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Mesmer, the placebo effect, and the efficacy paradox: lessons for evidence based medicine and complementary and alternative medicine

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ABSTRACT

Drawing on Isabelle Stengers' discussion of the investigation of Mesmer and the starring role that experimentation plays in the rationality of modern medicine, this paper examines longstanding tensions between the realms of evidence based medicine and complementary and alternative medicine. While evidence based medicine often claims the ability to demarcate between pseudoscience and science, and complementary and alternative medicine often claims that evidence based medicine involves a kind of pseudo-logic that is unable to capture all forms of efficacy, I argue that both of these claims are unfounded. Unpacking the similarities between the commission that evaluated Mesmer's magnetism and the structure of evidence based medicine, a significant gap is revealed in today's system of knowledge production within medicine. In order to demonstrate the efficacy of a novel treatment within a randomized controlled trial, the treatment must be shown to improve clinical outcomes significantly more than a placebo control. However, some treatments improve clinical outcomes, but operate primarily through placebo responses, leading to effective medicines being labelled 'ineffective' within randomized controlled trials. This phenomenon is known as the efficacy paradox and appears most frequently in chronic conditions and in relation to complementary and alternative medicine, in which placebo responses are common. It is argued that the realms of evidence based medicine and complementary and alternative medicine have much to learn from each other, in that one has neglected the vast potential of producing clinical benefit through placebo responses, while the other has neglected the understanding that can be gained through experimentation.

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Introduction: Mesmer and modern medicine

In her paper 'The Doctor and the Charlatan', Isabelle Stengers is concerned with a fascinating moment in the history of medicine, in which questions of evidence, imagination, and experimentation collide. She describes the moment as such:

The scene takes place in Paris in 1784. Two commissions have been appointed to investigate the practices of the Viennese doctor Franz Anton Mesmer. Their main task is to put the principles underlying his practices to the test. According to Mesmer's practice, his patients gather around a tub that contains a magnetic fluid, which has the power to effect the cures on which his reputation is based... [One of the commissions] asked an accomplice magnetiser to magnetise a 'likely subject' without warning him, to pretend to magnetise another

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person, or even, the subject having had his eyes blindfolded, to magnetise one part of his body while announcing another part was to be magnetised. The commission was then able to conclude that *'the fluid is powerless without imagination, while the imagination without the fluid is able to produce the effects that are attributed to the fluid'*. (Stengers, 2013, pp. 13–14, emphasis added)

Drawing upon this case, Stengers' examines the ways in which modern medicine understands its own rationality, and the crucial part that experimentation plays in operationalizing that rationality. While Stengers' discussion covers a significant amount of territory, I am primarily interested here in three points that she makes in relation to the investigation of Mesmer.

The first of these concerns the types of evidence that were sought within the investigation. As Stengers observes, from the perspective of the commission, 'the cure proves nothing' (Stengers, 2013, p. 14). Even if it were the case that the individuals subjected to magnetization found relief from their ailments, such relief was not considered relevant to the investigation. The second point relates to the commission's understanding of what occurred within the investigation. Stengers reports that one member the commission, the botanist Antoine Laurent de Jussieu, criticized the commission for merely substituting 'a hypothetically "simple" cause, imagination, for another simple cause, fluid' (Stengers, 2013, p. 22). Instead of seeking to understand why townspeople were flocking to Mesmer and reporting the disappearance of symptoms after they'd experienced magnetism, the commission suggested that it was only the 'imagination' that was responsible, a concept equally as murky as Mesmer's mysterious 'fluid'. Finally, Stengers suggests that this understanding is limited, in that the 'imagination' is incompatible with the rationality of experimentation. 'From the experimental point of view, the question of imagination emerges as an obstacle', she argues (Stengers, 2013, p. 24).

In the following discussion, I examine and expand upon these three points. First, I consider the ways in which modern medicine continues to conclude that 'the cure proves nothing', as it places randomized controlled trials at the center of evidence based medicine, and excludes the 'imagination' through the use of placebo controls. Second, I look closely at the positive role that the 'imagination' can play in medical encounters, especially in the treatment of chronic conditions. In particular, I discuss recent evidence related to the placebo effect and how it links to today's 'charlatans', those who practice complementary and alternative medicine. Finally, I depart from Stengers' analysis with regards her discussion of the conflict between experimentation and the imagination. Drawing on growing evidence from placebo studies, I argue that the imagination, rather than providing an obstacle that modern medicine must grapple with, is a powerful instrument of healing that can, and ought to be, subjected to experimental investigations. Finally, I end with recommendations related to how the fields of evidence based medicine and complementary and alternative medicine might learn from each other, in order to better reach their shared goal of developing greater tools to improve health.

Within this analysis, questions central to the theme of pseudo global health which are being explored within this special issue, come to the fore. Evidence based medicine is often thought to be a tool for demarcating between genuine and fake treatments, medicines, or tools for healing. The line between that which is scientific and efficacious and that which is pseudoscientific and inefficacious, is thought to fall directly out of its structure. As I will show below, however, something real and powerful is being excluded from this process of demarcating between the real and the fake, leading to a preponderance of false negatives in the domain of chronic conditions. On the other hand, practitioners of complementary and alternative medicine often eschew the tools of evidence based medicine, claiming that the exclusive focus on specific forms of measurement is unable to capture the processes of healing taking place within their domain. However, in doing so, those within complementary and alternative medicine set aside fruitful tools of inquiry, deeming them inauthentic within a particular context, while authentic in another. In what follows, I hope to demonstrate that these dichotomous lines drawn between what's real and what's fake, in terms of medicine and methodology, are more slippery than one might think.

The commission continues: evidence based medicine

As a result of the remarkable advances it affords with regards to precision, prediction, and the exclusion of biases, science has come to embrace experimentation as the pinnacle of knowledge production, and medicine has followed suit. Evidence based medicine (EBM) aims to identify which interventions are truly efficacious and which interventions only appear to be so through the use of highly controlled experiments. Central to EBM is a hierarchy of evidence, which places the randomized control trial (RCT) above clinical case studies and expert opinion, and meta-analyses and systematic reviews of RCTs at the top. The RCT offers investigators the ability to determine to what degree the intervention being tested contributes to changes in clinical outcomes, and to what degree these changes are the result of other factors impacting the results of the trial (e.g. natural course of the illness, regression to the mean, placebo responses).¹ By comparing the results of the active arm, which includes participants who have received the intervention being tested, and the placebo arm, which includes participants who have received a placebo control, researchers can determine to what extent the active ingredients are responsible for any clinical improvements. As such, a clear demonstration of the efficacy of a novel intervention tends to involve a randomized controlled trial in which the intervention contributes to positive clinical outcomes that are significantly better than those produced by the placebo arm.² Ideally, both participants and researchers are blinded with regards to the randomization process, so this knowledge does not compromise the results.

As Stengers points out, the imagination that replaced Mesmer's fluid has not been lost within this system. 'Under the label of the "placebo effect", the curing power of trust, hope and "faith healing" are today systematically set out in the protocols that determine the elevation of a chemical formula to the status of a medicine' (Stengers, 2013, p. 15). The role of the placebo effect in these protocols is that of providing a threshold. By comparing each intervention with a placebo control, designed to mimic the active intervention in every way except with regards to the 'active ingredient' (e.g. a placebo surgery may involve anesthetic and an incision, a placebo pill may involve side effects), outperforming the placebo effect is the minimum requirement for any intervention within EBM. In this way, the imagination provides a baseline that new treatments ought to surpass in order to enter the ranks of evidence based medicine, paving the way to regulatory approval and coverage by payers.

While the embrace of evidence based medicine has led to the development and identification of countless effective treatments that continue to extend and save lives every day, critiques of this dominant approach to medical research have been growing (Mykhalovskiy & Weir, 2004). While EBM's hard endpoints, selective sampling, and randomization contribute to greater precision with regards to the conclusions drawn, they tend to detract from the generalizability and clinical applicability of results, particularly with regards to multimorbidities and patients underrepresented in clinical trials (e.g. racial and ethnic minorities, women) (Fan & Uretsky, 2017; Goldenberg, 2006; Horwitz, Hayes-Conroy, Caricchio, & Singer, 2017; Lambert, 2006). As Rosengarten and Savransky have argued, RCTs aim to produce abstractions that can generalize to all situations, but such a task is not only impossible, but can render some features of a trial invisible and lead to the prioritization of rigorous evidence over situated relevance (Rosengarten & Savransky, 2019). Others have pointed out that EBM focuses on outcomes to the neglect of causal understanding, is susceptible to manipulation by industry, fails to recognize the relationship between evidence and context, and is too quick to assume that one size of research will be suitable for all research questions (Brody, 2001; Dobrow, Goel, & Upshur, 2004; Greenhalgh, Howick, & Maskrey, 2014; Verhoef, Casebeer, & Hilsden, 2002). The growing recognition of these concerns can be seen in EBM's shift away from relying primarily on RCTs and towards alternative trial designs, such as adaptive and pragmatic trials, as well as attempts to complement RCTs with evaluations of plausibility and adequacy (Montgomery, 2017; Sugarman & Califf, 2014; Victora, Habicht, & Bryce, 2004). While these critiques are important, I am concerned here with another shortcoming of EBM, one that is acknowledged less frequently by critics and yet is very significant.

The efficacy paradox: ‘the cure proves nothing’

A remarkable consequence of the structure of evidence based medicine today is that the same experimentation that has contributed to its success also threatens its goal of determining which treatments are most effective. Harald Walach calls this phenomenon ‘the efficacy paradox’. In describing this paradox, Walach asks the reader to imagine two hypothetical treatments, treatment X and treatment Y, for chronic pain. Treatment X has a very large positive clinical effect on chronic pain, but the placebo control for treatment X also does; in this case, treatment X will not pass the threshold of outperforming the placebo arm of the trial, and so will be deemed inefficacious. Treatment Y, on the other hand, may have a small positive clinical effect on chronic pain, but one that is significant in comparison to the placebo control for treatment Y, which has a negligible impact on chronic pain. In this case, treatment Y will pass the threshold, and be considered to have demonstrated its efficacy. The incredible result of this scenario is that treatment X may be much more effective at treating chronic pain than treatment Y, and yet treatment Y will be the one to be approved by regulators, integrated into health systems, and funded by payers. Treatment X, in contrast, will be considered ineffective and excluded from care, merely because it impacts chronic pain primarily through placebo mechanisms (Walach, 2001). As Stengers remarks in response to the case of Mesmer, ‘the suffering body is not a reliable witness. It can happen that it will be cured for the “wrong reasons” ’ (Stengers, 2013, p. 16).

In a recent discussion of Walach’s efficacy paradox, Zhang and Doherty suggest the phenomenon occurs ‘when the effect of a treatment being examined in RCTs, or a recommendation in evidence based guidelines, differs markedly from the benefits observed when that treatment is used in clinical practice’ (Zhang & Doherty, 2018, p. 82). Furthermore, as will be discussed in more detail below, evidence indicates that instances of this paradox are not uncommon, particularly when it comes to treatments for chronic conditions. This suggests that, in some cases, evidence based medicine is failing to identify the most effective available treatments, and instead promoting those that are less effective. Rather than focusing only on *whether* treatments are able to bring about clinical improvements, RCTs put weight on *how* treatments are able to bring about clinical improvements, and this emphasis may be standing in the way of their ability to bring effective treatments to light.³

Below the threshold: the placebo effect

How is it possible that evidence based medicine could manage to reject a treatment that is most effective and promote one that is less effective? The structure of the RCT in relation to the placebo control requires it. When the imagination was relegated to the position of the threshold over which novel interventions must pass, treatments that were brought about via placebo responses were, by definition, unable to pass the threshold.⁴ This means that any positive clinical outcomes brought about by placebo mechanisms within a clinical trial are seen as irrelevant to the findings of the trial.

As we learn more and more about the placebo effect, however, it becomes clear that the phenomenon is both powerful and ubiquitous, particularly in relation to some conditions. Increasing evidence suggests that placebo effects are brought about primarily through cognitive processes, such as expectations and beliefs, as well as conditioned processes, that involve repeated pairings of a stimulus and response (Fabrizio Benedetti, 2009). Placebo responses can be brought about by words spoken by health care professionals or one’s social network, the history one has with a particular treatment or context, as well as what one believes about what interventions are likely to work for them (Colloca & Benedetti, 2009; Enck, Benedetti, & Schedlowski, 2008). As a result of the diversity of causes of placebo responses, some have proposed that the phenomenon should be reconceptualized as ‘contextual healing’ or a ‘meaning effect’ (F. G. Miller & Kaptchuk, 2008; Moerman, 2002). Importantly, some conditions appear to be very responsive to placebo treatments while others remain unresponsive. Chronic conditions, particularly those characterized by pain,

depressed mood, and anxiety, as well as those categorized as functional somatic syndromes, appear to frequently show robust placebo responses (Coryell & Noyes, 1988; Hayden, 1991; Kirsch, 2010; Patel et al., 2005). Viruses, tumors, and broken bones, do not seem to be impacted by placebo treatments.⁵

Today's mesmerism? Complementary and alternative medicine

Many are likely to think of complementary and alternative medicine (CAM) as a contemporary form of mesmerism. Largely dismissed as pseudoscientific, and yet widely popular, CAM remains on the outside of evidence based medicine and is unlikely to disappear anytime soon (Segar, 2011). Practices that fall under the heading of CAM include, among others, homeopathy, reiki, Traditional Chinese Medicine, massage therapy and chiropractic techniques, meditation, and aromatherapy. Like Mesmer, many practitioners of CAM may be harnessing the imagination in order to bring about positive outcomes for their clients.⁶ If this is the case, these practices will fail the test of experimentation, as Mesmer did, because evidence based medicine does not permit treatments that operate via the imagination to enter its fold. As Christine Barry points out,

Mythological, ritualised and culturally embedded aspects of all healing systems, biomedicine included, can in themselves possess great healing potential. Orthodox medicine can be blind to such aspects of its own praxis in its claim to scientific legitimacy, and these elements are not studied in the RCT. Yet it is often these very aspects that attract patients to CAM. (Barry, 2006)

As Barry suggests, any context of healing can contribute to placebo responses. And yet, there is reason to think that placebo responses may occur more frequently and have a greater impact on placebo-responsive conditions within some forms of CAM. The features that characterize many CAM practices, the conditions CAM clients tend to seek help for, as well as the comments of both practitioners and clients, all suggest that this may be the case. While it is difficult to make generalizations with regards to CAM treatments, given their number and diversity, features that are common to many of these practices include long consultations, expressions of warmth and empathy from practitioners, time devoted to the mutual development of explanation, as well as the instillation of hope (Carter, 2003; Ernst, 2001; Kaptchuk & Eisenberg, 1998; Stub, Foss, & Liudden, 2017). These features are known to increase placebo responses across a variety of conditions (Friesen & Blease, 2018; Howe, Goyer, & Crum, 2017; Kaptchuk et al., 2008). Furthermore, the types of conditions that individuals seek out CAM treatments for most often overlap considerably with the types of conditions that tend to show the most robust responses to placebo treatments, including chronic pain, mood disorders such as depression and anxiety, and functional somatic syndromes such as fibromyalgia and irritable bowel syndrome (Barnes, Bloom, & Nahin, 2008; Bausell, Lee, & Berman, 2001). Finally, interviews with CAM practitioners and clients reveal that aspects of these treatments that are likely to enhance placebo responses are often seen as central to the practices (e.g. understanding and explanation, holistic care, a meaningful therapeutic alliance, belief in the treatment) (Astin, 1998; Sirois, Salamonsen, & Kristoffersen, 2016; Stub et al., 2017).

CAM and chronic conditions: where the harm lies

Taking these points together, this suggests that evidence based medicine may be excluding effective treatments from its ranks, especially when it comes to some types of conditions, particularly chronic conditions characterized by pain, anxiety, and psychosomatic symptoms, and some types of treatments, particularly those operating within CAM. Biomedicine has little to offer patients by way of promising treatments for these conditions; unsurprisingly, those seeking treatment from CAM practitioners, many of whom are struggling with such chronic conditions, often report feeling dissatisfied with the treatment they have received within conventional medicine (Vincent & Furnham, 1996). Walach suggests that the efficacy paradox is 'frequently true for

CAM therapies', in which placebo responses (which he calls 'non-specific effects') are especially significant (Walach, 2001, p. 215). While conventional medicine may also produce treatments that bring about change primarily through placebo effects, these are likely to be less common because of structural factors and theoretical commitments that prevent clinicians from engaging in long consultations with their patients, approaching multiple morbidities holistically, and spending time mutually developing hope and explanations.

This means that some CAM treatments, which may be the best available treatments for some chronic treatments involving pain and anxiety, are being thrown into the 'ineffective' pile of medicine, despite our having nothing better to offer those suffering from these conditions. Because modern medicine's rationality is based on the embrace of experimentation and the exclusion of healing through the imagination, individuals are being denied coverage for treatments that might offer them greater relief than available treatments, merely because of the way the relief is brought about. As Kaptchuk has asked, 'Should a person with chronic neck pain who cannot take diazepam because of unacceptable side effects be denied acupuncture that may have an "enhanced placebo effect" because such an effect is "bogus"?' (Kaptchuk, 2002). Surely we do not want the way in which a treatment provides relief to take precedence over the effectiveness of that treatment. And yet, that is precisely the effect of the system of evidence based medicine we have embraced.

Experimentation as an obstacle

Reflecting on the investigation of Mesmer and the commission's conclusions, Stengers presents the imagination as a barrier that stands in the way of modern medicine's commitment to experimentation as the route to knowledge. She observes that 'experimental procedure requires that what one is dealing with can become capable of engendering "experimental facts" ' but also notes that 'subjects can't be stopped imagining, interpreting, or taking up a position on what they are being subjected to, or on what they feel', concluding that it is impossible to incorporate the imagination into an experimental protocol in line with modern medicine's rationality (Stengers, 2013, p. 23). Since experimentation requires the isolation of a variable, and the ability to demonstrate the ways in which the variable is the cause of a particular effect, the imagination is a poor candidate for experimentation. Stengers asserts,

Imagination is not a true variable because the experimenter is not free to control the variations. He cannot, for example, tell the subjects what they are supposed to be imagining and stop them incorporating 'parasitical' elements that would transform the meaning of the experimental situation. (Stengers, 2013)

Many proponents of CAM also maintain that their practices cannot be subjected to experimentation, at least not within the boundaries set out by evidence based medicine. Some have suggested that the effectiveness of CAM cannot appropriately be measured within an RCT because the impact of treatment may be altered by the process of blinding either patients or practitioners, by randomizing patients to treatments they may not want or believe in, or by damaging the therapeutic relationship (Carter, 2003; Margolin, Avants, & Kleber, 1998; F. G. Miller, Emanuel, Rosenstein, & Straus, 2004). Others argue that individual components of CAM practices cannot be examined in isolation, but must be measured as part of the whole system of practice (Verhoef et al., 2005). Interestingly, these arguments only serve to underscore the importance of placebo responses within these practices by highlighting features known to bring about placebo effects, such as the therapeutic alliance and the beliefs and expectations of patients.

Experimentation as a tool

While I agree with much of Stengers' analysis of the case of Mesmer's investigation, I do not share her pessimism in relation to the ability of modern science to tame the imagination within its protocols. The field of placebo studies offers countless examples of successful cases in which the effects of the

imagination on one's wellbeing have been captured within RCTs. Rather than resisting the manipulation of the experimenter, the imagination can be directed to expect particular consequences as a result of treatment, or can simply be placed within a context of healing or not.

A simple and yet powerful example of impact of the imagination can be found in the hidden treatment paradigm. After randomizing post-operative patients into two groups and connecting them to a morphine drip that can be activated from an adjoining room, half of the patients were told when the morphine entered the drip, while the other half were not told (although they did know it would be administered at some point). Results of this experiment show the remarkable effect that the belief that one is receiving treatment for pain can have on one's experience; those that were unaware of when morphine was administered required a significantly higher dose in order to reduce pain by 50% (Colloca, Lopiano, Lanotte, & Benedetti, 2004).

Another randomized control trial examined which aspects of homeopathic treatment predicted the relief of symptoms for 56 participants with rheumatoid arthritis, who were randomized to either receive or not receive a homeopathic consultation, and then further randomized to receive either a homeopathic treatment or a placebo treatment. It was found that those who received a homeopathic consultation reported significant improvements in terms of pain, swollen joints, mood, and their weekly global assessments, as compared to those that did not receive the consultation. No significant difference was found between groups that received the homeopathic and placebo treatments (S. Brien, Lachance, Prescott, McDermott, & Lewith, 2011). Qualitative research accompanying this RCT suggests that patients who engaged in the homeopathic consultations reported that what participants found most effective were the opportunities to receive emotional support, explore their illness and self, and gain advice during the consultation (S. B. Brien, Leydon, & Lewith, 2012).

Taken together, these experiments, along with many others that corroborate them, suggest that the imagination that was deemed to be responsible for the effects brought about through Mesmer's magnetism can in fact be subjected to experimentation (Kaptchuk, 2011; Levine & Gordon, 1984). Beyond these trials, discussions of how to best capture placebo effects within scientific investigations are ongoing. The balanced placebo design, which includes four conditions: receiving an active treatment and being told one is receiving an active treatment, receiving an active treatment and being told one is receiving a placebo treatment, receiving a placebo treatment and being told one is receiving an active treatment, receiving a placebo treatment and being told one is receiving a placebo treatment, allows for the possibility for determining to what extent changes are the result of placebo and pharmacological components.⁷ Similarly, the balanced cross-over design involves telling all participants that they will receive placebo treatment during half of the trial and active treatment during the other half of the trial, while in fact four conditions receive: placebo-active, active-placebo, active-active, and placebo-placebo, allowing for expectancy effects to be differentiated from effects of the active treatment⁸ (Enck, Klosterhalfen, & Zipfel, 2011). Others have suggested that the use of a virtual experimenter could limit the introduction of bias within an experimental protocol and solve problems related to the difficulty of blinding clinician-investigators, while others point to the importance of drawing on qualitative methods to capture how participants understand their own placebo responses (Horing, Newsome, Enck, Babu, & Muth, 2016; Kaptchuk et al., 2009).

Stengers might object, however, drawing on the observations of Jussieu, that one obstacle to measuring the imagination arises because the belief that one is not being magnetized may be 'capable of annulling other effects', suggesting that not only can the imagination bring about positive healing effects but it can reduce or undo them (Stengers, 2013, p. 23). However, many experiments concerning the nocebo effect, where expectations or conditioning negatively impact health outcomes or increase pain experiences, have also been conducted (F. Benedetti, Lanotte, Lopiano, & Colloca, 2007). While Stengers is right to argue that the imagination is not a variable that is easy to isolate and turn on and off experimentally, she is too quick to conclude that its effects cannot therefore be captured, as creative experimental designs suggest otherwise.

Looking forward: CAM, EBM, and mutual learning

While Stengers predicts that both the placebo and the charlatan will inevitably disappear as medicine continues to progress, the placebo as it settles into its role as a control within clinical trials, and the charlatan 'because, to the extent that medicine increases its effectiveness, he will lose, for his part, his power of parasitical seduction', I predict an alternate ending to the story of modern medicine, one that embraces the placebo and the charlatan into the fold of experimentation (Stengers, 2013, p. 20). In this ending, both EBM and CAM undergo critical examinations of their theoretical commitments and practices, and engage in a process of mutual learning.

What can EBM learn from CAM?

What EBM can learn from CAM is that for some conditions, clinical improvement might be brought about primarily via placebo responses, and if there are therapies able to bring about that relief, they should not be excluded from the realm of interventions deemed efficacious. This means that examinations of how and when clinical benefits are brought about, whether via placebo mechanisms or other routes, ought to be made routine. Zhang and Doherty recommend that RCT reporting should include an analysis of the proportional contextual effects (PCE) that are brought about through placebo components of treatment, as well as those effects that are brought about through the 'active' components of a treatment, pointing out that 'for many chronic painful conditions the majority of treatment benefits result from contextual [placebo] effects rather than the specific effects of individual treatments' (Zhang & Doherty, 2018, p. 85). Examinations of trials involving patients with osteoarthritis, rheumatoid arthritis, and fibromyalgia revealed that the average proportional contextual effects for pain relief in RCTs in these conditions are 75%, 63%, and 64% respectively (Abdullah, 2015; Chen et al., 2017; Zou et al., 2016). These are benefits we do not want to miss out on.

Beyond mere reporting, regulators should create routes whereby treatments that are able to improve clinical outcomes by way of placebo effects are made available to those most likely to benefit from them. Permitting the inclusion of treatments that operate primarily through placebo mechanisms, particularly for conditions that are placebo-responsive, is likely to lead to improvements for patients, practitioners, and the public. Most importantly, more treatments will become available to those that are suffering from chronic conditions related to pain, anxiety, and complex, psychosomatic symptoms. As Walach points out, 'to just dump all these effects in the huge waste bin of medical research and dub these effects as "nothing but placebo" is, at best, scientific stupidity' (Walach, 2001, p. 217). Furthermore, creating space for placebo-based treatments within EBM will bring help to close the gap between efficacy and effectiveness, bringing the realm of research closer to what is seen in clinical practice (Naudet, Falissard, Boussageon, & Healy, 2015; Zhang & Doherty, 2018). This does not mean that CAM treatments or other treatments that are able to harness placebo mechanisms in order to benefit patients need to be seen as on par with biomedical interventions that do not depend on placebo responses to bring about their effects. However, these forms of interventions need to be evaluated in relation to the conditions being treated, with an eye to what is likely to be effective for which conditions and which patients.

Finally, clarifying the role the imagination plays within CAM can help to bring clarity to public debates about its value. Wayne Jonas describes the current state of affairs:

Current data indicates that acupuncture is effective for low back pain compared to no treatment, but is no more effective than sham needle control treatments. Proponents of acupuncture use this information to say that acupuncture is effective for low back pain, and detractors use the same information to say that acupuncture is not effective for low back pain. Both are right and both are misleading. These kind of statements confuse the public, policy makers and a good percentage of practitioners. (Jonas, 2005)

By recognizing the importance of treatments that draw on placebo responses for some conditions and drawing a line between these kinds of treatments and treatments that operate through other mechanisms, this confusion can be alleviated.

What can CAM learn from EBM?

Similarly, the realm of complementary and alternative medicine has much to learn from evidence based medicine, in that embracing experimental exploration of the imagination can have a positive impact on the public, clients, and clinicians. Most importantly, uncovering which components contribute to positive clinical outcomes within CAM practices can help to develop an understanding of what impact these practices are likely to bring about in relation to different ailments, so that patients and the public can make educated decisions when they are seeking complementary or alternative treatments. Currently, claims made by CAM practitioners are often very wide in scope, both in terms of how and what they are able to treat. Restrictions must be made, however, with regards to which practices should be given regulatory support and which conditions CAM practices can claim to treat. If long consultations involving warmth, empathy, and understanding are part of what leads to positive changes, it is important to distinguish between homeopathy, which regularly involves such consultations, and the expensive body vibe stickers available through Gwyneth Paltrow's wellness brand Goop that are said to promote healing (goop.com). Experimentation can help to reveal these distinctions. Furthermore, while evidence suggests that some kinds of conditions are often impacted by placebo treatments, there are also many that are not. While only a small minority of patients visit CAM practitioners in hopes of finding an alternative cancer treatment, such patients are more likely to have reduced survival rates in comparison to those who seek biomedical treatment (Johnson, Park, Gross, & Yu, 2018). Clarifying the scope of which conditions CAM practices are best able to treat could help to counteract misleading information about the extent to which CAM therapies are likely to be successful in impacting different health conditions.

Additionally, developing a better understanding of what components of CAM therapies contribute to positive clinical outcomes can help to improve these practices. If experimentation reveals that spending time exploring one's emotions and finding an explanation for one's suffering makes a difference to clients, but ingesting a component of an endangered species within a prescribed remedy does not, a practice that involves these two components can be modified to involve less harms and produce the same benefits. As Ernst has argued, 'If patients are helped by treatment X, which is entirely devoid of risks but not better than a placebo, these patients are obviously benefiting from a placebo effect. And there is nothing wrong with that. However, instead of perpetuating the myth that treatment X has specific effects, we should be honest and endeavour to understand its non-specific (placebo) effects' (Ernst, 2002).

Of course, there are important limitations to the recommendation that CAM embrace experimentation. While many proponents of CAM are in favour of building an evidence base, they are often restricted in their ability to do so as a result of the costs of trials, the push-back against EBM within CAM communities, and the distance from 'science-based epistemology' that is common in CAM (Barry, 2006, p. 2650). Furthermore, RCTs are far from the only form of evidence that matters, and the many criticisms of EBM that have been raised still stand. Rather than disparaging EBM's embrace of experimentation, however, I argue CAM should look more closely at what it might gain from engaging in further examination of its practices.

Conclusion

Reflecting on the work of the commission in charge of the investigation of Mesmerism, Stengers reports that it 'allowed for elimination, for the destruction of pretensions, and refutations, but it remained silent on the cures that were actually observed' (Stengers, 2013, p. 22). The efficacy paradox, which reveals the ways in which placebo-based treatments which sometimes offer the best chance of relief to individuals suffering from chronic conditions, are systematically excluded from the ranks of evidence based medicine, demonstrates that this is still the case today. It's time to step away from the commission's approach, which holds that 'the cure proves nothing' and

allow for clinical outcomes to speak louder than the way in which those outcomes were brought about (Stengers, 2013, p. 14). It's also time to step away from conceiving of any treatments that operate through placebo mechanisms as shams. As Julia Segar points out, 'shedding the moral baggage attached to much of the discussions about CAM which seek to portray these therapies as either "fake" or "real" would allow more fruitful lines of enquiry' (Segar, 2011). Rather than excluding all treatments that rely on placebo responses for their effects, EBM should make space for these treatments when they are the best interventions we have, and rather than hiding in a shroud of mystery, CAM should examine the ways it is able, and unable, to contribute to wellbeing.

Notes

1. Three armed RCTs, which include an active arm, a placebo control arm, and a waitlist arm, distinguish between what changes are the result of the natural course of the illness and regression to the mean (as these will be present in all arms) and what changes are the result of placebo responses (as these will be present in only the active and placebo control arm).
2. For treatments for some medical conditions, demonstrating efficacy over and above the placebo arm is less important than showing an impact on particular endpoints associated with improvements. This is most often the case for conditions which have known biomarkers (e.g. malaria), and not often the case for the chronic conditions that tend to be most responsive to placebo treatments (discussed in more detail below).
3. This is not to suggest that the structure of RCTs is the only, or even primary, factor restricting the development and approval of effective treatments, as many other factors (e.g. market forces, regulations) play a significant role as well. See (Cloatre, 2019) in this issue for a fascinating discussion of how the law and biomedicine operate in relation to traditional healing.
4. I use placebo effects, placebo responses, and the imagination interchangeably in this paper, referring to the positive outcomes brought about via placebo mechanisms; these outcomes are distinct from placebo controls (e.g. used to determine efficacy in a trial) or placebo treatments (e.g. a sugar pill or sham surgery).
5. Although important secondary outcomes, such as cancer related fatigue, appear to be responsive to placebo treatments (de la Cruz, Hui, Parsons, & Bruera, 2010).
6. This is not to say anything with regards to the efficacy of specific components of CAM practices, but merely to suggest that these practices are likely to be more effective in bringing about placebo responses than many encounters within Western biomedicine. Also see (Hornberger, 2019) in this issue for an illuminating discussion of alternative ways of conceiving of 'efficacy' in CAM.
7. As noted by (Enck et al., 2011), it is important to also include a manipulation check within the balanced placebo design, as some participants may be skeptical that they have been told the truth about what they have received.
8. Effects resulting from conditioning are not accounted for within this model.

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