The substantia innominata (SI) forms part of the basal forebrain that provides major cholinergic innervation to the cerebral cortex and hippocampus, and has an essential role in cognitive function. Cholinergic loss is a central feature of dementia with Lewy bodies (DLB) and contributes to the clinical symptom phenotype. The objective was to investigate grey matter (GM) and white matter (WM) changes in the SI from magnetic resonance (MR) images in DLB, Alzheimer’s disease (AD) and healthy older subjects using voxel-based morphometry (VBM). Methods: One hundred and twenty seven subjects' (39 controls, 48 AD, 41 DLB) underwent 3T T1 MR imaging as well as clinical and cognitive assessments. VBM was undertaken using SPM8 and used a SI mask image to define the brain volume subspace for voxel analyses. Group differences in GM and WM volumes and selected behavioural correlates were assessed using the general linear model, with age and total intracranial volume as nuisance variables. Results: Effects were identified using an uncorrected threshold of P uncorrected \(\leq 0.05\), followed by family-wise error (FWE) correction for multiple comparisons (P FWE \(\leq 0.05\)) within the SI volume subspace. Conclusions: In DLB, GM loss is more pronounced than in AD and appears to be associated with dementia severity and cognitive fluctuations. GM atrophy of the SI may shed light in understanding some of the clinical manifestations of DLB, while relative preservation of WM volume could also have positive implications for cholinergic intervention.