Data supplement to: Verdejo-Garcia et al. Neural substrates of cognitive flexibility in cocaine and gambling addictions. *Br J Psychiatry* - doi: 10.1192/bjp.bp.114.152223

Table DS1 Demographic and clinical characteristics of the three study groups by DRD2 genotype. Statistics report results from the 2-way analyses of variance with DRD2 genotype and Group as factors

	Controls Mean (SD)		Gamblers Mean (SD)		Cocaine Users Mean (SD)		p-value
Demographic variables	A1+	A1-	A1+	A1-	A1+	A1-	
N	6	12	7	10	5	13	
Age (years)	32.17 (4,58)	30.67 (4,94)	31.57 (6,08)	35.80 (8,87)	33.00 (8,86)	34.77 (6,30)	0.477
Gender (male/female)	6 / 0	11 / 1	6 / 1	9 / 1	4 / 1	13 / 0	0.364
Laterality (right/left)	6 / 0	11 / 1	6 / 1	10 / 0	5 / 0	13 / 0	0.144
Years of education	10.00 (1.26)	10.83 (2.17)	11.00 (2.08)	9.80 (2.20)	10.8 (2.28)	9.38 (1.26)	0.197
Verbal IQ	102.50 (8.80)	109.08 (8.59)	104.43 (9.52)	101.40 (6.20)	102.60 (8.53)	100.31 (7.42)	0.184
Clinical variables							
Age at onset cocaine use (years)					20.20 (3.56)	21.69 (6.58)	0.641
Monthly amount cocaine use (gr)					10.90 (16.51)	19.15 (28.44)	0.554
Duration cocaine (months)					50.80 (51.53)	41.04 (30.90)	0.624
Abstinence cocaine (months)					1.64 (1.92)	3.15 (6.32)	0.613
Age at onset gambling (years)			21.33 (6.47)	23.50 (10.09)			0.647
Monthly amount gambling (h)			45.83 (41.23)	43.30 (44.96)			0.912
Duration gambling (months)			24.00 (25.01)	25.80 (26.34)			0.895
Abstinence gambling (months)			6.50 (3.73)	8.17 (8.11)			0.645
Age at onset tobacco use (years)	24.5 (9.19)	15.50 (1.38)	14.50 (2.12)	15.83 (3.97)	16.00 (3.65)	15.60 (2.27)	0.023
Monthly tobacco use (cig)	180.00 (169.70)	321.67 (240.37)	750.00 (212.13)	640.00 (309.84)	545.00 (340.73)	572.00 (388.04)	0.800
Duration tobacco (months)	18.00 (8.49)	95.83 (115.69)	120.00 (16.97)	194.00 (112.16)	120.00 (176.09)	144.60 (103.32)	0.866
Age at onset alcohol use (years)	19.40 (1.52)	19.00 (6.96)	16.33 (1.53)	16.25 (2.06)	20.75 (5.19)	16.82 (4.05)	0.578
Monthly alcohol use (SDU)	9.20 (10.33)	10.56 (10.01)	16.00 (6.93)	18.50 (27.78)	28.25 (23.21)	32.83 (32.40)	0.985
Duration alcohol (months)	110.40 (31.06)	68.94 (62.94)	89.33 (73.90)	65.00 (63.53)	117.00 (131.59)	79.25 (83.13)	0.972
GHQ Somatic Symptoms	0.00 (0.00)	0.58 (0.97)	2.00 (3.16)	1.75 (0.50)	2.00 (2.65)	1.31 (1.75)	0.639
GHQ Anxiety	1.17 (2.86)	1.33 (1.92)	2.17 (2.79)	1.25 (1.89)	4.00 (3.61)	1.69 (2.14)	0.442
GHQ Social Dysfunction	0.67 (1.63)	0.92 (1.73)	1.17 (2.04)	1.00 (2.00)	0.00 (0.00)	1.54 (2.03)	0.563
GHQ Depression	0.50 (1.22)	0.42 (0.90)	1.67 (2.88)	1.00 (0.816)	0.33 (0.58)	1.77 (2.62)	0.467

SD, standard deviation; IQ, intelligencequotient; gr, grams h, hours; cig, cigarettes; SDU, standard drinkingunits, GHQ, General HealthQuestionnaire.

Table DS2 Regions showing significant activations during 'Correct vs. Incorrect responses' and 'Incorrect vs. Correct responses' across groups

	BA	Side	MNI Coordinates X	Y	Z	Volume (mm^3)	T-value
Correct vs. Incorrect							
Striatum		L	-28	-2	2	315944	8.02
Amygdala		L	-28	-4	-24	*	4.94
Posterior Insula	13	L	-38	-2	14	*	6.52
Striatum		R	28	-12	0	*	6.75
Amygdala		R	28	-2	-12	*	6.42
Posterior Insula	13	R	40	4	8	*	6.77
Middle Cingulate Gyrus	24, 32	R/L	6	-32	42	*	7.22
Posterior Cingulate Gyrus	31	R/L	-4	-56	22	*	6.51
Occipital Cortex	17, 18, 19	R/L	14	-100	10	*	6.31
Superior Temporal Gyrus	22	R	48	-32	10	*	4.92
Superior Temporal Gyrus	22	L	-64	-26	14	*	4.43
Rostral ACC	24	R/L	4	36	8	*	6.22
Superior Frontal Gyrus	8, 9, 10	L	-18	40	46	*	6.61
Superior Frontal Gyrus	8, 9, 10	R	14	56	32	*	4.19
Angular Gyrus	39	L	-44	-66	30	*	6.57
Angular Gyrus	39	R	48	-72	30	*	4.02
Lateral OFC	11, 47	L	-28	32	-22	9608	6.07
Lateral OFC	11, 47	R	44	36	-4	3480	5.12
Incorrect vs. Correct							
SFG/Supplementary motor area	8	R/L	2	16	54	7560	6.37
dlPFC	9, 46	R	46	22	28	2584	4.41
Anterior Insula-OFC	13, 47	R	34	24	-2	4352	5.21

BA, Brodmann area; ACC, Anterior Cingulate Cortex; SFG Superior Frontal Gyrus; OFC, Orbitofrontal cortex; *, Part of the large cluster

Table DS3 Regions showing significant activations and deactivations during 'Final reversal errors minus Perseverative errors' across groups, and between-group differences

	BA	Side	MNI Coordinates X	Y	Z	Volume (mm^3)	T-value
Activations							
Dorsal ACC/SFG	6, 8, 32	R/L	0	20	42	11088	7.56
Anterior Insula / OFC	13, 47	R	36	18	-4	6472	7.04
Anterior Insula / OFC	13, 47	L	-36	16	-10	3608	6.87
Inferior Parietal Lobule	7,40	R	40	-50	46	15344	6.20
Inferior Parietal Lobule	7, 40	L	-38	-52	46	15480	5.99
Dorsolateral Prefrontal Cortex	9, 10, 46	R	48	28	30	20224	5.95
Ventrolateral PFC	10, 47	R	34	58	-8	*	5.49
Occipital Lobule	17, 18	R/L	-12	-84	4	23112	5.52
Thalamus / Putamen		L	-10	-16	-8	7408	5.45
Thalamus / Putamen		R	16	0	-2	5872	5.35
Dorsolateral PFC	9	L	-44	32	28	4584	4.25
Deactivations							
Posterior Cingulate Gyrus	31	R/L	-8	-64	26	10408	5.63
Angular Gyrus	39	L	-48	-68	22	*	5.20
Superior Frontal Gyrus	9	R/L	-14	46	38	16544	5.25
Medial Frontal Gyrus / ACC	10	R/L	2	50	6	*	4.66
Parahippocampal Gyrus	35	L	-22	-22	-29	2296	3.95
Controls>Cocaine Users							
Ventrolateral PFC	47	R	46	48	-2	784	4.51
Dorsolateral PFC	9	R	26	48	36	544	3.84
Controls> Gamblers							
Ventrolateral PFC	47	R	42	46	-6	472	3.52

BA, Brodmannarea;ACC, Anterior CingulateCortex; SFG, Superior Frontal Gyrus;OFC, Orbitofrontalcortex; PFC, PrefrontalCortex;*, Partof thelargecluster

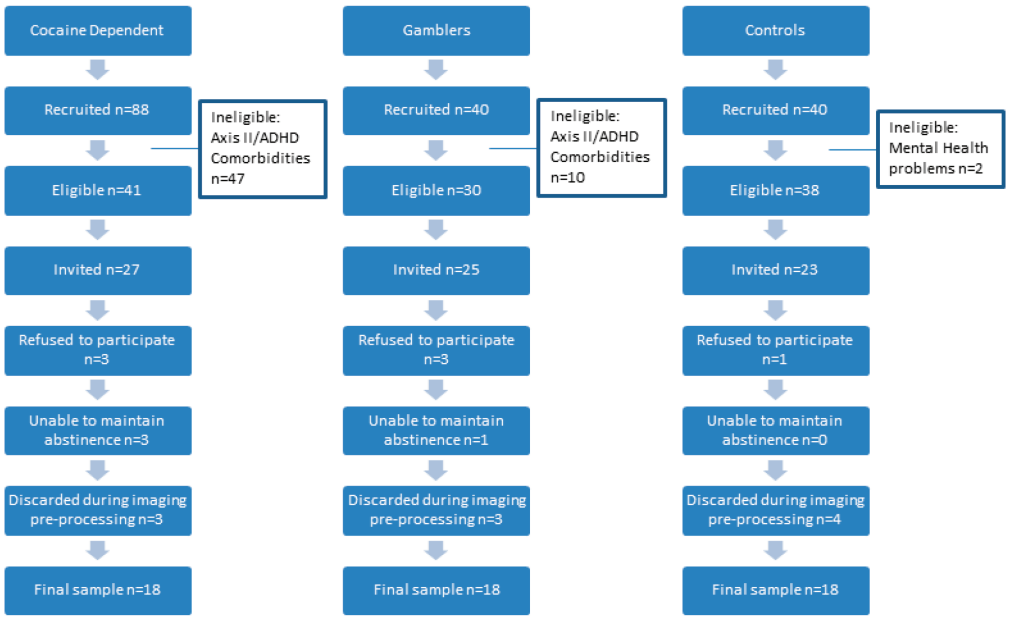

Fig. DS1 Flowchart of the recruitment process

Notes. *Eligibility*: Numbers represent participants excluded due to ADHD or Axis II comorbidities. Other Axis I comorbidities were also assessed, but we did not keep track of the number of participants excluded for this reason. *Invited to participate*: Eligible participants were consecutively invited to the scanning session up until achievement of intended sample size (n=20 per group). Discarded during imaging pre-processing: due to excessive movement artifacts or random behavioural responses.

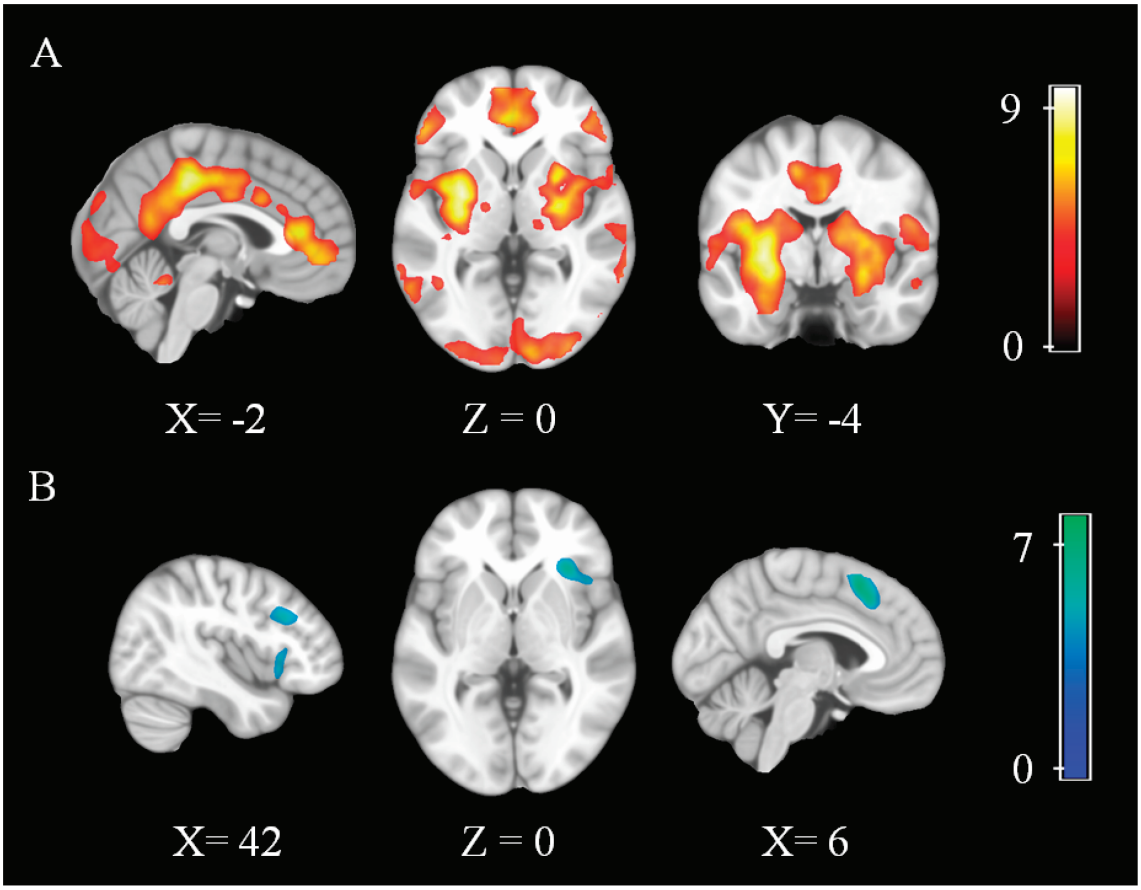

Fig. DS2 Regions of brain activation associated to correct/incorrect responses

Notes: Brain regions showing significant activations across groups during correct responses v. incorrect responses (A) and during incorrect responses *v*. correct responses (B). X and Z denote coordinate in standard MNI space. Right hemisphere is always displayed on the right. Colour bar indicates *T* value.

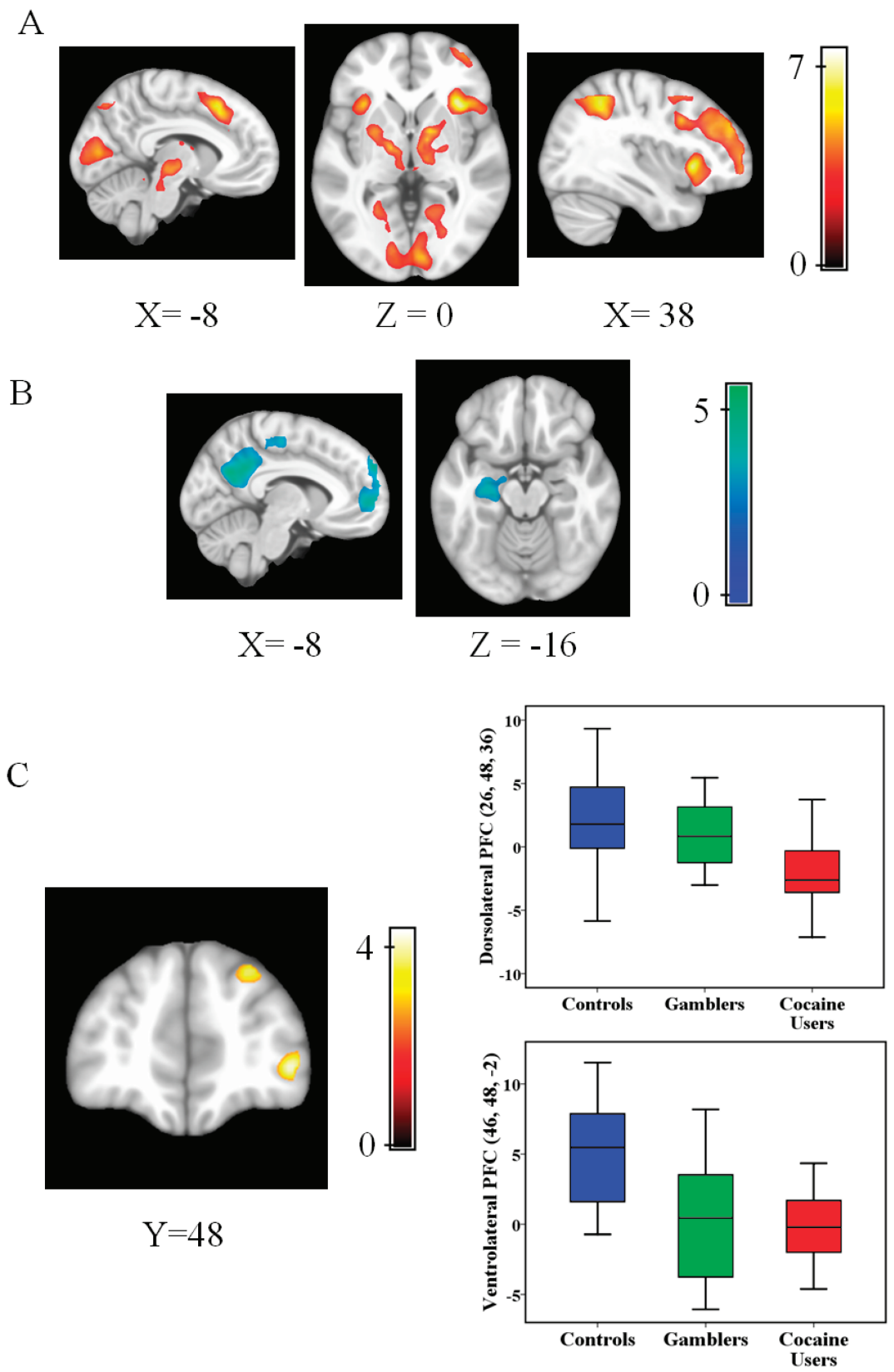

Fig. DS3 Brain activations, deactivations and between-group comparison during final reversal errors *v.* perseverative errors.

Brain regions showing significantly increased activations (A) and deactivations (B) during final reversal errors *v.* perseverative errors. Between-group analysis (C) revealed that the right dorsolateral and ventrolateral prefrontal cortex was significantly less active in cocaine users and gamblers compared to healthy controls (box-plots represent the mean group activation observed in these clusters). X, Y and Z denote coordinate in standard MNI space. Right hemisphere is always displayed on the right. Color bar indicates *T* value.

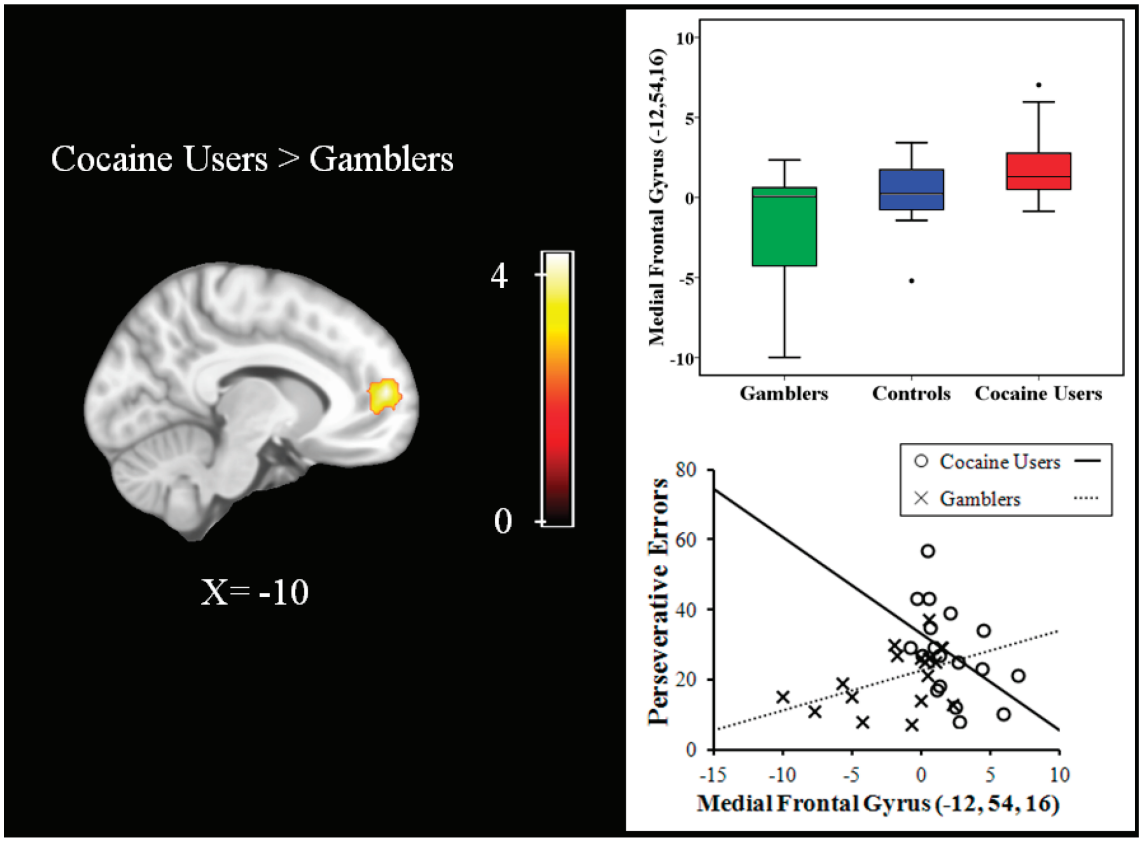

Fig. DS4 Brain activations associated to perseverative errors in cocaine users.

We observed a significantly increased activation of the medial frontal gyrus during perseverative errors *v.* probabilistic errors in cocaine users compared to gamblers (A). The box-plot represents the mean group activations observed in this cluster (B). The scatter-plot represents the correlation between imaging findings and the number of perseverative errors in cocaine users and gamblers (C). X denotes coordinate in standard MNI space. Color bar indicates *T* value.

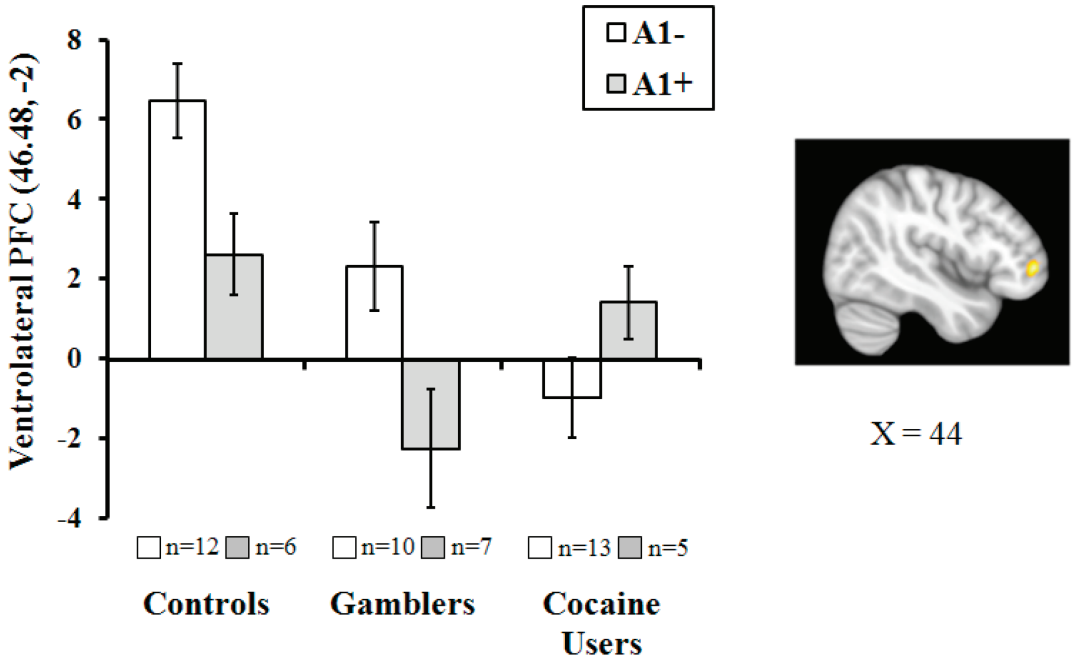

Fig. DS5 Group x genotype interactions.

Ventrolateral prefrontal cortex activation during final reversal errors *v.* perseverative errors as a function of group and DRD2 genotype.