

# Allelic Imbalance in SZ (Supplemental Material 1)

This is a document containing supplemental figures and tables for the “Comparison of Quantitative Trait Loci Methods: Total Expression and Allelic Imbalance Method in Brain RNA-seq” manuscript.

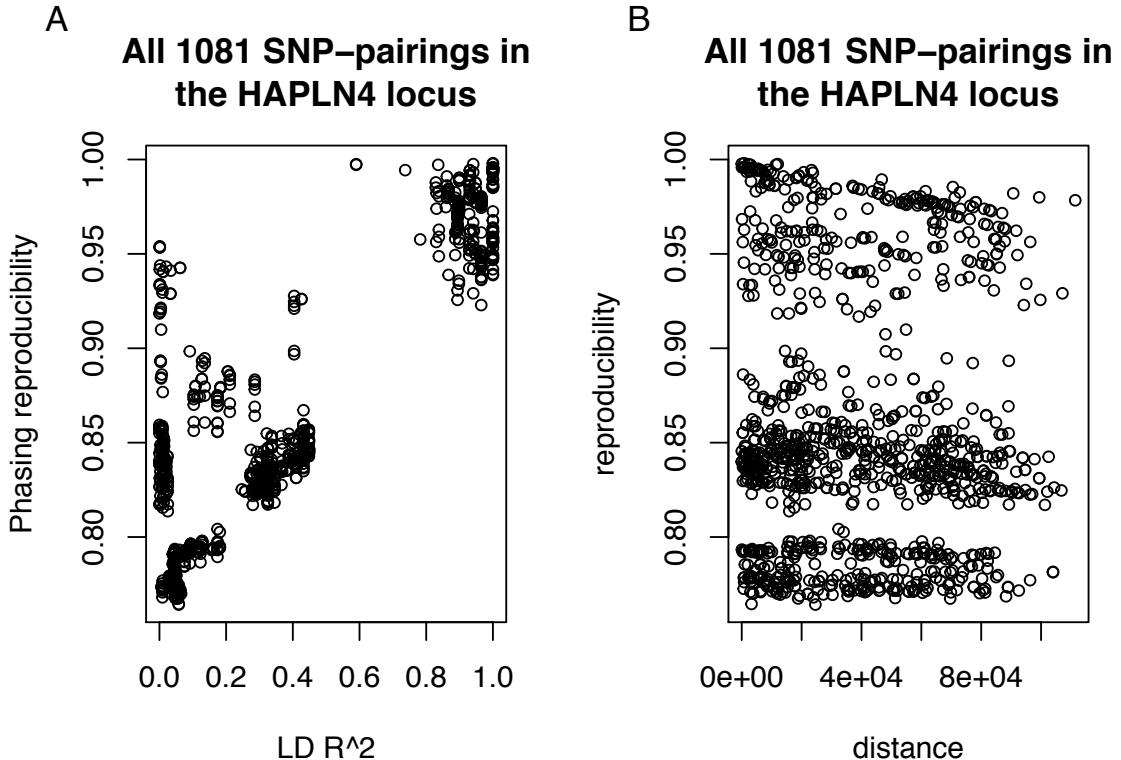


Fig S1-1: Illustration of the phasing quality of SNPs in the HAPLN4 region. All risk-SNP regions were phased using the Shapeit2 tool in order to link risk-SNPs with txSNPs. The fundamental mechanism of phasing is to determine likely parent of origin for all txSNPs that are heterozygous, by assigning alleles as being either of parent 1 (P1) origin or parent 2 (P2) origin. According to Shapeit2 notation, this is denoted with a vertical bar |, such that for example an A/G heterozygous SNP can be either A|G or G|A, meaning that the A-allele was inherited from the parent 1 or the parent 2, respectively.

A default execution of Shapeit2 provides one guess of likely haplotype, so the degree of probability is not directly available. However, as suggested by Shapeit2 authors a probability can be calculated by iterating through the same phasing using different random seeds. The phasing reproducibility between any two SNP is then defined as the fraction of iterations where the two SNPs have the same results with different random seeds; a value of 1 indicates perfect reproducibility and 0.5 indicates random choice.

We used this approach to investigate the relation between reproducibility and linkage disequilibrium (LD) R<sup>2</sup>, as well as between reproducibility and distance. This is illustrated here for all pairwise combinations of SNPs in the HAPLN4 region. For A) reproducibility and LD, we un-surprisingly found that all SNP-pairs in perfect LD ( $R^2=1$ ) achieve almost completely perfect phasing reproducibility. However, importantly SNP-pairs that are not in LD ( $R^2=0$ ) also can achieve reproducibility-values above 0.9. Moreover, in this region no SNP-pair had worse reproducibility than 0.78. For B) reproducibility and distance, we found that at the investigated distance (400KB) there was only a weak tendency towards diminished phasing reproducibility with distance.

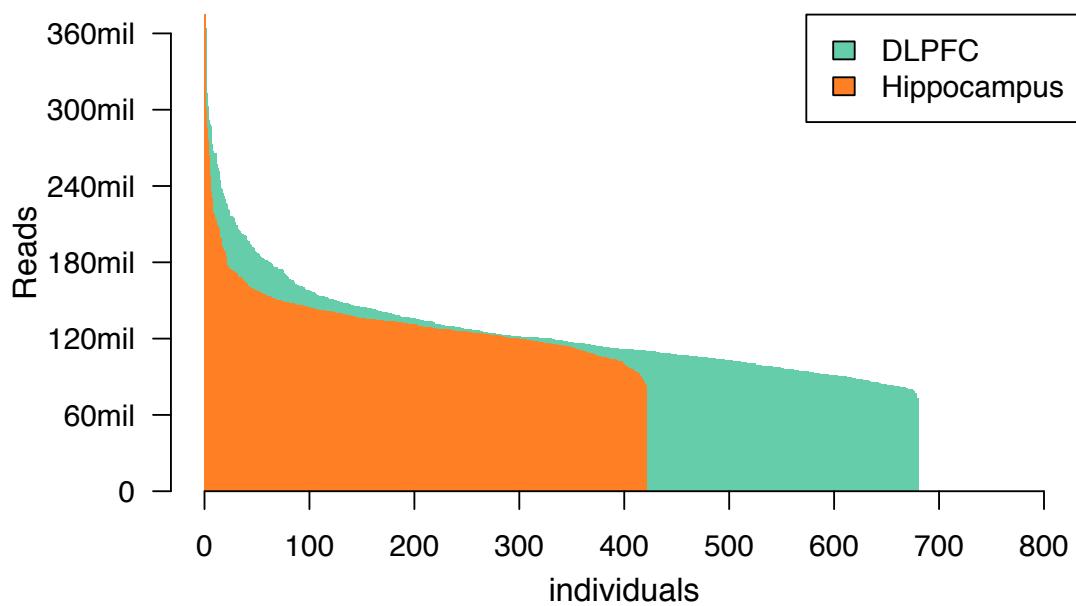


Fig S1-2: Pair-end reads in each fastq file for respective individual

	DLPFC	Hippocampus	Both
Mean	127133556	134174615	129825914
SD	39665006	30281344	36510189

Table S1-1: mean and standard deviation values for read counts in fastq files

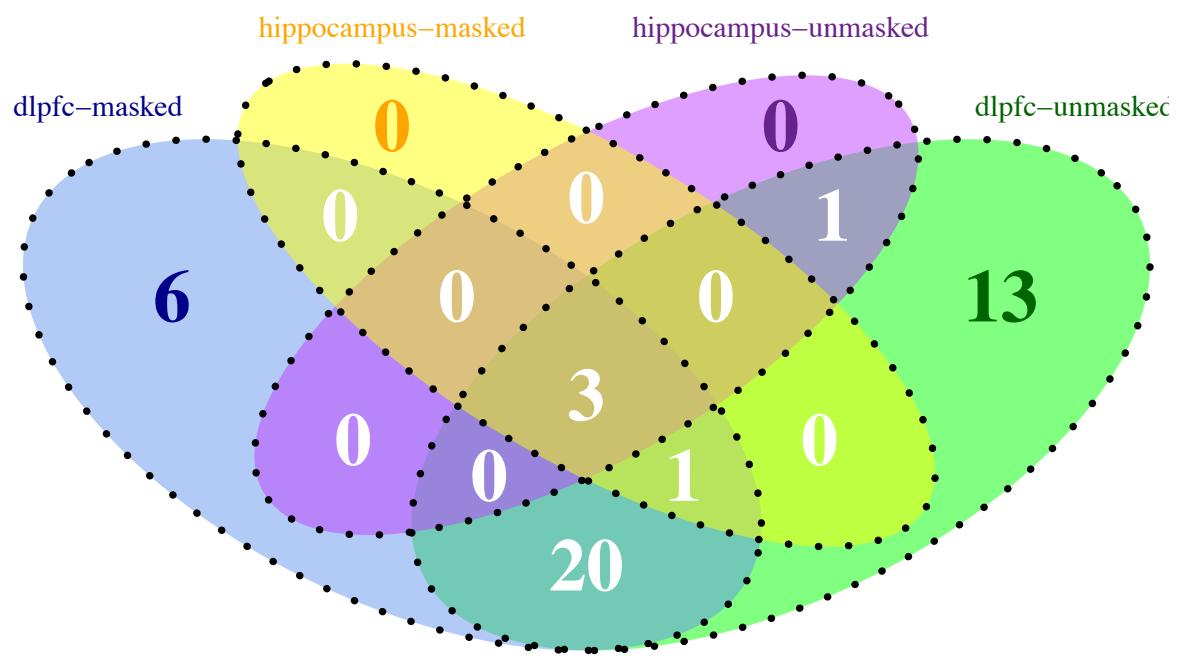


Fig S1-3: The number of aeQTLs found in respective tissue and alignment using significance thresholds set according to FDR5% as in main text table 1

	mean	sd	txSNPs
dlpfc.masked	0.506	0.127	247978
dlpfc.unmasked	0.517	0.125	239262
hippocampus.masked	0.505	0.161	137116
hippocampus.unmasked	0.513	0.160	135948

Table S1-2: A table of reference frequency and number of txSNPs in all genes and samples used for the calculation

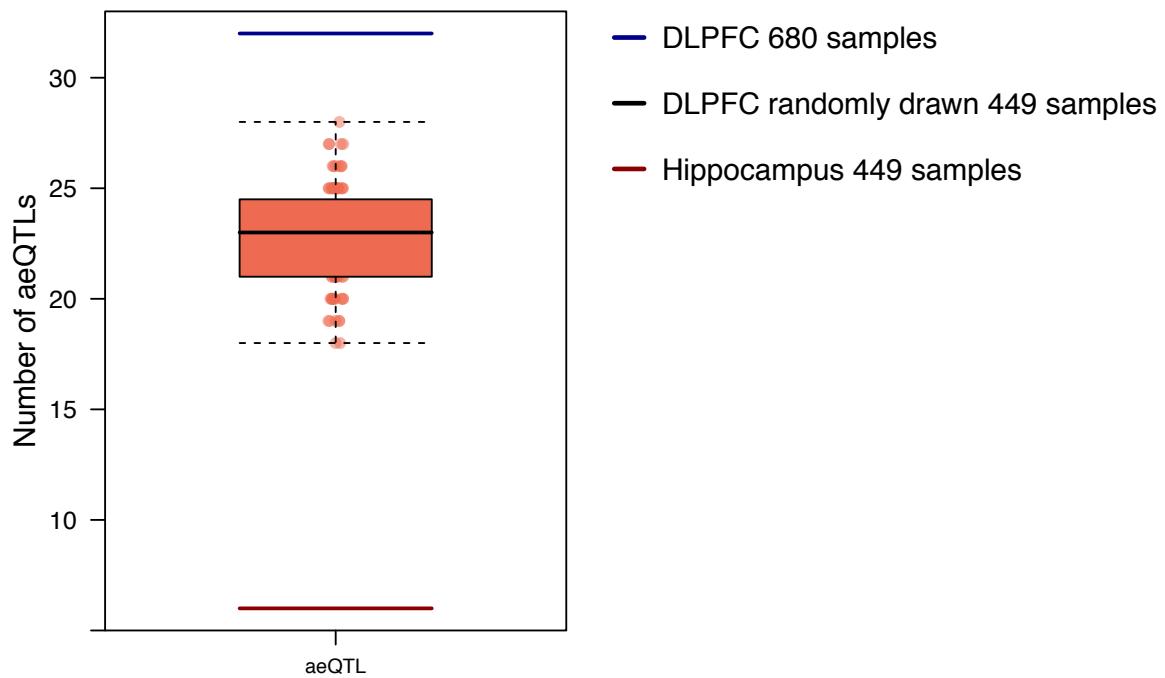


Fig S1-4: Figure demonstrating the amount of aeQTLs found for DLPFC( $n=680$ ) using the same sample size as Hippocampus( $n=449$ ). The DLPFC dataset was downsampled down to 449 and investigated for aeQTLs 100 times.

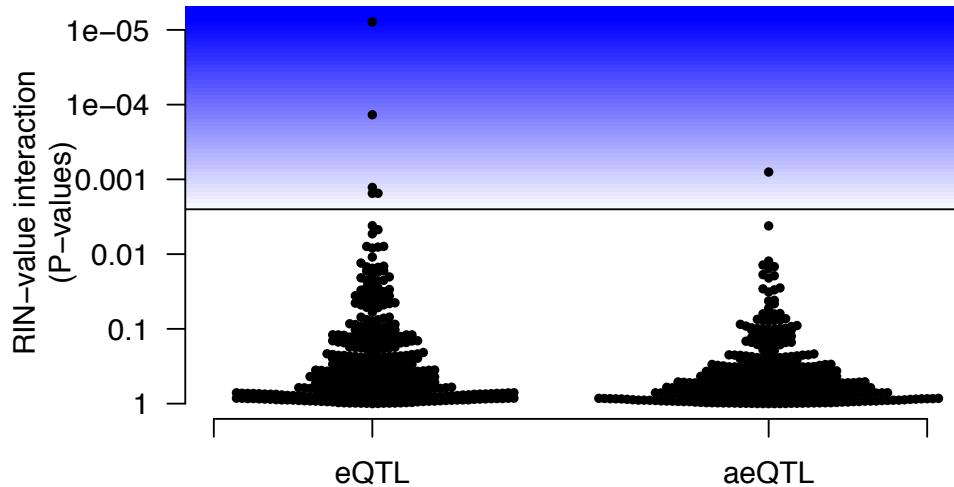


Fig S1-5: Calculation of RIN-interaction values for eQTL and aeQTL. Each dot shows the interaction P-value for all SNP-gene pairs. A binary RIN value cutoff was set at RIN 8. For the eQTL analysis 5 pairs were significant after multiple testing correction, in aeQTL analysis 1 pair was significant ( $P < 0.0025$ ).

### LRRN3 – rs13240464

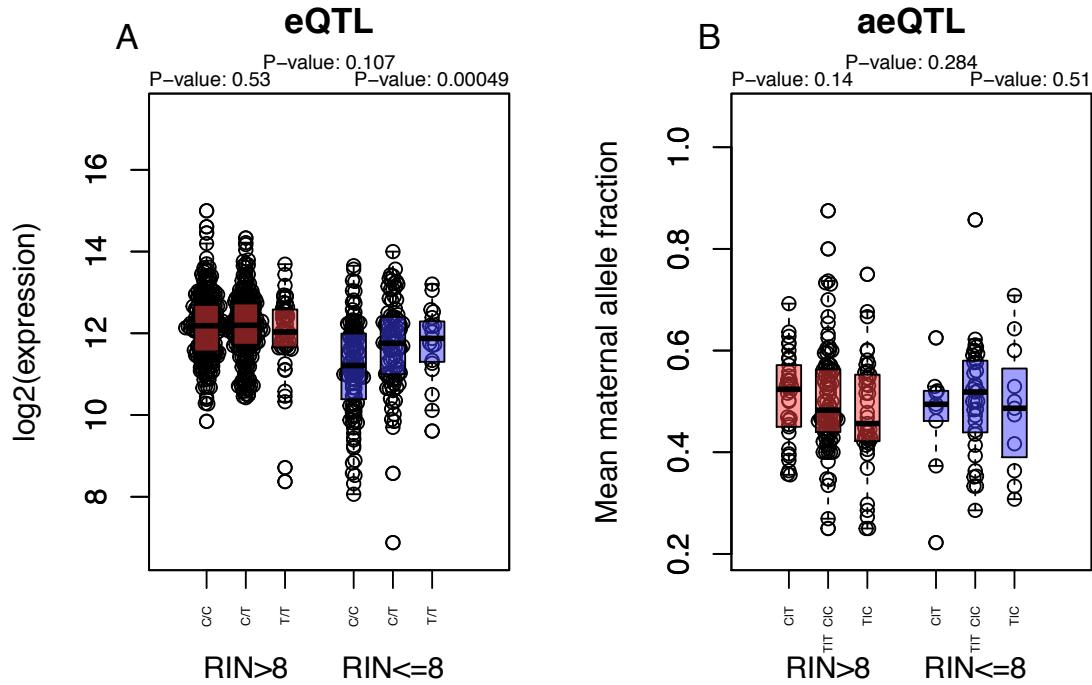


Fig S1-6: The eQTL for LRRN3 and risk-SNP rs13240464, stratified by RIN value. This plot illustrates an eQTL with potential interaction effects caused by RNA-degradation: when testing eQTL effect A), there was a significant interaction between RIN-value and risk-SNP genotype ( $P_{\text{interaction}}=1.36\text{e-}04$ ), with lower RIN values giving rise to a stronger eQTL effect. B) This was not the case for aeQTL ( $P_{\text{interaction}}=0.37$ ). Neither the non-stratified by RIN, but RIN-corrected eQTL ( $P= 0.107$ ) nor the aeQTL ( $P= 0.284$ ) for this gene-SNP pair were significant after multiple testing

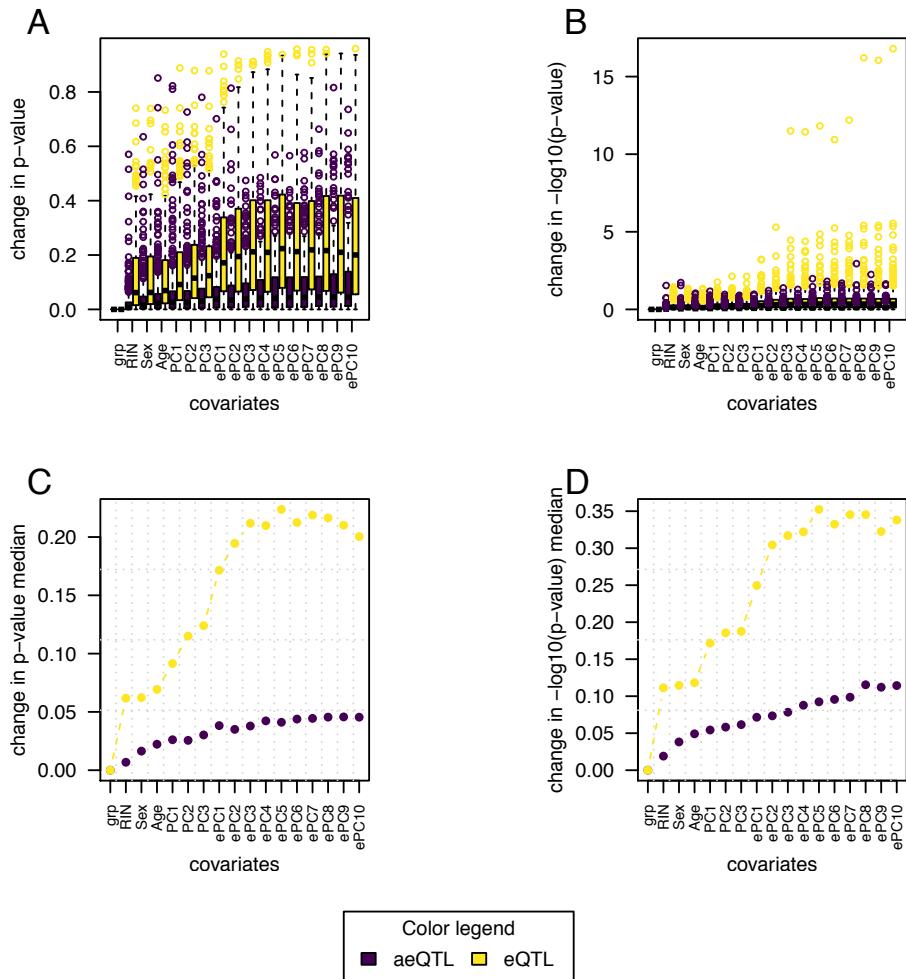


Fig S1-7: Covariates impact on p-values in aeQTL versus eQTL. All testable 371 gene-snp pairs in DLPFC have been included in this analysis, comparing the change of p-value distributions of aeQTL(purple) and eQTL(yellow). For each step to the right on the x-axis one more covariate is added, indicated as x-axis labels. For example, the third point's p-value was calculated using the formula  $\text{expr} \sim \text{grp} + \text{RIN} + \text{Sex}$ . A) Changes in raw p-value, calculated by  $|\text{pvalue1} - \text{pvalue0}|$ , giving more effect of pvalues in the higher p-value range. B) Performing the same comparison, but starting with p-values which had been  $-\log_{10}$  transformed, to give more effect on changes in the lower range of p-values. Taking the median from each p-value change using C) raw p-value and D)  $-\log_{10}$  p-value, the pattern for both variants are very similar, indicating a similar effect of each additional covariate on the whole p-value range. In general, the aeQTL analysis shows little impact of covariate usage compared to eQTL analysis.

Gene	RiskSNP	Pos	Dist (Kb)	Ref/Ant	aeQTL (est)	aeQTL txSNP (est)	aeQTL txSNP (pval)	aeQTL txSNP	aeQTL txSNP	Reads	Genegroup (ind)	
AIKBH5	rs8082590	chr17:18	-154	[G]/A	4.1e-05	-0.027	0.99	0.00098	rs13284	110	57/116/54	
AIKBH5	rs8082590	chr17:18	-153	[G]/A	0.012	0.031	0.0076	0.00023	rs1563371	84	57/116/54	
B4GALT5	rs7267548	chr20:48	-119	T/[C]	0.012	0.1	0.0046	0.0048	rs7693	18	10/16/4	
B4GALT5	rs7267548	chr14:104	23	[G]/T	0.016	0.029	0.0079	0.0027	rs11540970	110	50/154/49	
C11orf37	rs12887734	chr16:30	66	[A]/G	0.016	0.046	0.0046	0.0048	rs2275271	19	10/20/4	
C11orf37	rs12887734	chr10:105	-202	[T]/A	-0.0084	-0.036	0.26	0.0001	rs788228	87	112/55/114	
C11orf37	rs11191419	chr11:58	-76	[A]/G	-0.0007	-0.024	0.13	3.9e-07	rs200470100	140	10/14/127	
C11orf37	rs11191419	chr11:58	-54	[A]/G	-0.0007	-0.032	0.13	3.9e-07	rs11086644	12	7/29/16	
C11orf37	rs9420	chr11:58	-54	[C]/T	0.036	0.13	0.035	0.00075	rs28371704	34	22/25/16	
C11orf37	rs9420	chr11:58	-54	[T]/D	-0.028	-0.058	0.0097	0.00027	rs7891420	1900	30/206/21	
CYP2D6	rs6002655	chr7:24747494_D	chr7:25	-11	[A]/G	0.0014	0.16	0.92	0.0013	rs6063162	8.7	7/10/8
DMD	rs6005094	chr20:37	-168	[A]/G	0.015	-0.085	0.028	9.2e-08	rs12328151	300	52/64/53	
DMD	rs6005094	chr22:34	-120	[G]/A	-0.015	-0.036	0.034	45/22/44	rs693	310	45/22/44	
GIGYF2	rs7232245	chr16:59	-60	A/[T]	-0.0036	-0.018	0.72	7e-07	rs1042665	4900	86/74/75	
GIGYF2	rs7232245	chr5:138	-51	C/[T]	0.00087	0.018	0.72	2.5e-06	rs111032	67	10/17/11	
HSPA9, SNORD63	rs3849046	chr5:138	-40	C/[T]	0.005	-0.043	0.017	0.00024	rs1042665	4900	51/143/41	
HSPA9, SNORD63	rs10043984	chr5:138	-40	C/[T]	0.005	-0.032	0.13	0.00024	rs11542821	18	34/41/40	
LCAT	rs8044995	chr16:68	205	[G]/A	0.033	0.035	0.00039	0.026	rs11542821	3.1	15/21/5	
LCAT	rs8044995	chr16:68	212	[G]/A	0.033	0.033	0.00039	0.026	rs11860411	2.9	8/7/13	
LCAT	rs8044995	chr16:68	212	[G]/A	0.033	0.052	0.00039	0.026	rs11860115	1.3	7/5/8	
LCAT	rs8044995	chr16:68	210	[G]/A	0.033	-0.025	0.00039	0.59	rs17851876	8.2	5/38/4	
LCAT	rs8044995	chr16:68	208	[G]/A	0.033	-0.011	0.00039	0.026	rs11064125	7.1	31/31/23	
LCAT	rs1023500	chr22:42	-14	[T]/C	-0.013	-0.076	0.082	1e-05	rs62240997	120	49/151/46	
LCAT	rs1023500	chr22:42	-14	[T]/C	-0.013	0.03	0.082	0.0021	rs62240998	150	46/150/60	
MADIL1, MIR4655	chr7:2025096_L	chr7:2	-7	D/[H]	-0.0071	-0.041	0.33	0.0011	rs693	41	96/22/92	
MADIL1, MIR4655	chr7:2025096_L	chr7:2	-7	D/[H]	-0.0071	-0.041	0.33	0.00025	rs11537347	42	86/28/83	
MAN2A2	rs4702	chr15:91	-37	[G]/A	0.0045	0.017	0.3	0.0029	rs4773	180	73/156/70	
MAN2A2	rs2905426	chr19:19	11	[G]/T	-0.0078	-0.037	0.078	0.00022	rs756397	29	51/71/49	
MAN2A2	rs2905426	chr19:19	116	[G]/T	-0.015	-0.11	0.013	8.1e-05	rs62021395	130	64/98/65	
NCAN	rs12323245	chr19:19	132	[T]/T	0.014	0.028	0.0029	0.00029	rs2228600	88	16/59/21	
NCAN	rs12323245	chr16:59	141	A/[T]	0.00025	-0.032	0.95	2.5e-05	rs17821543	1800	23/7/36	
NLRP4	rs6002655	chr22:43	122	C/[T]	-0.011	-0.031	0.0083	0.00029	rs1134157	40	8/48/6	
NLRP4	rs6002655	chr22:43	122	C/[T]	-0.011	-0.031	0.0083	0.00029	rs17821543	1800	23/7/36	
NOGFB	rs6704768	chr22:34	-165	[G]/A	-0.0059	-0.018	0.023	2.4e-07	rs709337	1500	95/46/120	
NOGFB	rs6704768	chr16:68	-165	[G]/A	-0.0059	-0.018	0.023	4e-05	rs6704768	1600	104/56/117	
NSUN6	rs7833279	chr10:19	-90	[T]/G	0.048	0.11	0.0032	1.7e-05	rs373252672	10	23/58/11	
PLCB2	rs5620728	chr15:41	-16	[G]/A	-0.015	-0.11	0.013	0.00027	rs17292804	3	21/4/13	
PPBP1R13B	rs12887734	chr14:104	-158	G/[T]	0.036	0.035	6e-04	0.016	rs10134157	23	30/14/25	
PPBP1R13B	rs12887734	chr14:104	-154	G/[T]	0.036	0.016	6e-04	0.013	rs10134157	40	8/48/6	
PPBP1R16B	rs6005094	chr16:68	-156	[G]/A	-0.029	-0.058	0.015	0.0013	rs47748136	31	11/27/8	
PPBP1R16B	rs6005094	chr16:68	-156	[G]/A	-0.029	-0.072	0.00081	0.0005	rs3745741	85	34/19/40	
PPMT7	rs8044995	chr16:68	-198	[G]/A	-0.029	-0.021	0.00081	0.0005	rs61746794	32	21/23/27	
PPMT7	rs8044995	chr16:68	-200	[G]/A	-0.029	-0.021	0.00081	0.0005	rs1064826	340	43/55/40	
PPMT7	rs8044995	chr16:68	-191	[G]/A	-0.029	-0.0082	0.00081	0.38	rs1131933	530	48/20/764	
PPMT7	rs8044995	chr16:68	-184	[G]/A	-0.029	-0.0065	0.00081	0.96	rs7567372	5.7	24/12/6	
PPRT1	rs12091307	chr16:30	114	[A]/G	-0.029	-0.035	0.3	0.00081	NaN	2.9	3/15/5	
PPRT1	rs3240117	chr12:57	-186	A/[C]	-0.01	0.11	0.00017	0.00017	rs141436390	31	7/13/8	
R3HDM2	rs6873913	chr19:50	45	[T]/G	-0.025	-0.075	0.088	1e-04	rs3187346	50	40/49/34	
RCN3	rs10043984	chr5:138	-70	C/[T]	-0.0031	-0.0099	0.89	0.00086	rs1046576	470	109/118/117	
RREP2	chr1..8424084_D	chr1:8	12	H/D	-0.0048	-0.04	0.15	2.9e-11	rs1064826	250	74/28/107	
RREP2	chr1..8424084_D	chr1:8	12	H/D	-0.0048	-0.026	0.15	9.2e-08	rs8627	420	79/136/99	
RREP2	chr1..8424084_D	chr1:8	6	H/D	-0.0048	-0.026	0.15	8.1e-05	rs11121172	240	87/22/121	
RPTN2	rs6434288	chr12:198	-132	[G]/A	-0.021	-0.03	0.021	0.0018	rs1058766	240	86/19/121	
RPS11, SNORD35B	rs56873913	chr19:50	92	[T]/G	-0.0051	-0.071	0.011	2.5e-05	rs7582536	43	120/3/104	
SDCCAG8, MIR4677	rs10803138	chr1:244	-24	A/[G]	-0.024	-0.059	0.015	0.0014	rs1755056	26	30/56/55	
SEZ6L2	rs12691307	chr16:30	29	[A]/G	0.015	0.033	0.032	4e-04	rs110927011	40	64/139/48	
SMC6	rs4523057	chr17:2	23	G/[T]	0.026	0.037	0.62	5.3e-06	rs749240	160	67/143/74	
SMC6	rs4523057	chr17:2	23	G/[T]	0.026	-0.042	0.62	0.0012	rs1885987	23	112/17/123	

Gene	RiskSNP	Pos	Dist (Kb)	Ref/Alt	aeQTL (est)	aeQTL txSNP (est)	aeQTL (pval)	aeQTL txSNP (pval)	Reads	Genogroup (ind)
SOX2, SOX2-OT	rs9841016	chr3:181	-291	[T]/A	-0.004	0.49	8.8e-26	rs73182316	610	39/188/49
STAT6	rs324017	chr12:57	-2	A/[C]	0.0074	0.11	0.25	rs4559	180	94/141/89
STAT6	rs324017	chr12:57	2	A/[C]	0.0074	0.055	0.25	rs524015	54	104/18/108
STAT6	rs324017	chr12:57	-2	A/[C]	0.0074	-0.032	0.25	rs703517	83	67/148/66
SUGP1	rs2905126	chr19:19	88	[G]/T	0.0074	0.079	0.25	rs1059513	35	18/60/16
TAOK2	rs12491307	chr16:30	-55	[A]/G	0.001	-0.03	0.93	rs1155053	240	60/86/57
TCF20	rs6002955	chr22:43	-6	C/[T]	-0.012	-0.1	0.81	rs3814833	280	95/56/12
TMEML10,	rs2535627	chr3:53	-23	[T]/C	-0.012	0.11	0.05	rs3403079	2.8	9/18/10
MUSTN1,TMEM110-								rs6787946	78	13/27/9
MUSTN1										
VPS45	rs140505388	chr1:150	-8	[C]/T	0.056	0.062	0.0018	rs2027349	5.2	18/39/21
WBPL1	rs1191419	chr10:105	38	[T]/A	-0.002	-0.034	0.00019	rs284858	46	103/110/105
WDR55	chr5_140143664_I	chr1:140	95	D/[I]	-0.0094	-0.1	0.14	rs59583033	9.6	31/26/11
AS3MT, BORCS7	rs5533108	chr10:105	118	G/[T]	-0.032	-0.13	0.14	rs00527	35	10/95/9
ATXN7	rs832187	chr13:64	-155	[C]/T	-0.004	-0.082	0.69	rs00056	46	40/45/27
BAG5	rs1288734	chr14:104	23	G/[T]	0.013	0.077	0.3	rs7693	210	21/73/25
C11orf31	rs9120	chr11:58	-19	[A]/G	0.0083	0.088	0.28	rs11570176	210	29/64/19
C11orf31	chr7_24747494_D	chr7:25	9	[I]/D	-0.056	-0.089	0.029	rs12975	39	22/43/18
DNNA5	rs10043984	chr5:138	27	C/[T]	0.022	0.077	0.056	rs26368	37	27/74/21
FA, M53C	rs2905126	chr19:19	111	[G]/T	0.038	0.093	0.022	rs6576223	39	20/45/24
HAPLN4	rs10043984	chr5:138	-190	C/[T]	0.047	0.042	0.42	rs1042665	4.00	33/88/29
HSPA9, SNORD63	rs3819046	chr5:138	-51	C/[T]	0.022	0.031	0.68	rs1042665	4.00	48/55/47
HSPA9, SNORD63	rs3819046	chr5:138	-41	C/[T]	0.022	-0.022	0.68	rs10117	380	61/52/60
KLC1	rs1288734	chr14:104	-49	G/[T]	-0.0028	0.19	0.8	rs1050850	27	7/55/10
LRP1	rs12820178	chr12:58	33	[G]/T	0.02	0.17	0.22	rs180154	110	5/180/5
PTPRF	rs1210892	chr1:44	13	[G]/A	0.0011	-0.073	0.9	rs1145702	160	57/63/60
RERE	chr1_84124984_D	chr1:8	12	[I]/D	0.0049	-0.053	0.55	rs1061826	68	42/21/55
SDCCAG8, MIR4677	rs10803138	chr1:244	61	A/[G]	-0.042	-0.11	0.0032	rs2275155	760	24/30/26
SEPT3	rs1023600	chr22:42	-52	[T]/C	0.003	0.067	0.65	rs701094	190	7/51/10
SF3B1	rs6134528	chr2:198	47	[G]/A	-0.0083	-0.027	0.13	rs4685	170	71/170
SOX2, SOX2-OT	rs9841016	chr3:181	-291	[T]/A	-0.007	0.24	0.45	rs7616347	89	5/12/7
SREBF2, MIR33A	rs1023600	chr22:42	64	[T]/C	-0.0057	-0.11	0.95	rs2229334	2900	14/53/15
STAT6	rs324017	chr12:57	-2	A/[C]	-0.028	-0.055	0.038	rs24015	19	36/5/36
TMEML10,	rs2535627	chr3:53	-27	[T]/C	-0.0055	-0.12	0.64	rs2878634	13	14/27/19
MUSTN1										
TOMM2	rs802890	chr17:18	210	[G]/A	-0.011	-0.043	0.026	rs4924822	66	68/43/74

Table S1-3: For DLPPC, similar to Table 1 in the main manuscript, but for individual txSNPs that were FDR5% significant.

Table S1-4: For Hippocampus, similar to Table 1 in the main manuscript, but for individual txSNPs that were FDR5% significant.

Gene	SNP	Pos	Dist (Kb)	Ref/Alt	Direction	aQTL	p-value	tssNPRReads	Individuals	Support per group
AS3MT, BORCS7	rs11191419	chr10:105	-2	T/A	up	3.1e-21	20	150	159/141/152	Ge,Ja,Re,Je,Js
APOPT1	rs12887734	chr14:104	0	G/T	down	2e-44	8	6300	126/64/116	Ge,Ja,Re,Js
ZMAT2	chr5_140143664_I	chr5:140	58	D/I	down	4e-22	2	250	162/36/143	Ge,Ja,Re,Js
HAPLN4	rs2905426	chr19:19	109	G/T	up	3.8e-19	12	230	103/163/106	Ge,Ja,Re,Js
CD46	rs7523273	chr1:208	8	A/G	up	5.4e-17	9	250	147/121/126	Ge,Ja,Re,Js
BRINP2	rs670165	chr1:177	29	C/T	down	1e-12	4	1600	84/375/93	Ge,Ja,Re,Js
NDUFA2	chr5_140143664_I	chr5:140	116	D/I	down	3e-12	2	77	134/85/107	Ge,Re
TOM1L2	rs1082590	chr17:18	186	G/A	down	3.8e-12	24	360	140/154/162	Ge,Ja,Re
FURIN	rs4702	chr15:91	0	G/A	down	5.3e-12	10	61	142/126/144	Ge,Ja,Re
ANP32E	rs140505938	chr1:150	-160	G/C	down	4.4e-10	8	680	49/312/56	Ge,Ja,Re
CKB	rs12887734	chr14:104	59	G/T	down	7.7e-19	3	8900	70/268/71	Ge
SPCS1	rs2335627	chr3:53	103	G/T/C	down	8e-09	3	240	120/135/104	Ge
SNX19	rs10791607	chr11:131	-28	T/G	up	1.6e-08	44	710	160/139/145	Ge,Ja,Re,Js
PTRRF	rs1210892	chr1:44	12	G/A	down	2.5e-07	17	1600	140/311/131	Ge
NEK4	rs2335627	chr3:53	40	T/C	up	4.8e-07	9	44	140/170/141	Ge,Ja,Re,Js
FAM57B	rs12691307	chr16:30	-96	A/G	up	6.6e-07	4	370	139/167/152	Ge,Ja,Re
LRP1	rs12826178	chr12:58	16	G/T	down	5.9e-06	32	150	25/455/23	Ge,Ja,Re
HSPH1, MOB4	rs6434928	chr2:198	-60	G/A	up	3.5e-05	9	51	127/149/151	Ge
HSPD1	rs6434928	chr2:198	-47	G/A	down	3.9e-05	6	280	142/211/125	Ge,Ja,Re
VPS45	rs140505938	chr1:50	-8	C/T	up	4.0e-05	5	120	20/30/24	Ge,Ja,Re,Js
PRMT7	rs8044995	chr16:08	-156	G/A	down	0.00027	9	520	86/288/103	Ge,a,Re,Ja,Js
ZFYVE21	rs12887734	chr14:104	-146	C/T	down	0.00034	7	420	1.18/255/103	Ge,Ja,Re,Js
FAM53C	rs10013984	chr5:138	27	C/T	down	0.00035	9	100	104/260/89	Ge,Ja,Re
AS3MT, BORCS7	rs53833108	chr10:105	80	G/T	down	6e-04	20	150	39/369/44	Ge,Ja,Re
IK, MIR3655	chr5_140143664_I	chr5:140	102	D/H	down	0.00066	5	160	96/130/81	Ge
CNL3	rs2335627	chr3:53	117	T/C	up	7e-04	9	410	153/167/144	Re
SNORD19, SNORD69, SNORD19B	rs12887734	chr14:104	-153	G/T	down	0.001	9	42	43/119/39	Ge
PPP1R13B	rs1339227	chr6:73	43	C/T	down	0.0012	21	420	130/365/108	Ge
RIMSL1	chr3_180594593_I	chr3:181	-107	D/I	up	0.0014	2	54	126/19/132	Ge
DNAJC19	rs12691307	chr16:30	66	G/A	down	0.0016	3	31	27/63/24	Ge
CDEPT	rs2905426	chr19:19	-98	G/T	down	0.0016	15	85	135/162/144	Ge,Ja,Re,Js
GATA2D	rs1685299	chr2:225	0	C/A	up	0.0018	24	820	96/217/96	Ge,Ja,Re
CUL3	rs7893279	chr10:19	-30	H/G	up	0.0023	2	23	39/241/31	Ge,Ja,Re

Table S1-5: For DLPC, similar to Table 1 in the main manuscript, but here all fetal samples were used

Gene	SNP	Pos	Dist (Kb)	Ref/Alt	Direction	aQTL	p-value	tssNPRReads	Individuals	Support per group
AS3MT, BORCS7	rs11191419	chr10:105	-2	T/A	up	2.2e-08	20	120	90/58/88	Ge,Ja,Re,Je,Js
ZMAT2	chr5_140143664_I	chr5:140	58	D/I	down	3.9e-09	2	180	97/34/78	Ge,Ja,Re,Je,Js
SNX19	rs10701097	chr11:131	-28	T/G	up	2e-07	44	970	98/212/90	Ge,Ja,Re,Je,Js
HSPD1	rs634928	chr2:198	-47	G/A	down	6.3e-06	6	380	73/157/71	Ge,Ja,Re,Je,Js
DNAJC19	chr3_180594593_I	chr3:181	-107	D/I	up	0.0015	2	37	79/21/64	Ge,Ja,Re,Je,Js
SDCTAG8	rs10803138	chr1:244	0	A/G	down	0.0022	4	730	54/148/54	Ge,Ja,Re,Je,Js

Table S1-6: For Hippocampus, similar to Table 1 in the main manuscript, but here all fetal samples were used