

WHITE MATTER LESIONS AND CEREBRAL PERFUSION IMAGING IN LATE-ONSET MAJOR DEPRESSION

R. B. Dalby¹, J. Ahdidan¹, M. Chakravarty^{2,3}, L. Sørensen⁴, R. Rosenberg¹, L. Østergaard², and P. Videbech¹

¹Centre for Psychiatric Research, Aarhus University Hospital, Risskov, Denmark, ²Center of Functionally Integrative Neuroscience, Aarhus University Hospital, Aarhus, Denmark, ³PET Center, Aarhus University Hospital, Aarhus, Denmark, ⁴Department of Neuroradiology, Aarhus University Hospital, Aarhus, Denmark

Introduction

Major depression (MD) is characterized by persistent negative emotions and thoughts that coexist with disturbances of sleep, energy, and cognition, such as deficits in memory, executive function, and language processing. Cognition works through complex neuronal circuitries, involving the orbito-frontal cortex and fronto-striatal pathways. Neuroimaging studies in MD have revealed abnormalities in regional cerebral blood flow (CBF) and glucose metabolism in multiple limbic and prefrontal cortical structures which may account for the cognitive dysfunctions seen in MD.

White matter lesions (WMLs) are punctuate or confluent signal hyperintensities in the cerebral white matter seen on T2-weighted magnetic resonance imaging (MRI) and are believed to reflect underlying small artery disease [1]; they increase with age and correlate with vascular risk factors, such as hypertension and smoking [2]. Reports in depression literature demonstrate an increased frequency of WMLs in MD, variably associated with poor treatment response and cognitive performance [3]. However, the impact of WMLs on the neuronal network and the concurrent role of cerebral perfusion are not yet fully understood. We therefore aim to characterize the association between cerebral perfusion parameters and WMLs in late-onset MD.

Methods

We examined 22 unselected, consecutive patients with first episode, late-onset MD and 22 controls, matched for age and gender, in a 3 Tesla Signa HDx GE whole-body MRI scanner (GE Medical Systems, Milwaukee, WI, USA). The MRI protocol comprised a 3D T1-weighted sequence, T2-weighted FLAIR, and perfusion weighted MRI using gradient echo EPI during injection of 0.1 mmol/kg gadobutrol (Gadovist, Bayer-Schering, Berlin). Vascular risk factors were assessed and converted to a composite score [4] for each subject. MRI images were transformed into a standard space with the use of a non-linear model with a final resolution of 2 mm. Number and volume of WMLs were analyzed with non-parametric tests. MRI data were analyzed with voxel-based two-tailed t-tests using FMRISTAT [5].

Results

Perfusion analyses showed significantly increased CBF in the anterior cingulate gyrus in patients compared with controls (see Figure 1), while our analyses showed no significant difference in the number or volume of WMLs between groups.



Figure 1. Cluster (red) with significantly increased CBF in patients with late-onset MD compared with controls.

Discussion

Increased CBF in the anterior cingulate gyrus is supported by existing literature, although data from this area is inconsistent [6]. The cingulate gyrus functions as an integral part of the limbic system, which is involved in emotion formation and processing, learning, and memory. Alterations in regional CBF in MD may represent a state-dependent correlate of responses to neurophysiological imbalances in MD or a disease-specific trait. Advanced MRI techniques such as perfusion imaging may contribute to our further understanding of WMLs and their association with MD and vascular risk factors, with possible implications for the future treatment and prevention of depressive disease.

1. Pantoni, L. & Garcia, J. H. *Stroke* 28, 652-659 (1997). 2. Liao, D. et al. *Neuroepidemiology* 16, 149-162 (1997). 3. Herrmann, L. L., Le, M. M. & Ebmeier, K. P. *J Neurol Neurosurg Psychiatry* 79, 619-624 (2008). 4. Wolf, P. A., D'Agostino, R. B., Belanger, A. J. & Kannel, W. B. *Stroke* 22, 312-318 (1991). 5. Worsley, K. J. et al. *Neuroimage* 15, 1-15 (2002). 6. Drevets, W. C. *Ann N Y Acad Sci* 29, 614-37 (1999).