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1 **Title**

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3 Bayesian learning models of pain - a call to action

4
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18
19 **Abstract**

20
21 Learning is fundamentally about action, enabling the successful navigation of a
22 changing and uncertain environment. The experience of pain is central to this
23 process, indicating the need for a change in action so as to mitigate potential threat
24 to bodily integrity. This review considers the application of Bayesian models of
25 learning in pain, which inherently accommodate uncertainty and action, which, we
26 shall propose are essential in understanding learning in both acute and persistent
27 cases of pain.

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29
30 **Highlights**

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32
- 33 • The experience of pain sits awkwardly in traditional stimulus-response paradigms
 - 34 • Accommodating uncertainty and action is imperative to learning models of pain
 - 35 • Bayesian models provide a normative, probabilistic account of learning in pain
 - 36 • Learning in pain is conceptualised as an ongoing prediction of the consequences of
37 action
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55 **Introduction**

56

57 The process of learning is fundamentally about action. In order to successfully navigate our
58 environment, we must continually learn about the ever-changing limits of our body and the
59 constraints that it imposes upon our interaction with the world. The experience of pain is
60 central to this process, indicating the point at which our bodily integrity is potentially
61 compromised through action.

62

63 The interaction between pain and learning can be better understood from an evolutionary
64 perspective, by adopting the concept of the explore-exploit dilemma [1]. When our bodily
65 integrity is threatened, we typically withdraw or rest (exploit) to allow sufficient recovery to
66 within bodily limits, at which point we decide to interact (explore) within our niche. We learn
67 over time when it is best to exploit and when to explore in order to promote adaptive
68 behaviour [2,3].

69

70 Learning in pain, however, is not straightforward, owing to the complexity that comprises
71 bodily integrity and worldly state. As a consequence, we find ourselves confronted with the
72 reality that in some cases pain persists, seemingly decoupled from acute protection and
73 adaptive behaviour. This necessarily goes beyond responding to and learning about a
74 nociceptive signal, extending to an overall appraisal of the bodily and sociocultural
75 environments in which we exist [4,5]. Adequately accounting for such a rich and diverse set
76 of interactions is the challenge faced in establishing a learning model in pain.

77

78 **Current application of learning models in pain**

79

80 Over the last 40 years, associative learning models have come to dominate our conception
81 of learning in pain [6]. These accounts are pervasive in different forms across the pain field,
82 from Pavlovian (habitual) to Operant (instrumental) conditioning in behavioural psychology
83 [7,8], extending to reinforcement learning and temporal difference models in computational
84 neuroscience [9–12]. Operationalised through the Rescorla-Wagner model, the heart of
85 associative learning models lies in the concept of an associative weight between stimulus
86 and response, ranging from immediate, reflexive stimulus-response (model-free) to more
87 complicated goal-directed actions, which alter proceeding stimuli (model-based) [13].

88

89 Through the application of associative learning theory, it is posited that persistent pain
90 reflects the generalisation of pain-related responses and maintained avoidance behaviour
91 [8,17]. This conceptualisation has shaped our understanding of pain in the behavioural
92 sciences, an influence seen from scientific investigation to clinical management.

93

94 Yet, the *experience of pain* sits awkwardly in these traditional stimulus-response models
95 [21,22]. In light of recent advances across neuroscience and behavioural domains, there is a
96 growing consensus that perceptual experience is a predictive process, in which learners
97 actively seek information to update their prediction of their internal and external environment
98 [23,24]. This is problematic for traditional associative learning models in pain for several
99 reasons. Firstly, pain is classically posited as a stimulus and conflated with nociception,
100 which downplays the significance of *pain as an experience* and its explanatory role within
101 theories of learning. Secondly, traditional associative learning models the state of the learner
102 as a series of punctate values at any given time [26], which belies the learner's uncertainty
103 [25–28]. Finally, associative models do not adequately accommodate the active nature of
104 the learner (i.e. being able to actively explore and intervene in their environment) [29]. It is
105 proposed that these challenges for traditional learning models may be overcome by taking a
106 Bayesian approach to learning in pain.

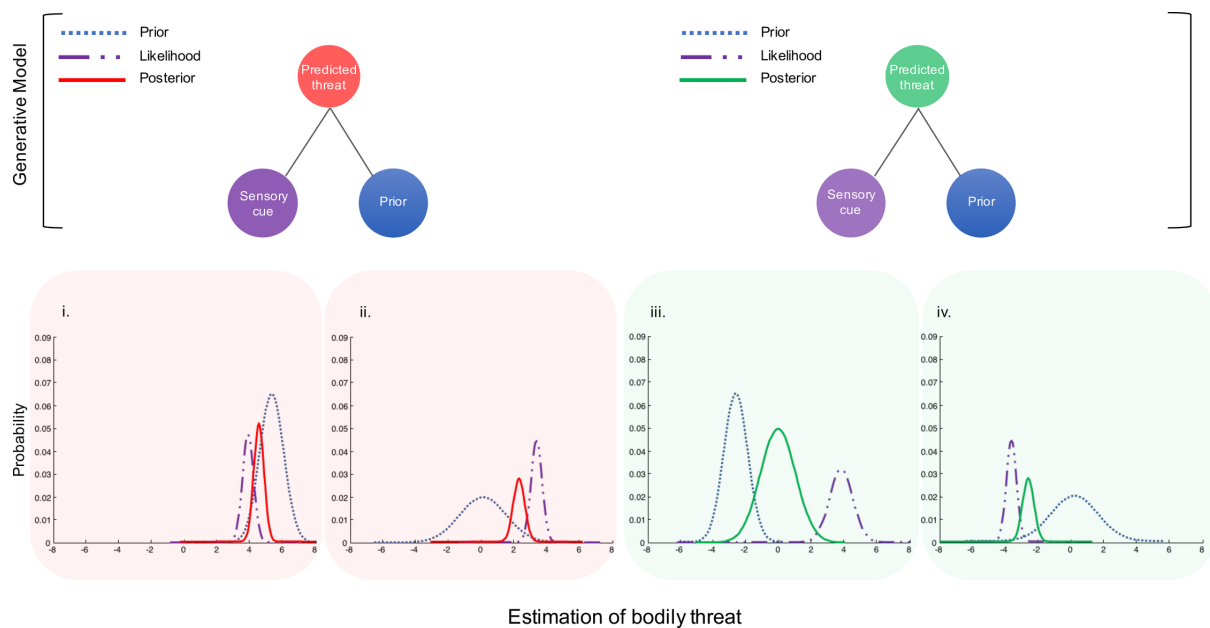
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108 **The Bayesian Framework**

109

110 Bayesian approaches to cognition comprise many distinct models and theories, used in a
 111 variety of domains, and spanning distinct levels of explanation. Often, these distinct
 112 approaches are grouped under the label 'Bayesian Brain hypothesis' [30,31], despite their
 113 many differences. This review will focus on the underlying Bayesian model that informs
 114 these approaches, specifying the Bayesian derivative where appropriate.

116 To date, the application of Bayesian models in pain has been limited to the description of
 117 perceptual experience, presenting pain as part of a probabilistic inference process that is
 118 shaped through the optimal integration of informative cues [27]. These models propose a
 119 mechanism for determining the hidden (latent) causes of encountered sensory information,
 120 summarised in a generative model [32]. In Bayesian terms, this is achieved through the
 121 weighted integration of prior experience and current (potentially multisensory) information,
 122 represented using probability distributions that reflect the agent's subjective uncertainty—the
 123 optimal integration of these probability distributions is given by Bayes' rule [33] (Fig. 1).
 124
 125



126
 127
 128 **Fig. 1. Generative models: Prediction of bodily threat (i-iv).** A generative model
 129 provides the framework from which predictions of the hidden causes of sensory
 130 consequences are generated (posterior), these are continually informed by multisensory
 131 sensory cues (likelihood) and previous encounters (prior). The relative precision, reflected in
 132 the probability density of these elements, influences the prediction. The more precise
 133 (narrow probability distribution), the greater the influence on the prediction. Threat panels
 134 (Left: i-ii) demonstrate the relative contribution of either a relatively precise prior (i) or precise
 135 likelihood (ii), the resultant prediction of threat is drawn toward the more precise source of
 136 information. In these cases, the sensory cue (likelihood) is the same in both panels, yet the
 137 relative precision of the prior determines the overall prediction of threat. Safety Panels
 138 (Right: iii-iv) demonstrate how the same relative precision can influence the prediction of
 139 negative threat, or safety. A precise prior, even in the presence of objective threat-based
 140 sensory cues, can influence the overall prediction to reflect safety (placebo effect) (iii).
 141 In contrast, an imprecise prior has less influence on the posterior (negative threat/safety) (iv).
 142 These hypothetical generative models demonstrate the possible decoupling of objective
 143 sensory information from experience, by accounting for the precision of the prior, which
 144 reflects the ongoing learning of the individual in keeping with previous experiences,
 145 homeostatic bounds and sociocultural constraints.

146

147 Although not directly about learning, these accounts expose the fundamental elements of
148 the Bayesian approach: a generative model, subjective uncertainty, and variable precision-
149 weighting. It is through the inherent encoding of the learner's uncertainty that Bayesian
150 models can shift away from specific associative weighting between variables towards a
151 learning account that is both predictive and active. This is a significant theoretical
152 development [26], which will form the basis of the proceeding review.

153 ***Learning under uncertainty***

154
155 In Bayesian approaches, learners are assumed to have only indirect access to the state of
156 their internal and external environment and must, therefore, infer their values on the basis of
157 their ambiguous and often incomplete information [34]. In contrast to associative learning models,
158 Bayesian models encode uncertain beliefs about the world as probability distributions [35].
159 They assume that learners maintain multiple hypotheses (with differing degrees of belief)
160 that reflect a range of candidate predictions about the state of the body and the world. This
161 invokes the notion of a generative model (Fig.1), which can be used to *generate* the
162 expected sensory consequences that may arise from hidden (latent) states of the
163 environment, and in absence of external stimulation [36,37].

164
165 According to Bayesian models, learning occurs through the adjustment of the prior
166 distribution (e.g. estimated threat), according to Bayes rule, when new sensory cues are
167 encountered. This asserts that over time a learner attempts to predict, with increasing
168 finesse, the state of the world. Rather than veridical reflections, these predictions are an
169 integration of probability distributions pertaining to the precision of the information.

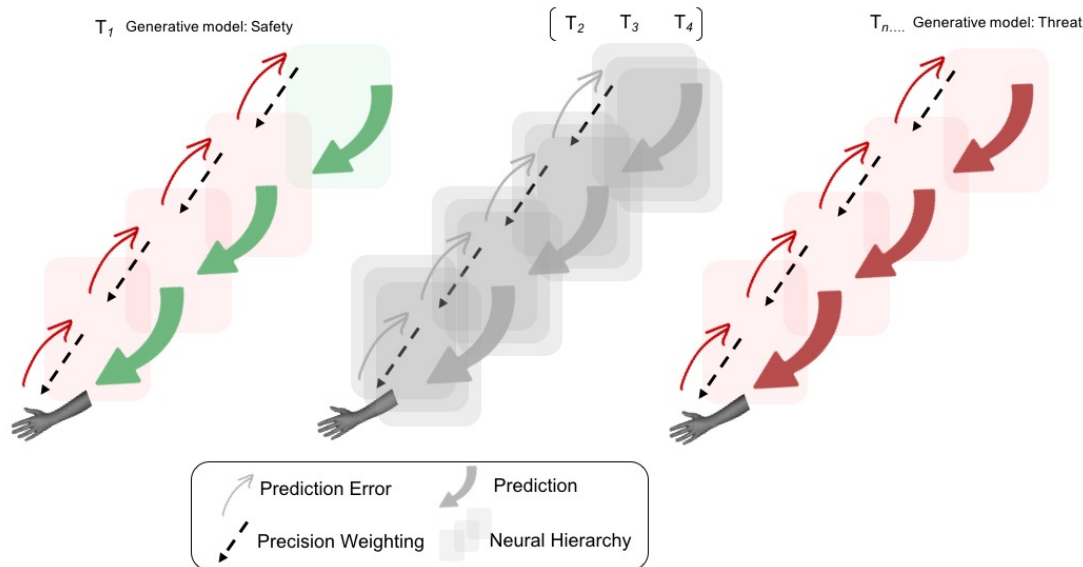
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171 An emerging framework, derived from a Bayesian approach, known as predictive processing
172 [23,38–40] casts the inferential process in probabilistic modelling as a matter of *prediction-*
173 *error minimisation*. According to this view, the learner's generative model gives rise to
174 multiple top-down predictions that are met by incoming sensory information (prediction
175 error). This is a competitive process, where the prediction that best captures the incoming
176 sensory information is selected, and perception arises as a result of successful prediction-
177 error minimisation¹.

178
179 The concept of prediction error here represents predictions and prediction-errors as
180 probability distributions, thus retaining the inherent encoding of uncertainty of an agent's
181 beliefs that is common to Bayesian approaches. In predictive processing, specifically, this
182 uncertainty is managed by precision-weighting mechanisms, which modulate the variance
183 associated with the respective distributions, in order to contribute to the overall goal of
184 minimising prediction error [41]. From this perspective, the learner's principle motivation is to
185 minimise the discrepancy between their prediction of the world and the sensory
186 consequences of it (prediction error), in order to ensure they maintain an accurate model of
187 their world (Fig.2). At a cortical level, it has been proposed that precision weighting of
188 prediction errors is mediated by dopamine, with the potential to influence both accurate and
189 aberrant learning [42–44].

190
191 As we shall explore, the learner can minimise prediction error in two ways: by updating the
192 parameters of their generative model in order to better predict the future sensory
193 consequences of action, or by holding the model fixed and altering their action within the
194 world to sample information that better reflects their predictions. These mechanisms are
195 described under the *Active Inference* framework [45].

196
197

¹ For a non-technical, conceptual introduction to the Predictive Processing framework see [23]. For an overview of how the free-energy principle applies to the brain see [57].



198
199

200 **Fig.2. Hierarchical Predictive Processing: from safety to threat.** Proposed within a
 201 neural hierarchy, generative models are shaped over time to reflect the precision weighting
 202 of information. There is a continual bidirectional flow of information at each level of the
 203 neural hierarchy involving top-down predictions, prediction error, and the precision-weighting
 204 of prediction error. Schematically represented over time, an initial generative model
 205 encompassing bodily safety entails the prediction of low bodily threat as a consequence of
 206 action. Over time, in the presence of prediction error (a deviation from predicted bodily
 207 safety or predicted bodily threat), the generative model is updated to reflect an alteration in
 208 action consequences, that of threat. It is suggested that the ability to flexibly update this
 209 prediction of threat, in the presence of new sensory evidence (e.g. safety cues), is
 210 imperative to the resolution of the need to experience pain.

211
212 **Active Learning**

213
214 The inherent uncertainty encoded in the agent's probability distributions not only satisfies
 215 learning paradigms that are typically challenging for associative theories (e.g backward
 216 blocking; see [26]), it crucially affords the agent an active role in reducing uncertainty. Active
 217 learning under this formulation is not simply the provision of an adequate sample space
 218 (spatial and temporal), it rests on the crucial ability of the learner to intervene in their world,
 219 sculpting the sensory consequences of their actions according to what is deemed most
 220 salient. The consequences of the learner's actions can either support or disconfirm the
 221 predictions of the consequences of action, offering multiple means by which to reduce
 222 uncertainty [46,47]. These considerations of active learning recognise ecological validity
 223 from the perspective of being in, and acting upon, the world, and where actions are taken
 224 based on the ongoing (motivational) homeostatic drives of the biological agent.

225
226 Active Inference²—a component of the predictive processing framework—extends these
 227 basic commitments and transforms the role of the learner in pain, from a passive processor
 228 of information, to a dynamic predictor of the relationship between the external and internal
 229 world. A key claim of the active inference model is that embodied action occurs as a result of

² For a review of active inference, which casts it as a process of descending projections (predictions) from motor cortex, see [43]. Other accounts have implicated the dopaminergic system as playing a key role in active decision-making, while also casting this within the framework of ecological psychology [44]. And, more recently, the active inference framework has been extended to incorporate homeostatic control [40, 51]. For a less technical overview, including empirical and theoretical support, see chapter 4 of [23].

230 an agent predicting (inferring) the outcomes of certain policies (e.g. reaching for a cup),
231 along with their associated precision estimations. The process of predicting future
232 consequences of actions (i.e. associated sensory information) leads to overt behaviour
233 through the activation of classical reflex arcs by downwards projections from motor cortex
234 [46]. An illustrative example would be a policy that controls an agent's task of reaching for a
235 cup. Prior to enacting the reaching behaviour, the predictions associated with grasping the
236 cup will be unfulfilled, and therefore result in error signals. However, instead of updating the
237 generative model, the agent can instead take actions that lead to the fulfilment of error
238 signals by actually reaching to grab the cup. In cases where the agent predicts that a certain
239 policy will also likely lead to the experience of pain (e.g. bending down to pick up a heavy
240 box), the agent may be reluctant to enact the respective behaviour, or choose to avoid it
241 altogether.

242
243 Seth [48] and others [51] have extended the active inference framework to account for
244 autonomic regulation, arguing that similar predictions generated by the AIC are sent to the
245 autonomic system via smooth muscles to activate autonomic reflexes in a similar manner as
246 earlier described in the case of proprioception. By focussing on the embodied nature of the
247 agent, active inference creates an intuitive segue that unites learning about the state of
248 external world (exteroception) with the state of the internal world (interoception). The same
249 predictive mechanisms that are responsible for predicting sensory states of the external
250 environment are also responsible for regulating the internal environment [48–50] and *for*
251 providing additional sources of information related to motivational drives [51]. Although often
252 separated in traditional theories, perception and action are entwined in active inference, due
253 to their dual-role in minimising uncertainty [15].

254
255 The proposition that a single underlying mechanism (i.e. precision-weighted prediction-error
256 minimisation) underlies learning about the condition of the body, has provided instrumental
257 guidance for describing the generation of aberrant bodily predictions and the development of
258 persistent pathological conditions [42,43,52–54]. It is suggested that persistent pain can be
259 formulated in such a way [55]. To illustrate this, the experience of pain is mapped onto the
260 'warning light' scenario, proposed by Adams et al, 2013:

261
262 *Consider a circumstance in which you are experiencing knee pain, you predict, with high*
263 *precision, that the consequences of your action in the world will compromise the integrity*
264 *of your body. Minor fluctuations in your interoceptive sensory cues (prediction errors) are*
265 *assigned high precision, which serve to confirm the prediction of potential threat and*
266 *propagate your experience of pain. You decide to visit your doctor who is unable to*
267 *determine a specific cause for your pain, they even present you with your x-ray that*
268 *shows "no structural cause for your pain". Your first thought is that your doctor has*
269 *missed something, that there must be something else going on, or that the x-ray has*
270 *been misinterpreted. From your perspective all of these are plausible hypotheses that*
271 *accommodate the evidence that is available to you. However, from the doctor's*
272 *perspective, without the knowledge that informs your prediction of bodily threat, your*
273 *suspicions seem irrational.*

274
275 This adapted account highlights the consequences of precision weighting of information in
276 the experience of pain. What is suggested is a decoupling between sensory input and
277 subjective experience, where the latter is dependent on the relative precisions afforded to
278 predictions and prediction error (Fig.2). The learner in pain updates the precision weighting
279 of information that reflects their generative model in a changing world, informing whether to
280 exploit or explore³. This places experiences of the body, whether well-defined through

³ Some have proposed that precision-weighting may also be responsible for the transient switching between online and offline control [41]—allowing an agent to deliberate about some future policy, prior to taking action within the world. Although generative models play a central role in guiding online

281 disease process or medically unexplained, on a continuum [55]. What distinguishes them is
282 the accuracy with which they account for the underlying physiological condition of the body.
283

284 Persistent pain, from this view, occurs as a consequence of precision: either via a precise
285 prediction of bodily threat (top-down) or through aberrant precision weighting of sensory
286 information (bottom up). In both cases, the prediction of bodily threat persists, and so with it
287 the experience of pain, detached from veridical evidence of tissue damage and
288 unchallenged by information assigned less precision. Altering the experience of pain this lies
289 in the ability to promote the flexible reassignment of precision weighting, which in turn alters
290 the individual's prediction about their body and the world.

291
292 The description of learning in pain thus becomes one that concerns optimal precision
293 weighting over time. Importantly, under normative models, optimality does not pertain to
294 accuracy. As such, aberrant but precise predictions of bodily threat (e.g. high precision-
295 weighting of noisy sensory signals), and an accompanying experience of pain, may persist in
296 the absence of an objective reality of threat. No more or less real, all experiences of the
297 body are a reflection of our evolutionary history, sociocultural present and action-oriented
298 future.

299

300 **Discussion**

301

302 One core pursuit of learning models in pain is to adequately accommodate the phenomena
303 of acute and persistent cases. That is, why do the majority of people experience pain as
304 transitory—an experience that efficiently promotes acute withdrawal, mitigating further
305 harm—while a significant minority continue to experience pain in a way that seemingly
306 contravenes optimal behaviour?

307

308 We have broadly considered Bayesian models and their relevance to learning in pain. It is
309 proposed that in order to accommodate the ecological validity of the learner in pain, the
310 concepts of uncertainty and active learning must be addressed. As such, derivatives of the
311 Bayesian model have been presented, which attempt to re-conceptualise the learner as an
312 action-oriented predictor of their environment.

313

314 An advantage of this approach is that learning in pain is considered under a unifying
315 framework. The experience of pain becomes a problem of precision-weighting, inherently
316 contextualised in relation to previous experience and future endeavour; both the resolution
317 and persistence of pain lies within one's ability to continually update the predictions of bodily
318 state.

319

320 The approaches that are described are not wholly opposed to the concepts present in
321 associative learning accounts (e.g. kalman filter and the Rescorla Wagner model) [26].
322 However, a probabilistic formulation of learning promotes an account that naturally extends
323 to the body and action [56], and is highly relevant to learning in pain, whereby the active
324 sampling of one's environment is fundamentally altered.

325

behaviour (i.e. active inference), by decoupling generative models from the incoming stream of sensory information (prediction errors), through the use of selective modulation of incoming prediction errors (precision-weighting), generative models may also guide deliberative processes such as planning and offline reasoning [41,51]. This flexible switching between offline and online control could be viewed as a type of arbitration mechanism for model-free and model-based forms of behavioural control, albeit one that may be best viewed as more of a continuum of cases, rather than a well-delineated set of options [41].

326 Bayesian formulations have proffered much, not least a unifying theory of mind [57]. Yet,
327 with such promise comes inevitable pitfalls [58–60], a number of which require consideration
328 here.

329

330 This review has focussed predominantly on the implementation of such models at an
331 instrumental level, describing the macro phenomena in pain-based learning, without delving
332 into the underlying neural architecture that such probabilistic models aim to account for [61].
333 Although increasing evidence supports the role of such realist applications in perception,
334 [39,42,62], including in pain [63,64], these are yet to mature into adequate models of
335 complex learning scenarios. Initial investigations comparing models of learning in pain,
336 including generic Bayesian models [65], suggest that there is work to be done to outperform
337 temporal difference models in computational neuroscience paradigms [66]. Consequently,
338 some have argued that the Bayesian Brain should be treated as an instrumental theory in
339 lieu of more developed mechanistic explanations [67]. An important question for the future
340 application of probabilistic models relates to the nature of our experimental paradigms in
341 pain. Using a model, designed to reflect an active learner who minimises uncertainty over
342 time, may demand an alteration in traditional stimulus-response protocols.

343

344 Associative learning theories would be considered incomplete without accounting for value,
345 reward or utility in relation to optimal behaviour. Bayesian generalisations of the Resorla-
346 Wagner model, embodied in the Kalman filter, assumes that the target of learning is the
347 problem of predicting immediate reward [68]. However, full active inference accounts aim to
348 replace the notions of reward, value or utility, by subsuming them all within the generative
349 model [13,69]. Whether these concepts can therefore be considered redundant, while still
350 accounting for the complexities of learning in pain and pleasure, is yet to be determined.

351

352 **Conclusion**

353

354 We have presented a broad overview of Bayesian models of learning in pain. From this
355 view, the experience of pain involves the continual prediction of the consequences of action
356 in relation to bodily threat. As such, learning in pain is both predictive and active. Although
357 there still exist many challenges to the full implementation of such probabilistic accounts, we
358 propose that at present, Bayesian derivatives (such as predictive processing and active
359 inference) can provide important considerations for researchers and clinicians alike.

360

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362

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