PCSK6 is associated with handedness in individuals with dyslexia.

Thomas S. Scerri, William M. Brandler, Silvia Paracchini, Andrew P. Morris, Susan M. Ring, Joel B. Talcott, John Stein, and Anthony P. Monaco.

Supplementary Methods

Ascertainment Criteria for Study Participants

Stage 1: Approximately two thirds of the families were ascertained if the proband had a British abilities scales (BAS) single-word reading score > 2 standard deviations (SD) below that predicted by their intelligence quotient (IQ) derived from their verbal and non-verbal reasoning scores and if at least one other sibling had a record of reading disability. These criteria identified some probands with high IQ scores and BAS scores within the 'normal' range. Therefore, for the remaining families the criteria were changed such that the subject's difference in their BAS single-word reading score had to be ≥ 1 SD below the population mean for their age-band, along with an IQ ≥ 90. Proband exclusion criteria included other disorders such as specific language impairment (SLI), autism or attention deficit-hyperactivity disorder (ADHD). We administered a battery of six psychometric tests to all the subjects, and we age-adjusted and standardized their scores against a normative control data set, as described elsewhere (1, 2). These included a series of reading measures including; single-word reading ability (READ), spelling ability (SPELL), phonological decoding ability (CCN), phonemic awareness (SPOON) and two of orthographic coding ability – one by an irregular word test (CCI) and the other by a forced

word choice test (OLSON). Individuals selected for the present study were within the normal range of IQ (>85), but had scores >1.5 SD below the mean for at least one of the 6 reading phenotypes. The subjects have a mean age of 11.4 years (SD 3.8, range: 6.3-25.4 years) and consisted of 139 males and 58 females.

Stage 2: The majority of these individuals are between 8 and 18 years old, have a BAS2 single-word reading score that is both ≤ 100 (at chronological age) and > 1.5 SD below that predicted by IQ.

ALSPAC: From age 7, all children were invited annually for assessments on a wide range of physical, behavioral, and neuropsychological traits, including reading-related measures. DNA is available from approximately 11,000 ALPSAC children. For the present study we assigned individuals from the ALSPAC cohort into a sub-group with RD (stage 3), and a sub-group representing the general population without a neurodevelopmental disorder. In both cases, subjects were excluded based on both a self-reported ethnicity of non-white and a performance IQ ≤ 85 at age of 8.5.

RD sub-group (stage 3): An assignment of RD was based on an age-adjusted single-word reading score ≤ -1 SD for both a 40-word reading test at 7.5 years and a 12-word reading test at 9.5 years; individuals missing either of these data points were excluded.

General Population sub-group: Individuals were excluded if they met criteria for one of the following neurodevelopmental disorders:

[A] Attention Deficit Hyperactivity Disorder (ADHD): Defined based on a DAWBA DSM-IV clinical diagnosis at 7.5 years; individuals missing this data point were excluded.

[B] Autistic features: a composite score of 7 measures from the Children's Communication Checklist (CCC) pragmatic aspects of communication (prorated) ≤ -3 SD at 7.5 years.

[C] Specific language impairment: If an individual met at least two of the following four criteria; i) a composite score of 7 measures from the Children's Communication Checklist (CCC) pragmatic aspects of communication (prorated) > -3 SD and ≤ -1 SD at age 7.5 years, ii) an age adjusted nonword repetition score ≤ -1 SD at 8.5 years, iii) an age adjusted WOLD comprehension score ≤ -1 SD at 8.5 years, and iv) a questionnaire asking if the individual has ever had speech/language therapy given at 9.5 years; some flexibility for missing data points was allowable in assigning SLI.

[D] Reading disability (as above for stage 3).

After excluding those who had not been genotyped or performed the Peg test, there were 197 individuals in the RD group (stage 3), and 2,667 in the general population group. The Peg test was performed at 7.5 years.

Table S1: Most highly associated SNPs with PegQ ($P<1\times10^{-4}$) under the additive model in stage 1.

Rank	Chr[a]	Marker	Position	Gene	Feature	Left Gene	Right Gene	A	B	AA	AB	BB	MAF	P	INFO	β[b]	SE	HWE P[c]
1	15_i	rs11855415	99692646	PCSK6	intron	SNRPA1	TM2D3	A	T	12.2	73.4	106.3	0.25	4.73E-07	0.95	-0.60	0.12	1.00
2	15_i	rs1871978	99680812	PCSK6	intron	SNRPA1	TM2D3	C	T	97.1	81.5	13.4	0.28	6.65E-07	0.98	0.58	0.12	0.59
3	15_i	rs4965830	99681512	PCSK6	intron	SNRPA1	TM2D3	A	T	81.3	93.3	17.3	0.33	8.55E-07	0.97	0.56	0.11	0.25
4	15_i	rs7182874	99682995	PCSK6	intron	SNRPA1	TM2D3	C	T	81.5	93.1	17.2	0.33	8.64E-07	0.97	0.56	0.11	0.25
5	18_i	rs7238095	64725259	CCDC102B	intron	TXNDC10	DOK6	A	C	52.3	101.1	38.4	0.46	1.05E-06	0.96	-0.52	0.11	0.47
6	15	rs9806256	99681096	PCSK6	intron	SNRPA1	TM2D3	C	T	13.0	81.0	98.0	0.28	1.11E-06	1.00	-0.56	0.12	0.59
7	18_i	rs2051294	64710365	CCDC102B	intron	TXNDC10	DOK6	A	C	52.5	101.1	38.2	0.46	1.42E-06	0.97	-0.51	0.11	0.47
8	1_i	rs1284855	209459736	-	-	FLVCR1	VASH2	C	T	25.0	67.1	99.8	0.30	3.96E-06	1.00	-0.47	0.10	0.03
9	1_i	rs6702876	209465840	-	-	FLVCR1	VASH2	C	G	25.0	67.3	99.7	0.31	4.17E-06	0.99	-0.47	0.10	0.03
10	6_i	rs12206319	142405419	-	-	LOC729076	LOC645503	C	T	115.4	64.6	12.0	0.23	7.89E-06	0.98	-0.53	0.12	0.68
11	15	rs752028	99686708	PCSK6	intron	SNRPA1	TM2D3	C	T	82.0	93.0	17.0	0.33	1.05E-05	1.00	0.50	0.11	0.25
12	6_i	rs12212141	142401465	-	-	LOC729076	LOC645503	A	G	112.9	66.1	12.9	0.24	1.19E-05	0.98	-0.51	0.12	0.55
13	6_i	rs4541765	142402402	-	-	LOC729076	LOC645503	C	T	112.9	66.1	12.9	0.24	1.19E-05	0.98	-0.51	0.12	0.55
14	9	rs10739976	94425992	FBP2	intron	HIATL1	FBP1	C	T	51.0	104.0	37.0	0.46	1.20E-05	1.00	0.46	0.11	0.25
15	6_i	rs11155233	142389959	-	-	LOC729076	LOC645503	A	T	113.9	65.4	12.6	0.24	1.21E-05	0.97	-0.51	0.12	0.54
16	6_i	rs13192891	142386917	-	-	LOC729076	LOC645503	A	G	113.9	65.4	12.6	0.24	1.21E-05	0.97	-0.51	0.12	0.54
17	6_i	rs4128460	142397679	-	-	LOC729076	LOC645503	A	G	113.9	65.4	12.6	0.24	1.21E-05	0.97	-0.51	0.12	0.54
18	6_i	rs9496232	142391771	-	-	LOC729076	LOC645503	A	G	113.9	65.4	12.6	0.24	1.21E-05	0.97	-0.51	0.12	0.54
19	6_i	rs11968035	142387385	-	-	LOC729076	LOC645503	C	G	12.6	65.4	113.9	0.24	1.21E-05	0.97	0.51	0.12	0.54
20	6_i	rs12213080	142389596	-	-	LOC729076	LOC645503	A	G	12.6	65.4	113.9	0.24	1.21E-05	0.97	0.51	0.12	0.54
21	6_i	rs7764878	142388438	-	-	LOC729076	LOC645503	C	T	12.6	65.4	113.9	0.24	1.21E-05	0.97	0.51	0.12	0.54
22	6_i	rs9496231	142391691	-	-	LOC729076	LOC645503	A	C	12.6	65.4	113.9	0.24	1.21E-05	0.97	0.51	0.12	0.54
23	8_i	rs6469727	90092828	-	-	LOC100129100	RIPK2	C	G	56.2	100.6	35.0	0.44	1.29E-05	0.99	0.46	0.11	0.47
24	6_i	rs11155234	142450400	NMBR	intron	LOC645503	VTA1	C	T	114.8	64.1	12.9	0.23	1.34E-05	0.98	-0.51	0.12	0.42
25	6_i	rs12210427	142430974	-	-	LOC645503	NMBR	A	G	114.8	64.1	12.9	0.23	1.34E-05	0.98	-0.51	0.12	0.42
26	3_i	rs4683019	45015686	EXOSC7	intron	ZDHHC3	CLEC3B	C	T	41.3	82.3	68.2	0.43	1.77E-05	0.98	0.42	0.10	0.10
27	10_i	rs7922735	119161661	-	-	PDZD8	EMX2OS	A	C	146.7	42.3	2.9	0.13	1.82E-05	0.51	-1.18	0.13	1.00
28	8_i	rs1155562	97042119	-	-	C8orf37	LOC643228	C	G	144.7	45.1	2.1	0.13	1.84E-05	0.99	-0.67	0.16	0.74
29	8_i	rs1484629	97044921	-	-	C8orf37	LOC643228	A	G	2.2	45.1	144.7	0.13	1.86E-05	0.98	0.67	0.16	0.74
30	15	rs3825921	99679686	PCSK6	intron	SNRPA1	TM2D3	C	T	66.0	98.0	28.0	0.40	1.97E-05	1.00	0.45	0.11	0.45
31	8	rs1586475	90067358	-	-	LOC100129100	RIPK2	A	G	35.0	96.0	56.0	0.44	2.01E-05	1.00	-0.45	0.11	0.66
32	4	rs17330237	184067228	ODZ3	intron	MGC45800	DCTD	A	G	145.0	39.0	5.0	0.13	2.01E-05	1.00	-0.62	0.15	0.21
33	3_i	rs4683031	45059406	-	-	CLEC3B	CDCP1	G	T	39.9	83.9	68.1	0.43	2.44E-05	0.98	0.41	0.10	0.14
34	3_i	rs6790660	45062035	-	-	CLEC3B	CDCP1	A	T	68.1	83.9	39.9	0.43	2.44E-05	0.98	-0.41	0.10	0.14
35	3_i	rs4323037	45067810	-	-	CLEC3B	CDCP1	A	G	39.9	83.9	68.1	0.43	2.45E-05	0.98	0.41	0.10	0.14
36	4_i	rs17330216	184067015	ODZ3	intron	MGC45800	DCTD	G	T	147.5	39.1	5.3	0.13	2.49E-05	0.91	-0.63	0.15	0.20
37	3_i	rs9852384	45032054	-	-	EXOSC7	CLEC3B	A	G	67.9	83.0	40.9	0.43	2.59E-05	1.00	-0.41	0.10	0.14
38	3_i	rs1520079	45055574	-	-	CLEC3B	CDCP1	G	T	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
39	3_i	rs9880792	45053186	-	-	CLEC3B	CDCP1	C	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
40	3_i	rs1004877	45042421	CLEC3B	near-gene-5	EXOSC7	CLEC3B	A	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
41	3_i	rs13320864	45037973	-	-	EXOSC7	CLEC3B	C	T	67.9	83.1	40.9	0.43	2.61E-05	1.00	-0.41	0.10	0.14
42	3_i	rs2372850	45049992	CLEC3B	intron	EXOSC7	CDCP1	C	T	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
43	3_i	rs2372851	45051312	CLEC3B	intron	EXOSC7	CDCP1	A	T	67.9	83.1	40.9	0.43	2.61E-05	1.00	-0.41	0.10	0.14
44	3_i	rs4683023	45037258	-	-	EXOSC7	CLEC3B	A	C	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
45	3_i	rs4683029	45051827	CLEC3B	intron	EXOSC7	CDCP1	A	G	67.9	83.1	40.9	0.43	2.61E-05	1.00	-0.41	0.10	0.14
46	3_i	rs6807133	45038769	-	-	EXOSC7	CLEC3B	C	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
47	3_i	rs9861505	45046032	CLEC3B	intron	EXOSC7	CDCP1	C	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
48	3_i	rs9868885	45050503	CLEC3B	intron	EXOSC7	CDCP1	A	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
49	3_i	rs9873373	45035897	-	-	EXOSC7	CLEC3B	A	T	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
50	3_i	rs9877793	45049271	CLEC3B	intron	EXOSC7	CDCP1	A	G	40.9	83.1	67.9	0.43	2.61E-05	1.00	0.41	0.10	0.14
51	3	rs2372862	45034615	-	-	EXOSC7	CLEC3B	A	G	68.0	83.0	41.0	0.43	2.62E-05	1.00	-0.41	0.10	0.11
52	3	rs939310	45050936	CLEC3B	intron	EXOSC7	CDCP1	C	T	41.0	83.0	68.0	0.43	2.62E-05	1.00	0.41	0.10	0.11
53	8_i	rs2874004	97051771	-	-	C8orf37	LOC643228	A	C	144.7	46.2	1.1	0.13	2.66E-05	0.97	-0.68	0.16	0.32
54	2	rs17447933	201177527	KCTD18	near-gene-3	LOC26010	KCTD18	A	G	142.0	47.0	3.0	0.14	2.85E-05	1.00	0.62	0.15	1.00
55	1	rs1284851	209461761	-	-	FLVCR1	VASH2	A	G	3.0	41.0	147.0	0.12	3.35E-05	1.00	-0.64	0.15	1.00

56	18_i	rs12970786	64735406	CCDC102B	intron	TXNDC10	DOK6	A	G	29.8	95.4	66.6	0.40	3.46E-05	0.97	0.44	0.11	0.65
57	18_i	rs12957393	64736422	CCDC102B	intron	TXNDC10	DOK6	A	G	66.6	95.4	29.8	0.40	3.46E-05	0.97	-0.44	0.11	0.65
58	3_i	rs6441877	45012674	EXOSC7	intron	ZDHHC3	CLEC3B	G	T	40.8	81.9	69.2	0.43	3.60E-05	0.98	0.40	0.10	0.08
59	3_i	rs6764088	45018997	EXOSC7	intron	ZDHHC3	CLEC3B	A	G	69.2	81.9	40.8	0.43	3.61E-05	0.98	-0.40	0.10	0.08
60	3_i	rs2280384	45024318	EXOSC7	intron	ZDHHC3	CLEC3B	C	G	69.2	81.9	40.8	0.43	3.62E-05	0.98	-0.40	0.10	0.08
61	18_i	rs12957357	64757780	CCDC102B	intron	TXNDC10	DOK6	A	G	29.0	94.9	67.9	0.40	3.67E-05	1.00	0.43	0.11	0.65
62	8	rs920198	97044680	-	-	C8orf37	LOC643228	C	T	153.0	37.0	2.0	0.11	3.73E-05	1.00	-0.68	0.16	1.00
63	15_i	rs8037547	67835908	-	-	LOC100133066	LOC100128431	A	T	21.1	90.4	80.4	0.35	3.80E-05	0.84	-0.49	0.12	0.63
64	1	rs11120063	209463420	-	-	FLVCR1	VASH2	C	T	148.0	41.0	3.0	0.12	3.91E-05	1.00	0.63	0.15	1.00
65	1_i	rs9429894	209463510	-	-	FLVCR1	VASH2	C	T	3.0	41.2	147.7	0.12	3.91E-05	0.99	-0.63	0.15	1.00
66	1_i	rs2644549	209468175	-	-	FLVCR1	VASH2	A	G	3.0	41.2	147.7	0.12	3.92E-05	0.99	-0.63	0.15	1.00
67	1_i	rs1284853	209459935	-	-	FLVCR1	VASH2	A	G	3.0	41.2	147.8	0.12	3.97E-05	0.99	-0.63	0.15	1.00
68	18	rs10503134	64751059	CCDC102B	intron	TXNDC10	DOK6	C	T	68.0	92.0	29.0	0.40	4.00E-05	1.00	-0.43	0.11	0.88
69	18_i	rs4891350	64740094	CCDC102B	intron	TXNDC10	DOK6	A	G	29.0	94.7	68.2	0.40	4.01E-05	0.99	0.43	0.11	0.76
70	9	rs3903098	74204474	-	-	LOC138971	LOC100130911	A	G	5.0	54.0	132.0	0.17	4.05E-05	1.00	0.56	0.14	1.00
71	18_i	rs12962796	64728848	CCDC102B	intron	TXNDC10	DOK6	G	T	64.7	96.1	31.2	0.41	4.06E-05	0.75	-0.49	0.12	0.66
72	3_i	rs17570449	45037099	-	-	EXOSC7	CLEC3B	C	T	64.7	84.6	42.6	0.44	4.26E-05	0.98	-0.40	0.10	0.18
73	3_i	rs13963	45052127	CLEC3B	missense	EXOSC7	CDCP1	A	G	39.2	82.7	69.9	0.42	4.40E-05	0.99	0.40	0.10	0.14
74	15_i	rs11637333	85336580	AGBL1	intron	LOC100132083	NCRNA00052	A	G	5.0	31.1	155.8	0.11	4.43E-05	0.99	0.62	0.15	0.05
75	15_i	rs11630354	85332015	AGBL1	intron	LOC727915	NCRNA00052	A	G	155.9	31.1	5.0	0.11	4.52E-05	0.98	-0.63	0.15	0.05
76	15	rs11636069	85335934	AGBL1	intron	LOC100132083	NCRNA00052	A	G	5.0	31.0	156.0	0.11	4.52E-05	1.00	0.62	0.15	0.05
77	15_i	rs11632067	85303427	AGBL1	intron	LOC727915	NCRNA00052	A	G	157.6	29.6	4.8	0.10	4.55E-05	0.89	-0.67	0.16	0.08
78	15_i	rs998860	85326320	LOC100132083	intron	LOC727915	NCRNA00052	C	T	156.4	30.6	5.0	0.11	4.57E-05	0.95	-0.64	0.16	0.10
79	15_i	rs11635786	85328022	AGBL1	intron	LOC727915	NCRNA00052	A	T	5.0	30.8	156.2	0.11	4.58E-05	0.97	0.63	0.16	0.04
80	3_i	rs2139538	45047539	CLEC3B	intron	EXOSC7	CDCP1	A	G	42.2	82.5	67.1	0.43	4.59E-05	0.98	0.40	0.10	0.08
81	9	rs11142070	87896981	-	-	RPS10P3	LOC497256	C	T	167.0	25.0	0.0	0.07	4.65E-05	1.00	-0.87	0.21	1.00
82	15	rs6494826	67836165	-	-	LOC100133066	LOC100128431	A	G	40.0	96.0	56.0	0.46	4.70E-05	1.00	-0.41	0.10	1.00
83	8	rs6468480	97034962	-	-	C8orf37	LOC643228	G	T	153.0	36.0	1.0	0.10	4.81E-05	1.00	-0.71	0.17	0.70
84	20_i	rs6091793	52008146	BCAS1	intron	SUMO1P1	CYP24A1	C	T	123.8	63.0	5.2	0.19	4.93E-05	0.94	-0.55	0.14	0.48
85	20_i	rs6091794	52008453	BCAS1	intron	SUMO1P1	CYP24A1	C	T	123.7	63.1	5.2	0.19	5.08E-05	0.95	-0.55	0.14	0.48
86	11_i	rs12364277	14253387	-	-	SPON1	RRAS2	A	G	171.9	19.8	0.2	0.05	5.15E-05	0.67	-1.14	0.28	1.00
87	3_i	rs3765173	45047773	CLEC3B	intron	EXOSC7	CDCP1	C	T	68.9	82.6	40.4	0.43	5.41E-05	1.00	-0.39	0.10	0.10
88	12_i	rs7314688	118186014	-	-	LOC144742	CCDC60	C	T	159.5	30.1	2.3	0.09	5.44E-05	0.85	-0.75	0.19	0.65
89	2_i	rs4972753	172949094	-	-	DLX2	ITGA6	C	T	5.1	46.4	140.5	0.15	5.48E-05	0.96	0.58	0.14	0.57
90	3	rs9819447	45032630	-	-	EXOSC7	CLEC3B	C	T	69.0	83.0	40.0	0.42	5.54E-05	1.00	-0.39	0.10	0.11
91	8_i	rs10106754	97061077	-	-	C8orf37	LOC643228	A	G	1.1	46.7	144.1	0.13	5.56E-05	0.95	0.66	0.16	0.32
92	8	rs11784307	81474832	-	-	LOC340443	ZBTB10	C	T	29.0	89.0	74.0	0.38	5.66E-05	1.00	0.41	0.10	0.76
93	8_i	rs1385251	97063766	-	-	C8orf37	LOC643228	C	T	144.1	46.7	1.1	0.13	5.75E-05	0.95	-0.66	0.16	0.32
94	1	rs6428233	191137268	-	-	EEF1AL12	KCNT2	A	G	120.0	59.0	12.0	0.22	5.84E-05	1.00	-0.47	0.12	0.20
95	8_i	rs185486	97071391	-	-	C8orf37	LOC643228	A	G	144.1	46.7	1.1	0.13	5.95E-05	0.95	-0.66	0.16	0.32
96	18_i	rs12327360	64762466	CCDC102B	intron	TXNDC10	DOK6	A	G	32.2	94.2	65.5	0.41	6.08E-05	0.99	0.42	0.10	0.88
97	18_i	rs12962140	64728564	CCDC102B	intron	TXNDC10	DOK6	A	C	26.4	93.3	72.1	0.38	6.10E-05	0.95	0.43	0.11	0.76
98	18_i	rs12965053	64725718	CCDC102B	intron	TXNDC10	DOK6	C	G	72.1	93.3	26.4	0.38	6.10E-05	0.95	-0.43	0.11	0.76
99	18_i	rs11660484	64725025	CCDC102B	intron	TXNDC10	DOK6	A	G	26.4	93.3	72.1	0.38	6.11E-05	0.95	0.43	0.11	0.76
100	3_i	rs871085	45000137	EXOSC7	intron	ZDHHC3	CLEC3B	C	T	42.0	84.3	65.5	0.44	6.40E-05	0.97	0.39	0.10	0.14
101	3	rs9821143	14699417	C3orf20	missense	C3orf19	FGD5	A	G	21.0	84.0	87.0	0.33	6.45E-05	1.00	-0.43	0.11	1.00
102	8_i	rs13275219	81422381	-	-	LOC340443	ZBTB10	C	T	85.7	84.1	22.0	0.33	6.56E-05	0.96	-0.43	0.11	0.87
103	8_i	rs1155294	97036729	-	-	C8orf37	LOC643228	A	G	152.7	37.4	1.8	0.11	6.72E-05	0.98	-0.66	0.17	0.70
104	8_i	rs1484630	97037642	-	-	C8orf37	LOC643228	G	T	1.8	37.4	152.7	0.11	6.83E-05	0.98	0.66	0.17	0.70
105	7_i	rs17455883	20179711	ITGB8	intron	MACC1	LOC100130234	A	T	14.0	83.0	94.9	0.29	6.92E-05	1.00	0.46	0.11	0.48
106	8_i	rs11987725	97038532	-	-	C8orf37	LOC643228	C	T	1.9	37.4	152.7	0.11	6.93E-05	0.98	0.66	0.17	0.70
107	7_i	rs17365084	20181667	ITGB8	intron	MACC1	LOC100130234	A	T	14.0	83.0	94.9	0.29	6.94E-05	1.00	0.46	0.11	0.48
108	3_i	rs9834046	14747361	C3orf20	intron	C3orf19	FGD5	G	T	118.8	64.1	9.0	0.21	6.94E-05	0.99	0.49	0.12	1.00
109	7_i	rs10239099	20182114	ITGB8	intron	MACC1	LOC100130234	C	G	14.0	83.0	94.9	0.29	6.95E-05	1.00	0.46	0.11	0.48
110	3_i	rs9811756	14722416	C3orf20	intron	C3orf19	FGD5	C	T	118.8	64.1	9.0	0.21	6.96E-05	1.00	0.49	0.12	1.00
111	7	rs17365098	20181699	ITGB8	intron	MACC1	LOC100130234	C	T	95.0	83.0	14.0	0.29	6.96E-05	1.00	-0.46	0.11	0.60
112	3_i	rs9822003	14724243	C3orf20	intron	C3orf19	FGD5	C	T	118.8	64.1	9.0	0.21	6.96E-05	1.00	0.49	0.12	1.00
113	3_i	rs13316767	14740126	C3orf20	intron	C3orf19	FGD5	C	T	118.8	64.1	9.0	0.21	6.97E-05	1.00	0.49	0.12	1.00
114	3_i	rs11710203	14741443	C3orf20	intron	C3orf19	FGD5	A	G	9.0	64.1	118.8	0.21	6.97E-05	1.00	-0.49	0.12	1.00
115	3_i	rs10212315	14732413	C3orf20	intron	C3orf19	FGD5	A	G	9.0	64.1	118.8	0.21	6.97E-05	1.00	-0.49	0.12	1.00

116	18_i	rs12965651	64696062	CCDC102B	intron	TXNDC10	DOK6	A	G	73.1	91.9	26.9	0.38	7.01E-05	0.97	-0.42	0.11	0.88
117	18_i	rs12970524	64726739	CCDC102B	intron	TXNDC10	DOK6	A	G	28.6	93.2	70.1	0.39	7.07E-05	0.92	0.43	0.11	0.88
118	18_i	rs10503133	64710977	CCDC102B	intron	TXNDC10	DOK6	A	G	26.3	93.3	72.3	0.38	7.07E-05	0.97	0.43	0.11	0.76
119	18_i	rs12970712	64710665	CCDC102B	intron	TXNDC10	DOK6	A	T	26.3	93.3	72.3	0.38	7.07E-05	0.97	0.43	0.11	0.76
120	18_i	rs8093895	64700838	CCDC102B	intron	TXNDC10	DOK6	G	T	26.3	93.3	72.3	0.38	7.08E-05	0.97	0.43	0.11	0.76
121	13_i	rs9318838	81571400	-	-	PTMAP5	LOC647313	C	T	27.1	91.8	73.0	0.38	7.09E-05	0.86	-0.45	0.11	1.00
122	9_i	rs4631540	118774799	-	-	LOC442434	DBC1	G	T	74.9	87.0	30.0	0.38	7.16E-05	0.87	0.43	0.11	0.65
123	8_i	rs7822342	81409254	-	-	LOC340443	ZBTB10	A	G	33.8	89.0	69.0	0.41	7.25E-05	0.99	0.40	0.10	0.65
124	6_i	rs2485800	93754453	-	-	LOC100128159	COPS5P	A	G	3.0	31.5	157.4	0.10	7.27E-05	0.63	-0.82	0.21	0.39
125	3_i	rs2056321	45058137	-	-	CLEC3B	CDCP1	A	G	51.3	86.9	53.6	0.49	7.30E-05	0.97	-0.39	0.10	0.19
126	8_i	rs6473223	81430710	-	-	LOC340443	ZBTB10	C	T	86.2	83.6	22.0	0.33	7.49E-05	0.96	-0.43	0.11	0.75
127	8_i	rs2202749	81436893	-	-	LOC340443	ZBTB10	A	G	22.0	83.6	86.2	0.33	7.51E-05	0.96	0.43	0.11	0.75
128	8_i	rs13275449	81438668	-	-	LOC340443	ZBTB10	A	G	86.2	83.6	22.0	0.33	7.51E-05	0.96	-0.43	0.11	0.75
129	8_i	rs12543811	81441440	-	-	LOC340443	ZBTB10	A	G	86.2	83.6	22.0	0.33	7.52E-05	0.96	-0.43	0.11	0.75
130	8_i	rs7837153	81445931	-	-	LOC340443	ZBTB10	A	C	22.0	83.6	86.2	0.33	7.55E-05	0.96	0.43	0.11	0.75
131	3	rs11128716	14720575	C3orf20	intron	C3orf19	FGD5	C	T	119.0	63.0	9.0	0.21	7.56E-05	1.00	0.49	0.12	0.83
132	8	rs10100514	97054468	-	-	C8orf37	LOC643228	C	T	2.0	46.0	144.0	0.13	7.58E-05	1.00	0.61	0.15	0.75
133	8_i	rs3739413	17574304	MTUS1	intron	PDGFRL	FGL1	A	T	118.7	66.2	7.0	0.21	7.74E-05	0.99	0.50	0.13	0.50
134	1	rs3121580	214880516	RRP15	intron	SPATA17	LOC728463	C	T	115.0	69.0	8.0	0.22	7.81E-05	1.00	-0.49	0.12	0.68
135	20_i	rs7272317	52050183	BCAS1	intron	SUMO1P1	CYP24A1	C	T	4.2	64.5	123.3	0.19	8.04E-05	0.97	0.54	0.14	0.24
136	20_i	rs12480106	52050416	BCAS1	intron	SUMO1P1	CYP24A1	A	G	123.2	64.5	4.2	0.19	8.07E-05	0.97	-0.54	0.14	0.24
137	8	rs6586625	17575863	MTUS1	intron	PDGFRL	FGL1	C	T	119.0	66.0	7.0	0.21	8.09E-05	1.00	0.50	0.13	0.67
138	20_i	rs2276494	52044629	BCAS1	intron	SUMO1P1	CYP24A1	C	T	123.8	64.1	4.0	0.19	8.17E-05	0.99	-0.54	0.14	0.14
139	20_i	rs2276496	52044595	BCAS1	intron	SUMO1P1	CYP24A1	C	T	4.0	64.1	123.8	0.19	8.17E-05	0.99	0.54	0.14	0.14
140	20	rs2024064	52046185	BCAS1	intron	SUMO1P1	CYP24A1	C	T	124.0	64.0	4.0	0.19	8.20E-05	1.00	-0.54	0.14	0.24
141	20	rs8124068	52043114	BCAS1	intron	SUMO1P1	CYP24A1	C	T	4.0	64.0	124.0	0.19	8.20E-05	1.00	0.54	0.14	0.24
142	20_i	rs6097716	52052205	BCAS1	intron	SUMO1P1	CYP24A1	C	T	4.3	64.7	122.9	0.19	8.40E-05	0.95	0.54	0.14	0.24
143	8_i	rs7006626	81410231	-	-	LOC340443	ZBTB10	A	C	79.0	89.8	23.1	0.35	8.61E-05	1.00	-0.42	0.11	0.87
144	12	rs12231356	70695815	TPH2	intron	TBC1D15	LOC283392	C	T	166.0	25.0	1.0	0.07	8.62E-05	1.00	-0.77	0.20	1.00
145	9	rs965474	94403753	FBP2	intron	HIATL1	FBP1	A	G	33.0	100.0	59.0	0.43	8.63E-05	1.00	0.41	0.11	0.46
146	7_i	rs1431091	136473566	PTN	intron	LOC100128744	LOC100128727	A	C	75.2	90.1	26.6	0.37	8.64E-05	0.88	-0.44	0.11	1.00
147	8_i	rs7462675	81426517	-	-	LOC340443	ZBTB10	A	C	85.1	84.8	22.0	0.34	8.92E-05	0.96	-0.43	0.11	0.87
148	9_i	rs6479554	94405553	FBP2	intron	HIATL1	FBP1	A	G	36.0	96.9	59.0	0.44	8.94E-05	1.00	0.41	0.10	0.77
149	8_i	rs6992476	81430261	-	-	LOC340443	ZBTB10	A	G	22.0	84.7	85.1	0.34	8.94E-05	0.96	0.43	0.11	0.87
150	8_i	rs12155779	96842645	-	-	C8orf37	LOC643228	A	G	25.9	91.8	74.1	0.37	8.95E-05	0.99	0.41	0.11	0.76
151	8	rs7822328	81409214	-	-	LOC340443	ZBTB10	A	G	23.0	89.0	79.0	0.35	9.01E-05	1.00	0.42	0.11	0.87
152	9_i	rs10781224	74206201	-	-	LOC138971	LOC100130911	C	T	6.8	54.5	130.7	0.18	9.05E-05	0.89	0.54	0.14	0.80
153	15_i	rs11633976	85410354	-	-	AGBL1	NCRNA00052	A	T	158.8	30.1	3.0	0.09	9.16E-05	0.95	-0.67	0.17	0.22
154	1_i	rs1587175	209453657	FLVCR1	intron	LQK1	VASH2	A	T	46.9	101.0	43.9	0.49	9.22E-05	1.00	-0.41	0.10	0.47
155	3_i	rs4682762	45049728	CLEC3B	intron	EXOSC7	CDCP1	C	T	53.2	84.0	54.6	0.50	9.23E-05	0.99	-0.37	0.10	0.11
156	3_i	rs6765447	45040740	-	-	EXOSC7	CLEC3B	A	G	54.6	84.0	53.2	0.50	9.25E-05	0.99	0.37	0.10	0.11
157	3_i	rs4682761	45038553	-	-	EXOSC7	CLEC3B	A	G	53.3	84.0	54.6	0.50	9.25E-05	0.99	-0.37	0.10	0.11
158	15	rs10518997	71343997	NEO1	intron	LOC729686	HCN4	A	G	101.0	80.0	11.0	0.27	9.38E-05	1.00	0.46	0.12	0.46
159	8_i	rs12542017	81414690	-	-	LOC340443	ZBTB10	C	T	79.4	89.4	23.0	0.35	9.46E-05	1.00	-0.42	0.11	0.87
160	3_i	rs4683021	45019882	EXOSC7	intron	ZDHHC3	CLEC3B	A	G	53.0	84.0	54.9	0.49	9.47E-05	1.00	-0.37	0.10	0.11
161	3_i	rs6441876	45012654	EXOSC7	intron	ZDHHC3	CLEC3B	C	G	54.9	84.0	53.0	0.49	9.47E-05	1.00	0.37	0.10	0.11
162	15	rs11637457	85373510	AGBL1	near-gene-3	AGBL1	NCRNA00052	C	T	159.0	28.0	5.0	0.10	9.47E-05	1.00	-0.61	0.16	0.02
163	3_i	rs7626251	45029153	-	-	EXOSC7	CLEC3B	A	G	53.0	84.0	54.9	0.50	9.48E-05	1.00	-0.37	0.10	0.11
164	3_i	rs6794	45027779	EXOSC7	missense	ZDHHC3	CLEC3B	C	G	54.9	84.0	53.0	0.49	9.49E-05	1.00	0.37	0.10	0.11
165	15_i	rs16939749	85379649	-	-	AGBL1	NCRNA00052	C	G	158.7	28.2	5.0	0.10	9.50E-05	0.99	-0.61	0.16	0.02
166	1_i	rs9429895	209463714	-	-	FLVCR1	VASH2	A	G	4.9	43.6	143.5	0.14	9.53E-05	0.95	-0.57	0.15	0.75
167	6	rs225613	142501956	-	-	NMBR	VTA1	C	T	14.0	68.0	109.0	0.25	9.56E-05	1.00	0.45	0.11	0.44
168	11	rs1790183	131453635	HNT	intron	LOC729229	OPCML	C	T	81.0	95.0	16.0	0.33	9.56E-05	1.00	0.45	0.11	0.14
169	3	rs11130040	45024190	EXOSC7	intron	ZDHHC3	CLEC3B	A	G	53.0	84.0	55.0	0.49	9.62E-05	1.00	-0.37	0.10	0.08
170	6	rs225626	142513987	VTA1	intron	NMBR	GPR126	G	T	109.0	69.0	14.0	0.25	9.62E-05	1.00	-0.44	0.11	0.57
171	6_i	rs225627	142514059	VTA1	intron	NMBR	GPR126	C	T	108.8	69.0	14.0	0.25	9.89E-05	1.00	-0.44	0.11	0.57
172	6_i	rs2842759	142478045	-	-	NMBR	VTA1	C	T	108.8	69.0	14.0	0.25	9.89E-05	1.00	-0.44	0.11	0.57
173	6_i	rs225638	142520826	VTA1	intron	NMBR	GPR126	A	G	14.0	69.0	108.8	0.25	9.89E-05	1.00	0.44	0.11	0.57
174	13_i	rs874497	27300332	-	-	GSX1	PDX1	C	T	111.8	68.9	11.3	0.24	9.98E-05	0.98	-0.46	0.12	0.84

[a] _i indicates the SNP was imputed, otherwise it was directly genotyped [b] The mean effect size of each copy of the minor allele measured in standard deviations [c] Hardy Weinberg Equilibrium P-values

Table S2: Association with reading, motor hand-skill, and cognitive traits for the SNPs tested in each stage (Bonferroni correction P=0.0018).

Trait	Marker	Stage 1	Stage 2	Stage 3	ALSPAC general population
Hand Motor Skill	rs11855415	0.28	0.46	0.75	0.34
	rs9806256	0.02	0.90	0.81	0.52
CCI	rs11855415	0.36	0.79	-	-
	rs9806256	0.30	0.91	-	-
CCN	rs11855415	0.24	0.28	-	-
	rs9806256	0.06	0.24	-	-
OLSON	rs11855415	0.20	-	-	-
	rs9806256	0.16	-	-	-
READ	rs11855415	0.98	0.28	0.41	0.31
	rs9806256	0.28	0.45	0.45	0.41
SPELL	rs11855415	0.90	0.26	-	-
	rs9806256	0.76	0.37	-	-
SPOON	rs11855415	0.86	-	-	-
	rs9806256	0.70	-	-	-
Performance IQ	rs11855415	0.91	0.65	0.81	0.48
	rs9806256	0.72	0.49	0.98	0.31
Verbal IQ	rs11855415	0.53	0.82	0.62	0.02
	rs9806256	0.20	0.53	0.76	0.05
Total IQ	rs11855415	0.67	0.94	0.86	0.11
	rs9806256	0.53	0.97	0.85	0.11

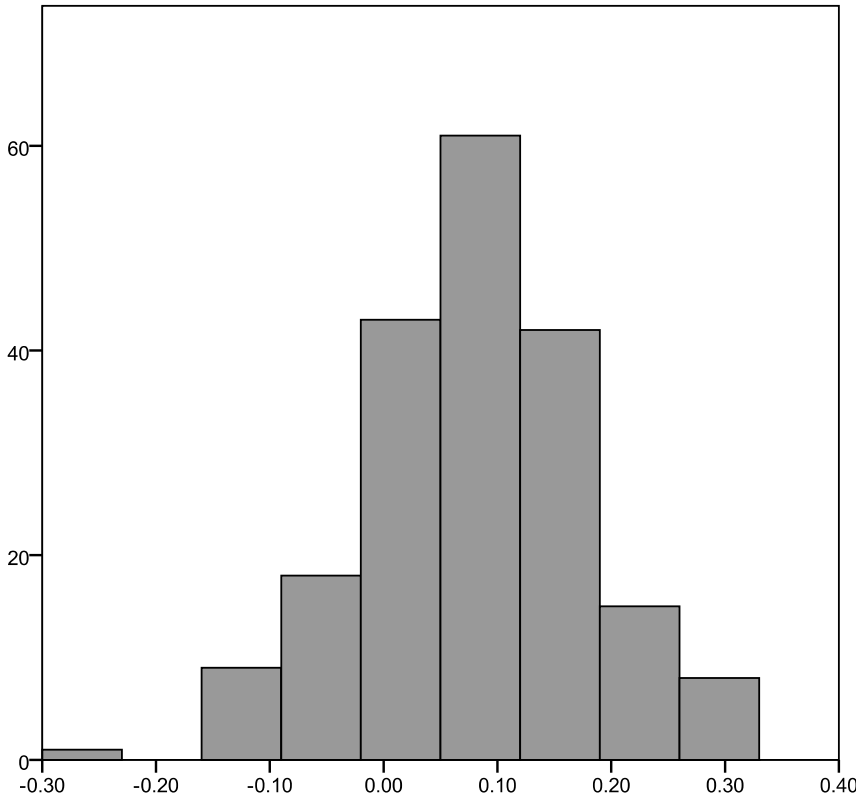

Figure S1: Distribution of PegQ scores for stage 1. N=197, mean=0.08, SD=0.099.

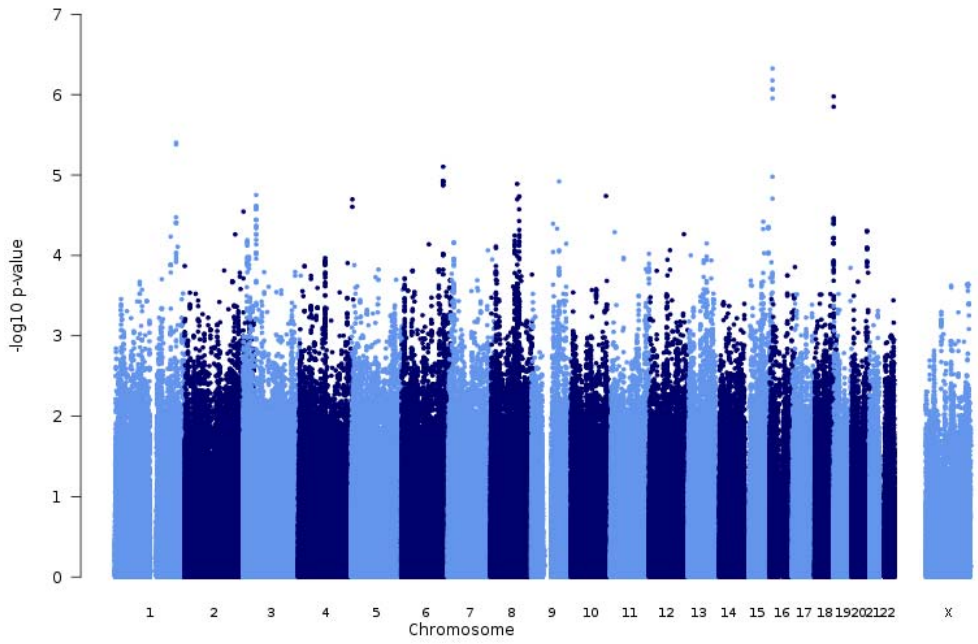

Figure S2: Manhattan Plot from the GWAS in stage 1. SNPs are plotted in order of chromosome and position along the X axis.

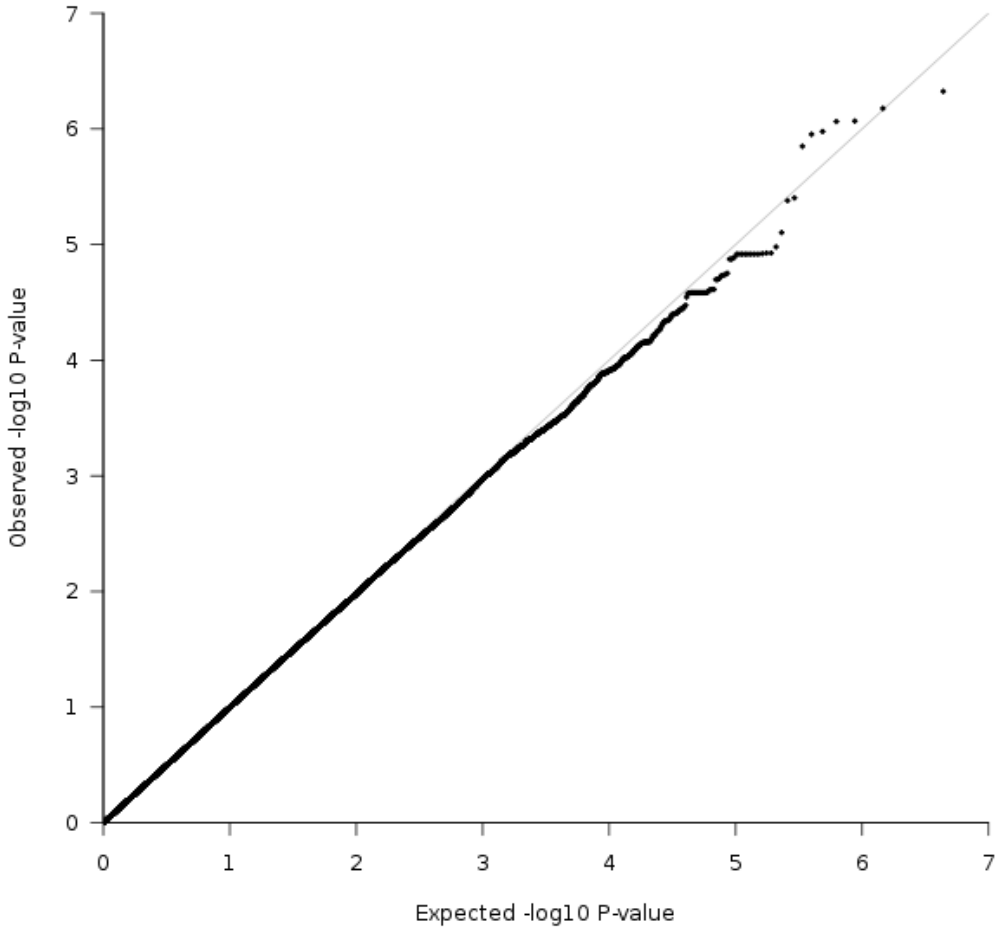

Figure S3: Q-Q Plot of all directly genotyped and imputed SNPs from stage 1.

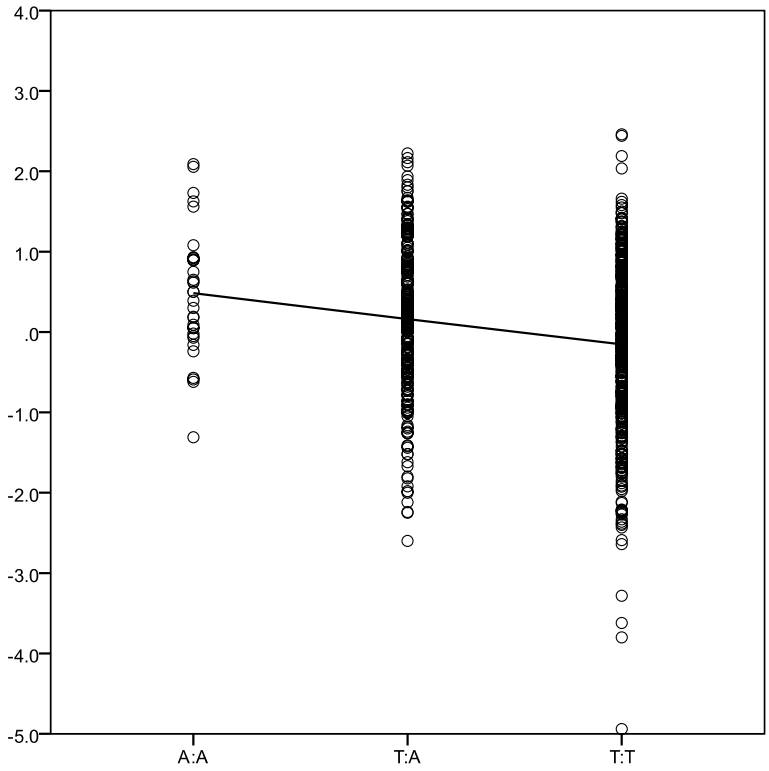

Figure S4: Plot of normalized PegQ (zPegQ, mean=0, SD=1) distribution (y-axis) for each genotype of rs11855415 (x-axis) in RD individuals in all 3 stages combined.

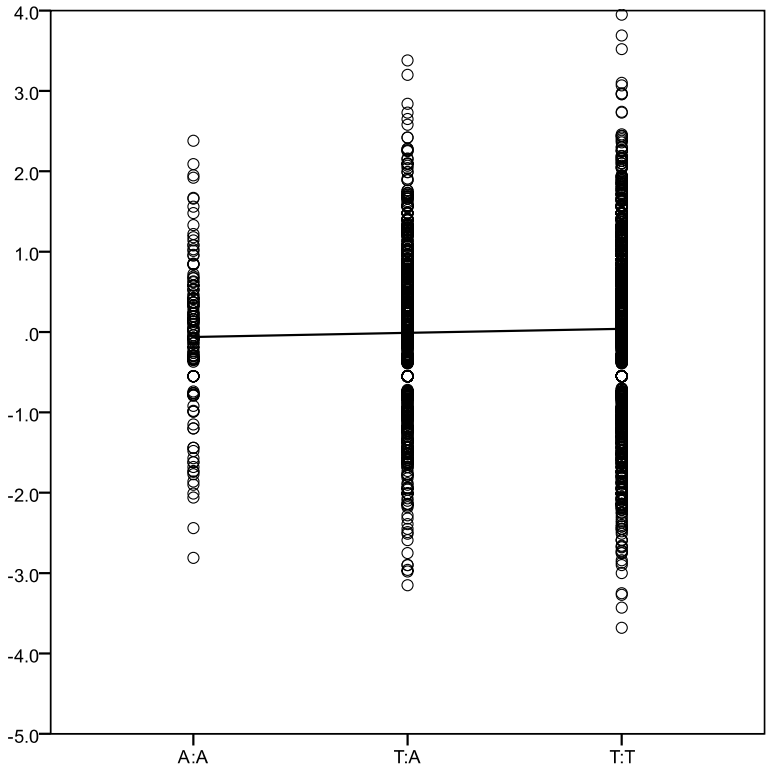

Figure S5: Plot of the normalized PegQ (zPegQ, mean=0, SD=1) distribution (y-axis) for each genotype of rs11855415 (x-axis) in individuals from the general population.

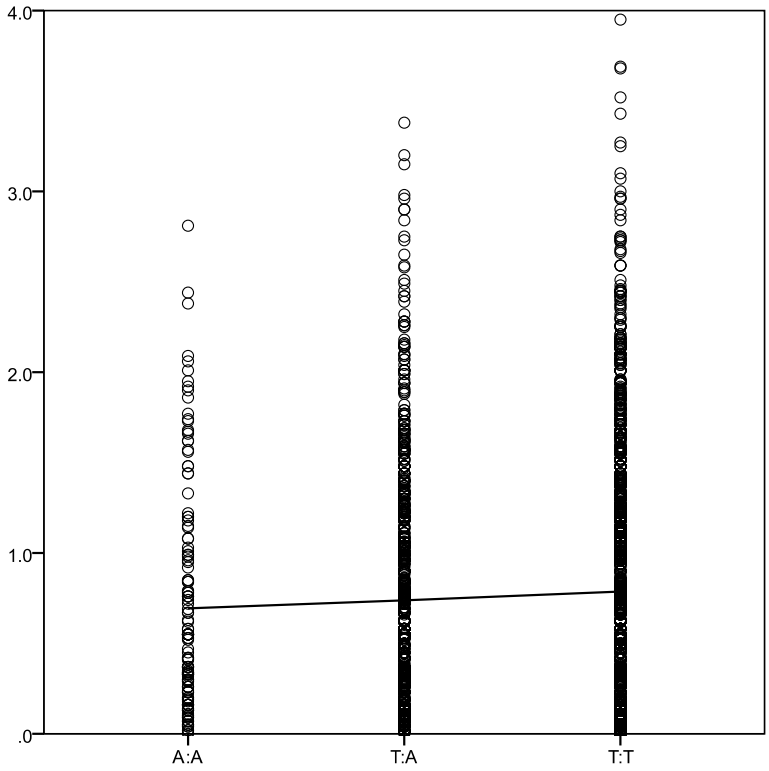

Figure S6: Plot of the absolute value of zPegQ (y-axis) for each genotype of rs11855415 (x-axis) in the general population.

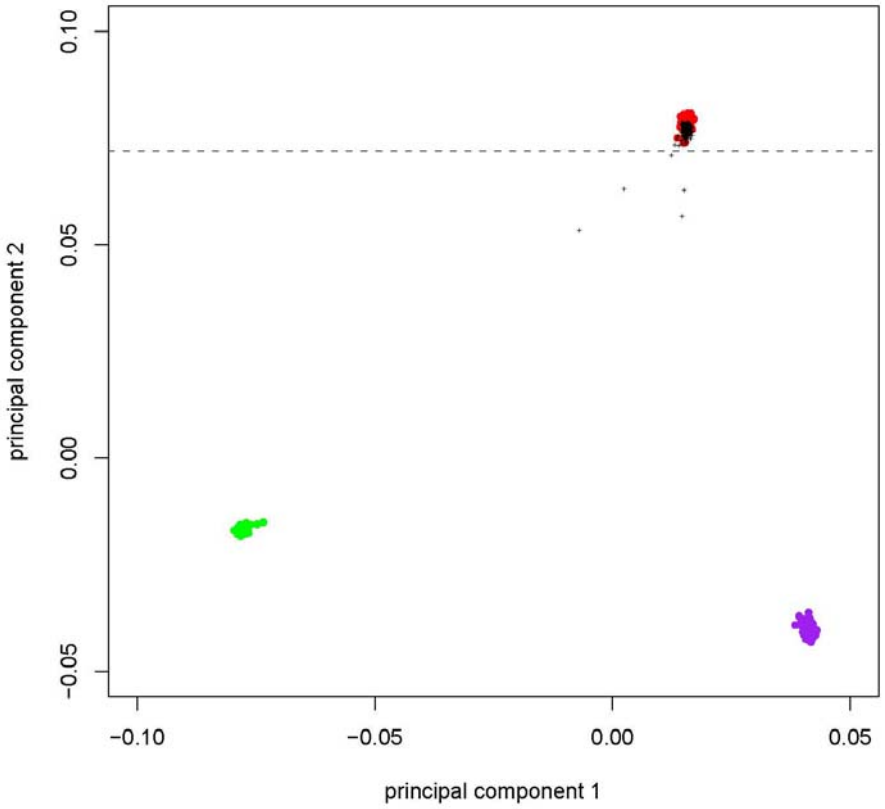

Figure S7: Ancestry Clustering based on principle component analysis of the original GWAS data. HapMap3 reference samples; CEU (red), JPT & CHB (purple) and YRI (green), are plotted alongside all individuals in the GWAS (black crosses). Based on this analysis, 4 samples with significant deviation from the CEU cluster were removed from the GWAS.

1 Fisher, S.E., Francks, C., Marlow, A.J., MacPhie, I.L., Newbury, D.F., Cardon, L.R., Ishikawa-Brush, Y., Richardson, A.J., Talcott, J.B., Gayan, J. *et al.* (2002) Independent genome-wide scans identify a chromosome 18 quantitative-trait locus influencing dyslexia. *Nat Genet*, **30**, 86-91.

2 Marlow, A.J., Fisher, S.E., Richardson, A.J., Francks, C., Talcott, J.B., Monaco, A.P., Stein, J.F. and Cardon, L.R. (2001) Investigation of quantitative measures related to reading disability in a large sample of sib-pairs from the UK. *Behav Genet*, **31**, 219-230.