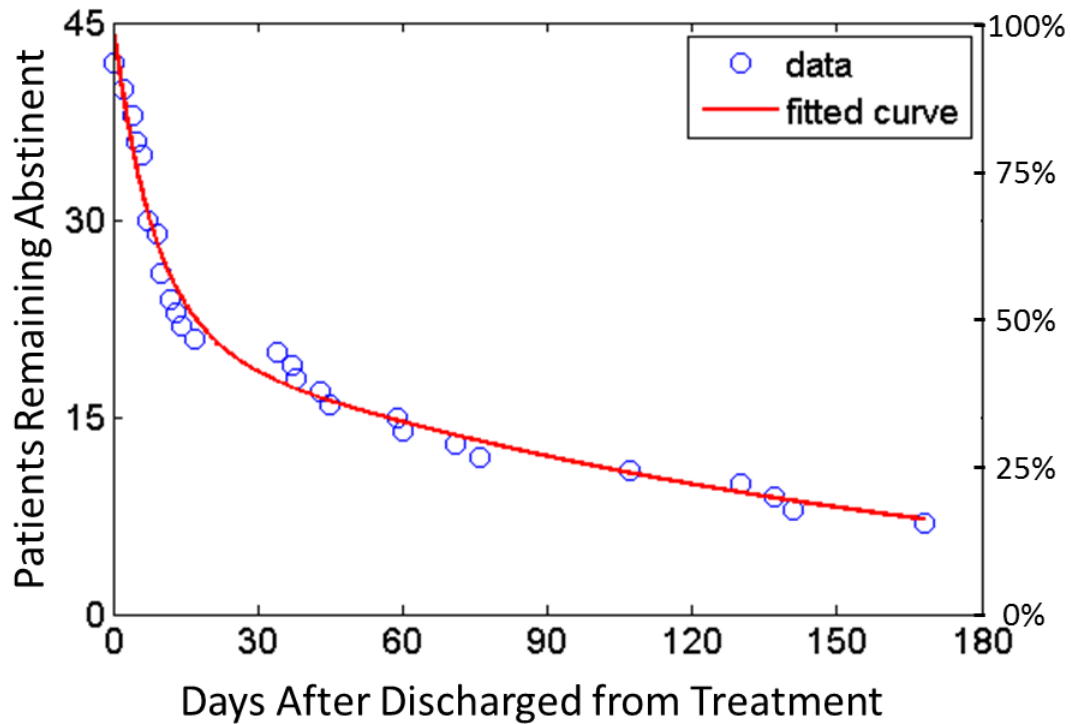
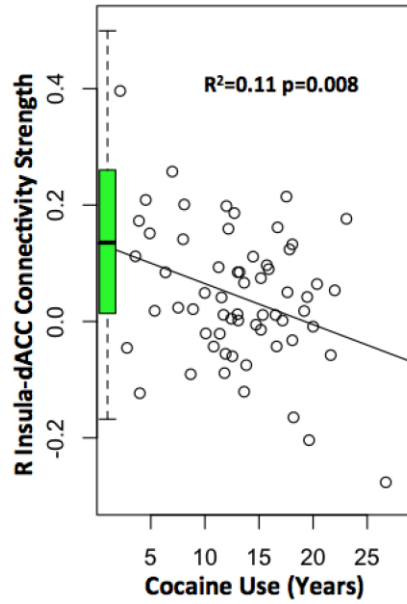


Salience and Default Mode Network Dysregulation in Chronic Cocaine Users Predict Treatment Outcome

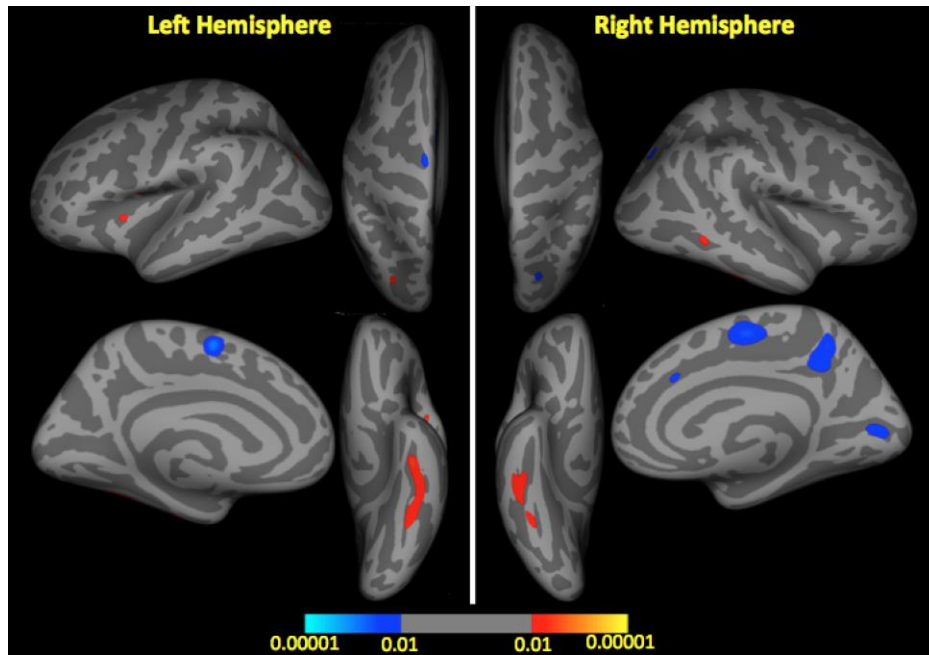
Supplementary Information



Supplementary Fig. 1 Frequency of patient remaining abstinent after discharged from treatment. The number of patients remaining abstinent (vertical axis, y) decreases along days after discharge from treatment (horizontal axis, x) as an exponential function: $f(y) = a \cdot \exp(b \cdot x) + c \cdot \exp(d \cdot x)$, in which the coefficients (with 95% confidence bounds) are given by $a = 23.05$ (19.29, 26.8), $b = -0.1171$ (-0.1525, -0.08183), $c = 21.6$ (18.36, 24.85), and $d = -0.006519$ (-0.008545, -0.004492).



Supplementary Fig. 2 Correlation between the rsFC strength and cocaine use measures. Negative correlation between the rsFC strength of the right insula-dACC circuit and years of cocaine use. Boxplots summarize the connectivity strength of the same circuits in the healthy control group.



Supplementary Fig. 3 Correlation between the cortical thickness and years of cocaine use. Note: color bar shows vertex-based p values, where blue color is for negative correlations and red is for positive correlations. No clusters survived after multiple comparison corrections.

Supplementary Table 1 Brain regions showing significant cortical thickness difference between non-treatment seeking cocaine users and matched healthy controls

Regions	Peak (Talairach)			Peak T-value	Cluster size (mm ²)
	x	y	z		
Right insula	38	-5	17	-3.61	1073
Left insula	-43	-4	15	-3.69	1259
Right temporal pole	35	2	-31	5.58	1274
Left temporal pole	-42	-2	-30	4.55	1290

Supplementary Table 2 Brain regions showing significant weaker resting-state functional connectivity in non-treatment-seeking cocaine users

Seed regions	Regions of difference	Peak (Talairach)			Peak T	Cluster size (voxels)
		x	y	z		
Right insula	RI_1: dACC (BA24/32/6/8)	4	30	37	-4.44	163
Left insula	LI_1: dACC (BA32/24/6/8)	10	32	20	-4.37	175
Right temporal pole	RTP_1: Left middle temporal gyrus (anterior & middle parts) (BA21/22/38)	-49	-5	-15	-3.90	228
	RTP_2: Right middle temporal gyrus (temporal pole and anterior parts) (BA21/38)	52	-2	-13	-4.41	207
	RTP_3: Right supramarginal gyrus (BA40/39)	52	-50	27	-4.33	176
	*RTP_4: Medial prefrontal cortex (BA10/32/9)	-10	49	16	-4.32	127
	RTP_5: Left superior/middle temporal gyrus, supramarginal gyrus (BA22/39/40)	-46	-53	19	-3.68	100
	RTP_6': Right medial superior frontal cortex (BA8)	16	42	50	-3.77	79
Left temporal pole	LTP_1: Cerebellum	-4	-56	-35	-4.34	134
	LTP_2': Right superior/middle temporal gyrus (BA38/21)	52	6	-18	-4.14	97

R/L: right and left; I: insula; TP: temporal pole.

*RTP_4 is the circuted used in Supplementary Table 4 and 5.

RTP_6' and LTP_2': a trend level of weaker rsFC with corrected $ps = 0.08$ and 0.06 .

Supplementary Table 3 The p values of correlations between the imaging measures and cocaine use measures.

P values	Tk RI	Tk LI	Tk RTP	Tk LTP	rsFC RI_1	rsFC LI_1	rsFC RTP_1	rsFC RTP_2	rsFC RTP_3	rsFC RTP_4	rsFC RTP_5	rsFC RTP_6'	rsFC LTP_1	rsFC LTP_2'
Use Year	0.47	0.17	0.64	0.91	0.008	0.345	0.38	0.75	0.71	0.10	0.99	0.99	0.13	0.23
Current use	0.63	0.53	0.30	0.20	0.81	0.91	0.32	0.59	0.63	0.07	0.14	0.00016	0.92	0.26

Tk: thickness.

RI: right insula; LI: thickness of left insula; RTP: right temporal pole; LTP: left temporal pole.

rsFC LI_1: rsFC strength of the circuit LI_1 (see Supplementary Table 2).

Supplementary Table 4 Statistic summary of cocaine relapse predictive models

Model	Model χ^2	Model p	$\Delta\chi^2$	Δp
1	6.32	.044	7.22	.007
2	13.43	.009	5.15	.023

Dependent Variable: Time to relapse up to 168 days

Model 1: Predictors: (Constant, Age, FD), years of education

Model 2: Predictors: (Constant, Age, FD), years of education, rsFC (R. TP - mPFC)

rsFC (R. TP - mPFC): resting-state functional connectivity between right temporal pole and medial prefrontal cortex (RTP_4 in Supplementary Table 2, Figure 1C)

Supplementary Table 5 Coefficients of cocaine relapse predictive models

Model		β (SE)	Exp(β)	Wald	P
1	Years of Education	-.24(.09)	.79	6.42	.011
2	Years of Education	-.25(.10)	.78	6.93	.008
	rsFC (R. TP - mPFC)	-2.37(1.10)	.09	4.62	.032

Dependent Variable: Time to relapse up to 168 days

Model 1: Predictors: (Constant, Age, FD), years of education

Model 2: Predictors: (Constant, Age, FD), years of education, rsFC (R. TP - mPFC)

β (SE): Coefficient (Standard Error)

rsFC (R. TP - mPFC): resting-state functional connectivity between right temporal pole and medial prefrontal cortex (RTP_4 in Supplementary Table 2, Figure 1C)