NeuroImage 172 (2018) 470–477

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Vascular reactivity in small cerebral perforating arteries with 7 T phase contrast MRI – A proof of concept study

Lennart J. Geurts [a,*], Alex A. Bhogal [a], Jeroen C.W. Siero [a,b], Peter R. Luijten [a], Geert Jan Biessels [c], Jaco J.M. Zwanenburg [a]

[a] Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands
[b] Spinoza Centre for Neuroimaging Amsterdam, Amsterdam, The Netherlands
[c] Department of Neurology and Neurosurgery, Brain Centre Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands

ARTICLE INFO

Keywords:
Cerebrovascular reactivity
Phase contrast MRI
Blood flow velocity
Cerebral perforating artery
Hypercapnia
White matter

ABSTRACT

Existing cerebrovascular reactivity (CVR) techniques assess flow reactivity in either the largest cerebral vessels or at the level of the parenchyma. We examined the ability of 2D phase contrast MRI at 7 T to measure CVR in small cerebral perforating arteries.

Blood flow velocity in perforators was measured in 10 healthy volunteers (mean age 26 years) using a 7 T MR scanner, using phase contrast acquisitions in the semioval center (CSO), the basal ganglia (BG) and the middle cerebral artery (MCA). Changes in flow velocity in response to a hypercapnic breathing challenge were assessed, and expressed as the percentual increase of flow velocity as a function of the increase in end tidal partial pressure of CO_2.

The hypercapnic challenge increased (fit ± standard error) flow velocity by 0.7 ± 0.3%/mmHg in the CSO ($P < 0.01$). Moreover, the number of detected perforators (mean [range]) increased from 63 [27–88] to 108 [61–178] ($P < 0.001$). In the BG, the hypercapnic challenge increased flow velocity by 1.6 ± 0.5%/mmHg ($P < 0.001$), and the number of detected perforators increased from 48 [24–66] to 63 [32–91] ($P < 0.01$). The flow in the MCA increased by 5.2 ± 1.4%/mmHg ($P < 0.01$).

Small vessel specific reactivity can now be measured in perforators of the CSO and BG, using 2D phase contrast at 7 T.

Introduction

With the increased SNR available in ultra-high field strength MRI, it has become feasible to measure increasingly smaller anatomical structures and their function in vivo. Recently, we developed a 2D phase contrast method at 7 T MRI, capable of measuring the time resolved blood flow velocity and pulsatility index in cerebral perforating arteries with diameters between 10 and 300 μm (Bouvy et al., 2016; Geurts et al., 2018). Abnormalities in these perforators, also referred to as cerebral small vessel disease (SVD), are a major cause of stroke and dementia (Pantoni, 2010; Wardlaw et al., 2013). Measuring hemodynamic properties of these small perforators may help to unravel the pathophysiological processes of SVD (Broderick et al., 1997; Lee et al., 2007; Mitchell, 2008; Mitchell et al., 2011).

A hemodynamic property that is relevant, is cerebrovascular reactivity (CVR). CVR is a physiological mechanism that contributes to cerebral autoregulation. To influence resistance and flow, vessel diameters change with perfusion pressure variation, but also with arterial CO_2 levels. Impaired CVR has been linked to white matter hyper-intensities, vascular dementia and an increased risk of stroke by a growing body of literature (Beishon et al., 2017; Reinhard et al., 2014; Reuck et al., 1999; Sam et al., 2016a, 2016b). CVR can currently be measured on a tissue level using blood oxygenation level dependent (BOLD) MRI, arterial spin labeling (ASL) or positron emission tomography (Halani et al., 2015;

Abbreviations: $PetCO_2$, end tidal partial pressure of carbon dioxide; SVD, small vessel disease; MCA, middle cerebral artery; CSO, semi oval center; BG, basal ganglia; TCD, transcranial Doppler ultrasound; MRI, magnetic resonance imaging; TE, echo time; TR, repetition time; FOV, field of view; BW, bandwidth; TFE, turbo field echo; Venc, encoding velocity; SNR, signal to noise ratio; BOLD, blood oxygenation level dependent; ASL, arterial spin labeling; T1w, T1 weighted; TONE, tilted optimized non-saturating excitation; CVR, cerebrovascular reactivity; R_v, velocity reactivity; R_ϕ, flow reactivity; R_d, diameter reactivity; ROI, region of interest; LME, linear mixed effects; CI, confidence interval; $N_{detected}$, number of detected perforators; V_{mean}, mean velocity.

* Corresponding author.
E-mail address: l.j.geurts-2@umcutrecht.nl (L.J. Geurts).

https://doi.org/10.1016/j.neuroimage.2018.01.055
Received 7 August 2017; Received in revised form 14 January 2018; Accepted 21 January 2018

Heijtel et al., 2014). CVR can also be measured at the level of the large intracranial arteries via Transcranial Doppler ultrasound (TCD) or phase contrast MRI (Leung et al., 2013). Currently there are no established methods to non-invasively assess reactivity in small arteries that are situated in between the large arteries and the tissue. Bridging this gap may help characterize reactivity in the cerebral vascular system as a whole. Now that 2D phase contrast MRI at 7 T can reliably measure blood flow velocity in perforators, it might be possible that it can also measure CVR in these small vessels (Geurts et al., 2018). Measuring CVR in perforating arteries with 2D phase contrast would complement existing methods and can help to pinpoint CVR impairments directly associated with local ischemia.

The aim of this paper is to determine whether it is feasible to measure CVR with the previously developed 2D phase contrast method in the cerebral perforating arteries of the semioval center and the basal ganglia. As a reference, we perform the same measurement in the middle cerebral artery as well. In all three experiments a baseline measurement was acquired, followed by a measurement in which the partial pressure of end tidal CO_2 ($PetCO_2$) was increased using a computer controlled gas delivery system. The change in blood flow velocity was taken as the primary outcome. Since increased blood flow increases blood signal through the T1-inflow effect, it becomes more likely that perforators are detected during the challenge (Bhogal et al., 2014; Brown et al., 2014; Geurts et al., 2018). Therefore, the change in number of detected perforators was taken as the secondary outcome. Systematic errors of CVR of the perforating arteries were qualitatively assessed through simulation.

Methods

Data acquisition

A group of 10 healthy volunteers was scanned using a 7 T MRI system (Philips Healthcare, Best, The Netherlands) and a 32 channel receive coil with volume T/R transmit coil (Nova Medical, Wilmington, MA, USA). The institutional review board of our hospital approved this study and all subjects provided written informed consent. A 2D phase contrast acquisition was performed at three anatomical locations during baseline breathing and hypercapnia. The phase contrast acquisitions were alternated with T1 weighted 3D turbo field echo (T1w) acquisitions for white matter segmentation. Interleaving structural scans with hypercapnic scans provided subjects with a rest period in which CO_2 values could fully return to resting values for subsequent baseline phase contrast scans. Baseline acquisitions were only started when CO_2 values had returned to normal. These scans also avoided potential problems due to (slight) changes in subject position over the duration of the exam, which would result in problems aligning the white matter segmentation with the 2D phase contrast results.

The planning of the three phase contrast slices is shown in Fig. 1. One slice was acquired in the perforating arteries of the semi-oval center (CSO, the white matter core underneath the cortical grey matter). The CSO contains perforators with very small diameters (10–300 μm), branching off from pial arteries. These perforators feed the capillary network of the white matter, the CVR of which is an area of active study (Sam et al., 2016a, 2016b). A group of larger perforators (diameters up to 1 mm) were measured with another phase contrast slice in the basal ganglia (BG, the subcortical nuclei of grey matter at the base of the brain). Their larger size ensures a higher blood signal and lower partial volume effect. The middle cerebral artery (MCA, the largest of the major arteries of the brain) was measured as a large reference vessel with known reactivity (Leung et al., 2013; Valdueza et al., 1999; Verbree et al., 2014). A phase contrast acquisition was performed in the MCA on one side, taking the side that allowed the most ease in planning (long straight segment without major branches).

The CSO acquisitions were performed first. To have a large number of successful reference measurements, the MCA acquisitions were acquired second. The BG acquisitions were performed last in the protocol, since these perforators, with intermediate diameters, were the least critical for answering the research question. If an acquisition showed excessive motion artifacts, it was performed again after the standard protocol, but only if the subject was still comfortable and within a maximum of 1 h of scanning.

All acquisition parameters can be found in Table 1. The excitation was performed with a Tilted Optimized Non-saturating Excitation (TONE) pulse (Atkinson et al., 1994; Geurts et al., 2018), and the flip angle increased from 50 to 90° in the feet-head direction. A turbo field echo factor of 2 was used, to acquire two velocity encoding cycles per acquired time point in the cardiac cycle. This resulted in an acquired temporal resolution of 114 ms (57 ms reconstructed through interpolation). To

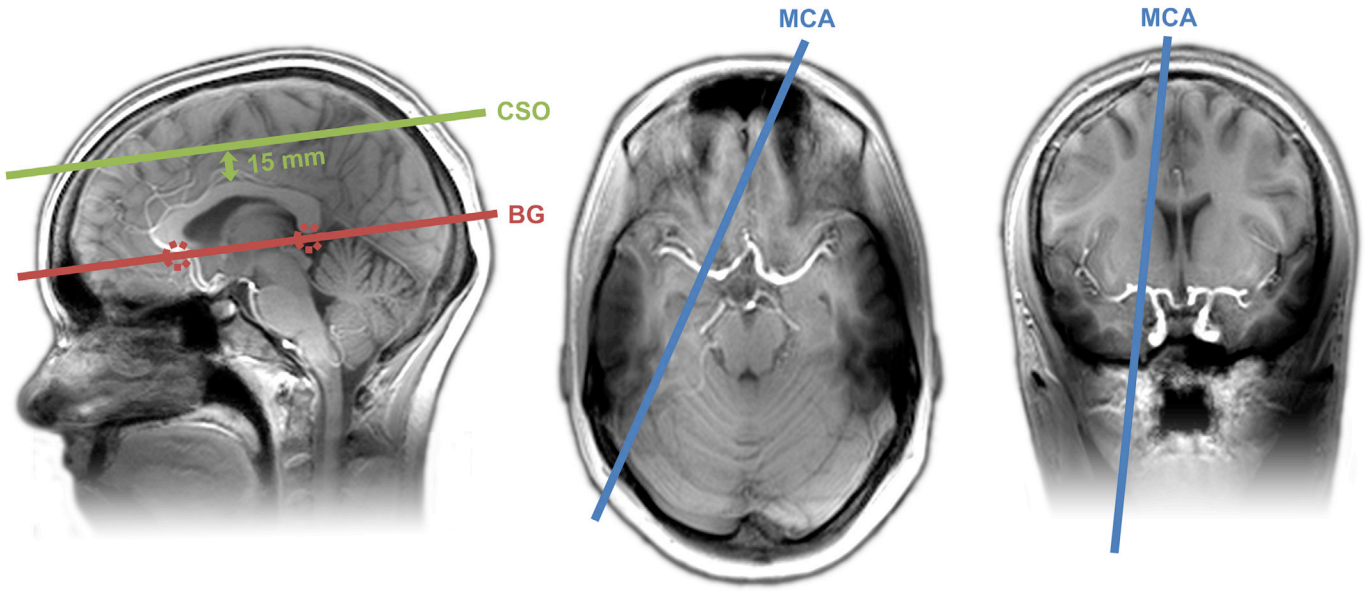

Fig. 1. Slice planning for the 2D phase contrast sequences. The left image shows the planning of the BG slice (in red) and the CSO slice (in green) on a sagittal T1 weighted image. The BG slice touches the underside of the corpus callosum, indicated by the dashed circles. The CSO slice is planned parallel to the BG slice and positioned 15 mm above the corpus callosum (Geurts et al., 2018). The center and right images show the planning of the MCA (in blue) on transverse and coronal T1 weighted images, respectively.