

Supporting Information

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SI Methods

Two-Tailed Testing. Our tensor-based morphometry results indicated that some brain regions were larger, with increased transferrin, and others were smaller. As this complex finding was not the initially expected result, we set out to ensure that both directional maps were, in fact, individually significant after multiple comparison correction on the entire single-direction map. To do this, we divided the brain map into two regions: one of all the voxels that showed a positive association and one of all the

voxels that showed a negative association. In each map, we then used a regional false discovery rate multiple comparison correction as before, at a false discovery rate correction threshold of 0.025, and both maps were still declared significant.

Subject Genotype Information for *HFE* Polymorphisms. For the H63D polymorphism (rs1799945), 22 subjects were homozygous for the minor G allele, 357 were homozygous for the major C allele, and 130 were heterozygous.

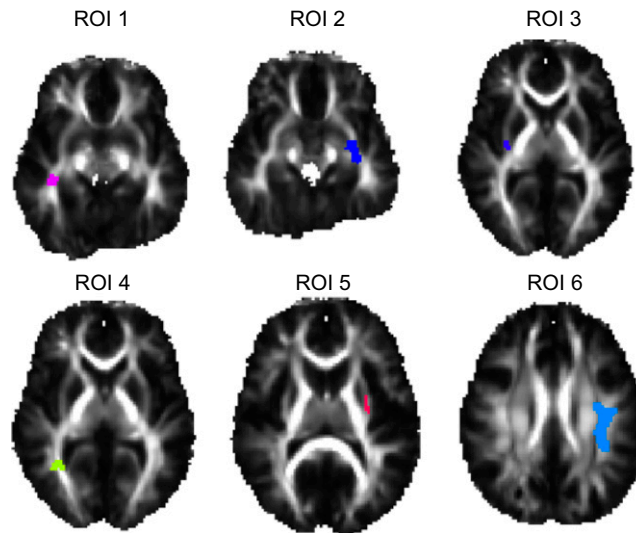


Fig. S1. Regions of interest for which genetic analyses were performed. Neighboring voxels found to have a significant cross-twin cross-trait correlation between FA and transferrin levels were clustered together into regions of interest at least 27 voxels in size.

Table S1. TF and HFE SNPs (n = 42) used for genetic associations with FA regions of interest, along with the minor allele frequency and the results of association for each of the six valid regions of interest

SNP	Gene	Allele	MAF	ROI 1		ROI 2		ROI 3		ROI 4		ROI 5		ROI 6	
				β -Value	P value	β -Value	P value	β -Value	P value	β -Value	P value	β -Value	P value	β -Value	P value
rs1130459	TF	A	0.415	-0.00223	0.22748	-0.00132	0.44226	-0.00110	0.46677	0.00019	0.91795	-0.00019	0.89086	-0.00070	0.70478
rs4459901	TF	C	0.323	-0.00070	0.74383	0.00054	0.78460	-0.00025	0.88603	-0.00152	0.47260	-0.00068	0.56178	0.00040	0.85001
rs4428180	TF	G	0.150	0.00553	0.05249	0.00110	0.67748	0.00300	0.19821	0.00026	0.92715	0.00102	0.62348	0.00280	0.32227
rs12493168	TF	G	0.150	0.00014	0.95997	-0.00105	0.68096	-0.00174	0.43912	0.00124	0.65049	-0.00004	0.98425	-0.00013	0.96171
rs8177190	TF	T	0.146	0.00300	0.36121	0.00205	0.50116	0.00304	0.25705	-0.00244	0.45250	0.00289	0.22826	0.00255	0.43272
rs8177191	TF	A	0.155	-0.00132	0.59484	-0.00437	0.05865	-0.00356	0.07995	-0.00319	0.19945	-0.00182	0.31781	-0.00317	0.19900
rs8177197	TF	A	0.336	-0.00008	0.96932	0.00023	0.90795	0.00001	0.99519	-0.00082	0.69634	-0.00082	0.59134	0.00077	0.71239
rs8177201	TF	C	0.137	0.00220	0.51036	0.00139	0.65350	0.00139	0.33770	-0.00189	0.56813	0.00277	0.25604	0.00156	0.63719
rs9880615	TF	G	0.169	0.00220	0.51036	0.00139	0.65350	0.00262	0.33770	-0.00189	0.56813	0.00277	0.25604	0.00156	0.63719
rs8177213	TF	C	0.292	-0.00008	0.96984	-0.00275	0.17382	-0.00161	0.36452	-0.00324	0.13495	-0.00021	0.89356	-0.00176	0.41470
rs4854759	TF	G	0.164	0.00220	0.51036	0.00139	0.65350	0.00262	0.33770	-0.00189	0.56813	0.00277	0.25604	0.00156	0.63719
rs4241357	TF	T	0.425	0.00054	0.77659	0.00098	0.58116	0.00004	0.98166	-0.00052	0.78599	-0.00129	0.35664	0.00144	0.44824
rs1799852	TF	T	0.075	0.00003	0.99342	0.00293	0.45770	0.00014	0.96712	0.00418	0.32031	0.00026	0.93337	0.00128	0.75988
rs3811658	TF	T	0.367	0.00037	0.85740	0.00088	0.64904	0.00049	0.77090	-0.00119	0.56505	-0.00129	0.39503	0.00028	0.89156
rs8177240	TF	G	0.346	0.00057	0.78636	0.00138	0.48296	0.00049	0.77675	-0.00120	0.56963	-0.00130	0.39836	0.00031	0.88288
rs8177252	TF	A	0.346	0.00057	0.78636	0.00138	0.48296	0.00049	0.77675	-0.00120	0.56963	-0.00130	0.39836	0.00031	0.88288
rs8177272	TF	A	0.358	0.00057	0.78636	0.00138	0.48296	0.00049	0.77675	-0.00120	0.56963	-0.00130	0.39836	0.00031	0.88288
rs2715631	TF	G	0.248	0.00041	0.85088	0.00134	0.50895	0.00242	0.17190	0.00393	0.06983	0.00264	0.09619	0.00111	0.60652
rs1880669	TF	T	0.394	-0.00084	0.67087	-0.00232	0.20779	-0.00244	0.13114	-0.00220	0.26540	-0.00104	0.47113	-0.00119	0.54390
rs3811647	TF	A	0.358	0.00057	0.78636	0.00138	0.48296	0.00049	0.77675	-0.00120	0.56963	-0.00130	0.39836	0.00031	0.88288
rs1358024	TF	T	0.177	-0.00163	0.52850	-0.00008	0.97515	-0.00035	0.87006	-0.00423	0.10219	-0.00249	0.18919	-0.00283	0.27092
rs1525892	TF	A	0.365	0.00057	0.78636	0.00138	0.48296	0.00049	0.77675	-0.00120	0.56963	-0.00130	0.39836	0.00031	0.88288
rs8177277	TF	C	0.093	0.00493	0.17634	0.00366	0.27786	0.00473	0.11113	0.00056	0.87743	0.00428	0.10716	0.00540	0.13325
rs2692695	TF	A	0.394	-0.00084	0.67087	-0.00232	0.20779	-0.00244	0.13114	-0.00220	0.26540	-0.00104	0.47113	-0.00119	0.54390
rs2715632	TF	T	0.248	0.00041	0.85088	0.00134	0.50895	0.00242	0.17190	0.00393	0.06983	0.00264	0.09619	0.00111	0.60652
rs2718806	TF	A	0.250	0.00037	0.86172	0.00068	0.73258	0.00226	0.19278	0.00393	0.06384	0.00194	0.21068	0.00097	0.64468
rs8649	TF	C	0.238	0.00041	0.85088	0.00134	0.50895	0.00242	0.17190	0.00393	0.06983	0.00264	0.09619	0.00111	0.60652
rs1358022	TF	G	0.248	0.00072	0.74117	0.00148	0.46619	0.00265	0.13702	0.00445	0.04116	0.00296	0.06338	0.00154	0.47835
rs1525890	TF	A	0.238	0.00072	0.74117	0.00148	0.46619	0.00265	0.13702	0.00445	0.04116	0.00296	0.06338	0.00154	0.47835
rs1525889	TF	C	0.363	0.00028	0.89284	0.00126	0.52223	0.00030	0.86099	-0.00164	0.43636	-0.00158	0.30709	-0.00008	0.97067
rs9824452	TF	A	0.155	-0.00003	0.99215	0.00030	0.90866	0.00024	0.91547	-0.00051	0.85433	0.00184	0.37032	0.00114	0.68163
rs1049296	TF	T	0.137	0.00307	0.23923	-0.00014	0.95291	-0.00063	0.76616	0.00017	0.94833	0.00153	0.42358	0.00018	0.94313
rs2715627	TF	C	0.248	0.00072	0.74117	0.00148	0.46619	0.00265	0.13702	0.00445	0.04116	0.00296	0.06338	0.00154	0.47835
rs1115219	TF	C	0.248	0.00072	0.74117	0.00148	0.46619	0.00265	0.13702	0.00445	0.04116	0.00296	0.06338	0.00154	0.47835
rs7638018	TF	G	0.363	0.00028	0.89284	0.00126	0.52223	0.00030	0.86099	-0.00164	0.43636	-0.00158	0.30709	-0.00008	0.97067
rs12595	TF	C	0.357	0.00028	0.89284	0.00126	0.52223	0.00030	0.86099	-0.00164	0.43636	-0.00158	0.30709	-0.00008	0.97067
rs2794719	HFE	C	0.405	-0.00116	0.55297	0.00163	0.37018	-0.00094	0.55618	0.00114	0.55737	0.00111	0.43745	0.00090	0.64122
rs1799945*	HFE	G	0.182	0.00234	0.34332	0.00697	0.00227	0.00301	0.13513	0.00424	0.08374	0.00675	0.00017	0.00366	0.13350
rs2071303	HFE	G	0.364	0.00233	0.37932	0.00410	0.04032	0.00178	0.31286	0.00423	0.04872	0.00501	0.00140	0.00252	0.23824
rs1800562	HFE	C	0.074	0.00604	0.12310	0.00765	0.03542	0.00316	0.32466	0.00014	0.97211	0.00148	0.60529	0.00994	0.01021
rs2858996	HFE	T	0.195	0.00078	0.86189	-0.00198	0.63617	-0.00261	0.47588	0.00208	0.64305	-0.00009	0.97805	-0.00500	0.26051
rs1572982	HFE	A	0.450	-0.00282	0.19515	-0.00288	0.15400	-0.00364	0.04051	-0.00200	0.35585	-0.00368	0.02057	-0.00082	0.70417

As a result of linkage disequilibrium, effectively 20 SNPs were tested. MAF, minor allele frequency. ROI, region of interest.

*After Bonferroni correction for the 120 tests performed ($P < 0.00042$), rs1799945, or the H63D polymorphism in the HFE gene, was significantly associated with the mean FA value in ROI 5, portions of the left external capsule ($P = 0.00017$).