Hemodynamic scaling of fMRI-BOLD signal amplitude in normal aging

S. S. Kannurpatti[1], M. A. Motes[2], B. Rypma[2], and B. B. Biswal[1]

[1]Radiology, UMDNJ-New Jersey Medical School, Newark, New Jersey, United States, [2]School of Behavioral and Brain Sciences, University of Texas at Dallas, Dallas, Texas, United States

Introduction: Vascular reactivity and resting cerebral blood flow (CBF) levels lead to inter-subject variability in functional magnetic resonance imaging (fMRI) studies using the Blood Oxygen Level Dependent (BOLD) contrast to a neural task. This variability is exacerbated in an aging population [1]. Hemodynamic scaling using Resting State Fluctuation Amplitude (RSFA) or Breath hold (BH) can mitigate intra and inter-subject BOLD signal variability to a large extent by minimizing vascular variability [2]. In this study, we investigated the BOLD signal variability during a motor and a cognitive task in young and old subjects. BOLD signal change was hemodynamically scaled using RSFA or BH, which led to a reduction in BOLD variability in both the young and old groups. The extent of reduction in BOLD signal variability in the older subjects was significantly larger than the young. This indicates that vascular variability in the elderly exacerbates age-related BOLD signal contrast variability in neural task-induced hemodynamic activity.

Methods: Twelve younger healthy human subjects (6M and 6F; mean age: 24 years; range: 19-27 years) and twelve older healthy subjects (5M and 7F; mean age: 58 years; range: 55-71 years) with no history of head trauma and neurological disease were scanned in a 3T PHILIPS MR-scanner. The Institutional Review Board of the University of Texas at Dallas approved all experimental procedures. Each subject performed a breath hold (BH), bilateral fingertapping (FTAP) and Digit-Symbol Substitution task (DSST). The MR scanner was equipped with a fixed asymmetric head gradient coil and a quadrature transmit/receive birdcage radio-frequency coil. Foam padding and a pillow were used to minimize subject head motion. High-resolution T1 weighted anatomical images were obtained from all subjects. Gradient echo-EPI images were subsequently obtained during rest, BH, FTAP and the DSST runs. 32 slices were obtained in the axial plane covering the entire brain. Imaging parameters were: FOV of 22 cm, matrix size of 64x64, TR/TE = 2000/30 msec and slice thickness of 4mm. 110 EPI images were obtained during each of rest, BH, DSST and FTAP tasks. Hemodynamic amplitude scaling was accomplished by dividing the BOLD signal response amplitude during the task (FTAP or DSST) with the BH-induced BOLD signal change or RSFA in the corresponding voxels [2]. The resting state data from one young subject was corrupted and data from all runs except the DSST task in one elderly subject was not considered for analysis due to excess motion.

Results and Discussion: Table 1 shows the BOLD signal amplitude change (percent change from pre-task baseline) for all tasks prior to and after hemodynamic scaling with RSFA or BH in younger subjects. Table 2 shows the same for older subjects. Hemodynamic scaling reduced the mean BOLD signal change during both motor and cognitive tasks in addition to significantly reducing the inter-subject variation in both younger and older subject groups. After hemodynamic scaling with BH, a relatively large reduction in the variation in the motor task-induced BOLD signal change was observed in the older subject group where the coefficient of variation (CV) reduced from 0.57 to 0.22. Such a large reduction in inter-subject variation was not evident in the younger subject group where the CV remained at 0.18 before and after hemodynamic scaling with BH. During the cognitive task, the inter-subject variation in the BOLD signal change reduced moderately from 0.31 to 0.28 in the older group and from 0.28 to 0.25 in the young. A similar trend was observed during scaling with RSFA. The above results indicate that variability in vascular sensitivity in the motor cortex may be more prominent in the elderly compared to the young.

Table 1: BOLD signal amplitude change in young subjects to a motor (FTAP) and cognitive (DSST) task and their values after hemodynamic scaling with RSFA or BH.

Subject (young)	FTAP			DSST		
	unscaled	scaled_RSFA	scaled_BH	unscaled	scaled_RSFA	scaled_BH
bh002	3.27	n.a	0.93	3.56	n.a	0.84
bh003	2.62	1.22	0.9	3.78	1.00	0.75
bh004	2.58	1.06	0.73	4.96	1.00	0.63
bh005	3.6	1.40	0.90	3.12	1.13	0.66
bh008	2.47	1.67	1.08	3.16	1.86	1.15
bh009	3.39	1.53	1.40	4.48	1.42	1.26
bh010	2.35	1.25	1.10	3.12	1.13	1.16
bh011	2.94	1.20	1.02	3.75	1.00	0.76
bh014	3.15	1.46	1.00	3.42	1.33	0.91
bh015	1.83	1.60	1.30	6.81	1.59	1.25
bh019	2.71	1.10	1.00	4.00	0.83	0.75
bh020	2.69	1.20	0.93	3.12	1.13	0.80
Mean	**2.80**	**1.34**	**1.02**	**3.94***	**1.22**	**0.91**
SD	**0.49**	**0.20**	**0.18**	**1.10**	**0.30**	**0.23**
CV	**0.18**	**0.15**	**0.18**	**0.28**	**0.25**	**0.25**

P<0.01 compared to FTAP prior to scaling in young subjects; paired t-test

Table 2: BOLD signal amplitude change in old subjects to a motor (FTAP) and cognitive (DSST) task and their values after hemodynamic scaling with RSFA or BH.

Subject (old)	FTAP			DSST		
	unscaled	scaled_RSFA	scaled_BH	unscaled	scaled_RSFA	scaled_BH
bh101	n.a	n.a	n.a	7.01	n.a	1.16
bh103	3.00	1.41	1.38	5.91	1.45	1.25
bh104	1.64	0.98	0.70	2.79	1.24	0.80
bh105	2.36	1.36	1.04	2.86	1.05	0.70
bh106	2.94	0.91	1.17	5.12	1.45	1.47
bh107	5.94	1.65	1.23	4.12	1.75	1.24
bh113	8.91	1.39	0.75	2.9	0.90	0.51
bh114	3.28	1.38	0.93	3.83	1.33	0.89
bh015	3.68	1.41	0.87	3.77	1.53	0.81
bh016	2.04	1.58	0.77	3.22	1.8	0.79
bh018	2.71	0.96	1.16	4.44	1.01	1.00
bh019	3.70	1.03	1.00	4.17	1.04	1.00
Mean	**3.65**	**1.28**	**1.00**	**4.18**	**1.32**	**0.97**
SD	**2.07**	**0.26**	**0.22**	**1.30**	**0.30**	**0.27**
CV	**0.57**	**0.20**	**0.22**	**0.31**	**0.23**	**0.28**

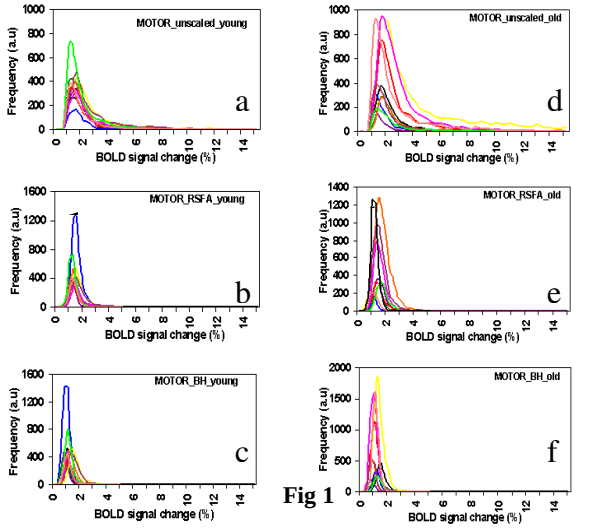

Fig 1

In younger subjects, the inter-subject variability was 0.18 (Table 1) for the motor task, but the same set of subjects performing the cognitive task during the same session had a relatively larger inter-subject variability (CV=0.28; Table 1). However, the inter-subject vascular variability as determined by the BH measurements was similar in regions activated by the motor and cognitive tasks (Data not shown). This result indicates that when the elderly performed the cognitive task, a relatively larger neural component contributed to the inter-subject variability in the BOLD signal change. Furthermore, in the older group, the cognitive task-induced inter-subject variability (CV=0.25; Table 2) was comparable to that observed in young subjects (CV=0.28; Table 1) while exhibiting a similar extent of inter-subject vascular variability as determined from the BH measurements (CV= 0.32). These results strongly support the hypothesis of a relatively greater neural than vascular contribution to the cognitive task-induced variability in the BOLD signal change in both younger and older subjects.

Considering the intra-subject variation, BOLD signal change during the motor task (FTAP) spatially varied between 1 to 15% in every subject. Fig 1a and d show the frequency distribution of the BOLD signal change during the FTAP task in young and old subjects respectively. Fig 1b and e show the frequency distributions of the BOLD signal change in response to the FTAP task in young and old subjects after scaling with RSFA, while Fig 1c and f after scaling with BH. Scaling with RSFA or BH consistently reduced the intra-subject variation in the BOLD signal change in every subject. The distributions after scaling with RSFA (Fig 1b and e) or BH (Fig 1c and f) were significantly narrower than the distributions prior to scaling in both young and old subjects (Fig 1a and d). A similar trend was observed for the DSST task.

Conclusion: Inter-subject BOLD signal response variability during motor task performance was largely vascular and may exacerbate BOLD signal amplitude variability in the elderly. However, cognitive task induced a BOLD signal amplitude variability that was largely neural, in both younger and older groups. These results suggest that age-related differences in BOLD signal during cognitive task performance, is principally a consequence of neural variability.

References: [1] D'Esposito, M., Zarahn, E., Aguirre, G.K., Rypma, B. Neuroimage 1999; 10:6-14. [2] Kannurpatti, SS Biswal. BB. *Neuroimage* (2008) 40:1567-1574.