Pain, Placebo, and Cognitive Penetration

ABSTRACT: There is compelling evidence that pain experience is influenced by cognitive states. We explore one specific form of such influence, namely placebo analgesia, and examine its relevance for the cognitive penetration debate in philosophy of mind. We single out as important a form of influence on experience that we term *Radical Cognitive Penetration,* and argue that some cases of placebo analgesia constitute compelling instances of this phenomenon. Still, we urge caution in extrapolating from this to broader conclusions about cognitive penetration in perceptual experience. Instead, we suggest that the cognitive penetration of pain raises distinctive psychological, epistemological, and ethical issues.

1. Introduction

An important long-standing debate in the study of perception concerns the phenomenon of cognitive penetration. This is the putative influence of states like beliefs and desires on the content of our perceptual experience; that is, whether what we see or hear can be influenced by what we believe, expect, or desire to be the case.

While the existence of cognitive penetration of perception remains controversial, similar questions about the influence of beliefs and desires can be raised for a range of other mental states, notably pain. Although it is widely acknowledged that pain experience can be impacted by one's outlook and expectations via placebo effects, there has been little philosophical exploration of how such effects might inform the broader cognitive penetration debate. It thus remains an open question whether there may be relevant similarities between cognitive influences on pain experiences and the putative cognitive penetration of perceptual experience.

In a notable recent attempt to explore these similarities, Gligorov (2017) argues that the case of pain is a clear and compelling case of cognitive penetration in which cognitive processes influence the sensory aspects of pain. Gligorov's argument relies on an extensive review of

empirical evidence supporting the existence of cognitive penetration in pain as well as an analysis of this literature through use of the gate theory of pain. While we are broadly in agreement with Gligorov's conclusion regarding the link between cognitive processes and pain perception, here we wish to expand her analysis through an examination of the implications of this phenomenon for the discussion of cognitive penetration in the philosophy of mind. Gligorov is clear that she is only putting forward an argument for the existence of cognitive penetration in pain, and that she does not wish to make claims about the influence of cognitive processes on other forms of perception.

In Section 2 of this paper, we briefly summarize current approaches to cognitive penetration in philosophy and cognitive science, and spell out a form of cognitive penetration, *Radical Cognitive Penetration*, that we take to be of primary interest in the contemporary debate. We go on in Sections 3 and 4 to examine in more detail one putative form of cognitive penetration of pain experience, namely placebo analgesia, and conclude (following Gligorov) that this should indeed be recognized a form of Radical Cognitive Penetration. In Section 5, we examine the relevance of this claim for the cognitive penetration debate. We argue that we should be cautious in inferring from the existence of cognitive penetration of pain to the empirical possibility of cognitive penetration of perceptual experience. Instead, we suggest that a number of distinctive and interesting psychological, epistemological, and ethical issues arise from the phenomenon of the cognitive penetration of pain experience.

Two brief points of clarification are worth quickly making before proceeding. First, we will use the term *perception* in this paper to refer narrowly to exteroceptive forms of sensation such as vision, audition, and touch. Framing things in this manner, pain and other interoceptive forms of sensation are thus not properly considered perceptual phenomena. This choice of terminology reflects our goal to compare what we believe is robust evidence for the cognitive penetration of pain experience with the more scanty and controversial evidence for the cognitive penetration of perception where this is understood as involving vision, audition, touch, and so on.

Second, we recognize that much of the following discussion may not seem particularly novel to those already familiar with placebo analgesia: the ability of our beliefs, desires, and expectations to influence clinical outcomes is long-standing and well-attested. What we take to be distinctive in the present endeavor, however, is our attempt to show that the phenomenon of

placebo analgesia exhibits many of the same features as those attested in alleged cases of the cognitive penetration of perception, as well as some important differences. Consequently, we suggest that cognitive science could glean important insights from comparing these two phenomena.

2. Cognitive penetration: an overview

2.1 – What's at stake in the cognitive penetration debate?

A major debate in philosophy of mind and cognitive science concerns cognitive penetration, that is, whether our thoughts, beliefs, and desires can influence what we see, hear, and otherwise perceive. Extensive experimental data, dating back at least as far as the work of psychologists such as Perky (1910), but proliferating especially in the last two decades, has been advanced in support of the claim that there are indeed 'top-down' effects from cognition to perception. Collectively, this has provided support for the thesis of cognitive penetration, which holds that our thoughts, beliefs, and desires can significantly affect how the world appears to us, by way of our perceptual experiences.

If it is true that our beliefs, desires, and other cognitive states can indeed directly influence our perceptual experience, a number of important conclusions follow. The first is straightforwardly epistemological: to the extent that perceptual experience is vulnerable to interference from a subject's beliefs and desires, it risks undermining the status of perception as a neutral source of evidence for forming beliefs (Macpherson, 2017). To give a simple example of the kind of case at issue, imagine two spectators are watching a tennis match between Djokovic and Murray, and Murray's serve is ruled to have clipped the net. Spectator A, a Djokovic supporter, agrees with the umpire's decision, and insists they saw the ball clip the net, but Spectator B, a Murray supporter, claims that he clearly saw the ball skim over the net without touching it. Assume further than both supporters have good vision and had a clear line of sight to the net. We can now ask whether their respective partialities to the two players genuinely led them to see events unfold differently. If the mechanisms of visual awareness are not subject to influence from viewers' attitudes and desires, then the answer to this will be no, and their different judgments in the two cases are likely due to a properly cognitive bias in judgment on the part of one or both of them, for which they can be held accountable as epistemic agents.

However, if their attitudes towards the two players *did* influence their visual experience prior to the operation of cognitive processes, then both players could be responding fully rationally given the evidence at their disposal, making this perhaps a case of blameless disagreement. This example is a little simplistic, but should give the reader an idea of the kind of case at the heart of the debate.

A second upshot of cognitive penetration of perception concerns the structure of the mind itself. A popular and influential framework for thinking about the mind holds that perceptual processing is *encapsulated* from cognitive attitudes like belief and desire, reflecting a modular architecture of the mind (Fodor, 1983). However, if it is possible for cognitive attitudes to directly influence perceptual experience in the way described above, then the evidence for this framework becomes somewhat less clearcut; rather than being organized into discrete processing modules, the mind might possess a much less clearly differentiated architecture in which no clear line can be drawn between expectations and perceptual representations (Clark, 2016).[1]

2.2 – Evidence and controversies

Many different experiments have claimed to show the existence of such cognitive penetration of perception. Some of this evidence has been taken to suggest that perceptual learning can influence the way we perceive even low-level properties such as hues (Goldstone, 1995; Hansen et al., 2006), and the perceived size of objects (Bruner, 1957). For example, one study by Levin and Banaji suggested that faces categorized as racially black rather than white are perceived as having a darker skin tone, even when luminance is controlled for (Levin & Banaji, 2006), while a study by Daas et al. suggested that men primed with sexual thoughts judge women's breasts to be larger than cases where men who have not been thus primed (Daas, Häfner, & Wit, 2013). A further important line of research concerns apparent distance and the influence of motor planning on perception. Thus one influential study suggested that people wearing a heavy backpack

[1] Some still endorse a modular account of perception while accepting the existence of cognitive penetration, perhaps on the grounds, that for example, perceptual representations have a different representational format from those of beliefs and expectations. However, the notion of modularity at stake would then be significantly different from that popularised by Fodor.

gauged distances to be longer than those who were unencumbered (Proffitt et al., 2003), while a further experiment (Witt, Proffitt, & Epstein, 2004) showed that when instructed to throw a heavy rather than light ball participants made greater estimates of the distance to a target, leading the authors of the study to suggest that the expectation of increased exertion involved in throwing the ball can affect how far away the target looks.

Nonetheless, the cognitive penetration debate remains convoluted and controversial. Many experimental findings that seemingly support cognitive penetration have been challenged on methodological and theoretical grounds. Firestone and Scholl, for example, point to a range of oversights and complications which, they claim, plague the current scientific literature on top-down effects on perception. These include failures of experiments to account for the "El Greco fallacy" (Firestone, 2013), the underappreciated role of memory in facilitating perceptual processing, 'demand characteristics' in which participants' reports are influenced by their beliefs about the purpose of the experiment, and attentional effects (Firestone & Scholl, 2015).

More fundamentally, however, there has been confusion and cross-purpose in the very notion of cognitive penetration, as has been widely pointed out (Macpherson, 2015). The term as influentially employed by Pylyshyn, for example, refers not to the capacity of cognitive states to influence perceptual experience, but more narrowly in relation to the possibility of the influence of cognition on unconscious early visual processing (Pylyshyn, 1999).[2] This is in contrast to how the term is often employed in the philosophy of perception (Macpherson, 2012), where the central question is typically whether perceptual *experience* is subject to such effects.

A further confounding factor concerns 'what counts' as cognitive penetration. There are entirely uncontroversial examples of ways in which our cognitive states can indirectly influence the inputs to perceptual processes, for example by causing us to redirect our eyes towards particular stimuli ('overt attention'). However, this is not taken to be of particular interest by any of the participants in the debate. A more complex case is presented by attention, and specifically *covert* attention, such as attendings that occur without shifts in gaze fixation. A growing body of experimental data (Carrasco, Williams, & Yeshurun, 2002; Fuller, Ling, & Carrasco, 2004)

[2] See also Mahon & Wu (2015) for a claim about cognitive penetration best understood in terms of influences on unconscious perceptual processing.

suggests that, even without moving our eyes, the selective allocation of attention to one visual stimulus rather than another can influence the contents of visual perception, including both the precision of information available to a given subject as well as more specific modulations of contrast and hue. However, while the seeming ability of covert attention to influence perceptual experience raises some interesting questions, it remains highly controversial whether these exhibit the same problematic epistemological features as cases involving direct, non-attentionally mediated influence of cognitive states on perception (Deroy, 2013; Mole, 2015).

2.3 – Radical Cognitive Penetration

Despite these disagreements and complexities, it is nonetheless possible to single out a specific extreme form of cognitive penetration that is of particular philosophical and psychological interest, which we will call *Radical Cognitive Penetration*. This is the putative influence over short timescales of a subject's beliefs, desires, and other cognitive states on their experience in a way that (i) is not directly mediated by attention, and (ii), involves a semantic or logical connection between the penetrated experience and the penetrating cognitive state or states.

It is worth saying something about both of these conditions. The first constraint reflects the fact that the relevance of attentional effects for the cognitive penetration debate remains disputed. Consequently, there will be those who question whether a notion of cognitive penetration that relied exclusively on attentional effects would raise any particularly novel interesting epistemological or architectural concerns like those discussed above. Far more controversial – and for present purposes, far more interesting – is the claim that our beliefs and attitudes can influence experience directly, without the need for attention as a mediating factor.

The second constraint mentioned above is necessary to capture something intuitively important about cognitive penetration, namely that there be a *meaningful* relation between the relevant cognitive and perceptual states. Consider a case in which someone develops a migraine after thinking about a forthcoming deadline, which causes them to see bright auras in their visual field. While this case strictly speaking involves the influence of cognition on perception, it arguably lacks at least one feature that makes cognitive penetration epistemologically and psychologically important, namely that the relation between the relevant cognitive and

perceptual states should involve a semantically intelligible connection between the two. To return to the example given earlier, if I am led to see Murray's serve as having clipped the net because of headache-induced visual perturbation caused by some belief entirely unrelated to the tennis, then my beliefs are only very indirectly relevant to my perceptual error; certainly, it would be a mistake to describe the situation as involving the systematic *biasing* of perception by cognition. If, by contrast, I am led to see Murray's serve as clipping the net via the cognitive penetration of my belief that Djokovic deserves to win, serious questions are raised about the broader capacity of our beliefs and partialities to undermine perception as a source of unbiased information.

If Radical Cognitive Penetration in the sense stated above does occur in the case of perceptual experience, it would follow that what a subject consciously sees or hears at a time can be influenced (in a semantically coherent way) by the cognitive states they happen to have at that moment. This would be of great significance, insofar as it would suggest that perceptual experience is vulnerable to epistemologically significant interference not merely from our distinct life experiences and learning histories, but from our beliefs and desires at a given moment. It thus raises the possibility that our awareness of the world is systematically undermined from one moment to the next by the distorting influence of beliefs, expectations, and desires.

Radical Cognitive Penetration is thus an important notion if we wish to get to the core of what is at stake in the debates about the cognitive penetration of perception. There are two other reasons worth mentioning, however, that lead us to believe Radical Cognitive Penetration is a particularly interesting way of framing the debate. The first that is that, unlike more subtle forms of cognitive penetration involving attention and perceptual learning, it is far from introspectively obvious that Radical Cognitive Penetration occurs at all for perception. If it does not occur, then it can potentially offer an important source of evidence in developing theories of the architecture of the mind and conscious experience, particularly concerning the question of whether perception is a modular process encapsulated from belief and desire.[3]

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[3] In this regard, it is worth noting that a leading family of theories of mind, namely the predictive coding approach, may be committed to a fairly high degree of radical cognitive penetration. See MacPherson (2017) for further discussion of this topic.

The second reason why we take Radical Cognitive Penetration to be of significance is that, as we shall argue, there is good evidence that it *does* in fact occur in the case of pain experience. That is, a subject may experience their pain quite differently at a given moment as a consequence of their beliefs and desires at that time, where there is an intelligible semantic connection between these cognitive states and their pain experience. In particular, as we shall now claim, the phenomenon of placebo analgesia may in some instances constitute such a case.

(3) Placebo analgesia as cognitive penetration

3.1 – Placebo and analgesia: an overview

As others have argued, pain experience is arguably susceptible to influence by cognition in a way that satisfies most definitions of cognitive penetration (Gligorov, 2017). This may not seem surprising to those acquainted with the clinical literature on placebo analgesia. However, in light of the nuances concerning the definition of cognitive penetration discussed above, some care is required to demonstrate that (at least some cases of) placebo analgesia entirely fulfill the criteria for Radical Cognitive Penetration. It is to this task that we now turn. In what follows, we briefly introduce the placebo effect and discuss evidence for placebo analgesia, before going on in Section 4 to explore several debunking explanations for this phenomenon that might suggest placebo analgesia is not a case of Radical Cognitive Penetration.

While the definition of the placebo effect is widely disputed, for our purposes, placebo effects can be thought of as beneficial effects on patient well-being resulting from patient expectations or conditioning processes.[4] Placebo effects are distinct from placebo controls used in clinical trials, which are designed to demonstrate the unique impact of the investigational intervention on the condition being treated, or placebo treatments used in practice, which are commonly used but often associated with deception (Howick et al. 2013). A closely related phenomenon is the nocebo effect, which resembles the placebo effect except that it involves negative effects rather than positive ones.

The placebo effect was first demonstrated in modern medicine by physician John Haygarth, who used sham treatments to produce real therapeutic outcomes, leading him to note

[4] For a review of the varieties of placebo analgesia and its broader philosophical significance, see Moerman (2017).

that, “to a degree which has never been suspected, [a] powerful influence upon diseases is produced by mere imagination” (Haygarth, 1800). Robust and consistent placebo effects have since been demonstrated across a wide variety of conditions, including, but not limited to, pain, depression, irritable bowel syndrome, chronic fatigue syndrome, and Parkinsonian symptoms, although other conditions, such as viruses and tumors, appear to be unresponsive to placebo treatments (Benedetti, 2009; Carvalho et al., 2016; Kirsch et al., 2008). Placebo effects can be brought about through a variety of means, including the perceived warmth of a practitioner, the color of a pill, or the description of a treatment given, and often operate in conjunction with other components of a treatment (Benedetti et al., 2007; de Craen et al., 1996; Howe, Goyer, & Crum, 2017).

Placebo *analgesia* refers specifically to placebo effects that lead to a reduction in the experience of pain. While it may be that other instances of the placebo effect also provide support for the existence of cognitive penetration, we have chosen this narrow focus for several reasons. First, is likely that there are several distinct mechanisms at play within different kinds of placebo responses, depending on the form of placebo treatment and type of condition, so to speak generally of all placebo effects would prove a cumbersome task. Secondly, a significant proportion of placebo research has focused on placebo analgesia, so there is a large evidence base to consider in relation to this phenomenon. Third, as mentioned above, cognitive processes such as beliefs and expectations appear to produce consistent and robust placebo analgesic responses. Finally, there are apparent similarities between perceptual experiences and pain experiences – such as their rapidity, automaticity, and sensory character – that mean this sub-phenomenon is most likely to give us insight into the cognitive penetration of perception.

3.2 – Evidence for Placebo Analgesia

There is a large and growing body of evidence for placebo analgesia. The hidden administration paradigm is a cornerstone of placebo studies. In this procedure, participants in one condition receive a painkiller that is administered overtly, so that they are aware of when the administration takes place and are able to watch a member of the clinical team administer it. In the second condition, participants are given a painkiller covertly, often intravenously initiated

from an automatic infusion machine in another room, so that they are unaware of when the drug is being administered and no clinician is present. In an exploration of this paradigm, Amanzio et al. (2001) examined the impact of four widely used painkillers on pain ratings of patients who had just undergone thoracic surgery. Regardless of the type of painkiller, they found that the dose required to reduce pain in the covert condition was 50% higher than that of the overt condition, and pain ratings in the first hour after surgery were significantly higher in the covert condition

Many other experiments seeking to examine the role of expectation in placebo analgesia have utilized the hidden administration paradigm and confirmed that the experience of watching a clinician administer a painkiller leads to a significant reduction in pain in comparison to covert administration, suggesting that one's beliefs and expectations regarding anticipated pain relief play a significant role (Benedetti et al., 2003; Bingel et al., 2011; Colloca et al., 2004; Levine & Gordon, 1984; Levine et al., 1981). It is noteworthy that these effects play out over the short-term: it is participants' specific belief about whether they have just received analgesics that influences the amount of pain experienced.

In another illustrative experiment, participants who had just had dental surgery received either real acupuncture or sham acupuncture to treat the pain. Here, pain relief depended on whether participants believed they were in the real acupuncture condition; those that thought they were receiving real acupuncture experienced significantly more pain relief (Bausell et al., 2005). Of course, in this experiment, it might be simply that those that felt greater pain relief (attributed to the natural reduction in post-surgical pain), surmised that they were in the real acupuncture condition as a result. However, there is evidence that those who think that acupuncture generally is an effective treatment for pain and that those who expect to personally benefit from it tend to report more pain relief, suggesting that expectations and beliefs related to the treatment are contributing as well (Kalauokalani et al., 2001; Linde et al., 2007).

Decreases in pain have also been associated with the belief that one is taking an expensive analgesic rather than a cheap one (Waber et al., 2008), watching someone else experience pain relief through a particular means (Colloca & Benedetti, 2009), and having a choice over which painkiller one takes (Rose et al., 2012). More invasive treatments (e.g. an injection vs. a pill) appear to contribute to greater pain relief (de Craen et al., 2000), while

'nocebo' words spoken along with administration (e.g. "This is the worst part of the procedure") can be hyperalgesic, leading to an increase in pain (Varelmann et al., 2010).

Prima facie, it looks as if placebo analgesia may constitute a compelling instance of Radical Cognitive Penetration of pain experience. Given the evidence above, it appears that one's beliefs and expectations with regards to the treatment one is receiving, as well as one's awareness of the administration, have a significant impact on one's immediate experience of pain relief. One interpretation would be that the belief that pain will be diminished itself directly inhibits the sensory processes underlying pain sensation. If this was correct, even in some cases, then it would constitute a demonstration of the ability of high-level cognitive states to directly modulate lower-level sensory representations. This in turn might provide an important analogue for the broad kind of architectural dynamics proposed by defenders of cognitive penetration in perception. However, as we will consider within the following section, there may be alternative explanations for placebo analgesia.

(4) Can we explain placebo analgesia without cognitive penetration?

While it is beyond serious doubt that patients' subjective and objective clinical outcomes relating to pain are influenced by their expectations and beliefs, it does not automatically follow that placebo analgesia involves the kind of direct influence on pain sensation that constitutes Radical Cognitive Penetration. We will now therefore examine some proposed explanations of placebo analgesia, and consider whether they might better explain the phenomenon than Radical Cognitive Penetration.

4.1 – Placebo as conditioned response

It has been widely hypothesized that a primary causal mechanism in many placebo effects is classical conditioning (Benedetti, 2009; Pacheco-Lopez et al., 2006; Schedlowski & Pacheco-López, 2010). For example, a subject who has previously experienced pharmacologically mediated pain relief via the administration of a given drug in capsule form might become conditioned to experience similar pain relief when a placebo capsule is given in its place. Indeed, given the established ability of classical conditioning to produce a number of typically

involuntary physiological changes, it would be surprising if such effects did *not* occur under appropriate circumstances. For example, Pavlov (1927) demonstrated that dogs who were given morphine when placed in an experimental chamber began to exhibit morphine-like symptoms immediately upon entering the chamber even prior to the morphine itself being administered. This raises the question of whether cognitive processes bring about placebo analgesia, or whether it might simply be a result of associations that have been formed between aspects of the placebo treatment and past pain relief. If the latter, then it would weaken the argument that it constitutes a bona fide case of cognitive penetration; as Brogaard and Chomanski put it, "top-down influence [relying on conditioning] is not a case of cognitive penetration because it rests on associative principles, which are non-inferential rather than a result of a chain of semantically-coherent inferential steps" (Brogaard & Chomanski, 2015).

Some types of placebo effects, such as those impacting the immune system, appear to only be brought about through the mechanism of conditioning (Benedetti, 2009; Pacheco-Lopez et al., 2006; Schedlowski & Pacheco-López 2010) . Conditioned immune responses have been observed across many species (Ader, 2003; Schedlowski, 2006) and have been hypothesized to have evolved "as an adaptive strategy in order to protect the organism and prepare it for danger"(Schedlowski & Pacheco-López, 2010). The role of conditioning in pain relief is more controversial, since unlike measurements of immune indicators, pain reporting involves a subjective dimension. Additionally, it can be difficult to tease apart the role of conditioning and cognitive processes within experiments investigating placebo effects because conditioning can impact expectations. Recent evidence, however, has demonstrated that placebo analgesia can be brought about through classical conditioning that individuals are unaware of (Jensen et al., 2012). This suggests that expectations may not be necessary for placebo analgesia to take place, although this hinges on a debate about whether expectations can be unconscious, in which case Jensen et al.'s results may be attributable to unconscious expectations (Colloca & Miller, 2011). Experiments have also demonstrated that placebo analgesic effects mediated by conditioning can be *overruled* through an expectation of hyperalgesia (Benedetti et al., 2003; Montgomery & Kirsch, 1997). This suggests placebo analgesia brought about through conditioning or expectations may operate through distinct mechanisms, and also that cognitive influences on pain experience may nullify conditioned responses.

4.2 – Placebo as demand characteristics

Several of the experiments cited above demonstrate a relationship between believing that one is receiving an effective treatment and the degree of pain relief reported (Bausell et al., 2005; Kalauokalani et al., 2001; Linde et al., 2007). This relationship can be seen in other forms of placebo response as well, and has been particularly robust in post-surgical ratings of quality of life, where one's belief that one is receiving the real (as opposed to sham) surgery has at times been a better predictor of outcome than which condition one was actually assigned to (Hyland & Whalley, 2008; Juergens et al., 2010; McRae et al., 2004). While these results suggest that beliefs can impact the experience of pain, they could also be interpreted as stemming from participant biases. In order to appease the experimenter or contribute to evidence for an intervention they believe in, participants may be reporting significant improvements in outcomes, while in actuality they are no better off.

In research specific to placebo analgesia, this highlights an important space between the experience of pain and reports of pain sensation. Pain outcomes are often measured by subjective reports, which do not allow researchers to distinguish between pain reports based on bias and pain reports based on a change in the experience of pain.

Despite this concern, growing evidence related to the physiology of placebo analgesia suggests that more is going on than can be explained by demand characteristics. There has been a surge in neuroscientific investigations of placebo analgesia in recent decades. Placebo analgesia brought about by expectations often involves the release of endogenous opioids in the brain, further corroborated by evidence that pain relief brought on through placebo treatments can be blocked by the opioid antagonist, naloxone (Amanzio & Benedetti, 1999; Benedetti, 1997, 2009). Interestingly, hyperalgesic placebo responses appear to be mediated through a distinct pathway involving the CCK system, and can be blocked by the CCK antagonist proglumide (Benedetti, 1997; Benedetti, Amanzio, et al., 2006; Hebb et al., 2005). Evidence also points towards the important role of the neural reward system in bringing about placebo analgesia (Benedetti, Arduino, et al., 2006; Gollub & Kong, 2011; Krummenacher et al., 2010; Scott et al. 2007, 2008), as well as decreases in activity in brain regions associated with pain (e.g. thalamus,

insula, ACC) during placebo analgesia (Wager et al., 2011; Wager et al., 2004). Taken together, this large body of evidence implies that placebo analgesia is not merely the result of participants reporting exaggerated pain relief in order to please experimenters or favor a particular therapeutic agent.

4.3 – Placebo as cognitive appraisal

Approaching a more fine-grained analysis of the mechanisms underlying placebo analgesia, one might maintain that the evidence still fails to demonstrate the existence of top-down effects of cognition on the sensation of pain on the grounds that placebo effects reflect changes in *appraisal* of pain rather than experience of pain. Arguably, just as there can be a gap between the experience of pain and the way one reports pain, there can also be a gap between the sensation of pain and the subjective appraisal of pain. Hence consider Lycan's example drawn from a John Grisham novel of an everyday description of pain that seems to pass unnoticed: "Every step was painful, but the pain was not felt. He moved at a controlled jog down the escalators and out of the building" (Lycan, 1996).

The idea that there can be a difference between the sensation of pain (that is, its felt intensity) and our appraisal of pain (how badly we believe it hurts) is highly controversial, and connects to further important debates about introspection and self-knowledge. Many would deny that the distinction between felt pain and appraised pain even makes sense: if someone sincerely claims to be in intense pain, then *ipso facto* they are in intense pain. The distinction is also typically irrelevant from a clinical perspective, insofar as there are good practical and ethical reasons for physicians to take sincere patient reports at face value.

From a philosophical perspective, however, it seems possible that some pain reports could involve a degree of introspective failure, in which participants overestimate or underestimate the underlying intensity of their pain sensation (see 5.2 for more discussion). Insofar as one takes dissociations between pain sensation and pain appraisal to be a possibility, one might raise a further doubt about the idea that pain involves cognitive penetration. Rather than influencing the underlying *sensation* of pain, it might be possible that placebo analgesia reflects effects on what people think or believe about their pain. This would contradict the idea

that cognitive states directly penetrate the sensory aspects of pain experience and hence tell against Radical Cognitive Penetration in the case of pain.

While it is likely that direct shifts in appraisal play a role in some forms of placebo analgesia, a growing consensus holds that there are multiple routes by which expectations lead to reduction of felt pain, some of which occur nociceptively and involve changing the pain sensation and the information about pain that reaches the brain, and others which occur during the appraisal of pain (Goffaux et al., 2007; Lorenz et al., 2005; Price & Barrell, 2000; Wager, Matre, & Casey, 2006). There is also growing evidence that expectations related to pain can impact spinal processing of pain, which is thought to occur downstream before any appraisal occurs (Eippert et al., 2009; Fields, 2004; Goffaux et al., 2007; Matre, Casey, & Knardahl, 2006)[5]. This suggests that the very *sensation* of pain is in fact modulated by relevant expectations and beliefs, challenging the view that pain sensations are somehow encapsulated from cognition.

There is further evidence that pain processing can be impacted by expectations, through a shift in perceptual decision-making, defined as "the inferential process underlying perception in which prior information is used to interpret sensory information" (Wiech et al., 2014). Wiech et al. explored how prior expectations concerning the likelihood that participants were about to experience a stimulus causing high-intensity pain or low-intensity pain (odds of 50/50, 80/20, or 20/80) impacted sensory pain processing as well as perceptual decision-making. Analysis of the data using a diffusion drift model revealed that changes in perceptual decision-making were primarily responsible for the influence of expectations on pain perception. This suggests that even before expectations have an opportunity to impact the sensory processing of a pain stimulus, expectations can influence unconscious inferences related to pain that will then impact how information related to pain is received; as Wiech et al. report, "incoming sensory information is not analyzed *de novo* but interpreted based on prior information"(Wiech et al., 2014, p. R680)[6]. The authors point out the link between their findings and research related to

[5] Note that there was no control condition in the experiment run by Goffaux et al. (2007) so the evidence is less strong.

[6] Consideration of the many ways in which experiences of pain can be impacted by expectations has led several researchers to suggest a shift towards a model of predictive coding, or Bayesian decision theory, in order to make space for the role of higher-order cognition in explanations of pain processing (Anchisi & Zanon, 2015; Buchel et

cognitive penetration in visual processing and it is to this link that we now turn. In the next section, we consider in what ways placebo analgesia might shine light on other forms of perception and in what ways it might not.

(5) Exploring the significance of placebo analgesia as Radical Cognitive Penetration

Drawing together the preceding arguments, we conclude that at least some cases of placebo analgesia plausibly satisfy the criteria for Radical Cognitive Penetration. In the experiments described above, it seems that the belief that one has received an analgesic can be sufficient to reduce the intensity of pain experience. This plays out over short-term timescales of a few hours, rather than depending on long-term conditioning or sensory learning. There is an intelligible semantic connection between the belief that a pain-alleviating drug was administered and the subsequent reduction in pain experience, and there are reasons to think that the effect does not just rely on shifts in attention or appraisal, but can involve modulation of nociceptive sensation early in the process of pain experience.

This suggests that we have evidence for at least one form of Radical Cognitive Penetration of experience, namely that which occurs in the case of pain. This is of potential significance, as we will now describe, for philosophers and cognitive scientists interested in the broader debate concerning cognitive penetration of perceptual experience. Additionally, we hope that by identifying an important conceptual bridge between the existing rich literature on cognitive penetration in perception and the similarly extensive body of clinical data on placebo analgesia, we might pave the way for further insights among those approaching pain from a clinical perspective. In what follows, we explore some of these issues, arranging them into two broad categories: first, those that pertain to the lessons of radical cognitive penetration for

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al., 2014; Jones, Brown, & El-Deredy, 2013; Wiech, 2016). Such a model would account for both ascending (bottom-up) and descending (top-down) effects, and the feedback loops between them, that can shape one's expectations and experiences of pain (Buchel et al., 2014). The concept of 'perception as inference' has also been offered as a guide, in order to tie cognitive processes more closely to perceptual processes and to do away with a picture of them as distinct (Wiech, 2016).

debates about the structure of the mind, and second, normative issues with relevance for epistemological and ethical questions.

5.1 – What can cognitive penetration of pain experience teach us about the mind?

It is tempting to regard Radical Cognitive Penetration of pain experience as a 'proof of concept' for cognitive penetration more broadly. After all, pain experience and perceptual experience arguably share a number of common features. Both are often taken to involve *nonconceptual* rather than conceptual content, for example (Tye, 2005) and to be evolutionarily more primitive than cognition proper (Feinberg & Mallatt, 2016). To the extent that there is cognitive penetration in pain experience, then, it might seem to motivate at least the possibility that such penetration could occur in perceptual experience.

However, some caution is required here. To be sure, the radical cognitive penetration of pain experience would seem to provide evidence that there can be semantically coherent influence from high-level cognition to more basic systems, even where these systems may differ in the kinds of representations involved (since pain sensations, like perceptions, arguably possess a sensory rather than propositional structure, yet are able to be influenced by beliefs to a high degree). Similarly, Radical Cognitive Penetration of pain experience would suggest that the mere automaticity of a process is not grounds for assuming it must be encapsulated from the influence of beliefs and desires: pain, after all, like perception is typically an involuntary sensation, yet we have argued that its subjective character can be heavily influenced by beliefs.

Nonetheless, there is nothing to prevent one who disbelieves in the phenomenon of cognitive penetration of perceptual experience from arguing that, as a matter of brute empirical fact, perceptual experience is unlike pain experience insofar as it cannot be directly influenced by beliefs.

While we do not wish to make any commitments in this regard, we nonetheless wish to now draw attention to three key ways in which perceptual experience and pain differ, such that radical cognitive penetration might occur differently in the two cases – if indeed it occurs at all in the case of perception.

A first important dissimilarity between pain and perception comes from the evidence for the release of endogenous opioids during placebo analgesia. This provides a fairly direct

mechanism by which appropriate beliefs might affect early nociceptive processing in a semantically coherent way: my expectation of diminished pain gives rise to a biochemical process that diminishes the intensity of pain sensation. There is to our knowledge no similarly broad biochemical mechanism by which the contents of perception could be appropriately influenced by belief states. In light of the more complex representational function of perception, one might question whether such a mechanism is even plausible. Somewhat crudely, it is hard see how any *hormonal* response could interact with early vision so as, for example, to cause me to see Murray's serve as having clipped the net. This is not to deny that there may be more sophisticated forms of influence from cognition to perception, such as the indirect influence of imagery (Macpherson, 2012), or the biasing of certain recognitional templates in long-term memory that might constitute bona fide cases of radical cognitive penetration in perception. However, these are markedly different from the straightforward diminution of nociceptive processing by hormonal release, and thus represent an important disanalogy between the possible mechanisms for cognitive penetration in perceptual and pain experience.

A second interesting reason why someone might claim pain differed from perception in respect of its vulnerability to influence by beliefs and goals is that pain sensations, as long as they are present, differ from most perceptual states insofar as they are *intrusive* (Martínez, 2015). Whereas I can usually ignore the noise of a bird outside my window or the drone of an air conditioning unit, it is normally much harder for me to do the same with a bad migraine or toothache. These latter sensations occupy 'center stage' in my mental landscape until acted upon. This reflects, of course, the fact that pains carry information that is frequently immediately relevant to an organism's survival, whereas much of our perceptual experience involves awareness of aspects of our environment that are not immediately relevant to our current goals.

This cognitive priority of pain sensations thus inhibits our ability to engage in other actions as long as we are subjectively aware of intense pains. Some adaptive advantage, then, might have been provided to organisms whose pain sensations were amenable to diminution or extinction in cases where they believed an appropriate response to them had been taken, thus freeing them to pursue other goals. By contrast, no clear parallel exists for perception, given that perceptual experience is rarely intrusive to the same extent as pain. Note that there are of course other states besides pain that have this intrusive character: hunger, thirst, fatigue, sexual arousal,

and other bodily states possess "interruptive and urgent functions" (Eccleston, 2018). Hence if it is pain's intrusive character that makes certain forms of cognitive penetration valuable or adaptive, we might expect to find something similar to be the case for other states with an essentially directive character, as discussed below.

Finally, and most speculatively, note that it is often maintained that perception critically differs from pain (as well as several other states, such as appetites and desires) in its *direction of fit* (Searle, 1983). Somewhat roughly, the contents of perception are such that they serve their purpose when an organism appropriately adjusts its cognitive state to reflect the condition of the world, thus possessing a 'mind to world' direction of fit. Perception operates in accordance with its constitutive function, then, when it leads us to accurately represent the world (Burge, 2010). If a creature's fleeting cognitive states were able to exert significant influence on its perceptual experience with the result that it *misrepresented* the world, then, this would amount to a failure of the proper purpose of perception.[7]

In contrast, pain (along with other states, such as hunger and thirst) is arguably characterized in part by having a *world-to-mind* direction of fit (Martínez, 2011); that is to say, its primary function is to motivate us to take appropriate action to change the world to satisfy some internal demand. According to one view of pain content, for example, experiencing pain in my leg can be understood in terms of a directive to alleviate that pain as much as possible and to protect the relevant body part (Klein, 2015).[8]

To the extent that mental states with a world-to-mind direction of fit are understood as injunctions to action, then, it is entirely compatible with their proper functioning that they be updated in light of beliefs about the actions we have already taken. Thus if a subject believes that appropriate responses to painful sensations have already been performed, as in the case of the administration of painkillers, the pain experience has already fulfilled at least one of its central

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[7] We recognize that there are complex issues here. For one, it seems possible that certain forms of cognitive penetration might lead one to *more* accurately or quickly represent the world, for example in cases of known illusion (though there may be broader epistemological reasons for ensuring that perceptual representations are not automatically updated in light of prior knowledge; see Egan, 2008). All that is at stake in the present discussion, however, is that the broad functional role of perception is importantly different from capacities such as pain.

[8] Of course, pain sensation does also provide useful information about injury and bodily damage (Tye, 1997). However, there is a striking phenomenological difference between, for example, *seeing* that one's leg is injured and *feeling* pain in one's leg. The latter experience is arguably immediately motivating in a way that the former is not, reflecting its world-to-mind direction of fit.

functions. There is hence a reason why we might expect pain representations to be susceptible to diminution or extinction once a subject believed they had been acted upon. No such similar phenomenon would be expected with comparable perceptual representations, which lack the constitutive connection to action that arguably applies in the case of pain.

There is a danger here, of course, of proving too much. Pain is not normally under our voluntary control to any great extent, and we are frequently burdened by pain even in contexts where we rationally realize that little can be done about it.[9] However, such cases differ from the contexts of placebo analgesia insofar as patients do not believe that they have undertaken effective measures to alleviate the pain. For example, it may be that in order for the relevant form of cognitive penetration to occur patients must not merely possess the belief that the pain experience is undesirable or unhelpful, but also that they have *already acted* to address it.

The above considerations are highly speculative. However, it is worth noting that, if there is some truth to this line of argument, we might expect cognitive penetration to be more common or more dramatic among other sensory states with a world-to-mind direction of fit, such as hunger or sexual arousal, and indeed, there is evidence to this effect. The perceived intensity of hunger sensations seems to be highly susceptible to influence from cognition, and via manipulatingparticipants' beliefs about much they have previously eaten it is possible to influence their subjective level of hunger (Brunstrom et al., 2012). In one study it was discovered that, without explicit memory of having previously eaten lunch, amnesic partients would eat lunch three times in fairly rapid succession (Rozin et al., 1998). Similarly, there is evidence showing that sexual arousal is subject to voluntary cognitive regulation. One neuroimaging study, for example, showed significantly decreased markers of sexual arousal among people watching an erotic film who were instructed to distance themselves from its content (Karama et al., 2002). Of course, (radical) cognitive penetration of the relevant appetitive states is only one explanation for these results, and we do not rest our argument on them, but they provide some intriguing evidence that we may do well to look for instances of cognitive penetration among sensations with a world-to-mind direction of fit.

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[9] However, note that there is considerable clinical data suggesting that self-hypnosis can be effective in the alleviation of pain. See, e.g.,(Olness and Ader, 1992).

In summary, then, we should not assume from the apparent occurrence of Radical Cognitive Penetration in the case of pain experience that such penetration is also likely to occur in perceptual experience. At most, the phenomenon of placebo analgesia suggests that certain facts about different forms of psychological processing – such as differences in representational format – are likely to be compatible with the occurrence of cognitive penetration. Constructively, we would suggest that to the extent that future experimental work bears out differences between the mechanisms or occurrence of cognitive penetration among states with world-to-mind and mind-to-world directions of fit, we might thereby glean insights into some of the key differences between different systems within the mind. If it were the case, for example, that states such as pain, hunger, arousal, and so on, are all found to be subject to quite dramatic forms of cognitive penetration, while perceptual systems are not, this might in turn lend support to the idea that there is a fundamental functional and even architectural distinction to be drawn between these two families of mental states, perhaps reflecting distinct evolutionary histories (a proposal considered by, among others, Godfrey-Smith, 2017, and Feinberg & Mallatt, 2016).

5.2 – Epistemological and ethical issues

We turn now to some possible epistemological and ethical upshots of the Radical Cognitive Penetration of pain experience. As noted above, Radical Cognitive Penetration is of interest in the case of perception partly for the threat that it may pose for experience as a source of justification. As MacPherson puts it, "the notion of cognitive penetration… is intended to pick out a certain problematic form of interaction between cognitive states and perception—problematic because the form of interaction undermines the role of perception as a theory or cognition neutral independent source of evidence for belief" (Macpherson, 2017). We can illustrate this point with an example much like that of the tennis match earlier on. Thus imagine Jack is looking at a steep hill. He is unsure of his physical ability to climb the hill, and as such (let us suppose) sees it as steeper. In this case, it seems reasonable to say that his perceptual experiences are problematically influenced by his cognitive states, and they provide a less reliable source of information about the objective features of the world they represent.

We can now ask whether, on the assumption that Radical Cognitive Penetration occurs in

pain experience, it raises similar epistemological issues. We believe that such cases are quite different, for several reasons. First, unlike perceptual experience, it is unclear whether we can even make sense of the notion of biasing or misrepresentation in the case of pain experience. As noted above, whereas perceptual experience functions to make us aware of interpersonally available features of the world, pain experience arguably serves primarily to motivate (or deter) certain kinds of action. Likewise, whereas it is relatively easy to assess whether someone is making a perceptual error, it is not clear how we could measure or even make sense of the idea that someone was making a mistake about their pain.

As a result, one might claim that illusions or errors in pain reporting are by definition impossible: someone who claims to be in pain is *de facto* in pain, and a person who sincerely claims their pain has diminished (perhaps as a result of placebo analgesia) should thereby be understood to be in less pain than they were previously.

Hence contrast the case of Jack just mentioned with that of Jill, who has a bad headache. She takes what she believes to be a powerful pain medicine, but which is in fact a sugar pill. She consequently sincerely reports feeling less pain. In this case, it hard to identify an epistemological problem analogous to that of Jack: if Jill's experience genuinely involves less pain, then no misrepresentation has occurred. If this line of thought is correct, then one of the central features that makes cognitive penetration epistemologically problematic in the case of perception simply does not apply to cognitive penetration of pain.

One might disagree with this particular understanding of pain experience, however. As noted in 4.3, above, we can at least in principle distinguish the sensory aspects of pain from our appraisal of pain. Granting this distinction, one might then suggest that our *appraisal* of pain might be at odds with the relevant pain sensation, leading us to over- or under-estimate the severity of a given pain on a particular occasion. A possible example of this comes from the phenomenon of 'dental fear'. As Rosenthal puts it, "[a] more dramatic case of mistaken introspective self-interpretation of qualitative states sometimes occurs in dental treatment. Patients occasionally seem, from a first-person point of view, to feel pain, although the relevant nerves are dead, missing, or anesthetized" (Rosenthal, 2005).

We do not rule out the possibility of such mismatches between pain appraisal and pain sensation. However, if there is indeed Radical Cognitive Penetration of pain experience in the

case of placebo analgesia, we suggest it *need not* involve this specific kind of error. Rather than misappraising their pain sensations, the cases of placebo analgesia that fulfill the criteria of Radical Cognitive Penetration, we have argued, are likely involve the modulation of low-level nociceptive processing through expectations, rather than shifts in appraisal. If this is right, then when participants in placebo analgesia conditions claim that their pain sensations have become less intense, it will follow that their judgments are quite correct. Consequently, we might consider placebo-induced pain relief to be every bit as real and medically warranted as pharmaceutical analgesia, relying, at least some cases, on very similar underlying mechanisms.

This in turn prompts difficult ethical challenges and opportunities, somewhat beyond the scope of this paper, but worth briefly noting. In particular, we recognize that physicians have both moral and legal obligations to alleviate avoidable pain and suffering on the part of their patients (Rich, 2001). To the extent that their ability to do this is enhanced by ethically leveraging the power of patients' expectations and beliefs to influence nociceptive processing, we might conclude that clinical obligations should extend to maximizing the positive power of cognitive penetration to diminish pain experience.

The idea that physicians might have some obligation to maximize the power of expectations in clinical analgesia prompts other worries of an epistemological and ethical character. As noted above, if someone is led to feel more or less pain as a result of having a belief, then this does not seem to directly involve problematic epistemological consequences: regardless of how it arises, to the extent that a subject's beliefs about their pains are genuinely reflected in their pain experience, they will be fully warranted. However, there may be cases in which the cognitive penetration of pain experience might *indirectly* lead to problematic epistemological and even ethical consequences, namely in cases where the pain experience is used to make mistaken inferences about some further state of affairs. Thus, imagine that Humpty-Dumpty suffers from severe migraines. His friend Jack advises him to try a new expensive, herbal supplement to alleviate the migraines. While Humpty-Dumpty has not heard of this supplement before, he trusts Jack enough to try his suggestion. He finds that shortly after taking it, his pain diminishes, and hence concludes that this supplement is effective for treating his pain.

Is Humpty-Dumpty's conclusion warranted? In a sense, yes: it is based on an accurate

observation that his pain experience diminished after taking the relevant supplement. However, if pain experience is indeed subject to cognitive penetration in the sense explored above, then this is not by itself evidence that the supplement is effective in any respect beyond placebo, hence making his conclusion potentially misleading.

Of course, cases like Humpty-Dumpty's are commonplace: many people use supplements, alternative medicines, and even clinically tested drugs for pain relief that may have little pharmacological effect on their symptoms aside from placebo analgesia. Insofar as their belief is simply that these treatments alleviate their pain, they may be fully warranted. However, there may be more serious epistemic upshots. For example, if a given pain treatment is deemed to be ineffective by the medical community, but a person finds it helpful in their own case, it may lead them to lose confidence in the broader advice of the medical community, or scientific methods more generally. This in turn might lead them to inappropriately reject or accept other treatments for conditions in which they are unlikely to benefit from a placebo effect (such as those involving viral or bacterial pathogens).

This is quite a different sort of worry from that raised by cognitive penetration of perception, but is nonetheless of potentially grave significance. However, it is again an ethically complex issue to address. If a doctor were to go out of her way to convince a patient that their preferred treatment was likely to be pharmacologically ineffective, it might deprive the patient of the pain relief provided by placebo analgesia, thereby raising worries about the ethical duties of clinicians to minimize pain as discussed above. On the other hand, if the clinician were instead to encourage the use of a medication that had no scientifically respectable mode of action, then she risks tacitly entrenching her patient's unscientific and potentially harmful beliefs.[10]

One compromise that has been suggested in the relevant clinical literature is so called 'open label' placebos, that is, the administration of placebos with the full awareness and consent of the patient. Strikingly, there is evidence that such open label placebos are effective for the relief of symptoms such as pain and fatigue (Carvalho et al., 2016) as well as for symptoms of irritable bowel syndrome (Kaptchuk et al., 2010). This perhaps offers a way that medical

[10] It is worth noting, however, that these issues become much more ethically charged when patients hold false beliefs or refuse effective treatments for life-threatening conditions such as cancer, while in the realm of pain relief, it is often worth harnessing the potent effects of placebo analgesia wherever they can be found.

professionals could obtain the clinical effects of placebo analgesia while minimizing the risk of misleading patients or entrenching misinformed beliefs.

(6) Conclusion

The primary target of this paper has been to argue for a specific empirical claim about the mind, namely that Radical Cognitive Penetration occurs in the case of pain, and explore some possible lessons that might be drawn from this for the broader cognitive penetration debate. In this latter regard, we have suggested that there are a variety of reasons why pain experience might be subject to radical cognitive penetration even if perceptual experience is not. If this turns out to be the case, it might in turn contribute to our understanding of the fundamental architectural divisions in the mind, such as those whose primary function is to represent the world and those directed at maintaining and protecting the body. Additionally, we have suggested that the epistemological considerations that make cognitive penetration of central importance in the case of perceptual experience do not straightforwardly apply to cognitive penetration of pain. Instead, cognitive penetration of pain experience presents distinctive epistemological, ethical, and clinical issues in its own right.

References

Ader, R. 2003. Conditioned immunomodulation: research needs and directions. *Brain, Behavior, and Immunity* 17 (1): 51–57. https://doi.org/doi:http://dx.doi.org/10.1016/S0889-1591(02)00067-3.

Amanzio, M., & Benedetti, F. 1999. Neuropharmacological dissection of placebo analgesia: expectation-activated opioid systems versus conditioning-activated specific subsystems. *Journal of Neuroscience* 19 (1): 484–494.

Amanzio, M., Pollo, A., Maggi, G., & Benedetti, F. 2001. Response variability to analgesics: a role for non-specific activation of endogenous opioids. *Pain* 90 (3): 205–215.

Anchisi, D., & Zanon, M. 2015. A Bayesian perspective on sensory and cognitive integration in pain perception and placebo analgesia. *PloS One* 10 (2): 0117270. https://doi.org/doi:10.1371/journal.pone.0117270.

Bausell, R.B., Lao, L., Bergman, S., Lee, W.L., & Berman, B.M. 2005. Is acupuncture analgesia an expectancy effect? Preliminary evidence based on participants' perceived assignments in two placebo-controlled trials. *Evaluation and the Health Professions* 28 (1): 9–26. https://doi.org/doi:10.1177/0163278704273081.

Benedetti, F. 1997. Cholecystokinin type A and type B receptors and their modulation of opioid analgesia. *Physiology* 12 (6): 263–268.

———. 2009. *Placebo effects: understanding the mechanisms in health and disease. Oxford;* New York, NY: Oxford University Press.

Benedetti, F., Amanzio, M., Vighetti, S., & Asteggiano, G. 2006. The biochemical and neuroendocrine bases of the hyperalgesic nocebo effect. *Journal of Neuroscience* 26 (46): 12014–12022. https://doi.org/doi:10.1523/jneurosci.2947-06.2006.

Benedetti, F., Arduino, C., Costa, S., Vighetti, S., Tarenzi, L., Rainero, I., & Asteggiano, G. 2006. Loss of expectation-related mechanisms in alzheimer's disease makes analgesic therapies less effective. *Pain* 121 (1–2): 133–144. https://doi.org/doi:10.1016/j.pain.2005.12.016.

Benedetti, F., Lanotte, M., Lopiano, L., & Colloca, L. 2007. When words are painful: unraveling the mechanisms of the nocebo effect. *Neuroscience* 147 (2): 260–271. https://doi.org/doi:http://dx.doi.org/10.1016/j.neuroscience.2007.02.020.

Benedetti, F., Maggi, G., Lopiano, L., Lanotte, M., Rainero, I., Vighetti, S., & Pollo, A. 2003. Open versus hidden medical treatments: the patient's knowledge about a therapy affects the therapy outcome. *Prevention & Treatment* 6 (1): 1.

Bingel, U., Wanigasekera, V., Wiech, K., Mhuircheartaigh, R.N., Lee, M.C., Ploner, M., & Tracey, I. 2011. The effect of treatment expectation on drug efficacy: imaging the analgesic benefit of the opioid remifentanil. *Science Translational Medicine* 3 (70): 70–14.

Brogaard, B., & Chomanski, B. 2015. Cognitive penetrability and high-level properties in perception: unrelated phenomena? *Pacific Philosophical Quarterly* 96 (4): 469–86. https://doi.org/10.1111/papq.12111.

Bruner, J.S. 1957. On perceptual readiness. *Psychological Review* 64 (2).

Brunstrom, J.M., Burn, J.F., Sell, N.R., Collingwood, J.M., Rogers, P.J., Wilkinson, L.L., Hinton, E.C., Maynard, O.M., & Ferriday, D. 2012. Episodic memory and appetite regulation in humans. *PLoS ONE* 7 (12). https://doi.org/10.1371/journal.pone.0050707.

Buchel, C., Geuter, S., Sprenger, C., & Eippert, F. 2014. Placebo analgesia: a predictive coding perspective. *Neuron* 81 (6): 1223–1239. https://doi.org/doi:10.1016/j.neuron.2014.02.042.

Burge, T. 2010. *Origins of objectivity*. Oxford: Oxford University Press.

Carrasco, M., Williams, P.E., & Yeshurun, Y. 2002. Covert attention increases spatial resolution with or without masks: support for signal enhancement. *Journal of Vision* 2 (6): 4–4.

Carvalho, C., Caetano, J.M., Cunha, L., Rebouta, P., Kaptchuk, T.J., & Kirsch, I. 2016. Open-label placebo treatment in chronic low back pain: a randomized controlled trial. *Pain* 157 (12): 2766–2772. https://doi.org/doi:10.1097/j.pain.0000000000000700.

Clark, A. 2016. *Surfing uncertainty: prediction, action, and the embodied mind*. New York, NY: Oxford University Press.

Colloca, L., & Benedetti, F. 2009. Placebo analgesia induced by social observational learning. *Pain* 144 (1–2): 28–34. https://doi.org/doi:10.1016/j.pain.2009.01.033.

Colloca, L., Lopiano, L., Lanotte, M., & Benedetti, F. 2004. Overt versus covert treatment for pain, anxiety, and Parkinson's disease. *Lancet Neurology* 3 (11): 679–684. https://doi.org/doi:10.1016/s1474-4422(04)00908-1.

Colloca, L., & Miller, F.G.. 2011. Role of expectations in health. *Current Opinion in Psychiatry* 24 (2): 149–155. https://doi.org/doi:10.1097/YCO.0b013e328343803b.

Craen, A.J. de, Roos, P.J., de Vries, A.L., & Kleijnen, J. 1996. Effect of colour of drugs: systematic review of perceived effect of drugs and of their effectiveness. *BMJ* 313 (7072): 1624–1626.

Craen, A.J. de, Tijssen, J.G., de Gans, J., & Kleijnen, J. 2000. Placebo effect in the acute treatment of migraine: subcutaneous placebos are better than oral placebos. *Journal of Neurology* 247 (3): 183–188.

Deroy, O. 2013. Object-sensitivity versus cognitive penetrability of perception. *Philosophical Studies* 162 (1): 87–107.

Eccleston, C. 2018. Chronic pain as embodied defence: implications for current and future psychological treatments. *Pain* 159 (September): S17. https://doi.org/10.1097/j.pain.0000000000001286.

Egan, A. 2008. Seeing and believing: perception, belief formation and the divided mind. *Philosophical Studies* 140 (1): 63.

Eippert, F., Finsterbusch, J., Bingel, U., & Büchel, C. 2009. Direct evidence for spinal cord involvement in placebo analgesia. *Science* 326 (5951): 404–404. https://doi.org/doi:10.1126/science.1180142.

Feinberg, T.E., & Mallatt, J.M. 2016. *The ancient origins of consciousness: how the brain created experience*. Cambridge, MA: MIT Press.

Fields, H. 2004. State-dependent opioid control of pain. *Nature Reviews: Neuroscience* 5 (7): 565–575. https://doi.org/doi:10.1038/nrn1431.

Firestone, C. 2013. On the origin and status of the 'El Greco fallacy.' *Perception* 42 (6): 672–674.

Fodor, J. 1983. *Modularity of Mind*. Cambridge, MA: MIT Press.

Fuller, S., Ling, S., & Carrasco, M. 2004. Attention increases perceived saturation. *Journal of Vision* 4 (8): 329–329.

Gligorov, N. 2017. Don't worry, this will only hurt a bit: the role of expectation and attention in pain intensity. *The Monist* 100 (4): 501–513.

Godfrey-Smith, P. 2017. The evolution of consciousness in phylogenetic context. In K. Andrews & J. Beck (Eds.), *The Routledge Handbook of Philosophy of Animal Minds.* New York: Routledge. https://doi.org/10.4324/9781315742250-21.

Goffaux, P., Redmond, W.J., Rainville, P., & Marchand, S. 2007. Descending analgesia–when the spine echoes what the brain expects. *Pain* 130 (1–2): 137–143. https://doi.org/doi:10.1016/j.pain.2006.11.011.

Goldstone, R.L. 1995. Effects of categorization on color perception. *Psychological Science* 6 (5): 298–304.

Gollub, R.L., & Kong, J. 2011. For placebo effects in medicine, seeing is believing. *Science Translational Medicine* 3 (70): 70–75. https://doi.org/doi:10.1126/scitranslmed.3002120.

Hansen, T., Olkkonen, M., Walter, S., & Gegenfurtner, K.R. 2006. Memory modulates color appearance. *Nature Neuroscience* 9 (11).

Haygarth J. (1800). *Of the imagination, as a cause and as a cure of disorders of the body: exemplified by fictitious tractors, and epidemical convulsions*. Bath: R. Crutwell.

Hebb, A.L.O., Poulin, J.F., Roach, S.P., Zacharko, R.M., & Drolet, G. 2005. Cholecystokinin and endogenous opioid peptides: interactive influence on pain, cognition, and emotion. In *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 29:1225–1238. 8. https://doi.org/10.1016/j.pnpbp.2005.08.008.

Howe, L.C., Goyer, J.P., & Crum, A.J. 2017. Harnessing the placebo effect: exploring the influence of physician characteristics on placebo response. *Health Psychology*. https://doi.org/doi:10.1037/hea0000499.

Howick, J., Bishop, F.L., Heneghan, C., Wolstenholme, J., Stevens, S., Hobbs, F.D., & Lewith, G. 2013. Placebo use in the united kingdom: results from a national survey of primary care practitioners. *PloS One* 8 (3): 58247. https://doi.org/doi:10.1371/journal.pone.0058247.

Jensen, K.B., Kaptchuk, T.J., Kirsch, I., Raicek, J., Lindstrom, K.M., Berna, C., Gollub, R.L., Ingvar, M., & Kong, J. 2012. Nonconscious activation of placebo and nocebo pain responses. *Proceedings of the National Academy of Sciences of the United States of America* 109 (39): 15959–64. https://doi.org/10.1073/pnas.1202056109.

Jones, A., Brown, C., & El-Deredy, W. 2013. *How does EEG contribute to our understanding of the placebo response?: insights from the perspective of Bayesian inference*. In L. Colloca, M.A. Flaten, & K. Meissner (Eds.), *Placebo and pain: from bench to bedside*. San Diego, USA: Academic Press.

Kalauokalani, D., Cherkin, D.C., Sherman, K.J., Koepsell, T.D., & Deyo, R.A. 2001. Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. *Spine* 26 (13): 1418–1424.

Kaptchuk, T.J., Friedlander, E., Kelley, J.M., Sanchez, M.N., Kokkotou, E., Singer, J.P., Kowalczykowski, M., Miller, F.G., Kirsch, I., & Lembo, A.J. 2010. Placebos without deception: a randomized controlled trial in irritable bowel syndrome. *PLOS ONE* 5 (12): e15591. https://doi.org/10.1371/journal.pone.0015591.

Karama, S., Lecours, A.R., Leroux, J.M., Bourgouin, P., Beaudoin, G., Joubert, S., & Beauregard, M. 2002. Areas of brain activation in males and females during viewing of erotic film excerpts. *Human Brain Mapping* 16 (1): 1–13.

Kirsch, I., Deacon, B.J., Huedo-Medina, T.B., Scoboria, A., Moore, T.J., & Johnson, B.T. 2008. Initial severity and antidepressant benefits: a meta-analysis of data submitted to the food and drug administration. *PLoS Medicine* 5 (2): 45. https://doi.org/doi:10.1371/journal.pmed.0050045.

Klein, C. 2015. *What the Body Commands*. Cambridge, Mass: MIT.

Krummenacher, P., Candia, V., Folkers, G., Schedlowski, M., & Schonbachler, G. 2010. Prefrontal cortex modulates placebo analgesia. *Pain* 148 (3): 368–374. https://doi.org/doi:10.1016/j.pain.2009.09.033.

Levin, D.T., & Banaji, M.R. 2006. Distortions in the perceived lightness of faces: the role of race categories. *Journal of Experimental Psychology: General* 135 (4): 501.

Levine, J.D., & Gordon, N.C. 1984. Influence of the method of drug administration on analgesic response. *Nature* 312 (5996): 755–756.

Levine, J.D., Gordon, N.C., Smith, R., & Fields, H.L. 1981. Analgesic responses to morphine and placebo in individuals with postoperative pain. *Pain* 10 (3): 379–389.

Linde, K., Witt, C.M., Streng, A., Weidenhammer, W., Wagenpfeil, S., Brinkhaus, B., Willich, S.N., & Melchart, D. 2007. The impact of patient expectations on outcomes in four

randomized controlled trials of acupuncture in patients with chronic pain. *Pain* 128 (3): 264–71. https://doi.org/10.1016/j.pain.2006.12.006.

Lorenz, J., Hauck, M., Paur, R.C., Nakamura,Y., Zimmermann, R., Bromm, B., & Engel, A.K. 2005. Cortical correlates of false expectations during pain intensity judgments–a possible manifestation of placebo/nocebo cognitions. *Brain, Behavior, and Immunity* 19 (4): 283–295. https://doi.org/doi:10.1016/j.bbi.2005.03.010.

Lycan, W.G. 1996. *Consciousness and experience*. Mit Press.

Macpherson, F. 2012. Cognitive penetration of colour experience: rethinking the issue in light of an indirect mechanism. *Philosophy and Phenomenological Research* 84 (1): 24–62.

———. 2015. *Cognitive penetration and nonconceptual content*.

———. 2017. The relationship between cognitive penetration and predictive coding. *Consciousness and Cognition* 47: 6–16.

Mahon, B., and Wu, W. 2015. *Cognitive penetration of the dorsal visual stream.* In J. Zeimbekis & A. Raftopoulos (Eds.). *The cognitive penetrability of perception: new philosophical perspectives*. Oxford: Oxford University Press.

Martínez, M. 2011. Imperative content and the painfulness of pain. *Phenomenology and the Cognitive Sciences* 10 (1): 67–90.

———. 2015. Pains as reasons. *Philosophical Studies* 172 (9): 2261–2274.

Matre, D., Casey, K.L., and Knardahl, S. 2006. Placebo-induced changes in spinal cord pain processing. *The Journal of Neuroscience* 26 (2): 559–563. https://doi.org/doi:10.1523/jneurosci.4218-05.2006.

Moerman, D.E. 2017. Philosophy and 'placebo' analgesia. In J. Corns (Ed.). *The Routledge handbook of philosophy of pain*, 378–87. New York, NY: Routledge/Taylor & Francis Group.

Mole, C. 2015. Attention and cognitive penetration. In J. Zeimbekis & A. Raftopoulos (Eds.). *The cognitive penetrability of perception: new philosophical perspectives*. Oxford: Oxford University Press.

Montgomery, G.H., & Kirsch, I. 1997. Classical conditioning and the placebo effect. *Pain* 72 (1–2): 107–113.

Olness, K., & Ader, R. 1992. Conditioning as an adjunct in the pharmacotherapy of lupus erythematosus. *Journal of Developmental and Behavioral Pediatrics* 13 (2): 124–125.

Pacheco-Lopez, G., Engler, H., Niemi, M.B., & Schedlowski, M. 2006. Expectations and associations that heal: immunomodulatory placebo effects and its neurobiology. *Brain, Behavior, and Immunity* 20 (5): 430–446. https://doi.org/doi:10.1016/j.bbi.2006.05.003.

Perky, C.W. 1910. An experimental study of imagination. *American Journal of Psychology(21),* 422–52.

Price, D.D., & Barrell, J.J. 2000. Mechanisms of analgesia produced by hypnosis and placebo suggestions. *Progress in Brain Research*, 122:255–271.

Proffitt, D.R., Stefanucci, J., Banton, T., & Epstein, W. 2003. The role of effort in perceiving distance. *Psychological Science* 14 (2): 106–112.

Pylyshyn, Z. 1999. Is vision continuous with cognition?: the case for cognitive impenetrability of visual perception. *Behavioral and Brain Sciences* 22 (3): 341–365.

Rich, B.A. 2001. Physicians' legal duty to relieve suffering. *Western Journal of Medicine* 175 (3): 151–52.

Rose, J.P., Geers, A.L., Rasinski, H.M., & Fowler, S.L. 2012. Choice and placebo expectation effects in the context of pain analgesia. *Journal of Behavioral Medicine* 35 (4): 462–470. https://doi.org/doi:10.1007/s10865-011-9374-0.

Rosenthal, D.M. 2005. *Consciousness and mind*. Oxford: Clarendon Press.

Rozin, P., Dow, S., Moscovitch, M., & Rajaram, S. 1998. What causes humans to begin and end a meal? A role for memory for what has been eaten, as evidenced by a study of multiple meal eating in amnesic patients. *Psychological Science* 9 (5): 392–96. https://doi.org/10.1111/1467-9280.00073.

Schedlowski, M. 2006. Insecta immune–cognitive interactions. *Brain, Behavior, and Immunity* 20 (2): 133–134.

Schedlowski, M., & Pacheco-López, G. 2010. The learned immune response: pavlov and beyond. *Brain, Behavior, and Immunity* 24 (2): 176–185. https://doi.org/doi:http://dx.doi.org/10.1016/j.bbi.2009.08.007.

Scott, D.J., Stohler, C.S., Egnatuk, C.M., Wang, H., Koeppe, R.A., & Zubieta, J.K. 2007. Individual differences in reward responding explain placebo-induced expectations and

effects. *Neuron* 55 (2): 325–336. https://doi.org/doi:http://dx.doi.org/10.1016/j.neuron.2007.06.028.

———. 2008. Placebo and nocebo effects are defined by opposite opioid and dopaminergic responses. *Archives of General Psychiatry* 65 (2): 220–231. https://doi.org/doi:10.1001/archgenpsychiatry.2007.34.

Searle, J.R. 1983. *Intentionality: an essay in the philosophy of mind*. Cambridge University Press.

Tye, M. 1997. *Ten problems of consciousness: a representational theory of the phenomenal mind*. Cambridge MA: MIT Press.

———. 2005. Another look at representationalism about pain. In M. Aydede (Ed.). *Pain: new essays on its nature and the methodology of its study*. Cambridge MA: MIT Press

Varelmann, D., Pancaro, C., Cappiello, E.C., & Camann, W.R. 2010. Nocebo-induced hyperalgesia during local anesthetic injection. *Anesthesia and Analgesia* 110 (3): 868–870. https://doi.org/doi:10.1213/ANE.0b013e3181cc5727.

Waber, R.L., Shiv, B., Carmon, Z., & Ariely, D. 2008. Commercial features of placebo and therapeutic efficacy. *JAMA* 299 (9): 1016–1017. https://doi.org/doi:10.1001/jama.299.9.1016.

Wager, T.D., Atlas, L.Y., Leotti, L.A., & Rilling, J.K. 2011. Predicting individual differences in placebo analgesia: contributions of brain activity during anticipation and pain experience. *Journal of Neuroscience* 31 (2): 439–452. https://doi.org/doi:10.1523/jneurosci.3420-10.2011.

Wager, T.D., Matre, D., & Casey, K.L. 2006. Placebo effects in laser-evoked pain potentials. *Brain, Behavior, and Immunity* 20 (3): 219–230. https://doi.org/doi:10.1016/j.bbi.2006.01.007.

Wager, T.D., Rilling, J.K., Smith, E.E., Sokolik, A., Casey, K.L., Davidson, R.J., Kosslyn, S.M., Rose, R.M., & Cohen, J.D. 2004. Placebo-induced changes in fmri in the anticipation and experience of pain. *Science* 303 (5661): 1162–67. https://doi.org/10.1126/science.1093065.

Wiech, K. 2016. Deconstructing the sensation of pain: the influence of cognitive processes on pain perception. *Science* 354 (6312): 584–587. https://doi.org/doi:10.1126/science.aaf8934.

Wiech, K., Vandekerckhove, J., Zaman, J., Tuerlinckx, F., Vlaeyen, J.W., & Tracey, I. 2014. Influence of prior information on pain involves biased perceptual decision-making. *Current Biology* 24 (15): 679–681. https://doi.org/doi:10.1016/j.cub.2014.06.022.

Witt, J.K., Proffitt, D.R., & Epstein, W. 2004. Perceiving distance: a role of effort and intent. *Perception* 33 (5): 577–590.