Cognitive control has been linked to both the microstructure of individual tracts and the structure of whole-brain networks, but their relative contributions remain unclear. To assess if the influence of tract microstructure on cognition is mediated by alterations in global network topology, we investigated changes in white matter network structure and their relationship with cognitive performance in Mild Cognitive Impairment (MCI). Structural networks were constructed from diffusion-weighted MRI in 25 patients with MCI and 20 matched healthy volunteers. Linear regression models were constructed for performance on cognitive control and episodic memory tasks, using global network metrics and microstructural measures from connections known to be critical to cognitive performance. Global efficiency and the mean clustering coefficient of structural networks were reduced in patients. They were related to cognitive control performance, but not episodic memory. The addition of a single tract measure to regression models led to an attenuation of the association between network metrics and cognition in patients, consistent with a mediation effect. The mediation effect of global network properties on cognitive control was stronger in MCI compared to controls, explaining 23-36% of the effect on control task performance. Network clustering was a significant mediator in the relationship between tract microstructure and cognitive control in both groups. These findings suggest that critical connections and topology of large-scale structural networks are both important for retention of cognitive control. Network topology partly mediates the relationship between cingulum microstructure and cognitive control. In contrast, episodic memory is less sensitive to global topology.