them in a way that is dynamic (i.e. flexible) and situated within (constrained and facilitated by) the broader socio-cultural context, including the interview situation and the discursive resources available in a particular society. Therefore, we talk about how people *conceptualise* placebos to convey the active, dynamic and situated nature of this process (rather than referring to mental models or representations which imply a more individualistic, static construct). We chose to conduct an inductive thematic analysis attending to latent and explicit themes to analyse the different ways in which participants conceptualised placebos and placebo effects. This approach allowed us to conduct a primarily data-driven analysis in a way which was faithful to published methodological guidelines (Braun & Clarke, 2006) and consistent with our assumptions, interview data, and aims.

Analytic methods

We followed the phases of thematic analysis set out by Braun and Clarke (2006), moving forwards and backwards between the phases and incorporating established qualitative coding techniques to enhance our analysis. Phase 1 focused on familiarisation with the data: the lead analyst (FLB) read and re-read every transcript,

noting initial ideas in the form of memos. Phase 2 focused on generating initial codes: FLB worked through each transcript in turn, annotating them with inductive codes which served to describe the meaning conveyed by a particular section of speech (coding unit) and/or something about the social context in which it was produced. Coding units varied in length and were bounded by changes in meaning rather than any punctuation that had been added at the transcription stage. Some codes retained participants' language ('in vivo' coding) in an effort to stay close to participants' understandings.

Phase 3 involved searching for themes. The primary focus was on delineating the ways in which participants conceptualised placebos. Thus all talk about placebos was analysed and initial codes applied to this talk were grouped together to develop an initial typology of different ways of conceptualising placebos. The secondary focus was on how conceptualisations of placebo related to other aspects of the participants' lives within and beyond the trial. Codes that seemed to be related however loosely to participants' conceptualisations of placebo context were grouped together into categories. This categorisation was guided by existing psychological theory about illness representations and treatment beliefs. Diagrams were used to explore the emerging typology of ways of thinking about placebos and how these related to the broader categories.

In Phase 4, the themes and categories were reviewed in relation to the initial codes and the transcripts as a whole, and the diagrams produced in Phase 3 were further refined. This was supplemented by producing a detailed written summary of each participant's talk about placebos to capture dynamic patterns within individuals and avoid an overly static interpretation focused on patterns across individuals. Further analyses of these summaries (including a deviant case analysis described in the Findings) helped to clarify how different ways of conceptualising placebos related to different understandings of IBS, acupuncture, and healing mechanisms, and were situated in a broader social context.

Phase 5 focused on naming and defining the themes, or in our case on naming and describing the different ways in which participants conceptualised placebos and their effects. This process of refinement continued into Phase 6 (writing up) which involved conveying the typology and the importance of context. To prevent idiosyncratic interpretation, all authors were involved in a process of review and negotiation to refine the analysis and check it for accuracy against the interviews. The different ways of conceptualising placebos were often found within the same participants. Thus, this is a typology of conceptualisations, not participants. Quotes were selected for vividness and typicality in illustrating analytic points; pseudonyms are used to protect participants' identities.

Findings

We identified four ways in which participants conceptualised placebos and placebo effects: placebos are necessary for research; placebo effects are fake; placebo acupuncture is not real acupuncture; placebos have real effects mediated by psychological mechanisms. Understandings of placebos were dynamic, and some participants talked about placebos in quite different ways across their three interviews. Exploring these differences highlighted the importance of the broader understandings of acupuncture, healing mechanisms in general, and IBS.

Placebos are necessary for research

Some participants saw placebo acupuncture as an essential feature of scientific medical research, which is consistent with the

findings from the Canadian consultation (Huston, 2007). One participant, Sam, who was a male biomedical doctor with experience as an investigator in clinical trials, saw placebos from this perspective, as a scientific necessity. Another, Ben, a man in his 50s who had previously taken part in other placebo-controlled studies, also talked about placebo treatments as intrinsic features of clinical trials, as scientific devices that the researchers used to find out if their treatment worked. A participant named David, speaking in his mid-point interview, believed that the risk of getting placebo was unavoidable and had to be accepted if one was to volunteer for a clinical trial – someone has to get placebo: “And if I’m in the placebo, I’ll be disappointed, but I will understand that it’s part of the program.” (David, male in his 60s).

Most participants, like Greta, explicitly talked about how they hoped that they would get real acupuncture: “[I am] trying to be optimistic, hoping that I’m getting the treatments and that I’m gonna feel better.” (Greta, female in her 20s, mid-point interview). Placebo acupuncture as a scientific necessity was imbued with undesirable characteristics through the language used to describe it, as a hoax, a phoney, and a fake. After finding out that he had been receiving placebo, Ben suggested that it might be the treatment that investigators give you if they don’t want you to get better, while before finding out what treatment he had received, David thought that his practitioner would not give him placebo acupuncture because she cared for him and he trusted her. Such perspectives are consistent with a therapeutic misconception that trial personnel prioritise the individual participant’s wellbeing, as occurs in usual clinical encounters (Appelbaum et al., 1987).

Placebo effects are fake

Placebos could be seen as ineffective or as having only illusory effects. An extreme view was that placebo acupuncture is incapable of producing any effects. For example, Sam thought he might be receiving placebo acupuncture and equated a lack of side-effects with placebo treatment: “I haven’t had any side effects. Obviously if it’s placebo, I shouldn’t.” (Sam, male in his 50s, mid-point interview). When asked how she felt about not knowing which treatment she would receive, Emily revealed that she thought she would be able to tell which treatment she was receiving based on its effects. If she did not get any benefit from treatment then she would assume she was receiving placebo acupuncture: “I think I would know, because if there’s no improvement I know it wouldn’t be the acupuncture.” (Emily, female in her 50s, baseline interview).

A closely-related view was that placebo acupuncture can produce only illusory effects. Greta thought that placebo acupuncture could produce illusory effects by tricking you into thinking you feel better when really you do not. This view emerged in her final interview when told that she had been receiving real acupuncture:

“I had a feeling I was getting it anyways, and I’m glad to know that I was, and knowing that I wasn’t just thinking, “Hmm...maybe I’ll feel better,” you know or thinking I’m feeling better when I’m not.” (Greta, female in her 20s, end-point interview)

Participants who saw placebo effects as fake typically talked about how responding to placebo acupuncture would have negative consequences, primarily for a person’s identity. Being ‘tricked’ into feeling better was seen as making a person appear gullible. For example, Abigail, a retired teacher in her 60s, talked about how she would feel pretty stupid, as if she made it up, if she found she had benefited from placebo acupuncture. Unsurprisingly, those interviewees who did not think that placebo acupuncture can produce any effects, did not express any concepts of how a placebo treatment works.

Placebo acupuncture is not real acupuncture

Participants in the RCT were told that they would be allocated at random to receive placebo or real acupuncture. In an attempt to avoid participants correctly guessing their treatment allocation (and thus threaten the validity of the single-blinded RCT), they were not told in advance what placebo acupuncture involved. Interviewees were curious about this placebo, and many developed their own ideas about what a placebo acupuncture treatment might involve. These theories about placebo acupuncture were entwined with participants’ theories about real acupuncture. They described placebo acupuncture as a fake treatment that differs from real acupuncture in a specific, important, and meaningful way. Whatever the interviewees saw as the active component of real acupuncture, they speculated that the placebo acupuncture was probably missing it. For example, Frances (female, in her 50s) and Kate (female, in her 20s) reported believing that the most important component of acupuncture that determined its effect was the application of acupuncture needles at precise locations on the body. They tentatively conceptualised placebo acupuncture as the application of acupuncture needles at points that were less effective or were associated with effects that were unrelated to IBS.

“I don’t know if the real acupuncture is just in different spots because I know I’m having needles put in, and I don’t know if the placebo acupuncture is just in different spots that are, perhaps, less effective.” (Kate, female in her 20s, mid-point interview)

Frances initially believed that placebo acupuncture involved real acupuncture needles applied at relaxation points (but not IBS points), and that placebo acupuncture could thus produce relaxation. However, when told at the end of the trial that placebo acupuncture did not pierce the skin Frances changed her mind and no longer believed that placebo acupuncture could produce any effects – her understanding of the possible effects of placebo acupuncture depended on her conceptualisation of real acupuncture.

Participants’ conceptualisations of real acupuncture ranged from very narrow to much broader and more holistic. In narrow conceptualisations the effects of acupuncture were attributed to the needles penetrating the skin in specific places: acupuncture was understood as working on a physiological level with the needles directly impacting the body. Other elements of acupuncture, such as the practitioner and the relaxing setting, were seen as important only in as much as they facilitated the correct application of the needles. For example, Greta expressed a physiological model of acupuncture in which needles are placed at specific points that trigger sensations in connected but distant parts of the body.

“I’m assuming that the points that she’s using are in some way related to, like, my GI tract or the nerves, you know, the connections to the body like from the brain to like the central nervous system wherever, but, like, I feel almost like a, I could, like when she would do the acupuncture and when she would leave, it wasn’t almost like once they were all in, it was kind of like some things would change and like, I felt like my GI tract.” (Greta, female in her 20s, end-point interview)

When real acupuncture was conceptualised more broadly, needle application was still important but other aspects were also essential. Acupuncture was seen as affecting the mind and the body: the acupuncturist had a central role in promoting healing and other elements, such as relaxation, were also valued as necessary and healing aspects of treatment. For example, Ben, who felt he had benefitted previously from other healing relationships such as those he had forged in a patient self-help group, felt that interacting with his acupuncturist helped him to develop a more positive

outlook which then inspired him to make positive lifestyle choices (which were not allowed according to the RCT protocol) that could benefit his health. David also saw the acupuncturist as central to his experience of acupuncture, as can be seen when he answered a question about the extent to which he thought the benefits he perceived were due to the acupuncture itself or his relationship with the practitioner.

“They go hand in hand [the practitioner and the acupuncture] I mean it’s, it’s, it’s, it’s the whole big picture, it’s all part of what makes the acupuncture successful, is making you feel comfortable for it. If I was with a group of people, uh, that I did not care for, then the acupuncture probably would not be as positive.” (David, male in his 60s, end-point interview)

Conceptualising real acupuncture narrowly tended to be accompanied by conceptualising placebo effects as fake or illegitimate, while conceptualising real acupuncture more broadly tended to be accompanied by seeing placebo effects as real and legitimate. There is some common-sense coherence to this pattern. When real acupuncture was conceptualised narrowly, placebo acupuncture was seen as lacking the single important, effect-giving, component of acupuncture. Thus placebo acupuncture could not have genuine effects. When real acupuncture was conceptualised broadly, placebo acupuncture was seen as lacking just one of the many effect-giving components of acupuncture. Here, placebo acupuncture could still have some of the same (real) effects of real acupuncture.

Placebos have real effects with psychological mechanisms

On occasion, a few participants conceptualised (real) placebo effects in more elaborate ways that involved psychological mechanisms. They did not link their ideas about psychological mechanisms of placebo to their ideas about the mechanisms of acupuncture: psychological conceptualisations of placebo were thus more “independent” of acupuncture and might be more likely to be invoked in other contexts. These participants found such psychological mechanisms intuitively appealing, and linked them to their understandings of IBS as (at least in part) an emotional illness. David and Ben thought that placebos work through the recipient having a generally positive attitude, a belief that one is having treatment, and a strong desire to get better. Both talked about “playing the game” to maximise the placebo response through cultivating such positive attitudes, beliefs, and desires. Both also thought that the practitioner (as an empathic caring professional who wanted to help them get better) is central to the process of producing placebo effects. Deb saw placebos as psychological treatments that work when one’s body is ready to heal. She believed that placebos could only produce effects that a person consciously expects or suggests to themselves.

“I would just be blown away if I had this much improvement if it wasn’t real. Well, I mean, if I had this much improvement with no real aid [...] You know, what does that tell me about what IBS is anyway? You know, then is it in my head? I mean if, if I wasn’t getting it and I improved, thinking I was getting an aid, then that tells me that it’s kind of controlled by something else but if I believe strongly enough that this was working ... Is that mind over matter? You know. Is that me telling myself that I can be healed?” (Deb, female in her 40s, end-point interview)

Participants who saw placebo effects as genuine and as underpinned by psychological mechanisms typically anticipated and displayed less negative interpretations of responding to placebo. Ben saw himself as a placebo responder with great inner resources

and a capacity for self-healing. Alan (who was in his 20s) and Ben interpreted their placebo responses as confirming their understanding of their IBS as a predominantly psychological or emotional condition. David saw the strength of his placebo response as proof of the healing power of feeling cared for by a practitioner within the context of a therapeutic relationship. However, these participants also expressed negative connotations of placebo responding: none expressed solely positive interpretations of placebo responding. For example, linking back to the conceptualisation of placebos as scientific tools, Ben was concerned that he might “throw” the results of the trial because he had got better in the placebo arm; also, he did not want to tell other people that he had benefited from placebo. Despite conceptualising placebo effects quite elaborately and relating them to psychological mechanisms, Deb said she might feel embarrassed or “kind of goofy” if she found out she was getting better while receiving placebo treatment. Thus even participants who believe that placebos can have real effects that are psychologically mediated might need some support to avoid distress on being told they have responded to placebo.

The importance of context

A broad pattern can be discerned from the analysis presented above. When placebo acupuncture was conceptualised as a fake treatment with no underlying rationale, it was seen as having fake or illusory effects that reflected poorly on the placebo responder. Conversely, when placebo acupuncture was conceptualised as having real effects underpinned by mind-body or psychological mechanisms, placebo effects were seen as more legitimate. Participants who saw placebo effects as real also shared a tendency to link this to a view of their IBS as partly or wholly caused or mediated by psychological factors. This suggests two interpretations, both of which are broadly consistent with the Common-Sense Model (Leventhal et al., 1992). Firstly, that having a more holistic understanding of healing, in which psychological mechanisms are not denigrated as trickery, might enable people to accept placebo effects as legitimate. Secondly, that having a more psychological understanding of IBS might enable people to see placebo effects as psychologically mediated and placebo responding as legitimate. However, a search for contradictory evidence revealed the need for a broader perspective. Of those participants who saw placebos as fake, some also saw their IBS as partly psychological and some also held elaborate views of mind-body healing mechanisms. These participants saw contextual aspects of treatment (such as social support, relaxation) as legitimate healing mechanisms and saw IBS as partly psychological, and yet, at times, displayed negative views of placebos. For example, Abigail saw her IBS as linked to psychological trauma and seemed to see social support as a legitimate pathway to healing but did not integrate this into her model of placebo effects. Instead, her view of placebo effects as fake dominated and she saw placebo responding in negative terms. Frances and Ben did not want to tell other people that they had benefited from placebo, further suggesting that placebo responding might not be socially acceptable. This contrasts with the apparent acceptability of acupuncture. Participants were able to cite the ancient system of Chinese medicine to legitimise acupuncture, as this quote from Emily illustrates: “And I believe in acupuncture. [...] there’s also some sort of philosophical reason why I do it, because I really believe in it. I really like the Chinese system.” Equivalent discourses that explicitly incorporate placebos and placebo effects into a larger system of medicine are difficult to imagine and appear to be marginalised. This could explain why negative views of the placebo in general were able to dominate some participants’ accounts despite them also expressing more nuanced understandings of psychological healing mechanisms.

Even David, who valued his placebo response, suggested that the term ‘placebo’ did not do justice to the effects that he had experienced from being in the trial, orienting to the negative and narrow interpretations of the term that were more commonly expressed by the other interviewees.

“even though you call me the placebo group, I don’t consider it totally placebo group because there are other benefits that came out of it that would not have happened if I’d not been in this study. So it may be placebo and I accept that, but there were other things that I know made me feel better because I was in this study.” (David, male in his 60s, end-point interview)

Discussion

RCT participants conceptualised placebos and their effects in a variety of ways. At their most negative, placebo effects were conceptualised as illusory effects produced by fake treatments which fooled their recipient and made them look gullible. At their most positive, placebo effects were conceptualised as valuable effects triggered by psychological aspects of treatment (e.g. attitudes, therapeutic relationship), experience of which could strengthen the recipient’s beliefs about their illness and/or healing mechanisms. Some ways of conceptualising placebo were intimately linked with ways of conceptualising real treatment in the context of this trial. For example, when participants understood placebo acupuncture as not real acupuncture, or had narrow understandings of real acupuncture (which focused on the needles) they tended to conceptualise placebo effects as fake or illegitimate. In comparison, when (sometimes the exact same) participants developed broader understandings of acupuncture (which emphasised needles *and* the therapeutic relationship) they tended to conceptualise placebo effects as real and legitimate. Other ways of conceptualising placebos were more generic, in that placebo acupuncture could be viewed as a treatment which had properties, mechanisms, and effects that were independent of real acupuncture. Overall, conceptualisations of placebos incorporated participants’ ideas about: how placebo acupuncture was being delivered, the purpose of the placebo condition in the RCT, the type of effects a placebo can have, the strength of placebo effects, the veracity of placebo effects, the mechanisms underpinning placebo effects, and the implications for a person of responding to placebo. Participants’ understandings of placebos were often linked to their understandings of IBS, acupuncture in particular and/or healing mechanisms in general, and also appeared to be shaped by the broader socio-cultural context.

Negative conceptualisations of placebos

That RCT participants hold negative conceptualisations of placebos is potentially problematic. Viewing placebos as ineffective can be seen as inconsistent with the literature on placebo effects and thus threatens the validity of informed consent. For certain conditions including IBS (Ford & Moayyedi, 2010), depression (Kirsch et al., 2008), osteo-arthritic pain (Zhang, Robertson, Jones, Dieppe, & Doherty, 2008), and insomnia (Bélanger et al., 2007), an understanding that placebos can produce specific beneficial effects is more consistent with the scientific literature on placebo effects and, if incorporated into participant information, could thus result in fuller informed consent. Furthermore, given that placebos are used in RCTs deliberately to control for placebo effects, all placebo-controlled RCTs should make it clear to potential participants that they might notice changes in their health even if they receive the placebo treatment.

Our analysis suggests additional undesirable consequences that flow from negative conceptualisations of placebos. We showed how seeing the placebo as a fake treatment, only capable of eliciting illusory benefits, can lead to the belief that to respond to a placebo is to be fooled. Previous survey work suggests that lay people commonly believe that placebo responding is linked to personality (Chen & Johnson, 2009) and anticipate feeling disappointed were they to discover they had been treated with a placebo (Fässler, Gnädinger, Rosemann, & Biller-Andorno, 2011) while RCT participants in one qualitative study described a fear of being a placebo responder (Stone, Kerr, Jacobson, Conboy, & Kaptchuk, 2005). One review suggests investigators are wary of telling participants that they have received a placebo for fear of causing distress (Shalowitz & Miller, 2008). People who see placebo effects as fake might be particularly at risk of experiencing such distress, if they have experienced benefit during a trial. Negative conceptualisations of placebos could also act as a barrier to participation in RCTs.

Changing trial participants’ conceptualisations of placebos

One way to alleviate the undesirable consequences of negative conceptualisations of placebos is to change the way in which participants are informed about placebos. Others have similarly suggested that patients should be informed of the possible effects of placebos at the informed consent stage, so that they focus on these possible effects rather than seeing the placebo as merely a “dummy” treatment (Di Blasi, Crawford, Bradley, & Kleijnen, 2005; Fassler, Gnädinger, Rosemann, & Biller-Andorno, 2009). RCT participants may be open to viewing placebos in more positive ways, as this would be broadly consistent with the therapeutic misconception: offering two treatments that can give health benefits (compared to offering one such treatment and one “dummy” treatment) is more consistent with the idea that trial personnel and procedures are interested in achieving health benefits for the individual participant as well as conducting scientific research. Experimental studies are now needed to develop materials and test whether encouraging participants to conceptualise placebos in less negative ways can improve informed consent and protect participants against distress on un-blinding.

The extensive scientific literature offers multiple ways of describing placebo effects to participants. Scientific models can be loosely categorised as: neuroscientific, in which the specific neuronal pathways underpinning placebo effects are the focus (Benedetti, Mayberg, Wager, Stohler, & Zubieta, 2005); psychological, with a focus on mechanisms such as conditioning and expectancy (Kirsch, 1997; Stewart-Williams & Podd, 2004); and anthropological, in which socio-cultural factors are emphasised (Kaptchuk, 2011; Moerman, 2006; Moerman & Jonas, 2002). The most elaborate and positive conceptualisations in our study described placebo effects as psychological effects triggered by positive attitudes and the experience of feeling cared for (by an acupuncturist and/or trial personnel). Participants did not talk about neuroscientific or cultural understandings of placebo effects. This suggests that a psychological level might be the most accessible level at which to begin describing placebos more fully to RCT participants.

An individual focus alone may not be successful. Our own findings highlight the need to examine dominant discourses of placebos and suggest that societal level interventions may be needed to challenge what appear to be established notions that placebos are fake treatments that have illusory effects. The beliefs of trial and healthcare personnel may also need to be challenged: nurses commonly attribute certain personality traits, such as psychological fragility, to placebo responders (Berthelot et al., 2001; Ernst & Abbot, 1997), and a meta-analysis showing that

anti-depressants and placebos are similarly effective in mild-moderate depression received particularly negative reactions in the professional and lay press (Kirsch, 2008).

How to describe placebos to RCT participants is particularly important for open-label studies, such as another recent RCT that found that open-label (i.e., non-deceptive and non-concealed) placebo treatment administered in a context of a persuasive rationale can elicit clinically significant placebo responses (Kaptchuk et al., 2010). In this open-label study, patients were provided with concepts that seemingly allowed them to have positive expectations and interpret their improvement in a positive light. A fuller understanding of how RCT participants conceptualise placebo and modify their beliefs in response to information might refine such an open-label treatment strategy.

Implications for placebo effect sizes

Encouraging RCT participants to have positive conceptualisations of placebos (in situations where placebos are expected to produce effects, such as conditions like IBS, insomnia, pain, and depression) would almost certainly have implications for the size of the placebo effect itself. Placebos are thought to have their effects partly through the recipient's conscious expectation of benefit (Benedetti et al., 2003; expectancy theory, Kirsch, 1997). In blinded RCTs, participants expect to receive either a placebo or a real treatment but their treatment allocation is kept masked, a situation which creates uncertainty and can lower expectations of benefit (Barlow et al., 2011; Stone et al., 2005). Following expectancy theory, lowered overall expectations of benefit could then reduce the observed effectiveness (of both placebo and verum treatments). Indeed, experimental data suggest that knowing one might receive a placebo can lessen its effects (Kirsch & Weixel, 1988). Similarly, it has been suggested that large placebo effects are observed in trials because high randomisation ratios create raised expectations of benefit (e.g. 16:1 against the placebo in migraine, Diener et al., 2006; more than 1:1 against the placebo in depression, Papakostas & Fava, 2009; Sinyor et al., 2010). Therefore, increasing patients' expectations of benefit from a trial by encouraging positive conceptualisations of placebo would probably increase the size of the placebo effect. This could improve the ecological validity of trials by making participants' overall expectations more similar to those held in usual care, where patients are typically more confident in expecting to receive a beneficial treatment (Barlow et al., 2011). However, there might also be negative consequences of enhancing RCT participants' expectations. For example, if placebo and drug effects are not simply additive (Paterson & Dieppe, 2005), then raising overall expectations could have differential effects on placebo and real drug arms and thus introduce bias (Kaptchuk, 2001). Increasing the size of the placebo effect might also make it more difficult to detect a verum treatment effect.

Strengths and limitations

The strengths of this analysis include the use of repeated interviews, which allowed us to understand that individual participants conceptualised placebos in multiple ways; the use of rigorous analytic procedures involving different multidisciplinary perspectives and the search for evidence contradictory to emerging interpretations about the importance of context; the relatively homogeneous sample of participants from a single RCT, which can help during initial explorations of phenomena. However, the use of a relatively homogeneous sample and no theoretical sampling does limit the validity of our work and means additional studies in other settings are needed to establish the range of conceptualisations and the transferability of our findings. In particular, it should be

remembered that our participants had all volunteered to take part in an acupuncture study and so might be expected to have more alternative or holistic beliefs about health than other patients. Also, our participants had received a placebo acupuncture (rather than, say, a placebo pill) and for some participants their beliefs about acupuncture were closely related to their beliefs about the placebo. That participants' conceptualisations of placebos varied in specificity is reminiscent of the distinction between generic and specific beliefs about medicines (Horne, Weinman, & Hankins, 1999) and suggests that there might be important differences in how people conceptualise different types of placebos. Qualitative work in multiple diverse settings, such as pharmaceutical and surgical RCTs, would help elucidate this.

Conclusions

In conclusion, it is possible to identify distinct ways in which participants in an RCT conceptualise placebos, and how people conceptualise placebos is linked to how they conceptualise illness and healing mechanisms in general. This paper has focused on how RCT participants conceptualise placebos. Given that physicians do not restrict their use of placebos to research settings but also use placebos in clinical practice (Sherman & Hickner, 2007; Tilburt, Emanuel, Kaptchuk, Curlin, & Miller, 2008), future research should also explore how members of the general public conceptualise placebos.

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