Supporting Information

Gauthier et al. 10.1073/pnas.0906232107

Table S1. Relevant clinical information for the 185 schizophrenia probands used in the present study

Subjects	Sex	Diagnosis	AO	IQ	ASQ score	ASD traits	Notes
S00146	M	SCZ	11	101	14		
S00149	F	SCZ	10	81	3	0	
S00150	M	SCZ	11	98	11	0	
S00152	F	SCZ	11	71	10	0	
S00154	M	SCZ	8	111	1	0	
S00155	M	SCZ	10	109	26	++	
S00157	F	SCZ	10	82	9	0	
S00158	M	SCZ	12	74	25	++	
S00160	F	SCZ	12	95	1	0	
S00161	F	Schizoaffective	11	73	1	0	De novo mutation in *SHANK3*
S00162	F	SCZ	10	85*	3	0	Estimated premorbid full scale intelligence quotient (FSIQ) is 85 based on school reports and evaluations
S00164	M	SCZ	9	100*	3	0	Estimated premorbid FSIQ is 100 based on A/B grades in mainstream academic setting and based on school evaluations
S00165	M	SCZ	12	115*			Estimated premorbid FSIQ is 115 based on premorbid academic performance and premorbid Stanford Achievement Test
S00167	M	SCZ	8	95	20	++	
S00168	M	SCZ	12	98	8	0	
S00170	M	SCZ	10	82	8	0	
S00171	F	SCZ	9	75*	11	0	Estimated FSIQ is 75 based on Stanford-Binet Composite Score of 81 as well as the below average to average results on additional tests
S00179	M	SCZ (paranoid)	16	125†			Depression, highest school level achieved = 9
S00180	F	SCZ (paranoid)	20				
S00181	M	SCZ (paranoid)	24				
S00183	M	SCZ (paranoid)	15				Comorbid mental retardation, depression
S00184	M	SCZ (paranoid)	20				
S00185	M	SCZ (paranoid)	24				
S00187	M	SCZ	17				
S00189	M	SCZ	17				
S00190	M	SCZ	21				
S00191	M	SCZ (paranoid)	29	97†			Highest school level achieved = 13
S00193	M	SCZ (undifferentiated)	19	101†			Comorbid mild mental retardation, highest school level achieved = 10
S00200	F	Schizoaffective	20				
S00201	M	SCZ					
S00203	M	Schizoaffective	13				
S00204	F	SCZ (catatonic)	20	76		+	
S00207	M	SCZ	18				
S00208	F	SCZ	20				
S00209	M	Schizoaffective	20				
S00210	M	Schizoaffective	18				
S00211	F	Schizoaffective					
S00212	M	SCZ					
S00213	M	SCZ (disorganized)	15	89†			Highest school level achieved = 13
S00219	M	SCZ	26				
S00220	F	SCZ					
S00223	F	SCZ	21				
S00224	M	SCZ					
S00231	M	SCZ					
S00233	M	SCZ	21				
S00235	F	Schizoaffective					
S00242	M	SCZ					

Table S1. Cont.

Subjects	Sex	Diagnosis	AO	IQ	ASQ score	ASD traits	Notes
S00245	F	Schizoaffective	15				
S00246	F	SCZ					
S00252	M	SCZ (undifferentiated)	30	ND		0	Mental retardation ruled out, no ASD traits according to ASQ
S00255	M	SCZ	20				
S00257	M	Schizoaffective	15				
S00259	F	SCZ (undifferentiated)	16	51†			Highest school level achieved = 10
S00261	M	SCZ (paranoid)	16	96†			Highest school level achieved = 12
S00263	M	Schizoaffective	18				
S00267	M	Schizoaffective	19				
S00270	M	SCZ					
S00271	F	SCZ	17				
S00272	M	SCZ	18				
S00274	M	SCZ	22				
S00276	M	SCZ	17–18				
S00278	F	SCZ					
S00279	M	SCZ					
S00281	M	Schizoaffective	14				
S00282	M	SCZ	14				
S00284	M	SCZ	17				
S00285	M	Schizoaffective	19	73	ND	0	De novo mutation in *SHANK3*
S02946	M	SCZ (paranoid)	23				
S02947	M	SCZ (paranoid)	18				
S02948	M	SCZ (undifferentiated)	18				
S02949	F	SCZ (residual)	24				
S02950	F	SCZ (undifferentiated)	19				
S02951	M	SCZ (disorganized)	26				
S02952	M	SCZ (paranoid)	24				
S02953	M	SCZ (residual)	16				
S02954	M	SCZ (paranoid)	19				Epilepsy
S02955	M	SCZ (undifferentiated)	22				
S02956	M	SCZ (residual)	19				
S02957	F	SCZ (paranoid)	24				
S02958	M	SCZ (paranoid)	20				
S02959	F	SCZ (disorganized)	17				
S02960	F	SCZ (paranoid)	24				
S02962	M	SCZ (paranoid)	19				
S02963	M	SCZ (paranoid)	23				
S02964	M	SCZ					
S02965	M	SCZ					
S02966	M	SCZ					
S02967	F	SCZ					
S02968	F	SCZ (paranoid)					
S02969	M	SCZ (paranoid)					
S02970	M	SCZ (paranoid)					
S02971	F	SCZ (paranoid)					
S02972	F	SCZ (undifferentiated)					
S02973	M	SCZ (paranoid)					
S02974	M	SCZ (disorganized)					
S02975	M	SCZ (paranoid)	26				
S02976	M	SCZ (paranoid)	24				
S02978	F	SCZ (paranoid, schizoaffective)	23				
S02980	M	SCZ	2				
S02981	M	Schizoaffective	21				
S02982	M	SCZ (paranoid)	25				
S02983	F	Schizoaffective	20				
S02988	F	SCZ					
S02991	M	SCZ					
S02992	M	SCZ					
S02993	F	SCZ	21				
S02994	M	SCZ	17				
S02996	M	SCZ	24				

Table S1. Cont.

Subjects	Sex	Diagnosis	AO	IQ	ASQ score	ASD traits	Notes
S02999	F	SCZ	18				
S03001	M	SCZ (undifferentiated)	15	83†			Highest school level achieved = 12
S03005	M	SCZ	22				
S03007	M	SCZ	16				
S03008	F	SCZ (paranoid)	20				
S03009	M	SCZ (paranoid)	19				
S03010	F	Schizoaffective	17				
S03011	F	SCZ (undifferentiated)	19	49†			Highest school level achieved = 10
S03012	M	SCZ (paranoid)	20				
S03013	M	SCZ (paranoid)	23				
S03014	F	SCZ (disorganized)	15				
S03017	M	SCZ (paranoid)	12				
S03042	M	SCZ	10	98	5	0	
S03044	M	SCZ	11	94	1	0	
S03051	M	SCZ	11	82	5	0	
S03058	F	SCZ	11	82	14	0	
S03059	F	SCZ	12	90*			Estimated IQ is 90 based on average school performance records in grades 1–7 (onset occurred in eighth grade)
S03061	F	SCZ	9	99	1	0	
S03064	M	SCZ	12	99	8	0	
S03066	M	SCZ	12	90	1	0	
S03067	F	SCZ	12	120			
S03068	M	SCZ	10	86	2	0	
S03071	M	SCZ	8	80	2	0	
S03074	M	SCZ	6	90*	2	0	Estimated FSIQ is 90 based on premorbid score (test composite score 92) on Stanford-Binet Intelligence Scale, Fourth Edition
S03076	M	SCZ	10	70	5	0	
S03077	F	SCZ	12	100*			Estimated FSIQ is 100 based on academic performance in mainstream school setting
S03082	F	SCZ	6	85*	2	0	Estimated FSIQ is 85 based on 2 years of mainstream school work
S03086	M	SCZ	10	130*	11	0	Estimated FSIQ is 130 based on honors student and advanced placement academic performance; also a presidential scholar
S03109	M	SCZ	12				
S03119	M	SCZ (paranoid)	17	120†			Highest school level achieved = 13
S03135	F	SCZ (paranoid)	16				
S05606	F	SCZ (paranoid)	26				
S05607	M	SCZ					
S05608	M	SCZ					
S05610	F	SCZ (paranoid)					
S05611	M	SCZ (paranoid)	26	128†			Depression, highest school level achieved = 12
S05612	M	SCZ (paranoid)	18	123†			Highest school level achieved = 11
S05614	F	SCZ (paranoid)	19				
S05615	M	SCZ (paranoid)	20				
S05616	M	SCZ (paranoid)	19				
S05617	M	SCZ (paranoid)	26				
S05618	M	SCZ (paranoid)	21				
S05619	M	SCZ (paranoid)	26				
S05620	M	SCZ (paranoid)	20				
S05621	F	SCZ (disorganized)	34	91			
S05622	M	SCZ (paranoid)	16				
S05623	M	SCZ (undifferentiated)	22				
S05624	M	SCZ (undifferentiated)	25				
S05626	M	SCZ (undifferentiated)	26				
S05627	M	SCZ (chronic)	27				
S05628	M	SCZ (disorganized)	20				Comorbid mental retardation
S05629	M	SCZ (disorganized)	20				
S05630	M	SCZ (undifferentiated)	27				
S05631	M	SCZ (paranoid)	19				

Table S1. Cont.

Subjects	Sex	Diagnosis	AO	IQ	ASQ score	ASD traits	Notes
S05632	M	SCZ (undifferentiated)	18				
S05633	M	SCZ (chronic)	21				
S05634	M	SCZ (chronic)	28				Depression
S05635	F	SCZ (paranoid)	22				
S05636	M	SCZ (undifferentiated)	20				
S05637	M	SCZ (paranoid)	23				
S05638	M	SCZ (chronic)	18				Epilepsy
S05639	M	SCZ (paranoid)	20				
S05640	M	SCZ (paranoid)	20				
S05641	M	SCZ (undifferentiated)	26				
S05642	M	SCZ (undifferentiated)	19				
S05643	M	SCZ (paranoid)	22				
S05644	F	SCZ (undifferentiated)	20				
S05645	M	SCZ (chronic)	18				
S05648	M	SCZ (paranoid)	32				
S05649	M	SCZ (undifferentiated)	20				
S05650	M	SCZ (paranoid)	26				
S05651	M	SCZ (paranoid)	26				
S05652	F	SCZ (residual)	20				
S05653	F	SCZ (chronic)	21				
S05658	M	SCZ	19				
S05662	M	SCZ (paranoid)	23				
S05666	M	SCZ (paranoid)	21				

AO, age at onset; ASD, autism spectrum disorder; ASQ, Autism Screening Questionnaire (score > 15 = autism); F, female; IQ, Intellectual Quotient; M, male; ND, not determined; SCZ, schizophrenia.

*These subjects had no formal premorbid IQ and no valid IQ score at admission but had documented premorbid school/academic functioning.

[†]Verbal IQ.

Table S2. Segregation of microsatellite markers in pedigrees 419 and 56

	PED 419					PED 56			
	Father	Proband	Brother	Brother	Mother	Father	Proband	Brother	Mother
	I-1	II-1	II-2	II-3	I-2	I-1	II-1	II-2	I-2
D3S1754	5,6	5,7	6,7	6,7	7,9	7,8	8,8	8,8	7,8
D4S3351	4,4	4,13	4,13	4,13	4,13	3,8	6,8	6,8	4,6
D6S1043	2,3	2,6	3,6	3,6	1,6	2,3	2,3	2,3	2,3
D8S1179	6,8	6,6	4,8	6,6	4,6	6,7	5,7	5,7	5,6
D15S659	2,6	2,1	2,4	2,1	4,1	2,7	1,7	1,7	1,1
D14S63	4,5	4,5	4,6	4,4	4,6	1,4	1,4	1,4	4,4
D7S531	4,6	4,4	4,4	2,4	2,4	2,2	2,3	2,4	3,4
D11S904	4,7	4,4	4,4	4,7	4,5	2,4	2,6	4,6	2,6
D19S215	2,6	2,6	1,6	1,2	1,2	2,6	2,6	1,2	1,2
D1S533	5,5	1,5	1,5	1,5	1,1	5,6	5,6	5,6	2,6
D2S1327	4,4	4,4	1,4	1,4	1,4	1,4	1,4	1,4	4,4
D9S1118	6,7	6,6	6,6	6,7	6,8	2,6	6,6	1,6	1,6
D10S677	2,5	5,6	2,6	4,5	4,6	4,4	4,5	3,4	3,5
D11S1984	5,7	5,7	5,5	5,7	5,5	3,7	3,5	5,7	5,5
D12S1294	3,6	3,3	3,3	3,3	3,3	5,8	4,8	5,8	4,5
D14S587	2,6	5,6	2,5	2,2	2,5	2,7	2,8	6,7	6,8
D16S748	1,1	1,1	1,2	1,1	1,2	6,6	2,6	2,6	2,2
D17S2196	ND	ND	ND	ND	ND	2,6	6,6	ND	6,7
G00111_M1-4	1,2	1,1	1,1	1,3	1,3	2,4	1,2	2,3	1,3
G00111_M2-3	2,2	1,2	1,2	2,3	1,3	1,1	1,1	1,3	1,3
G00111_M3-1	1,2	1,2	1,2	1,2	1,1	2,2	1,2	1,2	1,1
G00111_M4-1	1,2	1,2	1,2	1,1	1,2	1,3	1,2	1,2	2,2
G00111_M5_2	1,2	1,1	1,1	1,3	1,3	NA	NA	NA	NA
G00111_M6-3	1,2	1,2	1,2	1,1	1,2	NA	NA	NA	NA
G00111_M7-1	1,1	1,3	1,3	1,2	2,3	2,3	2,3	1,2	1,3

NA, not applicable; ND, not determined.

Table S3. List of *SHANK3* variants detected in our SCZ and CTL cohorts

Variant type	Variants	mRNA nucleotide	Genomic position	Allele frequency SCZ (n = 370)	Allele frequency CTL (n = 570)	PolyPhen	SIFT	SNAP	Probands
Variants observed in SCZ cohort only									
Silent	S341S	c.1023G > A	49469938	2	0				S00233, S05631
Missense	H494Q	c.1479C > G	49482990	1	0	PD	PT	NA	S00272
Missense	R536W	c.1606C > T	49484091	1	0	PD	PD	PD	S00161 (PED 56)
Silent	I631I	c.1893C > T	49490153	1	0				S00142
Silent	P681P	c.2043C > G	49491379	1	0				S00149
Missense	S952T	c.2856G > C	49505982	1	0	PT	PD	NA	S02974
Missense	G1011V*	c.3032G > T	49506159	1	0	PD	PD	NA	S05615
Silent	E1022E	c.3066G > A	49506193	1	0				S02969
Nonsense	R1117X	c.3349C > T	49506476	1	0				S00285 (PED 419)
Missense	P1134H	c.3401C > A	49506528	1	0	PD	PD	PT	S00167
Silent	A1160A	c.3482T > C	49506607	1	0				S03042
Silent	K1179K	c.3558G > A	49506664	4	0				S00263, S00233, S05635, S03014
Variants observed in CTL cohort only									
Silent	Y122Y	c.366C > T	49463905	0	1				S06581
Silent	S297S	c.891C > T	49468639	0	1				S06197
Silent	A737A	c.2211C > T	49500287	0	3				S06412, S06445, S06598
Silent	S1293S	c.3879C > T	49507006	0	1				S06262
Missense	R1298K	c.3893G > A	49507020	0	1	PT	PT	PT	S06436
Silent	S1338L	c.4013C > T	49507140	0	1				S06216
Missense	I1546V[‡]	c.4636A > G	49516046	0	1	PT	PT	NA	S06647
Silent	S1636S	c.4908C > T	49516318	0	1				S06442
Common variants									
Missense	I245T	c.734T > C	49464446	123	184	PT	PT	PT	>3
Missense	A721T	c.2161G > A	49500237	9	16	PT	PD	PT	>3
Silent	P770P	c.2313G > A	49501007	2	3				>3
Silent	Y999Y	c.2997C > T	49506124	5	14				>3
Silent	S1121S	c.3380C > T	49506490	3	1				>3
Missense	V1333G[†]	c.3999T > G	49507125	1	2	PD	PT	PT	>3
Silent	P1649P	c.4962C > T	49516357	2	2				>3
Missense	P1654T[§]	c.4960C > A	49516370	1	4	PD	PT	PT	>3

CTL, control; n, number of unrelated chromosomes tested; NA, not applicable; PD, predicted damaging; PT, predicted tolerated; SCZ, schizophrenia. cDNA sequence as described (1).

*Present in ASD (2).

[†]Present in CTLs (2).

[‡]Present in ASD (3).

[§]Present in unaffected siblings of ASD and CTL (1, 2).

1. Moessner R, et al. (2007) Contribution of SHANK3 mutations to autism spectrum disorder. *Am J Hum Genet* 81:1289–1297.
2. Durand CM, et al. (2007) Mutations in the gene encoding the synaptic scaffolding protein SHANK3 are associated with autism spectrum disorders. *Nat Genet* 39:25–27.
3. Gauthier J, et al. (2009) Novel de novo SHANK3 mutation in autistic patients. *Am J Med Genet B Neuropsychiatr Genet* 150B:421–424.

Table S4. Variation within the *SHANK3* coding region. Substitutions were tabulated by comparing human and chimp (*Pan troglodytes*) orthologous DNA sequence alignments

	Synonymous variants	Nonsynonymous variants
Interspecific substitutions	16	3
Intraspecific polymorphisms	24	3

Table S5. PCR primer pairs used to determine parental origin of the de novo mutations

Type	Primer name	Ampliconsize (bp)	Forward primer (5′-3′)	Reverse primer (5′-3′)
$(TG)_n$	G0111_M1-4	210	GCACCCACGCCAGTCAT	TTCATAGTTTCAATAAGCCACAA
$(TG)_n$	G0111_M2-3	229	ACATTGAGGGGTCTGGATACTG	CCCCGCTGCACCCTCGTCA
$(TC)_n$	G0111_M3-1	278	GGAACGGAGGAAAGCGGTCTGC	TGGGGCACATGTTCCAGTTGG
$(CA)_n$	G0111_M4-2	266	ATAGGCTCCCGGCTTCAGCACT	CAATTTTGCGGGCAGGATTCAG
$(TG)_n$	G0111_M5-2	255	GTTCTTGGGTCCTCCTGGCTCCTC	TGGTGCCGCCCTCCACACTT
$(CA)_n$	G0111_M6-3	350	TCAGGAGGCCGAGGCAAGATAATC	CCTCCTGGGCTCAAGCTACTCTGC
$(TG)_n$	G0111_M7-1	283	CGCGCCGGCAAGTTCCTG	TGTCCGCTCGCTGCACCCTGTA

Table S6. Primer pairs used for screening of the *SHANK3* gene

Exon	Amplicon name	Amplicon size (bp)	Forward primer (5′-3′)	Reverse primer (5′-3′)
1	G00111_001	325	GCGCTCCGTTCCCCGGCGCGA	CCTCCGCGAACCGCGGCCGAA
2	G00111_033	320	GACCTGAGCTCACGAGCCCGCT	CTGCCGTGCCCTTCACTGGTC
3	G00111_003	233	GGGGTTTGTGCATGGACTC	ACTGTGGTCAGCCCCAAG
4–5	G00111_004	502	AGGCTTGCCGGAGGAAG	GCAGCCTCAGTATCCACACC
4–7	G00111_034	1047	GAGGAAGGCGGGTGATGTTCA	AGTATATCCACACTCGGTGCA
8	G00111_005	247	GCGCATGTGCTGTTGTG	CCTTCCAGGGAAGAACCAAG
9	G00111_006	234	CTGGCGAGGCAAAGCTG	GCCCCTTTATGTCACCACTG
10	G00111_007	427	TAACATCTGGAAAGCCTGGG	GCTCCTCCTGGCTCAGGTC
11	G00111_326	602	CCCGGCATCGCGTCCGTCACCTA	CCACATCGCAGGGGCCTCCAATGG
12	G00111_009	275	ACCTGCTCCTGAGGTGGG	CCATGTGGATTTAGCACCAAG
13–14	G00111_010	556	GTGTGGGCAGAGACTGGTG	GAAGCTGAAGACATCCCTGAG
15–16	G00111_011	508	ACTCGGAGGTTGCTGTGTG	ATGTGGGCCTGAAGTCAAAG
17	G00111_036	384	ACCTGAACAAGATCCTGGCAC	CACCCATTCACCTCTGACCTG
18	G00111_013	188	GGTGGGGAAATGAGTGTGG	CTGGAACCTCCTCACACACC
19	G00111_014	286	GGTTGGGGAGGACATGG	CTCTCACCTCCGTCAAGAGG
20	G00111_015	243	CTCACCTCTGGCTTAGGAGG	TGTCCTTCAAACCCAAGTCC
21	G00111_044	609	GGTCCCCAGGAACCTCTC	ACCTGCAGCTGCTTCACC
21	G00111_017	676	TATCCCGAGCGGCAGAAG	GTGAGCTGGGGTCCAGG
21	G00111_029	607	CTACAGCCCTCCCGCTC	CTGCCACAGCCGCTGAC
21	G00111_041	570	CTCATCGTTGTGCACGC	GGAGGTGTGGGTGTCAGTG
21	G00111_114	488	CCAGGGCAGCTCAGAGG	GGTCCCTGAAGGTCACCG
21	G00111_119	520	GGGAACTCACTGACACCCAC	CAGGAGAGCCAGAGAACAGAC
24	G00111_039	600	CCGTAGGATCCCACCCTTTA	GCCTAGGTGGATGCTCTCCAG
24	G00111_040	460	CTTCGTGGTGCGCAGCGTGAG	ACAGCAAACAGGACGATTCA

Exons 22 and 23 were not tested because they are not expressed in isoforms found in brain tissue.