Purpose: We evaluated the relationship between white matter (WM) tract disintegration and gray matter (GM) atrophy in patients with Alzheimer's disease (AD), mild cognitive impairment (MCI) and controls, using diffusion tensor imaging (DTI) and an optimized voxel-based analysis.

Methods: Two hundred thirty one individuals (61 controls, 116 MCI and 54 AD) were included. Voxel-based WM tract statistics was used to obtain whole-brain maps of WM bundles for FA. Voxel-based morphometry (VBM) was conducted to detect regions of gray matter (GM) atrophy in the AD, MCI group relative to the control group. FA maps were processed to make voxel-wise comparison of tract based analysis in whole brain between each the two groups. The relationship between locations of abnormalities in the WM and GM were examined.

Results: Patients with AD showed significant GM atrophy in posterior cingulate gyrus (BA31, 32) to the precuneus, the middle temporal lobe (BA19), the superior frontal (BA9) to the anterior cingulate (BA 32), the medial frontal lobe (BA 11, BA25), the hippocampus, the parahippocampal gyrus (BA30/34) and the insula, and WM tract disintegrity of the uncinate fasciculus, posterior cingulate fasciculus and fornix compared with the control and MCI groups. These abnormalities in the AD group were caused by either structural changes in GM atrophy or neural dysfunction due to functional disconnections in the WM tract.

Conclusions: The GM atrophy resulting from WM tract disintegration or GM atrophy itself may be the first step in the AD process, resulting in anatomically congruent correlations between WM disintegration and regional GM atrophy. Using tract based spatial statistics and voxel based analysis, both of which are useful in investigating GM and WM changes in individuals with neurodegenerative disorders.