The hemodynamic response characteristics underlying the age-related change of brain activation during motor execution

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Introduction

Brain areas are additionally activated in elderly subjects [1,2]. It was suggested that this additional recruitment of brain areas in elderly subjects was consistent with the compensation hypothesis and characterized neuroplasticity at the systems level in the aging brain, rather than dedifferentiation hypothesis [2]. On the other hand, age-related reduction of BOLD signal (hemodynamic response function; HRF) has been reported in the primary visual area [3]. These age-related changes are of interest from the viewpoints of early detection of cognitive impairments. In this study, we investigated the characteristics of the HRF underlying the age-related change in order to estimate how the hemodynamic response is contributing to the statistical evaluation. Sequential finger tapping task was used, since it strongly demands activities of both primary and higher motor areas.

Material and Methods

Twenty-two healthy normal young (Y; under 50 years old, 11 males) and 22 healthy normal elderly subjects (E; between 60 and 75, 11 males) who gave written informed consent participated in this study. Two fMRI sessions were designed; 1) Sequential finger tapping task (2-3-4-5) at 1.5Hz paced by a prompting visual cue, 3 task blocks for each of right and left side interleaved with rest blocks, each 18 sec (TAP), 2) gripping and opening movements of bilateral hands paced by visual presentation of the hand posture for each condition, 3 sec for each movement, 5 task and 6 rest blocks, each 18 sec (GRIP). The visual stimuli were generated using E-prime (PST, Pittsburgh). Functional data were obtained using a T2* weighted gradient recalled echo EPI sequence (TR = 2000 ms, TE = 24 ms, 39 axial slices, 3 mm thick, FOV = 19.2 cm) on a 3T MRI scanner. The functional images were realigned, normalized and the center coordinates of the ROI (3x3x3 pixels in the MNI coordinate normalized at 3mm) were determined by using SPM5 (2nd level analysis, $p<0.001$). The time series of the BOLD signal was extracted using a Matlab module (BAX [4]).

Results

In these three comparisons, the total cluster size of the elderly was significantly larger than that of the younger (GRIP and TAP-L; $p < 0.003$, TAP-R; $p < 0.015$). Fig.1 shows the global activation detected by tapping by right (TAP-R) or left fingers (TAP-L) in each age group. In the contrast of elderly against young subjects, activation in the following areas was augmented ($p<0.01$). 1) TAP-R: right d/vPMA, SMA, BA3, SPL; 2) TAP-L: left anterior operticulum, SPL, BA4, right SMA, vPMA, BA46/10, CG/ACG, para-hippocampal gyrus; 3) GRIP: bilateral middle and posterior inferior frontal lobe, SMA, SPL (BA7), superior occipital gyrus (BA19), inferior and lateral occipital gyrus (BA37). The augmented activation mostly represented the difference of the HRF amplitude between the initial and post-stimulus peaks (Fig.2). In young subjects, a clear dip can be observed between these two peaks, while the curve is more flat in the elderly. The reduction of M1 activation on the contralateral side or augmentation on the ipsilateral side was not significant ($p<0.01$) in the elderly subjects, although the % HRF was slightly reduced (Fig.3). In GRIP, activation in caudate nuclei and putamen was bilaterally decreased in the elderly. The % HRF has shown that the age-related reduction depended on the decreased HRF amplitude in the latter half of the task block and lack of post-stimulus peak (Fig.4).

Discussion

It was demonstrated that augmented activation in the elderly subjects mostly depend on the elevated amplitude of the BOLD signal between the initial and post-stimulus peaks, while the % amplitude of these two peaks was close between the two age groups. Different HRF shape between the age groups and across the brain areas may give biases in statistical evaluation. For example, the difference between the age groups in ACG/CG may be underestimated. The age-related augmentation was observed in the higher motor areas and the associated areas involved in visuo-motor transformation. It represented the neuronal network recruited for complex movements. On the other hand, such augmentation was not observed in the M1 in both of TAP and GRIP. This observation suggested that the neuronal demanded was augmented to support cognitive processing for motor regulation rather than motor execution itself. In conclusion, it will be recommended to consider the potential bias induced by the non-linear dynamics of HRF to assess the age-related change of brain activation.

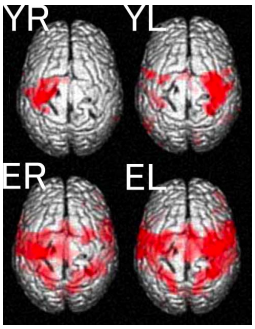

Fig 1 Activation by TAP
In the elderly subjects, the activation in the higher motor areas was increased. E: elderly, Y; young

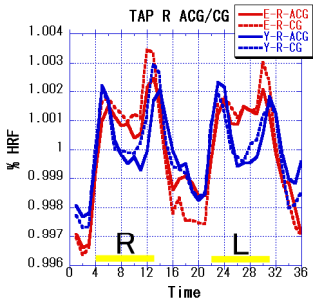

Fig 2 % HRF in ACG/CG by TAP
Mid-dip is clearly observed in the young subjects. Red: E, Blue: Y, Solid: R, Dashed: L, Yellow: Task

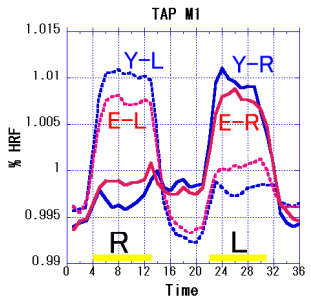

Fig 3 % HRF in M1 by TAP
The % HRF of the elderly is reduced on the contralateral side and increased on the ipsilateral side.

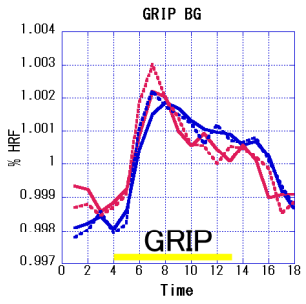

Fig 4 % HRF in BG by GRIP
After the initial peak, the BOLD signal of the elderly decrease faster than that of young subjects.

References

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