Figure S1 - Related to Figure 2a and Figure 3a: Fear responses during late Acquisition and early Test, presented separately for each CS type. a) Mean SCR for each CS type. b) Mean amygdala activity for each CS type. As in Figure 2 and Figure 3, t-tests were conducted to contrast the fear responses for the Target CS+ and Control CS+ in early Test. * $P<.05$. 
Figure S2- Induction likelihood of Target CS+ for each run (15 trials) of the daily Neural Reinforcement sessions. a) Mean induction likelihood for each run. Dashed line indicates a chance level of 50%. b) Variability of performance (s.d.) per run, averaged across participants. The gradual increase of Target CS+ likelihood suggests that the V1/V2 activation pattern for Target CS+ was successfully reinforced through the Neural Reinforcement sessions.
Figure S3 - Related to Figure 2b&c, and Figure 3: Correlation analysis for Neural Reinforcement session data. Same labeling as in Figure 2b&c, except the correlation is between activity level in amygdala and induction likelihood (V1/V2) in a&b, and between activity level in VMPFC and induction likelihood (V1/V2) in c&d. Error bars represent standard errors.
Figure S4 - Related to Figures 2&3: Absence of brain activity difference between two CS+s during late Acquisition and early Test in V1/V2 ROI used for the Neural Reinforcement session. Same labeling as in Figure 2a left and right panels, except the dependent measure here is the level of activity (arbitrary unit) in V1/V2. The difference between the Target CS+ and Control CS+ was not significant in late Acquisition ($t(16)=0.473$, $P=.643$) and in early Test ($t(16)=-0.198$, $P=.846$), suggesting that reduction of fear responses to the Target CS+ is unlikely to be due to the indirect effect of altered V1/V2 reactivity to the Target CS+. 
Figure S5 - Related to Figure 4c. A whole-brain searchlight analysis highlighting the voxels \((P<0.05,\) uncorrected) that showed significant correlation between the degree of information transmission during Neural Reinforcement and SCR reduction in early Test. Supplementing the result shown in Figure 4c, voxels in VMPFC were significantly anticorrelated with SCR reduction. A white horizontal line corresponds to the MNI coordinates where z=0.
Figure S6 - Related to Figure 4b: Results of a Psychophysiological Interaction (PPI) analysis examining the connectivity between striatum and a seed region of V1/V2 during the Neural Reinforcement sessions. Here, we particularly examined the connectivity of V1/V2 with striatum because it was predicted that striatum may have specifically interacted with V1/V2 during the Neural Reinforcement sessions, given striatal involvement has been implicated in reinforcement learning\textsuperscript{18,19}. The analysis revealed that voxels in caudate showed stronger connectivity during the trials with high Target CS+ likelihood in V1/V2 (>50%) than during the trials with low likelihood (<50%). Voxels showing significantly stronger connectivity on the high likelihood trials are highlighted ($P<0.05$; multiple corrections with permutation procedure\textsuperscript{21}).
Figure S7 - Related to Figures 2&3: Weak trends of possible generalization of fear reduction effect to “novel context.” a) Because we conducted all experimental sessions within the MRI scanner, it limited our ability to renew the context to test fear responses. As
an exploratory attempt, we changed the background from black to light gray to form a “novel” context. b) This was conducted 10 min after Test with original context, within the same session. c) SCR, amygdala activity and VMPFC activity in a novel context, averaged across all participants as in Early Test in main text Figures 2a, 3a&amp;b. Here we observed a weak trend of reduction of fear response for Target CS+ in SCR and amygdala activity (t(16)=1.321, \(P=0.205\); t(16)=1.218, \(P=0.241\); both two-tailed, for SCR and amygdala activity, respectively). One limitation was that Test in the original context might have in itself further reduced fear responses due to repeated presentation of the CS+s without US. As such, in the novel context, SCR was small even for Control CS+ (as compared to Figure 2a), and amygdala response was close to zero. This likely limited our ability to test for potential fear reduction in Target CS+. VMPFC activity did not differ between Target and Control CS+ (t(16)=0.800, \(P=0.937\), two-tailed). d) SCR, amygdala activity and VMPFC activity in the novel context, averaged across the participants who showed positive amygdala response to Control CS+ in this novel context (10 out of 17 participants). Fear responses were reduced for Target CS+, with SCR result reaching significance (t(9)=2.323, \(P=0.045\), two-tailed) and amygdala response approaching so (t(9)=2.005, \(P=0.076\), two-tailed). Error bars represent standard errors.

Future study could manipulate context more rigorously and/or manipulate the appearance of Target CS+ (e.g., tilt of grating) to further examine whether the effect of DecNef may generalize to novel contexts as well as other similar visual stimuli.
Supplementary Method

Apparatus for stimulus presentation

Visual stimuli were projected on a translucent screen by an LCD projector (DLA-G150CL, Victor). The projector spanned 20 × 15 deg in visual angle (800 × 600 resolution) and had a refresh rate of 60 Hz. All stimuli were generated with Psychtoolbox 3 running on Matlab.

Retinotopy session

We first conducted a standard retinotopic mapping experiment to define V1/V2 in each participant. Briefly, we first identified V1/V2 using conventional rotating wedge and expanding ring as stimuli, whose maximum radius (7.5 deg) was identical to the radius of a grating stimulus used in the subsequent sessions. Second, to further localize the subregions of V1/V2 that particularly corresponded to the visual field stimulated by the grating (1.5-7.5 deg in eccentricity), we presented a localizer stimulus. The localizer stimulus was a 16 sec duration of flickering colored checkerboard that was first presented within an annulus (1.5-7.5 deg) for 8 sec, and then presented inside the inner circle of annulus (1.5 deg radius) for another 8 sec. This localizer stimulus was presented in three runs of 14 trials. To maintain fixation, participants were asked to press a key with their right index finger when they noticed a change in the fixation color.

The obtained fMRI signals were preprocessed with mrVista software developed at Stanford University (http://vistalab.stanford.edu/software/). The functional images went through 3D motion correction without spatial and temporal smoothing. Then, the images went through rigid-body transformations to be aligned to the structural image for each participant. The fMRI signals from only the grey matter was extracted using a grey matter
mask. After the preprocessing, slice-timing was corrected, and runs were averaged for each stimulus type (wedge, ring, and localizer stimulus), before they were sent to a coherence analysis to define V1/V2 based on the activity related with stimulus presentation.

fMRI session for MVPA
Prior to the fMRI session for MVPA, we controlled for the luminance of three colors using flicker photometry\(^3\). The luminance of green and gray were each adjusted to be perceptually isoluminant to red with a fixed luminance. A trial was repeated 10 times per color (i.e., green or gray). On each trial, a red patch flickered with either a green or gray patch at 30 Hz. Participants were instructed to minimize perceived flicker by pressing keys to either increase or decrease the luminance of green or gray patch. The adjusted levels of luminance were kept constant for each participant throughout the rest of sessions.

During the fMRI session for MVPA, we presented a vertical grating containing a square-wave with a spatial frequency of 1 cycle/deg, which altered between black and one of three colors (red/green/gray). A grating was flickered at 0.5 Hz (6 sec total, three repeated sequence of 1.5 sec grating period and 0.5 sec blank).

There were 8 trials per color (e.g., red) in each of 12 runs. The order of color was randomized within each run. To maintain fixation, participants were instructed to press a key upon perceiving a luminance change of a fixation disc at the center of screen.

The obtained fMRI signals went through the preprocessing in the same manner as in Retinotopy session. Following preprocessing, the fMRI signals from the localized V1/V2 were further processed in the following steps: After removing a linear trend, the time-course in each voxel was z-transformed within each run to minimize the baseline
differences across the runs. The fMRI signal was averaged across 3 repetition times (TRs) which corresponded to the grating presentation period (6 sec). The signals were shifted by six seconds (3TRs) to compensate for the hemodynamic delay.

We used sparse logistic regression (SLR) to construct a color classifier. SLR automatically selected the voxels relevant for the discrimination of grating color from the voxels in the localized region within V1/V2. We trained the decoder using 192 data points obtained from 192 trials (across all 12 fMRI runs). The constructed decoder had an average of 107.65 voxels (+/- 68.93 s.d.) in V1/V2. The decoding accuracy was estimated with leave-one-run-out cross validation. The accuracy of the decoder to classify red versus green grating was 72.09% on average (+/- 9.24 s.d.), which was significantly above chance (50%) (t(16) = 9.86, P<.001; one-sample t-test, two-tailed). This decoding accuracy was similar to previous studies which successfully modified the targeted behaviours with similar neurofeedback procedures using MVPA. This suggests that the currently achieved decoding accuracy was sufficient to expect subsequent behavioural change (i.e., fear reduction) through the reinforcement of the decoded activation patterns. Although the decoder accuracy was modest initially, that only one out of the two CS+s was selectively paired with reward may also have enhanced the discriminability of the patterns over the days of Neural Reinforcement.

Acquisition session
Prior to Acquisition session, the intensity of electric shock was individually adjusted so that it was uncomfortable but tolerably painful. The intensity of electric shocks was set to each participant's tolerable level and delivered to participants' left wrist through an BrainAmp Ag/AgCl sintered MR electrode connected to a Digitimer constant current stimulator.
(DS7A-SP; Digitimer, Welwyn Garden City, UK). Skin conductance response (SCR) was recorded using BrainAmp Ag/AgCl sintered MR electrodes filled with skin conductance electrode paste. Two electrodes were attached to the distal phalanges of index and middle fingers of right hand.

Neural Reinforcement session

Neural Reinforcement was achieved using real-time fMRI with feedback control, and was motivated by previous studies that have shown successful modulation of neural activity using similar approach\(^8,9\). The Neural Reinforcement sessions were conducted for three consecutive days (see Main text). Each trial had a sequence of an induction period (6 sec), a fixation period (7 sec), a feedback period (1 sec), and an inter-trial interval (6 sec) (Figure 1e). Participants were instructed to remain fixated on the fixation point at the center of screen. During the induction period, V1/V2 activation pattern was analyzed online to estimate the likelihood that the currently achieved brain activation patterns represented the patterns for Target CS+ (red or green) that were previously decoded from the fMRI session for MVPA. This means that, the to-be-induced CS+ (e.g., red grating) served as Target CS+ while the other CS+ (e.g., green grating) served as Control CS+ which did not go through the Neural Reinforcement session. The color assignment for Target and Control CS+ was counterbalanced across participants (red as Target, N=9; green as Target, N=8) and was fixed throughout the Neural Reinforcement sessions. We applied the decoder constructed from another session (i.e., the fMRI session for MVPA) to each Neural Reinforcement session, by first aligning the scanning coordinate of each Neural Reinforcement session to match that of the fMRI session for MVPA\(^5,6\). We then applied
online motion correction with the Turbo BrainVoyager software (Brain innovation) in respect to the first EPI scan of the fMRI session for MVPA.6.

During the feedback period, the size of a white disc was presented to indicate the likelihood of an induction of the V1/V2 patterns for Target CS+ on that trial. The size of disc was determined as follows: First, we extracted the time-course of fMRI signals from the voxels selected for the constructed decoder (see the fMRI session for MVPA), and shifted the signals by 3TRs (i.e., 6 sec) to adjust for the hemodynamic delay. Second, after removing a linear trend, the fMRI signal time-course was z-score transformed for each voxel using the fMRI signals obtained during the 20 sec period following the initial 10 sec period from each fMRI run. Third, the processed fMRI signals for each voxel were averaged across the 3 TRs corresponding to Induction period from each trial. Lastly, we calculated the likelihood that the patterns of averaged fMRI signals represented Target CS+ using a decoder constructed from the fMRI session for MVPA. The disc size (i.e., radius) was proportional to the calculated likelihood of Target CS+ (0-100%). The feedback disc was presented inside a ring with a 5 deg radius, which indicated the maximum possible disc size. The disc size corresponded to the monetary reward of maximum 300 yen (US $2.5) per run. After each run, texts were presented on the monitor to inform the amount of monetary reward earned from the current run as well as the accumulated amount from the previous runs on that day. After completing the Neural Reinforcement session each day, participants received their monetary reward in cash. On each day, participants went through 12 fMRI runs with 15 trials each (20 sec per trial). Two participants were unable to complete all 12 runs in one of the three daily Neural Reinforcement sessions due to technical difficulty, so they instead performed additional run(s) on the other daily sessions to compensate for the missed run(s).
On Day 1 of the Neural Reinforcement session, the occurrence of Target CS+ pattern was around chance level (50.2± s.e. 4.1%; \( t(16)=.05, P=.96, \) two-tailed). Subsequently, Target CS+ likelihood exceeded chance level on Day 2 (58.9±3.1%) and Day 3 (57.2±3.3%) (\( t(16)=2.89, P=.01, t(16)=2.20, P=0.04, \) respectively), providing neural evidence of successful feedback reinforcement of the Target CS+ pattern. The effect of day was significant (ANOVA; \( F(2, 15)=3.62, P=.038 \)), which was primarily due to the increase of Target CS+ likelihood from Day 1 to Day 2 (\( P=.089, \) Bonferroni-corrected). Figure S2 more closely demonstrates that the occurrence of the Target CS+ pattern increased gradually across the runs of the Neural Reinforcement sessions. Although the improvement in induction of the Target CS+ patterns was somewhat modest, subsequent behavioural change was expected given that previous study with similar reinforcement techniques\(^5\) have successfully modified the targeted behaviours with similar degree of induction improvement (i.e., 5~10%). Such modest improvement of induction would be expected to be sufficient for fear reduction if we assume that the fundamental mechanism of fear reduction with our procedure was counter-conditioning (i.e., pairing of reward with induced Target CS+ patterns) rather than mere exposure (i.e., occurrence of Target CS+ patterns). In counter-conditioning, the absolute frequency of Target CS+ occurrence was not the most critical factor. It is sufficient to facilitate counter-conditioning so long as such pattern was consistently and selectively paired with reward. Over the 3 days, there was a sufficiently large variability in the trial-wise induction likelihood within each participant (across-participant mean of SD for the likelihood, 45.1%), hence exposing participants to a full range of contingency between the induction likelihood and its corresponding reward.

SCR was recorded during the Neural Reinforcement session, and was analyzed in the same manner as in Acquisition session while treating the onset of the induction period
as the onset of CS. Mean SCR for each Neural Reinforcement session is shown in Figure 2a (middle panel). To examine whether SCR was modulated by the likelihood that Target CS+ was induced in V1/V2, we examined the correlation between the trial-wise SCR and V1/V2 likelihood separately for each day of Neural Reinforcement session (Figure 2b&c). As neither SCR nor V1/V2 likelihood was normally distributed (see Figure 2b for the exemplar participant’s data), a Spearman correlation was used (In Figure 2b, \( \rho \) denotes the Spearman correlation coefficient, while the Pearson correlation coefficient \( r \) is also shown as a reference). The value of \( \rho \) was Fisher-transformed and averaged across participants (Figure 2c), which revealed no correlation between SCR and V1/V2 likelihood of Target CS+. Yet, because lower V1/V2 likelihood of Target CS+ corresponded to higher likelihood of Control CS+, it may be that increased likelihood of both Target and Control CS+ leads to increase in SCR. To test this possibility, we rectified the trial-wise likelihood by calculating the difference from 50% likelihood (i.e., representing neither Target CS+ nor Control CS+) to estimate the general likelihood of CS+ (without Target/Control distinction), and examined whether such rectified likelihood may correlate with SCR. However, even after rectification, CS+ likelihood showed no correlation with SCR during the Neural Reinforcement sessions (for Day 1, Day 2, and Day 3, \( \rho = -0.021 \pm 0.084 \) s.d.; \( \rho = 0.004 \pm 0.087 \); \( \rho = 0.006 \pm 0.081 \). As in Figure 2c, the \( \rho \) value was Fisher-transformed and averaged across participants).

**Test session**

A day after the last day of the Neural Reinforcement session, we conducted the Test session in the original context (i.e., black background color, Figure S7a) to measure fear responses to Target CS+, Control CS+, and CS- (see Main text). After a 10-minute break,
another session starting with reinstatement was repeated in the same procedure except that the background color of CSs was changed from the original color (black) to a novel color (light gray) to form a novel context (Figure S7a&b). In both original and novel context (Figure 2a, Figure S7c&d, respectively), to estimate fear responses in early Test, we calculated the mean SCR during the first 2 trials for each CS type. We presented four unsignaled USs intermittently presented across a 60 sec period 10 minutes before the Test session to activate the fear memory (i.e., Reinstatement). A trial sequence was identical to Acquisition session, except that there was no trial with US. After CS- was presented on the first trial to capture irrelevant orienting response (see main text), Target and Control CS+ were presented on the second and third trials, in counterbalanced order, and the order of remaining trials was randomized.

Analyses

**SCR analysis**

The amplitude of a skin conductance deflection within a 0.5 to 4.5 sec window from the onset of CS was measured. SCR amplitude was square-root transformed and then scaled to the average of US magnitude during Acquisition, following previous procedures. To compute SCR for each CS+, SCR for CS- was subtracted away as baseline for each participant.

**fMRI analysis**

To functionally define an amygdala ROI that represents fear responses, we first defined anatomical amygdala boundary with freesurfer segmentation. Then, we selected voxels
within this anatomical boundary that showed greater activity for all US trials and the last 2 trials of each CS+ (i.e., fear relevant trials) relative to fixation during the Acquisition session (at a threshold of \( P < .5 \)). To functionally define a VMPFC ROI, we first created an anatomical mask of a sphere with 15 mm radius centered around previously reported MNI coordinates \([0, 40, -12]\) which was estimated based on the representative literature\(^{12-14}\).

We then selected voxels within the sphere ROI that showed smaller activity for all US trials and the last 2 trials of each CS+ relative to fixation during Acquisition (\( P < .5 \)). Because it has been reported that there is considerable variability in the hemodynamic response function (HRF) in the amygdala\(^1\), to efficiently estimate activity in that region, we employed individually estimated HRFs based on the actual response for the US trials and last 2 CS+ trials, using a function from the mrVista software which estimates HRF based on the time course of fMRI signals for the relevant signal conditions (i.e., US trials and last 2 CS+ trials) relative to noise (i.e., fixation) (http://vistalab.stanford.edu/software/).

Analyses in areas other than the amygdala were conducted using the standard HRF (difference-of-gamma) implemented in mrVista.

To estimate activity for each CS presented in different phases of experiment, we obtained Beta coefficient from a GLM analysis applied to the averaged time course within each ROI, which reflected weight of the HRFs needed to fit the data. For the Acquisition session, a GLM was constructed with seven event types (Early 6-trials of Target CS+, Control CS+, CS-, Late 2-trials of Target CS+, Control CS+, CS-, as well as all US-trials). For the Test session, a GLM was constructed with seven event types (Very first CS- trial; Early 2 trials of Target CS+, Control CS+, CS- (i.e., 2nd and 3rd CS-); Remaining-trials of Target CS+, Control CS+, CS-). For Acquisition and Test, early and late trials were coded
as separate event types, to highlight the activity for late Acquisition and early Test as in the SCR analyses.

The estimates of activity for late Acquisition (left panels) and Early Test (right panels) are shown in Figure 3a&b for the amygdala and VMPFC, respectively. For the Neural Reinforcement sessions, a GLM was constructed with two event types (an induction period and feedback period) to estimate the activity in the amygdala and VMPFC (the middle panels of Figure 3a&b, respectively). Moreover, to examine whether the activity in the amygdala and/or VMPFC during the Neural Reinforcement session was modulated by the likelihood that Target CS+ was induced in V1/V2 (Figure S3), we further estimated the trial-wise activity for each ROI: First, after regressing out the fMRI signal explained by the feedback onsets, we averaged the fMRI signal across the three time points (i.e., 3 TRs) encompassing the 6 sec induction period. Here, the hemodynamic delay of 6 sec was considered. Then, we examined the relationship between the trial-wise activity and the V1/V2 likelihood with a Spearman correlation. Figure S3a&c show an example participant’s data to demonstrate the correlation between the induction likelihood and the activity in the amygdala or VMPFC, respectively (Pearson correlation coefficient $r$ is also shown as a reference). The Spearman correlation coefficient rho was Fisher-transformed and averaged across participants for amygdala and VMPFC (Figure S3b&d, respectively). Yet, as described earlier in the section of the Neural Reinforcement session in Supplementary Method, because lower V1/V2 likelihood of Target CS+ corresponded to higher likelihood of Control CS+, the increase of likelihood for both Target and Control CS+ may have led to the fluctuations in the hemodynamic responses in the amygdala and/or VMPFC. We therefore rectified the V1/V2 likelihood by calculating the difference from 50% (i.e., representing neither Target CS+ nor Control CS+) to estimate the general
likelihood of CS+ (without Target/Control distinction), and examined whether such rectified likelihood may correlate with the activity levels in the amygdala and/or VMPFC. However, similarly to the results with SCR, even after such rectification, CS+ likelihood showed no correlation with amygdala and VMPFC activity level during the Neural Reinforcement sessions (For the correlation with the amygdala on Day 1, Day 2, and Day 3, rho=.020±.079 s.d.; rho=.002±.087; rho=.020±.100. For VMPFC, rho=-.011±.098; rho=-.009±.083; rho=-.024±.100. As in Figure S3, the rho value was Fisher-transformed and averaged across participants).

MVP Analysis

To binary decode the colors of the grating (i.e., red and green) from the fMRI signal in V1/V2, we built a decoder using sparse logistic regression (SLR) which automatically selects relevant features (i.e., voxels) for MVPA\textsuperscript{4,16}. We used SLR over other algorithms such as support vector machine (SVM) for three reasons: First, SLR is advantageous when the number of features greatly exceeds the number of data sets\textsuperscript{4}. Secondly, SLR can output the predicted class in terms of its likelihood, which allowed us to give a fine increment of feedback during Neural Reinforcement reflecting the likelihood that the current activation patterns belonged to the Target CS+ (red or green, counterbalanced). Lastly, previous studies\textsuperscript{5,6} using SLR have succeeded in modifying behaviours through neurofeedback.

SLR uses a linear discriminant function (LDF) which discriminates two classes, S\textsubscript{1} and S\textsubscript{2} (Target CS+ and Control CS+, respectively), based on the weighted sum of the value from each feature (voxel),

\[
f(x; \theta) = \sum_{d=1}^{D} \theta_d x_d + \theta_0.\tag{1}
\]
Where \( x = (x_1, \ldots, x_D)^T \in \mathbb{R}^D \) is the input vector of each feature (i.e., fMRI signal in a voxel) in \( D \) dimensional space, and \( \theta = (\theta_0, \theta_1, \ldots, \theta_D)^T \) is the weight vector including a bias term \( (\theta_0) \). The boundary between the two classes is represented as the hyperplane where \( f(x; \theta) = 0 \). Logistic regression outputs the likelihood of category \( S_1 \) (i.e., Target CS+) for an input feature through the logistic function,

\[
p = \frac{1}{1 + \exp(-f(x; \theta))} \equiv P(S_1 | x). \tag{2}
\]

Here, \( p \) equals to 0.5 when \( f(x; \theta) = 0 \) (i.e., the boundary). \( p \) approaches 0 or 1 when \( f(x; \theta) \) becomes closer to plus or minus infinity (away from the boundary), respectively.

Given that our data set had a smaller number of samples relative to the number of features (voxels), logistic regression was not directly applicable. Therefore, we implemented the dimensionality reduction by automatically pruning out irrelevant voxels. More detailed description of this automatic relevance selection can be found in Yamashita et al.\(^4\).

The constructed decoder was used in Neural Reinforcement, to estimate the trial-wise likelihood of Target CS+. The estimated likelihood was then reflected as the size of disc to give a feedback to the participants on each trial. As the decoder was built to classify the V1/V2 activation patterns into either Target CS+ (e.g., red grating) or Control CS+ (e.g., green grating), the induction likelihood of 100% and 0% corresponded to the induction of Target CS+ and Control CS+, respectively. Therefore, the likelihood of 50% corresponded to the equal likelihood of Target CS+ and Control CS+. The SLR decoder built with hundreds of features (i.e., voxels) is expected to show bimodal response (i.e., likelihood clustered around 0% or 100%), because an argument within the logistic function takes either large positive or negative value. This bimodal nature of the decoder output was beneficial in clearly informing the participants with their success in manipulating their brain activity.
Whole brain “Information Transmission” analyses with searchlight method

To examine whether any brain region was engaged when the Target CS+ pattern was induced in V1/V2, we conducted a whole brain MVPA with a searchlight method\textsuperscript{17}. Specifically, we estimated the degree to which the trial-wise likelihood of Target CS+ in V1/V2 can be reconstructed from the activation patterns elsewhere in the brain, by moving a sphere ROI (radius=15 mm, M=266 voxels) centering each voxel of the whole brain. The ability of a given sphere ROI to reconstruct the V1/V2 likelihood was used as the estimate of information transmission between V1/V2 and the sphere ROI\textsuperscript{5,6}. We adopted such information theoretic approach to detect the co-occurrence of Target CS+ between V1/V2 and elsewhere in the brain, because it ensures sensitivity in detecting the occurrence of Target CS+ outside of V1/V2. That is, one alternative approach to estimate the Target CS+ occurrence outside of V1/V2 could be to construct a decoder for each sphere ROI and estimate the Target CS+ likelihood within such ROI during DecNef, independently from the Target CS+ likelihood of the V1/V2. However, decoding of red/green colors outside the visual area has been shown difficult\textsuperscript{6}, making it likely to observe only near-chance likelihood of Target CS+ outside of V1/V2. Therefore, in order to have sensitivity in detecting the non-random occurrence of Target CS+ in other brain regions, we examined the co-occurrence of Target CS+ in V1/V2 and other regions.

The analysis was conducted to yield a whole brain map highlighting the voxels that showed significant information transmission with V1/V2 during the Neural Reinforcement sessions (Figure 4b). This analysis included the whole grey matter, amygdala, and striatum (~32000 voxels). The amygdala and striatum were included in this analysis given these
areas are generally implicated in fear learning and reinforcement learning, respectively. More detailed procedure is as follows.

We first tested the sensitivity of the information transmission analysis on the fMRI data during the fMRI session for MVPA. We trained a decoder to reconstruct the V1/V2 likelihood from the activation patterns in each sphere ROI. Here, the decoder was constructed with sparse-linear-regression decoder. The decoders were trained with a leave-one-run-out cross validation procedure using the entire data set (i.e., 12 runs of the fMRI session for MVPA). That is, the likelihood for the trials in a given run (i.e., test set) was estimated based on the decoder build from the trials in rest of the runs (i.e., training set).

Because both the V1/V2 likelihood and the likelihood in each sphere ROI were at least partly driven by the common externally presented grating stimuli, we expected some information transmission between V1/V2 and other visual areas during the fMRI session for MVPA. To estimate the reconstructability of V1/V2 likelihood from each sphere ROI, we calculated Pearson correlation between the trial-wise estimates of the Target CS+ likelihood in each sphere ROI and the likelihood of Target CS+ in V1/V2. Here, the likelihood in V1/V2 was estimated using the same decoder built for online feedback during the Neural Reinforcement session (see fMRI session for MVPA for details). This correlation analysis was repeated for each sphere ROI, yielding a whole brain map of the Fisher-transformed correlation coefficient (i.e., information transmission). These analysis steps were conducted within the naive coordinate of each participant.

To perform a group level analysis, the map of each participant was non-linearly projected to the MNI coordinates and spatially smoothed by a Gaussian filter (FWHM=6 mm). Then, t-test on the Fisher-transformed correlation coefficient was performed for each voxel (against chance level, 0). To properly correct for multiple testings, a threshold for the t-values
was determined with a permutation procedure\textsuperscript{21} with which a t-value was iteratively (1000 times) calculated based on the randomized data set in order to find the threshold defining 5 percentile of the histogram of the t-values. Any voxel with t-value above the threshold was considered to be significant and is shown in Figure 4a. As was expected, the results showed that there was a widely spread information transmission mostly in, yet not confined to, the visual cortex (Figure 4a). This result ensured the sensitivity of the searchlight analysis to detect information transmission outside the V1/V2, if there is any.

We next applied the same searchlight analysis procedures to estimate information transmission outside V1/V2 during the Neural Reinforcement sessions. Here, the likelihood in V1/V2 was the same as the estimates computed online during the Neural Reinforcement session. The decoders were built using the entire data set from the fMRI session for MVPA. The result showed that significant information transmission with V1/V2 was much more confined to the lower visual areas (Figure 4b), compared with the result for the fMRI session for MVPA (Figure 4a). However, one of the exceptions was the striatum, mainly the left caudate (Figure 4b), a brain region implicated in reinforcement learning\textsuperscript{18,19}. Therefore, it appears that repetitive pairing of reward with the induced Target CS+ pattern in V1/V2 led to significant engagement of the striatal area (i.e., caudate) implicated in reinforcement learning.

"Information Transmission" in VMPFC during Neural Reinforcement and fear reduction

We next conducted ROI-based analyses to examine whether information transmission in particular brain region was related with fear reduction. Here, we particularly examined the amygdala and VMPFC given their distinct roles in conventional fear extinction learning\textsuperscript{13,22} as well as two striatal subregions, namely the caudate and ventral striatum, given their roles in reinforcement learning\textsuperscript{18,19}. Note that these ROI-based analyses were not subject to
“double dipping,” because the ROIs were anatomically defined in this analysis (see definition of ROIs), and were not functionally defined based on the estimates of information transmission. For each ROI, we took the median of the correlation coefficient (“information transmission”) estimated with the aforementioned searchlight method. We then analyzed the across participant correlation between information transmission in each ROI and SCR reduction (Target CS+ versus Control CS+) during Test. We here used Spearman rank correlation, given Pearson correlation prefers larger sample size. The analysis revealed a significant negative correlation between information transmission in VMPFC and SCR reduction (Spearman’s rho=-.522, \( P = .034 \)), suggesting that participants with less VMPFC engagement showed more successful fear reduction (Figure 4c). To supplement the ROI-based analysis, we also conducted a whole brain analysis to highlight voxels showing significant correlation between information transmission and SCR reduction. Consistently with the ROI-based analysis, the whole brain analysis revealed that information transmission in some VMPFC voxels was negatively correlated with SCR reduction (Figure S5). Meanwhile, the SCR reduction did not correlate with information transmission in the amygdala, caudate, or ventral striatum (rho=-0.081, \( P = .758 \); rho=-.378, \( P = .136 \); rho=.039, \( P = .884 \), respectively). Information transmission in none of the ROIs showed significant correlation with the reduction of amygdala response (amygdala, rho=.282, \( P = .272 \); VMPFC, rho=.262, \( P = .308 \); caudate, rho=.137, \( P = .599 \); ventral striatum, rho=-.118, \( P = .653 \)).

Functional connectivity between V1/V2 and striatum during Neural Reinforcement

As the core of the DecNef procedure is to reinforce the Target CS+ patterns in V1/V2 with reward, we hypothesized that striatal area previously implicated in reinforcement learning may have particularly interacted with V1/V2 during the Neural Reinforcement
sessions. Therefore, we conducted a PPI analysis to examine the differential functional connectivity between V1/V2 and the striatum, as a function of the Target CS+ likelihood in V1/V2 (i.e., psychological variable). In the PPI analysis, we selected V1/V2 as a seed region, with the assumption that V1/V2 is likely to initiate change in its connectivity with other brain areas given Target CS+ was induced in V1/V2. Here, the trials were grouped as high (>50%) versus low (<50%) likelihood trials.

The PPI analysis revealed that the connectivity between V1/V2 and the striatal area, particularly the caudate, was stronger during the high likelihood trials than during the low likelihood trials (Figure S6). Although the connectivity does not denote the directionality of interaction, given that Target CS+ was induced in V1/V2, it is likely that the Target CS+ patterns induced in V1/V2 led to the increase of sensitivity in the striatum to the Target CS+ induction. As the caudate is implicated in reinforcement learning, the interaction of V1/V2 with the striatum suggests a potential neural mechanism underlying a counter-conditioning.

The details of PPI analysis are as follows: PPI analysis was conducted with SPM8 (http://www.fil.ion.ucl.ac.uk). The PPI term was created by multiplying the deconvolved activity of the seed region (V1/V2) and the regressor of the Target CS+ likelihood (i.e., psychological variable), which coded the high versus low likelihood trials as 1 and -1, respectively. The PPI term was then reconvolved with a canonical HRF. The main effects of Target CS+ likelihood and the seed region time course were included as the regressors of no interest. Additional parameters of no interest were the initial rest period (30 sec), the feedback period and the fixation period each coded separately for the high and low likelihood trials, motion parameters, day of the Neural Reinforcement sessions, as well as experimental runs. The PPI analysis was confined to the time course averaged across the
12 s time window covering the induction period and the following rest period, in order to exclude the secondary activity evoked by the external feedback (i.e., disc size reflecting the induction likelihood). The hemodynamic delay of 6 sec was adjusted. The PPI analysis used the voxels within the V1/V2 which were activated during the induction period (irrespective of Target CS+ likelihood) relative to the fixation period with a liberal threshold (uncorrected $P<.1$). These analysis steps were conducted at individual participant level, and after non-linear transformation to the MNI coordinates, summarized at group level to yield a map of significant voxels showing differential connectivity with V1/V2 as a function of Target CS+ likelihood ($P<0.05$; corrected with permutation procedure) (Figure S6).

MRI parameters
Participants were scanned in a 3T MRI scanner (Trio, Siemens) with a head coil at the ATR Brain Activation Imaging Center. fMRI signals were acquired using a gradient EPI sequence. During the experiments, we obtained 33 contiguous slices (TR = 2000 ms, TE = 30 ms, voxel size = $3 \times 3 \times 3.5 \text{ mm}^3$, field-of-view = $192 \times 192 \text{ mm}$, matrix size = $64 \times 64$, slice thickness = $3.5 \text{ mm}$, 0 mm slice gap, flip angle = 80 deg.) oriented parallel to the AC-PC plane, which covered the entire brain. We also obtained T1-weighted MR images (MP-RAGE; 256 slices, TR = 2250 ms, TE = 3.06 ms, voxel size = $1 \times 1 \times 1 \text{ mm}^3$, field-of-view = $256 \times 256 \text{ mm}$, matrix size = $256 \times 256$, slice thickness = $1 \text{ mm}$, 0 mm slice gap, TI = 900 ms, flip angle = 9 deg.).
Supplementary Table 1. Post-experiment interview on induction strategy during Neural Reinforcement

<table>
<thead>
<tr>
<th>Participant No.</th>
<th>Reported strategies</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>In my head, I was doing math I just learnt in school. I tried to focus on the calculation process. When I got poor feedback (smaller disk), I also tried to imagine it to become bigger.</td>
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<tr>
<td>2</td>
<td>I repeatedly went through my students’ names in my head.</td>
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<td>3</td>
<td>I tried to plan and imagine activities, such as where I may want to visit one day or what I want to do.</td>
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<td>4</td>
<td>I mainly imagined playing sports such as soccer. But I also tried some other things such as imagining music.</td>
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<td>5</td>
<td>I imagined dancing to music, especially the movements in my hands. I repeated the same songs, around three, in my head.</td>
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<tr>
<td>6</td>
<td>I imagined many different events and activities, such as school activities and sports. I tried to imagine a mixture of events rather than a simple single event.</td>
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<tr>
<td>7</td>
<td>I imagined a various things such as being in a classroom or my plan for the coming weekend. I tried to visualize my thoughts.</td>
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<tr>
<td>8</td>
<td>I tried not to think of anything, keeping a clear mind. I felt that less I thought about, better the feedback was.</td>
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<tr>
<td>9</td>
<td>On day 1, I did calculation such as addition. On day 2, I was planning my schedule. On day 3, I was playing my favourite music videos in my head.</td>
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<tr>
<td>10</td>
<td>I tried to focus on fixation point, and then think of a various things.</td>
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<tr>
<td>11</td>
<td>On day 1, I counted up numbers from 1 and so forth. From day 2, I played my favourite music in my head.</td>
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<tr>
<td>12</td>
<td>I visualized past memories or my plans in future.</td>
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<tr>
<td>13</td>
<td>On day 1 I imagined a small animal moving around. From day 2, I imagined simpler geometric shapes.</td>
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<tr>
<td>14</td>
<td>On day 1, I imagined various body movements. From day 2, I tried to imagine playing darts.</td>
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<tr>
<td>15</td>
<td>I tried to fixate on the screen then imagine the space around my body, especially my hands or chest.</td>
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<tr>
<td>16</td>
<td>I tried to imagine a various body movements of my own. Such as throwing a ball with my non-dominant hand, using chopsticks, or working out in gym.</td>
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<tr>
<td>17</td>
<td>I visualized my good memories, such as playing with my niece.</td>
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</table>
Supplementary References


