

**Table S1. rs12807809 association with cognitive measures**

NRGN-rs12807809									
Cognitive function	Test or Subscale	sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient	95% Confidence Interval	p
				CC	CT	TT	B	of B regression coefficient	
<b>Current IQ</b>	Full Scale IQ	cases	329	102.8 (15.4)	98.6 (18.4)	100.1 (18.4)	(-)1.03	(-)2.103-0.043	0.06
		controls	2243	109.8 (14.2)	112.8 (14.2)	113.6 (14.6)			
<b>Working Memory</b>	WAIS Digit Span	cases	329	13.5 (3.0)	13.4 (3.6)	13.6 (3.7)	(-)0.104	(-)0.382-0.173	0.46
		controls	2243	13.7 (4.1)	14.3 (3.8)	14.3 (3.9)			
	WMS Spatial Span	cases	234	16.2 (3.8)	14.9 (3.4)	15.2 (3.2)	(-)0.064	(-)0.539-0.411	0.791
		controls	395	16.8 (3.7)	17.3 (3.5)	17.2 (3.3)			
<b>Episodic Memory</b>	WMS Logical Memory I	cases	235	25.6 (11.1)	23.8 (8.3)	24.7 (8.9)	0.309	(-)0.759-1.377	0.57
		controls	396	27.9 (7.9)	31.9 (6.4)	30.2 (6.5)			
	WMS Logical Memory II	cases	235	29.4 (9.6)	26.4 (10.1)	27.1 (10.4)	(-)0.276	(-)1.492-0.940	0.656
		controls	396	31.3 (7.8)	34.7 (7.6)	34.4 (7.1)			
<b>Attention/Vigilance</b>	CPT (3,7 version)	cases	332	4.35 (0.59)	4.14 (0.99)	4.18 (0.88)	0.003	(-)0.089-0.095	0.95
		controls	507	4.79 (0.46)	4.76 (0.57)	4.75 (0.58)			

**Schizophrenia Risk Allele='T'=major allele**

Positive Regression co-efficient indicates Sz risk allele associated with worse performance on cognitive test

Table S2. rs9960767 association with cognitive measures

TCF4- rs9960767

Cognitive function	Test or Subscale	sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient	95% CI of B regression coefficient	p
				AA	AC	CC			
<b>Current IQ</b>	Full Scale IQ	cases	327	99.4 (18.2)	102.7 (18.6)	93.3 (7.8)	0.537	(-)1.247-2.322	0.555
		controls	2193	113.2 (14.4)	113.3 (14.5)	142 (n/a)			
<b>Working Memory</b>	WAIS Digit Span	cases	327	13.6 (3.8)	13.7 (2.9)	12.0 (5.2)	0.405	(-)0.056-0.866	0.085
		controls	2193	14.2 (3.8)	14.7 (4.0)	21.0 (n/a)			
	WMS Spatial Span	cases	228	15.1 (3.2)	15.3 (3.5)	18.5 (2.1)	(-)0.100	(-)0.852-0.652	0.794
		controls	384	17.3 (3.4)	16.7 (3.7)	n/a			
<b>Episodic Memory</b>	WMS Logical Memory I	cases	229	24.2 (8.6)	25.6 (8.8)	27.5 (17.7)	(-)0.201	(-)1.877-1.474	0.814
		controls	385	31.0 (6.6)	29.6 (6.4)	n/a			
	WMS Logical Memory II	cases	229	26.7 (10.4)	28.9 (9.4)	24.0 (14.1)	0.177	(-)1.739-2.092	0.856
		controls	385	34.5 (7.2)	33.8 (8.0)	n/a			
<b>Attention/Vigilance</b>	CPT (3-7 version)	cases	330	4.17 (0.90)	4.18 (0.95)	3.64 (0.91)	(-)0.127	(-)0.265-0.012	0.073
		controls	501	4.78 (0.56)	4.61 (0.66)	n/a			

**Schizophrenia Risk Allele='C'=minor allele**

Positive Regression co-efficient indicates Sz risk allele associated with worse performance on cognitive test

**Table S3. rs6932590 association with cognitive measures**

**MHC-rs6932590**

Cognitive function	Test or Subscale	sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient	95% CI of B regression coefficient	p
				CC	CT	TT			
<b>Current IQ</b>	Full Scale IQ	cases	336	102.0 (18.7)	98.6 (18.3)	100.1 (18.2)	0.909	(-)0.022-1.839	0.056
		controls	2217	113.4 (14.4)	114.3 (15.1)	112.7 (14.1)			
<b>Working Memory</b>	WAIS Digit Span	cases	336	14.2 (4.5)	13.6 (3.7)	13.6 (3.7)	0.131	(-)0.108-0.370	0.284
		controls	2217	14.3 (3.8)	14.4 (3.9)	14.2 (3.8)			
	WMS Spatial Span	cases	235	15.9 (3.6)	15.5 (3.2)	14.8 (3.3)	0.362	(-) 0.045-0.768	0.081
		controls	395	17.6 (3.6)	17.2 (3.3)	17.1 (3.4)			
<b>Episodic Memory</b>	WMS Logical Memory I	cases	236	25.4 (7.9)	23.9 (8.7)	24.6 (8.9)	(-)0.335	(-)1.252-0.582	0.473
		controls	396	29.9 (7.2)	30.8 (6.7)	30.9 (6.4)			
	WMS Logical Memory II	cases	236	26.4 (10.9)	26.8 (10.7)	27.0 (10.0)	0.002	(-)1.043-1.047	0.997
		controls	396	33.9 (8.9)	34.8 (6.6)	34.2 (7.4)			
<b>Attention/Vigilance</b>	CPT (3,7 version)	cases	340	4.17 (0.98)	4.21 (0.88)	4.13 (0.94)	0.077	(-)0.001-0.155	0.053
		controls	511	4.93 (0.49)	4.79 (0.58)	4.72 (0.58)			

**Schizophrenia Risk Allele='T'=major allele**

Positive Regression co-efficient indicates Sz risk allele associated with worse performance on cognitive test

**Table S4. rs3131296 association with cognitive measures**

**MHC-rs3131296**

Cognitive function	Test or Subscale	sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient	95% CI of B regression coefficient	p
				AA	AG	GG			
<b>Current IQ</b>	Full Scale IQ	cases	336	101.0 (n/a)	101.3 (18.4)	99.3 (18.2)	(-)0.107	(-)1.351-1.137	0.866
		controls	2239	109.5 (11.3)	113.6 (14.6)	113.3 (14.5)			
<b>Working Memory</b>	WAIS Digit Span	cases	336	15.0 (n/a)	13.7 (4.1)	13.6 (3.6)	(-)0.044	(-)0.363-0.277	0.79
		controls	2239	13.7 (3.8)	14.3 (3.9)	14.3 (3.8)			
	WMS Spatial Span	cases	235	-	14.4 (3.1)	15.3 (3.3)	(-)0.369	(-)0.956-0.219	0.219
		controls	395	17.8 (2.5)	17.2 (3.1)	17.2 (3.4)			
<b>Episodic Memory</b>	WMS Logical Memory I	cases	236	-	24.6 (8.5)	24.4 (8.8)	0.563	(-)0.759-1.885	0.403
		controls	397	29.8 (3.9)	31.4 (6.7)	30.6 (6.6)			
	WMS Logical Memory II	cases	236	-	27.2 (11.3)	26.8 (10.0)	0.615	(-)0.891-2.121	0.423
		controls	397	33.3 (7.7)	34.9 (7.5)	34.3 (7.2)			
<b>Attention/Vigilance</b>	CPT (3,7 version)	cases	340	4.67 (n/a)	4.34 (0.85)	4.12 (0.93)	0.107	(-)0.007-0.221	0.067
		controls	513	4.88 (0.58)	4.79 (0.53)	4.75 (0.59)			

**Schizophrenia Risk Allele='G'=major allele**

Positive Regression co-efficient indicates Sz risk allele associated with worse performance on cognitive test

**Table S5. rs13219354 association with cognitive measures**

**MHC-rs13219354**

Cognitive function	Test or Subscale	sample	n	Mean (SD)			Regression Coefficient	95% CI of B regression coefficient	p
				CC	CT	TT			
<b>Current IQ</b>	Full Scale IQ	cases	336	97.5 (6.4)	100.5 (18.0)	99.5 (18.3)	0.968	(-)0.312-2.248	0.138
		controls	2234	115.0 (15.0)	114.1 (14.0)	113.1 (14.5)			
<b>Working Memory</b>	WAIS Digit Span	cases	336	16.0 (0.0)	13.2 (3.6)	13.7 (3.7)	0.033	(-)0.299-0.364	0.847
		controls	2234	14.8 (3.9)	14.3 (3.8)	14.3 (3.9)			
	WMS Spatial Span	cases	235	-	15.3 (3.4)	15.1 (3.3)	0.2	(-)0.349-0.749	0.474
		controls	398	17.9 (4.4)	17.3 (3.3)	17.2 (3.4)			
<b>Episodic Memory</b>	WMS Logical Memory I	cases	236	-	23.4 (7.8)	24.6 (8.9)	(-)0.275	(-)1.513-0.963	0.663
		controls	399	32.6 (6.0)	30.3 (6.9)	30.8 (6.6)			
	WMS Logical Memory II	cases	236	-	26.9 (10.2)	26.8 (10.9)	0.525	(-)0.886-1.936	0.465
		controls	399	37.2 (9.2)	34.5 (6.7)	34.2 (7.4)			
<b>Attention/Vigilance</b>	CPT (3,7 version)	cases	340	4.27 (0.11)	4.22 (0.82)	4.15 (0.94)	0.102	(-)0.005-0.209	0.063
		controls	516	4.98 (0.50)	4.83 (0.57)	4.73 (0.58)			

**Schizophrenia Risk Allele='T'=major allele**

Positive Regression co-efficient indicates Sz risk allele associated with worse performance on cognitive test

**Table S6. Results of rs6904071 association with cognitive domains separately in cases and controls in German and Irish samples**

German Sample

Cognitive function	Test or Subscale	Sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient <sup>a</sup>	95% CI	p
				AA	AG	GG			
<i>General Cognitive Ability</i>	Full Scale IQ	cases	342	106.5 (17.8)	100.8 (17.7)	99.3 (18.5)	2.434	(-1.215-6.083)	0.190
		controls	2244	114.5 (13.9)	113.8 (14.5)	113.0 (14.5)	0.863	(-)0.206-1.931	0.113
<i>Verbal Working Memory</i>	WAIS Digit Span	cases	342	16.4 (4.6)	14.0 (3.5)	13.3 (3.7)	0.989	0.247-1.732	0.009
		controls	2244	14.7 (4.0)	14.3 (3.9)	14.2 (3.8)	0.138	(-)0.150-0.426	0.348
<i>Spatial Working Memory</i>	WMS Spatial Span	cases	239	18.5 (3.73)	15.3 (2.98)	14.91 (3.40)	0.872	0.099-1.644	0.027
		controls	399	17.8 (3.79)	17.3 (3.11)	17.11 (3.43)	0.254	(-)0.364-0.804	0.364
<i>Immediate Episodic Memory</i>	WMS Logical Memory Immediate	cases	240	29.2 (8.6)	24.8 (8.2)	23.9 (9.0)	1.308	(-)0.771-3.387	0.216
		controls	400	31.6 (7.4)	30.6 (6.5)	30.7 (6.6)	0.171	(-)0.922-1.264	0.758
<i>Delayed Episodic Memory</i>	WMS Logical Memory Delayed	cases	239	30.0(11.5)	28.8 (9.4)	25.8 (10.5)	2.544	0.133-4.954	0.039
		controls	400	36.7 (9.1)	34.7 (6.6)	34.1 (7.4)	0.966	(-)0.236-0.217	0.115
<i>Attention/Vigilance</i>	CPT (3-7 version)	cases	346	4.59 (0.67)	4.28 (0.83)	4.10 (0.95)	0.210	0.027-0.393	0.024
		controls	517	4.90 (0.49)	4.85 (0.56)	4.71 (0.58)	0.116	0.031-0.201	0.007

Irish Sample

Cognitive function	Test or Subscale	Sample	n	Mean (SD)	Mean (SD)	Mean (SD)	Regression Coefficient <sup>a</sup>	95% CI	p
				AA	AG	GG			
<i>General Cognitive Ability</i>	Abbreviated Full Scale IQ	cases	300	92.5 (19.3)	91.5 (18.0)	90.5 (18.1)	1.213	(-)0.2870-5.295	0.559
		controls	148	131.0 (11.5)	121.5 (14.9)	121.8 (14.6)	1.636	(-)0.2485-5.756	0.434
<i>Spatial Working Memory</i>	CANTAB Spatial WM	cases	365	-1.08 (0.92)	-0.97 (1.29)	-0.96 (1.34)	0.029	(-)0.289-0.230	0.824
		controls	140	0.26 (0.83)	0.26 (0.75)	0.17 (0.84)	0.079	(-)0.153-0.310	0.503
<i>Delayed Episodic Memory</i>	WMS Logical Memory Delayed	cases	377	6.5 (3.3)	7.7 (3.2)	7.0 (3.3)	0.427	(-)0.207-1.062	0.187
		controls	145	16.2 (1.6)	13.4 (2.5)	13.0 (2.6)	0.837	0.118-1.556	0.023
<i>Attention/Vigilance</i>	CPT –IP (3 letters)	cases	257	2.27 (1.50)	1.97 (0.87)	1.95 (1.04)	0.031	(-)0.209-0.271	0.799
		controls	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Table S7. Results of rs6904071 association with cognitive domains adjusted for delayed episodic memory in combined sample

Cognitive function	Participant Numbers	Unadjusted Analysis Combined Cases and Controls		Adjusted for Delayed Episodic Analysis Combined Cases and Controls	
		B	p	B	p
<i>General Cognitive Ability</i>	<i>Controls 544</i> <i>Cases 537</i>	0.13	0.012	0.019	0.674
<i>Verbal Working Memory</i>	<i>Controls 542</i> <i>Cases 600</i>	0.117	0.021	0.05	0.289
<i>Spatial Working Memory</i>	<i>Controls 537</i> <i>Cases 598</i>	NS		NS	
<i>Immediate Episodic Memory</i>	<i>Controls 545</i> <i>Cases 616</i>	0.098	0.036	0.038	0.067
<i>Attention/Vigilance</i>	<i>Controls 389</i> <i>Cases 488</i>	0.143	0.012	0.08	0.136

NS - Non-significant

See text and main tables for details of cognitive tests used for each domain

<b>Table S8.</b> Demographic and Clinical details by rs6904071 genotype in German and Irish samples										
<b>German Sample</b>	<b>Cases</b>					<b>Controls</b>				
	<b>AA (n=10)</b>	<b>AG (n=93)</b>	<b>GG (n=236)</b>	<b>F value/<math>\chi^2</math></b>	<b>p</b>	<b>AA (n=83)</b>	<b>AG (n=636)</b>	<b>GG (n=1528)</b>	<b>F value/<math>\chi^2</math></b>	<b>p</b>
Age (s.d.)	38.3 (12.2)	37.3 (10.8)	39.4 (11.2)	1.17	0.313	51.1 (16.3)	51.7 (15.7)	51.6 (15.6)	0.053	0.95
Gender (% female)	60	40.2	38.6	1.85	0.4	55.4	52.2	50.9	0.89	0.64
Education (% completing high school)	60	68	63.7	6.5	0.593	79.5	74.2	74.9	1.6	0.809
Medication mg (s.d.)	442.2 (396.1)	914.1 (1008.3)	944.4 (1273.3)	0.924	0.398					
<b>Irish Sample*</b>	<b>Cases</b>				<b>Controls</b>					
	<b>AA/AG genotype (n=117)</b>		<b>GG (n=263)</b>	<b>F value/<math>\chi^2</math></b>	<b>p</b>	<b>AA/AG genotype (n=62)</b>		<b>GG (n=86)</b>	<b>F value/<math>\chi^2</math></b>	<b>p</b>
Age (s.d.)	40.0 (11.6)		41.2 (12.0)	0.755	0.386	37.3 (13.2)		36.6 (12.8)	0.038	0.96
Gender (% female)	23.0		29.4	1.74	0.19	50.0		47.7	0.08	0.78
Education (Years)	13.0 (2.4)		13.0 (2.4)	0.002	0.97	16.2 (2.1)		16.0 (2.4)	3.6	0.06
Medication mg (s.d.)	518 (549.3)		619(616)	2.6	0.1					

\* In the Irish sample AA and AG genotypes were combined for this analysis given small sample sizes in controls - examining genotype groups separately did not alter the results which all remained non-significant



Table S9. Principal Component Analysis of rs6904071 with Cognitive Phenotypes									
Cognitive Domain	Test	No Principal Component (PC)		First PC		2 PCs		3 PCs	
		Regression Coefficient	p	Regression Coefficient	p	Regression Coefficient	p	Regression Coefficient	p
Episodic Memory	Logical Memory Delayed	0.9077	0.1634	0.929	0.152	0.93	0.152	0.9434	0.146
General Cognition	Full Scale IQ	1.285	0.214	1.362	0.186	1.373	0.182	1.383	0.179
Attention/Vigilance	CPT 3-7 version	0.153	0.004	0.153	0.004	0.153	0.004	0.152	0.004