**Telling the Truth about Pain:**

**Informed Consent and the Role of Expectation in Pain Intensity[[1]](#footnote-1)**

Nada Gligorov

Abstract

Healthcare providers are expected to both relieve pain and to provide anticipatory guidance regarding how much a procedure is going to hurt. Fulfilling those expectations is complicated by the cognitive modulation of pain perception. Warning people to expect pain or setting expectations for pain relief not only influences their subjective experience, but it also alters how nociceptive stimuli are processed throughout the sensory and discriminative pathways in the brain. In light of this, I reconsider the characterization of placebo analgesia as pharmacologically inert and the use of it as deceptive. I show that placebo analgesia exploits the same physical mechanisms as proven analgesics and argue that it should be utilized to relieve pain. Additionally, I describe factors to help identify situations in which clinicians have the obligation to disclose the potential for pain coupled with ways of mitigating the risk of high-intensity pain by setting positive expectations.

1. Introduction

Healthcare professionals have the obligation of truth-telling, which includes the requirement to inform patients of the relevant risks and benefits for any proposed medical intervention or treatment (Beauchamp & Childress, 2009). The importance of truth-telling is usually buttressed by respect for autonomy, another fundamental principle of medical ethics (Beauchamp & Childress, 2009). In addition to truth-telling, healthcare professionals are also obligated to minimize harm and maximize benefits (Beauchamp & Childress, 2009). These obligations come to a head in the context of placebo and nocebo effects where communicating about the potential benefits or risks can influence the efficacy of treatment or the likelihood of side effects. The proposed solutions to the conflict between these obligations usually rely on the balancing of truth-telling, as a way of respecting autonomy, with beneficence or minimizing harm (Alfano, 2015; Annoni & Miller, 2016; Bostick, Sade, Levine, & Stewart, 2008; Cohen, 2014; Foddy, 2009; Fortunato, Wasserman, & Menkes, 2017; Wells & Kaptchuk, 2012). The tug of war between the principles rests on the view that placebos are physiologically inert, have no objective medical explanation, and that clinicians utilizing placebos are deceiving a patient when they aim to establish positive treatment expectations (Bostick et al., 2008). Similarly, nocebo effects are described as most prevalent for vague and nonspecific phenomena such as dizziness, palpitations, or pain, and are contrasted with physiologically or biologically based effects of treatment (Wells & Kaptchuk, 2012).

In this paper, I focus on the effects of attention, expectation and learning on pain perception. I challenge the view of that the changes in pain intensity that result from setting either positive or negative treatment expectations are unrelated to physiologic or biologic processes. To support my view, I show that attention, expectation, learning, and reappraisal of noxious stimuli affect how nociceptive stimuli are processed throughout the sensory and discriminative pathways in the brain. For example, expectation of high-intensity pain will increase the likelihood that a low intensity noxious stimulus will be perceived as being of high intensity (Wiech et al., 2014). Similarly, cognitive processes result in analgesia by inhibiting early pain processing in the spinal cord (Eippert, Finsterbusch, Bingel, & Buchel, 2009) and in later stages by inhibiting processing in the somatosensory cortices (Petrovic, Petersson, Ghatan, Stone-Elander, & Ingvar, 2000). The cognitive modulation of pain is thought to both underlie placebo analgesia and to contribute to the effectiveness of proven analgesics (Bingel et al., 2011).

In light of this evidence, I assess aspects of the definition of pain proposed by the International Association for the Study of Pain (IASP), including their characterization of pain as subjective and their claim that the concept of pain is learned in childhood. I do this to argue that conceptions of pain ought to accommodate the evidence for the cognitive penetration of pain. In particular, I emphasize that pain should be characterized as a psychological phenomenon causally related to physical or biological changes. I also show how the concept of pain and an individual’s ability to experience pain relief is acquired through learning and through communication with clinicians. Keeping in mind that cognitive penetration of pain leads to changes in processing throughout the pain system, I argue that the use of placebo analgesia does not require deception and it does not give rise to a conflict between the commitments to truth telling and beneficence. In addition, I argue that facts about how much a procedure might hurt are not independent of the disclosure for the potential for pain and that minimizing expectations of pain is not deceptive and does not introduce the dilemma between truth telling and minimizing harm even when it comes to nocebo.

2. The cognitive modulation of pain

The currently dominant scientific theory of pain is the gate control theory, which characterizes pain as a three-aspect phenomenon that requires the activation of the pain matrix in the brain (Moayedi & Davis, 2013).[[2]](#footnote-2) The three elements of pain include: the sensory and discriminative dimension of pain, which is the intensity, location, quality, and duration of pain; the affective and motivational elements of pain, which include unpleasantness and the flight response to noxious stimuli; and the cognitive and evaluative aspects of pain, which can mediate the experience of pain based on cultural values, the context in which the stimulus is experienced, and a person’s state of mind. Based on gate control theory, pain should not be identified with just one of its three elements, such as unpleasantness or intensity; instead pain requires the activation of the entire pain system and the contribution of all its three elements. This multidimensional description of pain is widely accepted in the scientific literature about pain and is the basis of the definition of pain adopted by International Association for the Study of Pain (IASP) (International Association for the Study of Pain, 2017).

The gate control theory of pain postulates a gate control mechanism in the spinal cord (R. Melzack & Wall, 1965). This gate control system modulates the input transmitted from nociceptors to the transmission cells (T cells) located in the dorsal horn of the spinal cord. When the output from the dorsal horn T cells is achieved, it is transmitted towards two distinct brain systems: “a) via neospinothalamic fibers into the ventrobasal and posterolateral thalamus and somatosensory cortex; and b) via medially coursing fibers, that comprise a paramedial ascending system, into the reticular formation and medial intralaminar thalamus and the limbic system” (Ronald Melzack & Casey, 1968, p. 427). These two distinct but interacting brain pathways realize the three distinct elements of pain and form the pain matrix in the brain. The pathway that projects into the thalamus and the somatosensory cortex underlies the sensory and discriminative aspects of pain, while the activation of the reticular formation and the limbic system contributes to the unpleasantness of pain and motivates avoidance of noxious stimuli. The cognitive and evaluative element of pain is localized in the neocortical areas of the brain. Based on gate control theory, the cognitive aspects of pain can have an inhibitory effect and can change the output from the dorsal horn, preventing the projection of the pain signal into the brain. Cognitive processes can affect both the sensory and discriminative aspects of pain as well as its affective and motivational aspects.

The three-aspect theory of pain groups together attention, expectation, and learning as potential cognitive modulators of the felt experience of pain. I will begin by describing the evidence that attention changes the felt intensity of pain. A number of functional brain imaging studies demonstrate that distraction away from noxious stimuli can reduce activation in the pain system in the brain areas that subserve the sensory, affective, and cognitive features of pain (Wiech, Ploner, & Tracey, 2008, p. 307). In a study by Tracey et al. 2002, participants received the same intensity stimulus, but the intensity ratings of the stimulus were lower for the participants who were distracted (Tracey et al., 2002). Brain imaging confirmed that the distracted participants had increased inhibitory activity in the midbrain and this inhibitory activity correlated with reports of lower intensity of pain. As distraction can diminish pain intensity, attending to pain can increase the intensity of pain--chronic pain syndromes, for example, might be the result of hypervigilance for pain (Eccleston, Crombez, Aldrich, & Stannard, 1997).

Expectation has also been shown to change pain perception. For example, the application of a low intensity noxious stimulus coupled with a warning to expect a high intensity stimulus produces the experience of high-intensity pain. Similarly, an expectation of a low intensity stimulus paired with the application of a high intensity stimulus results in a less painful experience (Wiech et al., 2008; Wiech et al., 2014). That expectation can modulate the intensity of pain is thought to be at the root of both placebo and nocebo effects.[[3]](#footnote-3) An individual who has taken an analgesic and has experienced pain relief will form an association between taking a pill of a certain type and pain relief, and this association will produce the pain relief, even when an individual is treated with a substance that does not contain any known analgesics. That expectation of pain relief, based on established associations, is the basis of placebo effects is supported by studies that indicate diminished placebo effects in individuals who have been unsuccessfully treated with analgesics in the past (Kessner, Wiech, Forkmann, Ploner, & Bingel, 2013).

Expectation can also contribute the effectiveness of proven analgesics. Bingel et al. (2011) demonstrated that patient expectations could influence the effectiveness of the pain reliever remifentanil (Bingel et al., 2011). Positive treatment expectations, i.e., anticipation of pain relief, doubled the analgesic effects of the drug, while negative treatment expectations, i.e., expectation of exacerbation of pain, diminished analgesic effects. Bingel et al. (2011) use functional magnetic resonance imaging (fMRI) to show the nociceptive stimulation resulted in the activation of the pain system. Imaging data was also used to corroborate the reports of pain intensity and to show the effects of analgesia in the brain. Furthermore, Kessner et al. (2013) demonstrated that prior experience with analgesia can impact the effectiveness of their current treatment, indicating both the impact of learning and the corollary expectations on pain perception (Kessner et al., 2013).

 Another way in which pain can be cognitively modulated is through the reappraisal, or reinterpretation, of a noxious stimulus. Impressions about whether a noxious stimulus is threatening can affect the intensity of pain, and an individual’s assessment of their abilities to cope with the threatening stimulus can effect pain perception. For example, pain intensity can be affected by the degree of control experienced by the individual. In situations where individuals think that they have greater control, pain is experienced as less intense even if the nociceptive input remains the same (Wiech et al., 2008). In addition, noxious stimuli perceived to be more life threatening, for example, are ranked as more unpleasant (Arntz & Claassens, 2004). Thus, reappraising a stimulus as less threatening diminishes the unpleasantness of pain. The valence of the cognitive appraisal of the pain affects both coping strategies and the intensity of pain for individuals suffering from chronic pain (Ramirez-Maestre, Esteve, & Lopez, 2008). Individuals with chronic pain who negatively appraise their pain tend to experience pain as more intense and they tend to have more difficulty coping with their pain. There is also indication that ability to cope through reappraisal depends on personality traits such as neuroticism or extrovertism, with extroverts being more likely to positively reappraise pain (Harkins, Price, & Braith, 1989).

A proposed mechanism for the cognitive modulation of pain is the descending pain modulatory system. The brain regions involved in this modulatory system include the frontal lobe, anterior cingulate cortex, insula, amygdala, hypothalamus, periaqueductal gray (PAG), nucleus cuneiformis (NCF), and rostral ventromedial medulla (Tracey & Mantyh, 2007, p. 380). Recent studies confirmed the involvement of the midbrain in the modulation of pain intensity caused by changes in attention. Tracey et al. (2002) showed that changes in pain rating intensity correlated with changes in activity in the PAG, an area in the midbrain. Additionally, the PAG has been shown to inhibit the processing of nociceptive stimuli in the dorsal horn of the spinal cord (Eippert et al., 2009). The descending pathway of pain modulation is thought to underlie both placebo and opioid analgesia.

That placebo analgesia recruits the descending pain modulatory system is supported by a study by Eippert et al. (2009), who documented the impact of expectation on processing of nociceptive stimuli in the dorsal horn (Eippert et al., 2009). Eippert et al. (2009) utilize fMRI to show that the application of a painful stimulation could be relieved through the administration of a placebo. Moreover, they demonstrated that administration of a placebo correlated with a decrease in response in the dorsal horn (Eippert et al., 2009). In effect, the expectation of pain relief resulted in the dampening of nociceptive processing in the spinal cord. The administration of the placebo also resulted in lowered pain ratings. Eippert et al. (2009) hypothesize that their study confirms gate control theory and that the changes in nociceptive processing are possibly due to the activation of the descending pain modulatory system (Eippert et al., 2009, p. 404).

Both attention and expectation correlate with decrease in activation in other parts of the sensory and discriminative pathway, such as the primary and secondary somatosensory cortices (SI and SII) (Wiech et al., 2008). For example, Petrovic et al. (2000) conducted a study to determine whether coupling a cognitively demanding task with nociceptive stimulation would affect the processing of the stimulus throughout the sensory and discriminative regions of the pain system (Petrovic et al., 2000). As part of their experimental design, they asked participants to complete a computerized maze test while administering a standard cold pressor test, i.e., immersion of a hand in freezing water (Petrovic et al., 2000). Utilizing positron emission tomography (PET), Petrovic et al. (2000) showed that in addition to changes in the PAG, shifting attention to the cognitive task reduced the activation in the somatosensory cortices SI and SII.

Additional brain imaging shows how neocortical processes can recruit the descending pathway of pain to promote analgesia. For example, reappraisal of pain that resulted in lower intensity of pain correlated with increased activity in the right anterior ventrolateral prefrontal cortex (VLPFC) (Wiech et al., 2008). Similarly, placebo analgesia can increase activity in the prefrontal cortex and decrease activity in parts of the pain system, including thalamus, insula, and ACC (Tracey & Mantyh, 2007, p. 382).

Taken together, these studies identify the regions of the brain that comprise the descending pain modulatory system and they confirm the neurocognitive inhibitory system posited as part of gate control theory. The evidence supports the view that attention, expectation and reappraisal can influence felt intensity of pain in a variety of different ways. Cognition can inhibit the processing of nociceptive stimuli in the spinal cord and in the midbrain, but it can also affect the processing of sensory and discriminative aspects of pain in the somatosensory cortex. This indicates that cognition can change the perceptual processing of pain all along the sensory and discriminative brain pathway.[[4]](#footnote-4)

3. Rethinking the Subjectivity of Pain

To assess the ethical implications of the evidence for the cognitive modulation of pain, I will first highlight some of the consequences that this evidence should have on the conception of pain in medical practice. I will examine what the literature on the cognitive penetration of pain can tell us about the subjectivity of pain and how individual conceptions of pain are formed through interaction with healthcare professionals.

I will begin with the characterization of pain as a subjective phenomenon and I will examine the ways in which this description is accurate. The IASP defines pain as subjective because of the dissociation between the experience of pain and the presence of a noxious stimulus. An individual can be in pain in absence of a noxious stimulus and one can fail to feel pain despite nociceptive stimulation. Thus, a person experiencing pain is the final arbiter of whether they arein pain. A similar sense of subjectivity permeates the scientific investigation of pain. For example, “an individual’s experience of pain, particularly pain of pathological origin, underscores the practical importance of appreciating a first-person experience from a third-person perspective….an individual’s subjective experience of pain can vary substantially from day-to-day despite being evoked by a temporally invariant stimulus” (Coghill, McHaffie, & Yen, 2003, p. 8538). The subjectivity of pain characterized in this manner is substantiated by the literature on the cognitive penetration of pain because it is clear that the strength of noxious stimulation does not always correspond with the felt intensity of the painful stimulus. As discussed earlier, distraction and expectation can diminish the felt intensity of pain even when the strength of the stimulus remains the same (Petrovic et al., 2000; Wiech et al.; 2008 Wiech et al., 2014). In addition, the same stimulus can be perceived of different intensity at different times by the same individual depending on the type of pain they are expecting to experience or their ability to reappraise the stimulus (Arntz & Claassens, 2004; Wiech et al., 2014).

Pain is also characterized as a psychological phenomenon. For example, the IASP definition of pain characterizes pain as primarily a psychological state, although they admit that those states likely have a proximate physical cause (International Association for the Study of Pain, 2017). In addition, when pain is characterized as being prone to placebo or nocebo effects, those effects are described as being psychological in the sense that they do not have a known biological etiology (Bostick et al., 2008; Wells & Kaptchuk, 2012). Although I do not wish to challenge the view that pain is a psychological phenomenon, I do wish to undermine the connotation that pain being psychological means that it is not a physical phenomenon as well. The dissociation between noxious stimuli and the experience of pain only disqualify noxious stimulation as the proximate cause of pain. But the localization of the pain system shows that there is correlation between the experience of pain and the activation throughout pain system, which establishes this physical process in the brain as the proximate cause of pain. This is true even when individuals are not being noxiously stimulated (Derbyshire, Whalley, Stenger, & Oakley, 2004). Additionally, the literature on the cognitive penetration of pain shows that the subjective experience of pain is the result of changes in the pain matrix; for example, the subjective experience of pain intensity is caused by the objective changes in the sensory and discriminative pathway of pain in the brain. The consequences of this on the obligations of physicians will be taken up in the next section of this paper.

I will now examine how learning and setting expectations over time contribute to the formation of the concept of pain for patients and ultimately how it affects perception of pain. Differences in the acquisition of the concept of pain through learning likely contribute to individual variances in pain perception. The IASP definition of pain includes the claim that our concept of pain is acquired through learning in our childhood (International Association for the Study of Pain, 2017). But the evidence for the cognitive penetration of pain seems to extend the period of learning into adulthood because treatment history with analgesics influence both the effectiveness of real analgesics and the susceptible to placebo analgesia. In addition, perceiving pain as being of certain intensity requires a history of experiences with pain. When individual patients are asked about the intensity of their pain, they are often expected to rank their pain on a scale, as mild, moderate, or severe (Hawker, Mian, Kendzerska, & French, 2011). These scales are often comparative; they require the patient to identify the level of their discomfort against the background of their past experiences. For example, in order for the patients to identify whether their pain is mild, moderate, or severe, they would have to have a background of pain experiences, such as childbirth, venipuncture, or a scraped knee, in order to identify their current pain as falling somewhere on that continuum of severity.

Given the evidence that learning can affect the felt intensity of pain, our overall concept of pain and our ability to rank pain depends in part on our interactions with healthcare professionals. For example, a phlebotomist telling a patient that venipuncture will feel like a pinprick increases the likelihood that the individual will experience low-intensity pain that feels like a pinprick.[[5]](#footnote-5) Furthermore, as an individual gains experience with blood draws, they will come to develop their own expectations of the level of pain intensity and their concept of the pain associated with drawing blood will be that it feels like a pinprick. Hence, both the initial experience of pain with venipuncture as well as the subsequent experience of pain in the same context will be determined partially by the expectations set initially by the healthcare provider. Exploring even further the formation of the concept of pain, most people learn to describe their pain and to categorize it as intense, throbbing, sharp, or dull, when they are asked to by their clinician. In these situations, the clinician attempts both to encourage the patient to describe their experience and to give them additional vocabulary to render the description more precise. This allows the patient to identify more of the sensory and discriminative aspects of pain. Additionally, the patient is learning to categorize their painful experiences as being intense, throbbing, sharp, or dull, and in doing so refining their concept of pain. In effect, each of us learns to identify pain and to establish a basis for rating pain experiences as mild or severe in part based on our experiences talking to healthcare professionals about our pain.[[6]](#footnote-6)

Expectation and learning can contribute to effectiveness of analgesics as well. The evidence presented in the previous section shows that an individual’s susceptibility to placebo analgesia as well as their likelihood of experiencing pain relief with the use of known analgesics might be increased by past experiences with successful analgesia.[[7]](#footnote-7) Furthermore, as was described earlier, the ability to reappraise pain may change its intensity or relieve it. An individual who is experiencing pain might not know whether the type of pain they are experiencing is associated with a life-threatening condition. A person experiencing abdominal pain might have the fear that their pain is a symptom of cancer. Once that fear is allayed and the patient is told that their pain is due to a benign abdominal condition, they might experience a decrease in the intensity of felt pain because they re-contextualizes the pain as not life-threatening. This individual could also use this experience in the future to correctly identify when they are experiencing similar discomfort and reappraise their pain as not being life-threatening. Hence, interactions with healthcare professionals and the way in which they communicate to patients about pain will not just contribute to their immediate experience of pain, but it will also shape the patient’s concept of pain which in turn will influence their future painful experiences as well as their ability to experience analgesia.

4. Placebos Analgesia as Real Analgesia

Placebos are usually described as being pharmacologically inactive (Beauchamp & Childress, 2009; Bostick et al., 2008), with their positive treatment effects often attributed to the contextual aspects of treatment and the purposeful deception by a healthcare professional. I will refrain from making general arguments about placebos, which have been recorded across a variety of different medical condition, and might have different basis for distinct conditions.[[8]](#footnote-8) When it comes to pain, however, there is evidence that placebo analgesia cannot be properly described as inert. Both the cognitive modulation of pain through expectation and pain relief through known analgesics exploit the descending modulatory system to diminish the intensity of pain (Tracey & Mantyh, 2007; Wiech et al., 2008) and can inhibit pain processing as early as in the spinal cord (Eippert et al. 2009). In addition, the effectiveness of known analgesics is enhanced by setting expectations of pain relief (Bingel et al., 2011), cognitive modulation of pain likely contributes to pain relief for all analgesics. Cohen and Shapiro (2013) argue that placebo treatments, which they call “comparable placebo treatment”, when they recruit similar biological mechanism as proven treatment challenge the distinction between placebos and proven analgesics as treatment for pain.

 One could raise an objection to the argument that placebo analgesia is real analgesia by pointing out that the cause of pain relief from a real analgesic is the pill and this is not the case for placebo analgesia. Annoni and Miller (2016), for example, argue that placebo effects are the result of aspects of the clinical encounter; rather than the result of the administration of placebo analgesia. It is clear that the clinical encounter or therapeutic communication with a clinician plays a role in placebo analgesia, as the expectation of pain relief is clearly primed by the interaction with a clinician and the context of the clinical setting. But other relevant factors for the establishment of a placebo response include the shape, size, and color of the pill (Ader, 2000). There is evidence, for example, that the color of the pill can influence the strength of the placebo effect (de Craen, Roos, Leonard de Vries, & Kleijnen, 1996; Moerman & Jonas, 2002). Moerman and Jonas (2002) interpret the importance of the color of the pill, for example, to be a demonstration that the pill itself is inert and that the color is the primary trigger of the placebo reaction. They argue that the individual is attributing meaning to the color of the pill and the placebo response relies on the ability of people to respond to meanings in the medical context (Moerman & Jonas, 2002). For example, red might be associated with danger or with hotness while blue might connote quietness or cool temperature (Moreman and Jonas 2002, p. 472). The evidence presented by Moerman and Joans (2002) about the importance of the color of the pill, does not exclude the pill as part of that trigger as well. The medical encounter and even the act of taking a pill are complex contexts that have a number of discrete elements. If we take the classical conditioning view of placebo analgesia the effect is established once an individual forms an association between taking a pill and the experience of pain relief. Given the complexity of the act and the context of taking a pill, any number of features could be the cause of placebo analgesia: it could be the pill; it could be the color of the pill; it could be the brand name of the pill; it could be who prescribes the pill; or it could be all those factors together. The research by Moerman and Jonas (2002) shows that certain features of the pill contribute to the placebo effect, but this research does not rule out that taking the pill contributes to the placebo response as well. Utilizing the approach proposed by Moerman and Joans (2002) we could argue that the pill is part of the meaning response; we attribute meaning to the pill in the same way as we attribute meaning to the color of the pill (Moreman and Jonas 2002, p. 472).

 Another objection could be raised with regard to the type of language used to introduce placebo analgesia. Cohen and Shapiro (2013) argue that introducing a placebo with general statement about the potential benefit of the treatment leaves room for equivocation. For example, a clinician could say: “I am giving you a pill that will relieve your pain.” And this general statement will have a different meaning for the clinician and for the patient. The clinician will understand the statement as stating that the administration of the pill will trigger the placebo effect, while the patient will understand that the pill will trigger a physiological effect that will relieve pain. This equivocation would result in deception because patients will think that they are receiving an active substance. Cohen and Shapiro argue, however, that providing more precise statements about the actual mechanisms of pain relief could diminish the amount of equivocation. They further argue that in situations where the biological mechanisms that underlie placebo effects and the effects of a proven medication are similar or the same, there would be no equivocation and it would not be deceptive to introduce placebos as treatment. When it comes to pain, the argument proposed by Cohen and Shapiro (2013) refutes the charge that introducing placebo as treatment is deceptive because both placebo analgesia and proven analgesics are thought to recruit the same biological mechanism, i.e., the descending pain modulatory system. Thus, even a very precise introduction of placebo analgesia would not require deception as the biological mechanism described would be the same as it is for proven analgesics.

 Given that I have argued that placebo analgesia should not be described as inert, I will now consider the impact of this argument on some recommendations for the ethical use of placebo. A recommended way of reconciling use of placebo with the obligation for truth telling is to disclose that one is administering or prescribing a placebo (Bostick et al., 2008). Considering the role of expectation in pain relief, the requirement of disclosure might have a negative impact on the effectiveness of the treatment. As described earlier, there are several elements that are required for the success of the placebo. There are the expectations set at each clinical encounter; each time positive expectations are established, they can contribute to pain relief. There is also the learned association based on past experiences of pain relief. Failing to preserve any of those elements might lead to a diminished analgesic effect. There is evidence that open-label placebos, which are placebos openly presented as such, are effective for the treatment of some condition, such as irritable bowel syndrome (Kaptchuk et al., 2010) and ADHD in children (Sandler & Bodfish, 2008). There is also a recent study showing efficacy of an open-label placebo for low back pain (Carvalho et al., 2016). In the Carvalho et al. study, participants who were given open-label placebos were also introduced to it in a way that fosters positive treatment expectations; they were informed about the benefits of placebos and how the body can automatically respond to the administration of the placebo. So it is not clear whether the pain relieving effects would persist without the description of placebos as having treatment properties. One could venture a prediction that disclosing that the patient is receiving a pharmacologically inert substance, without describing the benefits of placebo, might create negative expectations at the time of treatment and diminish efficacy. Even with the possibility that the learned association would result in analgesia despite the disclosure that one is administering a placebo, I would argue that this is not the right approach to placebo administration for the treatment of pain. First, as I argued, placebo analgesia should not be characterized as inert, and telling the patient that they are being treated with an inert substance would be inaccurate. Second, based on the evidence for the cognitive penetration of pain, a clinician prescribing placebo analgesia would have a justified expectation of the effectiveness of the treatment. And informing the patient that the clinician expects that taking this pill will treat the pain would not be misleading. There is of course always uncertainty with regard to whether an individual will benefit from any particular treatment, and placebo analgesia might fail to be successful in relieving pain. But the possibility that placebo might prove unsuccessful in relieving pain does not render the clinician’s recommendation deceptive as long as the recommendation rests on the demonstrated effectiveness of placebo analgesia in relevant populations.

 Other recommendation for the ethical use of placebo rest on the justification for the occasional obligation to deceive patients. Foddy (2009) argues, for example, that in order to garner the full benefit of placebo, a clinician might have to deceive the patient by providing the patient with a dishonest positive prognosis. Foddy argues that the real value of the deception in the context of placebo is that it can “drive expectations higher than an honest prognosis can” (Foddy, 2009 p. 8). The evidence for the impact of cognition on pain perception, however, challenges the view that facts about the likelihood for pain relief, i.e., an “honest prognosis”, can be set independently of the influence of positive expectations conveyed either by the clinician during the encounter or the learned expectations the patient already brings to the medical encounter. And if the likelihood of pain relief to be conveyed in an honest diagnosis are not set independently of positive expectations, then it is inaccurate to characterize setting positive expectations as deception. Deception requires departure from the truth in a way that does not exist in the context of placebo analgesia. Thus, the permissibility of the use of placebo does not need to rest on the justification of deception in the clinical context.

5. Nocebo Effects, Minimizing Harm, and Informed Consent

Despite the strong evidence for the cognitive modulation of pain, it is still the case that no matter how expectations are set certain injuries or medical procedures will hurt. Although I have described the dissociation between noxious stimulation and the experience of pain, strength of the noxious stimulus remains an important contributor to the overall activation of the pain system, and ultimately to the experience of pain. Nonetheless, as pain is prone to nocebo effects, warning somebody of the potential for intense pain increases the likelihood of high-intensity pain. One of the factors that should be used to adjudicate the obligations to disclose is the likelihood that a medical intervention will hurt, with the higher likelihood of pain enhancing the obligation to disclose this potential.[[9]](#footnote-9) A way to determine the likelihood of pain is to base it on the intensity of the noxious stimulus. For example, a blood draw is thought to be a low intensity stimulus, while a lumbar puncture is thought to be a higher intensity stimulus, and the pain predicted is expected to track the strength of the stimulus. Even in situations where there is a high likelihood that a medical intervention will cause high-intensity pain, however, it is important to remember that how much something hurts is the result of number of different factors that include the strength of the stimulus but is not solely dependent on it. If each individual experience of pain rests on factors that include contextual feature of the medical encounter, the expectations set by the clinician, and so on, estimates of how much a lumbar puncture hurts, for example, are also based on factors other than just the strength of the stimulus. And as almost everything about each individual instance of a medical procedure, except for the stimulus, can be variable, the hurt experienced by each individual are likely to be variable as well. Thus, even in situations where there is high likelihood of pain, there is still justification for creating positive expectations because those can diminish the felt intensity of pain.

Another way to adjudicate whether an individual should be warned about the potential for pain is based on whether the patient has a reasonable alternative to the proposed procedure or treatment. In situations where a particular procedure is required for diagnosis or there are not less invasive tests (and we know the patient wants to pursue treatment), the patient might not benefit from being warned about the potential for high-intensity pain because they will not use this warning to refuse the procedure. For example, an individual for whom it is recommended that they undergo a lumbar puncture in order to determine whether they have a life-threatening infection might simply not have alternative diagnostic procedures at their disposal, and warning the patient that the procedure might be significantly painful would fail to be either beneficent or to promote the patient’s autonomy. If we conceptualize autonomy as the capacity for self-government and not disclosing information as limiting this capacity (Foddy, 2009), not disclosing the potential for high intensity pain would not limit the patient’s autonomy. For the patient who wishes to pursue the diagnostic tests and for whom there are not better options, disclosing the potential for high-intensity pain will not enlarge the choices available to the patient and yet it will increase the likelihood that the pain will be experienced as intense. In this situation and situations sufficiently like this one, the best course of action is to minimize the expectation for intense pain. This does not mean failing to warn a patient that the procedure might hurt, but it means that a clinician ought to choose words that do not prime the patient to experience pain. Here again, it would be false to characterize what the clinician is doing as lying or deceiving the patient, for two reasons: First, utilizing only the strength of the stimulus to predict intensity of pain will result in inaccurate predictions. Second, facts about how much the procedure will hurt vary for any given patient because they are inextricably linked with the context within which the procedure is administered, the way in which this medical intervention is introduced, the patient’s individual history with pain, and their endogenous expectation for how much a medical procedure could hurt. A clinician in this situation could not be confident that a procedure would lead to high intensity pain, but they would have good reason to believe that their characterization of a lumbar puncture as significantly painful, will increase the likelihood that the stimulus is experienced a very painful by their patient.

 As described in the second section of this paper, aiding the patient maintain a sense of control while experiencing noxious stimulation can be used as a strategy to diminish pain intensity (Wiech et al., 2008). Thus, it might be important for healthcare professionals to allow the patient to have control over whether the painful stimulation will continue. For example, a clinician might say to their patients that they can ask for the procedure to stop at any point if they are experiencing too much discomfort. A further strategy for curbing the intensity of pain is to encourage the reappraisal or the contextualization of the sensation. For example, before a lumbar puncture, if the clinician explains that the needle will go into the spine at a location where there is minimal risk that the needle will cause any damage to the spinal cord. In this way, by assuaging a common fear associated with the procedure, the patient might feel that the procedure is not as dangerous as they previously thought and experience pain of lesser intensity. As I described earlier in the paper, pain unpleasantness diminished when the noxious stimulus was reappraised as less life threatening or dangerous (Arntz & Claassens, 2004).

 In situations where a patient has alternatives and might make a choice to decline a treatment or medical procedure because of its painful side effects, a clinician has an increased obligation to convey the possibility for pain to the patient. There are a number of different approaches to the scope of informed consent. One of the dominant approaches is the reasonable person standard (Beauchamp & Childress, 2009). Informed consent dos not require of a clinician to disclose all possible sequelae associated with an intervention; rather, they are asked to make a choice about what they think a reasonable patient might want to know. When it comes to disclosing the potential for pain, a clinician could make the safe assumption that most patients would want to be informed about the potential for pain. Most people prefer to avoid or minimize pain, and it is reasonable to assume that a potential for pain might be a significant factor for any individual contemplating consent to treatment or to a diagnostic test. Thus, the reasonable standard for informed consent would lead a clinician to disclose when a medical intervention has the potential for pain. But, as it was stated earlier, the level of pain severity associated with each medical intervention is in part based on the cognitive penetration of pain, and the ability to predict what type of pain, whether low or high intensity, will be experienced is compromised because changes in the context, in the communication style of the healthcare professionals, the amount of fear or anxiety patients experience during the medical encounter will affect their experiences. Thus, a patient ought to be apprised that although some people experience pain during the intervention, there is uncertainty about whether the procedure will have the similar effect for each particular patient.

 When the patient and a clinician have had an opportunity to become acquainted or have a long-term therapeutic relationship, the disclosure of the risk for pain should be more nuanced and take into account the individual patient. This is sometimes called the subjective standard for the scope of informed consent (Beauchamp & Childress, 2009). The clinician selects the information for disclosure based on their knowledge of the patient’s values and preferences and tailors the disclosure to only those facts that are likely to be of importance to that particular patient. As was mentioned in the previous section, personal coping styles can affect the experience of pain. For example, there is indication that the ability to reappraise pain is more difficult for some individuals who are coping with chronic pain. Those who feel that pain is affecting their life more negatively, feel the pain more intensely. A clinician or other healthcare professional could enhance the treatment of chronic pain by aiding the patient in reappraising their pain. They could help the patient identify all the ways in which they are still able to enjoy daily activities and encourage the patient to continue to engage in activities that give them pleasure. Additionally, as the literature on pain suggests, certain types of personal traits could place patients at risk for experiencing pain more intensely (Harkins et al., 1989). Given that negative expectations, such as fear or worry that an intervention will be very painful, put people at risk for experiencing high-intensity pain, assuaging fears and establishing positive expectations should be considered part of the treatment course for individuals who are particularly fearful of medical encounters. Fortunato et al. (2017) argue for a personalized approach that would take into account each patient’s nocebogenic traits, and used them as potential biomarkers for nocebo susceptibility. A personalized approach should be taken with any patient who is particularly anxious or fearful of medical interventions or medical encounters. Similarly, for individuals who are not anxious or fearful of medical encounters, the way to improve and promote the treatment of pain would entail maintaining their positive expectations.

6. Conclusion

In this paper, I presented evidence that attention, expectation, learning, and reappraisal can influence the felt intensity of pain. I showed how expectation of pain relief can inhibit the sensory processing of noxious stimuli and contribute to placebo analgesia. I’ve also described the evidence that the effectiveness of proven analgesics is enhanced through positive treatment expectation. As expectations of pain relief can inhibit the processing of noxious stimuli, expectation of pain can enhance their processing and heighten the experience of pain. I emphasized that cognitive penetration of pain indicates that the subjective experience of pain results in changes throughout the sensory and discriminative pathway of pain. Given that the subjective experience of pain mirrors changes in sensory and discriminative processing in the brain, I argued for the need to reconsider the approach to placebo analgesia and to the obligation of truth-telling for medical interventions that might hurt. I challenged the characterization of placebo analgesia as inert and showed that clinicians utilizing placebo analgesia are not deceiving patients. Additionally, I described a number of parameters to help clinicians identify situations in which they have an obligation to disclose the potential for pain coupled with ways of mitigating the risk of high-intensity pain by setting positive expectations.

References:

Ader, R. (2000). Classical conditioning in the treatment of psoriasis. *Cutis, 66*(5), 370-372.

Alfano, M. (2015). Placebo Effects and Informed Consent. *American Journal of Bioethics, 15*(10), 3-12. doi:10.1080/15265161.2015.1074302

Annoni, M., & Miller, F. G. (2016). Placebo Effects and the Ethics of Therapeutic Communication: A Pragmatic Perspective. *Kennedy Institute of Ethics Journal, 26*(1), 79-103.

Arntz, A., & Claassens, L. (2004). The meaning of pain influences its experienced intensity. *Pain, 109*(1-2), 20-25. doi:10.1016/j.pain.2003.12.030

Beauchamp, T. L., & Childress, J. F. (2009). *Principles of biomedical ethics* (6th ed.). New York: Oxford University Press.

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). doi:ARTN 70ra1410.1126/scitranslmed.3001244

Boerner, K. E., Birnie, K. A., Chambers, C. T., Taddio, A., McMurtry, C. M., Noel, M., . . . Riddell, R. P. (2015). Simple psychological interventions for reducing pain from common needle procedures in adults: systematic review of randomized and quasi-randomized controlled trials. *The Clinical journal of pain, 31*(Suppl 10), S90.

Bostick, N. A., Sade, R., Levine, M. A., & Stewart, D. M. (2008). Placebo use in clinical practice: Report of the American Medical Association Council on Ethical and Judicial Affairs. *Journal of Clinical Ethics, 19*(1), 58-61.

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. doi:10.1097/j.pain.0000000000000700

Coghill, R. C., McHaffie, J. G., & Yen, Y. F. (2003). Neural correlates of interindividual differences in the subjective experience of pain. *Proceedings of the National Academy of Sciences of the United States of America, 100*(14), 8538-8542. doi:10.1073/pnas.1430684100

Cohen, S. (2014). The nocebo effect of informed consent. *Bioethics, 28*(3), 147-154.

Cohen, S., & Shapiro, H. (2013). “Comparable placebo treatment” and the ethics of deception. *Journal of Medicine and Philosophy, 38*(6), 696-709.

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

Derbyshire, S. W., Whalley, M. G., Stenger, V. A., & Oakley, D. A. (2004). Cerebral activation during hypnotically induced and imagined pain. *Neuroimage, 23*(1), 392-401. doi:10.1016/j.neuroimage.2004.04.033

Eccleston, C., Crombez, G., Aldrich, S., & Stannard, C. (1997). Attention and somatic awareness in chronic pain. *Pain, 72*(1-2), 209-215. doi:Doi 10.1016/S0304-3959(97)00030-4

Eippert, F., Finsterbusch, J., Bingel, U., & Buchel, C. (2009). Direct Evidence for Spinal Cord Involvement in Placebo Analgesia. *Science, 326*(5951), 404-404. doi:10.1126/science.1180142

Foddy, B. (2009). A Duty to Deceive: Placebos in Clinical Practice. *The American Journal of Bioethics, 9*(12), 4-12. doi:10.1080/15265160903318350

Fortunato, J. T., Wasserman, J. A., & Menkes, D. L. (2017). When Respecting Autonomy Is Harmful: A Clinically Useful Approach to the Nocebo Effect. *The American Journal of Bioethics, 17*(6), 36-42. doi:10.1080/15265161.2017.1314042

Gligorov, N. (2016). Objectifying Pain *Neuroethics and the Scientific Revision of Common Sense* (pp. 117-137): Springer.

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.

Harkins, S. W., Price, D. D., & Braith, J. (1989). Effects of Extraversion and Neuroticism on Experimental Pain, Clinical Pain, and Illness Behavior. *Pain, 36*(2), 209-218. doi:Doi 10.1016/0304-3959(89)90025-0

Hawker, G. A., Mian, S., Kendzerska, T., & French, M. (2011). Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care & Research, 63*(S11), S240-S252. doi:10.1002/acr.20543

International Association for the Study of Pain. (2017). IASP Taxonomy. Retrieved from https://www.iasp-pain.org/Taxonomy

Kaptchuk, T. J., Friedlander, E., Kelley, J. M., Sanchez, M. N., Kokkotou, E., Singer, J. P., . . . Lembo, A. J. (2010). Placebos without Deception: A Randomized Controlled Trial in Irritable Bowel Syndrome. *Plos One, 5*(12). doi:ARTN e1559110.1371/journal.pone.0015591

Kessner, S., Wiech, K., Forkmann, K., Ploner, M., & Bingel, U. (2013). The Effect of Treatment History on Therapeutic Outcome: An Experimental Approach. *Jama Internal Medicine, 173*(15), 1468-1469. doi:10.1001/jamainternmed.2013.6705

Kong, J., Spaeth, R., Cook, A., Kirsch, I., Claggett, B., Vangel, M., . . . Kaptchuk, T. J. (2013). Are all placebo effects equal? Placebo pills, sham acupuncture, cue conditioning and their association. *Plos One, 8*(7), e67485.

Melzack, R., & Casey, K. L. (1968). Sensory, motivational and central control determinants of pain: a new conceptual model. In D. R. Kenshalo (Ed.), *The skin senses* (Vol. 1, pp. 423–439). Springfi eld: C.C.Thomas.

Melzack, R., & Wall, P. D. (1965). Pain Mechanisms - a New Theory. *Science, 150*(3699), 971-&. doi:DOI 10.1126/science.150.3699.971

Moayedi, M., & Davis, K. D. (2013). Theories of pain: from specificity to gate control. *J Neurophysiol, 109*(1), 5-12. doi:10.1152/jn.00457.2012

Moerman, D. E., & Jonas, W. B. (2002). Deconstructing the placebo effect and finding the meaning response. *Annals of Internal medicine, 136*(6), 471-476.

Petrovic, P., Petersson, K. M., Ghatan, P. H., Stone-Elander, S., & Ingvar, M. (2000). Pain-related cerebral activation is altered by a distracting cognitive task. *Pain, 85*(1-2), 19-30. doi:Doi 10.1016/S0304-3959(99)00232-8

Ramirez-Maestre, C., Esteve, R., & Lopez, A. E. (2008). Cognitive appraisal and coping in chronic pain patients. *European Journal of Pain, 12*(6), 749-756. doi:10.1016/j.ejpain.2007.11.004

Sandler, A. D., & Bodfish, J. W. (2008). Open-label use of placebos in the treatment of ADHD: a pilot study. *Child Care Health and Development, 34*(1), 104-110. doi:10.1111/j.1365-2214.2007.00797.x

Tracey, I., & Mantyh, P. W. (2007). The cerebral signature and its modulation for pain perception. *Neuron, 55*(3), 377-391. doi:10.1016/j.neuron.2007.07.012

Tracey, I., Ploghaus, A., Gati, J. S., Clare, S., Smith, S., Menon, R. S., & Matthews, P. M. (2002). Imaging attentional modulation of pain in the periaqueductal gray in humans. *Journal of Neuroscience, 22*(7), 2748-2752.

Wells, R. E., & Kaptchuk, T. J. (2012). To Tell the Truth, the Whole Truth, May Do Patients Harm: The Problem of the Nocebo Effect for Informed Consent. *American Journal of Bioethics, 12*(3), 22-29. doi:10.1080/15265161.2011.652798

Wiech, K., Ploner, M., & Tracey, I. (2008). Neurocognitive aspects of pain perception. *Trends in Cognitive Sciences, 12*(8), 306-313. doi:10.1016/j.tics.2008.05.005

Wiech, K., Vandekerckhove, J., Zaman, J., Tuerlinckx, F., Vlaeyen, J. W. S., & Tracey, I. (2014). Influence of prior information on pain involves biased perceptual decision-making. *Current Biology, 24*(15), R679-R681. doi:10.1016/j.cub.2014.06.022

1. Final version published in *AJOB Neuroscience*, 9(3): 173-182. [↑](#footnote-ref-1)
2. The pain matrix is also sometimes referred to as the pain system, and in this paper I will use both designations interchangeably. [↑](#footnote-ref-2)
3. For an overview of how classical conditioning theory can account for placebo effects, see (Alfano, 2015). [↑](#footnote-ref-3)
4. For a defense of the cognitive penetration of pain against some recent criticism of cognitive penetration, see (Gligorov, 2017) [↑](#footnote-ref-4)
5. For a meta-analysis that supports the claim that different descriptions of the sensation associated with venipuncture affects the actual experience of pain with common needle procedures, see (Boerner et al., 2015). [↑](#footnote-ref-5)
6. For more on how healthcare professionals contribute to the learning of the concept of pain, see (Gligorov, 2016) [↑](#footnote-ref-6)
7. There is evidence that placebo analgesia does not generalize across analgesics; rather, placebo effects are specific to the analgesic the individual has been successfully treated with in the past (Kong et al. 2013). [↑](#footnote-ref-7)
8. For an overview of the different sources of placebo effects, see, Alfano (2015). [↑](#footnote-ref-8)
9. Cohen (2014) has argued that that the obligation to minimize harm might in some situations outweigh the obligation to disclose and that in circumstances where pain is particularly susceptible to suggestions, the obligation to minimize harm is greater than the commitment to autonomy. My argument here does not rest on the primacy nonmaleficene, but it does not conflict with it either, because I am aiming to address situations in which pain is less susceptible to suggestion. For example, in situations where pain is the result of tissue damage that we know is very likely to produce pain in individuals with intact pain perception. [↑](#footnote-ref-9)