Stress testing the brain at 7T with breath holding

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Introduction

Cerebrovascular Reactivity (CVR) is a valuable clinical parameter in the evaluation of patients with vascular diseases [1 ,2]. Transcranial Doppler (TCD) is widely used to access CVR. Over the last decade MRI appeared as an alternative modality. It provides whole brain coverage and allows the study of regional differences in CVR [3]. The 'stress test for the brain' can be induced by invasive methods like injection of acetozolamide and inhalation of carbon dioxide and non invasive methods like hyperventilation and breath holding (BH). BH can be easily performed in a clinical setting [4] at 1.5 and 3T. Correlation between BH and invasive methods has been reported [5,6]. However, signal changes induced by BH at 1.5 and 3T are limited to 2-4% and variations are large [7]. This makes it difficult to differentiate between normal and impaired CVR. Here we report on the possibility of using BH in combination with BOLD fMRI at 7T. We provide normative values for an easy to perform BH task in healthy volunteers.
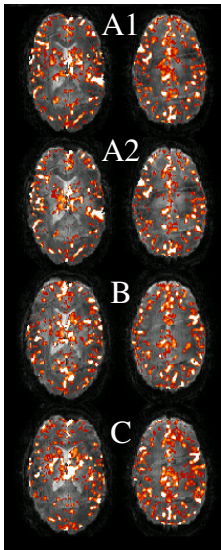
Methods

Fig 1: *Activated voxels*

Nine volunteers participated in this study. All measurements were performed on a 7T scanner (Philips) using a 16 channel head coil (Nova Medical). Each subject performed 4 times a BH paradigm: two times in a single session (scans A1 and A2) and in two consecutive sessions with repositioning of the subject in between the sessions (scans B and C). Care was taken to have similar spatial coverage. Sessions A and B/C were separated by one week while the order was balanced over subjects. The BH paradigm consisted of 5 periods of BH interleaved with 30s of normal breathing. The first 4 BH periods lasted 21s, the last one "as long as possible" (ALAP). Data from the respiratory belt of the scanner was logged and used to evaluate task performance and the length of the ALAP condition. 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 $1.5 \times 1.5 \times 1.5$mm^3. The data was realigned and scanner drift was removed prior to data analysis. Average signal and standard deviation (SD) over time were determined for each voxel. A voxel was considered activated by the BH task, if there were at least 3 consecutive time points were the signal was more than 2 SD higher than the average signal. Time courses of activated voxels were averaged, smoothed and maximum signal change and time to peak were determined.

Fig 2: *Signal change of 21s vs ALAP BH*

Results & Discussion

Figure 1 shows an example of voxels that were activated by the BH paradigm in the same subject over 4 scans. On average over all subjects and scans, 16±5% of the brain voxels were activated. No effects of repositioning of subjects or the interval between scans could be detected therefore data of subjects was pooled over scans. Table 1 shows the average signal change for each subject. Note the relatively low signal change in subject 1. Inspection of the recorded respiratory data revealed that this subject had difficulty in performing the 21s of BH. The other eight subjects could perform the task without difficulty. Averaged over all subjects, signal change was 6.4±1.4%. This is a threefold increase compared to 2.0±0.6% with 20s of BH recently reported using a 3T scanner [7]. Maximum signal change was reached approximately 6s after the end of the BH period indicating that the maximum obtainable effect is probably larger. This is shown in figure 2. The maximum signal change in the ALAP condition is slightly above the signal change in the 21s BH condition in most subjects. Inspection of signal time courses showed that the signal change reached a plateau in the ALAP condition in most cases. Figure 3 shows the duration of the ALAP period versus the maximum signal change with a tentative nonlinear fit to the data. Although the spread in signal change is considerable and clearly more data are required, it is this type of normalization graph that is needed to be able to detect impaired CVR in patients.

Fig 3: *Duration vs signal change ALAP condition*

Conclusion

A simple BH paradigm was used to measure CVR in healthy volunteers at 7T. 21s of BH gave rise to a BOLD signal change of more than 6% which means a 2- to 3-fold increase in signal change when compared to 1.5 and 3T. The observed signal change was close to what could be reached in the ALAP condition. This indicates that 21s of BH is the minimum time for a fixed length BH period to assess CVR and shows that task performance should be evaluated. In patients that are not capable of holding their breath for 21s, the ALAP test may be more suitable. Normalization of the signal change to correct for the duration of the ALAP period is necessary in that case. Further research is needed to determine whether this allows a differentiation between patients with impaired CVR and healthy volunteers. The increased BOLD contrast at 7T provides definitely a step towards a simple 'stress test for the brain' in a clinical setting.

Subject	1	2	3	4	5	6	7	8	9	Mean
Signal change ±SD (%)	3.9±0.5	8.0±1.0	6.6±0.2	5.8±1.6	7.3±1.3	5.6±0.8	7.1±0.9	6.7±1.3	6.1±0.8	6.4±1.4%

References

[1] S. Haller et al. Radiology 249(1):251-258, 2008, [2] H. Marcus and M. Cullinane. Brain 124(3):457-467, 2001, [3] A. Kastrup et al. NeuroImage 10:675-681, 1999, [4] A. Kastrup et al. Stroke 29:2641-2645, 1998, [5] A. Kastrup et al. MRI 19:13-20, 2001, [6] M. Muller et al. Stroke 26:96-100, 1995, [7] A. Scout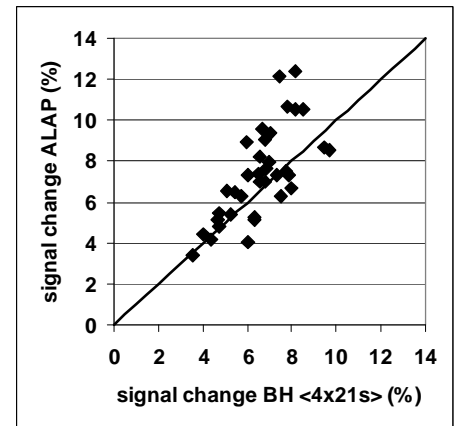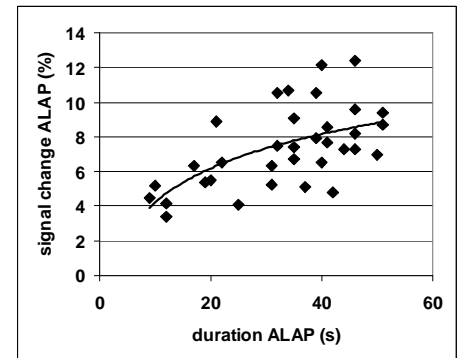en and C. Schwarzbauer, NeuroImage 43:250-257, 2008.