

Cortical Thickness and Cerebral Blood Perfusion Abnormalities Correlated with Depression in a Geriatric Population. Duygu Tosun¹, Douglas G. Peters¹, Ruth T. Morin², R. Scott Mackin^{2,3}. 1) Department of Radiology and Biomedical Imaging, University of California San Francisco. 2) Mental Health Service, San Francisco VA Medical Center. 3) Department of Psychiatry, University of California San Francisco.

Introduction: Major depressive disorder (MDD) is associated with increased risk for illness, dementia, and mortality. MDD in the elderly, also known as Late Life Depression (LLD), is especially common and debilitating with an incidence of 15% of adults over the age of 65. LLD is a complex disorder with many contributing psychological, social, and wellness factors. In addition, cognitive deficits relating to processing speed, executive dysfunction, and memory, symptoms generally associated with neurodegenerative diseases such as Alzheimer's Disease and Vascular Dementia, are recognized as important features of LLD. Yet, it is unclear to what extent neurobiological features are unique to LLD and not etiologically due to Alzheimer's disease (AD) and vascular disease pathologies, which are associated with greater incidence of depression symptoms. The goal of this study was to examine the cortical thickness¹ and cerebral blood flow reduction patterns in a large LLD population (n=117 LLD, 218 controls) to determine neurobiological factors unique to LLD.

Methods: LLD subjects with and without mild cognitive impairment (MCI) were pooled from the Alzheimer's Disease Neuroimaging Initiative (ADNI)-Depression study utilizing 3T Siemens MRI systems. Nondepressed subjects were pooled from ADNI GO and ADNI2 cohorts. Anatomical 3D-T1 volumetric MRIs (TR/TE/TI=2300/2.95/900ms; 1.1 x 1.1 x 1.2mm) were obtained to measure cortical thickness. Axial 2D ASL MRIs (eyes open; TR/TE=3400/13ms; 4.0 x 4.0 x 4.0mm) were collected to measure cerebral blood flow (CBF). T1 and ASL images were processed in parallel using FreeSurfer v5.1 to estimate dense cortical thickness and CBF surface map and regional measures. Surface-based cortical thickness and cortical CBF maps were smoothed by Gaussian filters of 10mm FWHM and 15mm FWHM, respectively. Surface cortical analysis was performed using FreeSurfer DODS while controlling for confounding effects of age, sex, education, APOE4+ status (genetic risk factor for AD), and delayed memory scores (measure of MCI severity).

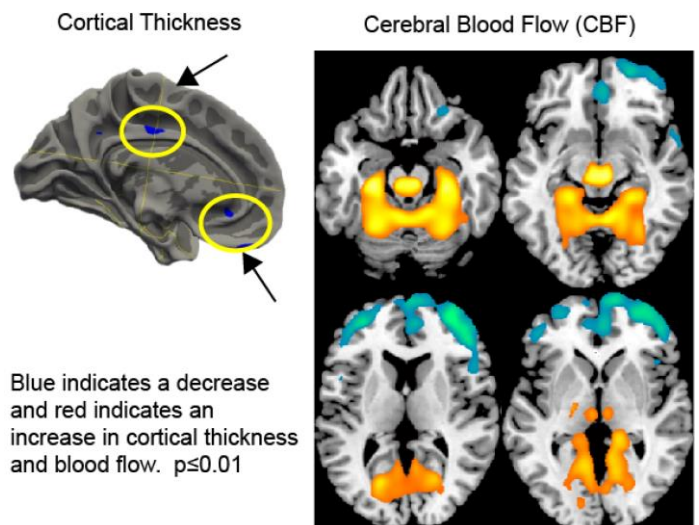
Results: The LLD group presented with thinner cortical thickness in the anterior and posterior cingulate gyrus. LLD was significantly associated with diffuse and bilateral CBF decreases in the frontal cortex and cingulate gyrus, as well as CBF increases in the basal ganglia, hippocampus, brainstem, and cerebellum (Fig. 1).

Discussion: Our current findings support previous literature that indicates cortical thickness thinning in the anterior and posterior cingulate. There was also a large difference in CBF between depressive group and controls. Decreased CBF in the frontal cortex may underlie atrophy in these regions. Increased CBF in the basal ganglia, hippocampus, cerebellum, and brain stem may reflect compensatory mechanism to increase oxygenation and nutrients to areas of the brain important for lower-level cognitive control and function where blood flow is preserved. Taken together, these findings are consistent with the concept of neurobiological mediation of MDD via neural networks comprising the orbitofrontal, medial prefrontal, and cingulate cortices with neuronal connections to the temporal cortex, parietal cortex, and basal ganglia. These findings are uniquely different from AD, which primarily affects the parietal and temporal cortices, and may indicate that blood flow is a more sensitive measure for identifying and measuring the neurobiological mechanism of LLD linked to synaptic dysfunction.

References:

1. Mackin, R. S. et al. Patterns of reduced cortical thickness in late-life depression and relationship to psychotherapeutic response. *Am. J. Geriatr. Psychiatry* 21, 794–802 (2013).

Fig. 1: Cortical Thickness and CBF in LLD



Highlights:

We found focal cortical thinning of the anterior and posterior cingulate gyrus in a late life depression (LLD) population, which is consistent with previous literature. However, we identify diffuse and spatially separate depression-specific changes in cerebral blood flow (CBF) that are distinct from Alzheimer's disease.