Structural Neuroimaging of Geriatric Depression

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KEYWORDS

- Geriatric depression • Late-life depression • Neuroimaging
- MRI • White matter hyperintensities
- Magnetic resonance spectroscopy

Neuroimaging has been a powerful tool in our search to identify neuroanatomic markers that provide information about the diagnostic and prognostic status of elderly patients with depressive symptoms. After decades of research, we now know several regions in the brain that are implicated in depression such as the anterior cingulate, orbitofrontal cortex (OFC), and the hippocampus. Successes in delineating the neural circuits in depression have closely paralleled progress in neuroimaging techniques and advances in image analysis. Such noninvasive methods are critical as access to the tissue of interest, the brain, is otherwise impossible except in postmortem samples.

Magnetic resonance (MR) or nuclear MR occurs when protons in the nuclei of certain atoms (usually hydrogen) are subjected to a static magnetic field, then exposed to a second oscillating magnetic field (pulse). During the application of the pulse, the alignment of the protons within the static magnetic field is disturbed. Following the application of the pulse, the misaligned protons relax and return to their original alignment emitting energy signals in the process. The relaxation times of different tissues vary, forming the basis of MRI.[1] MR-based methods such as MR morphometry, diffusion tensor imaging (DTI), and MR spectroscopy (MRS), among others, are used to detect differences between the brains of depressed and nondepressed elderly. Readers interested in further details about individual methods, their strengths and weaknesses in the context of geriatric depression, are referred to the excellent review by Hoptman and colleagues.[1]

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Several differences in the structure of the brain between depressed and nondepressed elderly have been found and replicated. In this article, the authors summarize some of the salient structural imaging findings in geriatric depression and their implications to the neurobiology of late-life depression. First, morphometric studies focusing on volumetric differences are discussed; followed by findings from studies that examine white matter pathology using different imaging techniques. Finally, the biochemical correlates of depression found by MRS are summarized.

VOLUMETRIC DIFFERENCES IN SPECIFIC BRAIN STRUCTURES

Volumetric studies examine differences in the volumes of different brain structures among patients with depression compared with those who are not depressed. This can be accomplished either by traditional morphometric studies that focus on a predetermined, specific structure, based on previous knowledge about pathophysiology, or by voxel-based morphometry (VBM) that is not biased toward any one structure and assesses anatomical differences throughout the brain.

Morphometric Studies

Most morphometric studies use T1-weighted images to compare the volumes of specific structures such as the hippocampus or a particular region in the frontal cortex. These areas are called regions of interest (ROI). This hypothesis-driven approach has identified several volumetric differences between depressed and nondepressed elderly.

The hippocampus

The hippocampus is one of the most commonly studied structures in depression. Studies in late-life depression have repeatedly demonstrated a reduction in hippocampal volume among the depressed.[2–7] Though some studies did find negative results,[8,9] two recent meta-analyses of MRI studies have confirmed that there is indeed an association between depression and decreased hippocampal volume.[10,11] It has been suggested that earlier negative findings may be due either to the inclusion of the amygdala along with the hippocampus[12] or lower resolution of images.[13] Further exploration of this association has revealed that age of onset of depression correlates negatively with hippocampal volume as patients with late-onset depression had smaller hippocampal volumes when compared with those with early onset depression and controls.[4] In a younger cohort of patients followed over 3 years, depressed participants exhibited greater decline in bilateral hippocampal volume.[14]

Evidence from animal studies indicates that the mechanism underlying decreased hippocampal volumes is stress-induced decrease in cell proliferation in the hippocampal region.[15,16] Further, administration of antidepressants has been shown to prevent such stress-induced suppression of neurogenisis.[17] Hippocampal volume reduction has also been shown to correlate with serotonin transporter promoter region polymorphism (5-HTTLPR) in which individuals who were homozygous for the L allele exhibited smaller hippocampal volumes.[18] A similar correlation with the val66met polymorphism of the brain-derived neurotrophic factor gene has been found to be positive in younger adults,[19] but was not replicated in an elderly sample.[20] Though decrease in hippocampal volume has been proposed as an endophenotype for depression, it is by no means specific as similar decreases occur in mild cognitive impairment and Alzheimer's dementia, which are common comorbidities in older adults with depression.[21,22]