Age-Related Change of Brain Activation During Virtual Performance of Combined Operation Task is Most Detected at Task Switching Timing – An ER-fMRI Study

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Introduction
Several investigations have reported that physical exercises improve cognitive functions of elderly (Geda 2010, Hogan 2013), suggesting their potential contribution to prevent cognitive decline. However, other review works pointed out that the effects still need to be confirmed (Uffelen 2008, Gates 2013). In order to investigate the conditions to predict valid applications of physical exercises, it is indispensable to establish a method to classify the subjects based on their cognitive and physiological status. For this evaluation, the cognitive effects of the tasks used in the exercises should be revealed. The fundamental problem to investigate the brain activation during motor execution is that most of the movements are hard to be actually performed during fMRI scans because of the narrow space in a magnet and head movements. In this study, we investigated the availability of a virtual performance task using a turnkey and direct visual feedback to the subjects. The task was designed from bean transfer test (BTT), one of physical test protocols for elderlies in Japan.

Material and Methods
An event-related fMRI task, virtual bean transfer test (VBTT), was designed by employing the visual components of BTT (Fig.1A). This consisted of three major operations using a 2 by 2 turnkey system. With the left-hand key, a small, round object (a bean) is clipped with two sticks representing chopsticks. Then, the object with chopsticks is moved to a round target (pot) with the right-hand key to put the bean in. The behavioral data were marked with 6 checkpoints. Functional imaging data were obtained from 24 elderly (over 60, 12 females) and 24 non-elderly (20 - 59, 12 females) healthy volunteers. Functional data were obtained using a T2*-weighted GRE-EPI sequence (TR = 3000 ms, TE = 30 ms, FA = 90 deg, 39 axial slices, 3 mm thick, 0.75 mm gap, matrix = 64 x 64, FOV = 192 mm, BW = 1420 Hz/Px, echo spacing = 0.77 ms) on a 3T-MRI scanner. During a VBTT session for 6 min and 30sec, 128 volumes of images were acquired. The functional data were realigned, normalized at 3 mm spatial resolution and smoothed using SPM8. The 6 time points in each trial were employed as the onset of 6 types of cognitive events (Fig.1A).

Results
In the activations representing the undivided trial (an event is covering whole part of one trial), the network for the upper visuo-spatial transformation tract and higher motor control was intensively observed in both age groups, while activation in the ventral visual pathway was also observed (two-sample t-test, p<0.05 corrected). Activations in bilateral BA2, 3, 4, 5, 6, 7, 18, 19, 37 and 40 were significant in both age groups. In young subjects additional peaks were detected in the right BA9, 13, 39 and left BA30. No differential peak was detected with a FEW threshold. In the partitioned maps representing the operation step by step, it was indicated that the activation representing the whole trial was contributed by different combinations of the steps across the age groups. In young subjects, major activations were detected at CP0, CP1 and CP4 (FEW, p<0.05), while they were detected at CP0 and CP2 in the elderly subjects (Fig.1B). Activations in the left BA 3, 5, 6, 40, 43 and the right BA7 were significantly augmented in the elderly group at CP2 (FEW, p<0.05). At lower threshold level (FDR, p<0.001), augmented activations in bilateral BA37 and 39 at CP1, in bilateral BA3, 6, left BA1, 2, 4, and right BA7 at CP3 and those in bilateral BA3, 6, 19, 22, 39, caudate head, left BA2, 38, 40, 42, right BA1, 4, 5, 7, 25, and thalamus at CP4 were detected in the young group.

Discussion and Conclusion
It has been pointed out that aging augment brain activation, suggesting the underlying neuro-physiological background of cognitive impairments. Two ideas, compensation (Heuninckx 2005) and dedifferentiation (Park 2004) hypothesis have been proposed. This age-related change of brain activation may be potentially an index to estimate subliminal cognitive decline, however, precise behavioral data are indispensable due to potentially reduced task performance in elderly subjects.

In this study, the activation was not significantly different between the two age groups when the contrasts were obtained from the events representing the whole trial processes of VBTT (i.e. CP0 to CP5), although a demand for visuo-spatial transformation by adjusting the asymmetric (two independent) rotation of the sticks will be higher in elderly subjects. This may be explained by the lower total frequency of object transference to the goal than that of clipping it in elderly subjects (higher errors in clipping beans). By introducing partitioning analysis using the accurate response time for each step of VBTT procedure, differential activation between the age groups could be extracted (Fig.1B). Even with strict threshold, augmentation of dorsal visual pathway in the elderly group could be detected at CP2 timing. Since CP2 is the timing to switch the action from clipping beans to transferring them to the target, this result suggests ‘switching cost’ was more sensitive index as age related change than the other task elements. By recording self-paced object manipulation in an interactive task, complex brain activation during a combined motor processing could be more precisely attributed to cognitive each element.

In conclusion, a virtual performance tasks may partially simulate the visuo-spatial cognitive processing of the movements to evaluate potential cognitive decline.