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ORAL PRESENTATIONS

In vivo vascular mapping of the human hippocampus using MICRO imaging

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Background

There is an urgent need for better detection and understanding of vascular abnormalities at the micro-level, where critical vascular nourishment and cellular metabolic changes occur. This is especially the case for structures such as the midbrain and hippocampus, where both the feeding and draining vessels are quite small. The hippocampus is a complex grey matter structure that plays an important role in spatial and episodic memory. It can be affected by a wide range of pathologies including vascular abnormalities. Being able to monitor vascular changes in normal aging in various hippocampal subfields will allow us to better understand vascular vulnerability across the hippocampus.

Methods

We recently introduced the concept of microvascular *in-vivo* contrast revealed origins (MICRO) protocol to image microcerebral vessels.[1-3] MICRO uses ferumoxytol, an ultra-small superparamagnetic iron oxides (USPIO) agent, to induce susceptibility in the arteries and veins; and by imaging with high resolution (0.22×0.44×1 mm^3) susceptibility weighted imaging sequence (SWI) at 3 T. Although the increased vascular susceptibility enhances the visibility of small sub-voxel vessels, the accompanying strong signal loss of the large vessels deteriorates the local tissue contrast. Hence, data are collected at different time points during a gradual administration (final concentration = 4 mg/kg) of ferumoxytol. Dynamically acquired SWI data were co-registered and combined (phase gradient-based adaptive combination or SWI_{PGAC}) to reduce the blooming artifacts from large vessels, preserving the small-vessel contrast.

Results

The presence of ferumoxytol helped to enhance the microvasculature, something that has previously only been demonstrated in cadaver brain studies. Figure 1 shows the difference between the pre-contrast SWI and SWI_{PGAC} data in visualizing the micro-vasculature across four healthy subjects. The intra-hippocampal and superficial major arteries (obtained through a non-linear subtraction method) and veins (obtained by averaging the T1-shortening map, pre-contrast quantitative susceptibility mapping (QSM) and pre-contrast R_2* maps) are used as an overlay in the third column to better visualize the major vessels penetrating and draining the hippocampus. The hippocampal fissure, along with the fimbria, granular cell layer of the dentate gyrus and cornu ammonis layers (except for CA1), showed higher micro-vascular density than the other parts of hippocampus. The CA1 region exhibited a significant correlation with age ($R=-0.37$, $p<0.05$, $n=37$). demonstrating an overall loss of hippocampal vascularity in the normal aging process. Moreover, the vascular density reduction was more prominent than the age correlation with the volume reduction ($R=-0.1$, $p>0.05$, $n=37$) of the CA1 subfield.

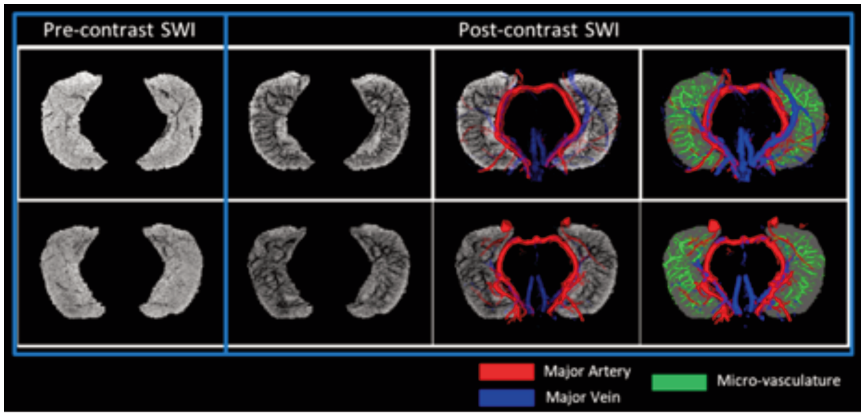

Figure 1. Revealing the microvasculature of the hippocampus using USPIO. Pre- and post-contrast SWI data, for three healthy controls (each in one row), are displayed with the overlays of major arteries (red), major veins (blue) and intra-hippocampal microvasculature (green). Although the pre-contrast SWI was able to highlight the presence of major veins due to the presence of deoxyhemoglobin, the vascular contrast from both arteries and veins was improved significantly on the post-contrast SWI data.

Conclusions

With this USPIO-induced increase in susceptibility comes the potential to study the cerebral micro-vasculature using high-resolution SWI. There was a strong negative correlation between hippocampal functional vessel density (FVD) (especially in CA1) and age. This FVD reduction was more prominent than volume reduction *vs* age, suggesting that vascular atrophy may precede reductions in tissue volume. Mapping the hippocampal vasculature has immediate implications for understanding the effects of normal aging and the etiology of many neurovascular diseases. MICRO imaging brings us into the decade of imaging the microvasculature of the entire human body.

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