

## 정신분열병 환자의 작동기억 이상에 대한 기능적 자기공명영상 연구

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### Working Memory Deficits in Patients with Schizophrenia : fMRI Investigation

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#### ABSTRACT

**O**bjective : Impaired processing of working memory is one of the cognitive deficits seen in patients with schizophrenia. This aimed at corroborating the differences in the brain activities involved in the process of working memory between patients with schizophrenia and the control subjects.

**Method** : Fourteen patients with schizophrenia and 12 healthy volunteers were recruited in this study. Functional magnetic resonance imaging(fMRI) was used to assess cortical activities during the performance of a 2 - back visual working memory paradigm using the Korean alphabet as mnemonic content.

**Results** : Group analysis revealed that left lateral prefrontal cortex and right parietal lobule showed decreased cortical activities in the patient group. On the other hand, an increased activation in left superior and middle frontal gyrus, left middle temporal gyrus, right cuneus, both occipital lobes, right fusiform gyrus and right cingulate gyrus. The activation in left anterior lobe and both declive of cerebellum was also increased.

**Conclusions** : This study showed a decreased activation in left lateral prefrontal and right parietal neural networks from the patient group and confirmed the earlier findings on the impaired working memory of patients with schizophrenia using fMRI investigation. The regions implicated in our study suggest an abnormal functioning of the fronto - parietal cortical areas that are critical to the information processing stream, which might be correspondent to common pathophysiology rather than a common etiology in schizophrenia.

**KEY WORDS** : Schizophrenia · Working memory · fMRI.

\*가

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# 서론

<sup>23)</sup>  
17)24-26)

가

PET SPECT

<sup>27)</sup>

가

가

fMRI

fMRI

(phonological loop)

(visuospatial sketchpad)

가

가 가

<sup>1)</sup>

가

(lateral prefrontal cortex)

(parietal cortex)

가

<sup>2)</sup>

가

## 방법

(DLPFC ; dorsolateral prefrontal cortex)<sup>3)4)</sup>

### 1. 연구대상

가

4

(DSM - )<sup>28)</sup>

14

( 8 , 6 )

<sup>5-7)</sup>

12

<sup>8)</sup>

18

45

75

<sup>9)</sup>

가

<sup>10)</sup>

가

(PET)

(SPECT)

(fMRI)

가

Brief Psychiatric Rating Scale(BPRS)<sup>29)</sup>

가

Mini - Mental State Examination(MM-

SE)<sup>30)</sup>

fMRI

가

Hollingshead<sup>31)</sup>

Raven's

Standard Progressive Matrices(SPM)<sup>32)</sup>

가

가

<sup>11-22)</sup>

fMRI  
가 2-back  
(80%)  
12 11  
chlorpromazine 가 (125~500 mg/day)  
(olanzapine 8, risperidone 4 )

## 2. MRI Parameters

1.5T MR scanner(Magnetom Vision

**Table 1.** Demographic and clinical characteristics of patients with schizophrenia and healthy comparison subjects

Characteristics*	Patients (n=12)		Comparison subjects(n=11)	
	Means	SD	Means	SD
Age(years)	27.8	7.3	24.6	6.6
Education(years)	12.8	2.5	14.0	2.2
I.Q. †	106.3	7.6	110.6	8.4
MMSE	29.2	1.3	29.5	0.7
Age onset	24.3	3.2		
BPRS Total score	25.1	3.6		
Medication dose ‡	351.5	105.2		

\* : Patients and healthy comparison subjects were matched throughout all the demographic variables (Mann Whitney U test, p>0.1)

† : Measured by Raven's Standard Progressive Matrices(SPM)

‡ : Chlorpromazine equivalent, mg/day

IQ : Intelligent Quotient, MMSE : mini-mental state examination, BPRS : Brief Psychiatric Rating Scale

Plus, Siemens, Erlangen, Germany) EPI(echo planar imaging) ( (TR)/ (TE)=3000/60msec, (flip angle)=90, field - of - view 240 x 240mm, matrix 64 x 64) BOLD (blood oxygenation level dependent)

fMRI  
1 6mm 22~24  
95 5 T1  
(equilibration)  
T1 (spin Echo sequence, TR/TE=100 msec/minimum, 256 x 128 in plane matrix, 6mm slice thickness) (co - registration)  
(normalization)

3D - FLASH(fast low - angle shot) sequence (sagittal orientation, TE/TR=4/9.7msec, FA=12, slice thickness=1.25mm, 256 x 192 in - plane matrix)

## 3. 기능적 자기공명영상을 위한 과제 패러다임

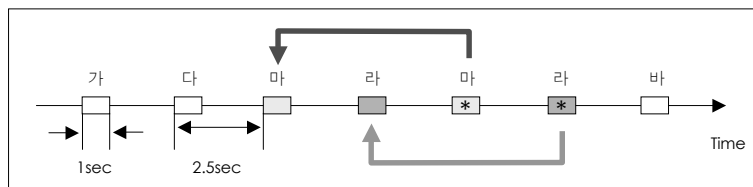
fMRI (가, , , ...)  
2-back

가  
( 1). Presentation software (Version 4.06, Neurobehavioral Systems, CA)

, MRI

가  
(viewing angle) 5

가  
가



**Fig. 1.** Illustration of the 2-back working memory paradigm : The visual cue, 1 second in duration, was presented every 2.5 seconds. An example illustrates that the target letter(marked with an asterisk) is the one which coincides with the letter that is presented two letters back in the time sequence.

1 2.5 30%  
 12 30 4  
 5 30 가  
 가 가  
 48

4. 영상 데이터의 분석  
 fMRI Random Field Theory<sup>33)</sup>

**Table 2.** Group activation at uncorrected  $p < 0.01$ . Anatomical location of the maximum activation is given along with its Brodmann's area nomenclature (BA)

(A) Comparison group					
Voxel level Z	Voxel P(unc)	Talairach coordinates{mm}			Region
		x	y	z	
4.25	0.000	48	35	9	Right Cerebrum, Frontal Lobe, Inferior Frontal Gyrus, Gray Matter, BA46
4.06	0.000	42	30	15	Right Cerebrum, Frontal Lobe, Middle Frontal Gyrus, Gray Matter, BA46
4.02	0.000	34	16	47	Right Cerebrum, Frontal Lobe, Superior Frontal Gyrus, Gray Matter, BA8
3.99	0.000	- 12	- 26	- 10	Left Brainstem, Midbrain, Gray Matter, Substantia Nigra
3.50	0.000	- 6	- 26	- 17	Left Brainstem, Pons
3.98	0.000	38	- 47	39	Right Cerebrum, Parietal Lobe, Inferior Parietal lobule, Gray Matter, BA 40
3.36	0.000	42	- 54	45	Right Cerebrum, Parietal Lobe, Inferior Parietal lobule, Gray Matter, BA 40
3.17	0.000	51	- 35	35	Right Cerebrum, Parietal Lobe, Inferior Parietal lobule, Gray Matter, BA 4
3.97	0.000	48	- 57	- 21	Right Cerebellum, Posterior Lobe, Declive
3.79	0.000	38	- 46	- 28	Right Cerebellum, Anterior Lobe, Culmen
3.60	0.000	32	- 63	- 25	Right Cerebellum, Posterior Lobe, Uvula
3.77	0.000	6	11	- 6	Right Cerebrum, Sub-lobar, Caudate, Gray Matter, Caudate Head
3.66	0.000	12	- 1	13	Right Cerebrum, Sub-lobar, Caudate, Gray Matter, Caudate Body
3.51	0.000	2	- 11	12	Right Cerebrum, Sub-lobar, Thalamus, Gray Matter
3.75	0.000	- 36	26	- 16	Left Cerebrum, Frontal Lobe, Inferior Frontal Gyrus, Gray Matter, BA47
3.64	0.000	- 48	23	- 13	Left Cerebrum, Frontal Lobe, Inferior Frontal Gyrus, Gray Matter, BA47
2.66	0.004	- 44	18	- 23	Left Cerebrum, Temporal Lobe, Superior Temporal Gyrus, Gray Matter, BA38
(B) Patient group					
Voxel level Z	Voxel P(unc)	Talairach coordinates{mm}			Region
		x	y	z	
4.32	0.000	- 48	- 69	- 13	Left Cerebrum, Temporal Lobe, Fusiform Gyrus, Gray Matter, BA19
4.16	0.000	- 48	- 72	- 3	Left Cerebrum, Occipital Lobe, Middle Occipital Gyrus, Gray Matter, BA19
4.39	0.000	32	- 92	- 12	Right Cerebrum, Occipital Lobe, Inferior Occipital Gyrus, Gray Matter, BA18
3.91	0.000	42	- 54	- 29	Right Cerebellum, Posterior Lobe, Tuber
3.80	0.000	48	- 67	- 12	Right Cerebellum, Posterior Lobe, Declive
3.46	0.000	48	15	- 7	Right Cerebrum, Frontal Lobe, Superior Temporal Gyrus
3.84	0.000	36	- 52	47	Right Cerebrum, Parietal Lobe, Superior Parietal Lobule, Gray Matter, BA7
3.62	0.000	28	- 56	47	Right Cerebrum, Parietal Lobe, Superior Parietal Lobule, Gray Matter, BA7
2.91	0.002	14	- 5	11	Right Cerebrum, Sub-lobar, Thalamus, Gray Matter, Ventral Anterior Nucleus
2.50	0.006	0	- 19	8	Inter-Hemispheric
2.36	0.009	16	6	3	Right Cerebrum, Lentiform Nucleus, Gray Matter, Putamen

SPM99 software( <a href="http://www.fil.ion.ucl.ac.uk">http://www.fil.ion.ucl.ac.uk</a> )	analysis method)	(random
(a least - square approach) <sup>34)</sup>	effect analysis method)	
	(error variance)	
Talairach <sup>35)</sup>	, 6mm	<sup>36)</sup> t Z
FWHM(full - width at half maximum)	3	(clusters of signifi-
가 (Gaussian kernel)		cant activation) (height) (spa-
(smoothing)		tial) ( $p<0.05$ ) (probability
		distribution ; $Z=2.58$ , $p<0.005$ )
SPM (general linear model)	<sup>37)38)</sup> Talairach	(Broadmann
(pixel)		
(individual - level analysis)	, area ; BA)	
SPM99 2	(hierarchical two - stage	

**Table 3.** Group comparison results at uncorrected at  $p<0.01$ . Anatomical location of the maximum activation is given along with its Broadmann's area nomenclature(BA)

(A) Comparison >Patient					
Voxel level Z	Voxel P(unc)	Talairach coordinates{mm}			Region
		x	y	z	
3.73	0.000	- 43	16	- 24	Left Cerebrum, Temporal Lobe, Superior Temporal Gyrus, Gray Matter, BA38
2.60	0.005	- 26	13	- 20	Left Cerebrum, Frontal Lobe, Inferior Frontal Gyrus, Gray Matter, BA47
3.61	0.000	21	- 30	16	Right Cerebrum, Sub-lobar, Caudate, Gray Matter, Caudate Tail
3.81	0.000	- 51	4	40	Left Cerebrum, Frontal Lobe, Middle Frontal Gyrus, Gray Matter, BA6
3.54	0.000	6	10	5	Right Cerebrum, Caudate, Gray Matter, Caudate Head
3.25	0.001	- 8	12	5	Left Cerebrum, Caudate, Gray Matter, Caudate Head
3.53	0.000	- 49	- 13	8	Left Cerebrum, Temporal Lobe, Superior Temporal Gyrus, Gray Matter, BA22
3.24	0.001	- 43	- 16	17	Left Cerebrum, Sub-lobar, Insula, Gray Matter, BA13
3.36	0.000	- 29	- 36	- 1	Left Cerebrum, Temporal Lobe, Sub-Gyral, Gray Matter, Hippocampus
3.26	0.001	- 8	- 27	- 7	Left Brainstem
(B) Comparison <Patient					
Voxel level Z	Voxel P(unc)	Talairach coordinates{mm}			Region
		x	y	z	
4.25	0.000	- 8	- 27	42	Left Cerebrum, Limbic Lobe, Cingulate Gyrus, Gray Matter, BA31
3.60	0.000	18	- 72	52	Right Cerebrum, Parietal Lobe, Precuneus, Gray Matter, BA7
3.47	0.000	2	- 10	40	Right Cerebrum, Limbic Lobe, Caudate Gyrus
3.44	0.000	32	- 54	- 18	Right Cerebrum, Posterior Lobe, Declive
2.56	0.005	48	- 66	- 18	Right Cerebrum, Posterior Lobe, Declive
3.18	0.001	- 18	- 62	- 24	Left Cerebrum, Anterior Lobe
2.17	0.015	- 32	- 62	- 24	Left Cerebrum, Posterior Lobe, Declive
3.09	0.001	42	- 82	6	Right Cerebrum, Occipital Lobe, Middle Occipital Gyrus, Gray Matter, BA19
2.97	0.001	- 36	- 80	28	Left Cerebrum, Occipital Lobe, Superior Occipital Gyrus
2.53	0.006	- 26	60	22	Left Cerebrum, Frontal Lobe, Middle Frontal Gyrus, Gray Matter, BA10
2.41	0.008	- 34	46	26	Left Cerebrum, Frontal Lobe, Superior Frontal Gyrus, Gray Matter, BA9

결 과

85.8 ± 9.6%, 93.6 ± 5.5% ,  
(Mann Whitney U test, Z= - 2.108,

1. 과제수행도

p=0.035).

fMRI

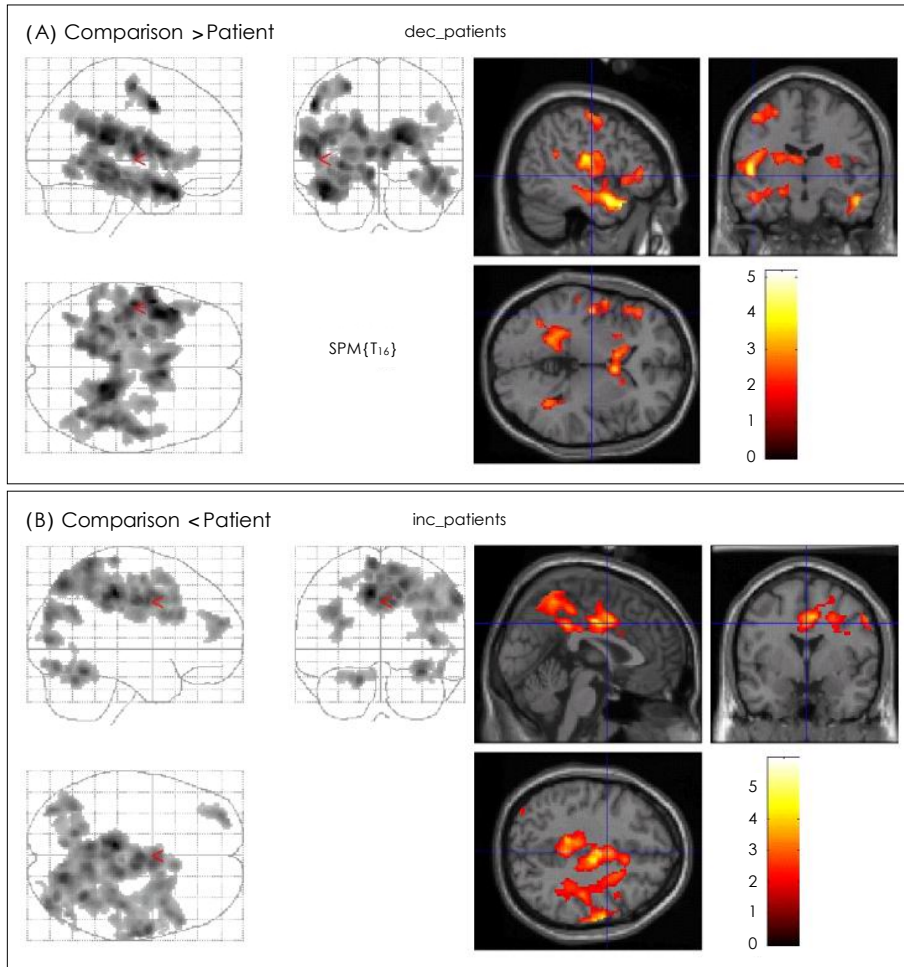


Fig. 2. The SPM results of the group comparison between schizophrenia group and matched healthy control group are shown on the glass window.

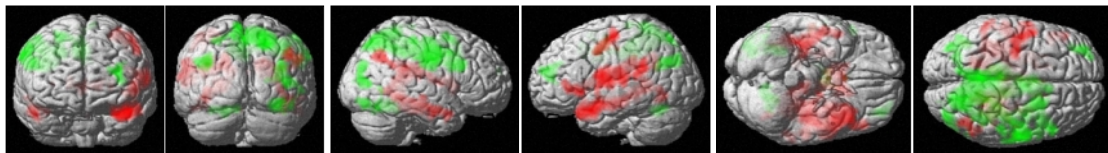


Fig. 3. Group activation results of patients and comparison subjects on a 3D rendered brain. Red areas indicate the regions in which patients had lesser activation than comparison subjects. Green areas indicate the regions in which patients had greater activation than comparison subjects (for all comparisons,  $p < 0.05$ , cluster size  $> 200$ , according to SPM99, uncorrected).

2. 기능적 자기공명영상 결과 : 개별적 효과(Individual effect)

(superior frontal gyrus),  
 (inferior frontal gyrus), (inferior parietal lobe)  
 (superior parietal lobule, BA7),  
 (middle occipital gyrus, BA19),  
 (inferior occipital gyrus, BA18),  
 (cingulate gyrus),  
 (fusiform gyrus)

fMRI ,<sup>39)</sup>

가<sup>17)24-26)</sup>

23)

11-22)

(tonsil)가  
 (tuber)  
 (decrive)

(lateral prefrontal areas, BA10/46)

<sup>40)41)</sup>

( 2).

3. 기능적 자기공명영상 결과 : 두군 간의 비교

( 3, 2, 3).

(signal)

(holding)

<sup>42)</sup>

Bertolino

proton

magnetic resonance spectroscopic imaging(H1 - MRSI) <sup>43)</sup>

N - acety-

lasparate

가

(precentral gyrus, BA6), (inferior frontal gyrus, BA47)

가

가

가가

(superior frontal gyrus, BA9), (middle frontal gyrus, BA10),  
 (middle temporal gyrus),

<sup>44)</sup>

(precuneus, BA7), (middle occipital gyrus, BA19),  
 (superior occipital gyrus), (cuneus),

가

(motor coordination)

(cingulate gyrus) (anterior lobe), (decrive) 가

<sup>45)46)</sup>

고 찰

가

Gold

<sup>47)</sup>

가

가

(neural substrate)

<sup>48)49)</sup>

fMRI

가

2 - back

18)

가

(problem solving)  
가 50)

중심 단어 :

참고문헌

가

가

(hypofrontality)

가

(hyperfrontality)

가

가

51)

가

(variability)

가

25)52)

(neural strategy) 가

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