EVALUATION OF THE VALIDITY OF TASK SWITCHING PARADIGM AS A COGNITIVE STRESS TEST

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Introduction: It has been pointed out that BOLD signal is augmented depending on aging (Aizenstein et al., J Cogn Neurosci 16, 786-, 2004). This phenomenon may be applied to detect potential cognitive decline by using the relationship with behavioral data. However, since the pattern and extent of age-related change depends on the task or stimuli (Nakai et al., ISMRM 2010 #1176), it is important to choose appropriate tasks that highly reproduce brain activation and are easy to perform for the elderly. From this point of view, we propose the divalent Task Switching Paradigm (TSP) as a cognitive stress test using fMRI. TSP is a recognition task that demands the subjects to periodically switch between a shape judgment task and a color judgment task. The brain areas that correspond to the working memory and learning system could be affected by switching tasks. In addition, TSP demands reconfiguration function. Reconfigration is a series of process which is retrieve goal states (what to do) and action rules (how to do it) (Monsell, TRENDS in Cogn Sci 7, 134-140, 2003). This cognitive process is strongly supported by caudate nucleus related to habit learning. We assume that the age-dependent change of caudate nucleus activity may reflect the status of reconfiguration, which integrates complex recognition in our daily life. In this study, we attempted to evaluate the validity of divalent Task Switching Paradigm (TSP) as a cognitive stress test to test this hypothesis.

Material and Methods: Fifteen healthy normal young (Y; mean age 24.46 ±6.19, 8 males) and 15 healthy normal elderly volunteers (E; mean age 67.33 ±4.58, 6 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. Participants performed divalent TSP. Red or blue and circle or square stimuli are presented continuously on display. Participants are required judging based on color (if upper) or shape (if downer). There are there speed condition; cue stimuli interval (CSI) were high speed (HS, 50ms), middle speed (MS, 650ms), low speed (LS, 1250ms) condition. All conditions consisted of 3 task and 4 rest blocks, all task consist 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 conducted to focus on the hit rate (%) as a dependent variable of the behavioral data. Two way ANOVA (age group × speed) revealed significant main effects of age ($F(1,28)=63.38$, $p<.001$), however, main effect of speed ($F(2,56)=1.34$, *ns*) and interaction effect between age and speed ($F(2,56)=.009$, *ns*) were not significant. In functional images, task dependent activation augmented depending on the velocity in both age groups. In the young group (Fig.1), the contrast of HS against MS was detected in middle occipital gyrus, the right superior parietal lobule, left temporal pole, while the contrast of MS against LS was detected in cerebellum vermis lobule VIII ($p < 0.001$, uncorrected, RFX). In the elderly, the contrast of HS against MS was observed in the left calcarine gyrus, cerebellum vermis lobule IX, right superior gyrus, and the contrast of MS against LS was detected in the right middle frontal gyrus, left caudate nucleus and right middle cingulated gyrus ($p < 0.001$, uncorrected, RFX). In right caudate nucleus, significant activation was observed in all conditions and in both age groups ($p < 0.001$, uncorrected, RFX). The contrast of Elderly against Young of caudate nucleus was observed in all conditions ($p < 0.001$, uncorrected, RFX). In HS condition, hit rate score was significantly correlated with the activation in left inferior frontal gyrus, left posterior cingulate, superior parietal lobule, right superior medial gyrus, right temporal gyrus in Young ($p < 0.001$, uncorrected, RFX). In contrast, activation in the right caudate nucleus and left middle occipital gyrus was significant in Elderly ($p < 0.001$, uncorrected, RFX).

Conclusion: The brain areas with augmented brain activation depending on the difficulty of TSP task were different between the two age groups. It is known that those areas are corresponding to the neuronal system for learning and the memories. In particular, it was observed that the contrast of Elderly against Young of right caudate nucleus and hit rate score was significantly correlated with the activation in the right caudate nucleus in the Elderly. It was suggested that right caudate nucleus has strong effects with changing goals and rules of task in the elderly. Evaluation of the activation in the caudate nucleus using TSP may be valid to represent the aging effects on reconfiguration function. These results showed that divalent TSP may be applied for clinical diagnosis to detect the influence of aging on both cognitive domain of visuo-spacial recognition and decision making objectively.

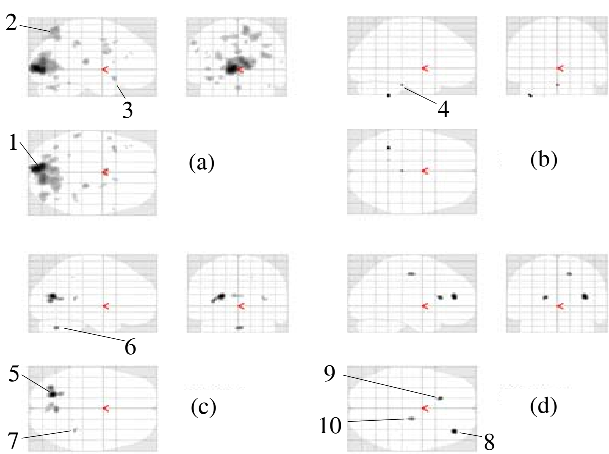

Figure 1. Results of the 2-sample-t-test in (a) HS minus MS in Y, (b) MS minus LS in Y, (c) HS minus MS in E, (d) MS minus LS in E

Table 1. Results of 2-sample-t-test comparing BOLD activations

	Location of peak voxel	Cluster size	Z	MNI cordination		
	High speed minus Middle speed in young					
1	Right Middle Occipital Gyrus	2243	5.4	−6	−88	2
2	Superior Parietal Lobule	376	3.85	10	−64	66
3	Left Temporal Pole	37	3.68	−38	16	−14
	Middle speed minus Low speed in young					
4	Cerebellum Vermis LobuleVIIIa	1	3.18	−36	−46	−44
	High speed minus Middle speed in elderly					
5	Left Calcarine Gyrus	166	4.27	−22	−68	16
6	Cerebellum Vermis Lobule IX	37	3.68	0	−64	−36
7	Right Superior Gyrus	13	3.4	36	−38	10
	Middle speed minus Low speed in Elderly					
8	Right Middle Frontal Gyrus	47	3.6	36	42	16
9	Left Caudate nucleus	15	3.44	−16	24	14
10	Right Middle Cingulate	18	3.36	16	−14	52