

Supplementary Table 1. Coordinates and mean percent methylation levels for all *SLC6A4* CpG sites assayed in the Discovery cohort. Number of participants with 0% methylation is indicated for each site. The sites assayed in all three samples are in bold font. All promoter sites are in the proximal promoter.

Assay ID	From ATG	From TSS	GRCh37/hg19 chr17	Region	Mean	SD	Number (%) participants with 0% methylation
ADS1818FS2	-12380	+497	28562219	intron 1	19.48	5.43	0 (0.00%)
	-12382	+495	28562221	intron 1	28.28	7.73	0 (0.00%)
ADS1818FS1	-12426	+451	28562265	intron 1	18.62	5.2	1 (1.25%)
	-12451	+426	28562290	intron 1	27.69	6.66	1 (1.25%)
	-12496	+381	28562335	intron 1	8.19	2.89	1 (1.25%)
ADS579FS1	-12758	+119	28562597	exon 1	0.038	0.34	79 (98.75%)
	-12766	+111	28562605	exon 1	2.19	1.38	21 (26.25%)
	-12771	+106	28562610	exon 1	7.82	2.02	1 (1.25%)
	-12784	+93	28562623	exon 1	8.41	2.01	0 (0.00%)
ADS579FS2	-12804	+73	28562643	exon 1	6.95	2.51	5 (6.25%)
	-12806	+71	28562645	exon 1	6.06	2.54	8 (10.00%)
	-12821	+56	28562660	exon 1	1.79	2.39	50 (62.50%)
	-12834	+43	28562673	exon 1	10.12	1.93	1 (1.25%)
	-12845	+32	28562684	exon 1	7.66	1.72	1 (1.25%)
	-12847	+30	28562686	exon 1	4.17	2.36	17 (21.25%)
	-12853	+24	28562692	exon 1	1.32	2.27	59 (73.75%)
	-12862	+15	28562701	exon 1	1.76	2.45	52 (65.00%)
	-12865	+12	28562704	exon 1	3.09	2.94	37 (46.25%)
	-12868	+9	28562707	exon 1	0.45	1.3	71 (88.75%)
	-12879	-3	28562718	promoter	1.58	2.27	53 (66.25%)
	-12887	-11	28562726	promoter	0	0	80 (100.00%)
	-12890	-14	28562729	promoter	0.21	1.1	77 (96.25%)
	-12893	-17	28562732	promoter	0	0	80 (100.00%)
	-12895	-19	28562734	promoter	0	0	80 (100.00%)
	-12899	-23	28562738	promoter	0	0	80 (100.00%)
-12911	-35	28562750	promoter	0.07	0.64	79 (98.75%)	
-12913	-37	28562752	promoter	0	0	80 (100.00%)	
ADS580FS1	-12945	-69	28562784	promoter	1.79	0.54	1 (1.25%)
	-12948	-72	28562787	promoter	1.44	0.81	3 (3.75%)
	-12975	-99	28562814	promoter	1.06	0.54	11 (13.75%)

	-12988	-112	28562827	promoter	1.55	0.63	7 (8.75%)
ADS580FS2	-13009	-133	28562848	promoter	2.87	0.45	1 (1.25%)
	-13011	-135	28562850	promoter	1.1	0.33	1 (1.25%)
	-13015	-139	28562854	promoter	1.21	0.36	2 (2.50%)
	-13017	-141	28562856	promoter	0.92	0.34	5 (6.25%)
	-13023	-147	28562862	promoter	2.24	0.45	1 (1.25%)
	-13025	-149	28562864	promoter	1.02	0.34	3 (3.75%)
	-13031	-155	28562870	promoter	1.89	0.38	1 (1.25%)
	-13046	-170	28562885	promoter	3.57	0.82	1 (1.25%)
	-13050	-174	28562889	promoter	1.59	0.47	2 (2.50%)
	-13064	-188	28562903	promoter	1.74	0.38	1 (1.25%)
	-13066	-190	28562905	promoter	0.76	0.53	22 (27.50%)
	-13071	-195	28562910	promoter	0.74	0.62	30 (37.50%)
	-13076	-200	28562915	promoter	0.88	0.67	26 (32.50%)
	-13083	-207	28562922	promoter	1.25	0.48	7 (8.75%)
	-13085	-209	28562924	promoter	0.66	0.6	34 (42.50%)
	-13089	-213	28562928	promoter	0.97	0.65	22 (27.50%)

Supplementary Table 2. Site-specific principal component loadings in the Discovery cohort presented for the five components with eigenvalues > 1.

DNS	Component (% variance accounted for)				
CpG site	1 (24.06%)	2 (13.12%)	3 (9.41%)	4 (7.22%)	5 (5.91%)
1	0.218	0.381	0.669	-0.006	0.156
2	0.158	0.515	0.534	0.009	0.423
3	0.442	-0.01	0.142	-0.546	0.005
4	0.584	-0.035	0.188	-0.459	-0.009
5	0.574	0.11	-0.245	0.237	-0.006
6	0.232	0.627	-0.236	0.338	0.142
7	0.429	0.177	-0.374	-0.381	-0.174
8	0.286	0.55	-0.326	0.126	0.313
9	0.405	0.278	0.132	0.432	-0.53
10	0.321	0.348	0.526	-0.019	-0.46
11	0.489	0.492	-0.037	-0.272	-0.185
12	0.543	0.013	-0.307	0.246	-0.298
13	0.73	-0.019	-0.263	-0.167	0.145
14	0.234	0.517	-0.302	-0.082	0.22
15	0.696	-0.17	-0.123	-0.114	-0.079
16	0.514	-0.483	0.074	0.162	0.179
17	0.574	-0.46	0.131	-0.007	-0.064
18	0.592	-0.157	0.379	0.323	0.094
19	0.608	-0.299	0.003	0.324	0.178
20	0.605	-0.421	0.028	0.009	0.248

Supplementary Table 3. Results from regression analyses in the Discovery cohort using amygdala reactivity as a dependent variable and the first principal component capturing 24.06% of all *SLC6A4* proximal promoter methylation variance as an independent variable. Covariates include age, gender, LESS Highest Impact, CTQ Total, 5-HTTLPR/rs25531 genotype, and current Axis I diagnosis (dummy coded: 0 = no, 1 = yes).

<i>SLC6A4</i> promoter methylation (PC 1)	ΔR^2	b	p
No Covariates			
Left amygdala	0.070	0.264	0.018
Right amygdala	0.042	0.204	0.070
With Covariates			
Left amygdala	0.079	0.284	0.012
Right amygdala	0.043	0.210	0.066

Supplementary Table 4. Location and mean percent methylation of all assayed *COMT* promoter CpG sites in the Discovery cohort.

				Percent methylation	
Assay ID	Position (relative to ATG)	Position (relative to TSS)	GRCh37/hg19 chr22	Mean	SD
ADS2791 FS1	-11466	-442	19938584	88.65	1.72
	-11446	-422	19938604	81.16	3.96
	-11442	-418	19938608	92.32	1.29
	-11440	-416	19938610	89.72	6.39
	-11434	-410	19938616	75.67	28.18
	-11430	-406	19938620	93.34	3.16
ADS2791 FS2	-11402	-378	19938648	95.01	2.38
	-11397	-373	19938653	91.41	1.46
	-11393	-369	19938657	91.76	6.21
	-11386	-362	19938664	87.36	1.62

SD = Standard Deviation

Supplementary Table 5. Site-specific principal component loadings in the Replication cohort presented for the five components with eigenvalues > 1.

TAOS CpG site	Component (% variance accounted for)				
	1 (30.41%)	2 (14.50%)	3 (10.34%)	4 (6.30%)	5 (5.21%)
1	-0.03	-0.101	0.793	-0.032	0.197
2	0.11	-0.319	0.634	-0.241	0.244
3	0.085	-0.385	0.607	-0.046	0.12
4	0.072	0.057	0.574	0.455	-0.471
5	0.717	0.007	-0.159	0.282	-0.009
6	0.283	0.841	-0.04	-0.117	0.106
7	0.753	-0.045	-0.214	0.191	0.254
8	0.443	0.252	0.012	0.452	0.455
9	0.761	0.275	-0.069	-0.312	-0.096
10	0.653	-0.339	-0.126	0.031	-0.137
11	0.75	-0.241	-0.092	0.07	-0.155
12	0.609	-0.119	0.039	-0.165	-0.518
13	0.717	-0.234	0.138	0.114	-0.104
14	0.645	-0.31	0.09	-0.24	0.049
15	0.762	-0.308	-0.083	-0.112	0.075
16	0.314	0.505	0.26	0.312	-0.083
17	0.212	0.69	0.305	0.104	-0.144
18	0.646	0.176	0.072	-0.414	0.055
19	0.781	-0.032	-0.021	0.198	0.234
20	0.278	0.768	0.188	-0.355	0.016

Supplementary Table 6. Results from regression analyses in the Replication cohort using amygdala reactivity as a dependent variable and the first principal component capturing 30.41% of all *SLC6A4* proximal promoter methylation variance as an independent variable in the Replication cohort. Covariates include age, gender, psychopathology risk, CTQ Total, and 5-HTTLPR/rs25531 genotype.

<i>SLC6A4</i> promoter methylation (PC 1)	ΔR^2	b	p
No Covariates			
Left amygdala	0.101	0.318	0.002
Right amygdala	0.009	0.096	0.354
With Covariates			
Left amygdala	0.076	0.287	0.009
Right amygdala	0.003	0.055	0.623