

Table DS1 Linear regression imaging outcome parameters

Imaging technique	Parameter	Region of interest	Model 1 ^a		Model 2 ^b		
			B (95% CI)	R ² , %	B (95% CI)	R ² , %	Significant predictors ^c B (95% CI)
1H-MRS (n=69)	NAA/Cr ratio	Mid-frontal grey matter	-0.017 (-0.137 to 0.103)	0.2	-0.056 (-0.200 to 0.087)	0.9	
		Mid-occipital grey matter	-0.013 (-0.113 to 0.088)	0.1	-0.021 (-0.144 to 0.103)	0.2	
		Left centrum semiovale	0.045 (-0.059 to 0.148)	1.1	-0.004 (-0.127 to 0.120)	0.0	
	Cho/Cr ratio	Mid-frontal grey matter	-0.013 (-0.033 to 0.007)	2.4	-0.008 (-0.031 to 0.016)	0.0	Cocaine 0.027 (-0.053 to -0.002)
		Mid-occipital grey matter	0.008 (-0.007 to 0.022)	1.5	-0.010 (-0.008 to 0.028)	1.5	Gender -0.019 (-0.035 to -0.003)
		Left centrum semiovale	0.015 (-0.004 to 0.034)	3.5	-0.000 (-0.023 to 0.022)	0.0	Cocaine 0.027 (0.003 to 0.051)
	ml/Cr ratio	Mid-frontal grey matter	-0.053 (-0.144 to 0.037)	2.9	-0.004 (-0.112 to 0.103)	0.0	
		Mid-occipital grey matter	-0.041 (-0.100 to 0.019)	2.8	-0.062 (-0.013 to 0.008)	4.3	Amphetamine 0.085 (0.008 to 0.162)
		Left centrum semiovale	-0.018 (-0.095 to 0.059)	0.3	-0.088 (-0.176 to 0.000)	5.4	Cocaine 0.144 (0.049 to 0.239)
Diffusion tensor imaging (n=68)	FA	Thalamus	-20.09 (-30.91 to -9.27)*	16.6	-18.76 (-32.14 -5.39)*	9.7	Gender -11.95 (-23.50 to -0.40)
		Globus pallidua	-10.48 (-31.73 to 10.76)	1.4	-14.06 (-40.58 12.47)	1.7	
		Putamen	-10.71 (-25.31 to 3.90)	3.0	-8.96 (-26.95 9.03)	1.5	
		Caudate nucleus	-14.32 (-29.96 to 1.31)	4.7	-15.27 (-34.36 3.81)	3.6	
		Centrum semiovale	-13.30 (-30.82 to 4.21)	3.4	-7.55 (-28.56 13.46)	0.8	Amphetamine -243.53 (-47.02 to -2.05)
	ADC	Thalamus	-2.18 (-10.8 to 5.43)	2.4	2.68 (-1.36 to 6.72)	2.4	Gender 4.84 (1.36 to 8.33)
		Globus pallidua	-0.78 (-1.97 to 0.42)	2.5	-0.75 (-2.20 to 0.71)	1.6	
		Putamen	-0.48 (-1.35 to 0.39)	1.9	-0.13 (-1.19 to 0.94)	0.1	
		Caudate nucleus	5.22 (-0.55 to 10.98)	4.7	6.05 (-1.04 to 13.15)	4.2	
Centrum semiovale	-0.98 (-2.18 to 0.22)	4.0	-1.10 (-2.59 to 0.39)	3.3			
Perfusion-weighted imaging (n=69)	rrCBV	Thalamus	0.094 (0.013 to 0.176)*	7.3	0.114 (0.007 to 0.220)*	6.4	
		Globus pallidus	-0.050 (-0.127 to 0.027)	2.5	-0.069 (-0.169 to 0.031)	2.9	
		Putamen	-0.006 (-0.063 to 0.052)	0.1	-0.010 (-0.083 to 0.063)	0.1	
		Caudate nucleus	-0.006 (-0.067 to 0.055)	0.1	-0.008 (-0.089 to 0.072)	0.1	
		Dorsolateral frontal grey matter	0.056 (-0.002 to 0.114)	5.3	0.057 (-0.019 to 0.133)	3.4	
		Mid-frontal grey matter	0.052 (-0.019 to 0.122)	3.1	0.018 (-0.072 to 0.108)	0.1	
		Occipital grey matter	-0.077 (-0.180 to 0.027)	2.9	0.038 (-0.089 to 0.165)	0.5	Gender -0.135 (-0.239 to -0.031); tobacco -0.133 (-0.252 to -0.014)
		Superior parietal grey matter	-0.009 (-0.089 to 0.071)	0.0	0.055 (-0.045 to 0.156)	1.7	Amphetamine -0.109 (-0.212 to -0.006)
		Temporal grey matter	0.111 (0.020 to 0.202)*	8.1	0.131 (0.013 to 0.249)*	6.8	
SPECT (n=47)	[¹²³ I]B-CIT binding ratios	Midbrain	-0.106 (-0.326 to 0.113)	2.1	-0.092 (-0.373 to 0.188)	1.0	
		Thalamus	-0.394 (-0.570 to -0.218)*	31.0	-0.343 (-0.566 to -0.121)*	15.2	
		Frontal grey matter	-0.090 (-0.152 to -0.028)*	16.4	-0.058 (-0.135 to 0.020)	4.3	
		Occipital grey matter	-0.029 (-0.101 to 0.043)	1.5	0.021 (-0.060 to 0.112)	0.8	Tobacco -0.078 (-0.155 to -0.001)
		Temporal grey matter	-0.160 (-0.254 to -0.066)*	21.1	-0.105 (-0.222 to 0.012)	5.9	

ADC, apparent diffusion coefficient; Cho, choline; Cr, (phospho)creatine; FA, fractional anisotropy; ml, myoinositol; MRS, magnetic resonance spectroscopy; NAA, N-acetylaspartate; rrCBV, regional relative cerebral blood volume; SPECT, single proton emission computed tomography.
a. Linear regression analyses with ecstasy use (dichotomised) as independent variable.
b. Linear regression analyses with ecstasy, amphetamines, cocaine and cannabis use (all dichotomised) as dependent variables, adjusted for covariates.
c. Other than ecstasy.
*P<0.05.

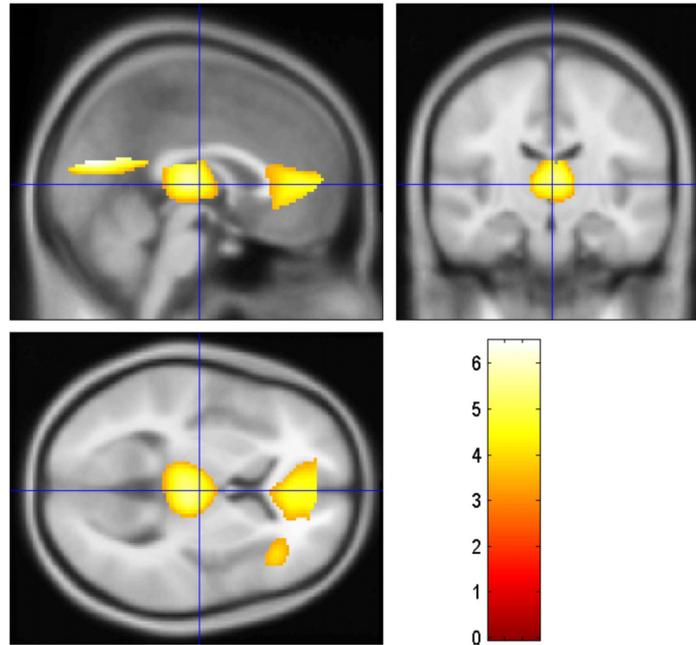


Fig. DS1 Clusters of significantly lower [¹²³I]β-CIT binding ratios in ecstasy users compared with non-users, superimposed on the standard brain.

The thalamic area showed the biggest cluster of significant difference ($Z_{\max}=5.07$, $P_{\text{corrected, cluster-level}}=0.001$; coordinates of the highest Z-value: 2, -22, 8). A second significant cluster of decreased [¹²³I]β-CIT binding ratios in ecstasy users was observed in the cingulate gyrus, although this should be interpreted with caution, because the highest Z-value was exactly in the midline ($Z_{\max}=4.42$, $P_{\text{corrected, cluster-level}}=0.007$; coordinates of the highest Z-value: 0, 42, 8). The clusters posterior on the sagittal slice are related to the upper boundary of the field of view and are likely to represent artefacts rather than real significant differences in [¹²³I]β-CIT binding.