

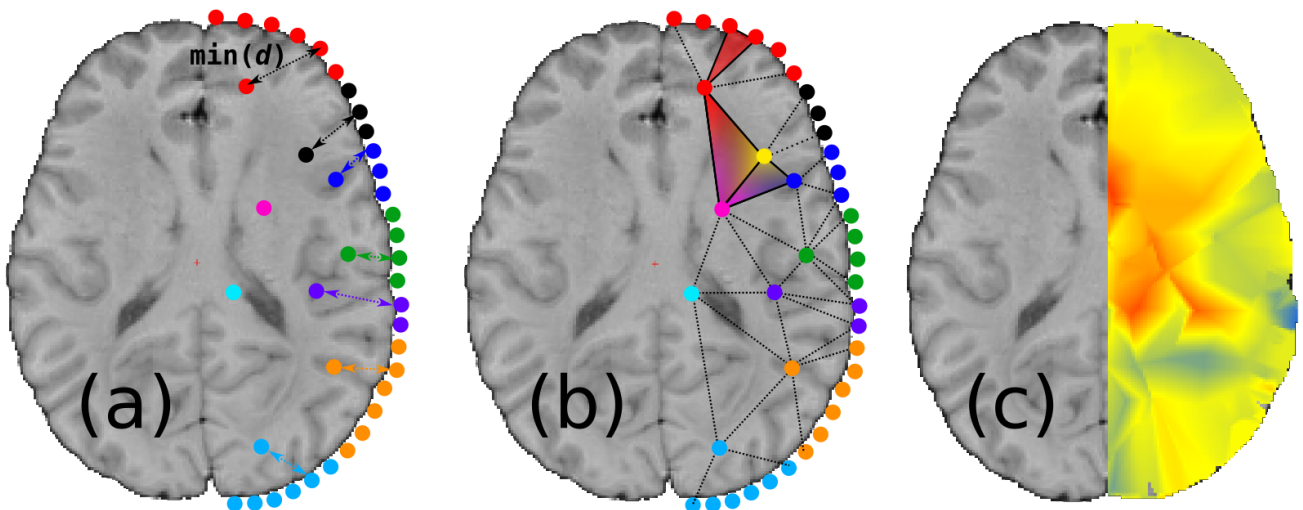
Supporting material

Oxytocin gene networks in the human brain: A gene expression and large-scale fMRI meta-analysis study

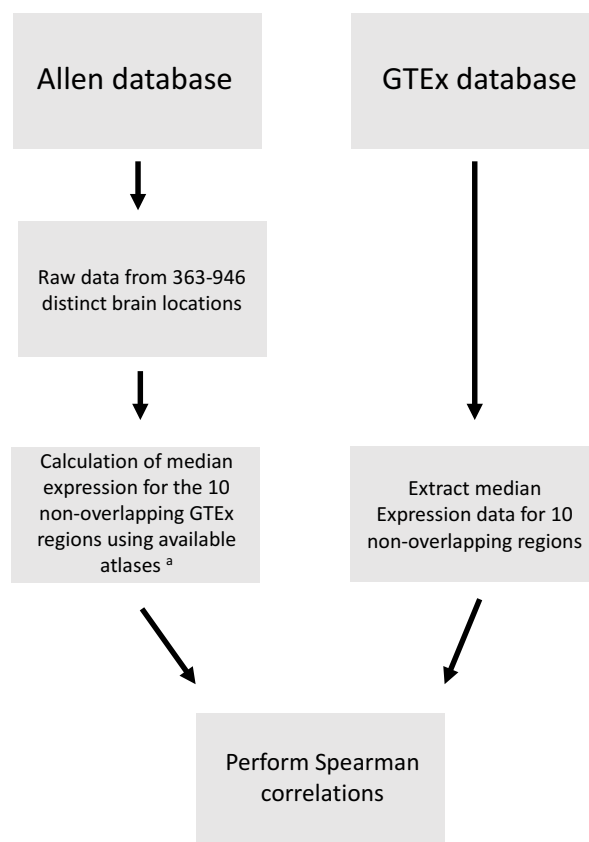
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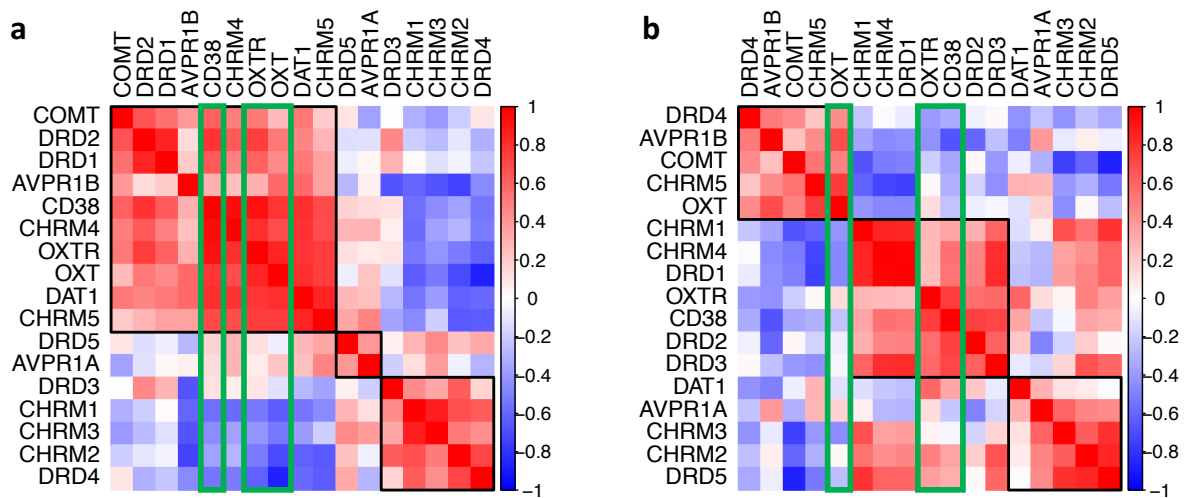
Supplementary Figure S1. Creation of expression maps. First, brain boundaries were labeled (a). Spaces were then divided into simplices, which were triangles in two-dimensional cases (note that not all possible triangles are marked in the image) (b). We then performed linearly interpolating within each simplex (c)



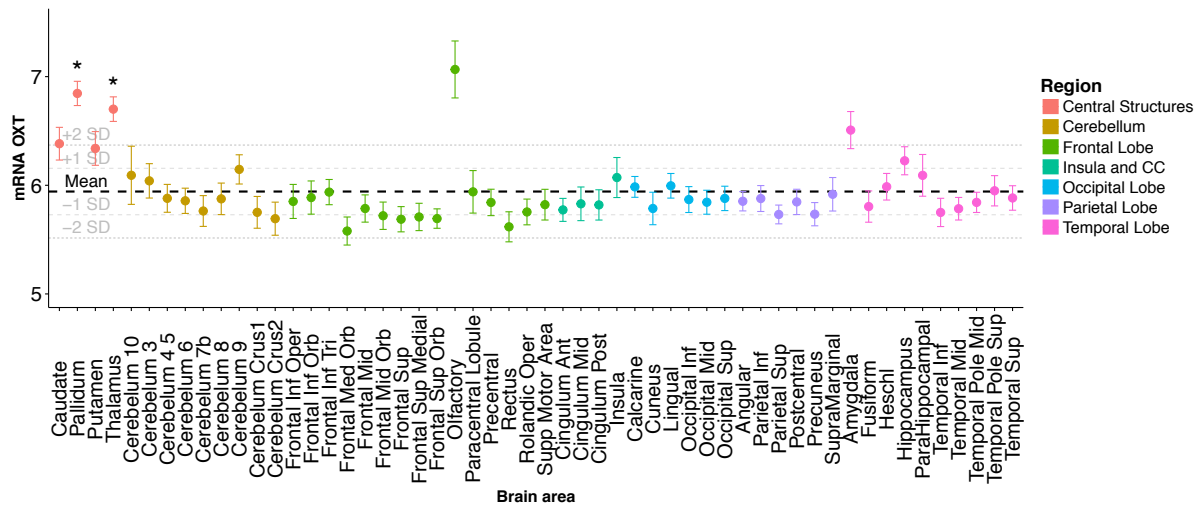
Supplementary Figure S2. The comparison of Allen and GTEx datasets. Median expression data from 10 distinct regions from the GTEx database were compared to the median expression of the same regions from the Allen database. Medians from the Allen dataset were extracted from the raw data by calculating 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



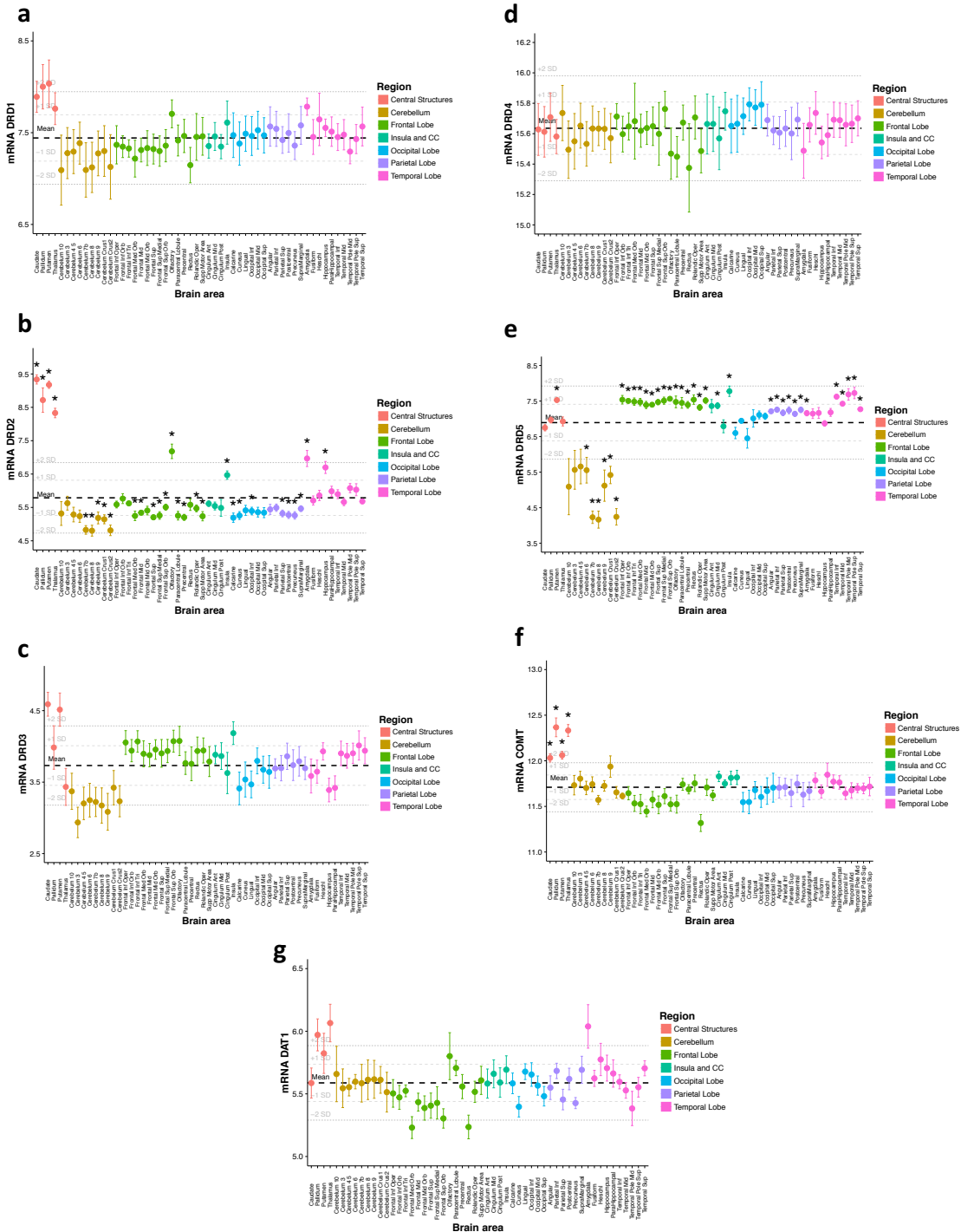
Supplementary Figure S3. Out-of-sample validation of the central co-expression of oxytocin, dopaminergic, muscarinic acetylcholine, and vasopressin gene sets. As described in Figure S2, median expression data was extracted from the Allen (a) and GTEx (b) datasets. Values represent Spearman correlation 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*, *CHRM4*, and *DRD1* genes.



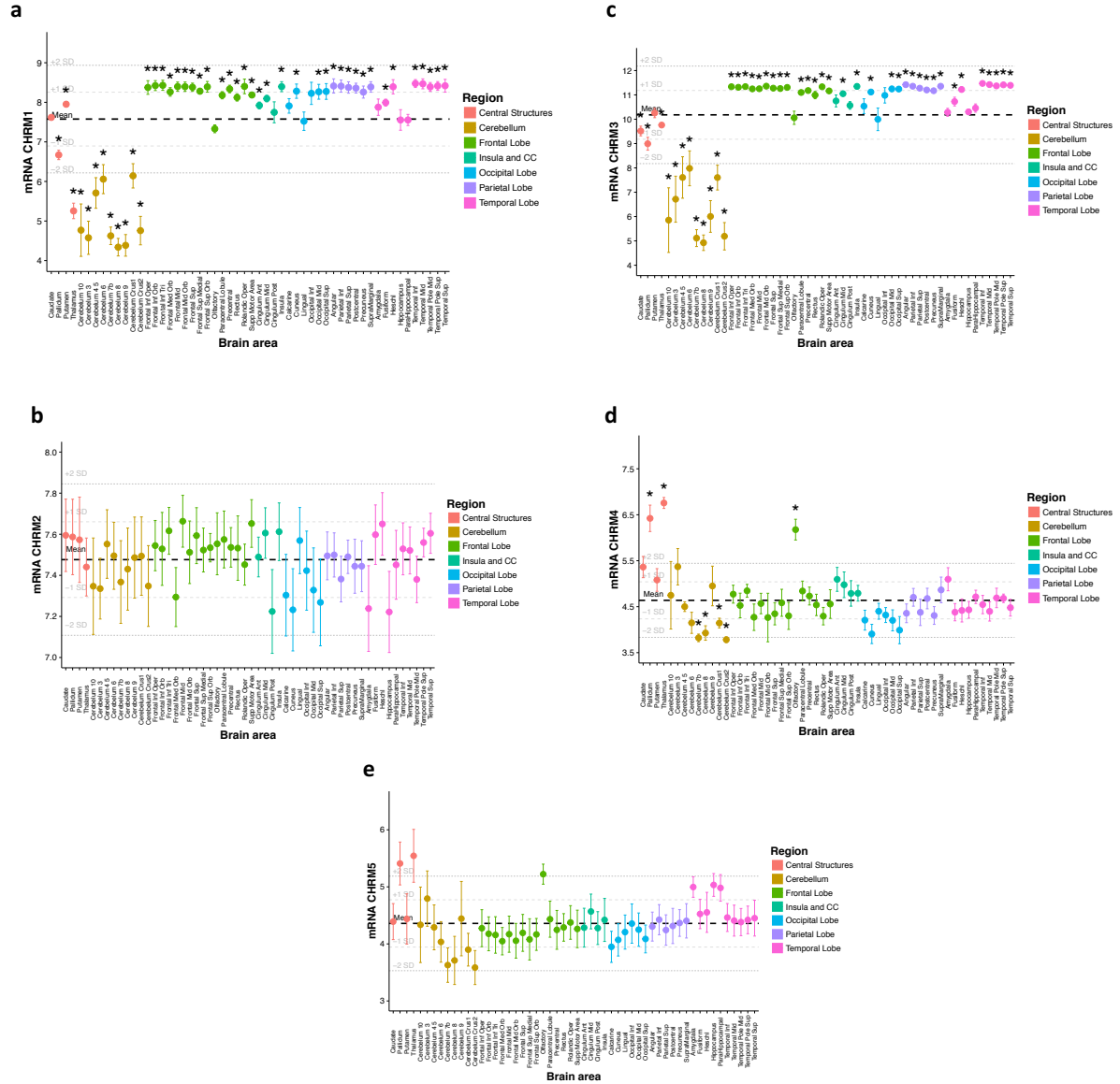
Supplementary Figure S4. The central expression of OXT. Means and standard errors are presented. * > 0.05 (FDR corrected).



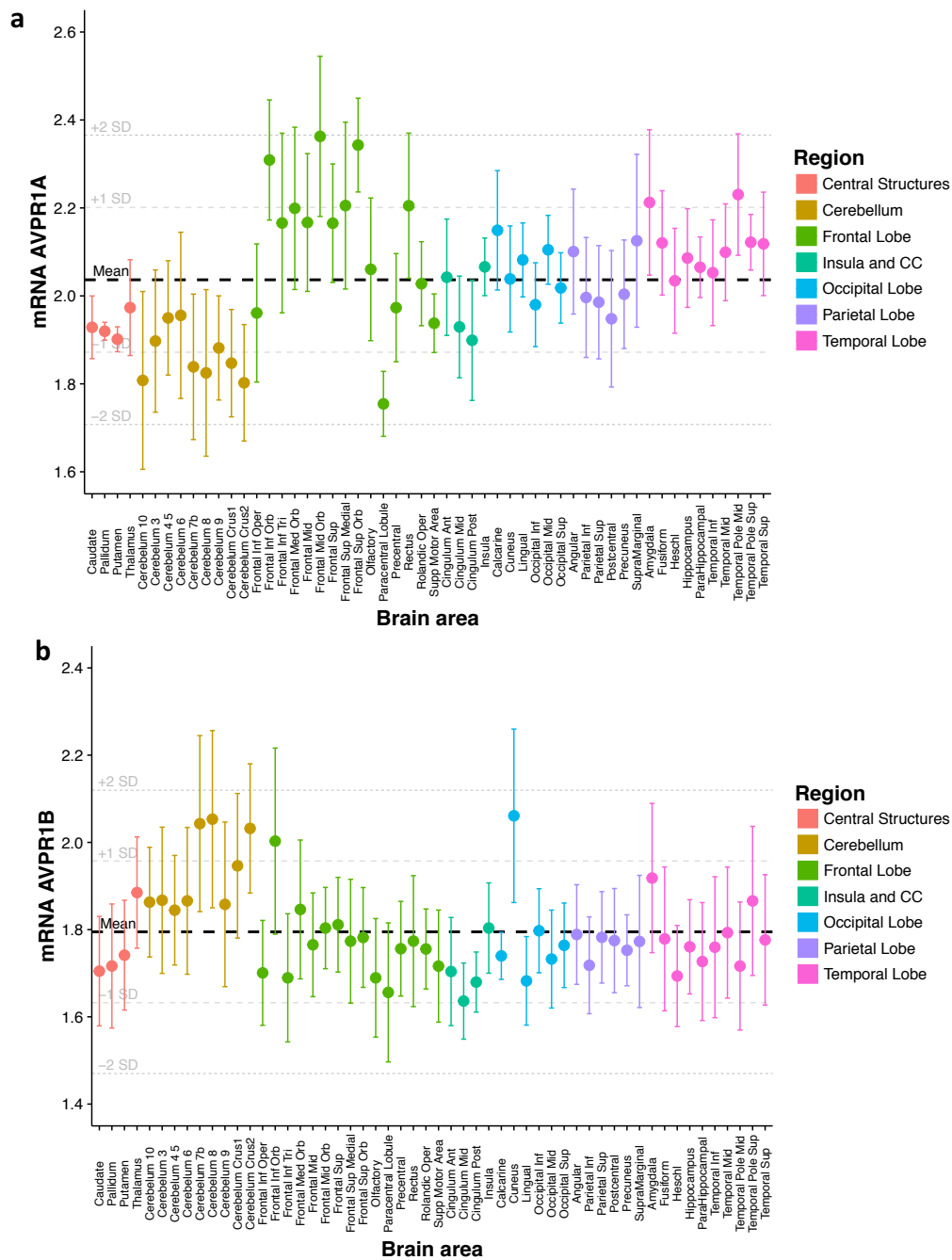
Supplementary Figure S5. The central expression of dopaminergic genes DRD1 (a), DRD2 (b), DRD3 (c), DRD4 (d), DRD5 (e), COMT (f), and DAT1 (g) Means and standard errors are presented. * > 0.05 (FDR corrected).



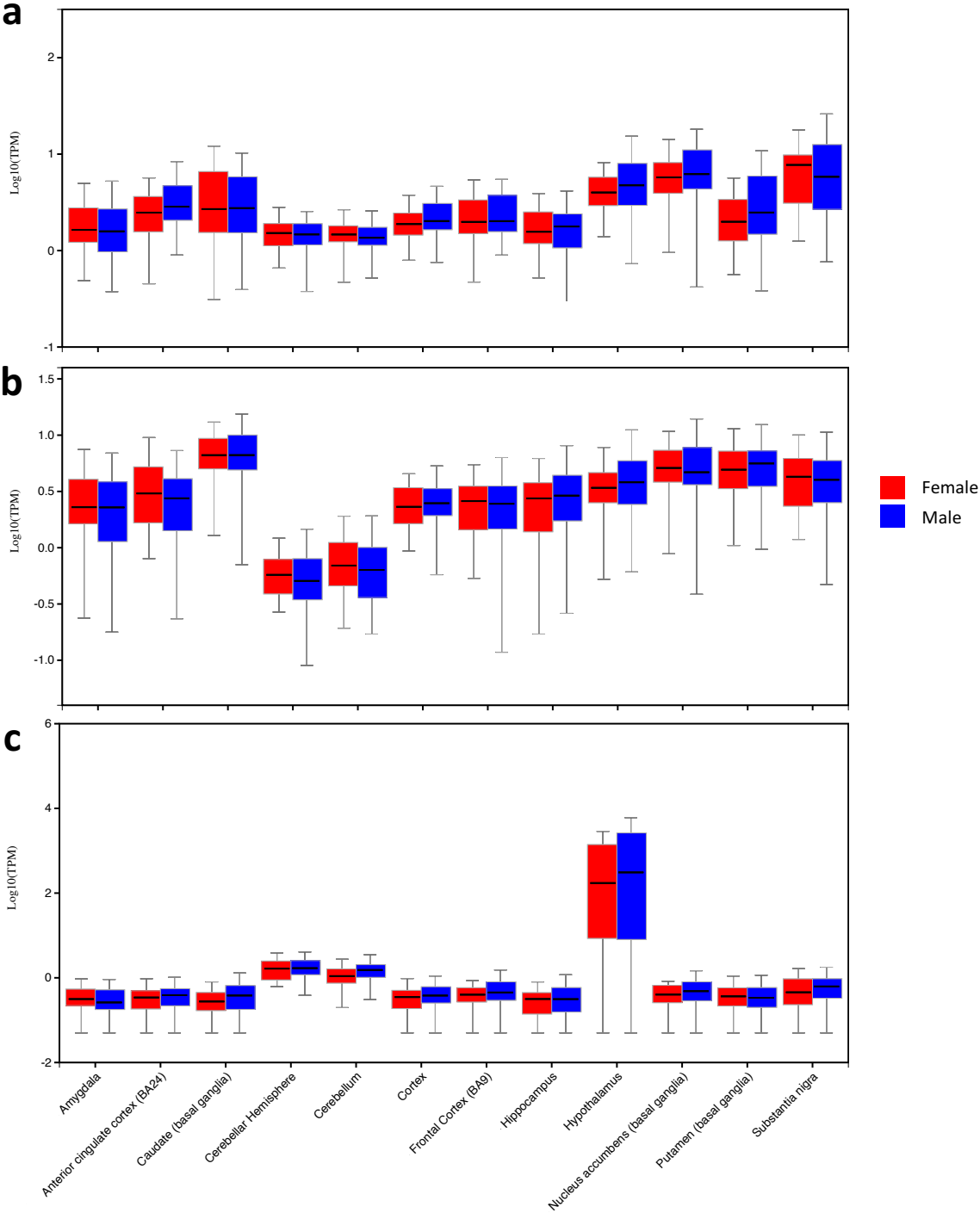
Supplementary Figure S6. The central expression of muscarinic acetylcholine pathway genes CHRM1 (a), CHRM2 (b), CHRM3 (c), CHRM4 (d), and CHRM5 (e). Means and standard errors are presented. * > 0.05 (FDR corrected).



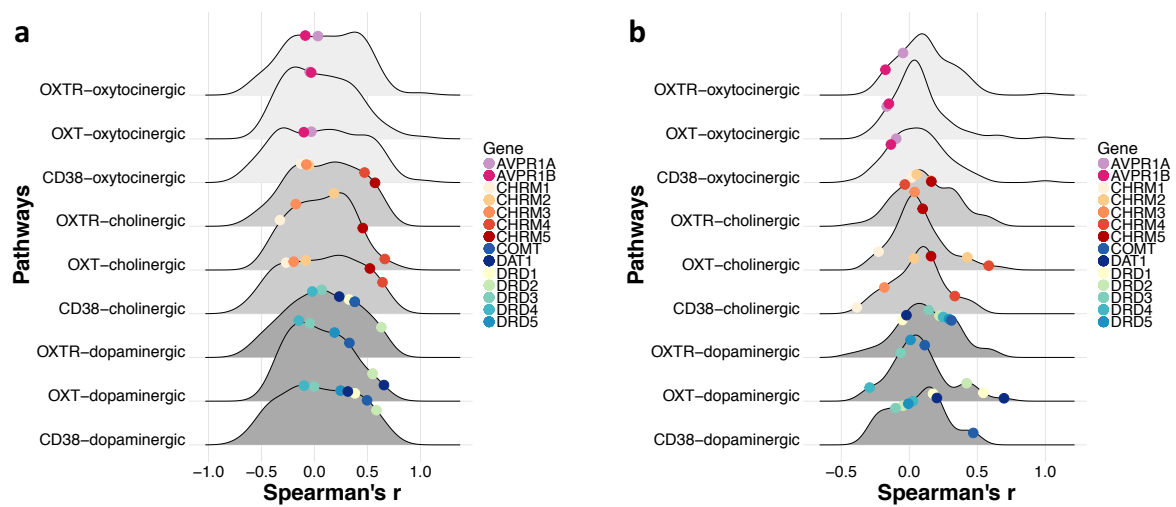
Supplementary Figure S7. The central expression of vasopressin genes AVPR1A (a), and AVPR1B (b). Means and standard errors are presented. * > 0.05 (FDR corrected).



Supplementary Figure S8. Sex differences in central oxytocin pathway mRNA expression. Box and whisker plots demonstrating median central expression of *OXT* (a), *CD38* (b), and *OXT* (c) in males (blue boxes) and females (red boxes) over 12 brain regions. Data was extracted from the GTEx database, with gene expression presented as log transformed units.



Supplementary Figure S9. Central co-expression of *OXTR*, *OXT*, and *CD38* with selected dopaminergic, muscarinic acetylcholine, and vasopressin gene sets across the brain and the cortex only. Spearman's correlation coefficients are presented for the full brain (a) and the cortex only (b). Spearman's correlations are visualized on a density distribution demonstrating all co-expression correlations between *OXTR*, *CD38*, and *OXT* and all genes in the complete oxytocinergic (n = 94), cholinergic (n = 79), and dopaminergic (n = 63) gene sets (see Dataset S1 for full lists). Genes of interest from each selected set are identified.



Supplementary Table S1. 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	946	Both

Supplementary Table S2. Probe details for top Spearman's correlations between oxytocin pathway genes and all remaining genes

	OXTR			CD38			OXT		
	Gene	Probe	ρ	Gene	Probe	r	Gene	Probe	r
Top 10 positive	NTSR2	A_23_P315212	0.798	LIX1	A_24_P226241	0.815	GSTCD	CUST_5255_PI416261804	0.81
	GLUD2	CUST_287_PI416408490	0.783	NTSR2	A_23_P315212	0.813	UMOD	A_23_P158775	0.80
	GLUD1	A_23_P138665	0.777	SPX	CUST_15484_PI416261804	0.810	WFDC10B	A_32_P951	0.80
	KCNN3	A_23_P126167	0.777	SLC14A1	A_23_P55616	0.803	THTPA	CUST_12922_PI416261804	0.78
	THBS4	A_24_P260443	0.762	PSAT1	CUST_8157_PI416261804	0.798	OR10H2	A_23_P50799	0.79
	HEYL	A_23_P430658	0.761	C18orf51	CUST_6268_PI416261804	0.790	SLC5A10	CUST_4603_PI416261804	0.79
	MLEC	A_23_P2554	0.761	ITGB8	A_23_P123060	0.787	SYDE1	CUST_1989_PI416261804	0.79
	LYPD1	A_32_P101031	0.752	HSDL2	A_23_P169197	0.784	KRT81	A_23_P25187	0.79
	KIAA1407	A_32_P54616	0.752	C9orf61	A_24_P209710	0.783	SEMA4G	CUST_3578_PI416261804	0.79
	ZC3HAV1	A_23_P425224	0.751	GLUD1	A_23_P138665	0.783	OR2B11	CUST_976_PI416379584	0.79
Top 10 negative	ST8SIA5	A_23_P379789	-0.621	RTN4R	A_23_P132175	-0.666	ATOH7	A_32_P78295	-0.32
	KLF9	A_23_P415401	-0.621	FAM153B	A_24_P280465	-0.671	DGKA	A_23_P105307	-0.32
	PAK7	A_24_P344666	-0.627	RNF165	A_23_P371276	-0.676	SLN	A_23_P150343	-0.32
	SLC6A7	CUST_1075_PI416261804	-0.629	SLITRK4	A_32_P131640	-0.677	LTK	A_23_P14853	-0.32
	C5orf13	A_24_P149124	-0.629	MICAL2	A_23_P24843	-0.679	CCKBR	A_23_P162010	-0.33
	SRPK1	A_23_P19543	-0.631	GALNT9	A_23_P252462	-0.682	GPM6A	A_23_P121545	-0.33
	KIAA0802	A_23_P360605	-0.634	PRSS3	A_23_P135257	-0.684	GARNL4	CUST_4993_PI416261804	-0.33
	RBFOX3	A_24_P142343	-0.639	NEUROD1	A_23_P209484	-0.698	RBFOX3	A_23_P364504	-0.34
	CADPS2	CUST_12165_PI416261804	-0.641	CHRD	A_23_P502047	-0.706	GALNT17	A_23_P111517	-0.35
	CHRD	A_23_P502047	-0.659	RBFOX3	A_24_P142343	-0.731	TMEM240	A_32_P161913	-0.35

Supplementary Table S3. Top 5 mental state correlations for OXTR, CD38, and OXT

brain mRNA maps submitted to NeuroSynth

Keyword	OXTR		CD38		OXT	
	r_s	Rank	r_s	Rank	r_s	Rank
Reward	0.351	90	0.332	141	0.131	4434
Regulation	0.307	84	0.258	355	0.053	6387
Anticipation	0.197	493	0.25	27	0.135	2980
Monetary	0.23	166	0.252	56	0.122	3371
Inhibition	0.093	3532	0.221	56	0.109	2631
Incentive	0.261	20	0.222	169	0.109	3471
Learning	0.073	7469	0.163	2491	0.117	4753
Seeking	0.129	1923	0.171	379	0.098	3900
Pain	0.22	1244	0.219	1266	0.143	3830
Unpleasant	0.201	1638	0.147	1701	0.154	1438
Aversive	0.198	245	0.149	1334	0.126	2308
Threat	0.201	87	0.154	512	0.095	2680
Anxiety	0.351	12	0.266	434	0.133	4111
Emotional	0.329	63	0.198	1069	0.053	6305
Stress	0.319	56	0.266	403	0.102	4973

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 represent the overall rank for correlation between the OXTR, CD38, and OXT gene maps and the given terms compared to all 20737 genes maps.