Cell Reports Medicine, Volume *3*

Supplemental information

Corticostriatal circuits in the transition to chronic back pain: The predictive role of reward learning

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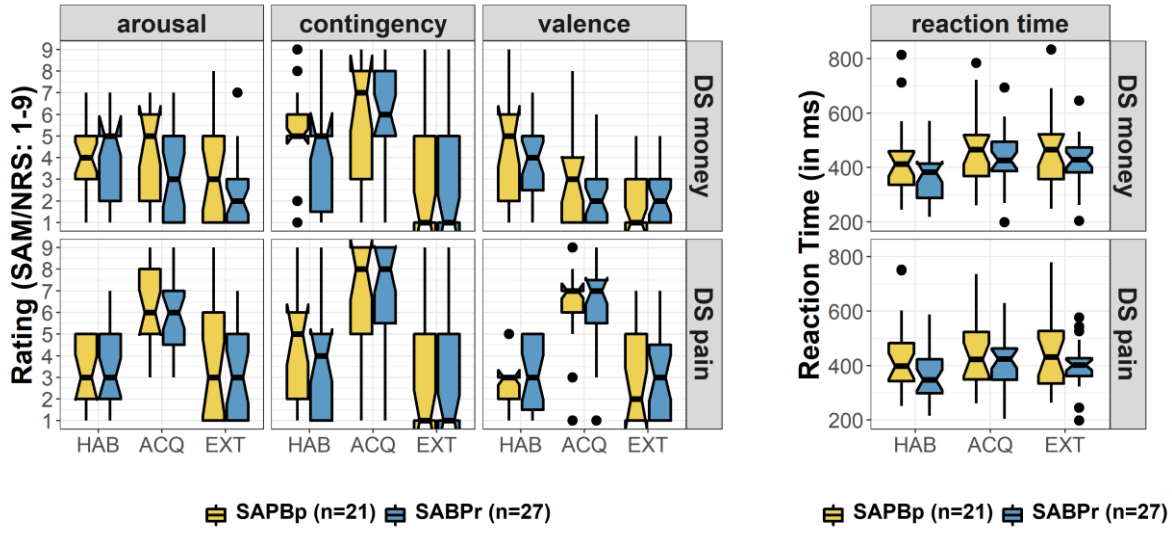
	Code	Diagnoses	Remitted	Acute
SABP	296.26	Major depressive disorder, single episode	10	
	296.30/296.36	Major depressive disorder, recurrent	2	2
	300.29	Specific phobia		1
	300.3	Obsessive-compulsive disorder	1	
	303.90	Dependence: Alcohol	2	
	304.xx	Dependence: Cannabis, Cocaine, Opioids	2	
	305.xx	Abuse: Opioids/Amphetamine/Cannabis/ Sedative-, hypnotic-, or anxiolytic-related	3	1
	307.51	Bulimia Nervosa	1	
	309.81	Posttraumatic stress disorder	1	
HC	296.26	Major depressive disorder, single episode	1	
CBP	296.26	Major depressive disorder, single episode	3	
	296.33/296.36	Major depressive disorder, recurrent	3	2
	300.01	Panic disorder, without agoraphobia		2
	300.22	Agoraphobia without history of panic disorder	1	
	303.90	Dependenc: Alcohol	1	
	304.10	Dependence: Sedative-, hypnotic-, or anxiolytic-related	1	
	305.xx	Abuse: Cannabis, Cocaine, Hallucinogen, Amphetamine	1	
	307.10	Anorexia Nervosa		1
	307.51	Bulimia Nervosa	1	

Supplementary table 1 reports comorbid metal disorders. Related to STAR Methods: diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM IV) in controls (HC), patients with chronic back pain (CBP) and patients with subacute back pain (SABP)

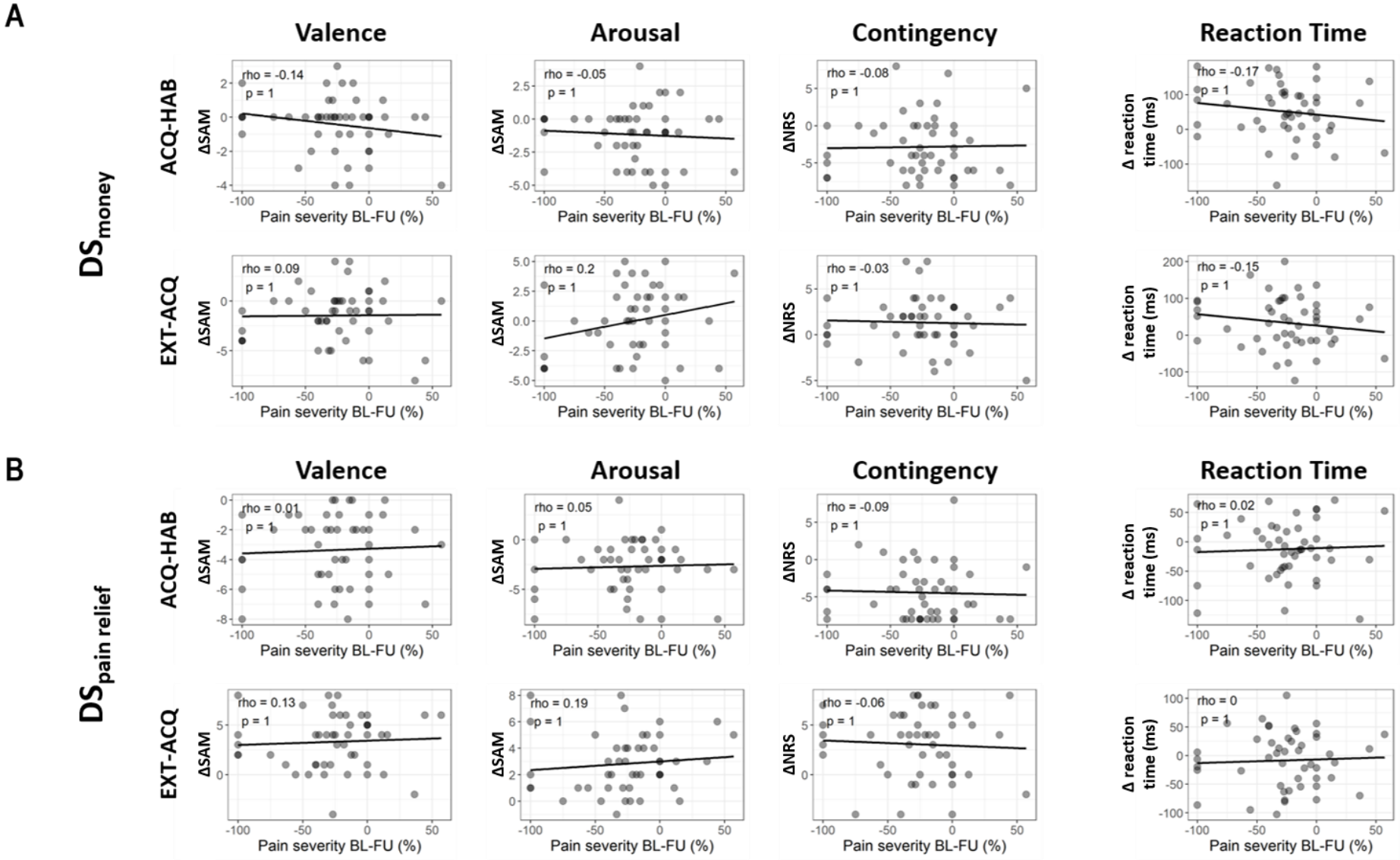


Supplementary Figure 1 depicts ratings and reaction times of patients with remitted and persistent SABP. Related to STAR Methods: *Boxplots show patients with remitted pain (SABPr, yellow) and persistent pain (SABPp, blue) at 6 months follow-up. Ratings of valence and arousal were assessed on a scale from 1 to 9 using the self-assessment manikins. Higher values indicate higher perceived arousal/valence/contingency. Abbreviations: DS: discriminative stimulus; HAB: habituation; ACQ: acquisition; EXT: extinction; SAM: Self-Assessment Manikin; NRS: Numeric Rating Scale; ms: milliseconds;*

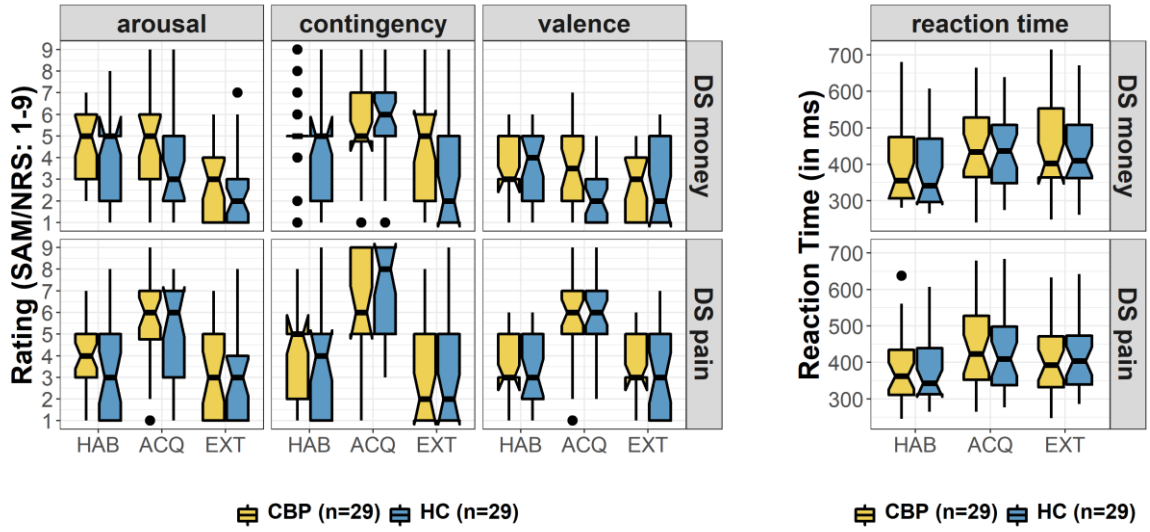
Analyses of perceived arousal, valence and contingency and reaction times to DS_{money} and $DS_{pain\ relief}$ in patients with persistent SABP and recovered SABP

		F-Tests			Posthoc-tests: SABP persistent		Posthoc-tests: SABP recovered	
		Group (SABPr – SABPp): F(df); p; ges	**Phase (HAB-ACQ-EXT): F(df); p; ges**	**Group x Phase F(df); p; ges**	**HAB-ACQ t(df); p; d**	**ACQ-EXT t(df); p; d**	**HAB-ACQ t(df); p; d**	**ACQ-EXT t(df); p; d**
DS_{money}	**Arousal**	F(1,46)=1.93; p=0.171; ges=0.020	**F(1.76,80.79)=7.25; p=0.002; ges=0.076**	F(1.76,80.79)=1.33; p=0.269; ges=0.015	t(20)=-1.02; p=0.96; d=-0.222	t(20)=2.57; p=0.054; d=0.562	t(26)=0.89; p=1.000; d=0.171	**t(26)=2.98; p=0.018; d=0.574**
	Valence	F(1,46)=0.61; p=0.441; ges=0.006	**F(1.55,71.1)=18.10; p<0.001; ges=0.171**	F(1.55,71.1)=0.69; p=0.472; ges=0.008	t(20)=2.09; p=0.150; d=0.455	t(20)=2.27; p=0.103; d=0.496	**t(26)=3.49; p=0.005; d=0.671**	t(26)=0.38; p=1.000; d=0.074
	Contingency	F(1,46)=0.095; p=0.759; ges<0.001	**F(1.68,77.31)=16.32; p<0.001; ges=0.174**	F(1.68,77.31)=1.10; p=0.330; ges=0.014	t(20)=-0.953; p=1.000; d=-0.208	**t(20)=2.96; p=0.023; d=0.646**	**t(26)=-3.72; p=0.003; d=-0.717**	**t(26)=3.97; p=0.002; d=0.763**
	Reaction time	F(1,46)=1.48; p=0.230; ges=0.028	**F(1.6,73.41)=15.65; p<0.001; ges=0.032**	F(1.6,73.41)=0.84; p=0.413; ges=0.002	t(20)=-2.31; p=0.095; d=-0.504	t(20)=0.43; p=1.000; d=0.093	**t(26)=-4.09; p=0.001; d=-0.787**	t(26)=2.02; p=0.16; d=0.389
$DS_{pain\ relief}$	**Arousal**	F(1,46)=0.26; p=0.614; ges=0.003	**F(2,92)=45.73; p<0.001 ges=0.307**	F(2,92)=0.67; p=0.515; ges=0.006	**t(20)=-8.22; p<0.001; d=-1.79**	**t(20)=4.67; p<0.001; d=1.02**	**t(26)=-5.34; p<0.001; d=-1.03**	**t(26)=5.34; p<0.001; d=1.03**
	Valence	F(1,46)=0.03; p=0.867; ges<0.001	**F(2,92)=53.72; p<0.001; ges=0.420**	F(2,92)=0.06; p=0.940; ges<0.001	**t(20)=-6.44; p<0.001; d=-1.40**	**t(20)=6.17; p<0.001; d=1.35**	**t(26)=-5.65; p<0.001; d=-1.09**	**t(26)=7.54; p<0.001; d=1.45**
	Contingency	F(1,46)=0.15; p=0.702; ges=0.001	**F(2,92)=44.86; p<0.001; ges=0.364**	F(2,92)=0.32; p=0.729; ges=0.004	**t(20)=-3.66; p=0.005; d=-0.799**	**t(20)=4.97; p<0.001; d=1.08**	**t(26)=-5.17; p<0.001; d=-0.995**	**t(26)=7.14; p<0.001; d=1.37**
	Reaction time	F(1,46)=2.39; p=0.129; ges=0.045	**F(1.76,81.16)=7.53; p=0.002; ges=0.014**	F(1.76,81.16)=0.89; p=0.404; ges=0.002	t(20)=-1.52; p=0.429; d=-0.332	t(20)=0.811; p=1.000; d=0.177	**t(26)=-3.23; p=0.010; d=-0.621**	t(26)=0.889; p=1.000; d=0.171

Supplementary table 2 Analyses of variances and posthoc-tests for perceived arousal, valence and contingency and reaction times to DS_{money} and $DS_{pain\ relief}$ in patients with persistent SABP and recovered SABP. Related to STAR Methods. The table shows results for analyses of variances and Bonferroni-corrected posthoc tests. All results that survived the corrected statistical threshold ($p_{bonf} < 0.05$) are depicted in bold. Abbreviations: DS: discriminative stimulus; SABP: subacute back pain; df: degrees of freedom; ges: generalized eta squared; d: Cohen's d; HAB: habitation phase; ACQ: acquisition phase; EXT: extinction phase;


A
Valence
Arousal
Contingency
Reaction Time
DS money
ACQ-HAB
EXT-ACQ
ΔSAM
ΔNRS
Δ reaction time (ms)
Pain severity BL-FU (%)
rho = -0.14
p = 1
rho = -0.05
p = 1
rho = -0.08
p = 1
rho = -0.17
p = 1
rho = 0.09
p = 1
rho = 0.2
p = 1
rho = -0.03
p = 1
rho = -0.15
p = 1
B
DS pain relief
rho = 0.01
p = 1
rho = 0.05
p = 1
rho = -0.09
p = 1
rho = 0.02
p = 1
rho = 0.13
p = 1
rho = 0.19
p = 1
rho = -0.06
p = 1
rho = 0
p = 1

Supplementary Figure 2: learning-related changes in perceived valence, arousal and contingency of the discriminative stimuli, as well as learning-related changes in reaction time to the discriminative stimuli do not predict the transition from subacute to chronic back pain. Related to STAR Methods. *Scatter plots and spearman correlation coefficients are depicted for the change in perceived valence (first column), perceived arousal (second column), contingency (third column) and the change in reaction time (fourth column, measured in milliseconds) for* ***A)*** *the discriminative stimulus of the monetary reward condition (DS_{money}) and* ***B)*** *the discriminative stimulus of the pain relief condition. The upper row depicts the difference between the habituation and acquisition phase (acquisition minus habituation), the lower row depicts the difference between the acquisition and extinction phase (extinction minus acquisition). Correlation coefficients are shown as Spearman's Rho and reported with Bonferroni-corrected p-values (corrected for 16 tests, yielding an uncorrected threshold of $p < 0.003125$). Abbreviations: DS: discriminative stimulus; BL: baseline; FU: follow-up; HAB: habituation; ACQ: acquisition; EXT: extinction; SAM: Self-Assessment Manikin; NRS: Numeric Rating Scale; ms: milliseconds;*

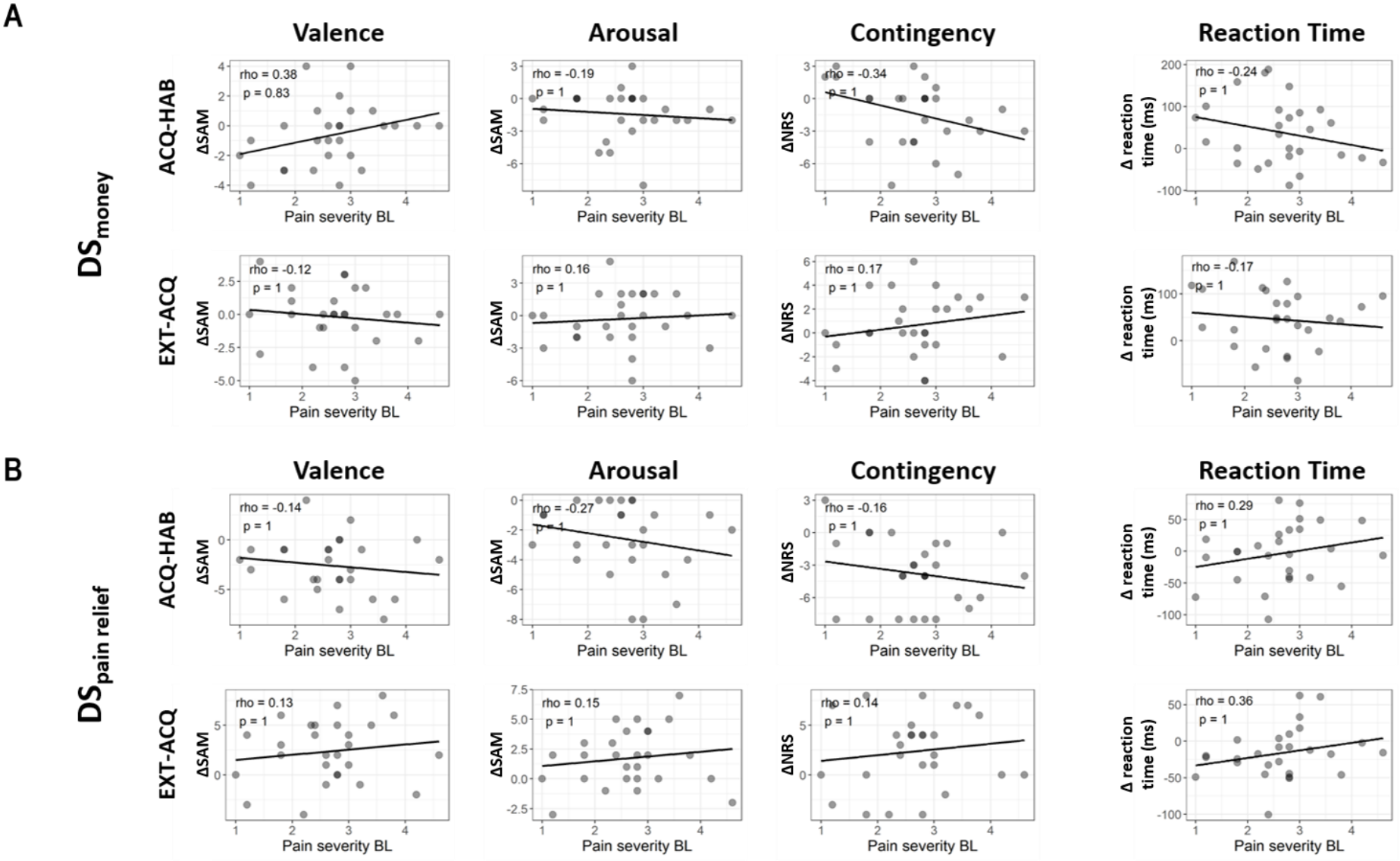


Supplementary Figure 3 depicts perceived valence, arousal and contingency of the discriminative stimuli, as well reaction time to the discriminative stimuli in patients with chronic back pain and controls. Related to STAR Methods. *Boxplots show patients with chronic back pain (CBP, yellow) and controls (HC, blue). Ratings of valence and arousal were assessed on a scale from 1 to 9 using the self-assessment manikins. Abbreviations: DS: discriminative stimulus; HAB: habituation; ACQ: acquisition; EXT: extinction; SAM: Self-Assessment Manikin; NRS: Numeric Rating Scale; ms: milliseconds;*

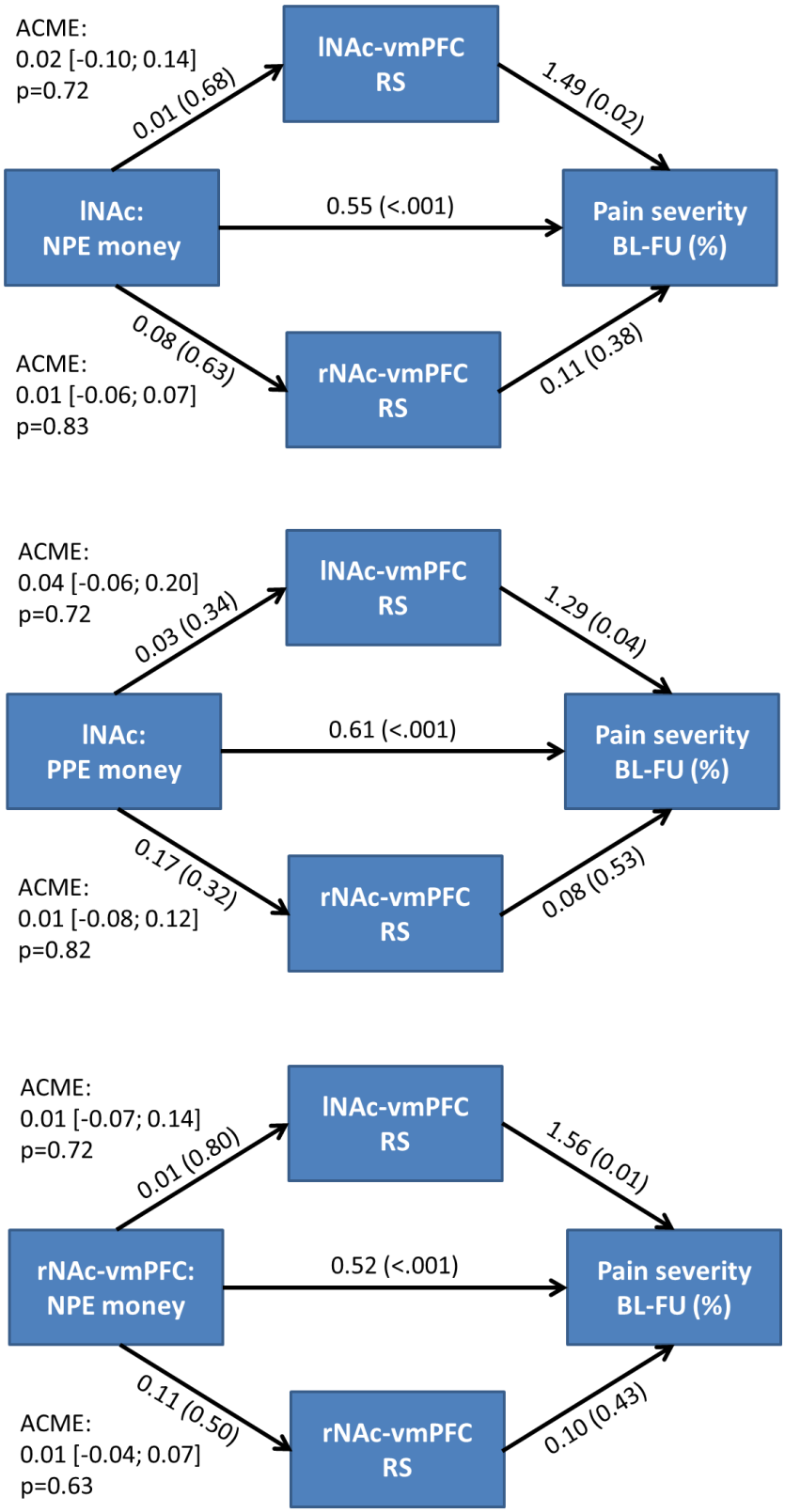
Analyses of perceived arousal, valence and contingency and reaction times to DS_{money} and $DS_{pain\ relief}$ in patients with persistent CBP and healthy controls

		F-Tests			Posthoc-tests: CBP		Posthoc-tests: HC	
		Group (CBP – HC): F(df); p; ges	**Phase (HAB-ACQ-EXT): F(df); p; ges**	**Group x Phase F(df); p; ges**	**HAB-ACQ t(df); p; d**	**ACQ-EXT t(df); p; d**	**HAB-ACQ t(df); p; d**	**ACQ-EXT t(df); p; d**
DS_{money}	**Arousal**	F(1,55)=2.85; p=0.097; ges=0.029	**F(2,110)=12.92; p<0.001; ges=0.091**	F(2,110)=0.43; p=0.65; ges=0.003	t(51.7)=0.72; p=1.00; d=0.193	**t(51.2)=2.83; p=0.02; d=0.752**	t(55.2)=0.12; p=1.00; d=0.032	t(53.7)=1.86; p=0.20; d=0.490
	Valence	F(1,55)=1.04; p=0.312; ges=0.011	**F(2,110)=4.44; p=0.014; ges=0.033**	F(2,110)=1.53; p=0.221; ges=0.012	t(54.5)=0.34; p=1.000; d=0.090	t(50.8)=1.40; p=0.507; d=0.371	t(54.6)=2.00; p=0.150; d=0.526	t(54.8)=-0.48; p=1.000; d=-0.127
	Contingency	F(1,55)=1.07; p=0.306; ges=0.012	**F(1.79,98.49)=17.99; p<0.001; ges=0.112**	F(1.79,98.49)=1.96; p=0.151; ges=0.014	t(54.1)=-1.09; p=0.843; d=-0-289	t(53.2)=2.02; p=0.144; d=0.535	**t(56.0)=-2.54; p=0.041; d=-0.668**	**t(55.0)=4.24; p<0.001; d=1.110**
	Reaction time	F(1,55)=0.32; p=0.577; ges=0.005	**F(1.63,89.56)=23.47; p<0.001; ges=0.043**	F(1.63,89.56)=0.95; p=0.376; ges=0.002	t(54.8)=-1.50; p=0.414; d=-0.399	t(54.8)=0.24; p=1.000; d=0.062	t(55.1)=-2.05; p=0.136; d=-0.538	t(56.0)=-0.20; p=1.000; d=-0.054
$DS_{pain\ relief}$	**Arousal**	F(1,55)=2.67; p=0.108; ges=0.025	**F(2,110)=32.91; p<0.001; ges=0.218**	F(2,110)=0.49; p=0.612; ges=0.004	**t(51.3)=-3.34; p=0.005; d=-0.886**	**t(54.6)=4.72; p<0.001; d=1.250**	**t(56.0)=-3.96; p<0.001; d=-1.040**	**t(56.0)=4.16; p<0.001; d=1.090**
	Valence	F(1,55)=0.05; p=0821.; ges<0.001	**F(1.61,88.63)=47.69; p<0.001; ges=0.341**	F(1.61,88.63)=0.24; p=0.736; ges=0.003	**t(48.1)=-4.90; p<0.001; d=-1.300**	**t(48.4)=5.24; p<0.001; d=1.390**	**t(56.0)=-6.19; p<0.001; d=-1.630**	**t(55.0)=6.04; p<0.001; d=1.590**
	Contingency	F(1,55)=0.42; p=0.518; ges=0.003	**F(1.76,96.93)=53.64; p<0.001; ges=0.372**	F(1.76,96.93)=1.65; p=0.200; ges=0.018	**t(50.2)=-3.79; p=0.001; d=-1.011**	**t(51.8)=5.86; p<0.001; d=1.560**	**t(55.2)=-6.99; p<0.001; d=-1.840**	**t(50.3)=6.92; p<0.001; d=1.820**
	Reaction time	F(1,55)=0.11; p=0.747; ges=0.002	**F(1.68,92.62)=27.08; p<0.001; ges=0.034**	F(1.68,92.62)=0.48; p=0.588; ges<0.001	t(54.7)=-1.61; p=0.342; d=-0.426	t(54.6)=0.58; p=1.000; d=0.153	t(54.0)=-1.76; p=0.253; d=-0.462	t(55.7)=0.21; p=1.000; d=0.055

Supplementary table 3 Analyses of variances and posthoc-tests for perceived arousal, valence and contingency and reaction times to DS_{money} and $DS_{pain\ relief}$ in patients with CBP and HC. Related to STAR Methods. The table shows results for analyses of variances and Bonferroni-corrected posthoc tests. All results that survived the corrected statistical threshold ($p_{bonf} < 0.05$) are depicted in bold. Abbreviations: DS: discriminative stimulus; HC: healthy controls; CBP: chronic back pain; df: degrees of freedom; ges: generalized eta squared; d: Cohen's d; HAB: habituation phase; ACQ: acquisition phase; EXT: extinction phase;


A
Valence
Arousal
Contingency
Reaction Time
DS money
ACQ-HAB
EXT-ACQ
ΔSAM
ΔNRS
Δ reaction time (ms)
Pain severity BL
rho = 0.38
p = 0.83
rho = -0.19
p = 1
rho = -0.34
p = 1
rho = -0.24
p = 1
rho = -0.12
p = 1
rho = 0.16
p = 1
rho = 0.17
p = 1
rho = -0.17
p = 1
B
Valence
Arousal
Contingency
Reaction Time
DS pain relief
ACQ-HAB
EXT-ACQ
ΔSAM
ΔNRS
Δ reaction time (ms)
Pain severity BL
rho = -0.14
p = 1
rho = -0.27
p = 1
rho = -0.16
p = 1
rho = 0.29
p = 1
rho = 0.13
p = 1
rho = 0.15
p = 1
rho = 0.14
p = 1
rho = 0.36
p = 1

Supplementary Figure 4: Learning-related changes in perceived valence, arousal and contingency of the discriminative stimuli, as well as learning-related changes in reaction time to the discriminative stimuli are not related to severity of chronic back pain. Related to STAR Methods. Scatter plots and spearman correlation coefficients are depicted for the change in perceived valence (first column), perceived arousal (second column), contingency (third column) and the change in reaction time (fourth column, measured in milliseconds) for ***A)*** *the discriminative stimulus of the monetary reward condition (DS_{money}) and* ***B)*** *the discriminative stimulus of the pain relief condition. The upper row depicts the difference between the habituation and acquisition phase (acquisition minus habituation), the lower row depicts the difference between the acquisition and extinction phase (extinction minus acquisition). Correlation coefficients are shown as Spearman's Rho and reported with Bonferroni-corrected p-values (corrected for 16 tests, yielding an uncorrected threshold of $p < 0.003125$). Abbreviations: DS: discriminative stimulus; BL: baseline; HAB: habituation; ACQ: acquisition; EXT: extinction; SAM: Self-Assessment Manikin; NRS: Numeric Rating Scale; ms: milliseconds;*



Supplementary Figure 5: Task-based prediction of chronicity was not mediated via functional connectivity of nucleus accumbens and ventromedial prefrontal cortex at rest shows. Related to Figures 2 and 3. The graphs depict results of mediation analysis with functional connectivity between vmPFC and left NAc (upper branch of the models) and right NAc (lower branch of the models) as mediating variable, encoding of monetary prediction error as independent and percentage change in pain severity from baseline to follow-up as dependent variable. Coefficients are given with p-values in round brackets in addition to the average causal mediation effect with 95 percent confidence intervals in square brackets for each model. Abbreviations: vmPFC: ventromedial prefrontal cortex; lNAc: left nucleus accumbens; rNAc: right nucleus accumbens; BL: baseline; FU: follow-up; RS: resting state; NPE: negative prediction error; PPE: positive prediction error; ACME: average causal mediation effect;

Correlation of BOLD responses in vmPFC and NAc with percent change in pain severity from baseline to follow-up				
	ROI	**Contrast**	**Pearson's correlation: r(df); p, p_{bonf}**	**ROC: Area under curve**
Parameter estimate of BOLD contrast	Left nucleus accumbens	Anticipation money	r(46)=0.07; p=0.632; pbonf=1	AUC=0.53; p=0.379; pbonf=1
		Anticipation pain relief	r(46)=-0.06; p=0.661; pbonf=1	AUC=0.44; p=0.758; pbonf=1
		DS money	r(46)=-0.34; p=0.018; pbonf=0.827	AUC=0.29; p=0.995; pbonf=1
		DS pain	r(46)=-0.17; p=0.235; pbonf=1	AUC=0.31; p=0.989; pbonf=1
		Positive prediction error: money	**r(46)=0.61; p<0.001; pbonf<0.001**	**AUC=0.77; p<0.001; pbonf=0.021**
		Negative prediction error: money	**r(46)=0.55; p<0.001; pbonf=0.002**	**AUC=0.83; p<0.001; pbonf<0.001**
		Positive prediction error: pain relief	r(46)=0.18; p=0.212; pbonf=1	AUC=0.63; p=0.068; pbonf=1
		Negative prediction error: pain relief	r(46)=0.12; p=0.416; pbonf=1	AUC=0.61; p=0.096; pbonf=1
		US pain	r(46)=0.36; p=0.012; pbonf=0.558	AUC=0.68; p=0.018; pbonf=0.806
	Right nucleus accumbens	Anticipation money	r(46)=0.08; p=0.598; pbonf=1	AUC=0.52; p=0.418; pbonf=1
		Anticipation pain relief	r(46)=0.07; p=0.628; pbonf=1	AUC=0.53; p=0.387; pbonf=1
		DS money	r(46)=0.00; p=0.999; pbonf=1	AUC=0.53; p=0.348; pbonf=1
		DS pain	r(46)=0.26; p=0.076; pbonf=1	AUC=0.56; p=0.261; pbonf=1
		Positive prediction error: money	r(46)=0.08; p=0.583; pbonf=1	AUC=0.53; p=0.379; pbonf=1
		Negative prediction error: money	r(46)=0.00; p=0.998; pbonf=1	AUC=0.48; p=0.590; pbonf=1
		Positive prediction error: pain relief	r(46)=-0.08; p=0.606; pbonf=1	AUC=0.48; p=0.598; pbonf=1
		Negative prediction error: pain relief	r(46)=-0.06; p=0.692; pbonf=1	AUC=0.49; p=0.565; pbonf=1
		US pain	r(46)=-0.11; p=0.445; pbonf=1	AUC=0.50; p=0.508; pbonf=1
	vmPFC	Anticipation money	r(46)=0.04; p=0.812; pbonf=1	AUC=0.41; p=0.849; pbonf=1
		Anticipation pain relief	r(46)=-0.06; p=0.670; pbonf=1	AUC=0.40; p=0.893; pbonf=1
		DS money	r(46)=0.25; p=0.089; pbonf=1	AUC=0.56; p=0.248; pbonf=1
		DS pain	r(46)=0.13; p=0.376; pbonf=1	AUC=0.41; p=0.849; pbonf=1
		Positive prediction error: money	r(46)=-0.10; p=0.518; pbonf=1	AUC=0.41; p=0.863; pbonf=1
		Negative prediction error: money	r(46)=-0.12; p=0.412; pbonf=1	AUC=0.44; p=0.758; pbonf=1
		Positive prediction error: pain relief	r(46)=0.10; p=0.502; pbonf=1	AUC=0.65; p=0.042; pbonf=1
		Negative prediction error: pain relief	r(46)=0.09; p=0.538; pbonf=1	AUC=0.66; p=0.029; pbonf=1
		US pain	r(46)=0.04; p=0.809; pbonf=1	AUC=0.48; p=0.582; pbonf=1

Supplementary table 4 Prediction of transition from subacute to chronic back pain with responses to different reward learning processes in the nucleus accumbens and ventromedial prefrontal cortex (vmPFC), related to Figure 2. The table shows correlations between the percentage change in pain severity from baseline to the six month follow-up and the BOLD response to different learning processes in the respective region. BOLD responses were extracted as parameter estimates from predefined masks extracted from neurosynth.org (see above). Correlations are reported as Pearson's correlation with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests yielding, a threshold of p < 0.00111). Additionally we divided patients in recovered patients if their pain severity decreased by 20% between the first

examination and the follow-up assessment patients and persistent patients in all other instances. Receiver operating characteristic (ROC) curves were created for classifying recovered and persistent patients with the respective parameter estimates extracted from our regions of interest. We report the area under each ROC curves as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests, yielding a threshold of $p < 0.00111$). All results that survived the corrected statistical significant ($p_{bonf} < 0.05$) are depicted in bold.

Correlation of functional connectivity with the vmPFC and the percent change in pain severity from baseline to follow-up				
	ROI	**Contrast**	**Pearson's correlation: r(df); p, p_{bonf}**	**ROC: Area under curve**
Functional connectivity with vmPFC	Left nucleus accumbens	Anticipation money	r(46)=0.00; p=0.982; pbonf=1	AUC=0.64; p=0.055; pbonf=1
		Anticipation pain relief	r(46)=0.05; p=0.739; pbonf=1	AUC=0.52; p=0.402; pbonf=1
		DS money	r(46)=-0.11; p=0.441; pbonf=1	AUC=0.51; p=0.475; pbonf=1
		DS pain	r(46)=-0.41; p=0.004; pbonf=0.165	AUC=0.39; p=0.907; pbonf=1
		Positive prediction error: money	r(46)=0.16; p=0.265; pbonf=1	AUC=0.57; p=0.217; pbonf=1
		Negative prediction error: money	r(46)=0.12; p=0.411; pbonf=1	AUC=0.64; p=0.055; pbonf=1
		Positive prediction error: pain relief	r(46)=0.01; p=0.948; pbonf=1	AUC=0.49; p=0.565; pbonf=1
		Negative prediction error: pain relief	r(46)=-0.04; p=0.786; pbonf=1	AUC=0.50; p=0.500; pbonf=1
		US pain	r(46)=-0.11; p=0.459; pbonf=1	AUC=0.46; p=0.704; pbonf=1
	Right nucleus accumbens	Anticipation money	r(46)=0.20; p=0.167; pbonf=1	AUC=0.53; p=0.379; pbonf=1
		Anticipation pain relief	r(46)=0.00; p=0.986; pbonf=1	AUC=0.53; p=0.363; pbonf=1
		DS money	r(46)=0.07; p=0.631; pbonf=1	AUC=0.54; p=0.340; pbonf=1
		DS pain	r(46)=0.13; p=0.372; pbonf=1	AUC=0.51; p=0.443; pbonf=1
		Positive prediction error: money	r(46)=-0.06; p=0.694; pbonf=1	AUC=0.54; p=0.340; pbonf=1
		Negative prediction error: money	**r(46)=0.52; p<0.001; pbonf=0.006**	**AUC=0.78; p<0.001; pbonf=0.021**
		Positive prediction error: pain relief	r(46)=0.14; p=0.348; pbonf=1	AUC=0.59; p=0.156; pbonf=1
		Negative prediction error: pain relief	r(46)=0.41; p=0.004; pbonf=0.191	AUC=0.66; p=0.026; pbonf=1
		US pain	r(46)=-0.13; p=0.397; pbonf=1	AUC=0.43; p=0.807; pbonf=1

Supplementary table 5 Prediction of transition from subacute to chronic back pain with task-based functional connectivity between ventromedial prefrontal cortex (vmPFC) and bilateral nucleus accumbens during different reward learning processes, related to Figure 2. The table shows correlations between the percentage change in pain severity from baseline to the six month follow-up and the task-based functional connectivity between the ventromedial prefrontal cortex and bilateral nucleus accumbens during different learning processes in the respective region. Parameter estimates were extracted from predefined masks extracted from neurosynth.org (see above), using a psychophysiological interaction (PPI) with the vmPFC as a seed region. Correlations are reported as Pearson's correlation with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests, yielding a threshold of p < 0.00111). Additionally we divided patients in recovered patients if their pain severity decreased by 20% between the first examination and the follow-up assessment patients and persistent patients in all other instances. Receiver operating characteristic (ROC) curves were created for classifying recovered and persistent patients with the respective parameter estimates extracted from our regions of interest. We report the area under each ROC curves as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests, yielding a threshold of p < 0.00111). All results that survived the corrected statistical threshold (p_{bonf} < 0.05) are depicted in bold.

Correlation of BOLD responses in vmPFC and NAc during habituation and extinction with percent change in pain severity from baseline to follow-up

	Phase(s)	Contrast	ROI	Pearson's correlation: r(df); p, pbonf	ROC: Area under curve
Parameter estimate of BOLD contrast	Habituation	DS money	lNA	r(46)=-0.09; p=0.560; pbonf=1	AUC=0.41; p=0.868; pbonf=1
		DS money	rNA	r(46)=0.08; p=0.570; pbonf=1	AUC=0.46; p=0.675; pbonf=1
		DS money	vmPFC	r(46)=0.33; p=0.023; pbonf=0.558	AUC=0.71; p=0.007; pbonf=0.159
		DS pain	lNA	r(46)=0.19; p=0.204; pbonf=1	AUC=0.60; p=0.128; pbonf=1
		DS pain	rNA	r(46)=0.12; p=0.413; pbonf=1	AUC=0.58; p=0.166; pbonf=1
		DS pain	vmPFC	r(46)=0.12; p=0.407; pbonf=1	AUC=0.66; p=0.026; pbonf=0.632
	Habituation < Acquisition	DS money	lNA	r(46)=-0.05; p=0.719; pbonf=1	AUC=0.51; p=0.451; pbonf=1
		DS money	rNA	r(46)=-0.08; p=0.602; pbonf=1	AUC=0.44; p=0.771; pbonf=1
		DS money	vmPFC	r(46)=0.12; p=0.435; pbonf=1	AUC=0.61; p=0.103; pbonf=1
		DS pain	lNA	r(46)=0.25; p=0.081; pbonf=1	AUC=0.66; p=0.032; pbonf=0.768
		DS pain	rNA	r(46)=0.15; p=0.322; pbonf=1	AUC=0.61; p=0.096; pbonf=1
		DS pain	vmPFC	r(46)=0.17; p=0.241; pbonf=1	AUC=0.72; p=0.005; pbonf=0.116
	Extinction	DS money	lNA	r(46)=-0.06; p=0.697; pbonf=1	AUC=0.47; p=0.637; pbonf=1
		DS money	rNA	r(46)=-0.03; p=0.836; pbonf=1	AUC=0.47; p=0.629; pbonf=1
		DS money	vmPFC	r(46)=0.10; p=0.496; pbonf=1	AUC=0.54; p=0.340; pbonf=1
		DS pain	lNA	r(46)=0.03; p=0.849; pbonf=1	AUC=0.46; p=0.697; pbonf=1
		DS pain	rNA	r(46)=-0.02; p=0.914; pbonf=1	AUC=0.49; p=0.557; pbonf=1
		DS pain	vmPFC	r(46)=0.16; p=0.288; pbonf=1	AUC=0.54; p=0.311; pbonf=1
	Acquistion > Extinction	DS money	lNA	r(46)=0.07; p=0.620; pbonf=1	AUC=0.55; p=0.296; pbonf=1
		DS money	rNA	r(46)=-0.01; p=0.922; pbonf=1	AUC=0.54; p=0.311; pbonf=1
		DS money	vmPFC	r(46)=-0.20; p=0.180; pbonf=1	AUC=0.37; p=0.935; pbonf=1
		DS pain	lNA	r(46)=-0.27; p=0.066; pbonf=1	AUC=0.37; p=0.943; pbonf=1
		DS pain	rNA	r(46)=-0.16; p=0.268; pbonf=1	AUC=0.39; p=0.904; pbonf=1
		DS pain	vmPFC	r(46)=-0.18; p=0.228; pbonf=1	AUC=0.27; p=0.997; pbonf=1

Supplementary table 6: Prediction of transition from subacute to chronic back pain with responses to discriminative stimuli (DS) during habituation, extinction and changes from habituation to acquisition and acquisition to extinction in the nucleus accumbens and ventromedial prefrontal cortex (vmPFC). Related to STAR Methods. The table shows correlations between the percentage change in pain severity from baseline to the six month follow-up and the BOLD response to different learning processes in the respective region. BOLD responses were extracted as parameter estimates from predefined masks extracted from neurosynth.org. Correlations are reported as Pearson's correlation with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 24 tests yielding, a threshold of $p < 0.00208$). Additionally we divided patients in recovered patients if their pain severity decreased by 20% between the first examination and the follow-up assessment patients and persistent patients in all other instances. Receiver operating characteristic (ROC) curves were created for classifying recovered and persistent patients with the respective parameter estimates extracted from our regions of interest. We report the area under each ROC curves as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 24 tests, yielding a threshold of $p < 0.00208$).

Prediction of chronicity with patterns of BOLD responses in vmPFC and NAc					
			Accuracy M±SD	**One-sample t-test (against Accuracy = 0.5): t(df); p; pbonf; d**	**ROC: Area under curve**
Pattern of BOLD contrast	Left nucleus accumbens	Anticipation money	0.48±0.39	t(47)=-0.40; p=0.69; pbonf=1; d=0.06	AUC=0.49; p=0.55; pbonf=1
		Anticipation pain relief	0.49±0.39	t(47)=-0.15; p=0.88; pbonf=1; d=0.02	AUC=0.49; p=0.57; pbonf=1
		DS money	0.52±0.39	t(47)=0.30; p=0.76; pbonf=1; d=0.04	AUC=0.51; p=0.46; pbonf=1
		DS pain	0.44±0.38	t(47)=-1.10; p=0.28; pbonf=1; d=0.16	AUC=0.43; p=0.81; pbonf=1
		Positive prediction error: money	0.47±0.39	t(47)=-0.54; p=0.59; pbonf=1; d=0.08	AUC=0.49; p=0.56; pbonf=1
		Negative prediction error: money	0.62±0.40	t(47)=2.09; p=0.04; pbonf=1; d=0.30	AUC=0.68; p=0.02; pbonf=0.85
		Positive prediction error: pain relief	0.44±0.37	t(47)=-1.08; p=0.29; pbonf=1; d=0.16	AUC=0.40; p=0.88; pbonf=1
		Negative prediction error: pain relief	0.44±0.37	t(47)=-1.03; p=0.31; pbonf=1; d=0.15	AUC=0.40; p=0.88; pbonf=1
		US pain	0.46±0.38	t(47)=-0.66; p=0.51; pbonf=1; d=0.10	AUC=0.40; p=0.89; pbonf=1
	Right nucleus accumbens	Anticipation money	0.40±0.36	t(47)=-1.88; p=0.07; pbonf=1; d=0.27	AUC=0.34; p=0.97; pbonf=1
		Anticipation pain relief	0.55±0.39	t(47)=0.91; p=0.37; pbonf=1; d=0.13	AUC=0.59; p=0.16; pbonf=1
		DS money	0.42±0.36	t(47)=-1.60; p=0.12; pbonf=1; d=0.23	AUC=0.38; p=0.92; pbonf=1
		DS pain	**0.71±0.34**	**t(47)=4.30; p<0.001; pbonf=0.004; d=0.62**	**AUC=0.8; p<0.001; pbonf=0.009**
		Positive prediction error: money	0.55±0.38	t(47)=0.84; p=0.40; pbonf=1; d=0.12	AUC=0.57; p=0.20; pbonf=1
		Negative prediction error: money	0.55±0.42	t(47)=0.81; p=0.42; pbonf=1; d=0.12	AUC=0.56; p=0.24; pbonf=1
		Positive prediction error: pain relief	0.53±0.40	t(47)=0.47; p=0.64; pbonf=1; d=0.07	AUC=0.56; p=0.25; pbonf=1
		Negative prediction error: pain relief	0.54±0.40	t(47)=0.65; p=0.52; pbonf=1; d=0.09	AUC=0.56; p=0.25; pbonf=1
		US pain	0.57±0.42	t(47)=1.18; p=0.24; pbonf=1; d=0.17	AUC=0.59; p=0.13; pbonf=1
	vmPFC	Anticipation money	0.40±0.40	t(47)=-1.81; p=0.08; pbonf=1; d=0.26	AUC=0.33; p=0.98; pbonf=1
		Anticipation pain relief	0.40±0.39	t(47)=-1.76; p=0.08; pbonf=1; d=0.25	AUC=0.35; p=0.97; pbonf=1
		DS money	0.57±0.40	t(47)=1.22; p=0.23; pbonf=1; d=0.18	AUC=0.59; p=0.13; pbonf=1
		DS pain	0.36±0.39	t(47)=-2.48; p=0.02; pbonf=0.75; d=0.36	AUC=0.31; p=0.99; pbonf=1
		Positive prediction error: money	0.41±0.41	t(47)=-1.47; p=0.15; pbonf=1; d=0.21	AUC=0.41; p=0.86; pbonf=1
		Negative prediction error: money	0.37±0.40	t(47)=-2.23; p=0.03; pbonf=1; d=0.32	AUC=0.33; p=0.98; pbonf=1
		Positive prediction error: pain relief	0.41±0.36	t(47)=-1.66; p=0.10; pbonf=1; d=0.24	AUC=0.34; p=0.97; pbonf=1
		Negative prediction error: pain relief	0.42±0.36	t(47)=-1.57; p=0.12; pbonf=1; d=0.23	AUC=0.36; p=0.96; pbonf=1
		US pain	0.60±0.41	t(47)=1.62; p=0.11; pbonf=1; d=0.23	AUC=0.63; p=0.05; pbonf=1

Supplementary table 7 Prediction of transition from subacute to chronic back pain with patterns of activation in the nucleus accumbens and ventromedial prefrontal cortex (vmPFC) in response to different reward learning processes, related to Figure 4. The table shows how good of patterns of activity in response to different reward learning processes classify recovered and non-recovered persons. Mean accuracy across subjects is reported and tested against chance level accuracy (50%) using a one-sample t-test with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests yielding an uncorrected threshold of p < 0.00111) and Cohen's d.

Additionally receiver operating characteristic (ROC) curves were created for correctly classifying persistent patients with the respective pattern of activity. We report the area under each ROC curves as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests yielding an uncorrected threshold of $p < 0.00111$).). All results that survived the corrected statistical threshold ($p_{bonf} < 0.05$) are depicted in bold.

Prediction of chronicity with patterns of functional connectivity to the vmPFC					
			Accuracy M±SD	**One-sample t-test (against Accuracy = 0.5): t(df); p; pbonf; d**	**ROC: Area under curve**
Pattern of functional connectivity to the vmPFC	Left nucleus accumbens	Anticipation money	0.54±0.35	t(47)=0.75; p=0.46; pbonf=1; d=0.11	AUC=0.58; p=0.19; pbonf=1
		Anticipation pain relief	0.54±0.36	t(47)=0.77; p=0.44; pbonf=1; d=0.11	AUC=0.59; p=0.15; pbonf=1
		DS money	0.44±0.33	t(47)=-1.19; p=0.24; pbonf=1; d=0.17	AUC=0.41; p=0.86; pbonf=1
		DS pain	0.53±0.36	t(47)=0.54; p=0.59; pbonf=1; d=0.08	AUC=0.56; p=0.25; pbonf=1
		Positive prediction error: money	0.54±0.38	t(47)=0.67; p=0.51; pbonf=1; d=0.10	AUC=0.56; p=0.25; pbonf=1
		Negative prediction error: money	0.49±0.36	t(47)=-0.26; p=0.80; pbonf=1; d=0.04	AUC=0.46; p=0.67; pbonf=1
		Positive prediction error: pain relief	0.64±0.34	t(47)=2.88; p=0.01; pbonf=0.27; d=0.42	AUC=0.73; p=0.003; pbonf=0.15
		Negative prediction error: pain relief	0.42±0.36	t(47)=-1.55; p=0.13; pbonf=1; d=0.22	AUC=0.38; p=0.93; pbonf=1
		US pain	0.52±0.34	t(47)=0.34; p=0.74; pbonf=1; d=0.05	AUC=0.52; p=0.41; pbonf=1
	Right nucleus accumbens	Anticipation money	0.41±0.37	t(47)=-1.61; p=0.11; pbonf=1; d=0.23	AUC=0.36; p=0.95; pbonf=1
		Anticipation pain relief	0.56±0.36	t(47)=1.17; p=0.25; pbonf=1; d=0.17	AUC=0.59; p=0.15; pbonf=1
		DS money	0.44±0.35	t(47)=-1.23; p=0.23; pbonf=1; d=0.18	AUC=0.42; p=0.83; pbonf=1
		DS pain	0.65±0.33	t(47)=3.16; p=0.003; pbonf=0.123; d=0.46	AUC=0.74; p=0.002; pbonf=0.101
		Positive prediction error: money	0.58±0.36	t(47)=1.49; p=0.14; pbonf=1; d=0.21	AUC=0.62; p=0.09; pbonf=1
		Negative prediction error: money	0.52±0.36	t(47)=0.32; p=0.75; pbonf=1; d=0.05	AUC=0.52; p=0.39; pbonf=1
		Positive prediction error: pain relief	0.49±0.35	t(47)=-0.21; p=0.83; pbonf=1; d=0.03	AUC=0.50; p=0.50; pbonf=1
		Negative prediction error: pain relief	0.52±0.38	t(47)=0.28; p=0.78; pbonf=1; d=0.04	AUC=0.56; p=0.25; pbonf=1
		US pain	0.50±0.35	t(47)=0.06; p=0.95; pbonf=1; d=0.01	AUC=0.49; p=0.53; pbonf=1

Supplementary table 8: Prediction of transition from subacute to chronic back pain with patterns of functional connectivity between the nucleus accumbens and ventromedial prefrontal cortex (vmPFC) in response to different reward learning processes. Related to STAR Methods. The table shows how good patterns of functional connectivity to the vmPFC in response to different reward learning processes classify recovered and non-recovered persons. Mean accuracy across subjects is reported and tested against chance level accuracy (50%) using a one-sample t-test with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests yielding an uncorrected threshold of p < 0.00111) and Cohen's d. Additionally receiver operating characteristic (ROC) curves were created for correctly classifying persistent patients with the respective pattern of connectivity. We report the area under each ROC curve as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests yielding an uncorrected threshold of p < 0.00111).

BOLD responses in vmPFC and NAc: correlation with pain severity in patients with CBP and dissociation between CBP and HC				
	ROI	Contrast	Pearson's correlation: r(df); p, p_{bonf}	ROC: Area under curve
Parameter estimate of BOLD contrast	Left nucleus accumbens	Anticipation money	r(27)=-0.29; p=0.120; pbonf=1	AUC=0.43; p=0.819; pbonf=1
		Anticipation pain relief	r(27)=-0.24; p=0.211; pbonf=1	AUC=0.43; p=0.807; pbonf=1
		DS money	r(27)=-0.06; p=0.764; pbonf=1	AUC=0.47; p=0.633; pbonf=1
		DS pain	r(27)=-0.34; p=0.073; pbonf=1	AUC=0.43; p=0.823; pbonf=1
		Positive prediction error: money	r(27)=0.27; p=0.160; pbonf=1	AUC=0.34; p=0.985; pbonf=1
		Negative prediction error: money	r(27)=0.31; p=0.103; pbonf=1	AUC=0.44; p=0.798; pbonf=1
		Positive prediction error: pain relief	r(27)=-0.03; p=0.864; pbonf=1	AUC=0.55; p=0.273; pbonf=1
		Negative prediction error: pain relief	r(27)=-0.04; p=0.833; pbonf=1	AUC=0.53; p=0.333; pbonf=1
		US pain	r(27)=0.09; p=0.632; pbonf=1	AUC=0.58; p=0.154; pbonf=1
	Right nucleus accumbens	Anticipation money	r(27)=-0.05; p=0.800; pbonf=1	AUC=0.40; p=0.901; pbonf=1
		Anticipation pain relief	r(27)=-0.24; p=0.209; pbonf=1	AUC=0.57; p=0.173; pbonf=1
		DS money	r(27)=0.20; p=0.288; pbonf=1	AUC=0.50; p=0.518; pbonf=1
		DS pain	r(27)=-0.01; p=0.978; pbonf=1	AUC=0.37; p=0.953; pbonf=1
		Positive prediction error: money	r(27)=0.25; p=0.184; pbonf=1	AUC=0.51; p=0.457; pbonf=1
		Negative prediction error: money	r(27)=0.08; p=0.662; pbonf=1	AUC=0.55; p=0.253; pbonf=1
		Positive prediction error: pain relief	r(27)=0.12; p=0.528; pbonf=1	AUC=0.44; p=0.798; pbonf=1
		Negative prediction error: pain relief	r(27)=0.07; p=0.724; pbonf=1	AUC=0.44; p=0.794; pbonf=1
		US pain	r(27)=0.08; p=0.699; pbonf=1	AUC=0.53; p=0.373; pbonf=1
	vmPFC	Anticipation money	r(27)=-0.36; p=0.056; pbonf=1	AUC=0.46; p=0.689; pbonf=1
		Anticipation pain relief	r(27)=0.29; p=0.132; pbonf=1	AUC=0.59; p=0.126; pbonf=1
		DS money	r(27)=-0.14; p=0.480; pbonf=1	AUC=0.62; p=0.064; pbonf=1
		DS pain	r(27)=-0.21; p=0.271; pbonf=1	AUC=0.51; p=0.445; pbonf=1
		Positive prediction error: money	r(27)=-0.09; p=0.651; pbonf=1	AUC=0.36; p=0.970; pbonf=1
		Negative prediction error: money	r(27)=-0.20; p=0.301; pbonf=1	AUC=0.45; p=0.752; pbonf=1
		Positive prediction error: pain relief	r(27)=-0.30; p=0.119; pbonf=1	AUC=0.41; p=0.892; pbonf=1
		Negative prediction error: pain relief	r(27)=-0.35; p=0.063; pbonf=1	AUC=0.42; p=0.839; pbonf=1
		US pain	r(27)=-0.07; p=0.731; pbonf=1	AUC=0.54; p=0.300; pbonf=1

Supplementary table 9: fronto-striatal encoding of reward learning is not associated with pain severity in patients with chronic back pain, related to Figure 5. The table shows correlations between the pain severity of patients with chronic back pain and the BOLD response to different learning processes in the respective region. BOLD responses were extracted as parameter estimates from predefined masks extracted from neurosynth.org (see above). Correlations are reported as Pearson's correlation with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests yielding a threshold of $p < 0.00111$). Additionally we created receiver operating

characteristic (ROC) curves for classifying patients with chronic back pain and controls with the respective parameter estimates extracted from our regions of interest. We report the area under each ROC curves as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests yielding a threshold of $p < 0.00111$). Al results that survived the corrected statistical threshold ($p_{bonf} < 0.05$) are depicted in bold.

Functional connectivity with vmPFC: Correlation with pain severity in patients with CBP and dissociation between CBP and HC				
ROI		**Contrast**	**Pearson's correlation: r(df); p, p_{bonf}**	**ROC: Area under curve**
Functional connectivity with vmPFC	Left nucleus accumbens	Anticipation money	r(27)=0.05; p=0.799; pbonf=1	AUC=0.44; p=0.802; pbonf=1
		Anticipation pain relief	r(27)=-0.18; p=0.361; pbonf=1	AUC=0.55; p=0.279; pbonf=1
		DS money	r(27)=0.01; p=0.976; pbonf=1	AUC=0.63; p=0.050; pbonf=1
		DS pain	r(27)=-0.11; p=0.572; pbonf=1	AUC=0.53; p=0.333; pbonf=1
		Positive prediction error: money	r(27)=-0.26; p=0.171; pbonf=1	AUC=0.61; p=0.070; pbonf=1
		Negative prediction error: money	r(27)=-0.27; p=0.154; pbonf=1	AUC=0.48; p=0.603; pbonf=1
		Positive prediction error: pain relief	r(27)=-0.21; p=0.283; pbonf=1	AUC=0.48; p=0.592; pbonf=1
		Negative prediction error: pain relief	r(27)=-0.05; p=0.801; pbonf=1	AUC=0.50; p=0.500; pbonf=1
		US pain	r(27)=0.03; p=0.870; pbonf=1	AUC=0.51; p=0.469; pbonf=1
	Right nucleus accumbens	Anticipation money	r(27)=-0.11; p=0.586; pbonf=1	AUC=0.45; p=0.727; pbonf=1
		Anticipation pain relief	r(27)=0.35; p=0.060; pbonf=1	AUC=0.49; p=0.579; pbonf=1
		DS money	r(27)=0.13; p=0.516; pbonf=1	AUC=0.37; p=0.952; pbonf=1
		DS pain	r(27)=-0.22; p=0.242; pbonf=1	AUC=0.52; p=0.397; pbonf=1
		Positive prediction error: money	r(27)=0.16; p=0.396; pbonf=1	AUC=0.48; p=0.615; pbonf=1
		Negative prediction error: money	r(27)=-0.01; p=0.965; pbonf=1	AUC=0.42; p=0.864; pbonf=1
		Positive prediction error: pain relief	r(27)=0.09; p=0.655; pbonf=1	AUC=0.34; p=0.982; pbonf=1
		Negative prediction error: pain relief	r(27)=0.18; p=0.340; pbonf=1	AUC=0.42; p=0.850; pbonf=1
		US pain	r(27)=-0.37; p=0.049; pbonf=1	AUC=0.53; p=0.338; pbonf=1

Supplementary table 10: Alterations in fronto-striatal functional connectivity during reward learning is not associated with pain severity in patients with chronic back pain. Related to STAR Methods. The table shows correlations between the pain and the task-based functional connectivity between the ventromedial prefrontal cortex and bilateral nucleus accumbens during different learning processes. Parameter estimates were extracted from predefined masks extracted from neurosynth.org (see above), using a psychophysiological interaction (PPI) with the vmPFC as a seed region. Correlations are reported as Pearson's correlation with degrees of freedom (df), uncorrected p-values and Bonferroni-corrected p-values (corrected for 45 tests yielding a threshold of $p < 0.00111$). Additionally we created receiver operating characteristic (ROC) curves for classifying patients with chronic back pain and controls with the respective parameter estimates for fronto-striatal connectivity. We report the area under each ROC curve as an estimate of sensitivity and specificity. Associated p-values for the comparison to a chance-level ROC curve (i.e. AUC = 0.5) are reported as uncorrected p-values as well as Bonferroni-corrected p-values (corrected for 45 tests yielding a threshold of $p < 0.00111$). All results that survived the corrected statistical threshold ($p_{bonf} < 0.05$) are depicted in bold