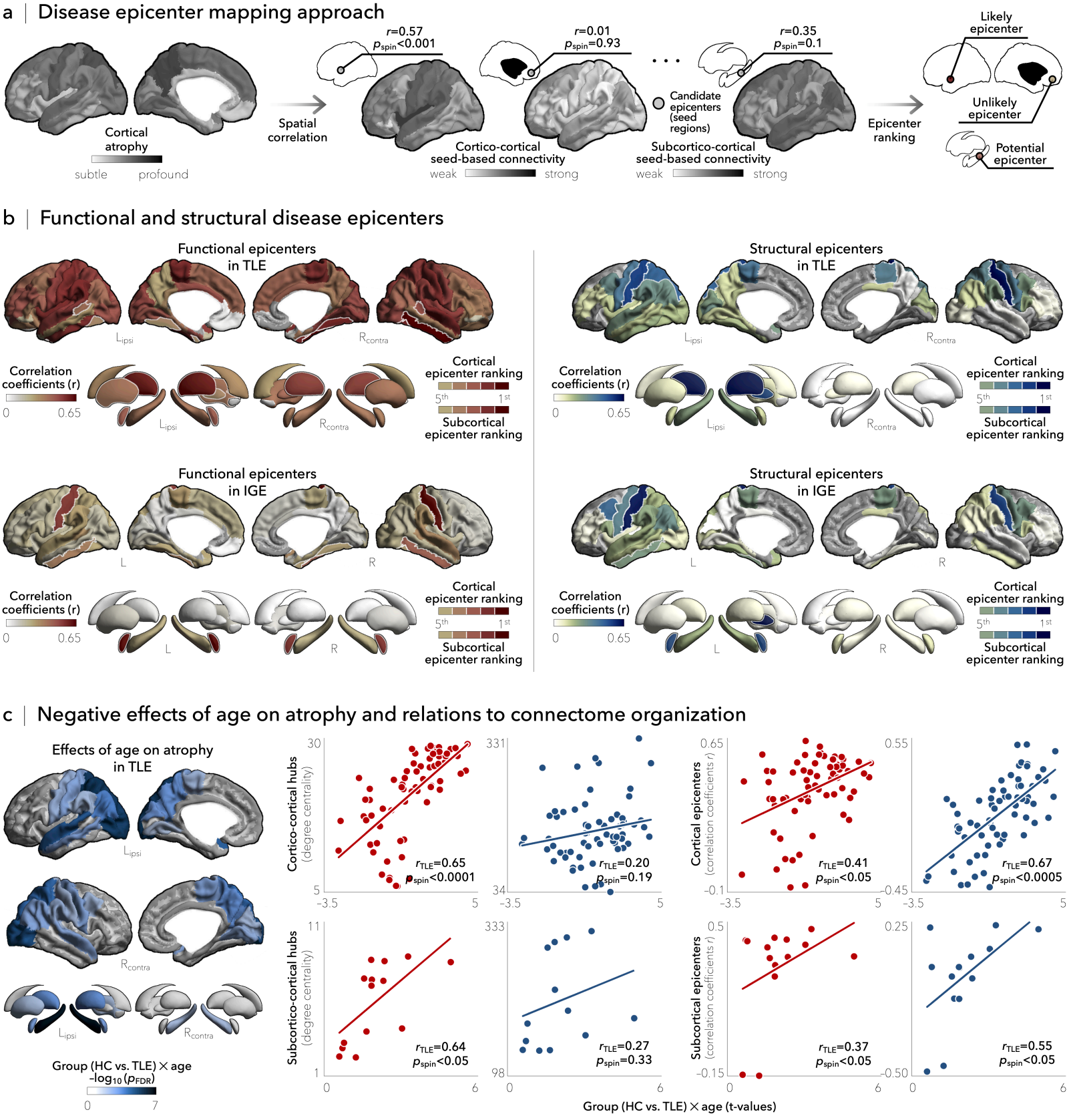

FIGURE 2. Syndrome-specific disease epicenters and negative effects of age on atrophy. **a** | Disease epicenter mapping schema. Spatial correlations between cortical atrophy patterns and seed-based cortico- and subcortico-cortical connectivity were used to identify disease epicenters in TLE and IGE. Epicenters are regions whose connectivity profiles significantly correlated with the syndrome-specific atrophy map; statistical significance was assessed using spin permutation tests. This procedure was repeated systematically to assess the epicenter value of every cortical and subcortical region, as well as in both functional and structural connectivity matrices. **b** | In TLE, bilateral temporal and sensorimotor cortical regions as well as several subcortical areas, including the thalamus, emerged as disease epicenters (p_{spin}<0.05). In IGE, highest ranked epicenters were located in bilateral fronto-central cortices and amygdala (p_{spin}<0.05). *=p_{spin}<0.1, *n.s.*=non-significant. **c** | Patients with TLE showed negative effects of age on cortical thickness in bilateral temporo-parietal and sensorimotor cortices (p_{FDR}<0.01), as well as on subcortical volume in ipsilateral hippocampus and bilateral thalamus (p_{FDR}<0.05). Negative $\log_{10}$-transformed FDR-corrected *p*-values are shown. Scatter plots depict relationships between the age-related effects and functional (*red*) and structural (*blue*) maps of degree centrality (*left*) and disease epicenters (*right*). Significant associations were observed between age-related effects and most hub and epicenters measures.