Comparison of Brain Structural Variables, Neuropsychological Factors, and Treatment Outcome in Early-Onset Versus Late-Onset Late-Life Depression

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Objective: *To compare differences in gray matter volumes, white matter and subcortical gray matter hyperintensities, neuropsychological factors, and treatment outcome between early- and late-onset late-life depressed (LLD) subjects.* **Methods:** *We conducted a prospective, nonrandomized, controlled trial at the outpatient clinics at Washington University and Duke University on 126 subjects, aged 60 years or older, who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for major depression, scored 20 or more on the Montgomery-Asberg Depression Rating Scale (MADRS), and received neuropsychological testing and magnetic resonance imaging. Subjects were excluded for cognitive impairment or severe medical disorders. After 12 weeks of sertraline treatment, subjects' MADRS scores over time and neuropsychological factors were studied.* **Results:** *Left anterior cingulate thickness was significantly smaller in the late-onset depressed group than in the early-onset LLD subjects. The late-onset group also had more hyperintensities than the early-onset LLD subjects. No differences were found in neuropsychological factor scores or treatment outcome between early-onset and late-onset LLD subjects.* **Conclusion:** *Age at onset of depressive symptoms in LLD subjects are associated with differences in cortical thickness and white matter and subcortical gray matter hyperintensities, but age at onset did not affect neuropsychological factors or treatment outcome.* (Am J Geriatr Psychiatry 2013; ■:■−■)

Key Words: Late-life depression, antidepressant, hippocampus, amygdala, neuropsychological factors, cognitive deficit, age at onset, vascular risk factors, white matter hyperintensities, treatment outcome

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http://dx.doi.org/10.1016/j.jagp.2013.02.005

INTRODUCTION

Studies of late-life depression (LLD) are important not only for the insights into the underlying pathophysiology of depression, but also because of the clinical significance of an expanding elderly population. LLD is a heterogeneous disorder, with outcome disparities in studies examining structural brain volumes, ischemic lesions, and neuropsychological deficits.[1–3] The conflicting results may be related in part to samples that differ in age at depression symptom onset.[4–6]

One difference between late-onset LLD (LOD), defined as depression onset at age 60 years or older, and early-onset LLD (EOD), defined as age at onset younger than 60 years, may be the contribution from underlying vascular disease. Multiple studies[1,7] have shown an association between cerebrovascular disease and depression in elderly adults.[8] LOD subjects have a higher burden of cerebrovascular disease, which may be an important contributing factor to the later development of depressive symptoms.[9] In contrast, EOD may be a more familial disorder with genetic predisposition.[10]

Our previous study[11] reported a significant correlation between white matter hyperintensities (WMHs), cognitive function, and vascular risk factors (VRFs), in support of the vascular depression hypothesis. However, this study did not examine the effect that age at onset of depressive symptoms exerts on WMHs, cognitive deficits, region of interest (ROI) gray matter volumes and cortical thicknesses, or treatment outcomes. The purpose of the current study is to compare ROI volumes and cortical thicknesses, deep white matter and nonwhite matter (subcortical gray matter) hyperintensities, neuropsychological factors, and treatment outcomes between EOD and LOD subjects.

METHODS

Participants

Patients were recruited from an ongoing National Institute of Mental Health study, Treatment Outcome in Vascular Depression, through advertising and physician referral to Washington University (WU) Medical Center and Duke University Medical Center. Patients were at least 60 years of age, met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition DSM-IV* (DSM-IV) criteria for major depression by Structured Clinical Interview for Axis I DSM-IV Disorders given by a research psychiatrist, and had a Montgomery-Asberg Depression Rating Scale (MADRS)[12] score of 20 or greater. Inclusion criteria, study measures, and study design have been described in detail elsewhere.[11] Patients were excluded if they had contraindications to magnetic resonance imaging (MRI), used psychotropic drugs, or had evidence of severe depression as defined by symptoms requiring hospitalization, risk of suicide, or history of failure to respond to two or more antidepressants. In addition, patients were excluded if they had a severe or unstable medical disorder or a known primary neurologic disorder. All participants were screened for dementia using the Clinical Dementia Rating scale (CDR)[13] and were excluded for CDR scores greater than 0.

Two hundred seventeen patients (120 at WU and 97 at Duke) enrolled in a 12-week treatment trial with sertraline. One hundred ninety participants completed the trial; 168 had complete imaging data. Subjects were divided into two groups: EOD (depression onset before age 60) and LOD (depression onset at age 60 or older). To match groups for age, the youngest 42 EOD participants were removed from the sample. Thus, 126 participants were included in the current analyses, 60 in the EOD group and 66 in the LOD group. Written informed consent approved by the relevant institutional review board was obtained for all subjects.

Comparison Group

For the purpose of creating a priori ROIs, a comparison group was recruited. The comparison group consisted of a sample of nondepressed subjects ($N = 57$) recruited from the community. Comparison subjects did not have a history of depression or current major depression. Of these 57 participants, 50 had complete, usable MRI scans.

Measures

Data were obtained from evaluations performed by research staff of the clinical research study at each site and included medical, psychiatric, demographic, MRI, and neuropsychological measures. Age at onset of depression was obtained from the subjects, all of