SUPPLEMENTARY INFORMATION

Aggregate *OXTR* Risk

In order to investigate whether any of the SNPs was contributing significantly more to the observed effects than the others, correlations were run between average connectivity values in subcortical and frontal regions modulated by the *OXTR* in ASD and TD groups (i.e., areas shown in Figure 2A,B) and aggregate risk on 3 of the 4 *OXTR* SNPs in an iterative fashion, leaving out one SNP at a time. While the strength of the correlation decreased in the analyses built on the 3-SNP aggregate scores, they remained significant in both ASD and TD groups ($p<0.05$). Further suggesting that no single risk allele disproportionately contributed to the reported effects, the strength of the observed correlations between aggregate risk allele dosage and connectivity did not differ significantly across any of these three SNP models.

Connectivity values were extracted from areas showing *OXTR*-dose-dependent modulation (i.e., areas shown in Figure 2) and correlated with age in the ASD and TD groups separately, as well as in the total sample, in order to determine whether finding were influenced by age. There were no significant associations ($p>0.05$). Furthermore, Leven's test for equality of variances was not significant when comparing ages in the TD and ASD sample, nor was there a difference in means between TD ($M=13.11$, $SD=1.85$) and ASD ($M=13.52$, $SD=2.20$) participants ($t(80)=0.91$, $p>0.05$, $d=0.20$).

NAcc-Frontal Connectivity in TD Youth

To further test whether increased NAcc-frontal connectivity in TD youth might reflect a compensatory neural mechanism in response to increased genetic risk, we divided our TD sample into high-risk (3-6 risk alleles) and low-risk (0-2 risk alleles) groups and tested the correlation between NAcc-frontal cortex connectivity and SRS scores in each group separately.

In the high-risk TD group, the significant correlation with SRS social cognition scores held ($r(25)=-0.34$, $p<0.05$, one-tailed), while in the low-risk group the correlation did not reach significance ($r(15)=-0.29$, $p=0.15$, one-tailed). Consistent with the notion that the observed relationship between increased NAcc-frontal connectivity and SRS scores may reflect a compensatory mechanism, we also found that connectivity between the NAcc and frontal cortex was significantly stronger in the TD high-risk group than in the TD low-risk group (M=0.19, 0.04, SD=0.14, 0.12, respectively; $t(39)=-3.38$, $p<0.01$, $d=1.10$).

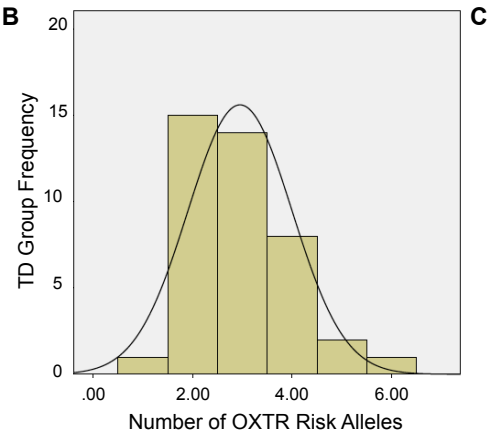
Medication Usage

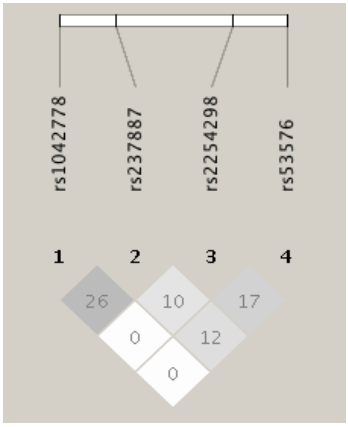
Twenty-seven of the ASD children reported current use of psychotropic medications: 7 were taking psychostimulants, 3 were taking atypical antipsychotics, 3 were taking a selective serotonin reuptake inhibitor (SSRI), 1 was taking an alpha 2 adrenergic agonist, 2 were taking both a psychostimulant and SSRI, 2 were taking both an atypical antipsychotic and SSRI, 1 was taking both a psychostimulant and a norepinephrine reuptake inhibitor, 1 was taking both a psychostimulant and an atypical antipsychotic, 6 of the remaining participants were taking a combination of three different classes of psychotropic medications and 1 was taking a combination of four different classes of medications. To assess whether medication status affected our findings in the ASD group, we directly compared parameter estimates from regions showing reduced NAcc functional connectivity as a function of increased *OXTR* aggregate risk between medicated and non-medicated participants; there was no difference in connectivity strength between the two groups.

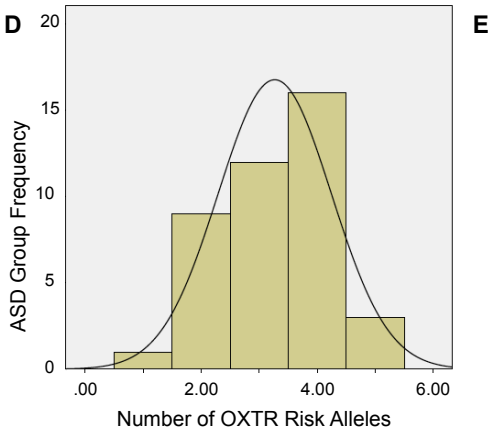
Supplementary Figure 1.

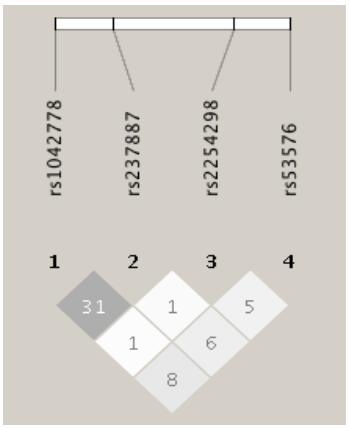
A

Polymorphism	Risk Allele	Genetic Score = 0	Genetic Score = 1	Genetic Score = 2
OXTR rs53576	A	GG	AG	AA
OXTR rs237887	A	GG	AG	AA
OXTR rs1042778	G	TT	TG	GG
OXTR rs2254298	A	GG	AG	AA



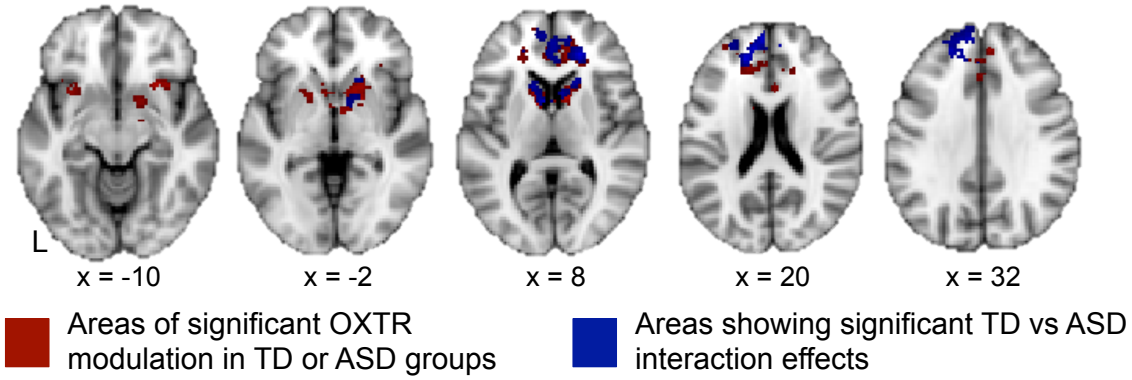






OXTR risk allele descriptives. (**A**) Additive risk scores were calculated by summing the number of ASD-associated risk alleles across four *OXTR* SNPs. (**B**) Distribution of the number of inherited ASD-associated risk alleles for the TD group (N=41). (**C**) Pair-wise linkage disequilibrium (LD) plot in 41 typically developing youth; LD values are r^2 x 100. (**D**) Distribution of the number of inherited ASD-associated risk alleles for the ASD group (N=41). (**E**) Pair-wise linkage disequilibrium (LD) plot in 41 youth with ASD; LD values are r^2 x 100.

Supplementary Figure 2.



Significant interactions by diagnostic group and number of risk allele. Regions in red represent the overlap of areas modulated by aggregate *OXTR* risk in TD and ASD groups (i.e., areas displayed in Figure 2). Areas showing significant interactions when comparing TD and ASD *OXTR* effects are displayed in blue.

Supplementary Table 1. Peak coordinates of NAcc connectivity.

		TD Positive Connectivity				ASD Positive Connectivity				TD Negative Connectivity				ASD Negative Connectivity				TD > ASD Connectivity			
		MNI Peak (mm)			Max *Z*	MNI Peak (mm)			Max *Z*	MNI Peak (mm)			Max *Z*	MNI Peak (mm)			Max *Z*	MNI Peak (mm)			Max *Z*
	R/L	x	y	z		x	y	z		x		z		x	y	z		x	y	z	
Accumbens	R	8	12	-4	13.2	10	10	-8	13.0												
Accumbens	L	-8	12	-4	13.1	-8	14	-4	13.1												
Angular Gyrus	R	62	-60	16	3.3																
Angular Gyrus	L	-58	-58	42	2.6																
Amygdala	R													24	-12	-12	3.0				
Amygdala	L													-30	-4	-24	4.7				
Caudate	R	12	14	14	5.6	18	26	2	7.9												
Caudate	L	-14	14	14	4.9	-14	22	0	10.3												
Cingulate Gyrus, Anterior	R	6	38	-4	8.7	14	44	6	7.4	4	4	32	3.7	10	-8	38	3.9				
Cingulate Gyrus, Anterior	L	-6	36	-4	9.0	-4	36	-2	9.0					-6	0	38	2.8				
Cingulate Gyrus, Posterior	R	6	-50	18	5.2													4	-48	30	3.6
Cingulate Gyrus, Posterior	L	-6	-52	18	4.8									-12	-16	36	3.6	-6	-50	26	3.0
Cuneal Cortex	R									24	-68	24	4.5								
Cuneal Cortex	L									-20	-76	22	4.6	-20	-76	26	2.7				
Frontal Medial Cortex	R	12	40	-14	5.9	12	46	-8	7.9												
Frontal Medial Cortex	L	-4	38	-14	7.0	-8	36	-20	5.9												
Frontal Operculum Cortex	L	-34	26	8	2.6	-40	22	8	3.1												
Frontal Orbital Cortex	R	22	30	-10	6.1	32	30	-4	4.5												

Frontal Orbital Cortex	L	-26	38	-10	5.0	-26	26	-16	6.3											
Frontal Pole	R	18	56	0	6.4	12	56	-4	7.7	52	38	16	4.0							
Frontal Pole	L	0	64	4	6.7	-4	66	10	5.7	-48	42	2	4.0					-12	42	54	3.7
Hippocampus	R									34	-12	-24	3.5	24	-34	-6	2.6			
Hippocampus	L									-22	-10	-20	3.2	-32	-16	-22	4.0			
Inferior Frontal Gyrus, Pars Opercularis	R									44	12	16	4.1							
Inferior Frontal Gyrus, Pars Opercularis	L									-46	14	22	4.2							
Inferior Frontal Gyrus, Pars Triangularis	R									42	30	12	3.6							
Inferior Frontal Gyrus, Pars Triangularis	L									-42	36	10	3.4							
Inferior Temporal Gyrus, Anterior	L	-48	-8	-26	2.9															
Inferior Temporal Gyrus, Posterior	R	50	-18	-24	2.6					56	-34	-28	3.6							
Inferior Temporal Gyrus, Posterior	L													-44	-24	-30	4.8			
Inferior Temporal Gyrus, Temporooccipital	R									46	-52	-10	4.9	58	-54	-16	3.3			
Inferior Temporal Gyrus, Temporooccipital	L									-46	-54	-22	3.6							
Insular Cortex	R	36	14	-12	3.2	34	14	-12	3.2	38	0	-6	3.8	38	-8	-2	4.1			
Insular Cortex	L	-36	10	-8	2.6	-40	16	-12	3.6	-42	0	-8	3.4	-36	-12	-2	3.5			
Intracalcarine Cortex	R									20	-64	6	4.9	20	-72	2	5.1			
Intracalcarine Cortex	L									-14	-72	10	4.9	-20	-76	2	3.9			

Lateral Occipital Cortex, Inferior	R									36	-84	-4	3.8	36	-60	12	3.7
Lateral Occipital Cortex, Inferior	L									-50	-72	-10	4.1	-38	-64	10	3.9
Lateral Occipital Cortex, Superior	R	44	-70	50	4.8					26	-60	46	5.8	26	-64	60	3.6
Lateral Occipital Cortex, Superior	L	-46	-78	36	5.1					-30	-82	20	5.7	-32	-82	20	4.1
Lingual Gyrus	R									14	-70	-2	4.9	22	-54	-8	4.2
Lingual Gyrus	L									-16	-52	-8	4.6	-8	-74	2	4.0
Middle Frontal Gyrus	R									40	4	54	4.8	36	16	60	3.4
Middle Frontal Gyrus	L					-26	24	44	3.5	-54	18	30	4.4	-30	-2	52	3.3
Middle Temporal Gyrus, Anterior	R	56	2	-32	3.2												
Middle Temporal Gyrus, Anterior	L	-60	-4	-26	3.2												
Middle Temporal Gyrus, Posterior	R	58	-16	-18	4.3												
Middle Temporal Gyrus, Posterior	L	-62	-16	-20	4.5												
Middle Temporal Gyrus, Temporooccipital	R									52	-54	0	4.0	48	-54	6	3.7
Middle Temporal Gyrus, Temporooccipital	L									-56	-58	-2	2.5	-50	-62	2	3.5
Occipital Fusiform Gyrus	R									24	-74	-12	4.0	28	-70	-6	3.8
Occipital Fusiform Gyrus	L									-30	-70	-10	4.5	-34	-72	-6	3.2
Occipital Pole	R									12	-90	18	3.4				
Occipital Pole	L									-18	-92	18	3.9				
Pallidum	R									22	-4	0	4.4	20	-2	0	6.1
Pallidum	L									-20	-4	0	3.9	-20	-6	0	4.7

Paracingulate Gyrus	R	2	50	-2	7.9	4	44	-2	7.5										
Paracingulate Gyrus	L	-10	50	2	8.4	-8	48	-4	7.9										
Parrahippocampal Gyrus, Anterior	R	16	0	-30	2.8									24	-18	-30	4.6		
Parrahippocampal Gyrus, Anterior	L									-20	-22	-26	2.6	-32	-14	-32	4.3		
Parrahippocampal Gyrus, Posterior	R													22	-28	-26	2.7		
Plamun Polare	R													44	-6	-16	2.8		
Postcentral Gyrus	R									46	-38	58	4.2	14	-38	48	3.6		
Postcentral Gyrus	L									-64	-22	40	4.0						
Precentral Gyrus	R									46	-8	54	4.4	50	0	54	4.0		
Precentral Gyrus	L									-46	-2	30	3.8	-44	-2	60	4.9		
Precuneous Cortex	R									12	-42	50	4.2	38	-2	56	4.8	10	-58	36	2.5
Precuneous Cortex	L	-8	-54	34	5.1					-8	-66	58	3.5	-4	-52	66	3.1	-12	-54	34	3.7
Putamen	R													34	0	4	4.7		
Putamen	L													-30	-4	6	3.8		
Superior Frontal Gyrus	R	20	32	40	4.6	6	44	38	2.9	18	2	66	4.0	18	-4	68	4.0	2	48	48	4.5
Superior Frontal Gyrus	L	-6	54	32	5.0	-20	28	36	5.0	-22	0	64	4.8	-24	-2	62	3.6	-12	30	58	3.2
Superior Parietal Lobule	R									36	-46	54	5.0	30	-38	44	4.0				
Superior Parietal Lobule	L									-32	-58	56	4.8	-22	-46	70	3.2				
Superior Temporal Gyrus, Anterior	L	-54	-4	-14	3.1																
Supramarginal Gyrus, Anterior	R									60	-34	44	4.8								
Supramarginal Gyrus, Anterior	L									-42	-40	42	5.5								
Supramarginal Gyrus, Posterior	R									38	-44	40	5.1								

Supramarginal Gyrus, Posterior	L									-48	-42	54	4.8				
Subcallosal Cortex	R	6	28	-6	7.7	6	30	-8	8.9								
Subcallosal Cortex	L	-6	30	-8	8.8	-4	32	-8	8.1								
Supplementary Motor Cortex	R									12	-2	58	4.1	2	-12	62	4.5
Supplementary Motor Cortex	L									-4	4	48	3.5	-12	-14	48	3.7
Temporal Fusiform Cortex, Posterior	R									40	-20	-28	3.4	30	-34	-24	3.7
Temporal Fusiform Cortex, Posterior	L													-36	-28	-20	3.4
Temporal Occipital Fusiform Cortex	R									30	-46	-12	4.5	40	-18	-30	3.5
Temporal Occipital Fusiform Cortex	L									-30	-60	-8	4.5	-28	-60	-12	4.4
Temporal Pole	R	42	22	-34	4.3	40	26	-24	4.7								
Temporal Pole	L	-36	24	-30	4.7	-40	22	-26	4.2								
Thalamus	R									8	-16	-4	5.0	8	-16	-4	5.5
Thalamus	L	0	-8	8	4.9	0	-10	10	5.3	-10	-24	2	4.0	-4	-18	-4	5.3

Coordinates are in Montreal Neurological Institute space. Results are presented at $z>2.3$, $p<0.01$ (corrected for multiple comparisons at $p<0.05$).

Supplementary Table 2. Areas modulated by number of *OXTR* risk alleles.

		TD OXTR+ Modulation				ASD OXTR- Modulation			
		MNI Peak (mm)			Max Z	MNI Peak (mm)			Max Z
	R/L	x	y	z		x	y	z	
Frontal Pole	L	-10	56	36	4.3				
Paracingulate Gyrus	L	-12	40	28	3.7	-8	36	24	3.2
Paracingulate Gyrus	R					12	44	14	4.6
Superior Frontal Gyrus	L					-24	54	22	2.8
Frontal Orbital Cortex	R					38	16	-22	4.0
Frontal Orbital Cortex	L					-34	16	-22	3.9
Insular Cortex	L					-34	16	-14	3.6
Insular Cortex	R					26	16	-12	3.8
Putamen	L					-24	12	-6	3.2
Putamen	R					16	12	-6	3.2
Pallidum	R					16	-2	2	3.5
Cingulate Gyrus, Anterior	L					-8	38	4	3.3
Caudate	L					-8	6	10	4.8
Caudate	R					12	4	14	4.0
Cingulate Gyrus, Anterior	R					4	26	16	4.4

Coordinates are in Montreal Neurological Institute space. Results are presented at $z>2.3$, $p<0.01$ (corrected for multiple comparisons at $p<0.05$).