Supplementary Material

Title
Brain network modularity predicts cognitive training-related gains in young adults

Abbreviated Title
Network predictors of training gain

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3.2.1 Baseline brain modularity and training-related gain

Correlations using the Power partition

	2%	4%	6%	8%	10%
Brain modularity vs. training-related gain	R=.178, p=.073	R=.205, p=.047	R=.197 P=.054	R=.198, p=.052	R=.189, p=.061

Multiple regression analysis using other cost thresholds for spectral-derived modularity

	Spectral: 4%		Spectral: 8%	
	B	*p*	*B*	*p*
Intercept	0.017	0.790	0.020	0.759
Group	0.374	<.001	0.377	<.001
Modularity	-1.337	0.106	-1.746	0.071
Group x Modularity	3.277	0.009	3.751	0.014

Multiple regression analysis for the Power partition

	Power: 6%		Power: Mean (2-10%)	
	B	*p*	*B*	*p*
Intercept	0.023	0.720	0.228	0.724
Group	0.377	<.001	0.377	<.001
Modularity	-2.331	0.090	-1.942	0.137
Group x Modularity	4.789	0.020	4.284	0.033

3.2.2 Baseline brain modularity, baseline cognition, and training-related gain

Correlations using the spectral-derived partition

	2%	4%	6%	8%	10%
Brain modularity vs. baseline Gf (all)	R=-.071, p=.402	R=-.102, p=.226	R=-.074, p=.381	R=-.081, p=.339	R=-.067, p=.426
Baseline modularity vs. baseline performance (all)	R=-.118, p=.162	R=-.158, p=.060	R=-.133, p=.113	R=-.087, p=.304	R=-.086, p=.309
Baseline modularity vs. training gain, c. baseline Gf (WM-REAS)*	R=.106, p=.197	R=.237, p=.027	R=.236, p=.027	R=.181, p=.071	R=.198, p=.054
Baseline modularity vs. training gain, c. baseline performance (WM-REAS)*	R=-.070, p=.287	R=.036, p=.385	R=.038, p=.379	R=.010, p=.469	R=.026, p=.417

*Note. * denote one-tailed tests for follow-up analyses*

Correlations using the Power partition

	2%	4%	6%	8%	10%
Brain modularity vs. baseline Gf (all groups)	R=-.096, p=.256	R=-.137, p=.103	R=-.141, p=.093	R=-.140, p=.096	R=-.130, p=.121
Baseline modularity vs. baseline performance (all groups)	R=-.135, p=.108	R=-.126, p=.133	R=-.107, p=.205	R=-.098, p=.244	R=-.091, p=.280
Baseline modularity vs. training gain, c. baseline Gf (WM-REAS)*	R=.147, p=.118	R=.164, p=.093	R=.151, p=.112	R=.150, p=.113	R=.141, p=.128
Baseline modularity vs. training gain, c. baseline performance (WM-REAS)*	R=.026, p=.416	R=.037, p=.382	R=.019, p=.439	R=.012, p=.462	R=-.003, p=.490

*Note. * denote one-tailed tests for follow-up analyses*

Multiple regression analysis using other cost thresholds for spectral-derived modularity

	Spectral: 4%		Spectral: 8%+	
	B	*p*	*B*	*p*
Intercept	0.396	<.001	0.395	<.001
Baseline Gf	-0.253	0.010	-0.239	0.017
Modularity	1.474	0.115	1.437	0.224
Baseline Gf x Modularity	-1.141	0.259	-1.074	0.440

	Spectral: 4%		Spectral: 8%+	
	B	*p*	*B*	*p*
Intercept	0.349	<.001	0.369	<.001
Baseline Perf	-0.432	<.001	-0.491	<.001
Modularity	0.660	0.385	0.267	0.774
Baseline Perf x Modularity	-3.038	0.019	-2.511	0.100

Multiple regression analysis for the Power partition

	Power: 6%		Power: Mean (2-10%)	
	B	*p*	*B*	*p*
Intercept	0.385	<.001	0.388	<.001
Baseline Gf	-0.250	0.012	-0.252	0.012
Modularity	1.439	0.341	1.465	0.318
Baseline Gf x Modularity	-2.733	0.150	-2.422	0.184

	Power: 6%		Power: Mean (2-10%)	
	B	*p*	*B*	*p*
Intercept	0.372	<.001	0.372	<.001
Baseline Perf	-0.471	<.001	-0.468	<.001
Modularity	0.586	0.631	0.556	0.640
Baseline Perf x Modularity	-3.254	0.109	-3.312	0.107

3.2.4. Controlling for in-scanner motion

As in-scanner motion can spuriously affect functional connectivity estimates (Power et al., 2012; Satterthwaite et al., 2012; Van Dijk et al., 2012; Satterthwaite et al., 2013), we confirmed that the relationship between baseline modularity and training-related gains was not due to motion.

Controlling for mean FD. In both groups, controlling for mean FD in the correlation analyses and including it as a predictor in the regression analyses did not substantially change the relationship between baseline modularity and training gain, even when factoring in baseline Gf and baseline performance (see below). Also, controlling for mean FD did not alter the findings in the association network and segregation analyses.

Baseline modularity: Controlling for mean FD did not substantially change the relationship between baseline modularity and training gain in the WM-REAS group (6% cost: $rp(65)=0.230$, $p=0.030$, one-tailed, BCa 95% CI [-0.040 0.459]) or the control group (6% cost: $rp(72)=-0.196$, $p=0.048$, one-tailed, BCa 95% CI [-0.351 -0.024]). Moreover, adding mean FD as a predictor in the regression analysis with training group, modularity, and an interaction term of training group and modularity did not significantly improve model fit (6% cost: $p(\Delta F)=0.480$).

Baseline modularity and baseline Gf: Including mean FD in the regression analysis did not improve model fit (6% cost: $p(\Delta F)=0.420$).

Baseline modularity and baseline performance: Including mean FD in the regression analyses did not improve model fit (6% cost: $p(\Delta F)=0.986$).

Association network and segregation analyses: Controlling for mean FD resulted in similar findings: training gain and association modularity $rp(65)=0.187$, $p=.065$, BCa 95% ci [-0.035, 0.394]; training gain and DMN modularity ($rp(65)=0.229$, $p=0.031$, one-tailed, BCa 95% CI [-0.018 0.450]). Training gain was still not significantly correlated with whole-brain segregation and association network segregation even after controlling for mean FD.

Results after motion censoring. We re-analyzed this dataset after removing 9356 out of 25740 volumes across subjects (36% of total volumes excluded after 573 volumes were flagged with FD > 0.2 mm). Although as expected by the reduced power of our analyses with this smaller dataset, the magnitude of the statistical significance of most of the analyses we performed was reduced. However, the patterns of relationships in the WM-REAS group between modularity, baseline Gf, baseline performance and training gain did not change direction.

Baseline modularity and baseline Gf: The two-factor model was significant $R^2=0.11$, Adjusted $R^2=0.08$, $F(2,65)=3.82$, $p=0.027$, with baseline Gf as a significant predictor ($\beta=-0.22$, $p=0.019$, BCa 95% CI [0-.41 -0.04]). Modularity was not a significant predictor ($\beta=1.13$, $p=0.258$, BCa 95% CI [-1.30 3.51]), although the results were in the same direction as the results of the unscrubbed data. A model with an interaction term was not a better fit ($p(\Delta F)=0.385$).

Baseline modularity, baseline performance, and interaction term: The three-factor model was significant, $R^2=0.46$, Adjusted $R^2=0.43$, $F(3,64)=18.13$, $p<0.001$. However, only baseline performance was a significant predictor ($\beta=-0.52$, BCa 95% CI [-0.66 -0.39], $p<0.001$). Modularity ($\beta=0.02$, $p=0.978$, BCa 95% CI [-1.74 1.86]) and the interaction of baseline performance and baseline modularity ($\beta=-1.73$, $p=0.161$, BCa 95% CI [-3.77 1.11]) were not significant predictors, although both results were in the similar direction as the results from the unscrubbed data.

Contributions of specific sub-networks to the relationship between global modularity and training gain. Modularity quantified using the predefined modules (Power et al., 2011) was correlated with modularity quantified using the spectral approach, $r(66)=0.714$, $p<0.001$, BCa 95% CI [0.50 0.86]. A repeated-measures ANOVA with a within-subjects factor of module showed that modularity differed across the 12 modules, $F(2.831,189.707)=290.404$, $p(GG)<0.001$, $\eta 2p=0.813$).

Modularity in the association system networks (DMN, FP, CO, VAN, DAN, Sal) and training gain in WM-REAS group: The correlation between association system modularity and training gain was significant, $r(66)=.207$, $p=.045$, one-tailed BCa 95% CI [-0.008 0.403], while the correlation between sensory-motor system modularity and training gain was not significant, $r(66)=.124$, $p=.158$, one-tailed BCa 95% CI [-0.109 0.348].

DMN modularity and baseline task performance. The correlation between training gain and DMN modularity was significant, $r(66)=.270$, $p=.013$, one-tailed BCa 95% CI [0.033 0.467]. The three-factor model of baseline task performance, DMN modularity and interaction of baseline task performance and DMN modularity was significant, $R^2=0.47$, Adjusted $R^2=0.44$, $F(3,64)=18.86$, $p<0.001$, with baseline performance as a significant predictor ($\beta=-0.49$, BCa 95% CI [-0.65 -0.34], $p<0.001$) and the interaction term as a near-significant predictor of training gain, ($\beta=-5.58$, BCa 95% CI [-11.95 0.08], $p=0.079$). DMN modularity itself was not a significant predictor ($\beta=-0.14$, BCa 95% CI [-3.01 5.29], $p=0.950$).