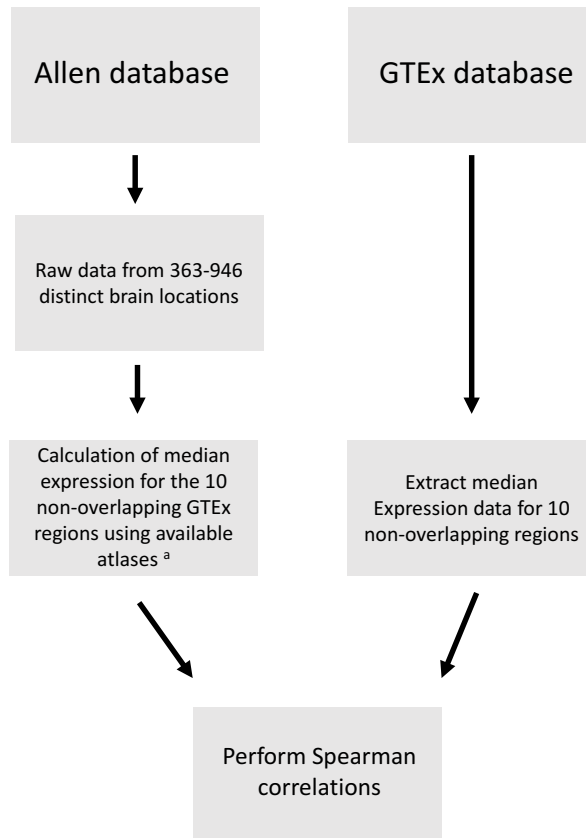
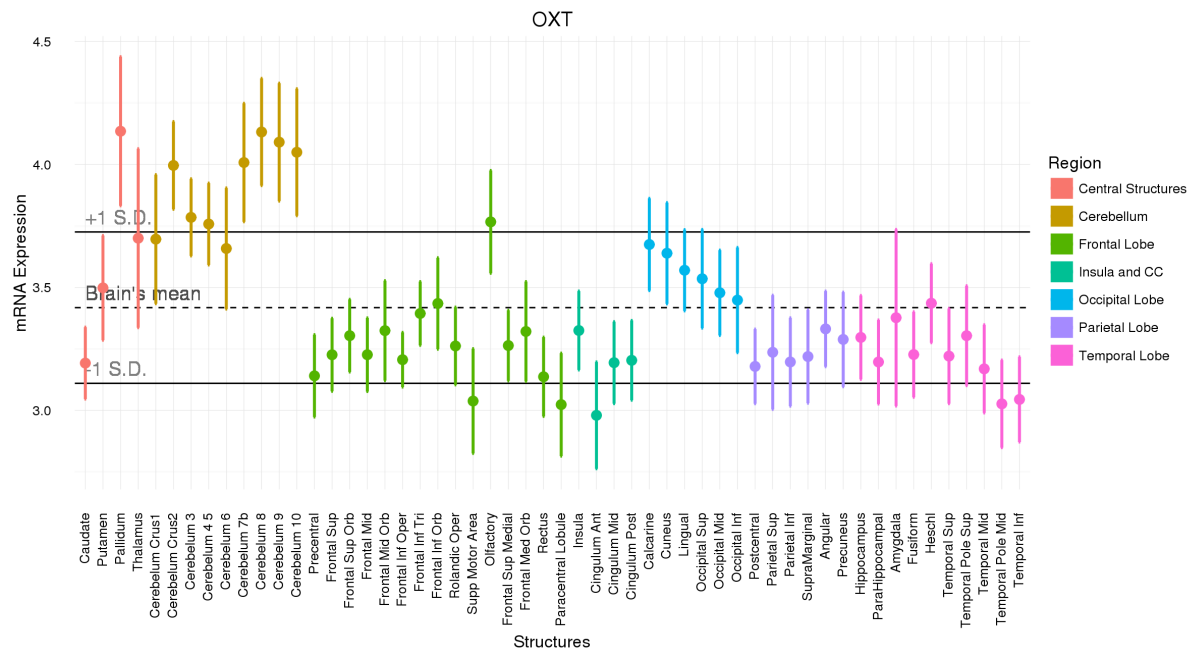


Oxytocin pathway gene networks in the human brain

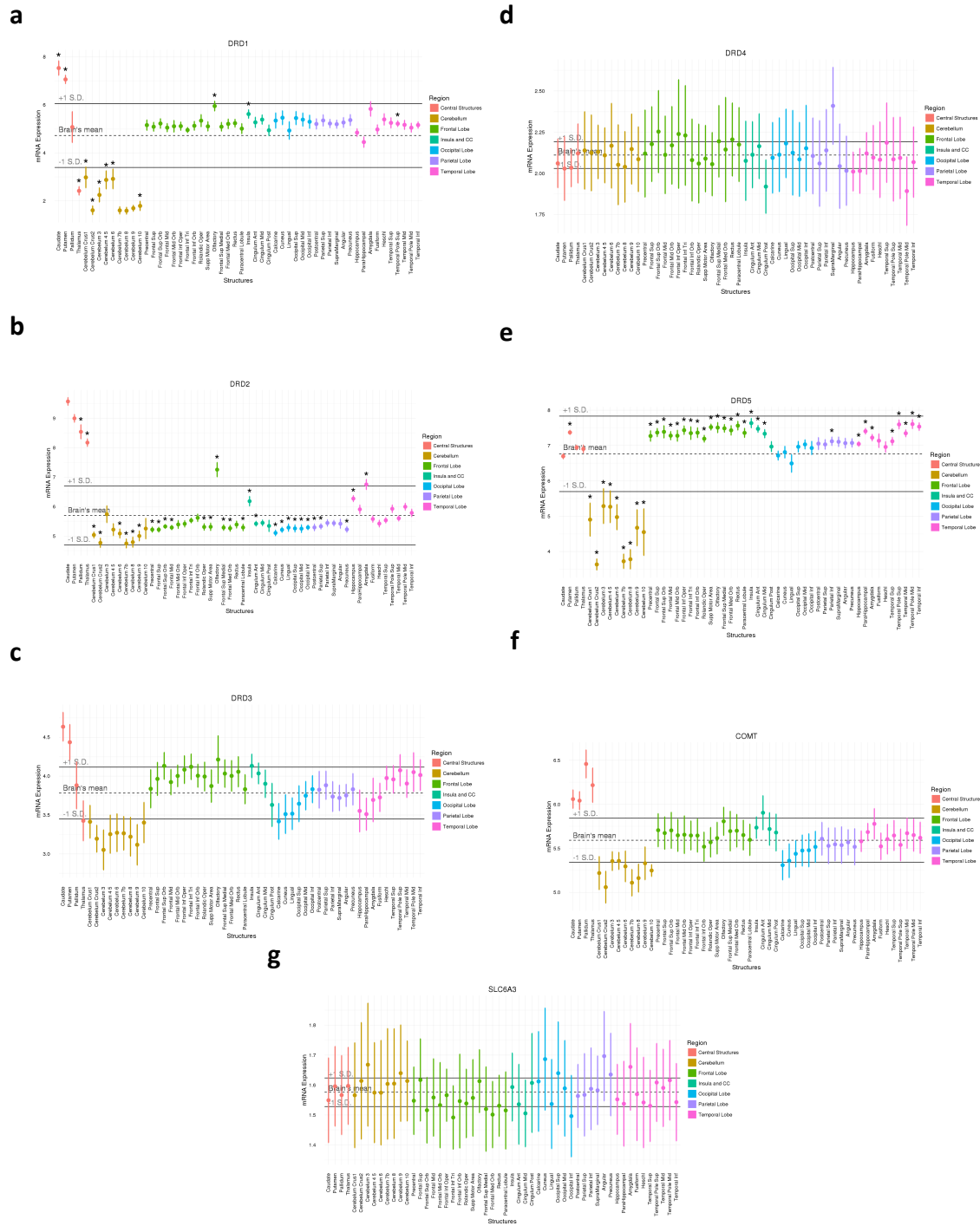
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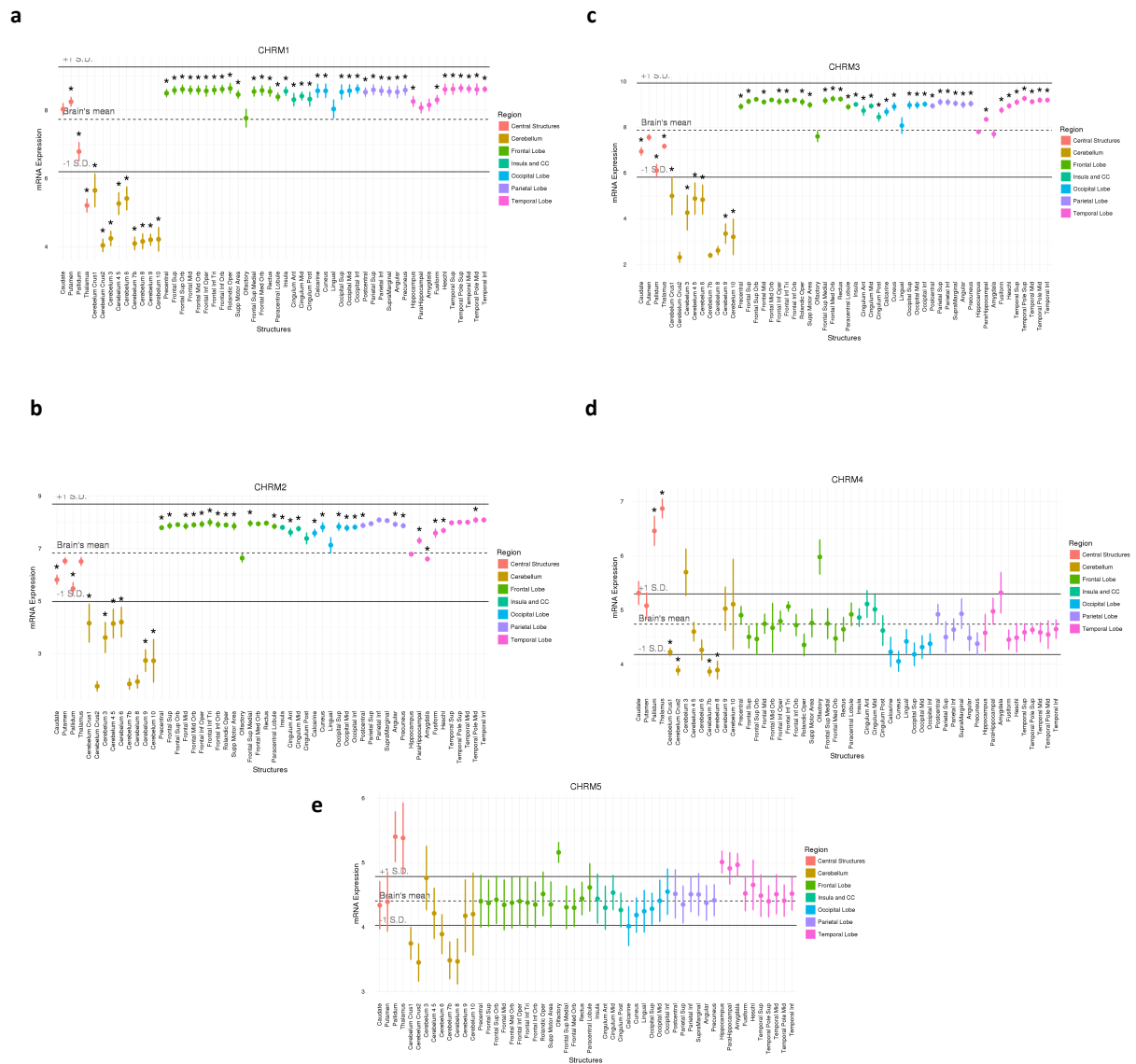
Supplementary Figure 1. The comparison of Allen and GTEx datasets. Median expression data from 10 distinct regions from the GTEx database were compared to the median expression of the same regions from the Allen database. Medians from the Allen dataset were extracted from the raw data by calculating the median expression of the GTEx regions using available atlases. Spearman correlations were then calculated to assess the relationship of these datasets. ^a AAL atlas: Amygdala, Caudate, Cerebellum, Hippocampus, Putamen; Talairach atlas: BA24, BA9, Hypothalamus, Substantia Nigra; “Hammers_mith atlas”: Nucleus Accumbens



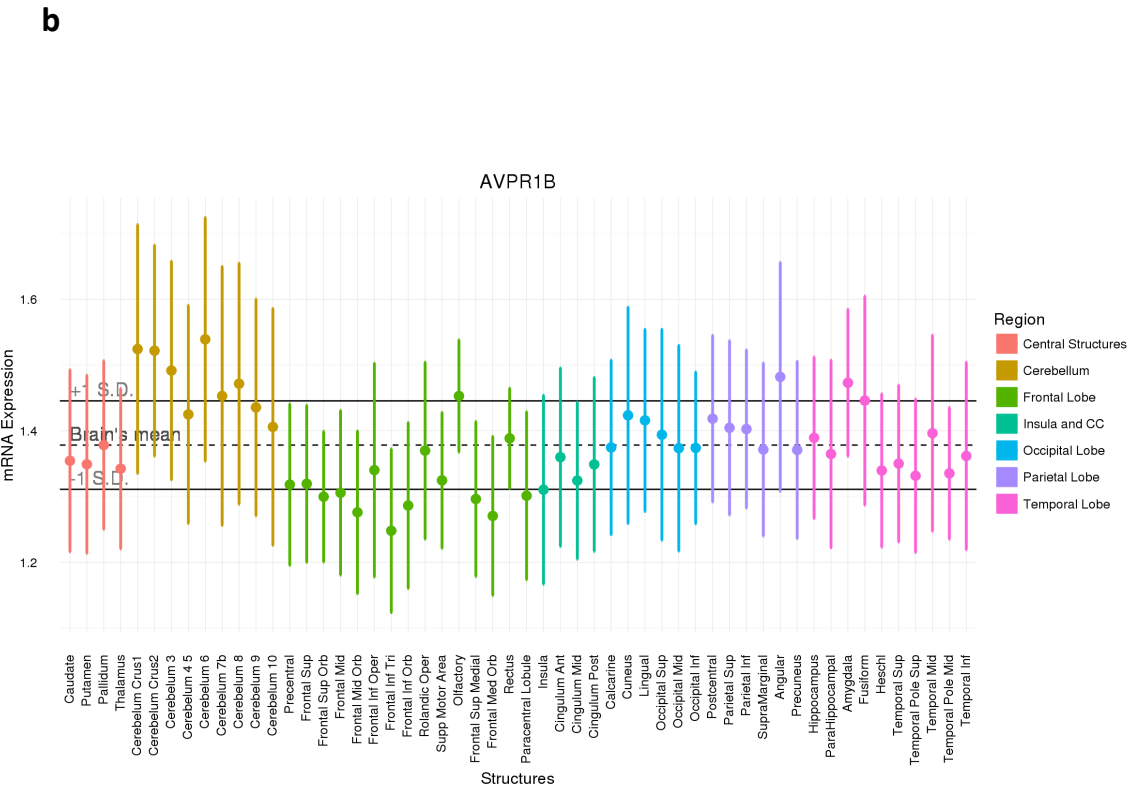
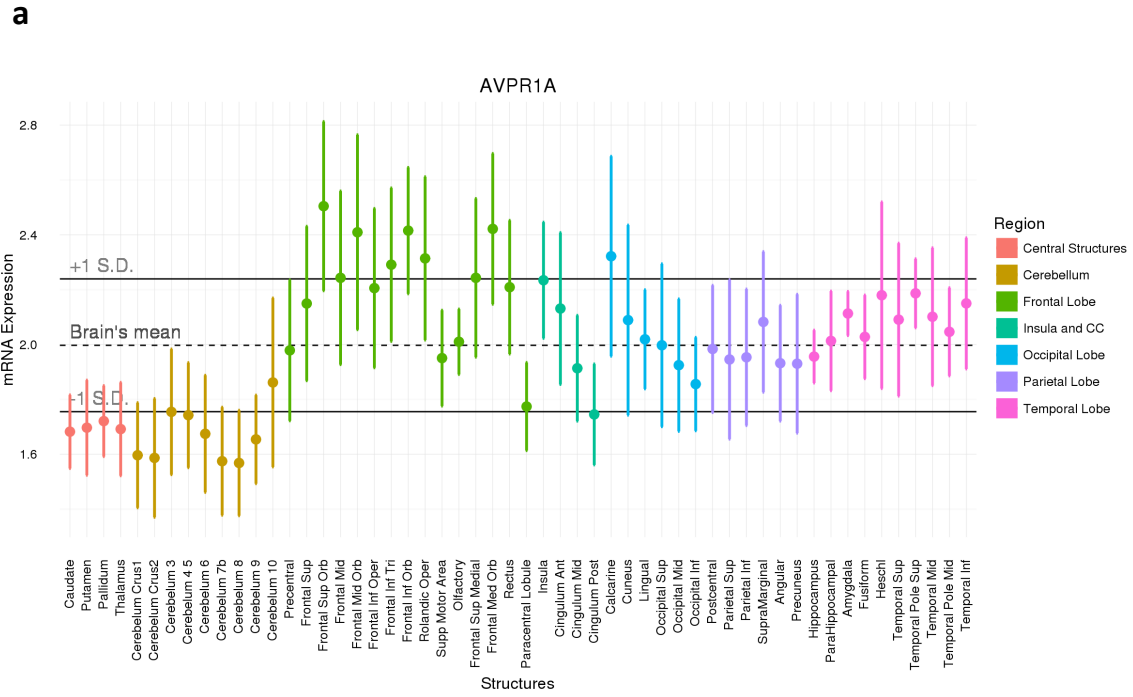
Supplementary Figure 2. The central expression of OXT. Means and standard errors are presented.



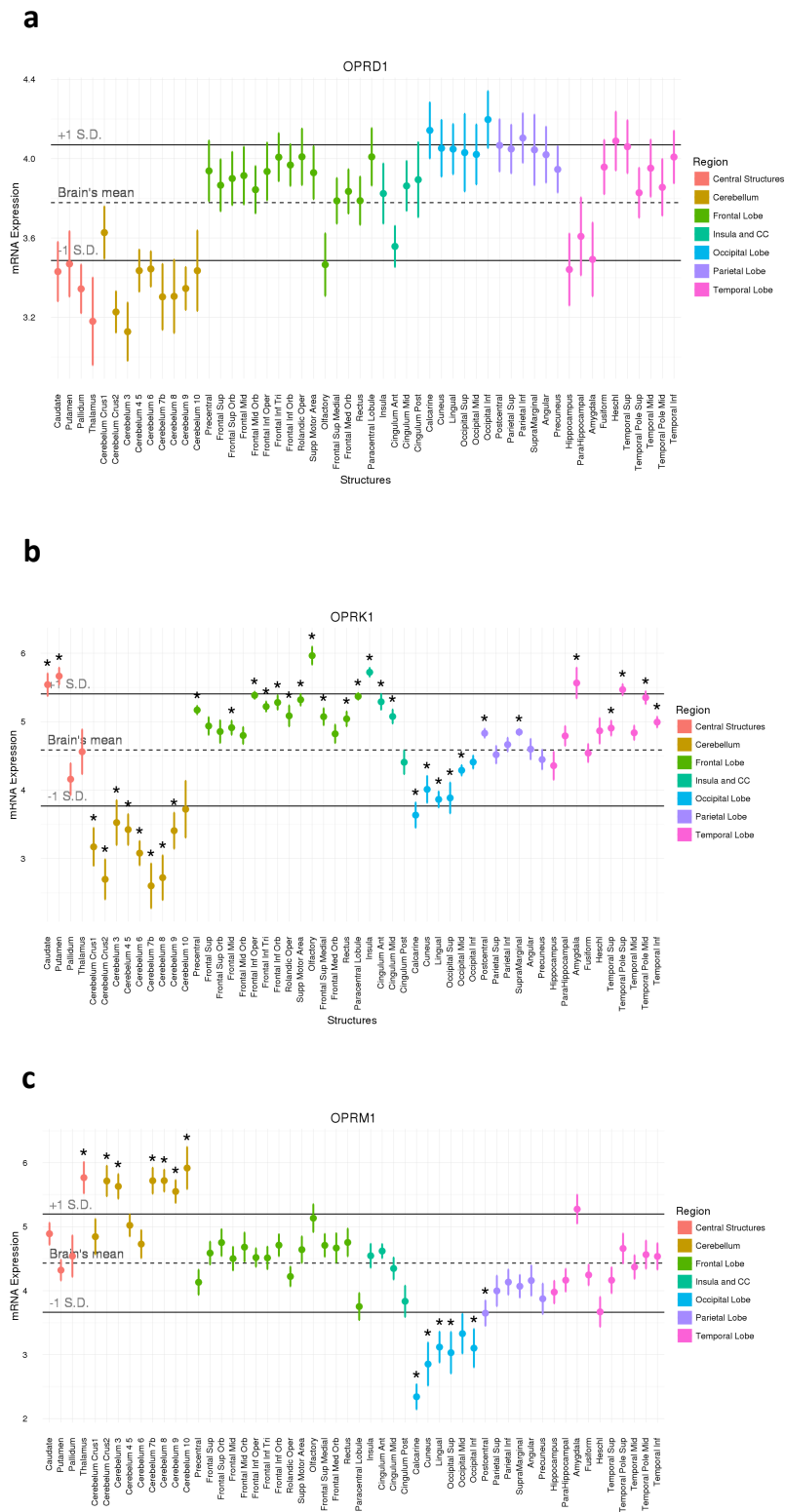
Supplementary Figure 3. The central expression of dopaminergic genes DRD1 (a), DRD2 (b), DRD3 (c), DRD4 (d), DRD5 (e), COMT (f), and DAT1/SLC6A3 (g) Means and standard errors are presented. Statistically significant two-tailed one-sample t -tests are shown. * $p > 0.05$ (FDR corrected).



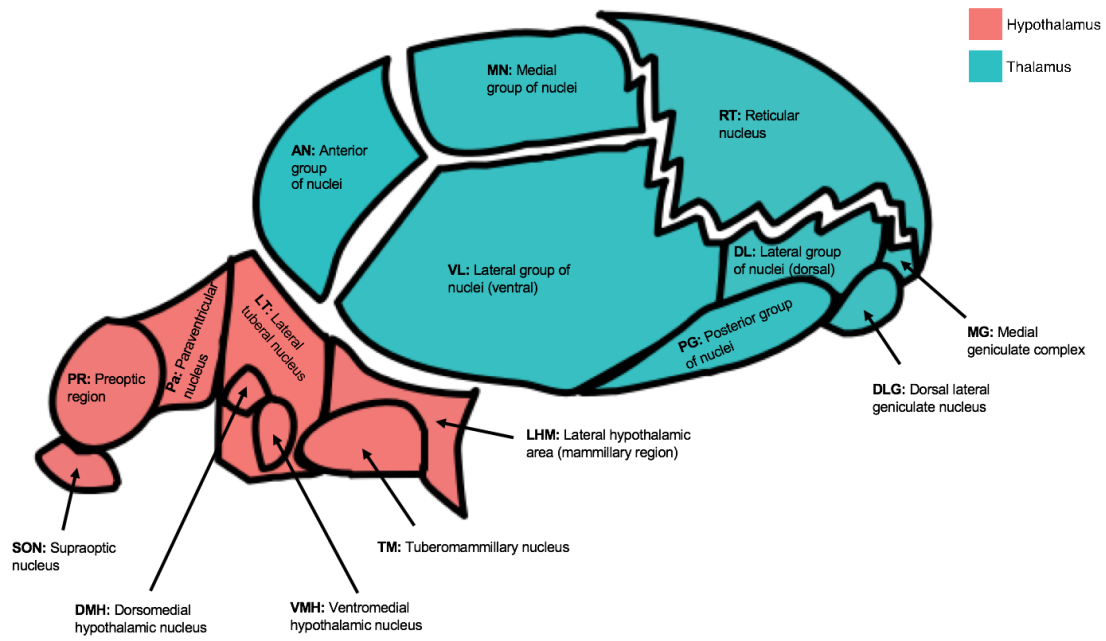
Supplementary Figure 4. The central expression of muscarinic acetylcholine pathway genes CHRM1 (a), CHRM2 (b), CHRM3 (c), CHRM4 (d), and CHRM5 (e). Means and standard errors are presented. Statistically significant two-tailed one-sample t -tests are shown. * $p > 0.05$ (FDR corrected).



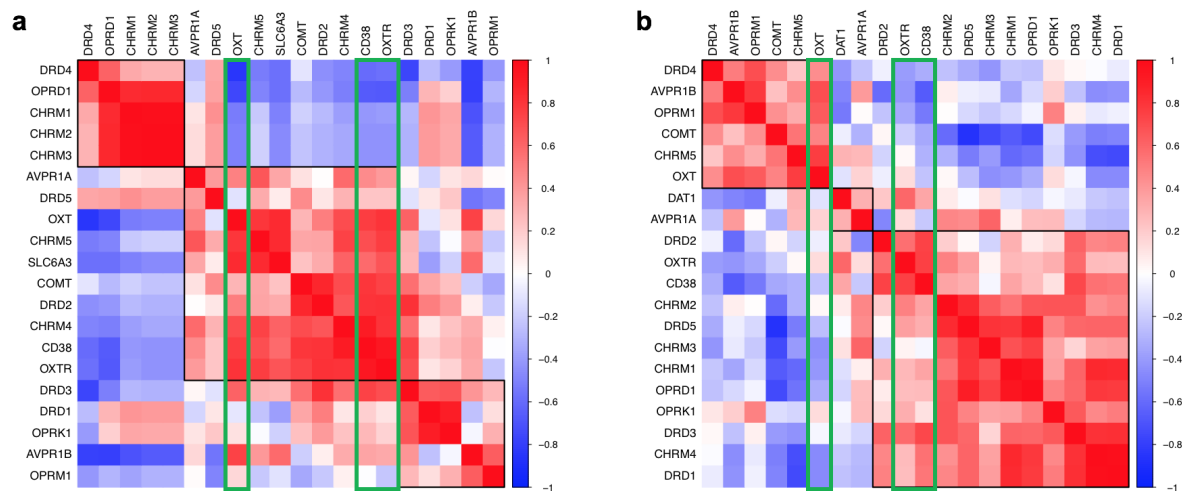
Supplementary Figure 5. The central expression of vasopressin genes AVPR1A (a), and AVPR1B (b). Means and standard errors are presented.



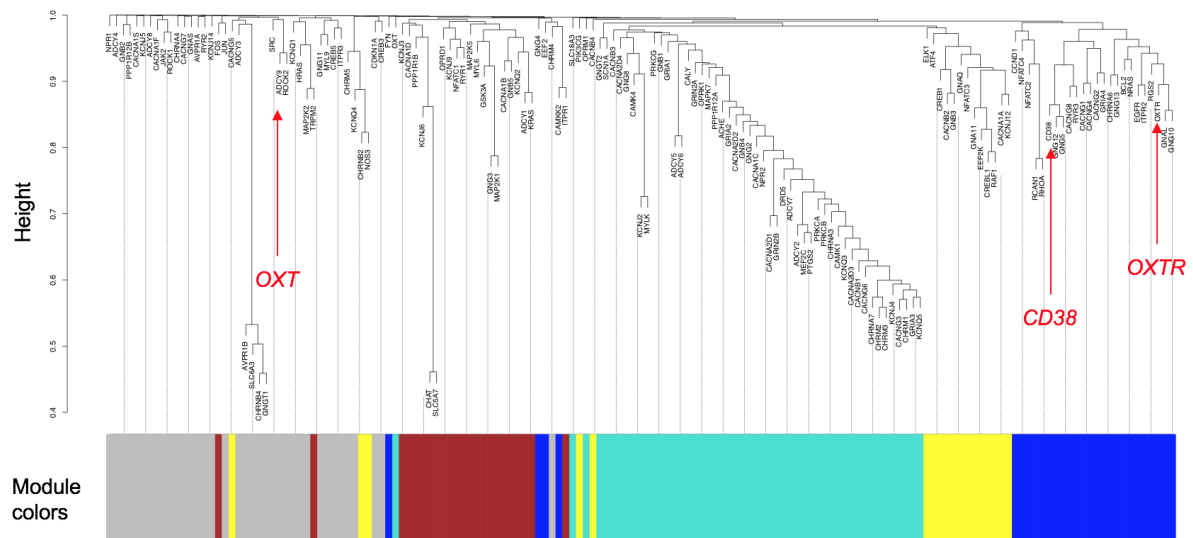
Supplementary Figure 6. The central expression of opioid genes OPRD1 (a), OPRK1 (b), and OPRM1 (c). Means and standard errors are presented. * > 0.05 (FDR corrected).



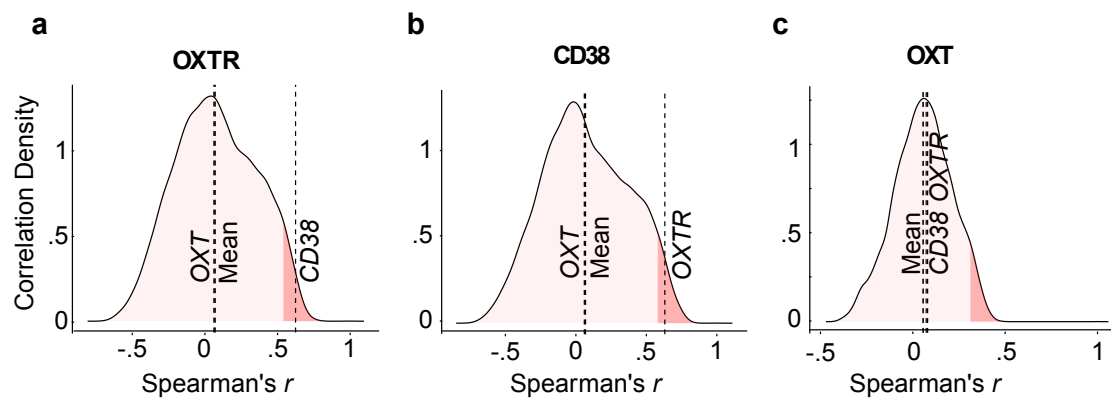
Supplementary Figure 7. Anatomical legend for thalamic and hypothalamic substructures.



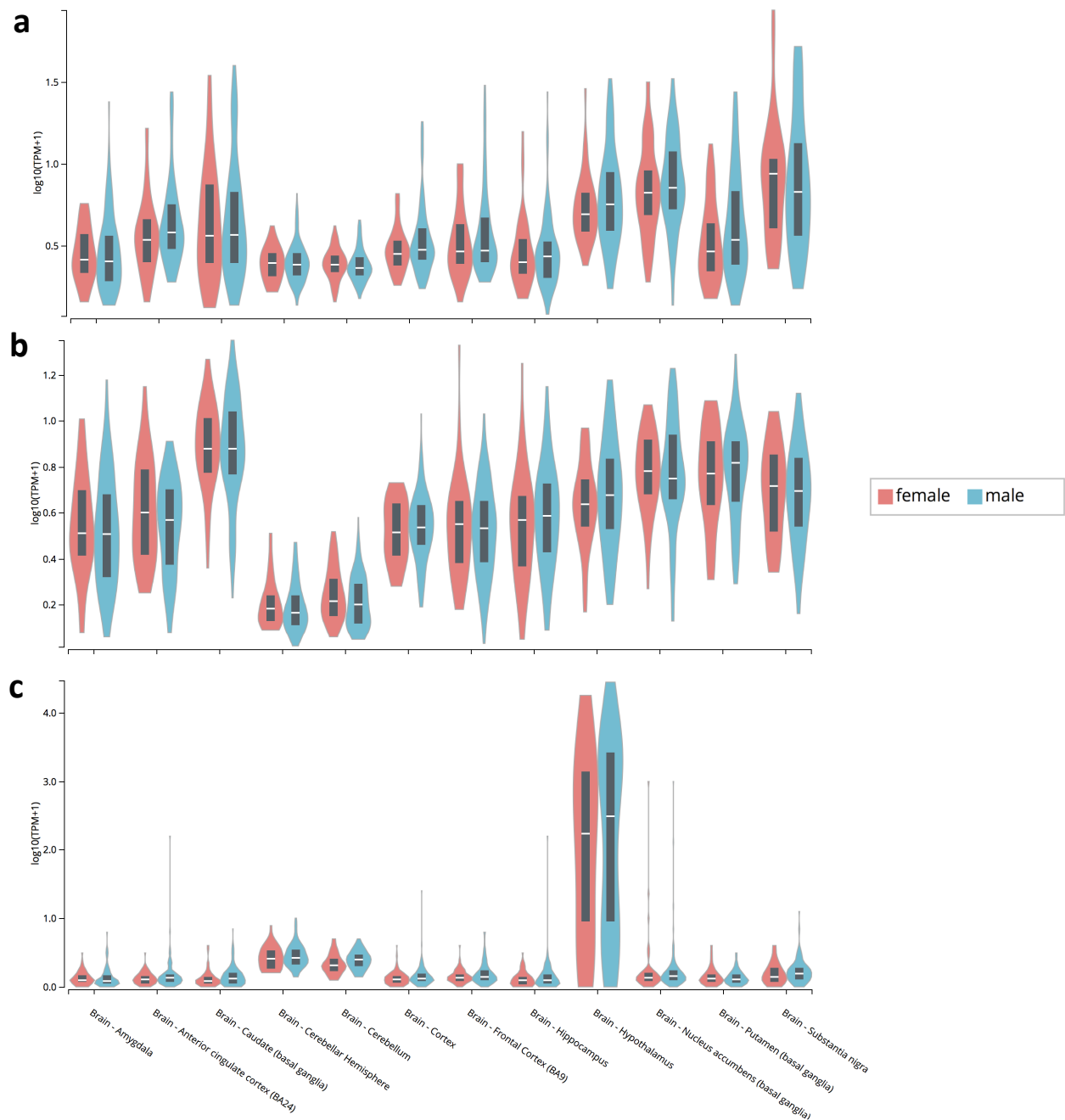
Supplementary Figure 8. Independent sample validation of the central co-expression of oxytocin, dopaminergic, muscarinic acetylcholine, vasopressin, and opioid gene sets. As described in Figure S2, median expression data was extracted from the Allen (a) and GTEx (b) datasets. Values represent Spearman correlation coefficients. Complete linkage clustering was used to identify 3 clustering groups (black squares). The key constituents of the oxytocin pathway (*OXTR*, *CD38*, *OXT*) were highlighted by green rectangles. In both datasets, *OXTR* and *CD38* clustered together, along with *DRD2*, and *CHRM4* genes.



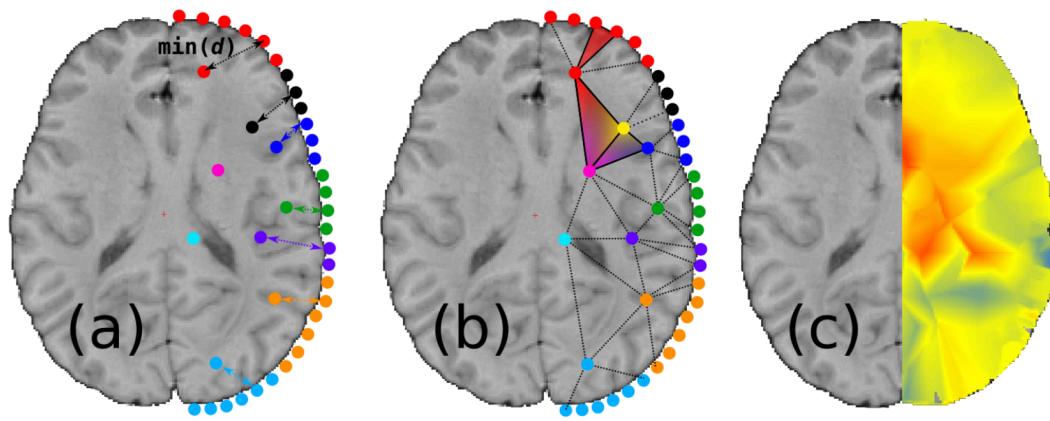
Supplementary Figure 9. WGNCA cluster dendrogram with modules and labelled genes. mRNA expression values of all oxytocin pathway genes in the brain were submitted for weighted gene co-expression network analysis. *OXTR* and *CD38* were clustered together in the same module. *OXTR*, *CD38*, and *OXT* are highlighted with red arrows and labelled in red



Supplementary Figure 10. Co-expression of oxytocin pathway genes against 20737 protein coding genes. Density plots visualize the distributions of correlations between *OXTR* (a), *CD38* (b), and *OXT* (c), and all other mRNA probes. For each oxytocin pathway gene of interest, the position of the other two oxytocin pathway genes of interest are shown. The correlation between *OXTR* and *CD38* is in the top 5% of all correlations, which is indicated by the dark red portions of the distributions.



Supplementary Figure 11. Sex differences in central oxytocin pathway mRNA expression. Box plots demonstrate median central expression of *OXTR* (a), *CD38* (b), and *OXT* (c) in males (blue boxes) and females (red boxes) over 12 brain regions, with 25th and 75th percentiles. Data was extracted from the GTEx database (<https://gtexportal.org>), with gene expression presented as Transcripts per million (TPM) as log transformed units.



Supplementary Figure 12. Creation of expression maps. First, brain boundaries were labelled (a). Spaces were then divided into simplices, which were triangles in two-dimensional cases (note that not all possible triangles are marked in the image) (b). We then performed linear interpolation within each simplex (c).

Supplementary Table 1. Probe details for top Spearman's correlations between oxytocin pathway genes and all remaining genes

	OXTR			CD38			OXT		
	Gene	Probe ID	r_s	Gene	Probe ID	r_s	Gene	Probe	r_s
Top 10 positive	LUPZ2	1029580	0.793	NTSR2	1045487	0.821	EPS8L2	1039716	0.492
	NTSR2	1045487	0.779	SLC14A1	1020063	0.811	FLYWCH2	1011181	0.473
	GLUD2	1056377	0.776	C12orf39	1038445	0.807	IL28RA	1033899	0.466
	GLUD1	1056379	0.771	AQP4	1024273	0.802	N4BP2	1041644	0.465
	MLEC	1048178	0.765	LIX1	1033799	0.799	MAP2K3	1052652	0.461
	THBS4	1050797	0.763	PSAT1	1027224	0.794	CCR10	1056267	0.453
	KIAA1407	1040552	0.759	PRTFDC1	1041054	0.782	CD14	1022645	0.451
	ZC3HAV1	1041166	0.748	HSDL2	1037724	0.78	C5orf56	1025314	0.446
	HEYL	1044845	0.743	ITGB8	1054914	0.78	CLDN3	1057991	0.443
	NAV2	1020830	0.741	GLUD1	1056379	0.777	CBX5	1010672	0.442
Top 10 negative	GABRD	1056608	-0.67	KCNJ3	1054823	-0.738	LHX2	1048690	-0.414
	KCNJ3	1054823	-0.66	AC021534.2	1019865	-0.724	NEK2	1053760	-0.412
	CHRD	1049481	-0.652	CHRD	1049481	-0.706	KCNV1	1044726	-0.41
	AC021534.2	1019865	-0.647	PAK7	1026139	-0.705	LOC339524	1020418	-0.401
	KIAA0408	1025969	-0.647	GABRD	1056608	-0.7	AK5	1027247	-0.397
	PAK7	1026139	-0.643	IGSF21	1037180	-0.7	CHSY3	1022072	-0.394
	KIAA0802	1019330	-0.632	GALNT9	1018522	-0.695	TRIM48	1016645	-0.394
	SRPK1	1051136	-0.632	ACTL6B	1043413	-0.692	ENC1	1049632	-0.393
	KIAA1456	1015411	-0.631	NEUROD1	1053753	-0.691	KCNJ4	1054822	-0.392
	SLC6A7	1051449	-0.631	MICAL2	1048322	-0.696	CTNNA2	1057852	-0.391

Supplementary Table 2. Top 5 mental state correlations for *OXTR*, *CD38*, and *OXT* brain mRNA maps submitted to NeuroSynth with rank and percentage out of all 20,737 protein coding genes

Cognitive state	Number of fMRI studies	<i>OXTR</i>				<i>CD38</i>				<i>OXT</i>			
		r_s	p -value	Rank	Rank percentage	r_s	p -value	Rank	Rank percentage	r_s	p -value	Rank	Rank percentage
Anticipation	301	0.215	< .0001	549	2.65	0.283	< .0001	13	0.06	0.082	0.0597	6382	30.78
Anxiety	449	0.297	< .0001	60	0.29	0.238	< .0001	495	2.39	0.022	0.3375	8056	38.85
Emotional	1708	0.293	< .0001	178	0.86	0.224	< .0001	793	3.82	0.005	0.4627	7802	37.62
Facial expressions	250	0.070	0.0906	2633	12.70	0.040	0.2261	5537	26.70	0.065	0.1098	3090	14.90
Fear	363	0.205	< .0001	481	2.32	0.117	0.0128	2673	12.89	0.079	0.0676	4421	21.32
Incentive	148	0.242	< .0001	49	0.24	0.239	< .0001	64	0.31	0.039	0.2303	7712	37.19
Learning	1144	0.074	0.0809	7825	37.73	0.110	0.0182	5773	27.84	0.161	0.0011	3328	16.05
Monetary	300	0.206	< .0001	452	2.18	0.263	< .0001	38	0.18	0.055	0.1493	6106	29.44
Motivation	189	0.234	< .0001	34	0.16	0.224	< .0001	69	0.33	0.047	0.1881	6368	30.71
Reward	922	0.324	< .0001	240	1.16	0.347	< .0001	114	0.55	0.078	0.0699	6102	29.43
Seeking	99	0.119	0.0115	1746	8.42	0.168	0.0007	234	1.13	0.088	0.0480	3853	18.58
Sexual	81	0.245	< .0001	19	0.09	0.177	0.0004	942	4.54	0.036	0.2448	7933	38.26
Stress	321	0.266	< .0001	358	1.73	0.263	< .0001	396	1.91	0.020	0.3490	8116	39.14
Taste	80	0.224	< .0001	393	1.90	0.238	< .0001	229	1.10	0.097	0.0321	4397	21.20
Unpleasant	132	0.156	0.0014	919	4.43	0.128	0.0072	1858	8.96	0.103	0.0252	3054	14.73

Note. After retrieving the mental state terms with the 5 strongest relationships with the *OXTR* map, we skipped duplicate terms when retrieving the 5 strongest relationships with the *CD38* map and the repeated this process (skipping duplicates) with the *OXT* map. Ranks and rank percentages represent the rank for correlations between the *OXTR*, *CD38*, and *OXT* gene maps and the given terms compared to all 20737 genes maps.

Supplementary Table 3. Detailed donor profiles

ID	Ethnicity	Gender	Age	Post-mortem interval (hours)	Number of brain samples	Hemisphere
1	Caucasian	Male	57	25.5	363	Left
2	Caucasian	Male	31	17.5	529	Left
3	Hispanic	Female	49	30.0	470	Left
4	Caucasian	Male	55	18.0	501	Left
5	African American	Male	24	25.0	946	Both
6	African American	Male	39	18.0	893	Both

Supplementary Table 4. Fit indices for scale-free topology

Power	Soft-thresholding power (adjusted R^2)	Mean connectivity	Median connectivity	Maximum connectivity
1	0.665	51.4	52.3	72.6
2	0.145	24.3	23.4	44.5
3	0.185	13.7	11.9	31.3
4	0.694	8.61	6.58	24.3
5	0.103	5.82	4.19	19.8
6	0.793	4.16	2.71	16.7
7	0.741	3.11	1.92	14.4
8	0.804	2.4	1.37	12.7
9	0.0672	1.91	0.906	11.2
10	0.828	1.55	0.608	10.1
12	0.781	1.08	0.29	8.27
14	0.795	0.791	0.161	6.93
16	0.213	0.604	0.0899	5.9
18	0.212	0.475	0.0533	5.08
20	0.93	0.382	0.0306	4.42

