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Decreased oxygen saturation in asymmetrically prominent cortical veins in patients with cerebral ischemic stroke

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ABSTRACT

Decreased oxygen saturation in asymmetrically prominent cortical veins (APCV) seen in ischemic stroke has been hypothesized to correlate with an increase of de-oxygenated hemoglobin. Our goal is to quantify magnetic susceptibility to define APCV by establishing a cutoff above which the deoxyhemoglobin levels are considered abnormal. A retrospective study was conducted on 26 patients with acute ischemic stroke in one cerebral hemisphere that exhibited APCV with 30 age- and sex-matched healthy controls. Quantitative susceptibility mapping (QSM) was used to calculate the magnetic susceptibility of the cortical veins. A paired *t*-test was used to compare the susceptibility of the cortical veins in the left and right hemispheres for healthy controls as well as in the contralateral hemisphere for stroke patients with APCV. The change in oxygen saturation in the APCV relative to the contralateral side was calculated after thresholding the susceptibility using the mean plus two standard deviations of the contralateral side for each individual. The thresholded susceptibility value of the APCVs in the stroke hemisphere was 254 ± 48 ppb which was significantly higher ($p < 0.05$) than that in the contralateral hemisphere (123 ± 12 ppb) and in healthy controls (125 ± 8 ppb). There was a decrease of oxygen saturation in the APCV ranging from 16% to 44% relative to the veins of the contralateral hemisphere. In conclusion, APCV seen in SWI correspond to reduced levels of oxygen saturation and these abnormal veins can be identified using a susceptibility threshold on the QSM data.

1. Introduction

Asymmetrically prominent cortical veins (APCV) seen in ischemic stroke have been introduced in several papers [1–5], with many presented as case reports [2–4,6,7]. In these observations, APCVs were typically identified if: 1) the diameter of the cortical veins in the ischemic hemisphere was larger than those in the contralateral hemisphere and/or 2) the length and visibility of veins was increased compared to those in the contralateral hemisphere. It has been proposed that APCV in the area of ischemia represent salvageable tissue [1–5,8]. The presence of APCV has been hypothesized to be related to increased deoxyhemoglobin (DHb) which is closely related with oxygen saturation and oxygen extraction fraction [4,9].

Understanding the difference in blood oxygen saturation between arteries and veins (Ya-Yv) could provide key information about cerebral oxygen demand and supply [10,11] of normal and diseased tissues. Previous MR studies to measure oxygen saturation have included T2 [12], T2* [13] and phase based methods [11,14,15]. Recently, phase based methods have had a resurgence in studying oxygen saturation of major veins which has been referred to as magnetic susceptometry [11,14,15]. The phase based method has been used to measure relative changes in oxygen saturation in traumatic brain injury in animals [16]. Susceptibility mapping (SM), using susceptibility weighted imaging (SWI), for measuring oxygen saturation was introduced by Haacke et al. [17] and has the potential to provide quantitative oxygen saturation estimations of cortical veins.

Ideally, to understand the changes of the brain's hemodynamics after stroke, perfusion measurements should be performed and then correlated with possible changes of oxygen saturation. For example,

Abbreviations: ΔYab, changes of oxygen saturation; APCV, asymmetrically prominent cortical veins; SM, susceptibility mapping; SWI, susceptibility weighted imaging; Y, oxygen saturation; ppb, parts per billion; DHb, deoxyhemoglobin.

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Table 1
Summary of sequence parameters.

Parameters	DWI	T2WI	SWI	MRA
TR (ms)	4000	5000	27	22
TE(ms)	96	96	20	3.59
Flip angle (degrees)	90	120	15	18
Field-of-view (mm × mm)	230 × 230	240 × 240	230 × 200	240 × 200
Resolution (mm × mm × mm)	0.6 × 0.6 × 5	0.6 × 0.6 × 5	0.5 × 0.5 × 2	0.8 × 0.8 × 0.8
Bandwidth (Hz/pixel)	1343	221	120	164
Number of slices	20	20	56	240
Acquisition time	1 min 01 s	1 min 45 s	2 min 58 s	7 min 02 s

if the cerebral blood flow decreases while the brain metabolism remains stable then it should be possible to see that oxygen saturation of the veins will decrease due to increased oxygen extraction fraction on blood with an already depleted supply. However, even without this direct measure, the presence of APCV can be used to infer such changes in perfusion. In this study, we hypothesize that it is possible to establish a susceptibility threshold above which one can infer that the level of deoxyhemoglobin in the cortical veins is abnormally high.

2. Materials and methods

2.1. Subjects

Data from 78 patients with acute ischemic stroke of one hemisphere were collected from December 2011 to March 2013. This study was approved by the local Institutional Review Board (IRB) of Tianjin First Central Hospital. Written consent from the patients or their relatives was stored in the hospital database and used for research. The inclusion criteria included: 1) the patients had available MRI data with SWI, diffusion weighted imaging (DWI) and MR angiography (MRA); 2) the lesion showed clearly recognizable hyperintensity on DWI and hypointensity on ADC which is a hallmark of acute ischemic infarction; 3) qualifying lesions only affected one hemisphere where there was occlusion of the middle cerebral artery, while the contralateral hemisphere was unaffected and served as a control; and 4) the cortical veins had to be visible bilaterally in order to measure their susceptibility.

Finally, 26 cases with APCV were included in this study. Thirty age and sex matched healthy controls were also recruited who had the same MRI protocol in order to measure the susceptibility value of cortical veins. All patients were evaluated for NIHSS (national institute of health stroke scale) within 24 hours before or after MRI examination. Additional information included: the time from symptom onset to MRI examination, the history of diastolic and systolic pressure, smoking behavior, and alcohol consumption. The MRA appearance and side of infarction were also recorded based on the imaging.

2.2. Imaging parameters

The SWI data were collected on a 3 T MRI Siemens system (Trio Tim, Siemens Medical Systems, Allegra, Germany) with a resolution of 0.5 × 0.5 × 2 mm^3. Routine T1WI, T2WI, DWI and MRA were collected for the diagnosis of acute infarction and for ruling out other lesions, such as tumor, hemorrhage, etc. The detailed parameters of the sequences are listed in Table 1.

2.3. Analysis of the data

The SMART (Susceptibility Mapping and phase Artifacts Removal Toolbox; Detroit, MI, USA) software tool was used to reconstruct the SM data. The processing included the following steps: Firstly, a high resolution SWI gradient echo sequence with velocity compensation in 3 directions was acquired with both the magnitude and phase images being obtained. Secondly, phase images were high-pass filtered using a central 96 × 96 homodyne filter [18]. Thirdly, phase k-space was interpolated by zero filling the phase images to a larger matrix size for the purpose of reducing the aliasing artifacts in the final SM data. Fourthly, skull stripping and complex thresholding were performed to remove unwanted regions of low signal [18]. Fifthly, a regularization threshold of 0.1 was used for the inverse process. A detailed description of the steps used in the processing of susceptibility mapping was outlined in our group's previous work [17].

SPIN (signal processing in nuclear magnetic resonance, Detroit, Michigan, USA) software was used to view and analyze the SM data. The susceptibility of the APCV in the area of the acute infarction and the corresponding veins in the control hemisphere were calculated directly from the SM data. The susceptibility values were measured from a maximum intensity projection (MIP) image over 16 SM slices (3.2 cm effective coverage) Fig. 1A. These MIPped SM images were chosen to run from the midbrain to the uppermost level of the brain in order to cover and include all major cortical veins while limiting any potential artifact from the sinus cavities. Two ROIs were drawn to include all of the veins in both hemispheres. A lower threshold of 90 ppb was applied to the MIPped SM data to highlight the cortical veins on the images as shown in Fig. 1B. This value was chosen because it is the lower end of susceptibility values for cortical veins in controls and therefore it removed most of the background tissue while preserving the signal from the cortical veins to be included in the analysis. The susceptibility of veins from the ischemic hemi-

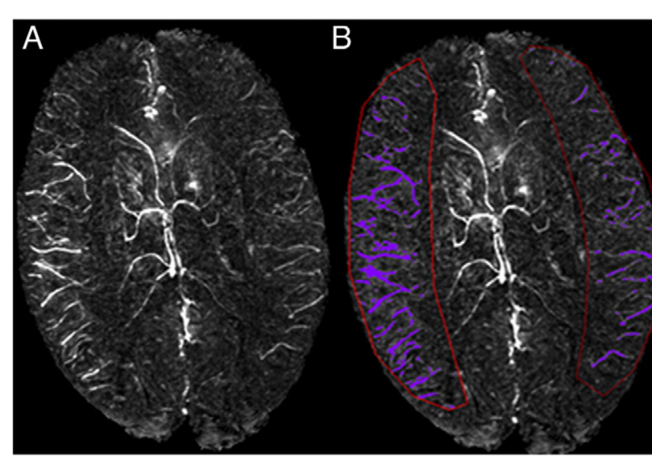

Fig. 1. Demonstration of the selection of cortical veins in control and ischemic hemispheres on SM. The original SM shows higher intensity in the right ischemic hemisphere (A) while the control left hemisphere still shows visible structures with lower susceptibility. The lower threshold of 90 ppb is set to highlight the cortical veins on the control side and determine the mean and standard deviation of the veins susceptibility (B) in this region. Note that the visibility of venous structures is increased in the ischemic hemisphere.