Cortical Thinning in Patients With Late-Life Minor Depression

Anand Kumar, M.D., Olusola Ajilore, M.D., Ph.D., Aifeng Zhang, Ph.D., Daniel Pham, M.S., Virginia Elderkin-Thompson, Ph.D

Objectives: *Clinically significant minor depression is among the most common mental disorders in the elderly individuals and is associated with considerable medical and psychosocial morbidity. Despite its clinical impact, the biological basis of minor depression in the elderly individuals remains poorly understood. The purpose of our current study was to examine cortical thickness in a sample of patients with late-life minor depression and non-depressed comparison subjects using magnetic resonance imaging (MRI).* **Design:** *Cross-sectional analysis.* **Setting:** *Community.* **Participants:** *Patients ($n = 16$; mean age $= 76.2 \pm 7.5$) met modified DSM (Diagnostic and Statistical Manual of Mental Disorders) criteria for minor depression and were free of other brain diseases. Healthy comparison subjects (HC; $n = 16$) were of comparable age and gender distribution.* **Measurements:** *All subjects were scanned on a 1.5-Tesla GE scanner and brain regions were outlined using Freesurfer Image Analysis.* **Results:** *Results show that patients with minor depression have cortical thinning in the right cingulate cortex compared to HC.* **Conclusions:** *These findings indicate that abnormalities in specific structures and associated neural circuitry may underlie minor and major depression in the elderly individuals and the pathophysiological abnormalities are comparable in major and less severe forms of the disorder.* (Am J Geriatr Psychiatry 2013; ■:■−■)

Key Words: Freesurfer, minor depression, MRI

OBJECTIVE

Clinically significant minor depression is a common psychiatric disturbance in late-life with prevalence estimates ranging from 5% to 10%.[1] Minor forms of depression are associated with considerable medical and psychosocial morbidity comparable to those observed in patients with major depressive disorder (MDD) − the more widely recognized and clinically severe form of the disorder.[2–5] Like individuals with MDD, older adults diagnosed with minor depression show increased suicide attempts, emergency room visits and tranquilizer use.[1,2,4] Clinical and health services studies have elaborated on the economic and psychosocial consequences of minor depression in the elderly individuals.[2,4,6,7] The prognosis of "subthreshold" disorders is unfavorable and these minor forms of depression are often chronic in nature.[8]

Received January 27, 2011; revised August 10, 2011; accepted October 20, 2011. From Department of Psychiatry, University of Illinois at Chicago, Chicago, IL (AK, OA, AZ); and Department of Psychiatry, University of California, Los Angeles, CA. Send correspondence and reprint requests to Anand Kumar, M.D., Department of Psychiatry, University of Illinois at Chicago, 1601 W. Taylor Street, Chicago, IL 60612. e-mail: akumar@psych.uic.edu

http://dx.doi.org/10.1016/j.jagp.2012.12.010

Not only is minor depression deemed risk factor forMDD, studies suggest there may be a genetic basis to minor depression.[9] Despite these clinical observations, the biological basis of minor depression in late life, unlike MDD, has received scant attention.[1,6]

The neuroanatomical basis of MDD has been relatively well characterized using magnetic resonance imaging (MRI). Principal findings suggest that MDD in late life is associated with a combination of smaller brain volumes in specific regions with an increase in high-intensity lesion volumes-—areas that appear bright on conventional T2-weighted FLAIR MRI.[10] Volumetric reductions and white matter hyperintensities have been identified in prefrontal subregions, the hippocampus, and subcortical nuclei in older adults diagnosed with MDD.[11–14] Volume decreases associated with late-life MDD have been correlated with duration of illness and age of disease onset, particularly measures of parahippocampal and inferior parietal regions.[15] Furthermore, smaller brain volumes and high-intensity lesions appear to be autonomous pathways to MDD in the elderly individuals.[10]

As previously stated, there is little work investigating the biological basis of minor depression. In an earlier study of minor depression in late life, we reported that the volume of the prefrontal lobe was significantly smaller in patients when compared with healthy comparison subjects.[16,17] More specifically, patients with late-life minor depression had frontal lobe volumes that were in between those of healthy comparison subjects and patients with late-life MDD.[17] The purpose of our current study was to expand on our earlier observation and determine whether cortical thickness, a reliable in vivo marker of gray matter structure, was lower in the prefrontal regions in patients diagnosed with latelife minor depression when compared with comparison subjects.[18] The thickness of the cortical mantle ranges from 1.5 to 3.4 mm in humans and extends from the pial surface of the brain to the boundary between the gray and white.[19] Cortical thickness, due to decreased variability in gray matter cytoarchitecture, is a sensitive measure of the structural integrity of the brain, comparable to such measures as gray matter density.[18,20] Cortical thinning has been observed in patients diagnosed with schizophrenia, Alzheimer disease, and mild cognitive impairment, a condition widely considered to be a precursor of Alzheimer disease.[21–23] Thinning of the cortical mantle, more marked in the right hemisphere, has also been identified in patients at increased familial risk for major depression[24] and correlated with measures of attention and emotional memory.

The focus of this study was on prefrontal lobes and its subregions including the anterior cingulate cortex, areas that are consistently implicated in the pathophysiology of mood disorders and formed the basis of the earlier report of minor depression from our laboratory.[11]

METHODS

Clinical

Sixteen patients diagnosed with minor depression (7 men, 9 women, mean age = 76.25, SD = 7.54) using modified DSM(*Diagnostic and Statistical Manual of Mental Disorders*) criteria,[25] and 16 nondepressed comparison subjects (7 men and 9 women, mean age = 75.06, SD = 5.42) were recruited from the community using identical outreach mechanisms described in detail elsewhere.[11] Data from the subjects recruited for this study have not been previously reported. Patients and comparison subjects had comparable medical comorbidities and were free of all neurological brain disorders including dementia. Minor depression was operationally defined as presence of low mood and/or loss of interest in activities and at least one additional symptom from the DSM checklist of 1-month duration.[17] All patients had 17-item Hamilton Depression Scale Scores of between 8 and 14 inclusive.[26] Twelve of the 16 patients diagnosed with minor depression reported duration of illness greater than 2 years thereby meeting criteria for dysthymic disorder (chronic clinical depression that does not meet criteria for MDD); however, none of the patients had a prior episode of MDD. The study was performed in accordance with UCLA's (University of California, Los Angeles) policies of the Human Subject Protection Committees, and written informed consent was obtained from all subjects after the procedures had been fully explained.

Magnetic Resonance Imaging

All subjects were scanned on a 1.5-Tesla GE Signa scanner (GE, Milwaukee, WI) using a coronal T1-weighted spoiled gradient/recall acquisition with the following parameters: repetition time = 42 ms, echo