Physiology & Relevance of Cerebrovascular Reserve

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Background:

In addition to cerebral hemodynamics in a resting condition also the cerebral hemodynamics can be investigated after a challenge. This challenge can also be called stress-test and the parameter that is measured is often called cerebrovascular reserve or cerebrovascular reactivity. To investigate the Cerebrovascular reserve two things are needed: first a measurement method that can quantitatively or semi-quantitatively (for instance percentage change) measure cerebral hemodynamics. Second, a challenge that typically causes a vasodilatory change in the stress or challenge condition. The results are typically expressed as the (percentage) change between the rest and the challenge (vasodilatory) condition. In most of the MRI methods described below this change can be visually shown on the brain tissue level; to depict regions with for instance preserved and impaired reactivity. Generally speaking a smaller change in the 'stress or challenge condition' is often found in patients with cerebrovascular disease which is explained by vasculature that has a lower capacity to dilate. It is often hypothesized that in patients with cerebrovascular disease, such as a stenosis or occlusion, the vasculature distal to the stenosis or occlusion (at the level of the resistance arterioles) are chronically dilated to compensate for the lower perfusion pressure. The dilated arteries have a lower capacity to further dilate after a challenge. In a model of hemodynamic impairment this stage of dilation of resistance arterioles (with an increase in cerebral blood volume; CBV) has been doped stage I (with stage II hemodynamic impairment the oxygen extraction fraction is increased to maintain oxygen metabolism).[1]
To investigate the health or disease status of the vasculature after a stress test is very common from the heart: in the last decade cerebrovascular reserve measurements have also gained popularity to investigate hemodynamic changes in the brain vasculature. It is hypothesized that hemodynamic changes (IE dilation of resistance arterioles) can be present even when the resting blood flow is within the normal range. In the past the most common method to measure cerebrovascular reactivity was blood flow velocity measurements changes of the brain vasculature in a rest condition and after a challenge. Typically, transcranial Doppler ultrasound was used for these flow velocity measurements after a carbondioxide or breath-holding challenge. Also other measurement methods such as SPECT before and after a challenge have been used in many patient studies.
In the current lecture we will describe MR Methods to measure the cerebrovascular reserve. To do so different measurements methods will be described and different challenging methods will be described with emphasize on the most commonly used methods. Finally the patients groups in which these cerebrovascular reserve measurements can be performed are indicated. For further reading, references can be checked below.[2-3]

MR measurement methods of cerebrovascular reserve:

The most widely available measurement of cerebral hemodynamics with a good signal-to-noise ratio and therefor attractive measurement times and image quality are blood oxygen level dependent (BOLD) MRI measurement similar to those used in functional MRI. These acquisitions are sensitive to the amount of deoxyhemoglobin in the veins; more deoxyhemoglobin will results in a decrease in BOLD MRI signal at the long echo times used for these acquisitions. Similar to fMRI, an increase in blood flow will cause a decrease in the amount of deoxyhemoglobin and an increase in the BOLD signal. When the hemodynamic reserve is tested a vasodilatory challenge will result in an increase the cerebral blood flow and a positive change in the BOLD signal. In this concept a healthy arterial vasculature has a

stronger positive BOLD signal change compared to patients with cerebrovascular disease (with already dilated resistance arterioles). BOLD MRI sequences are available on all MRI scanners and processing of data is relatively straightforward. Still, a drawback of BOLD MRI measurements is that the only the percentage change in signal is measured and no quantitative measurement of for instance cerebral blood flow (or volume). As known from fMRI the BOLD measure is a composite of both changes in oxygenation, cerebral blood volume and cerebral blood flow. Arterial spin labeling (ASL) MRI has the ability to measure the cerebral blood flow quantitatively. When arterial spin labeling MRI is performed before and after a challenge both the percentage and quantitative change in cerebral blood flow can be used as a measure of cerebrovascular reserve. A drawback of ASL MRI is the lower signal-to-noise ratio relative to BOLD MRI. ASL includes a subtraction step of the acquired imaging pairs: subtraction of the label from the control image. With the rest and challenge condition another subtraction step is added. This two subtraction steps make ASL a low SNR method to measure cerebrovascular reserve.
Other MRI methods that can be used to measure the cerebrovascular reserve at the brain tissue level are CBV based methods such as VASO and other methods such as contrast injection; although contrast injection is cumbersome because of the contrast that is still present when the second measure is performed with a short delay which makes quantification of (changes) in signal difficult. Other methods that are quantitative at a vascular level include (2D and 3D) phase contrast MR angiography measurements which can also measure the cerebrovascular reserve in the larger vasculature when performed before and after a challenge.

MR challenging methods of cerebrovascular reserve:
Challenges for cerebrovascular reserve testing include inhalation of carbondioxide which increase the cerebral blood flow. Also breath-holding can be used to do so and breath-holding can be used as a challenge although breath-holding is less controlled compared to inhalation of a gas mixture with carbondioxide. Another challenge that was also often used with SPECT cerebrovascular reserve measurements is the intravenous injection of a vasodilatory medication (Acetazolamide/Diamox). Other challenges that are explored are short breath-holds ore the use of resting state fMRI signal (breathing related signal fluctuations) or hyperoxia.

Patient groups
Patient groups of interest are patients with acute, subacute or chronic cerebrovascular disease in which the cerebrovascular reserve is often impaired secondary to the presence of a stenosis or occlusion in the brain feeding vasculature. Recently, MRI measurements of cerebrovascular reserve have also been used more widely in other patients groups such as patients with vascular cognitive impairment, aging patient populations or in patients with non-vascular disease such as brain tumors. When a simple cerebrovascular reserve test is used which only requires a limited amount of MRI scantime this test can in principal be applied as an add-on to the structural MRI sequences and for instance cerebral blood flow measurements in rest. Although cerebrovascular reserve measurements are, similar to the evaluation with stress test of the coronary arteries, promising, the exact place in clinical MRI imaging protocol and clinical patient management has yet to be determined.

References

1. Derdeyn CP et al. Brain. 2002 Mar;125(Pt 3):595-607.
2. Donahue MJ, Strother MK, Hendrikse J. Novel MRI approaches for assessing cerebral hemodynamics in ischemic cerebrovascular disease. Stroke. 2012 Mar;43(3):903-15.
3. Bokkers RP et al. Cerebral autoregulation measured at the brain tissue level with arterial spin-labeling MR imaging. Radiology. 2010 Jul;256(1):201-8.