Expectation generation and its effect on subsequent perception in pain and vision

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In line with Bayesian predictive coding theories of brain function, cue-based expectations affect perception. However, it remains unclear how multiple cues are integrated into expectations, how these expectations affect subsequent perception, and if these processes are modality-specific or modality-general. Here, 45 participants observed multi-value cues and reported their expectations regarding the painfulness of thermal stimuli or visual contrast of flickering checkerboards. The mean, variance, and skewness of the cues were experimentally manipulated. Then, participants observed the same cues, followed by thermal and visual stimuli, during an fMRI scan. Expected and perceived stimuli were indeed higher following cues with higher mean in both modalities, but the effects of cue variance were mostly not consistent with Bayesian or other previous theories. Instead, computational models indicated that people placed a larger weight on extreme values in both modalities, particularly low-pain cues. fMRI analysis showed that the effect of expectations on pain ratings was mostly mediated by brain systems related to cognitive and affective processing, rather than nociceptive pain. Our findings suggest that people's expectations and perception are affected by extreme values, with some similarities and some differences across modalities.

Keywords: Bayesian; Brain; Expectations; fMRI; Pain; Prediction; Predictive Coding; Vision

Introduction and experimental design

Current theories of perception, such as the "Bayesian brain" (Friston 2010; Friston 2012; Knill and Pouget 2004) and predictive coding (Clark 2013), posit that the brain represents the world with an internal generative model, and prediction-based expectations combine with the incoming sensory information to form perceptions. This broad framework raises three important, unanswered questions: First, how do people integrate information provided by multiple sensory cues into expectations? Previous studies, particularly in the context of pain, have used multi-value cues, and mostly focused on the mean of available information and rarely on its variance (Grahl et al. 2018; Koban et al. 2019; Yoshida et al. 2013; Zhang et al. 2023). However, other properties of the cue distribution may affect the generated expectation, such as outliers or inliers (de Gardelle and Summerfield 2011; Spitzer et al. 2017), and such nonlinear weighting has not been studied in pain. Second, how do expectations affect subsequent perception, and do these processes follow Bayesian updating rules? Bayesian theories suggest that the expectation (prior belief) combines with incoming sensory information (likelihood) to form the perception (posterior belief). In line with this framework, previous studies have shown that perception assimilates to predicted values (Atlas et al. 2010; Koban et al. 2019; Summerfield and de Lange 2014; Yoshida et al. 2013). Bayesian models further predict that more certain expectations affect perception to a higher degree (Büchel et al. 2014; Pouget et al. 2013; Summerfield and de Lange 2014). However, studies in pain have provided mixed evidence (Zaman et al. 2021). This raises the third question: Are these processes modality-dependent or modality-general? For example, uncertainty may be aversive particularly in the threatful context of painful stimuli.

Here, we address these fundamental questions by directly testing with behavioral, computational, and neuroimaging analyses, how different properties of the cue distribution affect the generated expectations, and how these expectations affect subsequent perception of visual and painful stimuli. N=45 participants completed two main tasks: In the *Expectation Task*, they saw multi-value cues consisting of a rating scale with 10 marked ratings, allegedly obtained from previous participants, and reported the expected painfulness of thermal stimuli or visual contrast of flickering checkerboards. The mean, variance, and skewness of each cue's values were experimentally manipulated. Then, in the *Cued-Perception Task*, performed during an fMRI scan, participants saw similar cues and then rated the painfulness or visual contrast of subsequent stimuli.

Expectation generation from multi-value cues

Replicating previous studies, expectations were higher for larger mean cue values in both modalities (linear mixed effects model, $p < .001$). The effect of the variance on expectations is less straightforward, because current theories suggest it affects the certainty or valence, rather than the value, of expectation. Surprisingly, expectations were higher when the variance was lower ($p < .001$), but this effect interacted with modality ($p < .001$), such that it was significant for pain ($p = .002$) and not for vision ($p = .802$). There was no interaction between the cue mean and variance ($p = .171$). Finally, expectations were higher for positively skewed cues, and lower for negatively skewed cues, compared to symmetric cues (both $p < .001$), indicating that expectations are drawn towards extreme values.

To test more directly how different values are weighted during expectation generation, we developed a computational model weighting each of the 10 cue values based on its relative location in the cue's distribution (inspired by Spitzer et al., 2017; Figure 1). Values were first rescaled to [0,1] and demeaned ($X_{i=1:10}$). Each value's weighting was based on a combination of (1) a power term modeling the weighting of inliers vs. outliers with the free parameter k:

(1) $$Wk_i = \frac{sign(X_i) * |X_i|^k}{X_i}$$

and (2) a logistic term modeling the weight of values that are smaller vs. larger than the cue mean with the free parameter b:

(2) $$Wb_i = \frac{1}{1+e^{(-b * X_i)}}$$

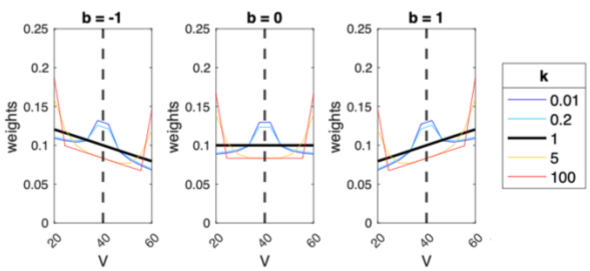

Figure 1. Simulations of the expectation model. Mapping of cue values, V (10 per cue), to weights for expectation computation, based on two free parameters: k (weighting of inliers vs. outliers) and b (weighting of values that are smaller vs. larger than the mean). When $k = 1$, inliers and outliers are equally weighted; when $k > 1$, outliers are weighted higher; when $k < 1$, inliers are weighted higher. When $b = 0$, smaller and larger values are equally weighted; when $b > 0$, larger values are weighted higher; when $b < 0$, smaller values are weighted higher. The dashed vertical line represents the cue mean.

The two weights were combined and normalized to [0,1]. Finally, expectation was computed as the dot product of the vector of cue values (V) and vector of weights (W). The model was fit to all trials, and the free parameters were optimized per participant and modality using OLS. The model fit the data well with averaged (across participants) $r = 0.94$. At the group level, participants weighted outliers significantly higher in both modalities (i.e., $k > 1$; Wilcoxon signed rank test, pain $p = .019$, vision $p = .008$), and also smaller values specifically in pain (i.e., $b < 0$; pain $p < .001$, vision $p = .446$). These findings strengthen the conclusion that extreme values drive expectations in both modalities, and further suggest an optimism bias towards "safety signals" of low-pain cues (which might be specific to our sample population of healthy young adults).

The effect of expectations on perception

Overall, pain ratings were only affected by the stimulus intensity level and the cue mean (both $p < .001$), while in vision there were also effects of the cue variance (higher variance leads to higher ratings, as in Yoshida et al., 2013, $p = .005$), cue skewness (positive > symmetric, $p = .040$), and an interaction between the cue mean and the cue variance (larger effect of the mean when variance is lower, in accordance with Bayesian theories, $p = .008$).

We then developed and compared five computational models of cue-based expectation effects on perceptual ratings and found that (1) for most participants, cue-based expectations affected the ratings (i.e., models including cue-based expectations were significantly better than models ignoring them); (2) most participants did not learn to down-weight (or ignore) the cues, although they were not predictive of actual stimulus intensity (i.e., models including a prediction-error based learning process did not improve the model fit significantly); and (3) these processes were largely modality-general (i.e., modality-specific models were not significantly better than modality-general models).

We tested the effect of the cues on fMRI activity during painful stimuli with two *a priori* validated pain neuromarkers: The Neurologic Pain Signature (NPS, (Wager et al. 2013)), which is sensitive and specific to nociceptive pain, and the Stimulus Intensity Independent Pain Signature (SIIPS, (Woo et al. 2017)), which captures higher-level, endogenous influences on pain construction independent of stimulus intensity and the NPS score. The NPS score was affected by the stimulus intensity ($p < .001$) and not by the cue mean, variance, skewness, or their interactions. Conversely, the SIIPS score was only affected by the cue mean ($p = .020$). As expected, there were no effects on the neuromarkers' score in vision. In addition, multilevel mediation analysis revealed that the SIIPS, and not the NPS, formally partially mediated the effect of the cue-based expectations on pain ratings (Figure 2). Whole-brain voxelwise multilevel mediation revealed that several individual brain regions also mediated the effect, including the thalamus and prefrontal cortex in pain, and visual and prefrontal cortex in vision.

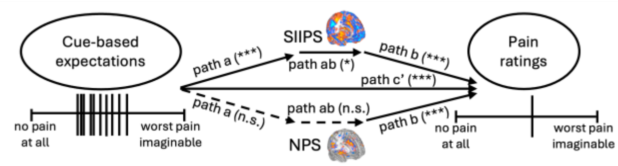

Figure 2. Multilevel mediation with neuromarkers.

Conclusions

Taken together, our findings suggest that perception is more complex than the recent Bayesian-driven focus on the mean and uncertainty of contextual information. More specifically, they show that extreme values have an important role in how people integrate information into expectations that later affect perception. Furthermore, these findings suggest that some aspects of expectation formation and their effect on subsequent perception are modality-general (e.g., the central influence of the cue mean and the importance of extreme values), while others are modality-dependent (e.g., the higher weighting of smaller values). Finally, participant-level perception models revealed meaningful individual differences across participants, with the minority of participants ignoring the cues completely, others learning to ignore them during the task, and the majority being consistently affected by the cues. Better understanding these differences between sub-populations and modalities would advance our knowledge of how people form predictions, how these predictions affect perception, and how these processes could be leveraged to improve well-being and clinical care.

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