

ORIGINAL ARTICLE

Visualization of calculation centres by functional MRI for neurosurgery

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Abstract

We performed functional MRI with several semantic tasks to visualize parietal lobe functions. Twenty subjects were studied, including 9 normal controls and 11 patients with brain lesions. The calculation task was to simply add 3 numbers projected on a screen. Functional MRI showed the active pixels in the bilateral interparietal sulcus (especially the dominant side) and mean values and standard deviation of left/right ratios of active pixels in the interparietal sulcus were 1.63 ± 0.57 in normal controls, and 1.64 ± 0.72 in neurosurgical patients. In 3 patients, postoperative functional MRI well reflected sequential changes of their calculation ability. This technique is simple to apply to evaluate the severity of dyscalculia not only for parietal lobe lesions, but also for other diseases, such as developmental dyscalculia, autism and dementia.

Key words: *Functional MRI, calculation, interparietal sulcus, neurosurgery.*

Introduction

Acalculia is a representative tetralogy in Gerstmann's syndrome. It is well known that brain injury of the parietal lobe in the dominant hemisphere impairs arithmetical functions.¹ Since the left inferior parietal lobule (IPL) and interparietal sulcus (IPS) are considered to be strongly related to the calculation ability, surgical strategy for the parietal and intraventricular lesions has been planned to preserve the lateral part of the parietal lobe, including the interparietal sulcus.

Functional magnetic resonance imaging (fMRI) has recently been developed to identify the hemisphere showing language dominance. Most language fMRI studies have shown activations in the inferior and middle frontal gyri using tasks such as word generation and categorization. We have reported more than 90% of brain lesion patients successfully underwent language-fMRI to identify the dominance.² Although technical difficulties to detect the receptive language area by fMRI remain, language-fMRI has been accepted for clinical use. We have considered that the parietal region is the next target to detect special functions by fMRI in the clinical setting. According to previous fMRI studies using volunteers, calculation tasks consistently evoked particular activation patterns around the IPS. In particular, the addition tasks demonstrated wider

activated areas such as bilateral inferior parietal lobule³ and IPS.^{4,5}

In this study, we established fMRI to detect the parietal lobe functions using addition task (addition-fMRI) and demonstrated the consistent activation patterns in normal controls and neurosurgical patients. In addition, three cases of parietal lesions showed that serial changes of addition-fMRI were well correlated with symptomatic fluctuations on neuropsychological tests. We here describe addition-fMRI is a simple, but new clinical tool to localize parietal lobe functions.

Materials and methods

Subjects

Twenty subjects were investigated and all were right-handed native Japanese speakers. The demographic data of all subjects is shown in Table I. This study was approved by our institutional review board, and a written informed consent was obtained from each subject before participation in the studies.

Normal controls

Initial studies were performed on nine neurologically normal volunteers (ages 22–37, all males) to confirm

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TABLE I. Demographic data of all subjects

Subject	Age	Sex	Diagnosis	Activation areas of addition-fMRI	Dyscalculia	L/R ratio of the IPS
Normal controls						
1	22	M	volunteer	Bilateral IPS, Left IPL	–	2.72
2	29	M	volunteer	Bilateral IPS	–	2.38
3	33	M	volunteer	Bilateral IPS	–	1.18
4	25	M	volunteer	Bilateral IPS, Left IPL	–	1.44
5	26	M	volunteer	Bilateral IPS	–	1.67
6	32	M	volunteer	Bilateral IPS	–	1.72
7	25	M	volunteer	Bilateral IPS, Left IPL	–	1.26
8	37	M	volunteer	Bilateral IPS	–	1.00
9	27	M	volunteer	Bilateral IPS, Left IPL	–	1.36
Neurosurgical patients						
10	49	F	Left frontal meningioma	Bilateral IPS, Left IPL	–	2.46
11	25	F	Right IV tumor	Bilateral IPS, Left IPL	–	3.17
12	56	F	Left parasagittal meningioma	Bilateral IPS	–	2.11
13	36	M	Left temporal AVM	Bilateral IPS	–	1.53
14	30	F	Left frontal glioma	Bilateral IPS, Left IPL	–	1.30
15	60	M	Right mild ICA stenosis	Bilateral IPS	–	1.19
16	62	F	Right parasagittal meningioma	Bilateral IPS, Left IPL	–	1.33
17	66	M	Right frontal meningioma	Bilateral IPS, Left IPL	–	1.86
18	49	M	Left parietal glioma	Bilateral IPS	–	1.48
19	55	F	Left parietal glioma	Bilateral IPS	+	1.00
20	34	F	Left IV meningioma	Bilateral IPS	+	0.64

IPS: interparietal sulcus, IPL: inferior parietal lobule, IV: intraventricular, AVM: arteriovenous malformation, ICA: internal carotid artery

the results of previous studies.^{3–5} They had no impairment of visual acuity or calculation ability.

Neurosurgical patients

Nine patients had no lesion in the left parietal region and no impairment of calculation ability. One case with a tumour in the left lateral ventricle underwent surgery to dissect the left interparietal sulcus and suffered from transient dyscalculia. Two patients suffered from mild dyscalculia because of left parietal lesions. All three cases with dyscalculia underwent addition-fMRI before and after surgery to compare fMRI activations and symptoms. The mean age of the subjects was 47.5 years old (from 25 to 66, 4 males and 7 females).

Functional MRI

All MR imaging was performed using a 3-tesla MR scanner with echo planar capabilities and a whole-head receive-only coil (Signa, General Electric, USA). During the experiments, foam cushions were used to immobilize the patient's head. fMRI was performed with a T2*-weighted echo planar imaging sequence (echo time; 35 msec, repetition time; 4000 msec, flip angle; 90°, slice thickness; 4 mm, slice gap; 1 mm, field of view; 240 mm, number of matrix; 64 × 64, number of slice; 24). Each fMRI session consisted of 3 dummy scan volumes, 3 activation periods, and 4 baseline (rest) periods. During each period, 5 echo-planar imaging volumes were collected, yielding a total of 38 imaging volumes. We used 2 different semantic tasks for fMRI such as letter-reading and addition.

Language dominance was identified using letter-reading task fMRI elsewhere.²

Calculation task

Thirty sets of 3 one-digit numbers were randomly presented on a liquid crystal display monitor with a mirror above the head coil allowing the patients to see the numbers. For the calculation task, subjects were asked to covertly add presented three numbers of each set. The sets were presented in a 300-millisecond exposure time with interstimuli intervals ranging from 2800–3200 milliseconds. During the rest phase, the subjects passively viewed random dots that were controlled to have the same luminance as the stimuli to eliminate primary visual responses.

After data acquisition, functional activation maps were calculated by estimating Z-scores between the rest and activation periods using Dr.View (Asahi Kasei, Tokyo, Japan). Pixels with Z-scores higher than 2.2 ($p < 0.05$) were considered to indicate real activation and were used for mapping. The result from each fMRI session was co-registered with 3D-MRI (by the Affine transformation). Further details of this analysis after data acquisition have been described elsewhere.² We counted the number of active pixels in the bilateral superior and inferior parietal lobules and the inner banks of IPS and calculated left/right (L/R) ratios of active pixels for each region. Non-paired Student's t-test was applied to identify functional lateralization of the parietal regions.

Three patients, who suffered from dyscalculia, underwent the Japanese version of the Wechsler Adult Intelligence Scale- Revised (WAIS-R) to

objectively evaluate calculation ability before and after surgery, as well as addition-fMRI.

Results

Language lateralization

The language dominance of all subjects was the left side, which was identified by reading-fMRI.

Normal controls

The active pixels were clustered mainly in the bilateral IPS in 5, and the bilateral IPS and the left IPL in 4 subjects, respectively. There were few active pixels in the bilateral superior parietal lobule or right IPL in controls. Mean numbers and standard deviation of active pixels were 22.11 ± 8.15 , 30.33 ± 13.27 , and 7.33 ± 9.71 in the right IPS, left IPS and left IPL, respectively (Fig. 1a). Since the active pixels were consistently and mainly clustered in the inner banks of the IPS, we focused on the IPS activations. The mean value and standard deviation of L/R ratio of the IPS (IPS-L/R ratio) were 1.63 ± 0.57 in the controls.

Neurosurgical patients

Although 2 cases have mild dyscalculia, active pixels of addition-fMRI were clustered mainly in the inner banks of the bilateral IPS and left IPL as well as in normal controls. Mean numbers and standard deviation of active pixels were 27.55 ± 22.83 , 39.00 ± 13.62 , and 8.55 ± 12.58 in right, left IPS and left IPL, respectively (Fig. 1b). The inner banks of the bilateral IPS showed obvious fMRI-activations in neurosurgical cases and the mean value and standard deviation of IPS-L/R ratio were 1.64 ± 0.72 , which is almost identical to that of normal controls. There was no significant difference in IPS-L/R ratio between normal controls and neurosurgical patients ($p > 0.05$). These results demonstrated that the inner bank of the bilateral IPS should play important roles and the IPS-L/R

ratio indicated the left parietal dominance by the calculation task in both of normal controls and neurosurgical patients.

We present two representative cases of dyscalculia and compared the results of addition-fMRI and WAIS-R (Figs. 2 and 3).

Representative cases

Case 18

A 49-year-old, right-handed man with a suspected high grade glioma in the left superior parietal lobule had weakness in his right leg and mild dyscalculia. MRI showed the IPS and IPL were markedly compressed by a cystic tumor of 50 mm in diameter. Active pixels of the addition-fMRI were restricted in the bilateral IPS and IPS-L/R ratio was 1.49, which indicated left-side dominance. In order to preserve the left IPS and IPL, we resected the brain tumour in the superior parietal lobule. Postoperative MRI demonstrated the resection had spared the left IPS. The number of active pixels on addition-fMRI was increased in the left IPS and 1.89 of IPS-L/R ratio 1 month after surgery was much better than preoperative value (Fig. 2). The calculation score of WAIS-R was increased, and indicating marked improvement of calculation ability.

Case 19

A 55-year-old, right-handed woman had suffered from mild apraxia and seizure for 5 years. MRI revealed an intra-axial lesion with 35 mm in diameter in the left IPL. Addition-fMRI demonstrated marked activation in bilateral IPS (Fig. 3a) and IPS-L/R ratio was 1, which did not indicate left parietal dominance. We resected the lateral wall of the left IPS, where the marked fMRI activation was observed, and her parietal symptoms, including calculation ability, were deteriorated after surgery. Serial addition-fMRI demonstrated activations became smaller in size within 3 months after surgery (Fig. 3b, 3c). Although preoperative IPS-L/R ratio was 1, it became 0.52 and

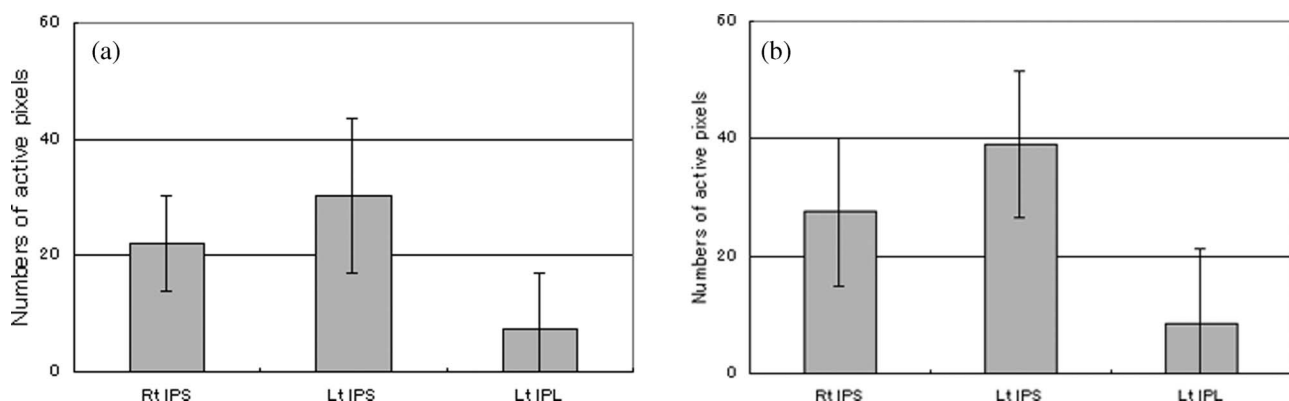


FIG. 1. Mean numbers and standard deviation of active pixels in right IPS, left IPS and left IPL: (a) in normal controls; (b) in neurosurgical patients.

0.29 14 days and 3 months after surgery, respectively (Fig. 3d). Severe dyscalculia has persisted with no significant recovery.

Discussion

Our fMRI results demonstrated that the bilateral IPS (especially the dominant side) played important roles as calculation centres, which were in concordance with a previous fMRI study of normal controls.⁴ There have been few reports about the functional mapping of calculation centres by electrocortical stimulation or fMRI in neurosurgical patients. In this study, addition-fMRI was simple to perform and consistently

disclosed the calculation centres in bilateral IPS in all normal controls and neurosurgical patients.

Compared to language-fMRI, it was relatively difficult to clearly indicate the hemispheric dominance of the calculation function by fMRI; however, at least in part, we would like to stress that the inner bank of IPS is indispensable for calculation tasks and $IPS-L/R < 1$ ratio might be the critical threshold to detect dyscalculia.

The findings of addition-fMRI changed depending on the patients' conditions. In case 19 with damage in the left IPS and IPL, calculation difficulty persisted with no recovery, whereas in case 18 with no damage in the left IPS, sacrificing the left superior parietal lobule enabled recovery from preoperative dyscalculia. On the basis, the left IPS in the dominant hemisphere is the most important region for calculation and the functional state could be objectively evaluated by addition-fMRI.

There have been no reports about serial fMRI investigations using calculation tasks in cases with neurosurgical operation. After decompression of the left IPS in case 18, calculation ability improved and postoperative addition-fMRI detected more active pixels than preoperatively. Similar recovery processes of addition-fMRI and symptoms were observed in case 20, who had transient deterioration of calculation ability. As far as we know, only one case report has shown postoperative recovery of dyscalculia after lesion resection in the superior parietal lobule⁶ with no fMRI investigation.

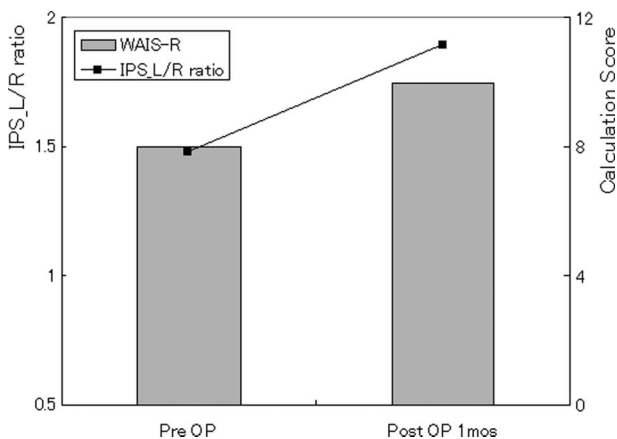


FIG. 2. IPS-L/R ratio and WAIS-R in case 18. IPS-L/R ratio and calculation score of WAIS-R were increased 1 month after surgery.

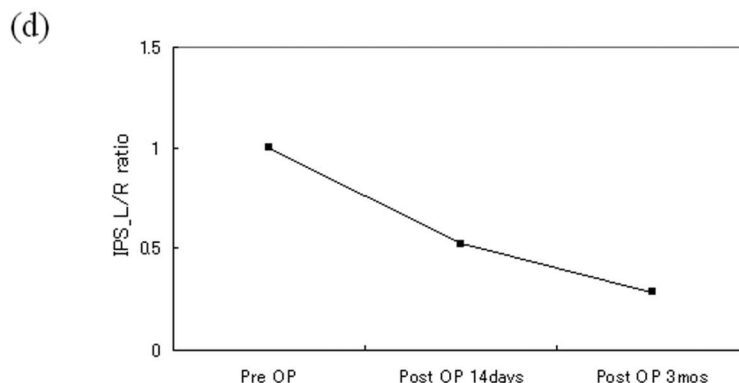
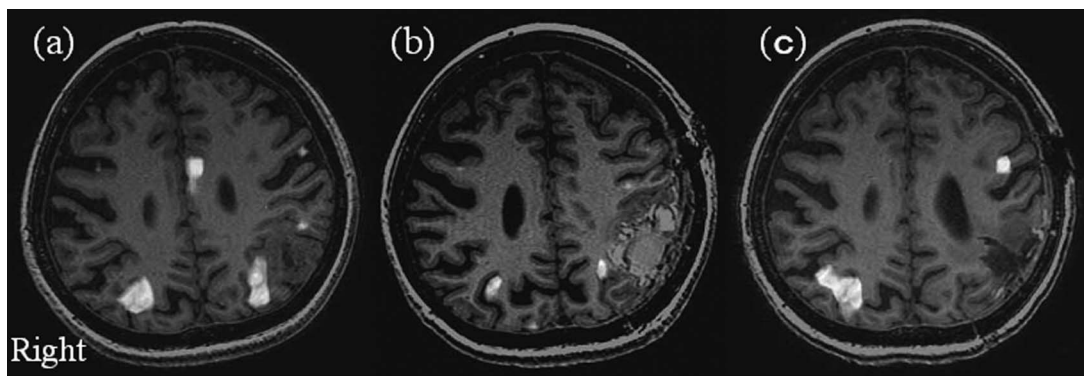


FIG. 3. Addition-fMRI in case 19. Preoperative addition-fMRI showed activation areas in bilateral IPS (a). The number of pixels in the left IPS decreased 2 weeks (b), 3 months (c) after surgery. The active pixels remained in the right IPS. Sequential changes of the IPS-L/R ratio in case 19, showing gradual decrease of the L/R ratio (d). Note that her dyscalculia persisted, which was correlated with the IPS-L/R ratio.

Holodny *et al.* reported decreased BOLD fMR activation of the motor and sensory cortices adjacent to a glioblastoma multiforme. That may have been due to a pressure effect or loss of vascular autoregulation.⁷ The decrease of BOLD fMR activation might be related to the mass effect or peritumoural oedema; however, we did not observe peritumoural oedema in case 18 and 19. Although it is still hard to mention increase of BOLD signal exactly reflects functional recovery of the brain, the facts of this study demonstrated positive possibility of fMRI to evaluate local brain conditions and functions.

Several groups achieved cortical mapping of calculation functions by electrocortical stimulation in the awake state.^{6,8–11} In general, electrocortical stimulation has several practical limitations, such as restricted time, patient's cooperation and position, anesthesia and difficulties of the various calculation tasks; therefore, functional mapping of the parietal regions by electrocortical stimulation includes several risks and is still challenging⁷. Instead of invasive procedures, non-invasive mapping using fMRI might be acceptable in the clinical scene. Addition-fMRI, which we proposed in this study, was non-invasive, simple, repeatable and reproducible. Furthermore, the obtained results evaluated preoperative state of the calculation ability in each patient and enabled us to identify the functioning of the affected cortical regions.

This addition-fMRI enables us to understand the patient's calculation function and anatomical information before surgery. So far, we don't think that preservation of left IPS takes priority over complete lesion resection. With this addition-fMRI results, we can explain postsurgical risks of calculation deficits to the patients before operation and determine surgical and postsurgical strategy.

The task which we used was quite simple and has significant scope for improvement. When calculation tasks are too easy for subjects, they will be achieved with little effort, resulted in little fMRI activation, while complicating tasks, which affect the task performance, might cause patient motion artifacts and little fMRI activation. It should be noted that the results of addition-fMRI could be modified, depending on patient conditions and individual ability. Our results using a simple addition task, however, showed distinct activation in parietal lobe and the IPS-L/R ratio well correlated with the WAIS-R score. We believe that our task was sufficiently acceptable for clinical practice in neurosurgery.

Addition-fMRI showed active pixels not only in IPS and IPL but also supplementary motor cortex, primary motor and Broca's areas. Duffau *et al.* indicated functional areas for multiplication and subtraction were in the inferior part of the angular gyrus and in the superior part immediately below the intraparietal sulcus by using electrocortical stimulation with awake craniotomy, respectively.⁶ We analyzed the pixels of addition-fMRI along IPS and demonstrated correlations of symptomatic changes

and number of fMRI pixels. Although this study design and results were rather simple compared to the Duffau's study, we would like to stress that addition-fMRI is practically useful in the clinical scene and IPS played an important role in the addition task.

These findings have been indirectly confirmed by the clear correlation between symptoms and addition-fMRI results. Our study demonstrated the positive possibility of fMRI for functional mapping of parietal lobe and indicated the IPS should be the key target for the analysis. These preliminary findings need to be confirmed by studying larger number of patients with parietal lesions and fMRI using multiple calculation tasks, such as multiplication, subtraction and division (calculation-fMRI). Further study, comparing calculation-fMRI with electrocortical stimulation under an awake craniotomy, might enable us to understand the whole calculation network.

Conclusion

This study emphasizes that the IPS in the dominant hemisphere is indispensable for calculation processes and can be identified by addition-fMRI. We believe that addition-fMRI is a useful technique for non-invasive preoperative mapping of calculation centres in clinical practice. Furthermore, the fMRI results well correlated with postsurgical calculation ability. This technique would be applicable to evaluate severity of dyscalculia in other diseases such as developmental dyscalculia, autism and dementia.

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