Brain Atrophy Rates in Normal Aging and Alzheimer Disease

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Abstract
The objectives of this study were to (1) compare atrophy rates associated with normal aging and Alzheimer disease (AD) using the semi-automated Boundary Shift Integral (BSI) method and manual tracing of the entorhinal cortex (ERC) and hippocampus and (2) calculate power of BSI vs. ERC and hippocampal volume changes for clinical trials in AD. We quantified whole brain and ventricular BSI atrophy rates and ERC and hippocampal atrophy rates from longitudinal MRI data in 20 AD patients and 22 age-matched healthy controls.

Keywords
Dementia, Boundary Shift Integral, Serial MRI, Longitudinal, Normal Aging, Alzheimer Disease.

Introduction
Alzheimer’s disease (AD) is characterized by progressive cerebral atrophy, which may be assessed by volumetric MRI. We describe a voxel-based analysis of nonlinear-registered serial MRI to demonstrate the most statistically significant ($P < 0.001$) regions of change at different stages of the disease. We compared presymptomatic ($n = 4$), mild ($n = 10$), and moderately affected ($n = 12$) patients with early- and late-onset AD, with age- and sex-matched controls, and demonstrated increasing global atrophy with advancing disease. Significantly increased rates of hippocampal atrophy were seen in presymptomatic and mildly affected patients. There was a shift in the distribution of temporal lobe atrophy with advancing disease; the inferolateral regions of the temporal lobes showed the most significantly increased rates of atrophy by the time the patients were mildly or moderately affected. Significantly increased rates of medial parietal lobe atrophy were seen at all stages, with frontal lobe involvement occurring later in the disease. Our results suggest that the sites showing the most significant rates of atrophy alter as the disease advances, and that regional atrophy is already occurring before the onset of symptoms. This technique provides insights into the natural history of AD, and may be a valuable tool in assessing the efficacy of disease-modifying treatments, especially if these treatments were to have region-specific effects. All four atrophy rates were greater among normal subjects who converted to MCI or AD than among those who remained stable, greater among MCI subjects who converted to AD than among those who remained stable, and greater among fast than slow AD progressors. In general, atrophy on MRI was detected more consistently than decline on specific cognitive tests/rating scales. With one exception, no differences were found among the four MRI rate measures in the strength of the correlation with clinical deterioration at different stages of the disease.

Reversibility of cerebral atrophy
While most cerebral atrophy is said to be irreversible there are some recent studies that show this is not always the case. A child who was treated with ACTH originally showed atrophy, but four months after treatment the brain was seemingly normal again.

Chronic alcoholism is known to be associated with cerebral atrophy in addition to motor dysfunction and impairment in higher brain function. Because some of the behavioral deficits have shown improvement after abstinence from alcohol, a study looked to see if cerebral atrophy could be reversed too. Researchers took CT scans of the 8 study participants in order to measure cortical volume over time. Although decrease in atrophy does not equate clinical improvement, the CT scans of 50% of participants showed partial improvement, giving hope that cerebral atrophy could be a reversible process.

References


