

Social network diversity predicts white matter microstructural integrity in humans



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Background

In rodents, reduced social contact is associated with decreased myelin integrity (Liu et al, 2012) and this relationship is mediated by increased activation of inflammatory pathways (Hermes et al, 2005). While pathophysiological inflammation is known to affect myelin integrity in primates (Hauser & Oksenberg, 2006), this relationship between characteristics of social network and white matter integrity has yet to be demonstrated in humans.

Hypothesis

More diverse and larger social networks will be associated with increased white matter integrity. This relationship will be associated with decreased levels of inflammatory activity.

Methods

Participants

Neurologically healthy adults (N=155; mean age = 40.7) were recruited via mass mailings to residents of Allegheny County, PA. All testing was approved by the local IRB.

Participant Characteristics

Demographics	
Men	78
Women	77
Age	30 - 50
Anthropometric Factors	
Body Mass Index (BMI)	18.48 - 42.32
Waist Circumference	25.5 - 47
Diastolic Blood Pressure (DBP)	54.25 - 99.75
Systolic Blood Pressure (SBP)	95.75 - 143.5
Psychosocial Factors	
SNI (Div)	2 - 12
SNI (#)	5 - 50
Smoking	0 - 1
Sleep quality (PSQI)	0 - 14
Income	13.57 - 61.38**
Years of Education	11 - 24
Positive Affect (PANAS)	1.9 - 5
Negative Affect (PANAS)	1 - 3.4
Biometabolites	
Glucose	45 - 169
Interleukin 6 (IL-6)	0 - 29.5 *
C-reactive protein (CRP)	-3.91 - 1.3 *
Low-density lipoprotein (LDL)	55 - 214
High-density lipoprotein (HDL)	22 - 126
Triglycerides	21 - 341

*log transformed

**adjusted and normalized

Imaging Acquisition Parameters

Siemens Trio MRI (Siemens Inc., USA) located at the Magnetic Resonance Research Center at the University of Pittsburgh Medical Center.

Diffusion Tensor Imaging (DTI): 30-directions, 3mm isotropic voxels, 43 slices, TR = 5800 ms, TE = 91ms.

White Matter Integrity Measures

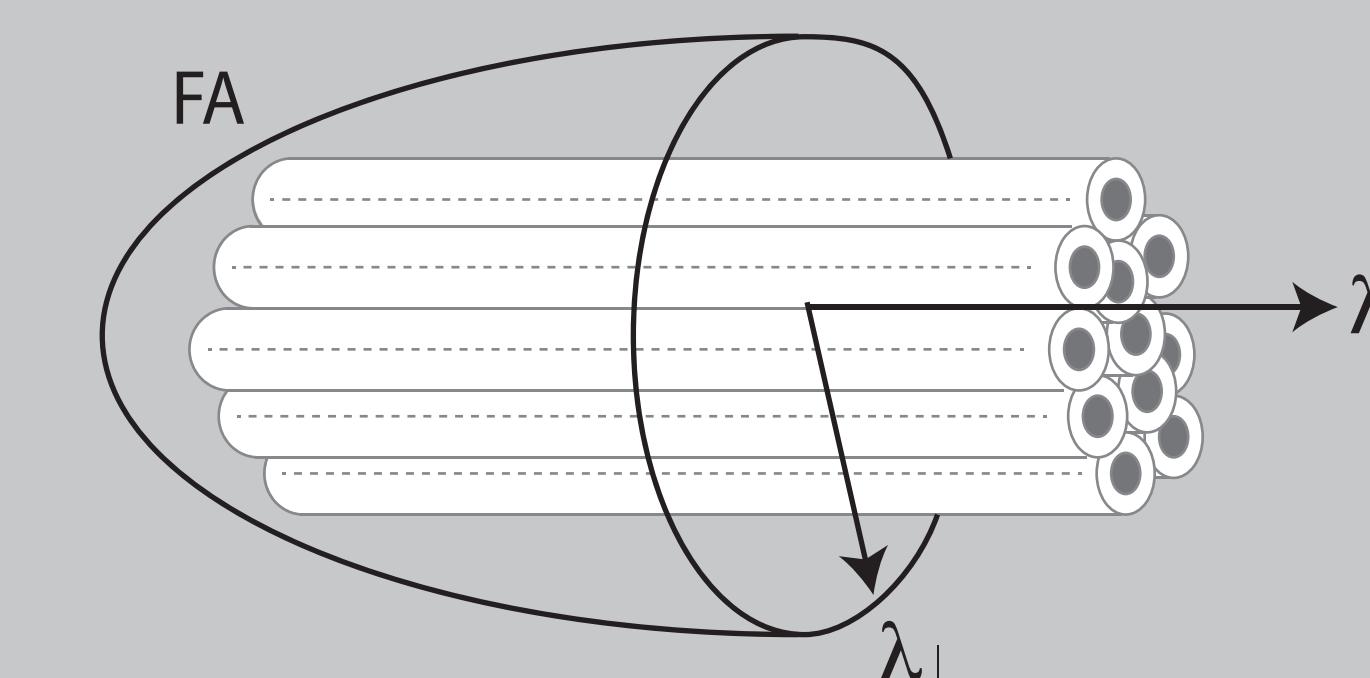
Fractional Anisotropy (FA): Degree of anisotropy of underlying water diffusion.

$$FA = \frac{\sqrt{3} \sqrt{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

Axial Diffusivity (λ_{\parallel}): Strength of water diffusion in principle anisotropy direction.

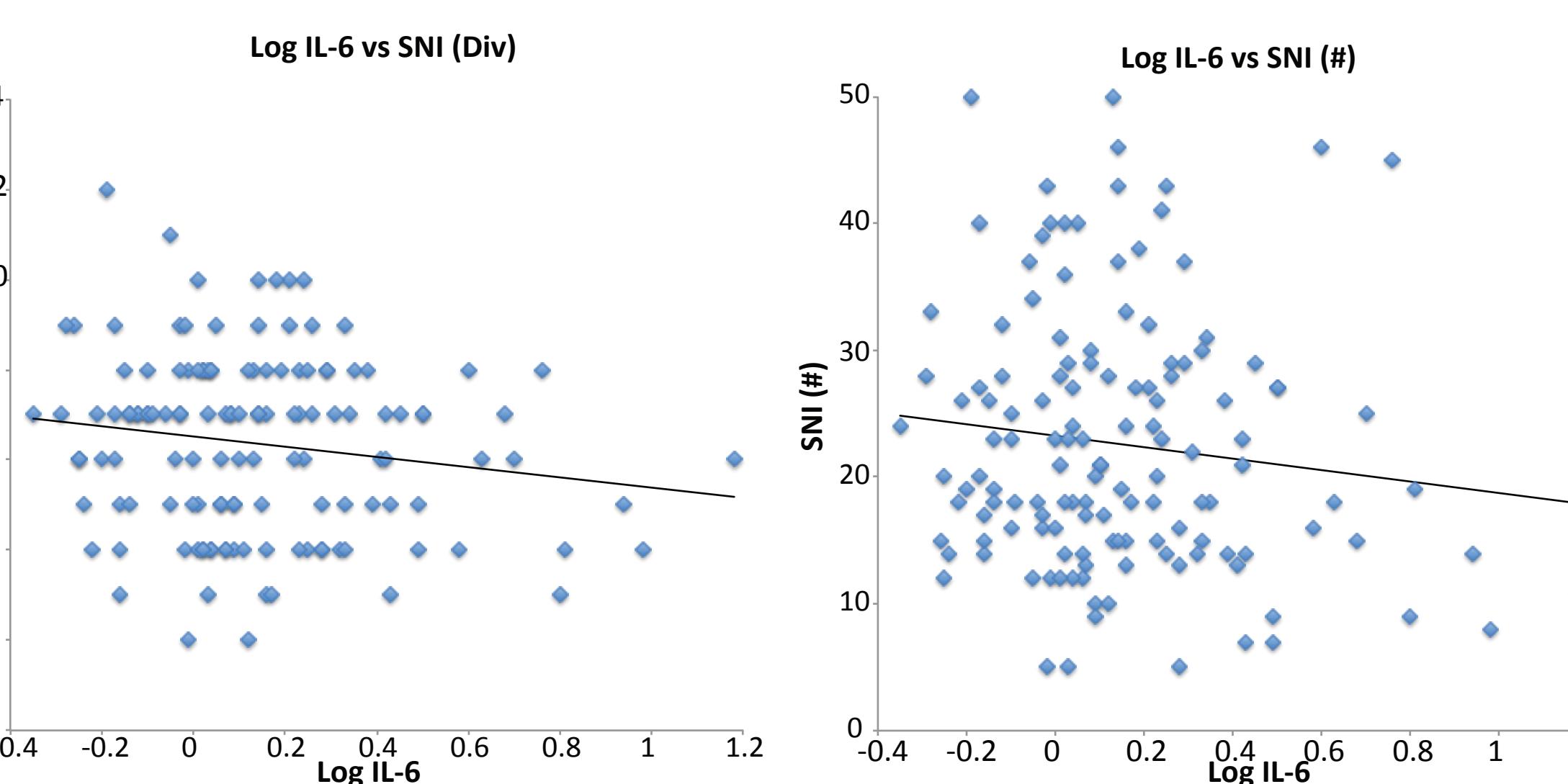
Radial Diffusivity (λ_{\perp}): Strength of water diffusion in the orthogonal plane to principle anisotropy direction.

$$\lambda_{\perp} = \lambda_2 + \lambda_3 / 2$$

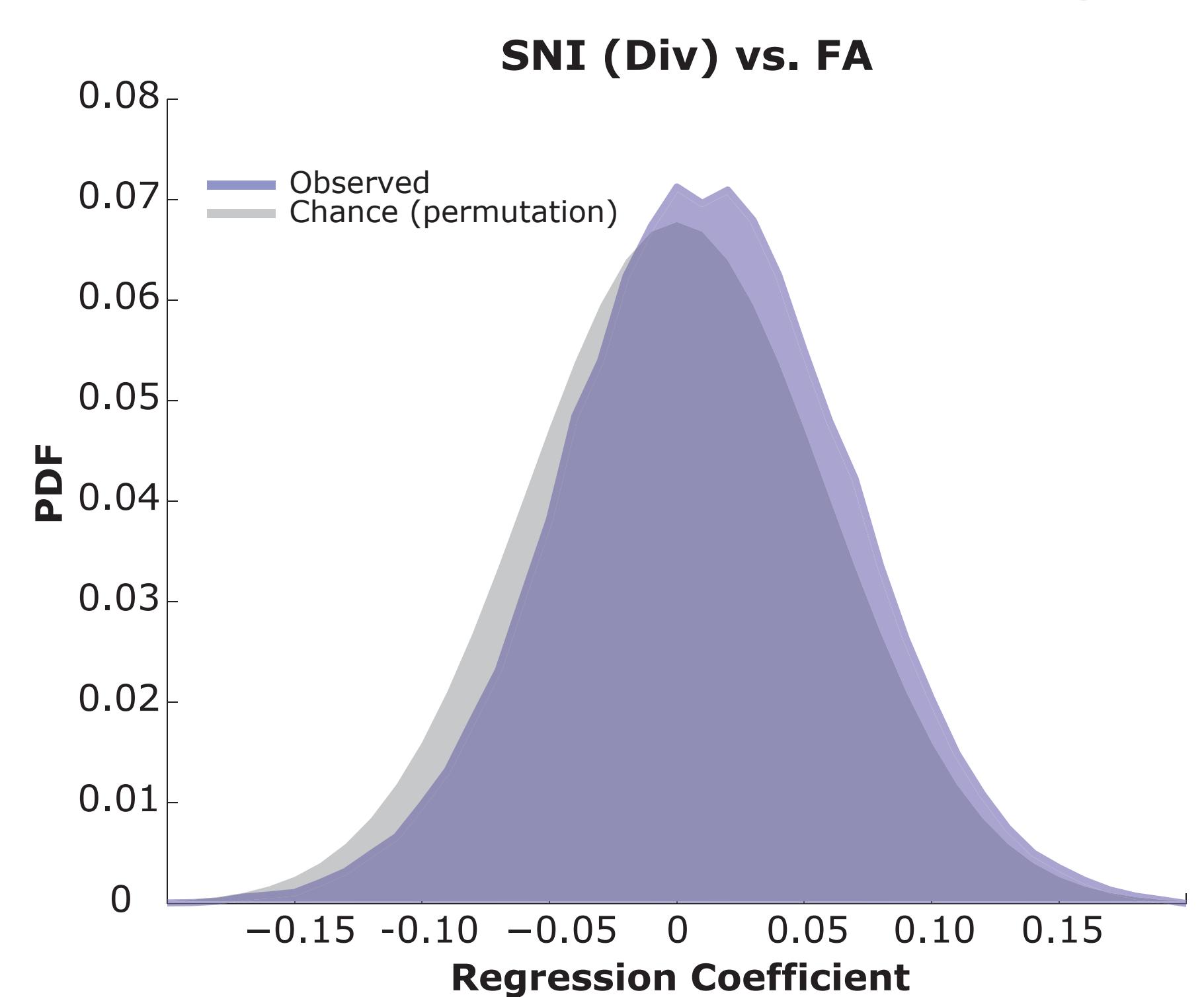


Inflammation and SNI

IL-6 was negatively associated with SNI (Div) ($r(128) = -0.194$, $p = 0.027$), but not SNI Size ($r(128) = -0.088$, $p = 0.319$), after controlling for age, sex, waist circumference, and years of education. These relationships to SNI were trending but not significant for CRP (Div: $r(137) = 0.04$, $p = 0.638$; Size: $r(137) = 0.125$, $p = 0.144$).

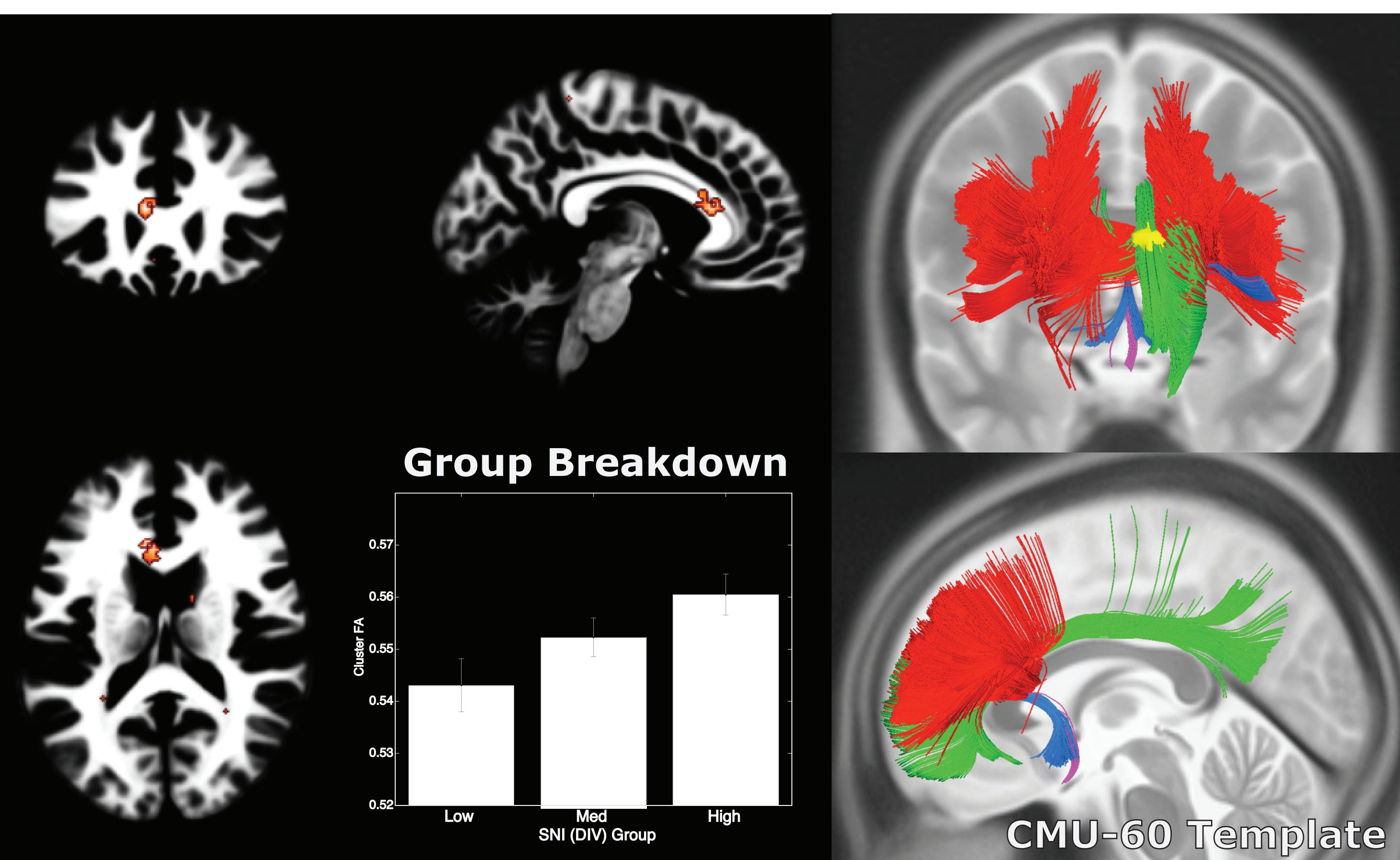


SNI associations with FA



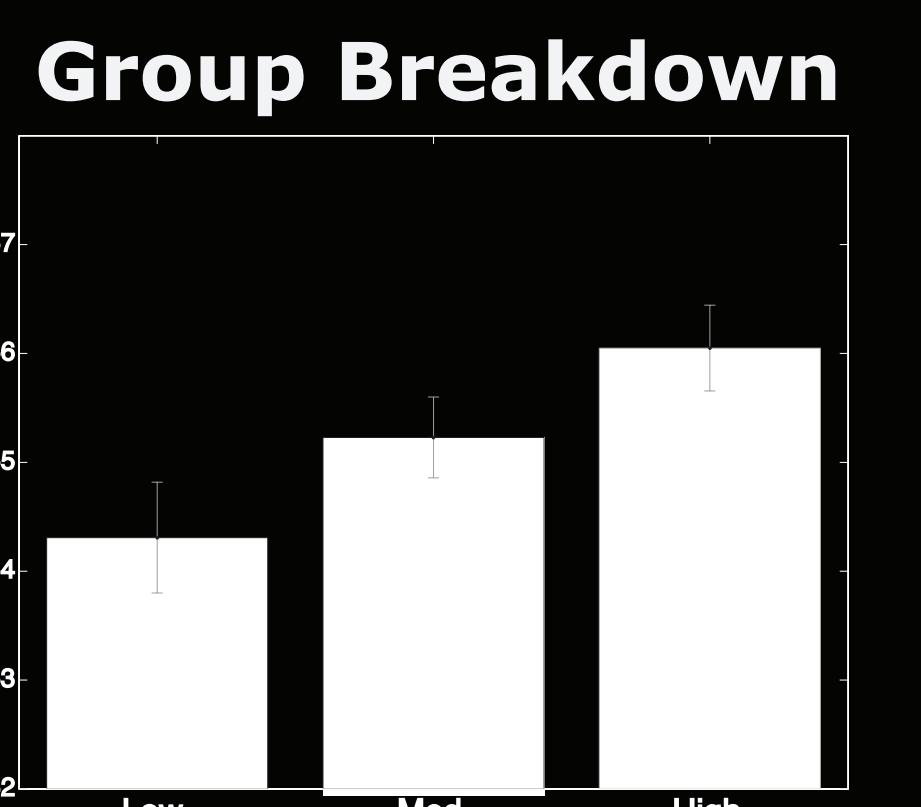
Across all white matter voxels there was a predominantly positive association between FA and SNI (Div). No such pattern was seen for size of a social network (not shown).

Significant Cluster



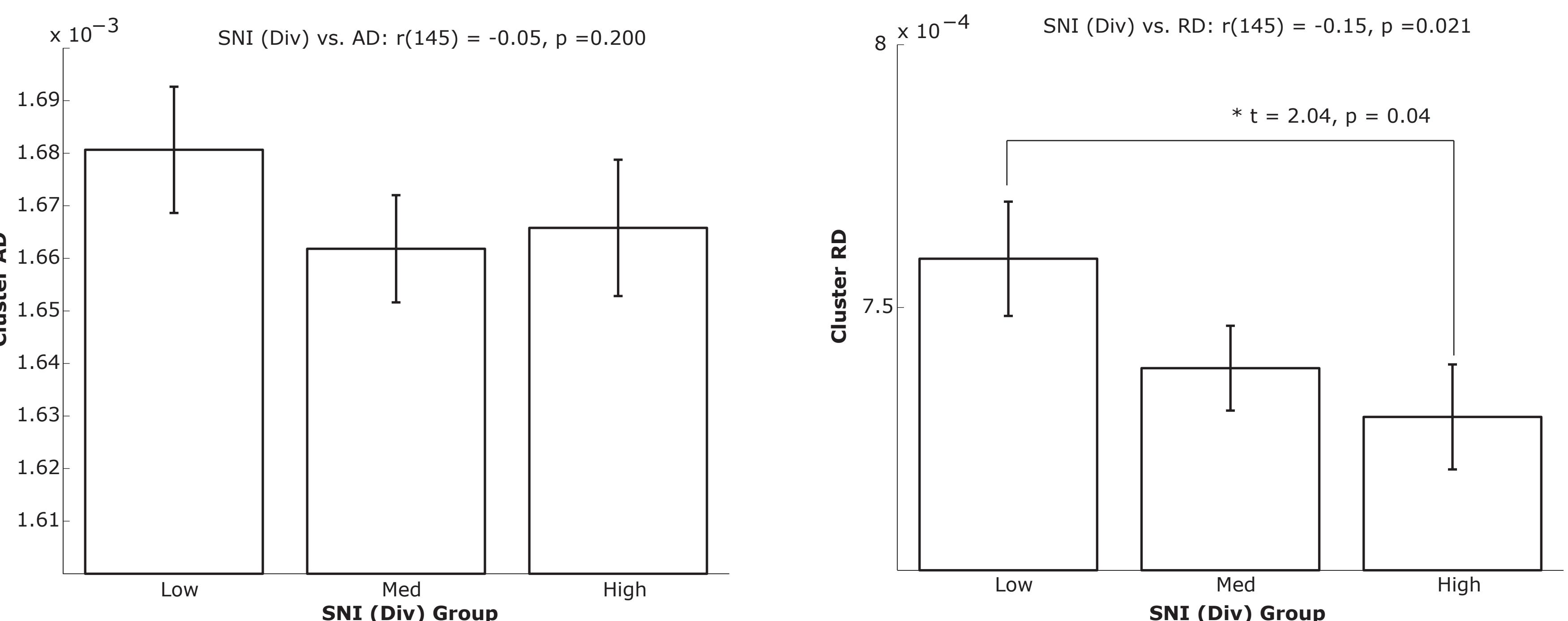
The SNI (Div) and FA association was strongest in a cluster near the genu of the corpus callosum (FDR < 0.05 , $k > 40$). This included fibers connecting the left and right dorsolateral prefrontal cortices (red fibers), areas of the cingulum (green fibers), and frontal subcortical projections to the nucleus accumbens (blue fibers) and hypothalamus (purple fibers).

Fiber Bundles



CMU-60 Template

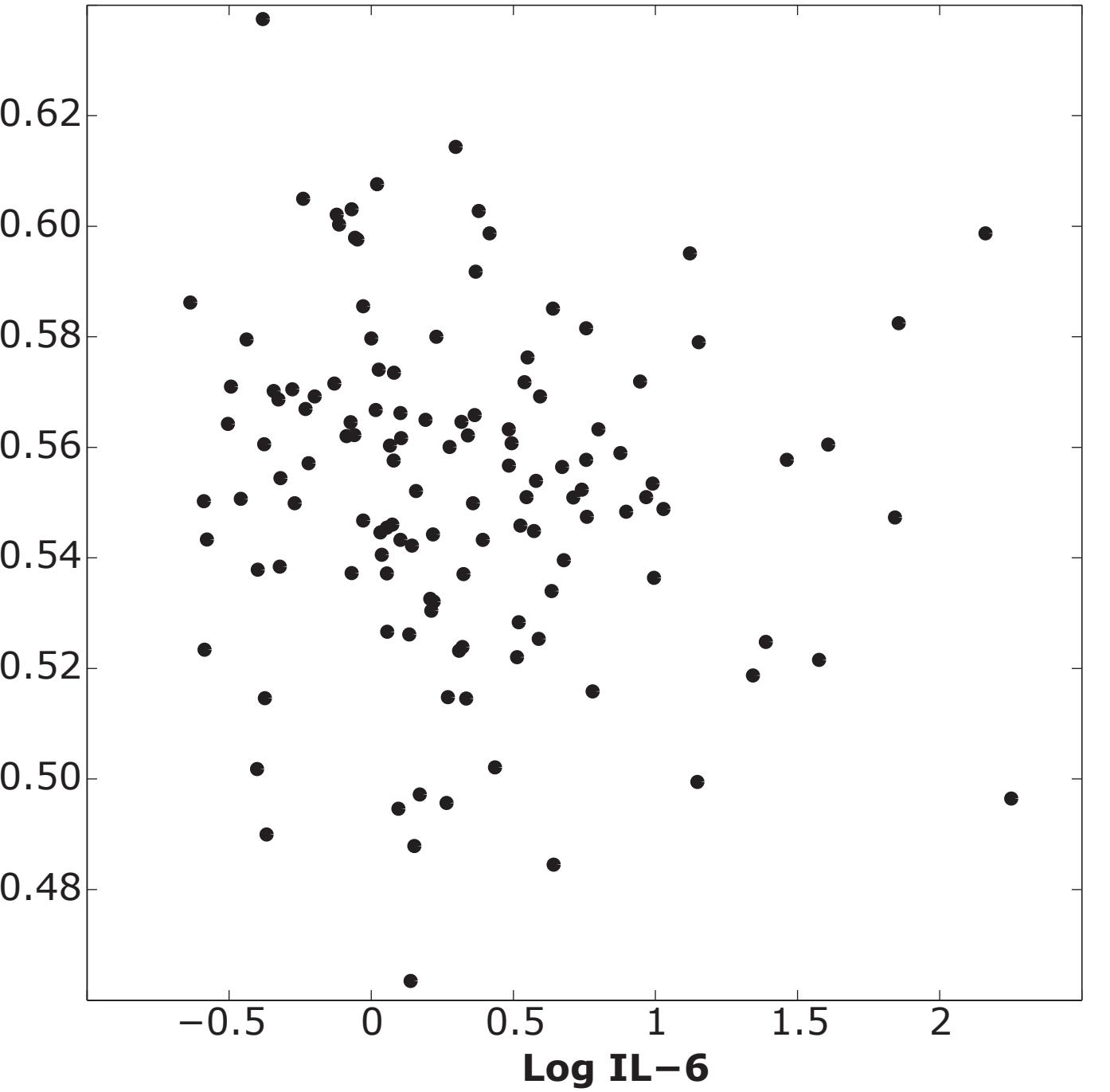
SNI and components of FA



Within the significant cluster, SNI (Div)-related differences in FA appeared to be driven by differences in the radial component of the DTI signal.

IL-6 and FA

Within the significant cluster, we found a simple correlation between FA and circulating levels of IL-6 ($r(126) = -0.14$, $p = 0.017$). The correlation with CRP was trending, but not significant ($r(135) = -0.12$, $p = 0.084$).



Potential mediating pathways

Overall, we were unable to find any factors that served as indirect mediators of the relationship between SNI (Div) and FA within the significant cluster, after controlling for age and sex.

Associations with cluster FA

	β	t	p
<i>Anthropometric Factors</i>			
Waist Circumference	-0.132	-1.613	0.109
DBP	-0.083	-1.023	0.308
SBP	-0.076	-0.929	0.354
<i>Psychosocial Factors</i>			
Smoking	-0.133	-1.601	0.112
Sleep quality	-0.114	-1.354	0.178
Income	0.093	1.118	0.266
Years of Education	0.047	0.571	0.569
Positive Affect (PANAS)	0.068	0.802	0.424
Negative Affect	0.086	1.006	0.316
<i>Biometabolites</i>			
Glucose (log)	-0.025	-0.302	0.763
IL-6 (log)	-0.111	-1.227	0.222
CRP (log)	-0.088	-1.031	0.304
LDL	-0.245	-3.107	0.002*
HDL	-0.002	-0.024	0.981
Triglycerides (log)	-0.067	-0.795	0.428

* p < 0.05, not correlated with SNI (Div)

Summary

- The diversity of a person's social network positively correlated with the microstructural integrity of white matter pathways in the brain, particularly in fibers connecting frontal areas.
- Patterns of white matter differences with social network diversity resembled patterns consistent with variation in myelin integrity.
- While inflammation was not a significant mediator, white matter integrity negatively correlated with levels of systemic inflammation.
- Future longitudinal studies, with larger sample sizes, are needed to determine whether changes in inflammation may mediate the relationship between social contact and white matter integrity.

References

- Liu, J, Dietz, K, DeLooyt, JM, Pedre, X, et al (2012). Impaired adult myelination in the prefrontal cortex of socially isolated mice. *Nature Neuroscience*, 15, 1621-3.
- Hermes, GL, Rosenthal, L, Montag, A, McClintock, MK (2005). Social isolation and the inflammatory response: sex differences in the enduring effects of a prior stressor. *Am J Physiol Regul Integr Comp Physiol*, 290, 273-82.
- Hauser, SL, Oksenberg, JR (2006). The neurobiology of multiple sclerosis: Genes, inflammation, and neurodegeneration. *Neuron*, 52, 61-76.