

## Supplemental Material

**Supplemental Table S1.** The association of IR on MWF in brain regions in subsample (n=121)

Region	Coordinates (millimeters)	T-Value	Observed extent threshold	Cluster level p- value
<b>IR positive direction cluster data</b>				
Inferior portion of anterior cingulate	0, 36, -12	4.76	433	.006
Right inferior temporal gyrus	32, 14, -40	4.31	1071	.000
Right superior temporal region	48, -6, -16	4.10	599	.002

Extent threshold (k) = 174 voxels,  $p < .005$ , uncorrected for positive and negative directional multiple regression analyses. All voxel-level p-values were  $p < .005$ .

Abbreviations: MWF = myelin water fraction; IR = insulin resistance.

**Supplemental Table S2.** The association of insulin on MWF in brain regions in subsample (n=121)

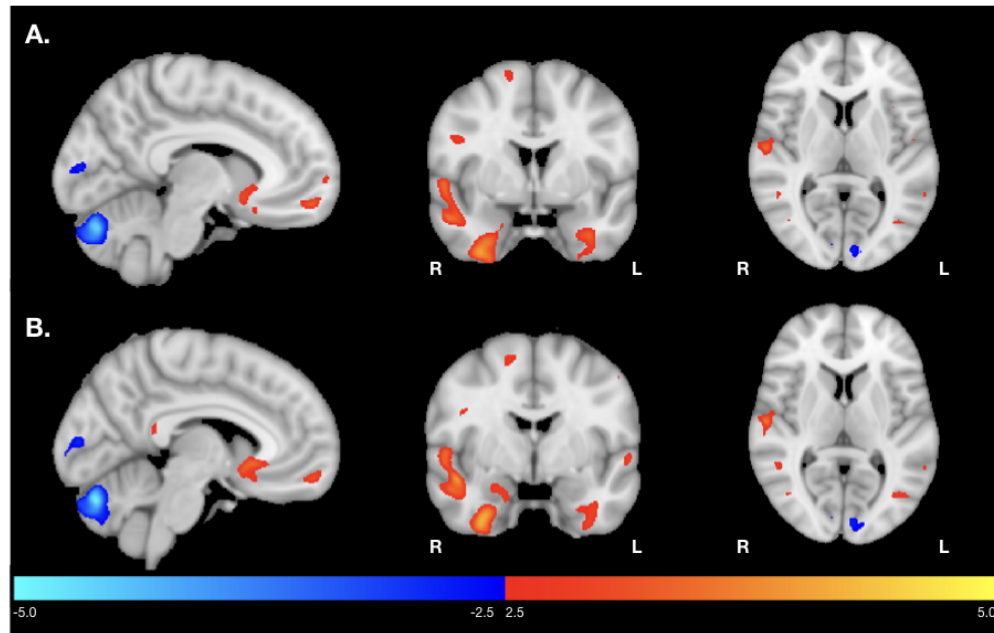
Region	Coordinates (millimeters)	T-Value	Observed extent threshold	Cluster level p- value
<b>Insulin positive direction cluster data</b>				
Inferior portion of the anterior cingulate	0, 36, -12	4.88	675	.001
Right hippocampal region	28, -10, -22	4.54	1931	.000
Left fusiform gyral area	-32, 2, -34	3.61	248	.028

Extent threshold (k) = 174 voxels,  $p < .005$ , uncorrected for positive and negative directional multiple regression analyses. All voxel-level p-values were  $p < .005$ .

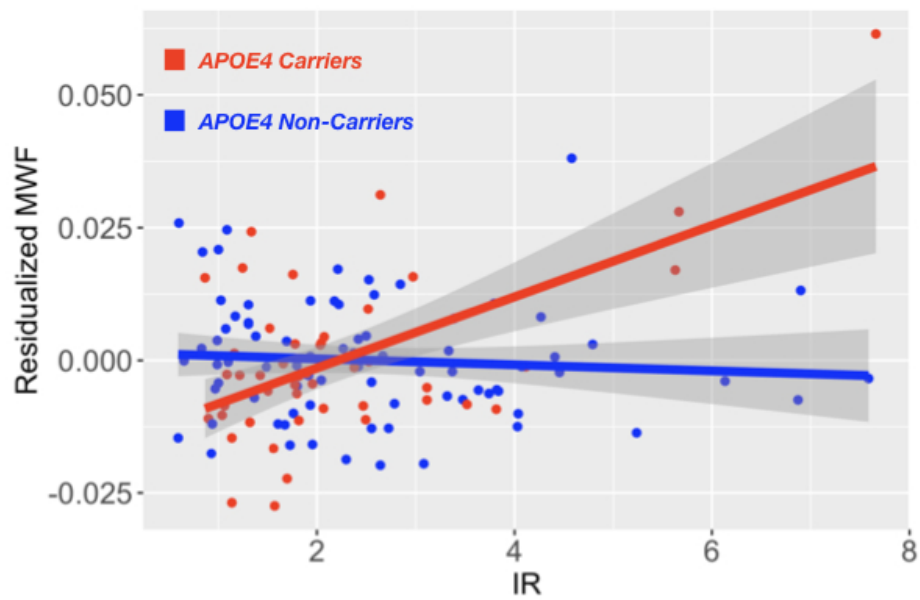
Abbreviation: MWF = myelin water fraction.

**Supplemental Figure S1:** Multi-slice rendering of voxelwise associations between MWF and A) Insulin and B) HOMA-IR performed in subset of non-outliers (n=121). T-statistics are displayed. Similar relationships between MWF and Insulin and HOMA-IR are observed, compared to analyses of full sample, however, the main effects in the negative direction (blue) appear to be attenuated.

**Supplemental Figure S2:** Multi-slice rendering of voxelwise APOE4 x IR interaction on MWF. T-statistics are displayed. While not surviving correction for multiple comparison, a cluster spanning the middle frontal and precentral gyri was observed, such that the association between HOMA-IR and MWF differed in APOE4 carriers and non-carriers. The mean MWF vs. HOMA-IR for APOE4 carriers and non-carriers is displayed in the corresponding scatter plot.



Supplemental Figure 1: Multi-slice rendering of voxelwise associations between MWF and A) Insulin and B) HOMA-IR performed in subset of non-outliers (n=121). T-statistics are displayed. Similar relationships between MWF and Insulin and HOMA-IR are observed, compared to analyses of full sample, however, the main effects in the negative direction (blue) appear to be attenuated.



Supplemental Figure 2: Multi-slice rendering of voxelwise APOE4 x IR interaction on MWF. T-statistics are displayed. While not surviving correction for multiple comparison, a cluster spanning the middle frontal and precentral gyri was observed, such that the association between HOMA-IR and MWF differed in APOE4 carriers and non-carriers. The mean MWF vs. HOMA-IR for APOE4 carriers and non-carriers is displayed in the corresponding scatter plot.