To Investigate the Cerebral Vasomotor Reactivity by CO2 Stimulus Using Cine PCMRI

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Introduction: The variation of blood flow in artery is generated by systole and diastole during one cardiac cycle. Using velocity-sensitive phase-contrast magnetic resonance imaging with retrospectively gated techniques (cine PCMRI), we can observe the velocity profile in one heartbeat. The techniques has been widely used in blood flow and CSF production rate [1,2]. Prior researches have shown that non-triggered 2D phase contrast magnetic resonance angiography (PCMRA) to be a useful tool for rapid flow measurement in phantom study [3] and human arteries [4].Cerebral vasomotor reactivity (VMR) is an index quantifying the capability of cerebral arterioles to dilate after extrinsic stimulation by vasodilators. Inhalation of carbon dioxide (CO2), with similar effect of vasodilatation as intravenous injection of acetazolamide, could serve as a stimulus of VMR, which has been demonstrated to be important in approaching cerebrovascular diseases such as transient ischemic attack [5]. In most studies, VMR was evaluated by the change of perfusion or blood flow before and after vasodilator stimulus. The blood flow is usually measured by Transcranial Doppler (TCD) which bases on the time-average flow of pulsatile flow in arteries, and the perfusion is acquired using the techniques which including xenon-enhanced computed tomography, dynamic susceptibility contrast magnetic resonance imaging, positron emission tomography and single photon emission tomography. Recently, PCMRA has been applied to investigate the cerebral VMR by breath-hold challenge [6] and carotid artery compression [7]. However, there is no study to observe on the difference between perfusion and blood flow for VMR evaluation. In this study, we aim to evaluate VMR of the human brain by blood-volume and blood-flow of both arteries and returning veins under graded CO2 inhalation (room air, 3%, 5% and 7%) on healthy volunteers using cine PCMRI.

Method: Six healthy subjects (mean age 29years,) given informed consent were recruited and were scanned with retrospectively gated 2D PCMRI using a 1.5T whole-body system (Siemens Vision plus, Erlangen, Germany). An oblique slice approximately vertical to the target vessels on a localizer MRA) slab in the sagittal plane was chosen to include the left (LICA) and right internal carotid artery (RICA), basilar artery (BA), sinus rectus (SR), superior sagittal sinus (SSS) (Fig 1). Cine 2D PCMRI measurements were performed with conventional protocol using optimal scan parameters (TR/TE= 29/7 ms; flip angel=30°; matrix size 115×256; FOV 120x240; Venc=150 cm/sec; slice thickness=5mm.). 64 cardiac phases were acquired and rearranged with retrospective electrocardiographic gating to form 32 images that represented sequential phases in a cardiac cycle. The scan time was 3 min 35 sec. Total four PC MRI scans were performed for different CO2 concentration (room air and 3%, 5% and 7% CO2 gas). At 3 min after CO2 gas inhalation, the PC-MRI was started with CO2 gas inhalation for 3%, 5% and 7% CO2 gas experiment. Quantitative blood flow values were calculated in the manually defined ROI regions according to the methods proposed by Huang et al. [2].The velocity profile and blood volume of each vessel in one heart beat was observed for different CO2 concentration. VMR index could be quantitative by the percentage change of increased flow for hypercapnia to normocapnia, (blood flow$_{(hypercapnia)}$ – blood flow$_{(normocapnia)}$) / blood flow$_{(normocapnia)}$ × 100%. Four types of VMR were defined in this study, $VMR_{sys\text{-}flow}$, $VMR_{mean\text{-}flow}$, $VMR_{dia\text{-}flow}$ and $VMR_{str\text{-}volume}$ computed by systolic blood flow, mean blood flow, diastolic blood flow and stroke volume, respectively.

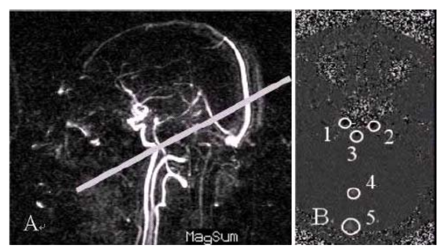

Fig1. (A) Sagittal localizer MRA. (B) Phase image with ROI (1) RICA (2) LICA (3) BA (4) SR (5) SSS.

Results: Fig. 2 depicted the mean blood flow in one cardio cycle from all subjects during the experiment (RICA shown only). The mean VMR indices of all vessels in systole, mean, diastole and stroke volume were graphically demonstrated in Fig. 3.

Discussion: Our results provided all VMRs as a nonlinear function of inhaled CO2 fraction. In all vessels, the $VMR_{str\text{-}volume}$ was 16% ~ 21% under 3% of CO2 inhalation, rose to 31% ~ 37% under 5% of CO2 inhalation and further climbed to 60% ~ 106% under 7% of CO2 inhalation. Although all four types of VMR analyses are similar and all they used to evaluate vessel reactive by vasodilator stimulus, the VMR interpretation is different in physiology. $VMR_{str\text{-}volume}$ is an increase percentage index of cerebral blood volume in vasodilator stimulus, but others ($VMR_{sys\text{-}flow}$, $VMR_{mean\text{-}flow}$, $VMR_{dia\text{-}flow}$) indicate the blood flow. Our result demonstrated the $VMR_{str\text{-}volume}$ is closer to $VMR_{mean\text{-}flow}$ under different CO2 induced hypercapnia comparing with other two blood flow VMR indexes.. Furthermore, $VMR_{sys\text{-}flow}$ and $VMR_{dia\text{-}flow}$ were near in 3% CO2, but widely separated in 5 and 7% CO2 condition (Figure 6). The finding was clearly observed in arteries, it reflected the increased ratio of blood flow by CO2-induced hypercapnia was not proportion in systole and diastole.

Acknowledgement: This work was supported by National Science Council, Taiwan, under Grant No. 99-2221-E-035-009-MY3.

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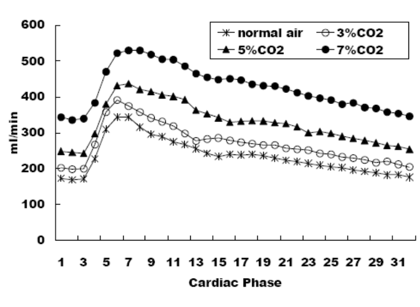

Fig2. The mean blood flow of RICA in one cardiac cycle as a function of time for the six subjects included in this study.

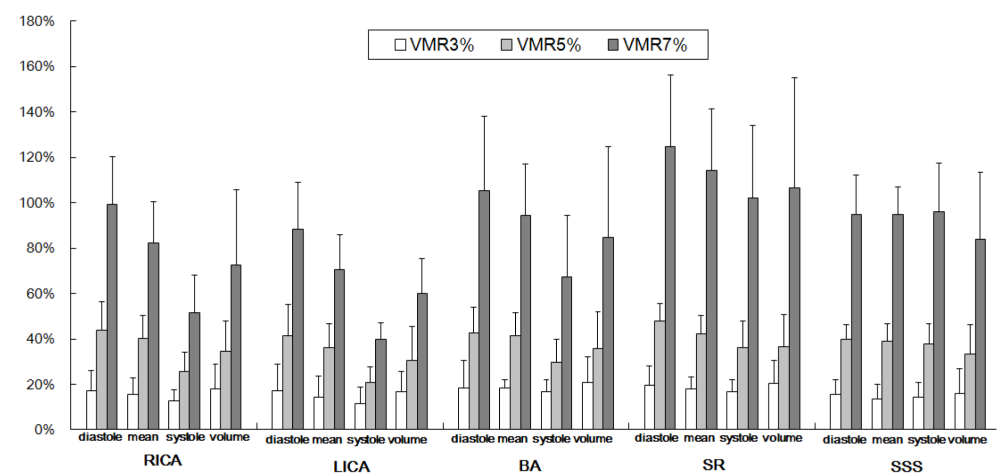

Fig3. Mean and SD of VMR in diastolic flow (diastole), mean flow (mean), systolic flow (systole) and stroke volume (volume) in five vessels for rom air to 3% CO2 (VMR3%), 5% CO2 (VMR5%) and 7% CO2 (VMR7%).