Aging Effects on Cerebrovascular Response to Breath Holdings as Measured by Blood Oxygenation-Level Dependent MRI

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Introduction

Alterations in cerebrovascular ultrastructure and hemodynamics due to normal aging may affect blood oxygenation-level dependent (BOLD) response to hypercapnia challenges (1). Previous 3-T BOLD MRI studies showed that fractional activation volumes and maximum signal changes during breath holdings were smaller in elderly than in young adults (2, 3). Recently, regional heterogeneity in cerebrovascular response to hypercapnia challenges was identified by positron emission tomography (PET) (4) and BOLD MRI (5); and age-related changes in regional cerebral blood flow (CBF) during CO_2 inhalation were demonstrated in a PET study (6). The present study was aimed to evaluate the regional difference in BOLD response during breath holdings between young and elderly adults.

Methods

Twenty healthy young (F/M = 10/10, 23 - 35 year-old, mean = 28.2 year-old) and twenty healthy elderly (F/M = 12/8, 52 - 78 year-old, mean = 64.4 year-old) adults were recruited for this study. There was no hypertension, diabetes, cerebrovascular disease, cardiovascular disease, neurological disorder, or other major medical problems in these subjects. The breath-hold paradigm comprised of one preparation stage (30-second natural breathing) and three one-minute periodic breath-hold cycles (15-second breath-hold and 45-second natural breathing). A total of 70 dynamic measurements were obtained. A single-shot T2*-weighted gradient-echo EPI sequence was applied for BOLD MRI at a 3T clinical scanner: TR/TE = 3000/35 msec, flip angle = 90°, slice thickness = 5 mm, matrix size = 64 x 64, and in-plane resolution = 3 x 3 mm^2. Image data were analyzed using SPM2. After preprocessing including motion correction, spatial normalization and spatial smoothing with a 5-mm Gaussian kernel, BOLD response to the breath-holding was identified by fitting to the general linear model. A delay of hemodynamic response function, identified by the whole-brain averaged signal time curve for each subject, was applied. Areas with significant changes in BOLD signal were then determined for each group using a one-sample t-test at the level of a FWE corrected $P < 0.05$. Two-sample t-test was applied to identify areas with significantly lower response in the elderly than in the young adults at a threshold of uncorrected $P<0.001$.

Results

Significant BOLD signal increases could be detected in both the cortical and subcortical gray matters, but not in the white matter. The area showed significant BOLD signal response was in a much smaller extent (50.1%) for the elderly as comparing to the young group (Figs. 1 and 2). There was significantly lower BOLD response in amygdala and dentate nucleus in the elderly compared to the young (green and blue arrows, respectively, in Fig. 3). Otherwise, there was no significant regional difference in BOLD response between young and elderly groups except some scattered along brain surface.

Fig. 1 Areas with significant BOLD response during 15-s breath-hold in 20 young adults

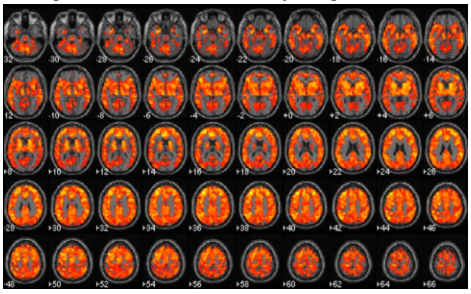


Fig. 2 Areas with significant BOLD response during 15-s breath-holding in 20 elderly adults

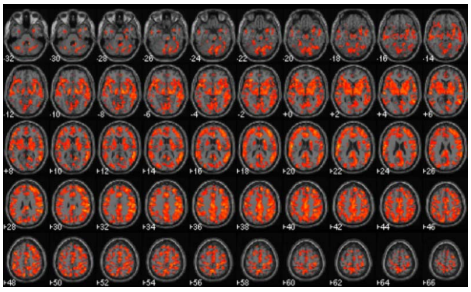
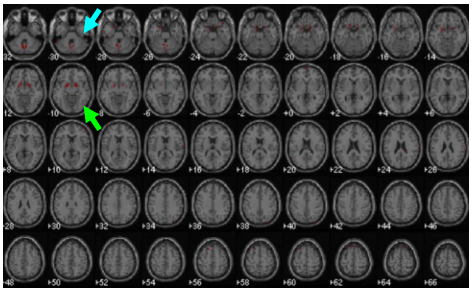


Fig. 3 Significantly lower response in amygdala and dentate nucleus in elderly than in young adults



Discussion

Elevated arterial CO_2 tension due to hypercapnia challenges induces vasodilatation and causes CBF increases. With the assumption that there is constant or little increase in oxygen consumption during a short period of hypercapnia stress, elevated CBF is expected to deliver more oxyhemoglobin than being extracted and leads to BOLD signal increases. This study showed that there were significant BOLD signal increases in cortical and subcortical gray matters during repeated 15-second breath-holdings and no significant BOLD response in the white matter, comparable with findings in previous studies (2, 3). The brain volumes with breath-hold regulated vasodilatation in the elderly were only about 50% of those in the young adults. The relative changes in BOLD signal during breath-holding were significantly smaller in the dentate nucleus of older brains than in younger ones, comparable with previous PET study (6). Furthermore, the present study showed that there was significantly less BOLD signal increase of amygdala in the elderly than in the young adults. Aging effects on cerebrovascular response to hypercapnia challenges should be considered when studying BOLD functional MRI or evaluating cerebral vascular reserve.

References

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