MR Imaging of Arterial Dysfunction in a Transgenic Mouse Model of Alzheimer’s Disease

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Introduction

Arterial spin labeling (ASL) magnetic resonance imaging (MRI) has demonstrated regional cerebral hyperperfusion in Alzheimer’s disease (AD) patients, as well as murine models of AD. It is well-recognized that cerebral arteries undergo microstructural changes in AD, including deposition of β-amyloid (i.e. cerebral amyloid angiopathy) and loss of smooth muscle cells, resulting in cerebrovascular dysfunction. While ASL MRI is used to study perfusion deficits at the capillary level, it does not provide information about the complete arterial tree. Currently, compromised arterial function can be assessed in mouse brain by several techniques. However, these methods are generally restricted to focal regions of the cortical surface. In order to assess the entire arterial system, we have developed a novel, non-invasive, quantitative approach based on in vivo 3D MRI data.

Methods

MR image volumes were acquired from 5 month-old (young, n = 9) and 18-20 month-old (aged, n = 15) APP transgenic (TG) and wild-type (WT) mice. Whole-brain anatomical images and 3D MR arteriograms (140x140x280 μm) were acquired on a 7T small animal MRI system. The MRI data was processed using a fully-automated pipeline. In order to derive quantitative information from the arteriogram, we utilized a region-of-interest (ROI)-based approach. The ROI labels (vessel segments) were nonlinearly mapped from a standardized atlas in reference space to each mouse brain MRI volume in native space via atlas-based segmentation. We then derived a quantitative measure, the “arterial index”, which is related to the apparent arterial cerebral blood volume (CBVₐ), for each ROI.

Results

Figure 1 shows the group-average arteriogram from all MRI scans. Note the excellent definition of the azygos pericallosal artery and its branches in the sagittal view. The penetrating cortical arteries can be readily visualized in the coronal view.

In Figure 2, the reduced arterial index in the TG mice can be appreciated in the arteries supplying the hippocampus, as well as in the branches of the azygos pericallosal artery. Figure 3 shows the ROI-based measures for several arterial territories for each of the groups, as well as change over time. Statistically significant deficits are seen in the TG mice in multiple regions. The retrosplenial cortex demonstrates the greatest reduction over time in TG relative to WT mice.

Conclusions

We have developed a novel, non-invasive, quantitative approach to investigate cerebrovascular abnormalities throughout the entire arterial system. Using this MRI technique, we have observed significant arterial dysfunction in young and aged APP TG mice. The assessment of regional arterial index arterial provides unique information regarding cerebrovascular physiology and complements ASL perfusion MRI measures.

Acknowledgments

We thank Drs. Felix Carbonell & Alex Zijdenbos (Biospective Inc.) for their contributions to the image processing and statistical analysis. We thank Dr. Edith Hamel for assistance with the mice, and Dr. Lennart Mucke and the Gladstone Institutes for use of the APP mice. This work was supported by funding from the Canadian Institutes of Health Research (CIHR) and Canadian Foundation for Innovation (CFI).