Abstract

Background: Older adults presenting with both a depressive disorder (DEP) and cognitive impairment (CI) represent a unique, understudied population. The classification of cognitive impairment severity continues to be debated though it has recently been subtyped into late (LMCI) versus early (EMCI) stages. Previous studies have found associations between treatment outcome and both cortical thickness and white matter hyperintensities (WMH), though report inconsistent directionality and affected regions. In this study, we examined baseline clinical characteristics and neuroanatomical features as prognostic indicators for older adults with comorbid DEP and CI participating in an open antidepressant trial.

Methods: Key inclusion criteria were diagnosis of major depression or dysthymic disorder with Hamilton Depression Rating Scale (HAM-D) score >14, and cognitive impairment defined by MMSE score ≥21 and impaired performance on the WMS-R Logical Memory II test. Patients were classified as EMCI or LMCI based on the 1.5 SD cutoff on tests of verbal memory, and compared on baseline clinical, neuropsychological, and anatomical characteristics. Mood was assessed using the Hamilton Depression Rating Scale. All patients underwent a baseline MRI scan and received open antidepressant treatment with citalopram for 8 weeks. Cortical thickness was extracted using an automated brain segmentation and reconstruction program (FreeSurfer). Vertex-wise analyses were conducted using general linear models to evaluate the relationships between cortical thickness and clinical variables.

Results: 79 DEP-CI patients were recruited, of whom 39 met criteria for EMCI and 40 for LMCI. The mean age was 68.9 and mean HAM-D was 23.0. LMCI patients had significantly worse global cognition and smaller right hippocampal volume compared to EMCI patients. EMCI patients had thicker right medial orbitofrontal cortex than LMCI. MRI indices of cerebrovascular disease did not differ between MCI subtypes. Remitters had greater deep WMH burden, left medial orbitofrontal gyrus thickness, and right superior frontal gyrus thickness than nonremitters. Greater HDRS depressive severity was positively correlated with right pars triangularis thickness. Stronger ADAS-Cog global cognitive performance was positively correlated with thickness in diffuse cortical areas.

Conclusions: Cognitive and neuronal loss markers differed between EMCI and LMCI among patients with DEP-CI, with LMCI being more likely to have the clinical and neuronal loss markers known to be associated with Alzheimer's disease. Samples of DEP-CI exhibit unique patterns of cortical thickness and WMHs compared to their non-CI peers. Cortical thickness may serve as predictor of treatment remission and relates to both depressive severity and global cognition.