INVESTIGATION OF AGE-RELATED CHANGES IN BLOOD OXYGENATION LEVEL DEPENDENCY SIGNALS DURING THE VISUOSPATIAL N-BACK USING FUNCTIONAL MRI

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Introduction: The N-back tasks are continuous-recognition measures that present stimulus sequences; for each item in the sequence, participants judge whether the stimulus matches the one presented N items ago. Since the memory storage capacity is limited, subjects are required not only temporary retention but also processing such as updating information. The N-back task has been examined in neuroimaging research and used for objective detection of age-related change of working memory (Braver et al., 1997; Manoach et al., 1997; Perlstein, Dixit, Carter, Noll, & Cohen, 2003; Ragland et al., 2002; Miller et al, 2009). However, there are few studies comparing the physiological data such as brain activation during visual N-back task since most studies were compared the behavioral data such as storage performance quantitatively. Although the physiological data was focused on, most studies used verbal stimuli (e.g., letters, words and digit). The evaluation of age-related change of visuospatial working memory by visual N-back using the functional neuroimaging is not examined. Since the verbal and the visuospatial working memory are assumed to be differential functions, it should be examined and discussed separately. Therefore, this study attempted to investigate the difference of activation during visual N-back task between young and elderly age using functional magnetic resonance imaging (fMRI).

Material and Methods: Twenty healthy young adults (mean age: 23.85 ±5.43, 9 males) and 20 healthy elderly volunteers (mean age: 67.35 ±4.27, 9 males) who gave written informed consent participated in this study. All participants were checked with visual acuity test, Mini Mental State Examination (MMSE), geriatric depression scale (GDS) and MHLW test to pre-evaluate the task performance. Visual stimuli were presented continuously on display. Participants were required to judge whether it matches the one presented N items ago. Experiment conditions were task difficulty (N = 1, 2, 3) and stimuli (meaningful drawing pictures and non-meaningful 4 × 4 matrix) and age group (young and elderly). This study was examined using a block design. All conditions consisted of 3 task and 4 rest blocks, all task consisted of 34 trials. Functional data were obtained using a T2* weighted gradient recalled echo EPI sequence (TR = 3000 ms, TE = 30 ms, 39 axial slices, 3 mm thick, FOV = 19.2 cm) on a 3T MRI scanner. The functional images were realigned, normalized and analyzed by SPM8.

Results: An ANOVA was used to assess the factors that influence the accuracy (%) as a dependent behavioral variable. Three-way ANOVA (N × stimuli × age group) detected the significant main effect of N ($F(2,76)=362.016$, $p < 0.001$), stimuli ($F(1,38)=170.489$, $p < 0.001$), age group ($F(1,38)=45.101$, $p < 0.001$), and the interaction between N, stimuli and age group ($F(2,76)=3.790$, $p < 0.05$). The results of 2-sample-*t*-test in meaningful minus non-meaningful stimuli condition revealed activation in ventral visual pathway ($p < 0.05$, FWE, RFX). The results of non-meaningful minus meaningful stimuli condition also show dorsal visual pathway ($p < 0.05$, FWE, RFX). In both age group, significant activation was observed in the bilateral visual cortex ([BA] 17, 18, 19), the inferior frontal gyri ([BA] 44), middle frontal gyri ([BA]46), the supplementary motor area ([BA] 6), the superior parietal lobule ([BA] 5, 7), the inferior parietal lobule ([BA] 39, 40), thalamus, Insula, and the fusiform gyri ([BA] 18) ($p < 0.05$, FWE, RFX). In addition, the activations in these areas of young were augmented depending on task difficulty. The results of 2-sample-*t*-test in elderly minus young revealed significant difference in the bilateral supplementary motor area ([BA] 6) and left middle ([BA] 21) and superior temporal gyrus ([BA] 22) ($p < 0.05$, FWE, RFX) in N=1 and 2 conditions.

Conclusion: The difference of visual information processing pathways revealed the activated area depending on the meaningfulness of the visual stimuli and the area irrespective of it. The comparison between age groups suggested that elderly might perform the visual task with assistance of verbal processing. Additionally, the change of activation depending on task difficulty shows reduction in the up-regulation of the regions responsible for visuospatial working memory in response to increasing task demands in the elderly. It was suggested that the impaired ability to regulate load of visuospatial working memory depending on age caused the decline of performance in elderly. This phenomenon may be applied for clinical diagnosis to detect the potential influences of aging in visuospatial working memory. The visual N-back task could evaluate not the presence or absence of aging effect but the degree of age-related change of visuospatial working memory objectively.

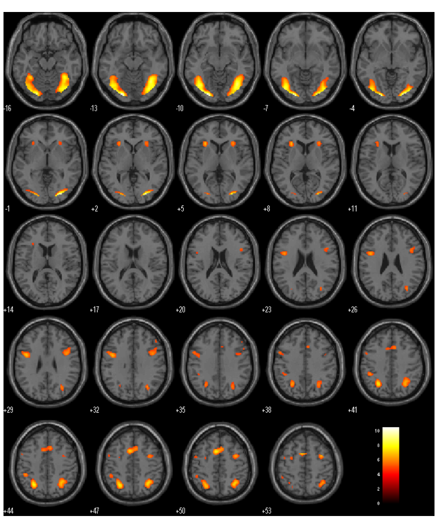
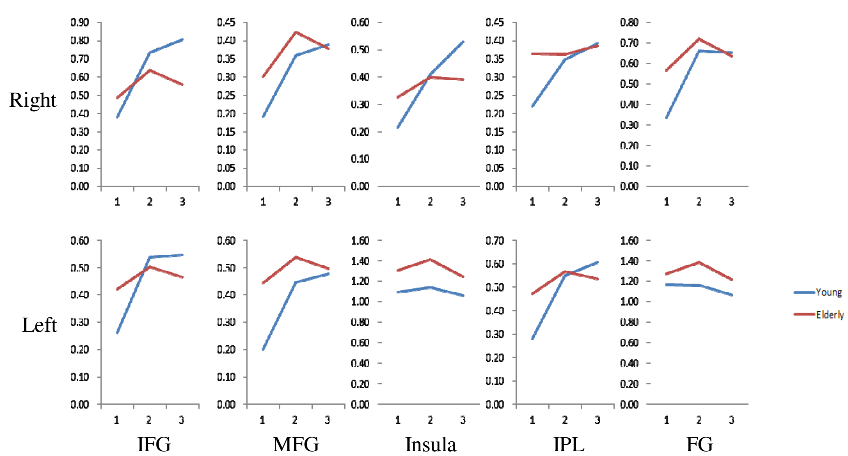


Figure 1. The results of the conjunction analysis of Young and Elderly groups. Statistical threshold was p <.05 for a cluster level with a FWE correction.



IFG: inferior frontal gyrus, MFG: middle frontal gyrus, IPL: inferior parietal lobule, FG: fusiform gyrus

Figure 4. The changes in the percent signal changes for the ROIs among the conditions. The age- and task difficulty-dependent augmentation of brain activation varied between the different brain regions. The X-axis stands for task difficulty (N), and the Y-axis shows percent signal changes (%).