

Associations between aversive learning processes and transdiagnostic psychiatric symptoms revealed by large-scale phenotyping

Supplementary materials

Control task

Participants completed a control task that required avoidance that was not dependent on learning, in order to quantify each subjects' avoidance ability resulting from non-learning related factors. This allowed us to control for general motor-related avoidance ability in further analyses and ensured that relationships between our behavioural variables and psychopathology were not simply a result of non-learning factors such as reaction time. This task was similar to the to the main task, however a group of asteroids was always positioned to appear at the same Y position as the subject's current location. As in the main task, subjects had to avoid asteroids, but this was dependent only on the ability to move out of the way of oncoming asteroids rather than the ability to learn their position.

Computational models

We tested a range of computational models of the behaviour on our task. We focused on probabilistic models, termed "asymmetric leaky beta" models due to the fact that they update in response to safety and danger asymmetrically, and incorporate a leak parameter to imbue them with the flexibility to update estimates in response to incoming information rather than assuming safety probabilities are fixed. The basic machinery of this model family, along with the full best fitting model, is described in the main text, however here we describe variations that we also tested in addition to the reinforcement learning models tested.

Asymmetric leaky beta

This is the most basic model, which the other models build upon. This is described in the main text and is identical to the winning model but without the softmax transform and stickiness function.

Softmax-transformed asymmetric leaky beta

This model builds upon the basic model described above by incorporating a softmax transform on the estimated optimal position, as described in the main text.

Variance weighted asymmetric leaky beta

This model weights the two screen locations based on their variance when calculating the optimal Y position. The location with the lowest variance is weighed most highly, as follows. Firstly, a variance bias measure was calculated, representing the ratio between the variance of the top and bottom zones (labelled X and Y here).

$$\sigma_t^{bias} = \frac{\sigma_t^X}{\sigma_t^X + \sigma_t^Y} \quad (1)$$

This bias measure was then used to weight the safety probability estimates of the two options, such that the probability estimate was highest for the option with the lowest variance. This weighting was itself dependent on a free modulatory parameter π , to allow the amount of variance weighting to differ on an individual subject basis.

$$Pw_t^X = P_t^X \cdot (1 - \sigma_t^{bias} \cdot \pi) \quad (2)$$

$$Pw_t^Y = P_t^Y \cdot (1 - (1 - \sigma_{bias})_t \cdot \pi) \quad (3)$$

Upper confidence bound asymmetric leaky beta

This model also incorporates uncertainty into the position calculation, through an upper confidence bound rule. This means that rather than using the mean of the distribution as the location's safety estimate, an upper part of the distribution is used, the exact level of which is estimated as free parameter ω .

$$UCB_t^X = P_t^X + \omega \cdot \sqrt{\sigma_t^X} \quad (4)$$

The position is then calculated as follows:

$$pos_t = \frac{(UCB_t^X - UCB_t^Y) + 1}{2} \quad (5)$$

Rescorla-Wagner

We also tested two reinforcement learning models for comparison. The first of these was a standard Rescorla-Wagner model (1) which updates safety estimates based on prediction errors (δ) weighted by a learning rate (α), which is estimated as a free parameter.

$$P_{t+1}^X = P_t^X + \alpha \cdot (\text{outcome}^X - P_t^X) \quad (6)$$

Probability estimates are combined in the same way as the beta models and are also then passed through a softmax function with a free inverse temperature parameter to decrease the likelihood of positions near the centre of the screen.

Dual learning rate Rescorla-Wagner

The second reinforcement learning model we tested was an extension of the Rescorla-Wagner model (2) that allowed better and worse than expected outcomes to have differential effects on safety updates by introducing a separate learning rate for each

$$\delta = \text{outcome}^X - V_t^X \quad (7)$$

$$P_{t+1}^X = P_t^X + \begin{cases} \alpha^+ \cdot \delta & \text{if } \delta_t > 0 \\ \alpha^- \cdot \delta & \text{if } \delta_t < 0 \end{cases} \quad (8)$$

Probability estimates are converted to a single position estimate as in the previous models.

Correspondence between real and model-generated data

While our winning model provided a better fit to the data than other candidate models, it is important to ensure that our model truly produced data that was similar to subjects' real behaviour. We checked this in two ways: First, we calculated the R^2 value and Pearson's correlation between the true data and data simulated from our model with the estimated parameters for each subject, to ensure that we did indeed achieve a high correspondence between model-generated and true data. As these data were heavily skewed, due a small number of subjects where the model did not provide a good fit to the data, we report the median and interquartile range of the scores across subjects. These were 0.44 (0.26) and 0.70 (0.16) for R^2 and Pearson's R respectively (Figure S1A), indicating good concordance between model-generated and true data.

Second, we checked that a basic pattern of behaviour that emerged in the true data was also present in the model-generated data. Subjects tended to change their position more following a dangerous outcome than a safe outcome, as would be expected if they are learning to avoid threat (as shown in Figure 2A). We repeated this analysis on our simulated data, and observed the same pattern of results (Figure S1B).

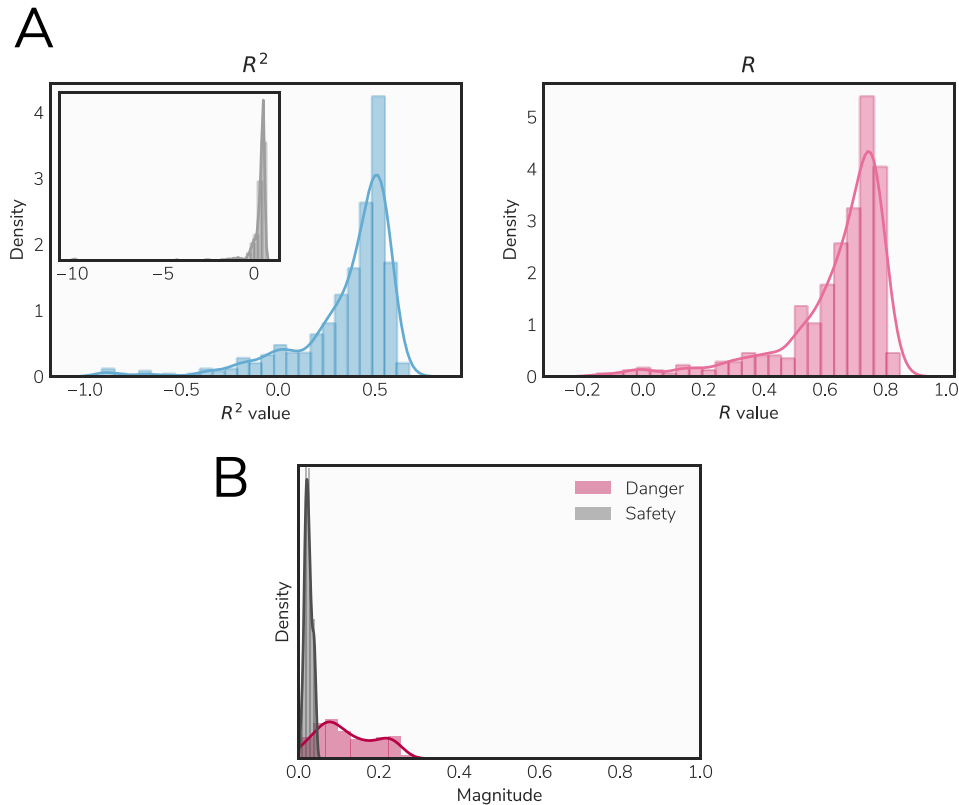


Figure S1. Correspondence between simulated and true data. A) Distributions of R^2 and R values across subjects, showing a high correspondence between the real and simulated data. The inset plot in the first panel shows the full distribution of R^2 scores (which can take any value below or equal to 1), including a small number of subjects with poor model fit, while the main figure shows the values between -1 and 1. B) Magnitude of position changes following dangerous and safe outcomes in simulated data, showing that simulated subjects tend to change position to a greater extent in response to danger than safety, as seen in data from real subjects.

A reduced set of questions for measuring transdiagnostic factors

We wished to investigate relationships with three transdiagnostic factors developed by Gillan et al., (2016). However, to reduce the number of questions used to determine scores on these three factors for each subject, and hence the time taken to complete the task, we used a data-driven approach to select the most important questions for determining factor scores. To achieve this, we used lasso regularised regression to predict each subject's factor score from responses to individual questions in data from the study by Rouault et al (3). Performing this analysis with a range of values of the hyperparameter C , which governs the degree of regularisation, produced a model that included varying numbers of questions as predictors. The ability of these models to predict the true factor scores was assessed using five-fold cross validation, whereby the model was trained on 80% of the data and tested on the remaining 20%, with this procedure repeated across combinations of training and test data and the prediction R^2 averaged across these five folds. Plotting this across values of C , and numbers of retained questions, allowed us to select a point at which we were able to achieve satisfactory accuracy with an acceptable number of questions. This resulted in a set of 63 retained

questions out of an initial 225 (Figure S2A, Table S1), which resulted in R^2 values of .91, .81, and .89 for the three factors (Figure S2B).

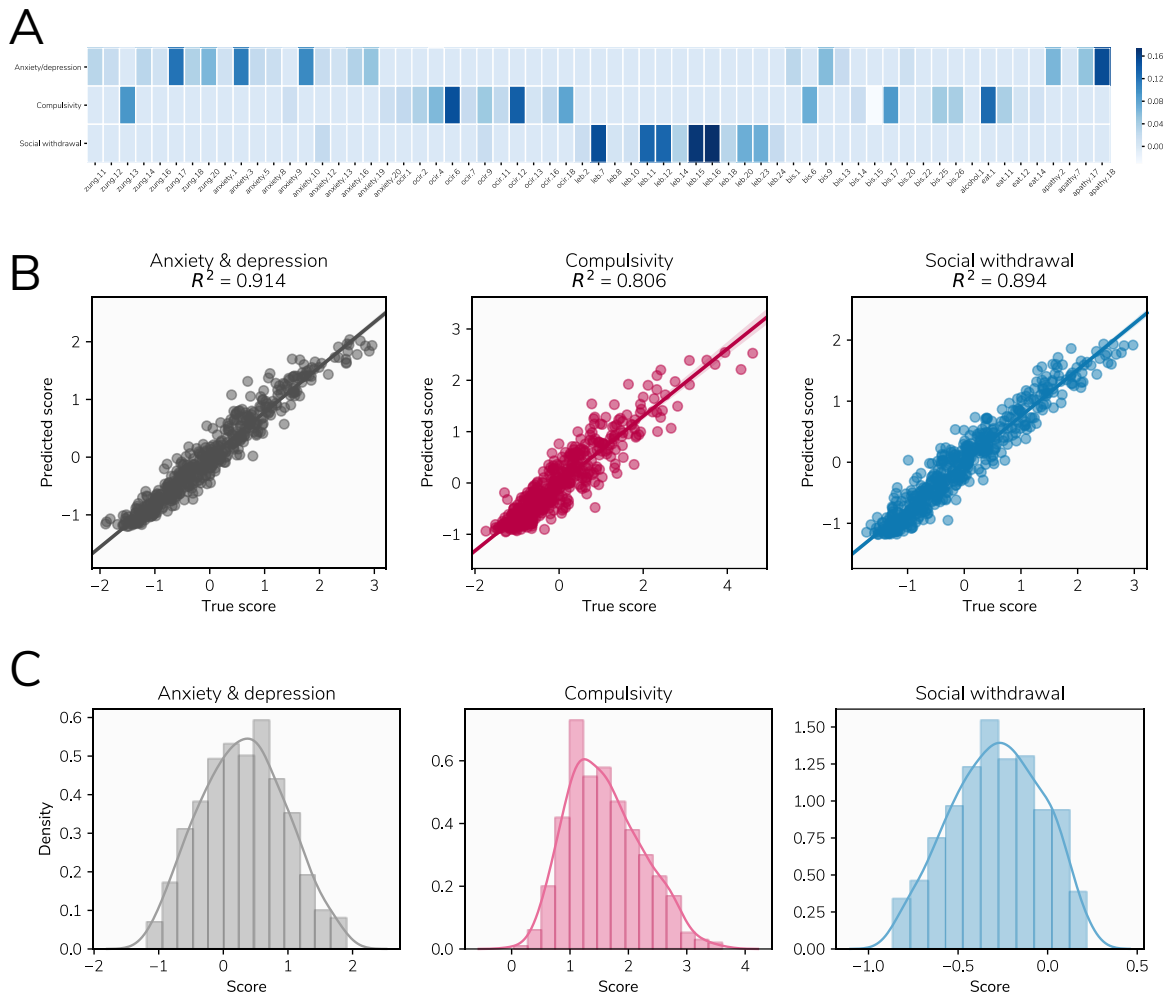


Figure S2. Result of question reduction procedure, finding a reduced set of questions that allow prediction of subject scores on the three transdiagnostic factors identified by Gillan et al. (2016). A) Weights of the retained questions in the regularised logistic regression model, demonstrating which questions are predictive of each factor. B) True factor scores from the study by Rouault et al. (2018) plotted against the cross-validated predicted factor scores from our model, demonstrating a high degree of accuracy. C) Distributions of factor scores in the data from the current study.

Table S1. Questions included in the reduced set of items used to approximate scores on the three factors derived by Gillan et al., 2016 (4).

Measure	Item numbers
Zung Depression Scale (5)	11, 12, 13, 14, 16, 17, 18, 20
State Trait Anxiety Inventory (trait subscale) (6)	1, 3, 5, 8, 9, 10, 12, 13, 16, 20
Obsessive Compulsive Inventory (Revised) (7)	1, 2, 4, 6, 7, 9, 11, 12, 13, 16, 18,
Liebowitz Social Anxiety Scale (8)	2, 7, 8, 10, 11, 12, 14, 15, 16, 18, 20, 23, 24
Barratt Impulsivity Scale (9)	1, 6, 9, 13, 14, 15, 17, 20, 22, 25, 26
Alcohol Use Disorder Identification Test (10)	1
Eating Attitudes Test (11)	1, 11, 12, 14
Apathy Evaluation Scale (12)	2, 7, 17, 18

Subjects with clinical levels of anxiety

Although we did not aim to recruit subjects with clinically-significant symptoms of anxiety, given the high prevalence of anxiety disorders it would not be unexpected to find subjects with such levels of anxiety in a large general population sample. We did not use any measure designed to diagnose anxiety disorders, and as such is impossible to determine for certain how many subjects would meet diagnostic criteria. However, it is possible to use approximate thresholds on other measures to provide an indication of the proportion of the sample who may have clinically significant anxiety symptoms. For our measure of trait anxiety, the STICSA (13), such a threshold has been identified by van Dam et al., (14). This study indicated that a score of 43 on the scale was able to distinguish individuals diagnosed with anxiety disorders from healthy controls with 74% accuracy. In our data, 144 of our 400 subjects (36%) scored above this threshold (Figure S3), indicating that a substantial proportion of our sample are likely to be experiencing clinically significant symptoms of anxiety.

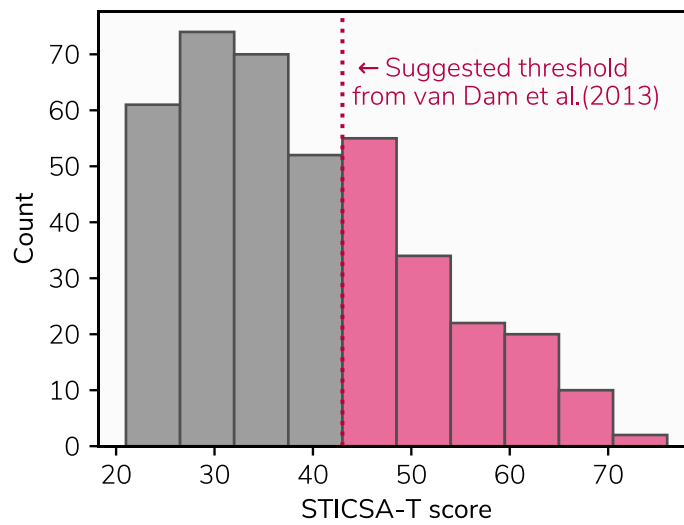


Figure S3. Proportion of subjects scoring above a threshold indicating likely presence of a clinical anxiety disorder determined by van Dam et al. (14). The dotted line indicates the threshold of 43 on the STICSA trait scale, while the histogram bars coloured pink represent subjects scoring above this threshold.

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