Structural and Functional Brain Changes in Late-Life Major and Minor Depression

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Introduction

Major depression (MDD) is common in older adults and is often associated with impairments on working memory tasks dependent upon the integration of prefrontal and anterior cingulate cortical regions[1]. Minor depression, or subthreshold depression (SD), is even more common in older adults[2]. There is increasing evidence that these symptoms share similar cognitive sequelae, neural correlates, and clinical outcomes with MDD[3]. However, cognitive neuroscience studies are needed to fully elucidate whether MDD and SD involve similar underlying neural circuitry. Moreover, whether this relation is affected by the severity of particular symptom dimensions (e.g., affective vs. somatic) is unknown.

Experimental

We have collected data in 19 healthy, dementia-free older adults. fMRI data were acquired while participants performed a working memory (n-back) and episodic memory (Memory Recall Paradigm) task. *Image Acquisition:* Scanning took place in the Siemans 3T head scanner at the UF McKnight Brain Institute using an 8-channel sensitivity encoding (SENSE) head RF coil. Functional images were acquired in 34 contiguous axial slices parallel to the anterior commissure-posterior commissure (AC-PC) line using a T2*-weighted EPI pulse sequence (TR=2000ms; TE=30ms; FA=90°; FOV=24cm; 64 x 64 voxels at 3.75mm^3). A whole-brain high-resolution 3D anatomical image was acquired using a T1-weighted 3D turbo gradient echo sequence with SENSE (176 1-mm thick sagittal slices; TR=2s, TE=4.13ms, FA=8˚, matrix=512 x 512mm, FOV=24cm). Functional images were normalized to a common mean, movement corrected, co-registered to a common reference image, and smoothed using a 3-dimensional Gaussian filter (8mm FWHM). fMRI data were preprocessed and analyzed using BrainVoyager QX software (BVQX version 2.1; Brain Innovation, Maastricht, The Netherlands). *Image Processing:* Image preprocessing consisted of: rigid-body 3D motion correction using trilinear interpolation, slice-scan time correction using sinc interpolation, spatial smoothing with an 8mm FWHM Gaussian kernel to accommodate between-subject differences in brain anatomy, and high-pass filtering of frequencies below 3 cycles per time course. The fMRI time series for each subjects' functional run were co-registered to their high-resolution anatomical volume using BrainVoyager's co-registration procedure and manually aligned when necessary. Spatial normalization was performed using the standard 9-parameter landmark Talairach method defined on each individual participant's anatomical volume. Structural data have not yet been analyzed. Because of difficulty recruiting participants with major depression, analyses focused on continuous measures of depressive symptoms. fMRI data were correlated with scores on the Center for Epidemiologic Studies Depression Scale (CES-D) and Beck Depression Inventory-II (BDI-II) as well as scores on the CES-D and BDI subscales.

Results and Discussion

Data analysis is ongoing, but earlier analyses revealed decreased activity in areas including the anterior cingulate, middle and superior frontal gyrus, and striatal regions in participants endorsing symptoms of anhedonia on the Beck Depression Inventory-II compared to controls (**Figure 1**). Anhedonia was also associated with increased activity in temporal regions. Interestingly, posthoc analyses unrelated to our primary aim showed a linear decrease in hippocampal activity during memory encoding between young-old (mean age 67.9, SD = 2.6) and middle-old (mean age 77.3, SD = 2.7) adults.

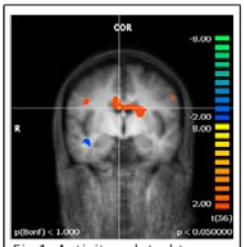

Fig 1. Activity related to anhedonic symptoms (N-15)

Conclusions

Our initial analyses support the hypothesis that low levels of depressive symptoms impact brain function and that particular symptom components may have distinct associations with brain function.

References

[1] Vasic, N, *et al*., Psychological Medicine, **39**, 977-987 (2009).
[2] Blazer, D.G., The Journals of Gerontology, **58**, 249-265 (2003).
[3] Beck, D.A., *et al*. International Journal of Psychiatry in Medicine, **26**,177-209 (1996).