

# The dynamics of pain avoidance

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# The dynamics of pain avoidance: the exploration–exploitation dilemma

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Pain can be described as an urge to escape from bodily threat and is a driver of avoidance learning.<sup>8,13,67,70</sup> Although avoidance can be helpful in the early phases of pain, it can interfere with individuals' valued life goals, causing disability and distress.<sup>15,32,65</sup> Specifically, when performed after an injury has healed, avoidance may prevent individuals from updating their knowledge about their body, resulting in the maintenance of avoidance even when pain is no longer present.<sup>37,49</sup> The idea that avoidance is a maintaining factor in disabling pain has inspired research about how avoidance is learned and can be reduced.<sup>8,37,67</sup> Despite this increased interest, current pain avoidance research has yet to fully acknowledge at least 2 observations in clinical practice. The first observation relates to avoidance reduction techniques (exposure-based therapies) and their laboratory parallels (eg, extinction with response prevention procedures). Across those techniques, there is often the assumption that performing the avoidance response is unnecessary when the injury has healed (often the case in chronic pain) and thus avoidance should be stopped. However, a feared movement will often remain painful, possibly urging individuals to continue avoiding such actions.<sup>8</sup> Second, pain avoidance is commonly conceptualized and tested as the result of simple learning processes, where individuals quickly learn to avoid performing movements paired with pain or harm.<sup>28</sup> However, in everyday life, pain avoidance emerges in dynamic environments, where individuals sometimes will not perform an action that is expected to increase pain or bodily harm but at other times they will.<sup>28</sup> These observations suggest that current avoidance research need to consider pain avoidance as a *dynamic* phenomenon, meaning that the benefits and the costs of avoidance may vary as a function of the goals and the contexts within it is expressed. In this topical review, we argue that reconceptualizing the dynamic nature of pain avoidance in terms of how individuals solve the so-called *exploration–exploitation* dilemma (EED) opens a new window on how to study and treat avoidance in chronic pain.<sup>27</sup> Specifically, we argue below that a EED framework offers a more informative approach for

investigating laboratory avoidance compared with the existing procedures (eg, conditioning).

## 1. Acquisition and maintenance of pain avoidance

Traditionally, avoidance has been argued to be the outcome of learning that situations are predictive of aversive events (eg, pain), and as such, the appropriate response should be emitted to prevent such events to occur.<sup>37,67,69</sup> Going beyond this traditional view, motivational accounts consider avoidance as the result of a trade-off between preventing pain with some cost, vs achieving a valued goal despite pain.<sup>4,7</sup> There are several ways to understand this trade-off. In this study, it is described in terms of the organism balancing between *exploration and exploitation*. Exploration is the search for novel information, whereas exploitation is using the knowledge already achieved (see 36 for alternative definitions). Exploration is typically associated with curiosity,<sup>40</sup> whereas exploitation has been associated with dedicated, purposeful, goal-directed actions over an extended period.<sup>19</sup> Learning usually starts with exploration, which then gradually converges to the exploitation of the knowledge that is associated with better outcomes.<sup>19</sup> Both exploration and exploitation are imperative for survival.<sup>14,22</sup> Explorative behavior enables the discovery of actions that lead to stronger rewards, and exploitation is the repetition of choices known to be favourable. However, both hold risks. Exploration may increase the risk of wasting unnecessary energy or the occurrence of unknown threats,<sup>5</sup> whereas exploitation may hold the risk that actions are repeated despite diminishing benefits.<sup>5,36,56</sup> How individuals balance their decisions between exploration and exploitation is a key topic of research in computer science,<sup>57</sup> machine learning,<sup>2</sup> and neuroscience.<sup>54</sup> Pain avoidance research may greatly benefit from that research, especially those from the computer sciences.<sup>48,58</sup>

The theoretical models of EED<sup>17,36,58</sup> (see **Fig. 1** for an example) describe how individuals learn to predict future salient events (either appetitive or aversive) by making a cascade of decisions that may lead to aversive or appetitive outcomes.<sup>54</sup> In each step (or state<sup>58</sup>), the individual makes predictions about the outcomes of each action. The predictions are based on multiple sources of information, broadly classified as (1) individual (eg, personal knowledge about a situation, stress levels),<sup>31</sup> (2) environmental (eg, the available resources in each situation), and (3) social (eg, knowledge acquired through others; refer to Refs. 20,24 for relevant research).

The integration of all this information results in so-called *prior knowledge* in Bayesian models, or *generative model* in active inference models (see also Refs. 56,61), about the actions/stimuli and their probability of being followed by aversive/appetitive outcomes. Using that prior knowledge,<sup>59,60</sup> individuals have the option to explore alternative ways to search for new or additional

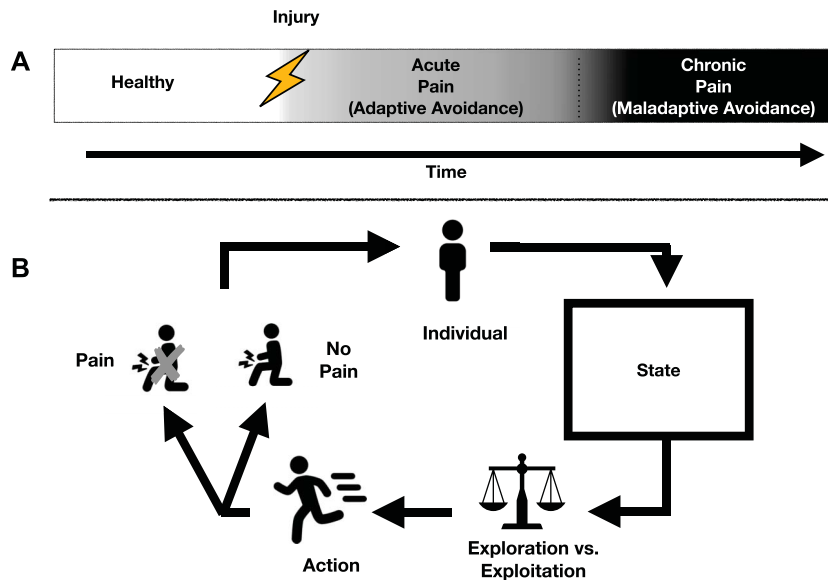
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**Figure 1.** Schematic of the differences between the standard acute/chronic pain distinction and the basic exploration–exploitation model. (A) According to the standard acute/chronic pain dichotomy, following an injury, the individual experiences acute pain, where avoidance is largely adaptive. If that pain persists for more than 3 months, then acute pain transforms to chronic pain and adaptive avoidance to maladaptive. (B) Example visualization of the EED decision process. In it, an individual enters a loop where they encounter different states. Based on the (prior) knowledge that the individual has, they need to balance between exploration and exploitation and perform an action (here running). After the action, an outcome is observed (here pain or no pain) after which the individual enters the next state, and a similar procedure is followed. See main text for more information. EED, exploration–exploitation dilemma.

knowledge (exploration) or decide to take advantage of the information they already have (exploitation). After deciding and having performed the chosen action, the outcome of the behaviour is observed, and the knowledge of the individual is updated accordingly. In case of expectancy confirmation, the prior knowledge is strengthened, whereas in the opposite case, the prior knowledge is weakened. The larger the discrepancy between the prediction and the actual event, the more learning occurs.<sup>38,50</sup>

In comparison to the current learning models for studying avoidance in pain,<sup>26</sup> these EED models can provide a better account of avoidance for at least 3 reasons. First, EED models can account for the dynamic nature of everyday behaviour, where avoidance may be expressed in some contexts (eg, when pain levels or risk of bodily harm are high) but stopped in other situations (eg, when pain levels remain but are low), depending on the current circumstances.<sup>30,62</sup> This dynamic character of avoidance aligns well with the dynamic nature of pain. For example, using experienced sampling methods (ESM), where participants report pain levels multiple times a day, Selby et al.,<sup>53</sup> showed that pain fluctuates over time in individuals committing self-injury. Experienced sampling methods could also be expanded to track avoidance as well (see also 9 for another ESM study with pain). Second, by focusing on variability in past experiences, EED can account for individual differences in excessive avoidance acquisition and reduction during exposure treatments, with earlier negative experiences<sup>23</sup> resulting in faster acquisition and slower extinction of avoidance behavior.<sup>35,63</sup> To illustrate, evidence suggests that exploration increases with more physical strength, cognitive capacity, and reduced levels of dopamine (see 4 for a review). It remains to be tested whether these individual differences also play a role in pain avoidance. A third reason is that research in the animal literature has extensively delved into EED, highlighting the continuity between human and nonhuman animals. Research on nonhuman animals has inspired human studies, offering fresh perspectives and challenges in

grasping complex human behavior (see Refs. 1, 36, 41 for the relevant literature). This involves human research on associative learning theory, which heavily leans on animal studies,<sup>11</sup> like those examining the role of conditioning in pain.<sup>67</sup> In addition, studies have explored decision making amid varying levels of uncertainty, aiming to compare human and nonhuman decision-making strategies, particularly in economic decision-making scenarios.<sup>10</sup>

Collectively, EED models can help in accounting for dynamic, real-life environments, holding promise that we can have a more accurate account of behavioural decision making in pain. In the next section, we expand on how EED models can help in reconsidering and expanding current views of the extinction of avoidance behavior in individuals with chronic pain.

## 2. Extinction of pain avoidance

One of the challenges in clinical practice is the reduction of disabling avoidance. Exposure-based treatments are becoming more prevalent and have demonstrated efficacy in reducing levels of pain-related fear.<sup>18,52,66</sup> The aim of exposure is to create a discrepancy between the prediction that certain pain-relevant (proprioceptive or interoceptive) stimuli lead to increased pain or bodily harm and the actual event (eg, that harm does not necessarily follow). For example, if a patient is afraid of bending because of an expected spine injury, they will be encouraged to bend, creating the surprising experience that this movement does not result in actual injury. These expectancy violations provide opportunities for new learning (eg, bending is safe) and are also in line with the theoretical models described in the previous section. Despite the ample evidence that exposure-based treatments successfully reduce pain-related fear, recurrence of fear and avoidance is common.<sup>8,55</sup> In this study, we suggest that exposure-based treatments can be seen as a way to optimize the balance between exploration and exploitation.<sup>68</sup>

First, drawing from the theoretical framework explained above (see **Fig. 1**), increasing curiosity between the actions that are expected to result in pain, and their actual outcomes will encourage exploration.<sup>16,40</sup> This can be done by increasing the uncertainty that pain will follow a pain-related stimulus or action. By this strategy, the information value of the pain-related stimulus or action increases, and thus, exploration is encouraged.<sup>40</sup> Second, encouraging individuals to engage in novel actions that are valuable on their own is likely to promote exploration (see 1 for relevant animal research). In addition, rewards for novel actions can be added, or reminding individuals that some feared actions can be followed by a rewarding outcome. Third, from the EED perspective, exposure can be considered a dynamic strategy that varies in time and context. Depending on the goal, the individual switches between exploring new actions and exploiting known ones. At the start of the treatment, new knowledge is acquired about the meaning of pain, and the associations between injury, pain, avoidance, and the disabling interference in daily life activities. After the exploration of this new knowledge, there could be a gradual shift in frequency from less exploration and more exploitation. In that sense, a key goal of exposure treatment is finding a balance between rest vs activity, stability vs change, and inflexibility vs flexibility through a sequence of behavioral experiments. The presented EED model could prove helpful also for interpreting other therapies than exposure. For example, pacing<sup>44</sup> or the regulation of boom-bust pattern of activities<sup>43</sup> can also be reconsidered as a strategy to shift between activity and rest, or how it is here explained exploration of novel actions or exploitation of known ones.

The EED also holds the potential to introduce a novel mechanistic framework for comprehending behavioural responses to pain, which can contribute to the development of treatments at an individual level. The progression of computational modelling<sup>29</sup> and machine learning presents modern algorithms that can enhance our understanding of the mechanisms underlying pain-related behavior. The combination of formal models and clinical knowledge could also help to better understand and reduce excessive pain avoidance. This is the case with computational medicine, where computational models are used to capture all information known about enabling the derivation of predictions regarding potential therapeutic targets.<sup>6</sup> In addition, this computational approach is already successful in areas like clinical psychology.<sup>3</sup> For instance, by identifying variations in reward reinforcement patterns on an individual basis, this knowledge can be translated into treatment paradigms that require enhanced reward stimuli compared with standard one-size-fits-all treatment protocols. It is timely for pain researchers to embrace the advancements in computational research and effectively translate those insights into the domain of pain.

### 3. Avenues for future research

The application of the EED in the field of pain offers new opportunities for the study of pain avoidance, and we present some research lines.

First, research has revealed various individual factors that can influence EED choices (see 36 for a review), but these await corroboration in the field of pain. Furthermore, it would be beneficial to examine individual difference variables that have been identified as relevant in the context of fear learning (eg, intolerance of uncertainty<sup>27,42</sup>), avoidance learning (eg, emotional stability<sup>33</sup>), or context (eg, where fear extinction takes place<sup>46</sup>). This knowledge could help in detecting which individual characteristics predict imbalances between exploration and exploitation behaviour. Identifying individual differences that

forecast a tendency toward increased exploitation could aid in tailoring personalized care for individuals with chronic pain. In this line of work, single case experimental designs<sup>25,45</sup> are particularly useful because they allow testing different treatments using idiographic measures without requiring large samples.

Second, certain clinical insights have not yet been incorporated into theoretical frameworks and experimental research. To illustrate, exposure-based protocols typically account for the dynamic nature of pain and formulate personalized protocols tailored to individual clients. This is currently not the case with formal theories of pain. Computational modelling enables the connection of theoretical models of psychological responses (eg, pain avoidance) to experimental observations.<sup>29</sup> For example, interoceptive psychopathology and pain have been explained through active inference models.<sup>47</sup> However, such models are often only informed by laboratory data and not so much of clinical data. The combination of formal models and clinical knowledge could also help to better understand and reduce excessive pain avoidance.<sup>64</sup>

Third, decision making implies that an explicit decision is made. Making no decision at all could also be construed as avoidance behavior,<sup>12,21,34,39</sup> such as is the case when postponing a serious surgical operation unless more information is acquired about the current condition of the patient. Such nondecisions seem to be just another instance of the EED, where individuals prefer sticking with the information they have, rather than risking experiencing pain by exploring new options.

Finally, a major challenge is how to model the complexity of real-world situations, where there is a panoply of options to choose from. In experimental studies so far, participants usually perform highly controlled tasks including few options and relatively simple probability distributions over pain and rewards following each option.<sup>27</sup> There is a need for studying EED in real-world environments using wearable sensors capturing moment-to-moment fluctuations,<sup>62</sup> eg, by using geolocation tracking to quantify exploration variability in daily movement patterns. To illustrate, Saragosa-Harris et al.<sup>51</sup> found that days of higher exploration were associated with greater positive affect and greater social connectivity, irrespective of age. Higher mean exploration was also associated with higher risk taking among adolescents.<sup>34</sup> These methods are promising, as they could be used to track the effects of exposure treatments on the exploration–exploitation balance in naturalistic settings of the patient.

### 4. Conclusion

In this review, we propose to study pain avoidance from the lens of the EED. To move beyond the idea that avoidance is something that once learned in acute pain and always will be performed in chronic pain, we suggest viewing behaviour as a chain of exploration–exploitation decisions irrespective of pain duration. The EED framework is a value-free new approach of pain avoidance considering its dynamic nature in real-life environments. Such view holds the promise for designing more refined individually tailored pain treatments.

### Conflict of interest statement

The authors have no conflict of interest to declare.

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### References

- Archer J, Birke LIA. Exploration in animals and humans. UK: Van Nostrand Reinhold, 1983.
- Auer P. Using confidence bounds for exploitation-exploration trade-offs. *J Mach Learn Res* 2003;3:397–422.
- Aylward J, Valton V, Ahn W-Y, Bond RL, Dayan P, Roiser JP, Robinson OJ. Altered learning under uncertainty in unmedicated mood and anxiety disorders. *Nat Hum Behav* 2019;3:1116–23.
- Claes N, Crombez G, Vlaeyen JWS. Pain-avoidance versus reward-seeking: an experimental investigation. *PAIN* 2015;156:1449–57.
- Cohen JD, McClure SM, Yu AJ. Should I stay or should I go? How the human brain manages the trade-off between exploitation and exploration. *Philos Trans R Soc Lond Ser B Biol Sci* 2007;362:933–42.
- Computational Medicine. Translating models to clinical care/science translational medicine. Available at: [https://www.science.org/doi/full/10.1126/scitranslmed.3003528?casa\\_token=C-mCz2Z3a-oAAAAA:dn2Tyb6ixy3zJ7TVY1lz7-zq9RfqPNW3v6oHO\\_ZWxl0nv0v4bl0WZg7\\_qONlftwzKpqYL8f9APVbQ](https://www.science.org/doi/full/10.1126/scitranslmed.3003528?casa_token=C-mCz2Z3a-oAAAAA:dn2Tyb6ixy3zJ7TVY1lz7-zq9RfqPNW3v6oHO_ZWxl0nv0v4bl0WZg7_qONlftwzKpqYL8f9APVbQ). Accessed January 26, 2024.
- Crombez G, Eccleston C, Van Damme S, Vlaeyen JWS, Karoly P. Fear-avoidance model of chronic pain: the next generation. *Clin J Pain* 2012;28:475–83.
- Crombez G, Eccleston C, Vlaeyen JWS, Vansteenwegen D, Lysens R, Eelen P. Exposure to physical movements in low back pain patients: restricted effects of generalization. *Health Psychol* 2002;21:573–8.
- Crombez G, Viane I, Eccleston C, Devulder J, Goubert L. Attention to pain and fear of pain in patients with chronic pain. *J Behav Med* 2013;36:371–8.
- De Petrillo F, Rosati AG. Variation in primate decision-making under uncertainty and the roots of human economic behaviour. *Philos Trans R Soc Lond Ser B Biol Sci* 2021;376:20190671.
- Delgado MR, Olsson A, Phelps EA. Extending animal models of fear conditioning to humans. *Biol Psychol* 2006;73:39–48.
- Dhar R. The effect of decision strategy on deciding to defer choice. *J Behav Decis Making* 1996;9:265–81.
- Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. *Psychol Bull* 1999;125:356–66.
- Eliassen S, Jørgensen C, Mangel M, Giske J. Exploration or exploitation: life expectancy changes the value of learning in foraging strategies. *Oikos* 2007;116:513–23.
- Fallon N, Brown C, Twiddy H, Brian E, Frank B, Nurmikko T, Stancak A. Adverse effects of COVID-19-related lockdown on pain, physical activity and psychological well-being in people with chronic pain. *Br J Pain* 2021;15:357–68.
- Friston KJ, Lin M, Frith CD, Pezzulo G, Hobson JA, Ondobaka S. Active inference, curiosity and insight. *Neural Comput* 2017;29:2633–83.
- Ghavamzadeh M, Mannor S, Pineau J, Tamar A. Convex optimization: algorithms and complexity. *FNT Machine Learn* 2015;8:359–483.
- Glombiewski JA, Holzappel S, Riecke J, Vlaeyen JWS, de Jong J, Lemmer G, Rief W. Exposure and CBT for chronic back pain: an RCT on differential efficacy and optimal length of treatment. *J Consulting Clin Psychol* 2018;86:533–45.
- Gopnik A. Childhood as a solution to explore-exploit tensions. *Philos Trans R Soc Lond Ser B Biol Sci* 2020;375:20190502.
- Goubert L, Vlaeyen JWS, Crombez G, Craig KD. Learning about pain from others: an observational learning account. *J Pain* 2011;12:167–74.
- Han Q, Quadflieg S, Ludwig CJH. Decision avoidance and post-decision regret: a systematic review and meta-analysis. *PLoS One* 2023;18:e0292857.
- Hills TT, Todd PM, Lazer D, Redish AD, Couzin ID. Cognitive Search Research Group. Exploration versus exploitation in space, mind, and society. *Trends Cogn Sci* 2015;19:46–54.
- Humphreys KL, Lee SS, Telzer EH, Gabard-Durnam LJ, Goff B, Flannery J, Tottenham N. Exploration—exploitation strategy is dependent on early experience. *Development Psychobiol* 2015;57:313–21.
- Karos K, Williams ACdC, Meulders A, Vlaeyen JWS. Pain as a threat to the social self: a motivational account. *PAIN* 2018;159:1690–5.
- Kazdin AE. Single-case experimental designs. Evaluating interventions in research and clinical practice. *Behav Res Ther* 2019;117:3–17.
- Kryptos A-M, Effting M, Kindt M, Beckers T. Avoidance learning: a review of theoretical models and recent developments. *Front Behav Neurosci* 2015;9:189.
- Kryptos A-M, Alves M, Crombez G, Vlaeyen JWS. The role of intolerance of uncertainty when solving the exploration-exploitation dilemma. *Int J Psychophysiol* 2022;181:33–9.
- Kryptos A-M, Crombez G, Alves M, Claes N, Vlaeyen JWS. The exploration-exploitation dilemma in pain: an experimental investigation. *PAIN* 2022;163:e215–33.
- Kryptos A-M, Crombez G, Meulders A, Claes N, Vlaeyen JWS. Decomposing conditioned avoidance performance with computational models. *Behav Res Ther* 2020;133:103712.
- Kryptos A-M, Moscarello JM, Sears RM, LeDoux JE, Galatzer-Levy I. A principled method to identify individual differences and behavioral shifts in signaled active avoidance. *Learn Mem* 2018;25:564–8.
- Lenow JK, Constantino SM, Daw ND, Phelps EA. Chronic and acute stress promote overexploitation in serial decision making. *J Neurosci* 2017;37:5681–9.
- Lerman SF, Rudich Z, Brill S, Shalev H, Shahar G. Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. *Psychosomatic Med* 2015;77:333–41.
- Lommen MJ, Engelhard IM, van den Hout MA. Neuroticism and avoidance of ambiguous stimuli: better safe than sorry? *Personal Individ Differ* 2010;49:1001–6.
- Luce MF. Choosing to avoid: coping with negatively emotion-laden consumer decisions. *J Consumer Res* 1998;24:409–33.
- Meacham F, T Bergstrom C. Adaptive behavior can produce maladaptive anxiety due to individual differences in experience. *Evol Med Public Health* 2016;2016:270–85.
- Mehlhorn K, Newell BR, Todd PM, Lee MD, Morgan K, Braithwaite VA, Hausmann D, Fiedler K, Gonzalez C. Unpacking the exploration–exploitation tradeoff: a synthesis of human and animal literature. *Decision* 2015;2:191–215.
- Meulders A. From fear of movement-related pain and avoidance to chronic pain disability: a state-of-the-art review. *Curr Opin Behav Sci* 2019;26:130–6.
- Miller RR, Barnet RC, Grahame NJ. Assessment of the Rescorla-Wagner model. *Psychol Bull* 1995;117:363–86.
- Minor J, Miller L, Ditrachs R. The effect of an undecided alternative on resolution of approach-approach and avoidance-avoidance conflict situations. *Psychon Sci* 1968;12:375.
- Modirshanechi A, Kondrakiewicz K, Gerstner W, Haesler S. Curiosity-driven exploration: foundations in neuroscience and computational modeling. *Trends Neurosci* 2023;46:1054–66.
- Mogil JS. Animal models of pain: progress and challenges. *Nat Rev Neurosci* 2009;10:283–94.
- Morriss J, Christakou A, van Reekum CM. Nothing is safe: intolerance of uncertainty is associated with compromised fear extinction learning. *Biol Psychol* 2016;121:187–93.
- Murphy SL, Kratz AL. Activity pacing in daily life: a within-day analysis. *PAIN* 2014;155:2630–7.
- Nielson WR, Jensen MP, Karsdorp PA, Vlaeyen JWS. Activity pacing in chronic pain: concepts, evidence, and future directions. *Clin J Pain* 2013;29:461–8.
- Onghena P, Edgington ES. Customization of pain treatments: single-case design and analysis. *Clin J Pain* 2005;21:56–72; discussion 69–72.
- Papalini S, Ashoori M, Zaman J, Beckers T, Vervliet B. The role of context in persistent avoidance and the predictive value of relief. *Behav Res Ther* 2021;138:103816.
- Paulus MP, Feinstein JS, Khalsa SS. An active inference approach to interoceptive psychopathology. *Annu Rev Clin Psychol* 2019;15:97–122.
- Pezzulo G, Parr T, Cisek P, Clark A, Friston K. Generating meaning: active inference and the scope and limits of passive AI. *Trends Cogn Sci* 2024;28:97–112.
- Philips HC. Avoidance behaviour and its role in sustaining chronic pain. *Behav Res Ther* 1987;25:273–9.

- [50] Rescorla R, Wagner A. A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. *Classical conditioning II: current research and theory*. Vol. 2. New York: Appleton-Century Crofts, 1972.
- [51] Saragosa-Harris NM, Cohen AO, Reneau TR, Villano WJ, Heller AS, Hartley CA. Real-world exploration increases across adolescence and relates to affect, risk taking, and social connectivity. *Psychol Sci*. 2022;33:1664–1679.
- [52] Schemer L, Schroeder A, Ørnbøl E, Glombiewski JA. Exposure and cognitive-behavioural therapy for chronic back pain: an RCT on treatment processes. *Eur J Pain* 2019;23:526–38.
- [53] Selby EA, Kranzler A, Lindqvist J, Fehling KB, Brillante J, Yuan F, Gao X, Miller AL. The dynamics of pain during nonsuicidal self-injury. *Clin Psychol Sci* 2019;7:302–20.
- [54] Seymour B, Daw ND, Roiser JP, Dayan P, Dolan R. Serotonin selectively modulates reward value in human decision-making. *J Neurosci* 2012;32:5833–42.
- [55] da Silva T, Mills K, Brown BT, Pocovi N, de Campos T, Maher C, Hancock MJ. Recurrence of low back pain is common: a prospective inception cohort study. *J Physiother* 2019;65:159–65.
- [56] Spelke ES, Kinzler KD. *Core knowledge*. *Develop Sci* 2007;10:89–96.
- [57] Sutton RS, Barto AG. *Reinforcement learning: an introduction*. Cambridge, Mass: MIT Press, 1998.
- [58] Sutton RS, Barto AG. *Reinforcement learning, second edition: an introduction*. Cambridge: MIT Press, 2018.
- [59] Tabor A, Thacker MA, Moseley GL, Kørding KP. Pain: a statistical account. *PLoS Comput Biol* 2017;13:e1005142.
- [60] Tenenbaum JB, Griffiths TL, Kemp C. Theory-based Bayesian models of inductive learning and reasoning. *Trends Cogn Sci* 2006;10:309–18.
- [61] Toates F. Exploration as a motivational system—a cognitive-incentive model. In: Archer J, Birke L, editors. *Wokingham, UK: Van Nostrand Reinhold, 1983*. Available at: <http://oro.open.ac.uk/66671/>. Accessed October 12, 2022.
- [62] Tottenham N, Shapiro M, Flannery J, Caldera C, Sullivan RM. Parental presence switches avoidance to attraction learning in children. *Nat Hum Behav* 2019;3:1070–7.
- [63] Trimmer PC, Higginson AD, Fawcett TW, McNamara JM, Houston AL. Adaptive learning can result in a failure to profit from good conditions: implications for understanding depression. *Evol Med Public Health* 2015;2015:123–35.
- [64] Van Damme S, Moore DJ. From the clinic to the lab (and back)—a call for laboratory research to optimize cognitive behavioural treatment of pain. *Transl Behav Med* 2012;2:102–5.
- [65] Vandael K, Vervliet B, Peters M, Meulders A. Excessive generalization of pain-related avoidance behavior: mechanisms, targets for intervention, and future directions. *PAIN* 2023;164:2405–10.
- [66] Vlaeyen J, Morley S, Linton S, Boersma K, Jong J. *Pain-related fear: exposure-based treatment for chronic pain*. Washington: IASP Press, 2012.
- [67] Vlaeyen JWS. Learning to predict and control harmful events: chronic pain and conditioning. *PAIN* 2015;156(suppl 1):S86–93.
- [68] Vlaeyen JWS, Crombez G. Behavioral conceptualization and treatment of chronic pain. *Annu Rev Clin Psychol* 2020;16:187–212.
- [69] van Vliet CM, Meulders A, Vancleef LMG, Vlaeyen JWS. The opportunity to avoid pain may paradoxically increase fear. *J Pain* 2018;19:1222–30.
- [70] Wall PD. On the relation of injury to pain. *The John J. Bonica lecture*. *PAIN* 1979;6:253–64.