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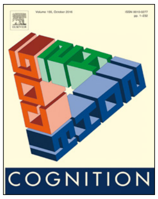

Original Articles

Sensitivity to pain expectations: A Bayesian model of individual differences

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ABSTRACT

The thoughts and feelings people have about pain (referred to as 'pain expectations') are known to alter the perception of pain. However little is known about the cognitive processes that underpin pain expectations, or what drives the differing effect that pain expectations have between individuals. This paper details the testing of a model of pain perception which formalises the response to pain in terms of a Bayesian prior-to-posterior updating process. Using data acquired from a short and deception-free predictive cue task, it was found that this Bayesian model predicted ratings of pain better than other, simpler models. At the group level, the results confirmed two core predictions of predictive coding; that expectation alters perception, and that increased uncertainty in the expectation reduces its impact on perception. The addition of parameters relating to trait differences in pain expectation improved the fit of the model, suggesting that such traits play a significant role in perception above and beyond the influence of expectations triggered by predictive cues. When the model parameters were allowed to vary by participant, the model's fit improved further. This final model produced a characterisation of each individual's sensitivity to pain expectations. This model is relevant for the understanding of the cognitive basis of pain expectations and could potentially act as a useful tool for guiding patient stratification and clinical experimentation.

1. Introduction

The experience of pain, like all other sensory experiences, is a result not only of the objective reality, such as the degree of tissue damage, but also of the sufferer's beliefs about pain. Conscious and unconscious thoughts and beliefs that people have about imminent pain are referred to as 'pain expectations' (Schrooten, Vlaeyen, & Morley, 2012). The effect of pain expectations on pain experience is evident in both laboratory and clinical experiments (e.g. Atlas & Wager, 2012; Bingel et al., 2011; Colloca, & Benedetti, 2006; Peerdeman et al., 2016; Tracey, 2010). In addition, neural correlates of the effect of expectation on pain perception have been established (Brown, Seymour, El-Deredy, & Jones, 2008; Ploghaus et al., 1999; Seymour et al., 2004; Tracey, 2010; Wager et al., 2004; Watson et al., 2009). Despite these advances there remains a significant gap in our knowledge regarding the specific cognitive processes that underpin pain expectations.

Predictive coding provides the dominant theoretical framework for understanding the effects of expectation on perception (Clark, 2013; Friston, 2003), including pain perception (Buchel, Geuter, Sprenger, & Eippert, 2014; Tabor, Thacker, Moseley, & Körding, 2017; Van den Bergh, Witthöft, Petersen, & Brown, 2017). Predictive coding stipulates that perception is biased towards the expected level of pain, and that this bias will be stronger when the expectation is more certain, since expectation uncertainty causes the suppression of top-down, prior-driven signals, leading to greater importance being placed on the bottom-up sensory input. A number of studies confirm that the specific predictions of predictive coding apply to pain perception, beyond the established biasing effect that pain expectations exert on pain experience. For example the effect of pain expectations is enhanced when expectations are more precise (Brown, Seymour, Boyle, El-Deredy, & Jones, 2008; Colloca, Petrovic, Wager, Ingvar, & Benedetti, 2010). Likewise formal Bayesian models provide a good fit to pain reports in placebo analgesia studies (Anchisi and Zanon, 2015; Jung, Lee, Wallraven, & Chae, 2017) and to neural data from the anterior insula (Geuter, Boll, Eippert, & Büchel, 2017).

Although predictive coding guides much of the research on the

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effect of expectations on perception, some findings appear to contradict its prediction concerning the impact of the precision of the expected pain. Watkinson, Wood, Lloyd, and Brown (2013) delivered two different distributions of pain stimuli, a unimodal and a bimodal distribution. The two distributions had the same mean pain level, but the bimodal distribution had a larger variance. According to predictive coding theories the mean expected level of pain should be the same in the two conditions, but the influence of this expectation on pain experience should be lower in the bimodal condition, as the larger variance of the bimodal distribution should cause greater expectation uncertainty. In direct contradiction with predictive coding, and in support of the alternative, Range Frequency Theory (Parducci, 1963), Watkinson et al., found that the expected mean level of pain had a stronger influence on the rating of three target stimulations in the bimodal condition, despite the greater uncertainty generated by the larger stimulation variance. Likewise, Yoshida, Seymour, Koltzenburg, and Dolan (2013) altered participant's expectations relating to upcoming pain stimulations by presenting fictitious pain ratings of the stimuli prior to their delivery. The mean and variance of the distribution of these ratings were manipulated. They found that increasing pain uncertainty contributed independently to increased pain experience, in contradiction with predictive coding. In addition, it is not clear from Yoshida et al. data whether uncertainty significantly modulated the bias induced by the mean of the fictitious pain ratings, as it should do according to the predictive coding framework. These findings suggest that further work is needed before predictive coding is accepted as a viable framework for understanding pain perception.

Over and above the conflicting findings around the impact of expectation uncertainty, we also know very little about how specific processes that underlie pain expectations are integrated. Unpacking the construct of pain expectations to its underlying information processing mechanisms requires a statistical model of the pain perception process to be formulated which accommodates parameters that describe different facets of pain expectations. Furthermore, in order for such a model to be useful in understanding an individual's response to both pain and placebo analgesia, it needs to be capable of predicting the effect of pain expectations not just at a group level, but also at an individual level, and not only qualitatively, but also quantitatively. For example such a model would need to be able to identify individuals that experience high levels of pain because they have a trait-like bias to expect high levels of pain (i.e. always expecting high pain, independent of context), and to distinguish such individuals from those who experience high pain because they are highly pessimistic in assessing the information they are given about a treatment, or because they are overconfident in their mildly-pessimistic expectations, so that they rely less on their sensory data. That level of understanding is necessary to allow an individual's response to treatment to be predicted, thus providing the basis for a tool that can support clinical decision making.

This paper details the construction and testing of a mathematical model of the impact of pain expectations on pain perception using experimental data garnered from a novel predictive cue task. The purpose of this model construction was threefold. Firstly, we wished to assess the effect of expectation uncertainty on pain perception in light of the conflicting past results mentioned above. Our second objective was to identify, using the experimental data, a number of putative cognitive processes that give rise to the umbrella term 'pain expectations'. Finally, leading on from the second objective, we wished to assess whether a model could be constructed that would enable individuals to be distinguished based on the aforementioned cognitive processes.

We collected two sets of experimental data via two separate experiments using independent samples. A series of increasingly complex statistical models were constructed and their performance was compared using the data from the first experiment. The simplest model (Model 1), where the pain participants experienced was influenced only by the actual, delivered pain, served as a baseline to compare to five other models, which successively included additional facets of pain expectations. The multi-modal model (Model 2) represented pain expectations with a multi-modal distribution, which peaked around each of the possible pain levels that participants could expect based on the cues they were given. In the 'Mean-only model' (Model 3) pain expectations were assumed to correspond to the mean of the expected pain (i.e. the average of the possible pain levels indicated by the cue). The 'Mean-and-variance model' (Model 4) was inspired by predictive coding, and took into consideration the variance of expected pain, a function of the discrepancy between the possible pain levels indicated by the cue. Like Model 3, Model 4 also allowed pain experience to be affected by the mean of the expected pain, but here the impact of mean expected pain was modulated by its uncertainty. Finally the 'Full model' (Model 5) additionally included the effect of cue-independent pain expectations in addition to the cue-dependent expectations used in Models 2, 3 and 4. In this formulation, cue-dependent pain expectations relate to those triggered on each trial by the cue, while cue-independent expectations capture more stable, trait-like differences in the propensity to believe that pain will be greater or weaker, independent of the effect of specific local cues. Thus, this model is organised into tiers, such that stable priors contribute to the shaping of more temporary priors triggered by the information provided by the cue. Finally, to satisfy the objective of creating a model that can characterise pain expectations at the individual level, we compared the winning group-level model to an individual-level variant that included individual-level random effects (Model 6). We considered the winning model to be able to usefully characterise pain expectations at an individual level if the 'individual-level' variant of the model was significantly better at predicting pain perception than its equivalent group level variant. The second experimental dataset was used for the purposes of conceptual replication; enabling validation of the findings from the first dataset, thus providing evidence that the winning model could predict outcomes in a dataset other than the one from which it was constructed (cf. Maloney & Zhang, 2010).

We hypothesised that the model comparison will provide support for the predictive coding framework. More specifically we predicted, based on neural evidence that the mean of probabilistic cues is computed and utilised in decision-making (Schultz, O'Neill, Tobler, & Kobayashi, 2011), that Model 3 will provide a better fit to the data than Model 2. We also predicted that Model 4 will provide a better fit to the data than Model 3, thus showing that expectation uncertainty significantly affects pain perception; and that the value of model parameter describing the effect of expectation uncertainty will show that increased uncertainty reduces the influence of pain expectations. Based on the vast clinical literature on individual differences in pain catastrophizing (Sullivan, Bishop, & Pivik, 1995) we hypothesised that Model 5 will provide a better fit for the data than Model 4, suggesting that both cue-dependent and cue-independent expectations have separate influences on pain perception. Finally, we hypothesised that when individual-level random effects are added to the winning model this will significantly improve the fit of the model to the data, suggesting that the model is able to characterise sensitivity to pain expectations at an individual level.

2. Method

2.1. General experimental design

Two experiments were conducted on independent samples. Experiment 2 was conducted for validation, with task delivery modifications introduced to enhance the translational impact of the approach. During each experiment participants performed a 'pain rating' task (Fig. 1). In each trial of the task, participants' expectations regarding the upcoming stimulation were manipulated. This manipulation was achieved by offering the participants a choice between two 'cues' expressing different probability distributions for the intensity of the upcoming stimulation in terms of the possible intensities and