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Authors
Cho, Sang-Soo
Kim, San-Eun
Kim, Yu-Kyeong
et al.

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Neural Substrates of Cognitive Skill Learning in Healthy Young Volunteers

Sang Soo Cho (psycog@chol.com)
Eun Jin Yoon (twobeats@snu.ac.kr)
Yu Kyeong Kim (yk3181@snu.ac.kr)
Sang Eun Kim (kse@snu.ac.kr)
Department of Nuclear Medicine, Seoul National University College of Medicine
28 Yongon-dong, Chongno-gu, Seoul, Korea

Jung-Mo Lee (jmlee@skku.edu)
Department of Psychology, Interdisciplinary Program of Cognitive Science, Sungkyunkwan University
3 Myungrun-dong, Chongno-gu, Seoul, Korea

Abstract

In the present study, we investigated the neural substrate related to the successful performance of cognitive skill learning using one of the typical form of incremental cognitive skill learning task, weather prediction task and FDG PET in voxel-wise analysis. The successful performance of weather prediction task was related with the high metabolic level of bilateral frontal and superior temporal areas as well as striatum. In the analysis in each learning period, the higher performance of the early learning period showed a positive correlation with metabolism of brain areas that are related with working memory, but in the intermediate learning period, frontostriatal connections are mainly involved. In the late learning period, metabolic correlation of higher performance was shown in brain areas that are related with automatic and implicit generation of candidate for response. The results suggest that despite apparent independence, multiple memory systems may interact cooperatively to solve the given task.

Background and Purpose

According to recent studies, there is growing consensus that multiple memory systems exist in the human brain (Rolls, 2000; Tulving, 2002). The main memory systems are declarative and nondeclarative memory systems, the former is associated with medial temporal and frontal regions and the latter is associated with basal ganglia, not impaired by lesion to the medial temporal lobe structure and frontal cortex (Knowlton et al 1994; Filoteo 2001).

Many cognitive neuroscience studies focus on double dissociation between patient groups, suggesting that the underlying neuronal substrate operates independently. However, a number of evidence reports that the two memory systems interact, even competition to produce optimize behavior for given stimulation or tasks (Ashby 1998; Poldrack and Rodriguez, 2004; Maddox 2004).

Probabilistic category learning is dependent on the nondeclarative memory system, assumed to be an incrementally learned cognitive skill across many trials. The striatal system is known to be involved in this learning, several disease with dysfunction of this brain area can impair the motor and cognitive skill learning as well as categorization (Knowlton et al., 1996a, 1996b; Westwater, Mc-Dowall, Siegert, Mossman, & Abernethy, 1998; Ashby et al., 2003), but possibly different memory systems and underlying brain structures are involved during initial learning (Ashby et al., 1998, 2003; Ashby and Jeffrey 2005).

An earlier study demonstrates that during probabilistic classification task, the frontostriatal system is activated while hippocampus is inactivated across the learning compare with a perceptual-motor control task (Poldrack et al., 1999). This suggests that the striatum and medial temporal structure interact during the course of the learning. Although Poldrack et al. showed successfully the time course of activation and deactivation of neural substrate during learning of cognitive skill, the performance related neural changes were can be differ. Recently Tulving et al. (1999) have proposed a distinction between `what' and `how' sites for neuroimaging data interpretation. What sites refer to activation loci yielded by the classic subtraction analysis, and their activity would reveal what the system is doing. In contrast, how sites refer to those loci yielded by brain/cognition covariance analysis, and their activity would reveal how well the system is performing a given task.

In this study, we investigate brain region that shows the metabolic correlation of performance level across the learning using FDG PET and weather prediction task.

Methods

Participants

Eighteen right-handed healthy subjects (age, 24 ± 2 y; 10 females/8 males) underwent brain FDG PET and neuropsychological testing. All the participants had no neurological and psychological problems and informed consent was obtained before participation. To confirm the handedness and emotional state, a handedness inventory and the Beck Depression Inventory were used.

Materials and Task

The procedure for the weather prediction task followed that used by Knowlton et al. (1994). The task was presented using a 15.1 inch plane monitor (in plain resolution 2024 × 768 pixels). The task required participants to decide which of two outcomes (rain or sunshine) will occur based on the combination of four cues on each trial. One, two, or three geometric shape cards appeared on the computer screen, and the two outcomes were occurred equal probability. There were 14 possible cue patterns; each cue was associated with one of the two weather outcomes with a fixed probability. Participants were instructed that they would be seeing one to three cues on each trial, and they should decide if the cues predicted sunshine or rain. The cues appeared 5 seconds on the computer screen.

The participant indicated his or her choice by pressing either the key labeled with a sun or rain icon on the keyboard. These two keys were on the opposite sides of the keyboard. If the response was correct, correct buzzer were delivered. If the response was incorrect, incorrect buzzer sounded. Then, the weather (sun or rain) corresponding to the correct answer appeared on the screen above the cues for 2 sec. Without a response within 5 sec, the trial was terminated, the incorrect buzzer sounded, and the correct answer appeared above the cues for 2 sec (these missed trials were not scored). Participants were allowed a short break (1 min) every 50 trials. Immediately after the total 150 trials were completed, they were administered a self report questionnaire that asked about the strategy of present task

PET scan

Three-dimensional acquisition method was adapted using a Phillips Allegro PET scanner. Static emission scans were started 40 min after the bolus injection of 4.8 MBq/kg FDG after at least 6 h fasting and continued for 15 min. Transaxial images were reconstructed by means of a filtered back-projection algorithm employing a 3D-RAMLA filter. Before the emission scan, subjects underwent a 5 minutes transmission scan for attenuation correction using a ^{137}Cs single-photon emitting point source. Scatter correction was performed using the standard software as supplied by the scanner manufacturer.

Analysis

The Total score of weather prediction task were used for the evaluation of cognitive skill learning. Additionally, the performance rate of the early, intermediate and late learning periods of weather prediction task were calculated to evaluate the performance changes according to learning processes. Scoring followed the guidelines of Knowlton et al. (1994). Responses were indicated to be correct for any given trial if the outcome selected was the outcome that was more strongly associated with the cue combination appearing on that trial.

Prior to statistical analysis, all the images were spatially normalized into the MNI standard template (Montreal Neurological Institute, McGill University, Montreal, Canada) to remove inter-subject anatomical variability. Spatially normalized images were smoothed by convolution, using an isotropic Gaussian kernel with 16-mm FWHM. The aim of smoothing was to increase the signal-to-noise ratio and to account for the subtle variations in anatomical structures. The count of each voxel was normalized to the average count of the whole gray matter with ANCOVA scaling in SPM 99. Simple correlation analysis between regional glucose metabolism and cognitive task performance was done by SPM99 in a voxel-wise manner ($P < 0.03$, uncorrected k=100).

Results

Weather prediction task

The result of weather prediction task was presented in figure 1. The total hit rate was 63.9±7.3%. Across the learning, the performance was increased; 58.1% in the first block, 63.5±10.4% in the middle block, and 70.8% in the late learning periods. The performance of each learning periods showed significant differences (F=6.260, df=2, $P < 0.01$). There was a significant correlation between the hit rates of first and intermediate learning periods (r= 0.49, $P < 0.05$). Based on the self report questionnaire that asked about the strategy of the task, most participants not only can't develop the strategy for the task but also can't find the hidden cue-outcome occurrence probability.

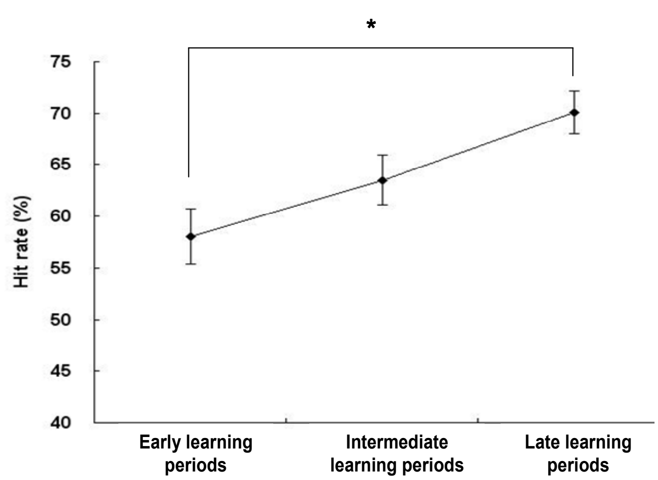

Figure 1: Performance of weather prediction task in each block. Error bar represent standard errors of the means (Error bar is standard error).

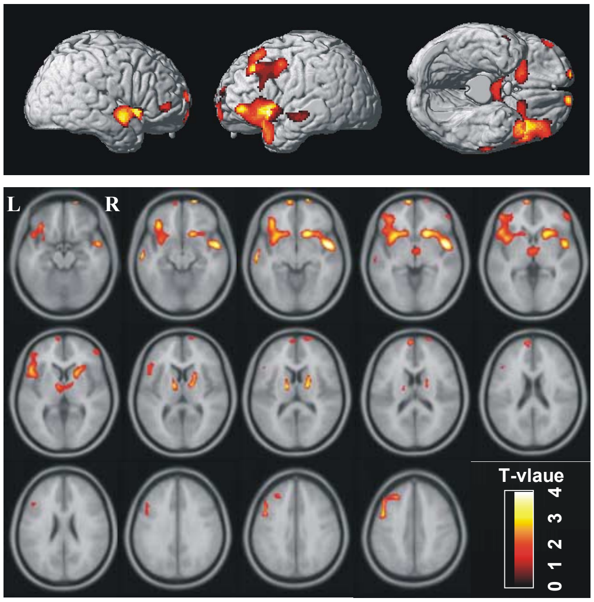

Figure 2: Metabolic correlation of weather prediction task total hit rate. The metabolic correlation are displayed on rendering and multislice images of standard MRI at the threshold of $P < 0.03$ uncorrected, K=100.

PET

The brain areas showing a positive correlation with the total score of weather prediction task were bilateral superior temporal and inferior frontal gyri, thalami and striatum and left precentral, middle, superior and medial frontal, middle temporal gyri and insula, suggesting that these regions are involved in weather prediction task (Figure 2).

However, block analysis revealed that the correlation pattern is different across the learning periods. Increased regional brain glucose metabolism correlated with high performance level of early learning periods in the right superior fontal gyrus, left middle temporal gyrus, and right inferior parietal lobule and supramarginal, posterior cingulate and medial frontal gyri. The performance of intermediate learning periods had the correlation in the medial frontal gyrus, insula, middle temporal gyrus, and inferior frontal gyri in the left and putamen, claustrum, superior temporal and superior frontal gyri in the right. Metabolic correlation was found in the bilateral cerebella, posterior cingulate gyri and superior temporal gyri for performance of late learning period (Figure 3, Table 1).

Discussion and Conclusion

We identified the neural substrates that are related with performance of cognitive skill learning. The successful performance of weather prediction task was related with the high metabolic level of bilateral frontal and superior temporal areas as well as striatum. These results are in agreement with a previous study showing frontostriatal activation during the probabilistic categorization learning (Poldrack et al., 1999). In the analysis in each block, the higher performance of the early learning period showed a positive correlation with metabolism of brain areas that are related with working memory, but in the intermediate

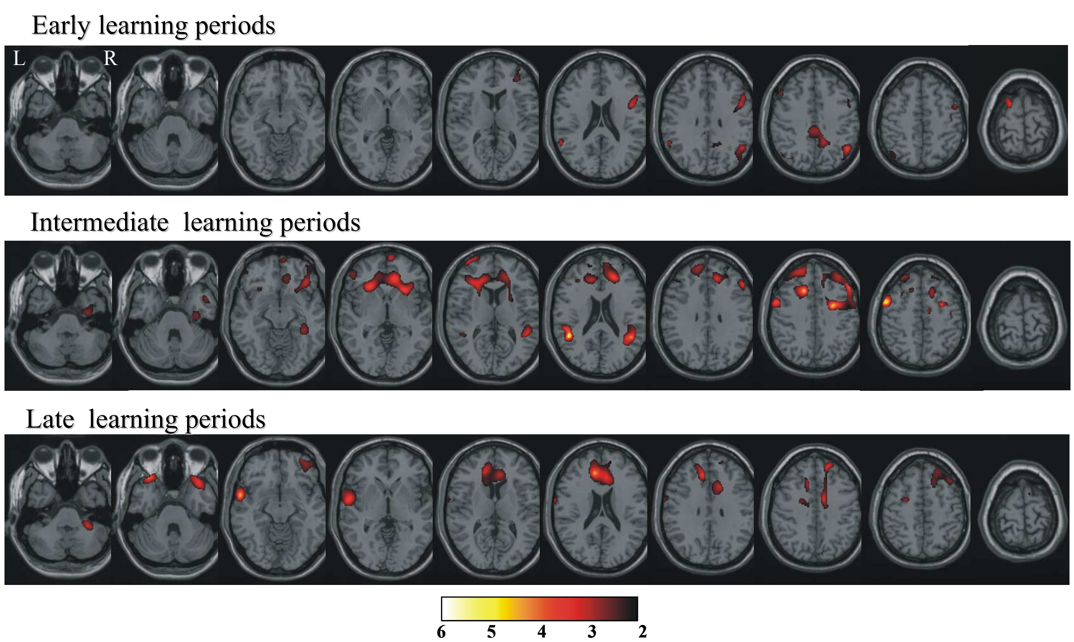

Figure 3: The change of metabolic correlation pattern during acquisition of a weather prediction task. The metabolic correlation are displayed on rendering and multislice images of standard MRI at the threshold of $P < 0.03$ uncorrected, K=100.

Table 1: Positive correlation between resting state regional brain glucose metabolism and performance score in each learning periods (Talairch coordinate).

	Region	BA	Coordinates			Z-value
			X	Y	Z	
Early learning periods						
Rt	Superior Frontal Gyrus	BA 6	20	7	64	3.86
Lt	Middle Temporal Gyrus	BA 21	-61	-12	-9	3.30
Rt	Inferior Parietal Lobule	BA 40	53	-42	24	3.27
Lt	Supramarginal Gyrus	BA 40	-46	-53	36	3.22
Rt	Posterior Cingulate Gyrus	BA 31	6	-27	35	2.75
Rt	Medial Frontal Gyrus	BA 6	14	18	47	2.69
Intermediate learning periods						
Lt	Medial Frontal Gyrus	BA 10	-8	61	14	3.15
Lt	Insula		-26	19	-4	3.91
Lt	Middle Temporal Gyrus	BA 21	-59	-22	-6	3.80
Lt	Inferior Frontal Gyrus	BA 45	-51	21	3	3.15
Rt	Putamen		22	4	11	3.65
Rt	Claustrum		28	19	1	3.63
Rt	Superior Temporal Gyrus	BA 38	40	14	-31	3.51
Rt	Superior Frontal Gyrus	BA 10	22	67	11	2.64
Late learning periods						
Lt	Cerebellum/Cerebellar Tonsil		-28	-41	-33	3.33
Rt	Cerebellum/Cerebellar Tonsil		34	-41	-40	2.53
Rt	Cingulate Gyrus	BA 31	18	-29	38	3.20
Lt	Cingulate Gyrus	BA 24	-10	-2	35	2.87
Rt	Superior Temporal Gyrus	BA 22	59	-2	0	2.85
Lt	Superior Temporal Gyrus	BA 38	-48	17	-16	2.36

$P < 0.03$ uncorrected; Lt, left; Rt, right; BA, brodmann area

learning periods, frontostriatal circuits are mainly involved. In the late learning periods, metabolic correlation of higher performance was shown in brain areas that are related with automatic and nondeclarative generation of candidate for response.

These results indicate that brain regions associated with the explicit memory system are recruited in early periods of nondeclarative learning procedure. Further, they suggest that frontostriatal circuits are involved only in late periods of nondeclarative learning procedure. These data demonstrate that despite apparent independence, multiple memory systems may interact cooperatively to solve the given task.

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Appendix

Probabilities for weather prediction task for each cue card combination

	Cue	P (Cue combination)	P (rain)	P (sunshine)
1	0001	0.14	0.143	0.857
2	0010	0.08	0.375	0.625
3	0011	0.09	0.111	0.889
4	0100	0.08	0.625	0.375
5	0101	0.06	0.167	0.833
6	0110	0.06	0.500	0.500
7	0111	0.04	0.250	0.750
8	1000	0.14	0.857	0.143
9	1001	0.06	0.500	0.500
10	1010	0.06	0.833	0.167
11	1011	0.03	0.333	0.667
12	1100	0.09	0.889	0.111
13	1101	0.03	0.667	0.333
14	1110	0.04	0.750	0.250