

Participants

Participants were screened with a semi-structured SCID-I interview to ensure that none of the following exclusion criteria were met (1): (i) major physical illnesses; (ii) current or previous major mood or psychotic disorders; (iii) current or previous substance misuse disorders.

Participants were assessed with the National Opinion Research Centre DSM-IV Screening for Gambling Problems (2) to establish that none had any history of problem gambling.

Psychometric Assessments

Participants completed the Beck's Depression Inventory (3), the trait Positive Affect Negative Affect Schedule (PANAS)(4). Trait impulsivity was measured with the I-7 questionnaire (5, 6) which has been used to discriminate between pathological and social gamblers (7) and between problem gamblers and healthy non-gambling controls (8). Verbal IQ was estimated using the National Adult Reading Test (9). All participants scored under 6 on the BDI, indicating an absence of recent depressive symptomology. As described in the main text, problem gambling was screened with the South Oaks Gambling Screening Questionnaire (SOGS)(10). Participants' scores on SOGS were mostly 0 and 1, with no score higher than 3.

Computer-simulated Slot-Machine Game

The slot-machine simulation was implemented using Presentation v.11.3 software (Neurobehavioral Systems, San Pablo, USA) (Fig. 1). The display consisted of a single winning line showing 3 fruit symbols. Available play credits were displayed at the top of the display in a purple font. The prizes delivered when the winning line showed 3 of the same fruit symbols were shown below in a traditional pay-off 'chart'.

On each play, participants waited for the presentation of a cue ('Click to play' positioned in the bottom-centre of the display) before making a single button-press with the index finger of their right-hand to start the slot-machine. Immediately after, the 3 fruit symbols 'spun' with a frequency of 5Hz. Following delays of between 4s and 10s (mean= 7s, Poisson distributed), all 3 reels stopped simultaneously to show the play outcome. When the reels stopped to display 3 identical fruits in a row, participants won monetary rewards (between 50p and £3). Near-misses consisted of play outcomes in which, viewing the display from left to right, the first 2 reels showed the same fruit while the third reel showed a different fruit ('AAB' displays). Other near-miss outcomes of the form 'ABB' or 'ABA' did not appear.

Play outcomes were displayed for a fixed interval of 4s followed by a blank display which remained in place for variable delays of between 3.5s and 9.5s (mean= 6.5s; Poisson distributed). The simulated slot-machine game was constructed so that 1/6 of all plays ended with winning outcomes (delivering a variable ratio of 6) and 1/5 ended with near-miss outcomes (delivering a variable ratio of 5). All other slot-machine game plays ended with losing outcomes consisting of 3 different fruits displayed along the pay line.

Finally, the slot-machine game also contained separate 'control' plays, which controlled for the gross visual and motor features of the slot-machine game by involving similar visual displays and identical motor commands, with the difference that all the fruit and credit symbols were replaced by coloured hashes ('#'). The event-structure and the delays between events in the control plays were identical to those of the game plays.

Supplementary Table T1. Demographic and psychometric details of 43 healthy adult volunteers who completed a simulated slot-machine game as part of a standard fMRI protocol. Twenty one participants had prior experience of the game before being scanned while 22 players had no prior experience. Verbal IQ (NART)= National Adult Reading Test (9); Recent depressive symptoms (BDI)= Beck's Depression Inventory (3); Trait positive/negative affect (PANAS-P/PANAS-N)= Trait Positive Affect Negative Affect Scale (4); Impulsivity (I-7)= Eysenck's Impulsivity scale (5, 6); Gambling problems (SOGS)= South Oaks Gambling Screening Questionnaire (10).

	Age	Gender	BDI	PANAS-P	PANAS-N	I-7	SOGS	IQ (NARTS)
Practiced	24.57±1.31	10/11	2.05±0.47	34.00±1.26	13.38±0.74	7.10±0.88	0.52±0.21	117.10±1.02
Unpracticed	24.27±1.43	11/11	1.41±0.41	36.55±1.34	13.77±1.01	7.18±0.98	0.32±0.12	117.64±0.92
Total	24.42±0.96	21/22	1.72±0.31	35.30±0.93	13.58±0.63	7.14±0.65	0.42±0.12	117.37±0.68

Procedure

On study visit 1, participants arrived at the University Department of Psychiatry and completed the screening as described above. Participants allocated to the practiced, but not the unpracticed, group played an extra session with the slot-machine game in a quiet testing room. Participants were told that winnings from the game would be exchanged for real money and would form part of their total experimental payment. Participants were given £10 credit at the start of the game; each play cost 25p. This practice game contained 120 plays and 16 control plays. Twenty plays terminated with winning outcomes, 24 plays terminated with near-miss outcomes, and 76 plays terminated with losing outcomes, delivered in a pseudo-random order. This schedule meant that every participant finished the slot-machine game with £4 final credit (i.e. they lost a total of £6 during the game).

This practice slot-machine game had an identical event structure to the slot-machine game played in the fMRI protocol, except that the blank display interval between plays was shortened to between 1s and 4s (mean= 2.5s; Poisson distributed). The clicks, reel spinning and delivery of game outcomes were each accompanied by distinctive 'slot-machine' sounds. The practice game contained 16 control plays, arranged so that 5 occurred in succession following the first 30 game plays, another 5 following the next 30, and the rest following the 90th game play. Finally, following instruction about how to play the slot-machine game, participants were given 7 introductory plays before playing the game proper.

On study visit 2, participants arrived at the Oxford Centre for Clinical Magnetic Resonance Imaging (OCMR) to play the slot-machine game inside the fMRI scanner. Game displays were back-projected onto a screen at the head-end of the scanner bore which participants viewed via a mirror positioned directly above their eyes and approximately one meter from

the screen. This slot-machine game consisted of 60 game plays and 10 control plays. Ten game plays terminated with winning outcomes, 12 with near-miss outcomes and 38 with straight losing outcomes, delivered in a pseudo-random order. Participants were given £5 credit to start with, and each play cost 25p. Participants ended with £2 (i.e. they lost £3 during the game). A total of 10 control plays were performed in the scanner, arranged such that 5 occurred in a row after the first 20 game plays and 5 more after the next 20 game plays. All participants completed 7 introductory game plays before being moved into the scanner.

Functional Image Acquisition

Participants were scanned at 3 Tesla with a Siemens MAGNETUM Trio scanner (Siemens Medical Solutions, Erlangen, Germany) while performing the computer-simulated slot-machine game. Functional data were collected as T2-weighted echo planar images, optimized for blood-oxygen-level-dependent (BOLD) signal contrast in orbitofrontal cortical regions (voxel size: 3*3*3 mm; TE: 30ms; TR: 3 seconds; 45 slices angled at 30° in anterior-posterior axis). A preparation pulse (1ms; 2mT/m) was used in the slice selection to compensate for through-plane susceptibility gradients when imaging orbitofrontal and medial temporal lobe regions (11). A 176 slice anatomical T1-weighted data set was also acquired with a slice thickness of 1mm for co-registration with the EPI data.

Pre-processing. Imaging pre-processing analysis was carried out with FEAT (FMRI Expert Analysis Tool) v.5.98 (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain; www.fmrib.ox.ac.uk/fsl). Images were high-pass filtered and realigned to correct for motion artefacts using MCFLIRT(12). Each volume was corrected for timing of slice acquisition and was smoothed with a Gaussian filter (full-width half-maximum 5mm). The skull and non-brain matters were removed from the brain using BET(13). Compensation for

geometric distortion and signal loss was carried out by measuring field inhomogeneities with a fieldmap sequence and using this information to geometrically unwarp the EPI images and apply a cost-function masking in registrations to ignore areas of signal losses(14). Individual timeseries were also examined using a model-free independent component analysis implemented in MELODIC (Multivariate Exploratory Linear Optimized Decomposition into Independent Components)(15) in order to remove any remaining artefacts.

Data analysis. Single-subject GLM results were estimated using Feat (FMRI Expert Analysis Tool v. 5.43; www.fmrib.ox.ac.uk/fsl)(16) and transformed, after spatial normalization, into standard (MNI152) space(12). Modelled events were convolved with gamma haemodynamic response functions (HRF). Temporal derivatives of the blurred original waveform were included (17). High pass temporal filtering was also applied to this model. Higher-level analysis was carried out with FLAME (FMRIB's Local Analysis of Mixed Effects)(18). Z (Gaussianised T/F) statistical images were thresholded using clusters at $Z > 3.09$ or 2.3, and a (whole-brain corrected) cluster significance threshold of $p < 0.05$ (19-21).

Clusters of identified activity that allowed comparisons between BOLD signals for the unpracticed and the practiced groups were extracted from functional ROIs identified by the contrasts between winning outcomes and losing outcomes (Supplementary Table T2 and Figure S1). These included (i) an area of the bilateral mid-brain incorporating the bilateral ventral tegmental area (VTA) and substantia nigra; (ii) the bilateral caudate nucleus; (iii) the bilateral ventral striatum including the nucleus accumbens; (iv) the bilateral amygdala; (v) the bilateral anterior cingulate cortex; (vi) the dorsomedial prefrontal cortex (including the medial superior frontal gyrus); and (vii) the bilateral anterior insular cortex.

Model. Winning outcomes and their values, near-miss outcomes and their values, and losing outcomes were all modelled as 1s impulses of neural activity. The value of near-misses were determined as the value of the first 2 fruits; e.g. the sequence 'grape-grape-pear' was modelled with a value of £2 as this was the prize for 3 grapes. The reel spins of the game were modelled in 2 ways. First, we modelled the start of the reel spins as 1s impulses. Separate impulse regressors were included for reel spins following winning, near-miss and losing outcomes. (These were included to test whether different game outcomes influenced signals elicited while watching the 3 reels spin on *subsequent* plays of the slot-machine; there were no such effects so these individual regressors are not discussed further.) Second, we modelled the extended signals associated with waiting for game outcomes as the whole jittered duration of the reel spins, collapsing across spins following the different game outcomes.

To explore the effects of trait impulsivity, I-7 scores were entered as covariates to identify areas of signal change that survived a threshold of $Z= 2.3$ (whole-brain cluster-corrected at $p < .05$). These were most apparent in differences between signals associated with winning and near-miss outcomes, collapsed across practiced and unpracticed groups (see main text). These ROIs covered the bilateral caudate, bilateral ventral striatum (ventral putamen), left amygdala and bilateral insular cortex (see Supplementary Table T4 and Figure S6 below).

Timecourse analysis. The timecourse of signals across the reel spin and the play outcomes are shown for illustrative purposes (22) only within regions of interest (ROIs) identified using a cluster corrected threshold of $p < 0.05$. To obtain signal changes within ROIs evoked by the slot-machine reel spins and outcomes, we performed a series of hemodynamic deconvolutions across each play of the game. BOLD amplitudes—expressed as % signal changes—were fit by hemodynamic response functions (HRFs) using GLMs. We separated

and resampled participants' timeseries data to align them into 2 slot-machine events: (i) reel spins that started following participants' click response at time 0 and; (ii) play outcomes which occurred after the reels stopped spinning. The resampling resolution was 0.1s.

Timeseries data and model fits were drawn separately for the practiced and unpracticed participants, and separate plots were drawn for plays ending with winning, losing and near-miss outcomes. We explored 2 hemodynamic models. In the first model, BOLD responses were modelled by regressors consisting of a 1s impulse of phasic activity at the time of reel spins and play outcomes convolved with the HRF. In the second model, the BOLD responses were explained by regressors consisting of tonic activity that lasted for the entire durations of the reel spins and play outcomes (of 4s), again convolved with the HRF. We compared these models using the sum of square errors (SSE) between the model and data. Overall, the impulse model provided a better fit to the timeseries data and is the one used here.

Matching analysis for practiced participants versus unpracticed participants. Matching for age, trait positive affect negative affect (PANAS)(4), depressive symptomology (BDI)(3), gambling problems (SOGS)(10), impulsivity (I-7) and estimated verbal IQ (NART)(9) was tested using one-way analyses of variance (ANOVAs) with the 2 between-subject factors of group (practiced participants vs unpracticed participants) and gender.

Behavioural data analysis. Mean reaction times (ms) for 'click' responses to start slot-machine plays were tested with repeated-measures ANOVA with the between-subject factors of group (practiced vs unpracticed) and gender, and within-subject factor of the immediately previous outcome (game plays following winning outcomes vs plays following near-miss outcomes vs plays following losing outcomes). Trait impulsivity scores (I-7) were added as

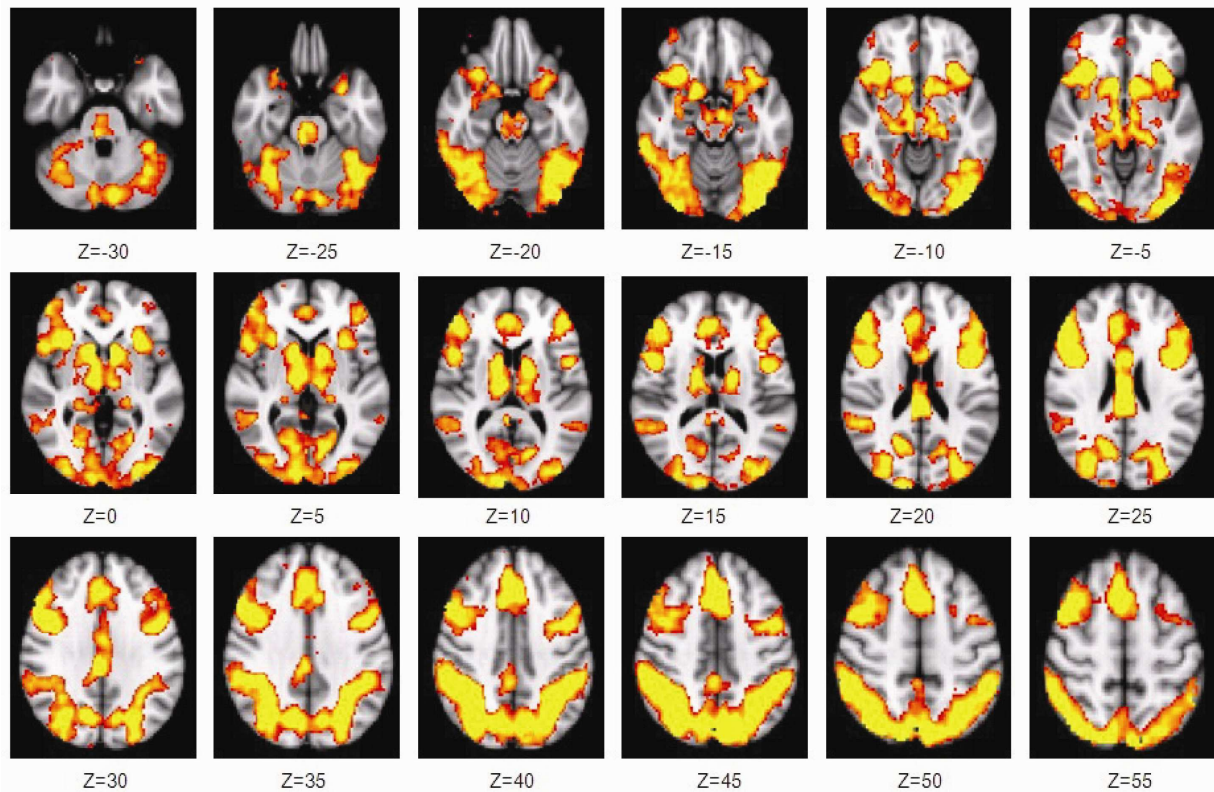
covariates in order to test whether variability in impulsivity influenced the speed of starting

new plays following different outcomes of the slot-machine game.

Supplementary Table T2. Group maximum Z-scores and MNI (Montreal Neurological institute) 'MNI152_T1_2mm' brain coordinates of BOLD amplitudes identified by the comparison between winning outcomes and losing outcomes, thresholded at $Z > 3.09$ and cluster-corrected at $p < 0.05$. VTA= ventral tegmental area; SN= substantia nigra.

Area	Side	Max Z	X	Y	Z
Midbrain (VTA/SN)		5.57	8	-28	-24
Ventral striatum	L	6.77	-8	10	-4
	R	6.37	10	10	-4
Ventral putamen	L	5.96	-14	8	-4
	R	6.11	16	10	-2
Caudate nucleus	L	7.18	-10	8	0
	R	6.60	12	8	6
Amygdala	L	4.64	-22	0	-16
	R	5.37	20	2	-16
Anterior cingulate	L	5.90	-2	6	26
	R	6.66	6	24	38
Posterior cingulate	L	6.67	-2	-32	24
	R	7.23	2	-30	26
Superfrontal gyrus	L	6.70	-2	26	40
	R	7.43	6	20	48
Middle frontal gyrus/sulcus	L	6.34	-42	14	22
	R	6.65	44	14	26
Inferior frontal gyrus	L	7.16	-32	24	-8
	R	7.74	34	22	-8
Insular cortex	L	7.31	-30	24	-8
	R	7.74	34	22	-8
Thalamus	L	6.01	-12	-2	8
	R	7.36	10	-14	6
Primary visual cortex	L	4.80	-2	-96	6
	R	5.88	12	-96	8
Inf. parietal sulcus	L	7.43	-32	-56	42
	R	7.86	40	-54	46

Supplementary Figure S1. Activation map for blood-oxygenation-level-dependent (BOLD) amplitudes evoked by winning compared to losing outcomes during play of a simulated slot-machine game in 43 healthy adults (collapsing across practiced and unpracticed groups). Signals were thresholded at $Z = 3.09$, whole-brain cluster-based corrected at $p < 0.05$, and then rendered onto the MNI (Montreal Neurological Institute) 'MNI152_T1_2mm' brain (see Methods). Contrast-dependent regions of interest (ROIs) identified included the midbrain (VTA/SN), ventral striatum, caudate nucleus, amygdala, anterior cingulate cortex (ACC), dorsomedial prefrontal cortex (dmPFC) and anterior insular cortex.



Testing the effects of prior experience on the neural signalling of reel spins and winning

outcomes: an omnibus multi- factorial repeated-measures analyses of variance

(ANOVAs) of BOLD responses to slot-machine play. β -values obtained from the GLM modelling of the timecourse described above were tested with repeated-measures ANOVAs with the between-subject factors of group (practiced vs unpracticed), gender, impulsivity (high vs low) and the within-subject factors of game event (reel spins vs winning outcomes) and ROI (mid-brain (ventral tegmental area/substantia nigra), ventral striatum, caudate nucleus, amygdala, anterior cingulate cortex (ACC), anterior insula vs dorsomedial prefrontal cortex (dmPFC)). Simple effects of practice and impulsivity were tested using univariate ANOVAs with the between-subject factors of group, gender and impulsivity. Practice produced different effects on the BOLD signals evoked by the reel spins compared to the winning outcomes of the slot-machine game as evidenced by the significant 2-way interaction between practice and game event, $F(1, 35)= 6.88, p < .05$. Analysis of the simple effects demonstrated that practice reduced signals evoked by the winning outcomes, $F(1, 35)= 6.021, p < .05$, but enhanced the signals evoked by the reel spins $F(1, 35)= 4.025, p = .05$.

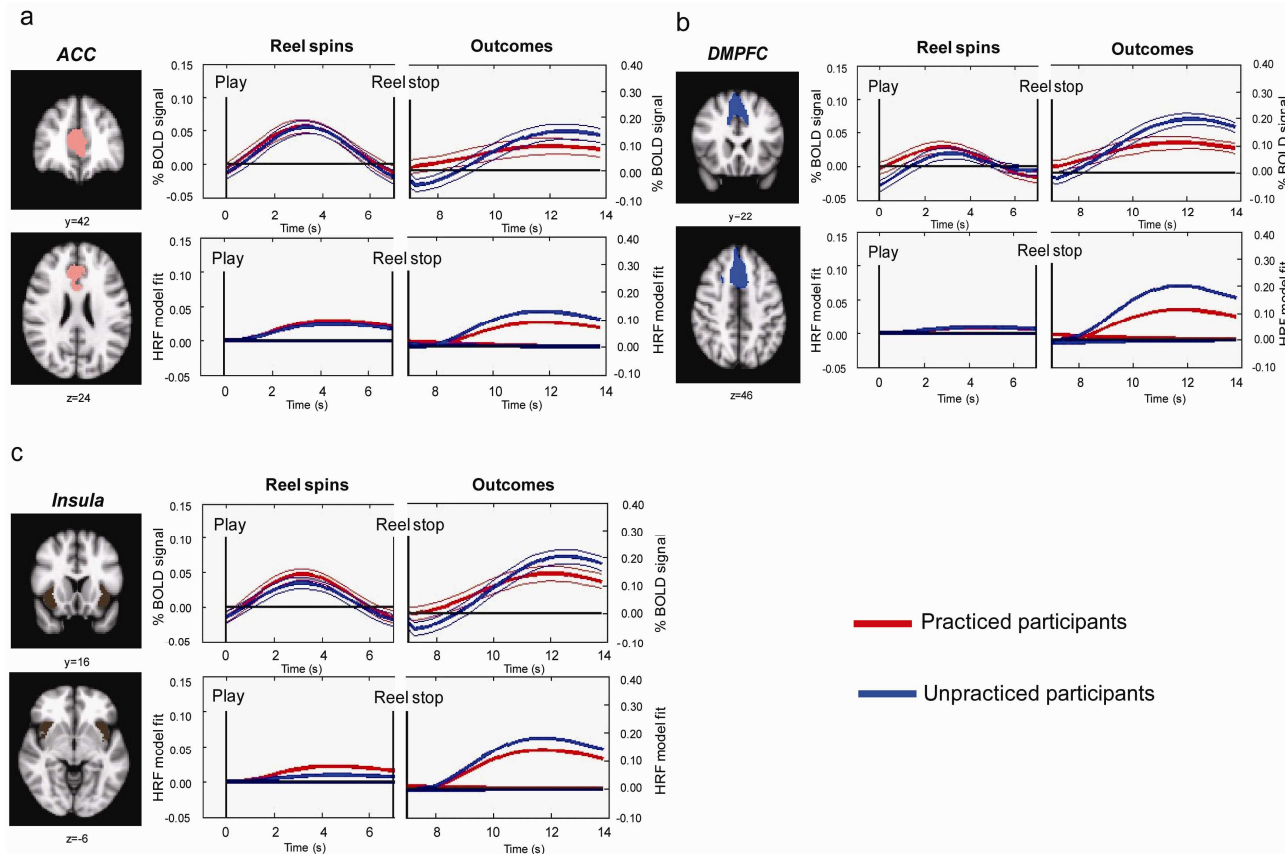
These distinct effects of practice were not reliably more or less pronounced in any of the 7 ROIs listed above, as evidenced by the non-significant three-way interaction between practice, game event (reel spins vs winning outcomes) and ROI, $F(6, 210)= 1.12$. Testing the BOLD amplitudes evoked by the winning outcomes revealed smaller signals evoked by winning outcomes in the practiced participants compared to the unpracticed participants in the ventral striatum, $F(1,35)= 9.093 p < 0.05$, and the caudate nucleus, $F(1,35)= 5.399 p < .05$, with a similar trend in the mid-brain, $F(1,35)= 3.134 p=0.085$. BOLD signals evoked by winning outcomes were also reduced within the dmPFC (see Supplementary Figure S2 below), $F(1, 35)= 8.71, p < 0.01$). By contrast, prior experience with the slot-machine game

significantly increased the BOLD signals evoked by the slot-machine reel spins within the ventral striatum, $F(1,35)= 4.339$ $p < 0.05$, and the amygdala, $F(1,35)= 6.193$ $p < .05$.

To test the claim that practice had larger effects upon winning outcomes compared to near-miss and losing outcomes, we also completed an ANOVA with the between-subject factors of practice, gender and impulsivity and the within-subject factors of outcomes (winning outcomes, near-misses, losing outcomes) and ROI. This demonstrated a marginal significant 2-way interaction between practice and game outcome, $F(2, 70)= 3.10$, $p = .05$.

Testing the effects of infrequency: BOLD responses to winning outcomes versus near-misses. It is possible that our finding that prior experience with slot-machine increased the BOLD signals evoked by reel spins but reduced the signals evoked by winning outcomes may reflect enhanced anticipation of infrequent, or otherwise salient, events but diminished processing of their delivery. One (partial) test of this idea is to compare the effects of practice upon BOLD responses to winning outcomes with the responses to the marginally more frequent near-miss outcomes. Two previous investigations suggest that near-misses evoke BOLD changes within the ventral striatum (23, 24). Therefore, we confined our tests to this structure using an ANOVA with the between-subject factors of practice, gender and impulsivity, and the within subject factors of outcome (winning vs near-miss). This demonstrated that practice had a significantly larger effect upon BOLD responses to winning compared to near-miss outcomes, $F(1, 35)= 5.16$, $p < .05$. Analysis of the simple effects confirmed that practice reduced the BOLD signals elicited within the ventral striatum by winning outcomes, $F(1, 35)= 9.09$, $p = .001$, but not by near-miss outcomes, $F(1, 35)= 2.27$.

Supplementary Figure S2. Timeseries plots of BOLD signals for the 3 regions of interests (ROIs) identified using the comparison between winning outcomes and losing outcomes of a computer-simulated slot-machine game (thresholded at $Z=3.09$, whole-brain cluster-corrected at $p < .05$). Coronal and axial slices are shown for each of the ROIs. MNI (Montreal Neurological institute) y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: % BOLD signal changes while watching the game reels spin (displayed for a mean of 7s following 'Play') and while watching the winning outcomes (displayed for 7s following 'Reel stop'). Reel spins and winning outcomes of the practiced participants are indicated by red lines and those of the unpracticed participants are indicated by blue lines. Means % signal values (relative to baseline) are shown with standard errors. Lower plots: hemodynamic response function (HRF) gamma model used to fit the BOLD % signals. An 'impulse' or phasic HRF with a mean response latency of 6s was used in the model. The anterior cingulate cortex (ACC) is marked in pink (a); dorsomedial prefrontal cortex is marked in blue (b); and anterior insula cortex is marked brown (c).

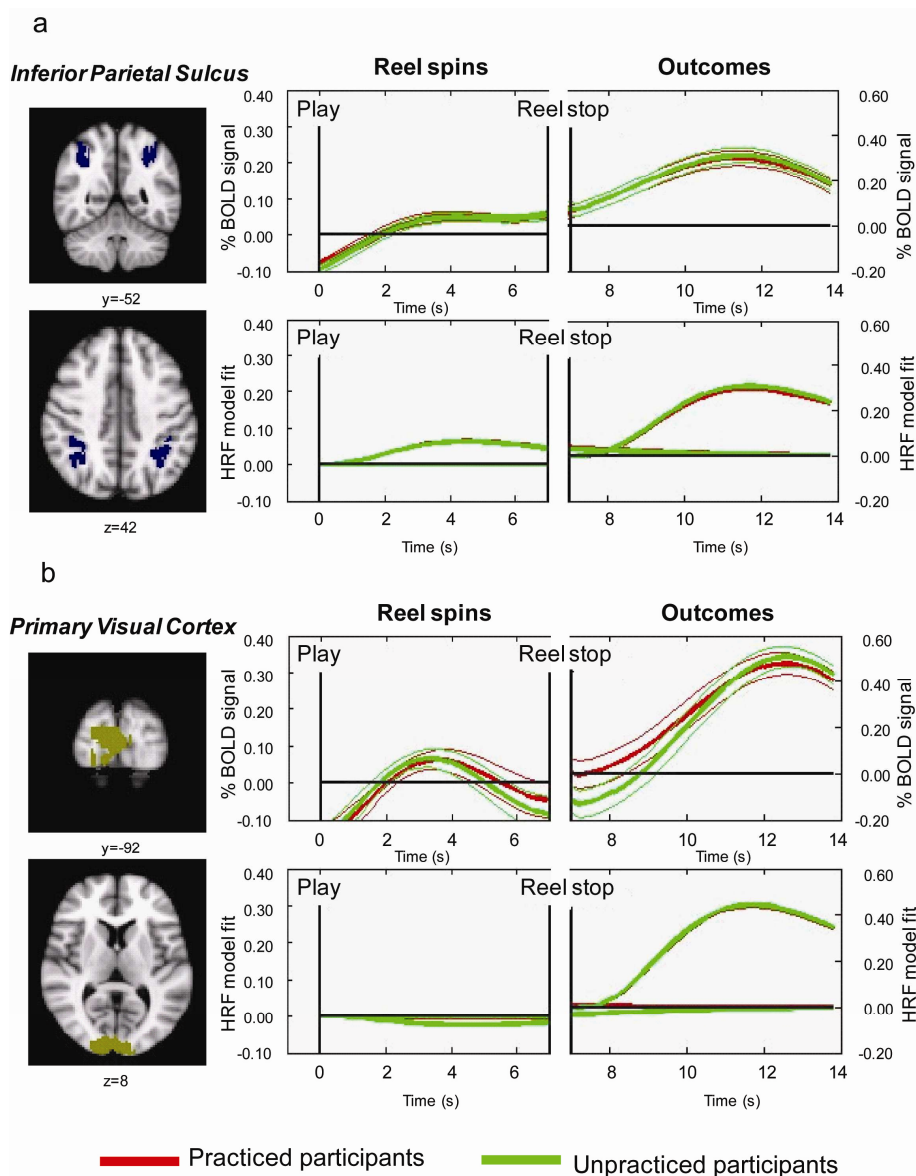


Testing the effects of practice on BOLD responses to slot-machine play in posterior

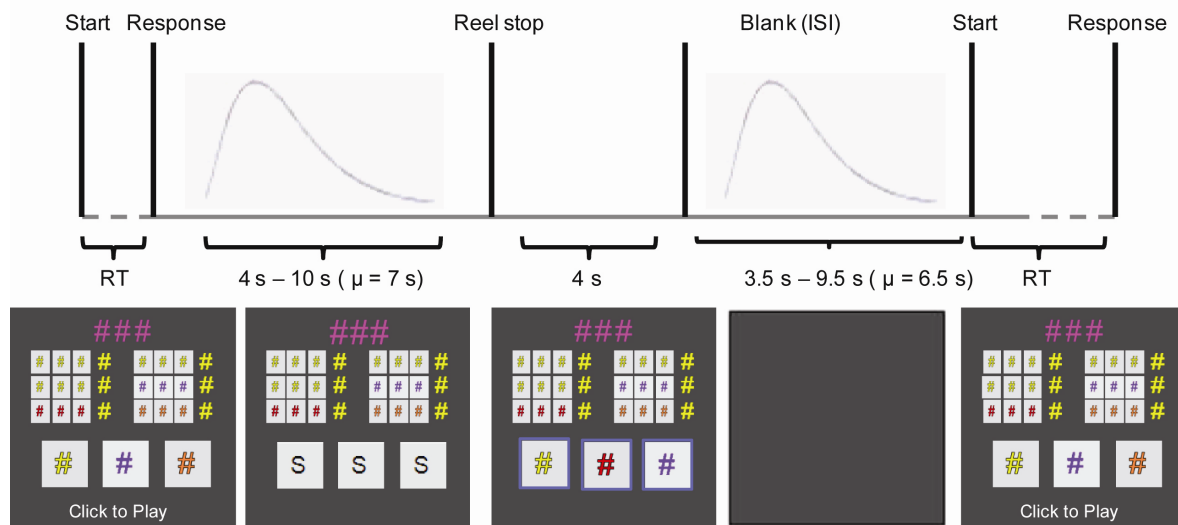
cortical regions (intra-parietal sulcus and visual cortex). We also tested the effects of prior experience with our slot-machine game on neural signalling within posterior cortical ROIs. These ROIs were also identified using the contrast between winning outcomes and losing outcomes thresholded at $Z= 3.09$ and whole brain cluster-corrected at $p < .05$. These centred round the intra-parietal sulcus and posterior visual cortex. The ANOVA had the between-subject factors of practice, gender and impulsivity, and the within-subject factors of game event (reel spins vs winning outcomes) and ROI (intra-parietal sulcus (IPS) and primary visual cortex). Overall, there was no indication that prior experience influenced the BOLD responses evoked by the winning outcomes differently from the BOLD responses evoked by the reel spins in these areas, as evidenced by a non-significant 2-way interaction between practice and game event, $F(1, 35) = .18$. Testing the effects of practice on signals evoked by winning outcomes and by the reel spins directly (and separately) did not yield significant main effects, $F(1, 35) = .1$ and $F(1, 35) = .06$, respectively.

We also compared the BOLD responses evoked by the reel spins and winning outcomes within the intra-parietal sulcus and ventral striatum, with an ANOVA having the between-subject factors of practice, gender and impulsivity and within-subject factors of game event and ROI (intra-parietal sulcus vs ventral striatum). This analysis showed that prior experience influenced BOLD responses to the winning outcomes and reel spins of the slot-machine differently within these 2 neural systems, as evidenced by a significant 3-way interaction between practice, game event and ROI, $F(1, 35) = 4.57$, $p < .05$. Analysis of the simple interaction effects showed that practice reduced BOLD responses to winning outcomes but increased BOLD responses to reel spins within the ventral striatum as indicated by a significant 2-way interaction between practice and game event, $F(1, 35) = 10.06$, $p < .05$. This simple interaction effect was not significant in the intra-parietal sulcal area, $F(1, 35) = .53$.

Supplementary Figure S3. Timeseries plots of BOLD signals during performance of a simulated slot-machine game within the 2 posterior regions of interests (ROIs) identified using the contrast between winning and losing outcomes (see above). Signals were thresholded at $Z=3.09$, whole-brain cluster-based corrected at $p < 0.05$, and then rendered onto the MNI (Montreal Neurological institute) 'avg152 brain' (see Methods). Coronal and axial slices are shown for each of the ROIs. MNI (Montreal Neurological institute) y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: % BOLD signal changes while watching the game reels spin (modelled for 7s following 'Play') and winning outcomes of the game (displayed for 7s following 'Reel stop'). Signal arising from plays completed by the practiced participants are indicated by red lines; plays completed by the unpracticed participants are indicated by green lines. Means % signal values (relative to baseline) are shown together with standard errors. Lower plots: hemodynamic response function (HRF) gamma models used to fit % BOLD signals. 'Impulse' or phasic HRFs with mean response latencies of 6s were used. The intra-parietal sulcus is marked in blue (a) and the primary visual cortical region is shown in yellow (b).

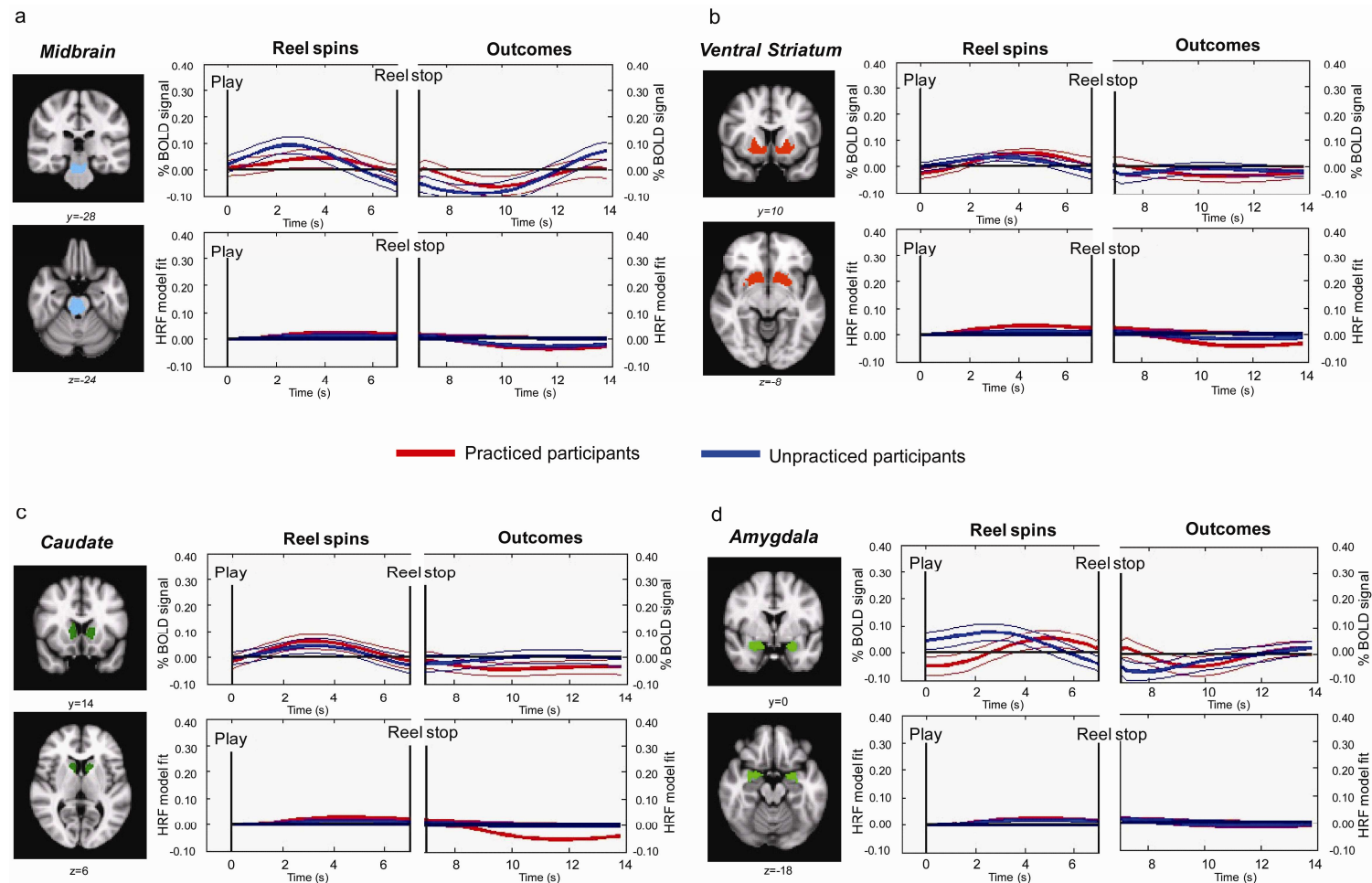


Supplementary Figure S4. Structure of the 'control' game for comparison with the simulated slot-machine. On being shown the cue 'Click to play', participants made a single button press to start the control game. All 3 reels displayed a random sequence of 6 coloured '#s', with a frequency of 5Hz. Three reels stopped following a Poisson-distributed latency of 4-10s (mean= 7s) and showed the game outcomes for a fixed 4s. The fMRI model included impulse regressors for reel spins and for control outcomes, and extended regressor for the jittered duration of reel spins. The display was blanked before the next play was started, with a Poisson-distributed inter-play interval (ITI) of 3.5-9.5s (mean= 6.5s). When this game was played outside the scanner, this latter ITI was shortened to a Poisson-distributed latency of 1.0-4.0s (mean= 2.5s). See Methods for more details.



Testing the BOLD signals evoked by the control game. Our findings are unlikely to reflect the visual and motor characteristics of the slot-machine game. The reel spins and, in particular, the control outcomes failed to evoke significant positive BOLD signals within the ROIs used to isolate reinforcement signalling in the slot-machine game. These ROIs were identified using the contrast between winning and losing outcomes thresholded at $Z = 3.09$ and whole brain cluster-corrected at $p < .05$ (Figure 2 and Supplementary Figure S2). While BOLD amplitudes elicited by the winning outcomes of the slot-machine game (collapsing across practiced and unpracticed participants) were all positive and significant (all β -values between 2.47 and 4.17), the amplitudes elicited by the control outcomes were small, negative and non-significant (β -values between -0.72 and -0.19). The exception was the significant negative response to control outcomes within the ACC, β -values= -1.14; $t(42) = -2.99$, $p < .01$.

Supplementary Figure S5. Timeseries plots of BOLD signals during performance of our control game within the same regions of interests (ROIs) identified using the contrast between winning and losing outcomes of the slot-machine game. Coronal and axial slices are shown for each of ROIs. MNI (Montreal Neurological institute) y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: % BOLD amplitudes while watching the control game reels spin (displayed for 7s following 'Play') and outcomes (displayed for 7s following the 'Reel stop'). Signals from plays completed by the practiced participants are indicated by red lines and those completed by the unpracticed participants are indicated by blue lines. Means % signal values (relative to baseline) are shown together with standard errors. Lower plots: hemodynamic response function (HRF) gamma models used to fit % BOLD signals. The mid-brain is marked in cyan (**a**); the ventral striatum is marked in red (**b**); the caudate is marked in green (**c**); and the amygdala is shown in light green (**d**).



Supplementary Table T3. Mean RTs (ms±standard errors) to start new plays following winning outcomes, losing outcomes and near-misses while playing a simulated slot-machine game in participants with and without prior experience of the game but split between high and low impulsive participants.

Low impulsive group (LI)

	RTs following winning outcomes	RTs after near-miss outcomes	RTs after losing outcomes
Unpracticed (n= 13)	1264.214 ± 105.00	1148.55 ± 135.19	1197.03 ± 118.84
Practiced (n= 11)	839.33 ± 111.53	842.73 ± 143.59	832.60 ± 126.23
Total	1051.77 ± 76.59	995.64 ± 98.61	1014.82 ± 86.68

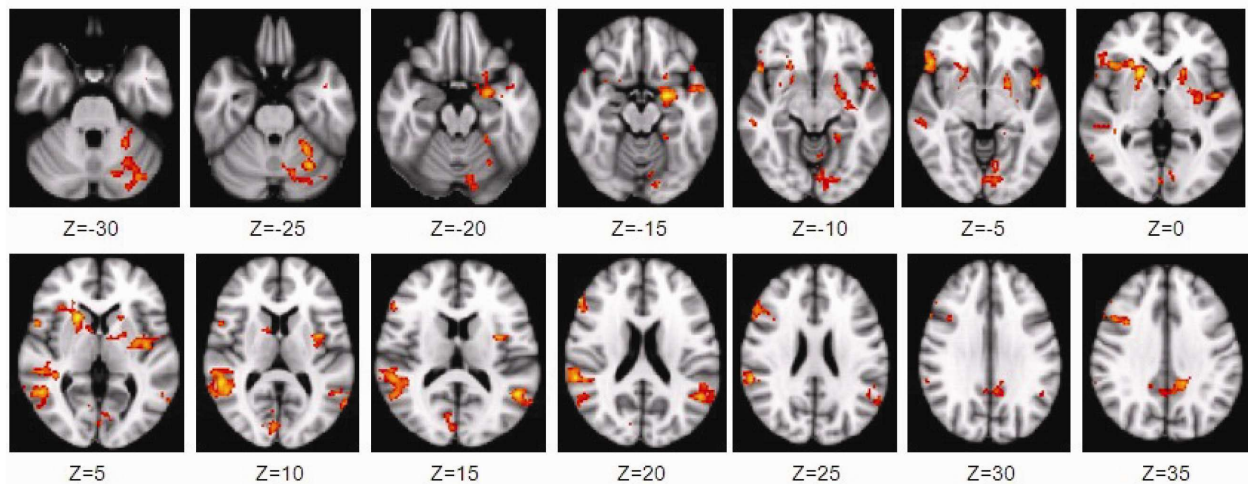
High impulsive group (HI)

	RT following winning outcomes	RT after near-miss outcomes	RT after losing outcomes
Unpracticed (n= 9)	1032.08 ± 130.24	1212.03 ± 167.68	1027.34 ± 147.40
Practiced (n= 10)	789.94 ± 116.49	897.23 ± 149.98	907.05 ± 131.84
Total	911.01 ± 87.37	1054.63 ± 112.48	967.22 ± 98.88

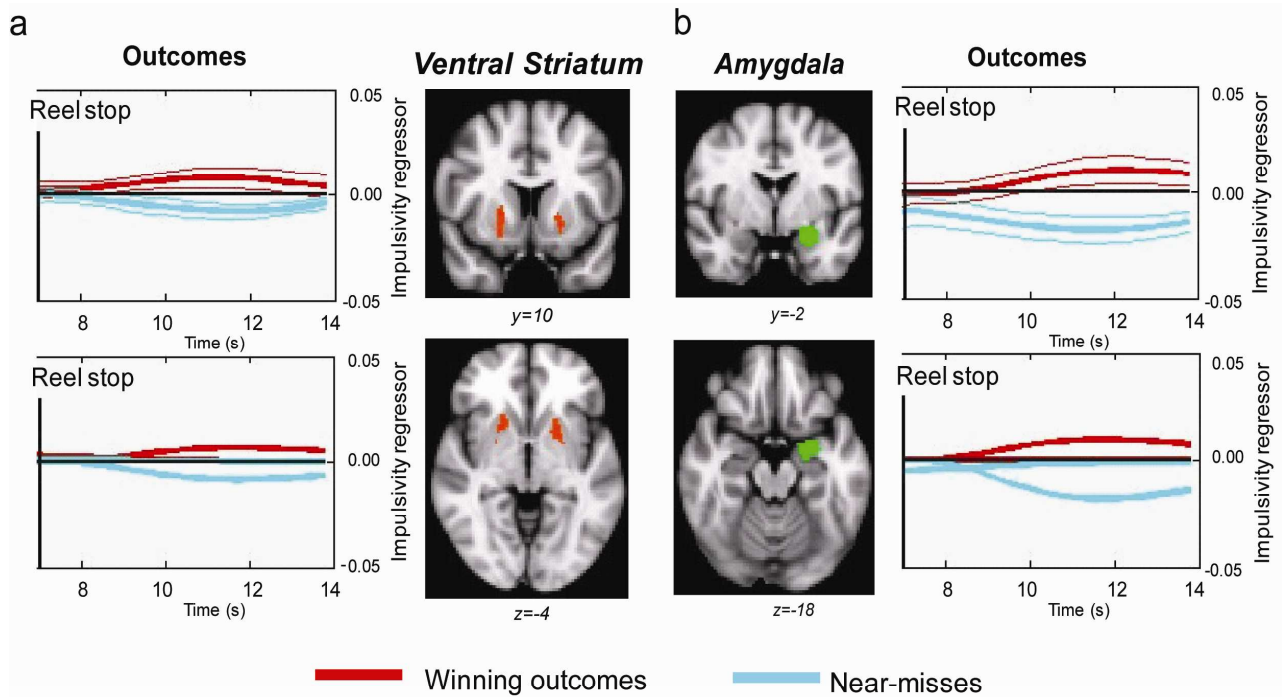
Supplementary Table T4. Z-scores and MNI (Montreal Neurological institute) 'MNI152_T1_2mm' coordinates of BOLD amplitudes associated with the positive covariate of I-7 scores on the winning minus near-miss outcomes contrast (Supplementary Figure S6) ($Z > 2.3$, cluster-correlated at $p < 0.05$).

Area	Side	Max Z	X	Y	Z
Ventral striatum	L	3.18	-18	6	-4
	R	4.10	20	16	2
Amygdala	L	3.94	-22	-4	-16
Caudate nucleus	L	3.04	-18	18	0
	R	4.18	18	18	2
Anterior insula	L	3.56	-34	-2	12
	R	3.12	38	22	0
Inferior frontal gyrus	L	2.90	-50	22	-12
	R	3.55	54	30	18
Middle temporal gyrus	L	3.41	-50	-54	12
	R	4.02	50	-54	6
Angular gyrus	L	3.95	-50	-54	14

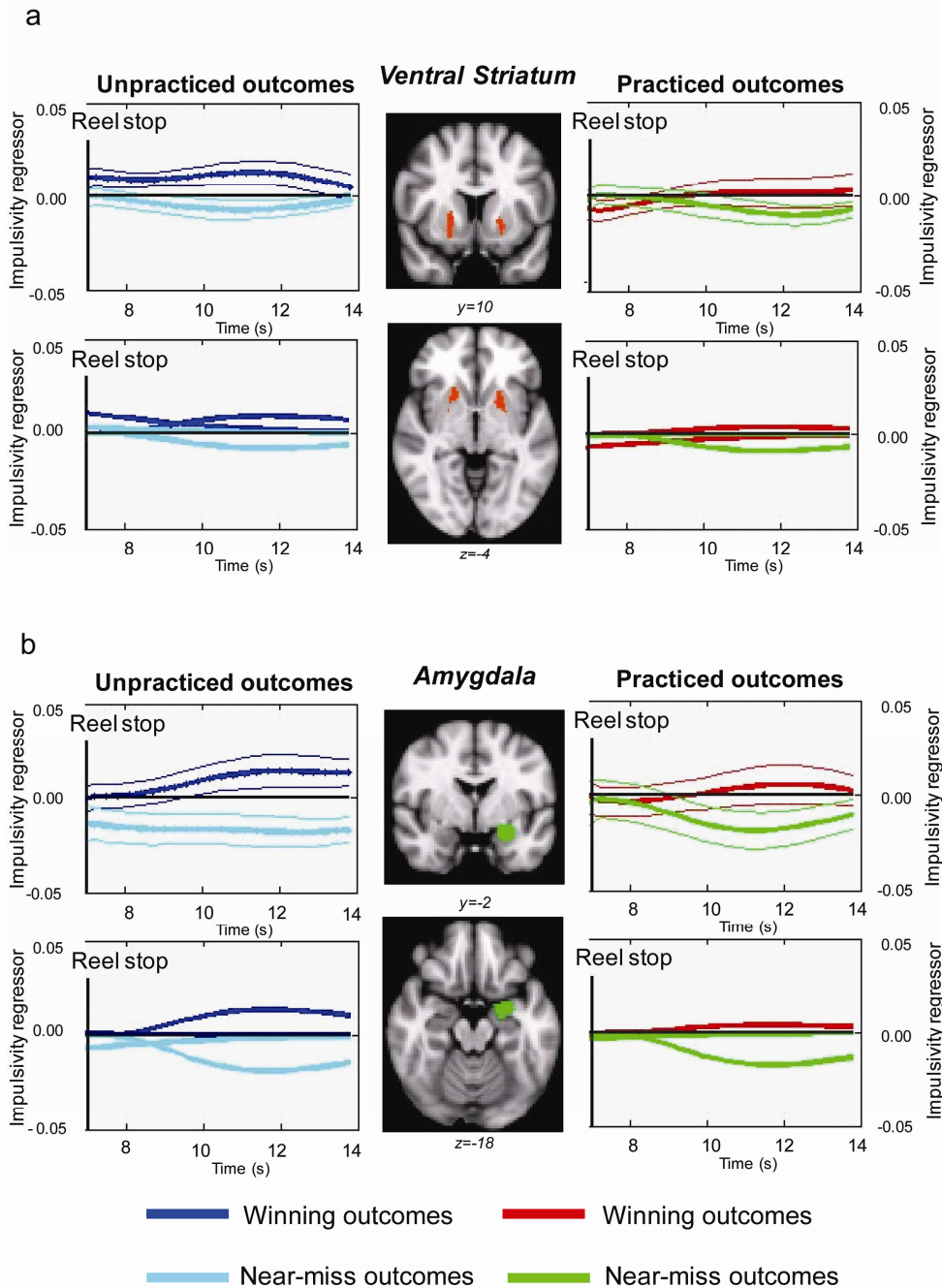
Supplementary Figure S6. Activation map for impulsivity-dependent BOLD signals in the comparison between winning and near-miss outcomes during performance of a simulated slot-machine game, collapsed across the 21 practiced healthy adult participants and the 22 unpracticed participants of the experiment. Signals were thresholded at $Z = 2.3$, with cluster-based correction at $p < 0.05$, and rendered onto the MNI (Montreal Neurological institute) 'MNI152_T1_2mm' brain. Contrast-dependent regions of interest (ROIs) identified included the ventral striatum and the amygdala (see main text for details).



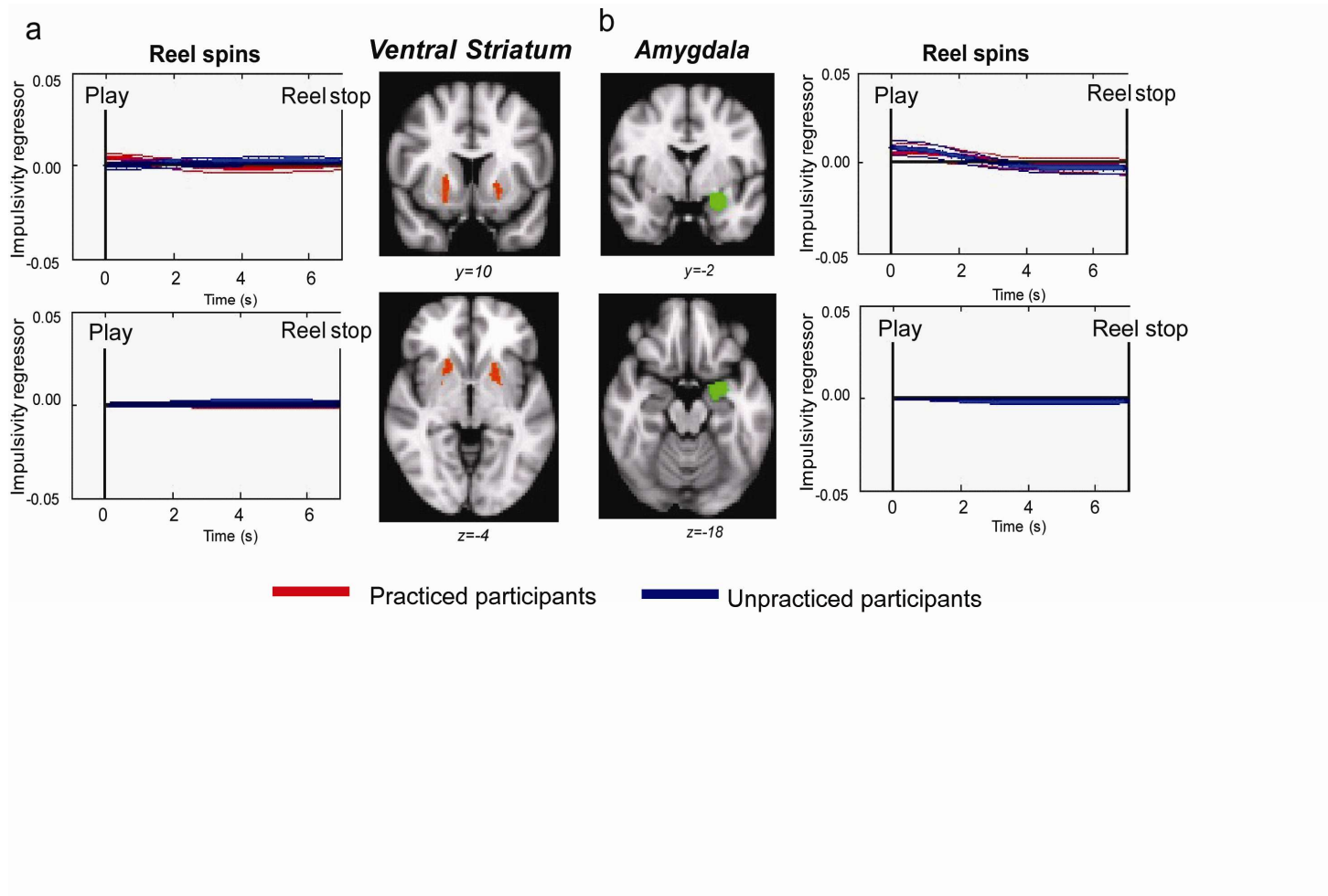
Supplementary Figure 7. Timeseries plots of BOLD signals within 2 regions of interests (ROIs) constructed using I-7 scores (5, 6) as a covariate in the comparison between winning outcomes and near-misses (thresholded at $Z=2.3$, whole-brain cluster-corrected at $p < .05$). Timecourse signals show influence of I-7 score against the baseline on the BOLD responses to winning outcomes and near-misses. Coronal and axial slices are shown for both ROIs. MNI (Montreal Neurological institute) y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: the regression coefficients of I-7 scores on % BOLD signal changes evoked by winning outcomes (indicated in red) and near-miss (indicated in cyan) outcomes (displayed for 7s following 'Reel stop'). Coefficient values are shown together with standard errors. Lower plots: the regression coefficients of I-7 scores on BOLD % signals fitted to the HRF gamma model. An 'impulse' or phasic HRF and mean response latency of 6s was used. The ventral striatum is marked in red (a); the amygdala is marked in light green (b).



Supplementary Figure S8. Timeseries plots of BOLD within 2 regions of interests (ROIs) constructed using the I-7 score (5, 6) as a covariate in the comparison between winning outcomes and near-misses (thresholded at $Z= 2.3$, whole-brain cluster-corrected at $p< .05$). Positive and negative signals show the influence of I-7 score on the BOLD signals associated with winning outcomes and near-misses, plotted separately for the 21 practiced and 22 unpracticed participants. MNI (Montreal Neurological institute) y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: regression coefficients of I-7 scores on % BOLD signal changes evoked by winning (blue for unpracticed; red for practiced) and near-miss outcomes of the game (cyan for unpracticed; green for practiced participants) (7s following 'Reel stop'). Regression coefficients are shown with standard errors. Lower plots: the regression coefficients of I-7 scores on % BOLD signals fitted to the hemodynamic response function (HRF) gamma model. An 'impulse' or phasic HRF and mean response latency of 6s was used. The ventral striatum is marked in red (a); the amygdala is marked in light green (b).



Supplementary Figure S9. Timeseries plots of BOLD within 2 regions of interests (ROIs) constructed using I-7 scores (5, 6) as a covariate in the comparison between winning outcomes and near-misses (thresholded at $Z=2.3$, whole-brain cluster-corrected at $p < .05$). Positive and negative signals show influence of I-7 score on the BOLD signals associated with reel spins averaged across all plays. Coronal and axial slices are shown for both ROIs. MNI y coordinates are provided below the coronal slices and z coordinates below the axial slices. Upper plots: the regression coefficients of I-7 scores on % BOLD signal changes evoked by reel spins in the practiced (indicated in red) and unpracticed (indicated in blue) groups (displayed for 7s following the trial start). Coefficient values are shown together with standard errors. Lower plots: regression coefficients of I-7 scores on BOLD % signals fitted to the hemodynamic response function (HRF) gamma model. An 'impulse' or phasic HRF and mean response latency of 6s was used. The ventral striatum is marked in red (a); the amygdala is marked in light green (b).



References

1. First M, Spitzer R, Gibbon M, Williams J. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P)* Biometrics Research: New York, 2002.
2. Gernstein D, Hoffman J, Larison C, Engelman L, Murphy S, Palmer A, et al. *Gambling impact and behavior study: report to the National Gambling Impact Study Commission.* National Opinion Research Center at the University of Chicago: Chicago, Illinois, 1999.
3. Beck AT, Steer RA, Brown GK. *Manual for the Beck Depression Inventory-II.* Psychological Corporation: San Antonio, TX, 1996.

4. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988; 54(6):1063-1070.
5. Eysenck SB, Eysenck HJ. Impulsiveness and venturesomeness: their position in a dimensional system of personality description. *Psychol Rep* 1978; 43(3 Pt 2):1247-1255.
6. Eysenck SBG, Pearson PR, Easting G, Allsop JF. Age norms for impulsiveness, venturesomeness and empathy in adults. *Personality and Individual Differences* 1985; 6:613-619.
7. Nower L, Derevensky JL, Gupta R. The relationship of impulsivity, sensation seeking, coping, and substance use in youth gamblers. *Psychol Addict Behav* 2004; 18(1):49-55.
8. Clarke D. Impulsivity as a mediator in the relationship between depression and problem gambling. *Personality and Individual Differences* 2006; 40(1):5-15.
9. Nelson H. *National Adult Reading Test (NART) Test Manual*. NFER-Nelson: Windsor, UK, 1982.
10. Lesieur HR, Blume SB. The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. *Am J Psychiatry* 1987; 144(9):1184-1188.
11. Deichmann R, Gottfried JA, Hutton C, Turner R. Optimized EPI for fMRI studies of the orbitofrontal cortex. *Neuroimage* 2003; 19(2 Pt 1):430-441.
12. Jenkinson M, Bannister P, Brady M, Smith S. Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *NeuroImage* 2002; 17(2):825-841.
13. Smith SM. Fast robust automated brain extraction. *Hum Brain Mapp* 2002; 17(3):143-155.
14. Jenkinson M. Fast, automated, N-dimensional phase-unwrapping algorithm. *Magnetic Resonance in Medicine* 2003; 49(1):193-197.
15. Beckmann CF, Smith SM. Probabilistic independent component analysis for functional magnetic resonance imaging. *IEEE Trans Med Imaging* 2004; 23(2):137-152.
16. Woolrich MW, Ripley BD, Brady M, Smith SM. Temporal Autocorrelation in Univariate Linear Modeling of FMRI Data. *NeuroImage* 2001; 14(6):1370-1386.
17. Friston KJ, *et al*. Event-related fMRI: characterizing differential responses. *Neuroimage* 1998; 7(1):30-40.
18. Woolrich MW, Behrens TEJ, Beckmann CF, Jenkinson M, Smith SM. Multilevel linear modelling for FMRI group analysis using Bayesian inference. *NeuroImage* 2004; 21(4):1732-1747.
19. Friston KJ, Worsley KJ, Erackowiak RSJ, Mazziotta JC, Evans AC. Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping* 1994; 1:214-220.
20. Forman SD, *et al*. Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): Use of a cluster-size threshold. *Magnetic Resonance in Medicine* 1995; 33(5):636-647.
21. Worsley KJ, Evans AC, Marrett S, Neelin P. A three-dimensional statistical analysis for CBF activation studies in human brain. *Journal of Cerebral Blood Flow and Metabolism* 1992; 12(6):900-918.
22. Kriegeskorte N, Simmons WK, Bellgowan PS, Baker CI. Circular analysis in systems neuroscience: the dangers of double dipping. *Nat Neurosci* 2009; 12(5):535-540.
23. Chase HW, Clark L. Gambling severity predicts midbrain response to near-miss outcomes. *J Neurosci* 2010; 30(18):6180-6187.
24. Clark L, Lawrence AJ, Astley-Jones F, Gray N. Gambling near-misses enhance motivation to gamble and recruit win-related brain circuitry. *Neuron* 2009; 61(3):481-490.

