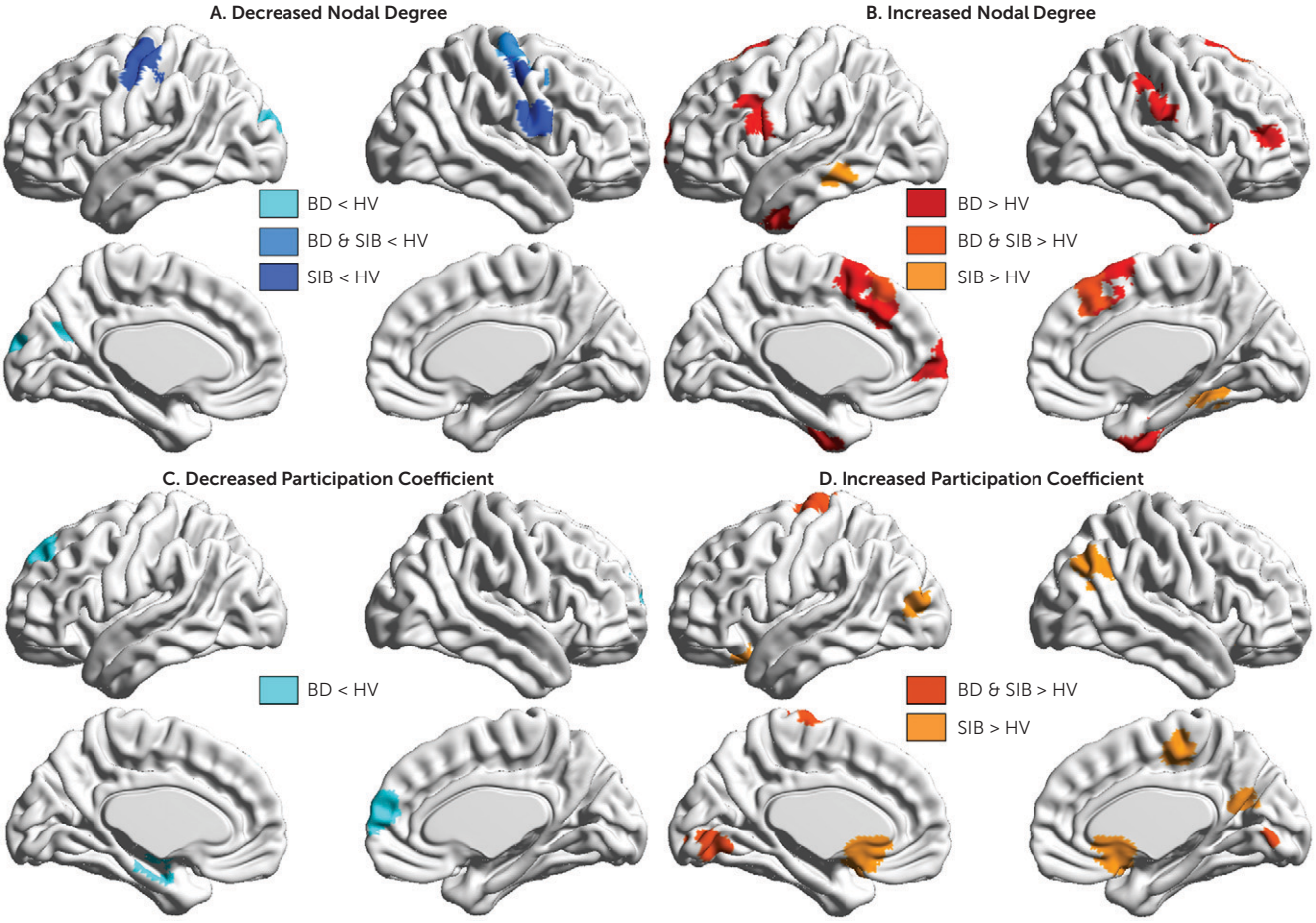
FIGURE 3. Altered Local Brain Topological Measures in Patients With Bipolar Disorder and Unaffected Siblings Relative to Healthy Volunteers[a]



[a] Panel A shows reduced nodal degree in patients with bipolar disorder (BD, N=78) and unaffected siblings (SIB, N=64) relative to healthy volunteers (HV, N=41). Panel B shows increased nodal degree in patients with bipolar disorder and unaffected siblings relative to healthy volunteers. Panel C shows reduced participation coefficient in patients with bipolar disorder relative to healthy volunteers. Panel D shows increased participation coefficient in patients with bipolar disorder and unaffected siblings relative to healthy volunteers. Significant difference between groups ($p<0.05$, following 5,000 permutations).

were associated with mesoscale and regional changes primarily in the default mode and sensorimotor networks, while global network properties appeared to be conserved both in patients and their siblings (Figure 4).

We found that global network properties in bipolar disorder were preserved in a manner consistent with previous studies examining the structural connectome topology (23) and the global resting-state fMRI signal power and variance in patients with bipolar disorder (24). This contrasts with findings in schizophrenia, where increased global signal variance and network randomization have been reported in patients (24) and their unaffected relatives (25). Although schizophrenia and bipolar disorder have overlapping clinical phenotypes and genetic risk factors (4, 26), preserved global brain organization in bipolar disorder may represent a major difference between the two disorders. This observation aligns with replicated reports of preserved premorbid and academic performance in patients with bipolar disorder (27) and superior academic performance in their relatives (28), which is not the case for schizophrenia (27, 28).

Our results suggest that mechanisms related to vulnerability to bipolar disorder affect brain organization at the mesoscale and at the regional level and that they particularly disrupt the connectivity of sensorimotor regions. Typically the sensorimotor network shows high within-system connectivity and relatively low integration with the rest of the brain (20). This connectomic signature is characteristic of "cohesive provincial" networks that are dedicated to the specialized processing of sensory stimuli and motor responses. In the present study, patients and relatives showed decreased within-module connectivity (indicative of reduced network cohesiveness) coupled with increased interaction of sensorimotor regions with regions outside their module (indicative of greater integration). In other words, the sensorimotor network in bipolar disorder behaves as an incohesive connector network which likely disrupts the processing of sensorimotor information within the brain. It is surprising that research to date has largely overlooked the evidence for sensorimotor dysfunction in bipolar disorder