Figures and figure supplements

The control of tonic pain by active relief learning

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Figure 1. Experimental paradigms. (a) Example trial in Experiment 1, which was an instrumental relief learning task (Ins) with fixed relief probabilities, yoked with identical Pavlovian task (Pav) within subject. In instrumental trials, subjects saw one of two images ('cues') and then chose a left or right button press, with each action associated with a particular probability of relief. In the yoked Pavlovian session, subjects were simply asked to press button to match the action shown on screen (appearing 0.5 s after CS onset). (b) Instrumental/Pavlovian session yoking and cue-outcome contingency in Experiment 1, arrows represent identical stimulus-outcome sequence. Note in contingency table, left and right button presses were randomised for both actions and cues. (c) Relief and no relief outcomes, individually calibrated, constant temperatures at around 44 °C were used to elicit tonic pain; a brief drop in temperature of 13 °C was used as a relief outcome (4 s in Experiment 1, 3 s in Experiment 2), but temperature did not change for the duration in no relief outcomes. (d) Example trial in Experiment 2, where subjects performed an instrumental paradigm (only) involving unstable relief probabilities. The cue-action representation was different to Experiment 1, and three cues were presented alongside each other with subjects required to choose one of the three using a button press. The position of each cue varied from trial-to-trial, and the same three cues were presented throughout. Tonic pain rating being taken before the outcome was experienced, not after as in Experiment 1. (e) Example traces of dynamic relief Figure 1 continued on next page
probabilities for the three displayed cues throughout all trials in eight sessions in Experiment 2, which required a constant trade-off of exploration and exploitation throughout the task. Dynamic relief probabilities also provide varying uncertainty throughout learning.

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Figure 2. Experiment 1: behavioural results. (a) Choice-fitted model comparison, TD model fit instrumental sessions choices best (TD: action-learning model with fixed learning rate, Hybrid: action-learning model with associability as changing learning rate, WSLS: win-stay-lose-shift model). Model frequency represents how likely a model generate the data given a random participant, while exceedance probability estimates how one model is more likely compared to others (Stephan et al., 2009). (b) Instrumental vs Pavlovian sessions SCRs (n = 15, sessions with over 20% trials <0.02 amplitude excluded). (c) Associability from hybrid model fitted trial-by-trial SCRs best in instrumental sessions (Assoc: associability, Hyb: hybrid model, RW: Rescorla-Wagner model). (d) Associability also fitted SCRs from Pavlovian sessions best. (e) Both pain and relief ratings did not differ significantly between instrumental and Pavlovian sessions (Participants’ ratings were averaged for each of the four categories shown, mean = 8 ratings per person per category).

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Figure 2—figure supplement 1. Experiment 1: raw skin conductance traces, where vertical lines are beginning of each trial when cue display starts (n = 15, excluded participants not shown, showing first non-excluded session from all participant).
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Figure 2—figure supplement 2. Experiment 1: filtered skin conductance traces (band-pass at 0.0159–2 Hz, 1 st order Butterworth), averaged across all trials within participant (n = 15, excluded participants not shown, shaded region represent SEM across all participants).
DOI: https://doi.org/10.7554/eLife.31949.006
Figure 2—figure supplement 3. Experiment 1: Model protected exceedance probability. Choice fitting remains similar to the original exceedance probability, however, SCR fitting comparison becomes less clear regarding best fitting model. DOI: https://doi.org/10.7554/eLife.31949.007
Figure 3. Experiment 1: neuroimaging results, shown at p<0.001 uncorrected: (a) TD model prediction errors (PE) as parametric modulators at outcome onset time (duration = 3 s). (b) Model PE posterior probability maps (PPMs) from group-level Bayesian model selection (BMS) within PE cluster mask, warm colour: TD model PE, cool colour: hybrid model PE (shown at exceedance probability P>0.7). (c) Axiomatic analysis of hybrid model PEs in instrumental sessions, ROIs were 8 mm spheres from BMS peaks favouring TD model PEs, in left putamen and VMPFC. (d) Associability uncertainty generated by hybrid model, as parametric modulators at choice time (duration = 0), in instrumental sessions. (e) Comparing pgACC activations across instrumental/Pavlovian paradigms, ROI was 8 mm sphere at [-3, 40, 5], peak from overlaying the pgACC clusters from Experiments 1 and 2.

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Figure 4. Experiment 2: behavioural results. (a) Model comparison showed that TD model fitted choices best (Bayesian: hierarchical Bayesian model, HMM: hidden Markov model, Hybrid: action-learning model with associability as changing learning rate). (b) SCRs measured on the side with thermal stimulation ('Stim side', left hand) were lower than those on without stimulation ('Non-stim side', right hand), but both were highly correlated. (c) Associability from state-learning hybrid model fit SCRs best, similarly to Experiment 1. (d) Trial-by-trial associability from hybrid model fitted pain ratings.

Figure 4 continued on next page
best compared with other uncertain measures (entropy: HMM entropy, surprise: TD model prediction error magnitude from previous trial, null model: regression with no predictors). (e) Regression coefficients with associability as uncertainty predictor were significantly negative across subjects.

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Figure 4—figure supplement 1. Experiment 2: raw skin conductance traces, where vertical lines are beginning of each trial when cue display starts (n = 20, excluded participants not shown, showing first non-excluded session from all participants).

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Figure 4—figure supplement 2. Experiment 2: filtered skin conductance traces (band-pass at 0.0159–2 Hz, 1st order Butterworth), averaged across all trials within participant (n = 20, excluded participants not shown, shaded region represent SEM across all participants). In Experiment 2, pain ratings took place immediately after cue display period, with variable length of rating time (participant terminates rating whenever they finish). This increased time gap between cue display and outcome account for the second peak in trial averaged SCR trace. DOI: https://doi.org/10.7554/eLife.31949.014
Figure 4—figure supplement 3. Experiment 2: model protected exceedance probability. Choice, SCR, rating fitting all remain similar to original exceedance probability figures.

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Figure 5. Experiment 2: neuroimaging results, shown at p<0.001 uncorrected: (a) TD model prediction errors (PE), at outcome onset time (duration = 3 s). (b) Model PE posterior probability maps (PPMs) from group-level Bayesian model selection, warm colour: TD model PE, cool colour: hybrid model PE (both shown at exceedance probability p>0.80). (c) Axiom analysis, separating trials according to outcomes and predicted relief values (bins 1–3 from low to high), BOLD activity pattern from striatum (putamen) satisfied those of relief PE. (d) Associability uncertainty generated by hybrid model correlating with pgACC activities, at choice time (duration = 0). (e) pgACC activation beta values across all subjects, ROI was 8 mm sphere at [-3, 40, 5], peak from overlaying the pgACC clusters from Experiments 1 and 2.
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Figure 5—figure supplement 1. Overlaying associability associated pgACC responses from both experiments (displayed at p<0.001 unc., crosshair at (-3, 40, 5)).
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Figure 5—figure supplement 2. Overlaying prediction error associated responses from both experiments (displayed at p<0.001 unc., showing overlapping dorsal putamen and amygdala clusters).

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