Divergent effects of expectations on behavior and brain

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Abstract

Expectations have a significant impact on sensory experiences, as evidenced by placebo and nocebo effects. In both cases, positive or negative outcomes are products of expectations, where an individual assimilates sensory experience with expectations. However, assimilation effects may not always occur, particularly when expectations are highly discrepant from sensory experience. Using a factorial experiment with different levels of cues and stimulus intensities, we find that higher expectations lead to higher pain ratings when expectations match incoming stimulus, indicating an assimilation effect. In contrast, when expectations and stimulus intensities do not match, expectations have less influence on outcome ratings, implying greater weighting on the stimulus input itself. Our results suggest that expectations and noxious input are weighted differently depending on congruence between expectations and pain experience. A computational model simulation supports these findings. Interestingly, the behavioral and neural results show opposite patterns, where low cues were associated with higher pain-predictive brain activation. Using our computational framework, further investigation is required to identify the discrepancy between the behavioral and neural results and understand the divergent effects of expectations on sensory perception.

Keywords: Prediction; Pain; Reinforcement Learning

Introduction

Expectations are mental models of the world, powerful enough to shape and influence our perceived sensory experiences. Prime examples are placebo effects, where subjective positive expectations lead to objectively better physiological outcomes despite an inert treatment (Benedetti, 2014; Wager et al., 2004). The idea of assimilating with expectations is well studied in the pain domain, where expectations for lower pain are associated with lower pain reports, i.e. placebo analgesia (Tracey, 2010), and vice versa when expecting greater pain (Colloca & Barsky, 2020).

However, in contrast to assimilation effects, expectations do not always drive outcome experience. When pain experience is drastically different from expectation, i.e. large prediction error, one may downweight the influence of expectations on outcome reports (Hird, Charalambous, El-Deredy, Jones, & Talmi, 2019).

What is the balance between these two competing effects? In order to answer these questions, a full factorial design with varying levels of cues and stimulus intensities are essential for identifying when assimilation processes are engaged versus not. Here, using neuroimaging and computational models, we investigate the effect of expectations on pain perception and further examine the context when assimilation vs downweighting occurs.

Method

Participant and design. Participants (N=84) performed a thermal heat task in an fMRI study: 2 cue (low/high) x 3 stimulus intensity (low 48 ℃/medium 49 ℃/high 50 ℃). Participants were first exposed to a high or low cue ("cue"), then indicated expectations of the upcoming stimulus intensity ("expectation rating"), received a thermal stimulation ("stimulus"), and reported pain experience ("outcome rating"; Figure. 1).

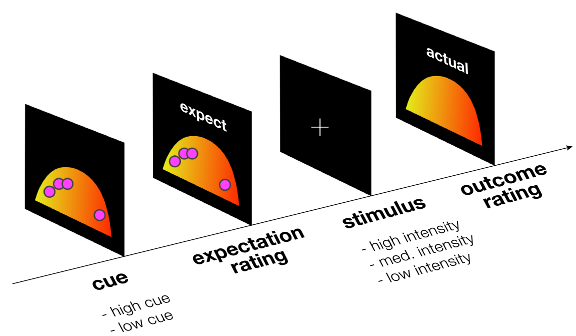

Figure 1: Schematic of one trial in a 2 cue x 3 stimulus intensity factorial design.

Analysis. *Behavioral data*: outcome ratings were modeled as a function of cue, stimulus intensity, and expectation ratings. *Neuroimaging data*: single trial estimates were extracted for "stimulus" epoch, and dot product was calculated between trial estimates and predefined neurological pain signature (NPS; Wager et al., 2013) as a proxy of pain-predictive brain states.

Computational model. The computational model consists of two main components: (1) pain outcome rating and (2) expectation rating.

$$Outcome(t) = (1-w) \times Stimulus(t) + w \times E_{Cue_i}(t) \quad (1)$$

$$\delta(t) = Outcome(t) - E_{Cue_i}(t) \quad (2)$$

$$E_{Cue_i}(t+1) = E_{Cue_i}(t) + \alpha \times \delta(t) \quad (3)$$

Pain outcome rating is a function of stimulus intensity and expectations (Equation 1), which allows for modeling assimilation effect of noxious input and expectations. Prediction error of pain is calculated as the difference between the pain outcome and the expectation of pain (Equation 2). Expectation of pain is updated by a reinforcement learning (RL) mechanism (Equation 3). In contrast to the assimilation effect, to account for the discrepancy between stimulus intensity and expectations,we introduce a weight parameter that is proportional to the inverse of the absolute difference between stimulus intensity and expectation. Therefore, when expectation and stimulus input are highly discrepant, lower weight is placed on the reported expectations and more on the noxious input itself (Equation 4).

$$w = \frac{1}{(1 + e^{\gamma \times |Stimulus(t) - E_{Cue_i}(t)|})} \quad (4)$$

Simulation. We used a computational model with an RL mechanism with two parameters: (1) α, and (2) γ. The lower learning rate means that the participant (or simulated agent) is learning the expectation of pain more slowly. We simulated models using the range of [0, 0.4] for the α, and [0.6, 0.8] for γ. The more γ is, the more it incorporates the discrepancy between the noxious stimulus and the expectation.

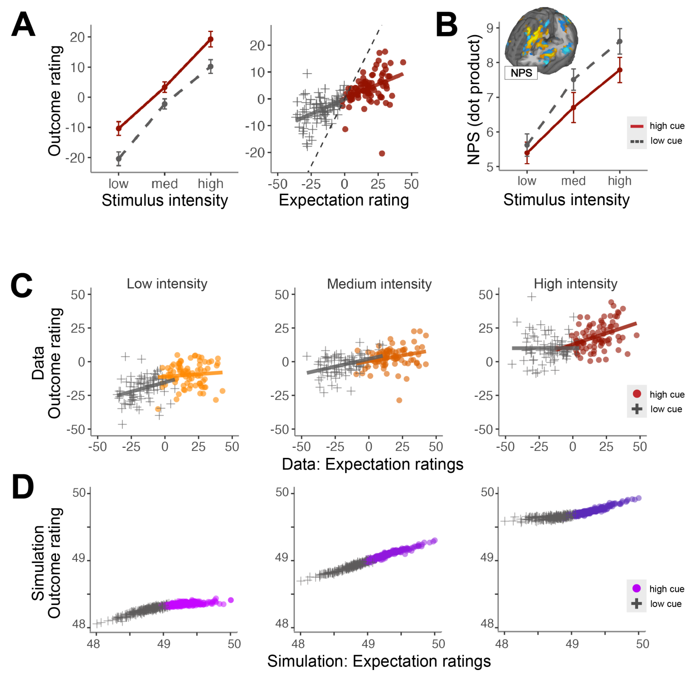

Figure 2: **A**) Behavioral results of cue x stimulus intensity & cue x expectation interaction. **B**) Neural results of cue X stimulus intensity interaction **C**) Behavioral results of cue x stimulus intensity x expectation interaction. **D**) Simulated results of cue x stimulus intensity x expectation interaction.

Results and Discussion

Behavioral results: Outcome ratings can be modeled as a function of cue, expectation ratings, and stimulus intensity

There is a significant 3-way interaction of cue, expectation rating and stimulus intensity ($p < .001$). In Fig. 2A, pain outcome ratings are higher for both higher cues ($p < .005$; left) and higher expectations ($p < .001$; right), suggesting an assimilation effect.

A different pattern is observed when examining outcome ratings as a function of cue, expectation rating, and stimulus intensity levels (Fig. 2C). While the assimilation effect was present when the cue was congruent with the stimulus intensity, when incongruent, expectations had less influence on outcome ratings. These results suggest that expectation ratings may be downweighted in certain situations.

Simulation results: Computational model captures the assimilation and downweighting of expectations depending on expectation-stimulus congruence

Using our computational model that allows for different weights depending on expectation-stimulus congruency, the model well simulates the behavioral patterns that we observed (Fig. 2D). When expectation is highly discrepant from the incoming noxious input, expectations play a smaller role in influencing perceived pain, thus has minimal impact on pain outcome ratings. For future directions, this model can serve as a framework for identifying assimilation processes versus not.

Neuroimaging results: Low cues are associated with greater pain experience, indicating a converse pattern from behavioral results

There is a significant cue effect on NPS patterns ($p < .005$; Fig. 2B). However, the direction of the cue effect is in contrast from the behavioral results; low cues are associated with higher NPS values, indicating greater pain-associated brain activation. Such findings suggest a threat analgesia effect, where low cues presumably lead to low expectations, resulting in greater pain when encountered with an unexpected high pain stimulus (Seidel et al., 2015).

To fully comprehend the divergent behavioral and neural effects of expectations on sensory experiences observed in the present study, refining the computational model and conducting additional neuroimaging analyses are essential.

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