The Dependency of Correlation between the BOLD Based Aging Index and MMSE Score on the Cognitive Contents

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Introduction

Since progressive MCI cases frequently convert to Alzheimer disease within a couple of years, risk estimation using neuroimaging techniques before clear positive sign detected by neuro-psychological tests is clinically important. It has been pointed out that BOLD signal is augmented depending on aging (Aizenstein et al., J Cogn Neurosci 16, 786-, 2004), mimicking the activation pattern of higher demand of the task performance. The physiological basis underling on this phenomenon is increase of the hemodynamic response amplitude of the pre-registered area, which is accompanied with low level response characterized by initial and post-stimulus peak (Nakai et al., ISMRM 2010, #1176). Two hypothesis, compensation and re-organization, have been proposed (Cabeza, Psychol Aging 17, 85, 2002) to explain this age dependent change, however, its clinical relevance has not been established. In order to clarify this point, we evaluated the correlation between the initial aging index based on BOLD contrast and change of MMSE score two years later.

Material and Methods

Twenty-two healthy normal young subjects (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. All subjects were checked with visual acuity test, Mini Mental State Examination (MMSE), geriatric depression scale (GDS) and MHLW test to pre-evaluate the task performance. Two sessions were conducted; 1) black and white checkerboard stimuli flickering at 8Hz in block design, 5 task and 6 rest blocks, each block 18sec (CB18), 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 block 18 sec (GRIP). 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) were determined by using SPM8 (RFX, $p<0.001$). BOLD based aging index (BAI) was computed by masking ($p < 0.05$) the individual activation maps of elderly subjects with the average activation of the young subjects and summing the total residual cluster size. Neuropsychological scores of the elderly subjects were re-evaluated 2 years later.

Results

In the GRIP experiment, the total cluster size was 7087±4054 in the elderly and 3483±2546 in the younger group. The correlation between initial MMSE score and BAI was not significant in both CB18 (Fig.1, r = 0.13) and GRIP (Fig.2, r = 0.063) experiment. However, the correlation between corrected MMSE change and aging index was positively modest in GRIP (r = 0.40), while it was not significant in CB18 (r = -0.16). Corrected MMSE score change (removal of the subjects reporting full score in both time) was employed due to unclearness of cognitive change. None of the initial GDS score, GDS change two years later or MHLW test was correlated with the BAI observed by GRIP or CB18 ($|r| < 0.1$). The correlation between age and MMSE score was not significant at the two observing points in this subject group (r = -0.129 and -0.17). On the other hand, the correlation between age and GDS grew negatively modest in the two years (r = -0.17 to r = -0.38).

Discussion

It was suggested that age-related augmentation of brain activation (BAI) observed in the early stage of the elderly group (60 ~ 75 years old) may be associated with the potential risk to converting MCI status, when BAI was evaluated using the task demanding complex visuo-motor process, while BAI did not correlate with the change of MMSE score by the checker board stimuli which does not demand higher cognitive process. This result suggests that BAI may represent two different types of demand at physiological level and neuronal circuit level, which can be discriminated by the cognitive contents of the tasks. The discrepancy between age-GDS correlation and BAI-GDS correlation is also compatible with the hypothesis that cognitive representation of BAI depends on the task contents.

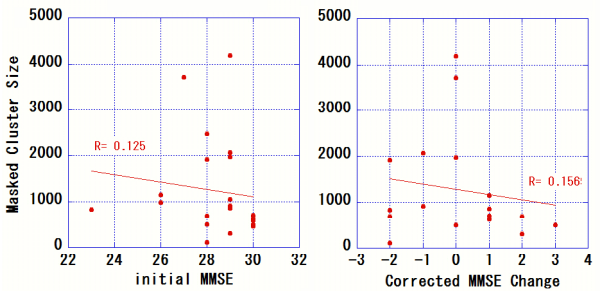

Fig.1 CB18

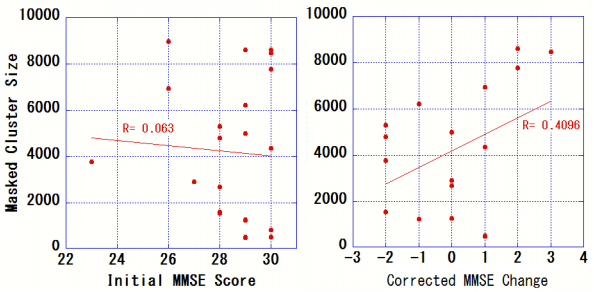

Fig.2 GRIP

Fig.1 and 2: Horizontal axis of corrected MMSE change indicates the difference between initial score and that of two years later. The unit of vertical axis is the number of voxels obtained by using the MNI template with 3x3x3 mm resolution.