The role of brain structure and executive function on visuoconstructional processing in late life depression

M. Lamar[1], E. Rhodes[1], O. Ajilore[1], A. Zhang[1], M. Caserta[1], and A. Kumar[1]
[1]Psychiatry, University of Illinois at Chicago, Chicago, IL, United States

INTRODUCTION

Research into visuoconstructional processing and aging suggests that executive functioning is key to successful performance. Given executive functioning deficits are observed in late life depression, we hypothesized that they would negatively impact visuoconstructional processing in these vulnerable older adults. The purpose of the present study was to examine the role of executive functioning in visuoconstructional abilities in late life depression and healthy aging taking into account other age-related structural and functional alterations including white matter and hippocampal volume.

METHODS

144 participants age 60 or older were recruited through clinic referrals and local advertisements. Unmedicated individuals with late life depression (n=57; mean age=69.0±8.1) met DSM-IV criteria for major depressive disorder and had scores of 15 or greater on the 17-item Hamilton Depression Rating Scale. 87 healthy controls (mean age=70.3±7.4) were also recruited. In addition to receiving a detailed mental status examination by a psychiatrist, all participants were assessed with a structured psychiatric interview (Structured Clinical Interview for DSM-IV). They also completed visuoconstructional tasks including WAIS-III Block Design, Visual Reproduction-Copy and the Rey-Osterrieth Complex Figure-Copy as part of a larger neuropsychological assessment. These measures were z-transformed and combined to create a visuoconstructional index (Cronbach's alpha=.76); additional indices representing executive functioning (Matrix Reasoning, Trails B, Stroop Color-Word Interference, WAIS-III Letter-Number Sequencing, Wisconsin Card Sort; Cronbach's alpha=.76), attention/information processing (Trails A, Stroop Color & Word Trials, WAIS-III Digit Symbol; Cronbach's alpha=.77) and verbal memory (California Verbal Learning Test short & long delay free recall; Cronbach's alpha=.94) were also derived.

113 participants (67 HC; 46 LLD) were scanned on a 1.5T Signa magnet. High resolution 3D MPRAGE (Magnetization Prepared Rapid Acquisition Gradient Echo) sequence was acquired for each subject using a SIEMENS Trio Tim 3T MRI Scanner. Parameters include: FOV=240X210mm, TR/TE/TI=2200/2.24/900ms, flip angle 9°, 224 contiguous coronal slices, in-plane resolution=0.9375X0.9375mm, acquisition matrix=256X224, slice thickness=0.9mm, NOA=1. White matter and hippocampal volumes were obtained using automated segmentation by the Freesurfer image analysis suite and manually reviewed for gross abnormalities or processing errors before being averaged across hemisphere and normalized for intercranial volume.

Individual ANOVAs investigated between-group differences on demographic, brain volume and cognitive indices. A stepwise linear regression was performed by diagnostic group with age, education and cognitive domain indices of executive functioning, attention/information processing, and verbal memory as predictor variables of performance variance for the visuoconstructional domain index. A second set of linear regression analyses by group were conducted incorporating white matter and hippocampal volumes into the set of predictor variables.

RESULTS

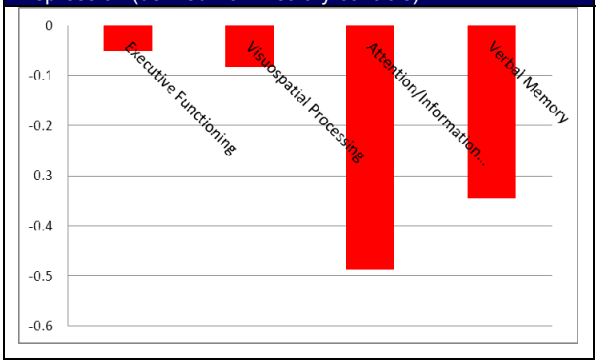
Groups did not differ on demographic, brain volumes (Table 1) or the visuoconstructional domain index; although performance on verbal memory and attention/information processing indices was better for the healthy controls when compared to the late-life depressed group (Figure 1).

Table 1. Participant Characteristics

Overall Sample	**LLD n=57**	**HC n=87**
Age	68.97 ±8.15	70.36 ±7.50
Education	15.94 ±2.59	16.21 ±2.28
Gender (M:F)	28:59	19:38
Mini-Mental State Exam	29.04 ±1.21	28.97 ±1.25
Geriatric Depression Scale*	19.64 ±4.82	1.99 ±1.68
Framingham Risk Stroke Profile	11.26 ±13.79	9.78 ±4.28
Cumulative Illness Rating Scale**	5.51 ±3.54	4.01 ±3.54
Neuroimaging Subset	**LLD n=46**	**HC n=67**
Hippocampal Volume (mm^3/cm^3)	5.5 ±1.0	5.6 ±1.0
White Matter Volume (mm^3/cm^3)	298.3 ±32.0	294.0 ±30.0

*p=0.001, **p=0.15

Figure 1. Z-scores of Cognitive Domain Indices for Late-life Depression (derived from healthy controls)



Indices of executive functioning and verbal memory significantly contributed to visuoconstructional performance variance (55%; p<0.001) in healthy controls. In contrast, only age significantly contributed to performance variance in late-life depression (37.5%; p<0.001). Incorporating white matter and hippocampal volumes into the set of predictors did not change the pattern of results in late-life depression; however, for healthy controls, the executive functioning index and white matter volumes significantly contributed to visuoconstructional performance variance (53%; p=0.03). Incorporating measures of stroke risk or medical comorbidity did not alter any of our reported results.

DISCUSSION

Executive functioning consistently contributed to visuoconstructional performance variance in healthy controls but not in late-life depression. Furthermore, increasing white matter volumes significantly contributed to increasing performance on the visuoconstructional index in healthy controls only. Given that healthy controls and depressed participants did not differ on age, white matter volume or executive functioning, the presence of depression may be accelerating or amplifying the contribution of age in this population (the only predictor variable that contributed to visuoconstructional performance variance in this population). Depression may cause increased burden on executive and non-executive tasks through multiple mechanisms including slowed information processing speed, medical comorbidity and/or subtle alterations in white matter not reflected in our gross measure of white matter volume. We are currently quantifying white matter damage using diffusion tensor and magnetic transfer imaging to assist with our investigation.

1. Fischl B et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. *Neuron* 2002;33:341-355.
2. Fischl B et al. Sequence-independent segmentation of magnetic resonance images. *Neuroimage* 2004;23:S69-S84.