

Relation between cerebral small vessel disease and vascular reactivity - a 7 Tesla study

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Introduction

Lacunar infarcts (LI) and white matter lesions (WML) are regarded as manifestations of cerebral small vessel disease. The pathogenesis of these lesions is still a matter of investigation. Several causes have been hypothesized, ranging from atherosclerosis in the perforating arteries to more diffuse alterations in the brain vasculature.^{1,2} If the changes underlying cerebral small vessel disease involve the vessel wall, as described in a process called lipohyalinosis,³ this may cause a loss of vascular reactivity in the brain. Functional assessment of the vasculature of the brain may provide valuable information about the impact of these vascular changes. This study investigated the relation between LI, WML and the vascular reactivity of the brain, measured through the BOLD-response at 7 Tesla.

Methods

Thirteen consecutive participants (9 men, 4 women, mean age 58.1, SD 7.6) with vascular disease or vascular risk factors and without non-lacunar infarcts on MRI from the Second Manifestations of ARterial disease (SMART) study were included. A BOLD fMRI scan with breath holding (BH) was made for all participants on a 7T scanner. The BH paradigm consisted of 5 periods of BH lasting 21s, interleaved with 30s of normal breathing. During the last BH period the subjects were asked to keep their breath as long as possible. Single shot Echo Planar Imaging (EPI) was used to measure the BOLD effect induced by the BH task. Scan parameters were: TR=3s, TE=20ms, SENSE factor 4, 96 volumes, 45 slices with no gap and a resolution of 1.5x1.5x1.5mm³. Multiple linear regression was applied to select activated voxels using a block model. The block was shifted by 4 volumes relative to the task to take into account the delayed BOLD response to the task. A linear term was included in the model to account for scanner drift. Estimated signal changes were used to create a T-map. The number of activated voxels was calculated by applying a threshold of Tcrit=2 to this map.

As a second measure for vascular reactivity whole brain (WB) signal change was calculated by averaging the estimated signal changes over a WB mask. This WB mask was created by setting a threshold on the first EPI volume and smoothing and eroding the result. The same mask was used to convert the number of activated voxels to a percentage of activated voxels.

The two measures were compared between patients with LI (n=4) and patients without LI (n=9) using Analysis of Covariance (ANCOVA), adjusted for age and sex. Multiple linear regression analysis was performed to identify if LI or WML contributed to the reduction in cerebrovascular reactivity after adjustment for age and sex.

Results

Figure 1 shows the activation pattern of one of the patients as a result of BH. The percentage of activated voxels was lower in patients with LI (mean 20.5%, 95% CI 16.1-24.8%) than in patients without LI (mean 31.2, 95% CI 28.3-34.0%, p=0.002) (figure 2). The difference in whole brain signal change was lower in patients with LI (mean 1.45, 95% CI 1.04-1.06) than in patients without LI (mean 0.90, 95% CI 0.28-1.51), although this was not significant (figure 3). Multiple linear regression analysis showed that the presence of LI significantly reduced the percentage of activated voxels (beta -0.996, p=0.004). For WB signal change, the presence of LI also resulted in a significant reduction (beta -0.866, p=0.019). WML showed no significant relation with the percentage of activated voxels or whole brain signal change.

Conclusion

Cerebral vascular reactivity measured through the BOLD-response at 7 Tesla is significantly reduced in patients with lacunar infarcts. The reduction in percentage of activated voxels and the whole brain signal change are associated with the presence of LI, independent of sex and age. Increase in WML is not associated with a reduction of either of these measures of cerebral vascular reactivity.

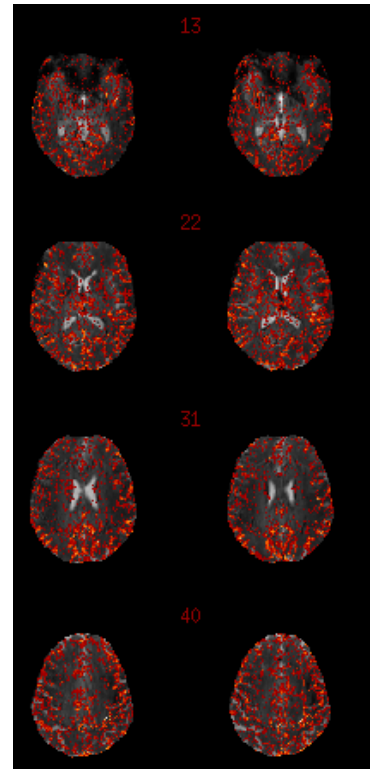


Figure 1
These images show the activation pattern in the brain after breathholding

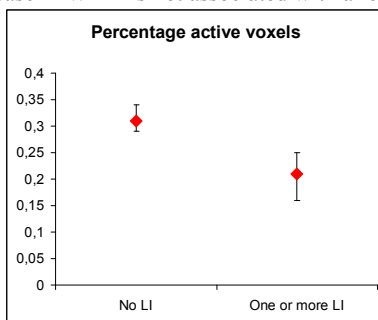


Figure 2
The mean percentage of active voxels after breathholding for patients without LI and one or more LI with 95% CI

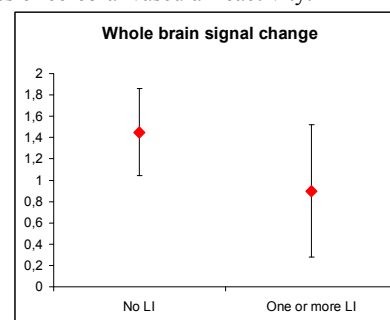


Figure 3
Mean whole brain signal change after breathholding for patients without LI and one or more LI with 95% CI

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