Bull Yamaguchi Med Sch 49(3-4):63-70, 2002

Functional magnetic resonance imaging Study of Cerebral Activation by a Simple Auditory Mental Addition Task: Problem Presentation Speed Adjusted for Individual Differences

Jun-ichi Ogasawara

Department of Neurology and Clinical Neuroscience, Yamaguchi University School of Medicine
1-1-1 Minamikogushi, Ube, Yamaguchi 755-8505, Japan
(Received November 8, 2002, revised January 9, 2003)

Key words: Functional magnetic resonance imaging, mental addition mathematical task, cognitive function, controlled task

Abstract We conducted a functional magnetic resonance imaging study of cerebral activation elicited by auditorily-presented and speed-adjusted simple mental addition tasks. The subjects were 8 healthy, right-handed men. We devised a method for determining the appropriate speed for auditory presentation of the mental addition task to each subject. A block design was used for this study. In the task state, simple mental addition problems were presented auditorily. In the control state, random numbers were presented auditorily. The left medial frontal gyrus, left cingulate gyrus, bilateral precentral gyri, left middle and inferior frontal gyri, bilateral insulae, left superior and inferior parietal lobuli, and right cerebellum were shown to be activated. Our findings indicate that the simple mental addition task is sufficient for activating cerebral areas associated with mental calculation when the difficulty of the mathematical task is controlled. The speed-adjusted simple addition task is useful for functional magnetic resonance imaging investigation of higher cognitive function.

Introduction

Patients with cerebral disease such as infarction, hemorrhage, or tumor can show dyscalculia or acalculia, although the mechanism of which is not sufficiently clear. Cerebral activation studies were recently shown to be useful for investigation of cognitive function.[1] Many such studies have used complex tasks for clarifying brain function, but patients with certain cognitive disorders and the very aged can not perform complex tasks. Simple tasks are more useful for clinical evaluation of patients or elderly persons. Thus, we have used simple tasks for investigation of arithmetic processing. There have been indications, however, that simple mathematical tasks are processed differently from complex mathematical tasks[2,3], and Dehaene et al. showed that simple addition and multiplication solutions are stored in and retrieved from rote verbal memory.[4] Therefore, mathematical tasks used in activation studies should be simple without being too simple.

Arithmetic operations are used in various daily life situations and are generally of four types: addition, subtraction, multiplication, and division. Selective impairment of each of these operations has been reported in patients with brain damage.[5,6] Thus, each operation may require a different cognitive process, and it is difficult to compare one operation with another in activation studies. Dixon et al. showed that mathematical principles are represented more by addition than by any other operation.[7] Cohen et al. showed dissociation between operations in patients with dyscalculia.[8] In these patients, arithmetic processing impairment often affects multiplication more severely than subtraction or subtraction more severely than multiplication, whereas the performance of addition in these patients is intermediate between that of multiplication and subtraction. Therefore, there is less possibility of severe impairment with respect to addition than to other operations in patients with dyscalculia. Understanding this is important in activation studies of the damaged brain. Most Japanese children first learn addition in elementary school. Addition is common in daily life and is used to explain the other mathematical operations. We hypothesized that addition is the best arithmetic task to use in testing patients with cognitive dysfunction. Many recent activation studies for mental calculation have involved subtraction, multiplication, or more complex arithmetic tasks[2,8−18]; few have involved simple mental addition tasks.[3,19,20] In addition, the tasks in these studies have not been controlled for individual mathematical abilities. The findings of one study suggested that functional optimization of arithmetic processing differs between perfect and imperfect performers.[11] Thus, we conducted a study in which the difficulty of arithmetic problems was adjusted on a per subject basis but the amounts difficulty of arithmetic work were nearly equal.

This study was undertaken with the aim of determining whether a simple mental addition task is enough to activate cerebral areas related to mental calculation when the difficulty of the task is controlled.

Materials and Methods

Subjects

The subjects were 8 healthy, right-handed men, aged 24 to 43 years, who graduated from a university or college. No neurological signs, significant medical conditions, or abnormal magnetic resonance (MR) image findings were present in these subjects. None had special mathematical ability. All provided informed consent to participate in the study.

Task design

We used a block design for this study. In the task condition, auditory addition problems were presented to each subject by artificial voice through headphones attached to a personal computer. The problem was as follows. A single-digit number was added to another single-digit number to yield a double-digit sum. The sum provided was either correct [for example, 9+6=15] or incorrect [for example, 8+4=13]. The subjects were required to judge mentally whether the given sum was correct or incorrect. The speed at which the problem presented was adjusted according to individual arithmetic ability determined before the MR examination. In the control condition, each subject laid with his eyes closed and random numbers were auditorily presented, i.e. 9, 7, 6, 3, etc.; the subject just listened to the random numbers. In alternating 35 sec epochs, subjects were presented with the arithmetic problem or the random numbers. One examination period was 280 sec.

Task presentation speed and performance

Because it is difficult to check task performance in the MR imaging unit, we examined task performance for each subject outside the unit just before scanning. One examination for checking his performance was same tasks and periods which were presented in the unit, the task and control conditions were both presented during this period. Each subject responded to the problems on a 10-key numerical pad. The # 1 key was used to indicate a correct sum; the # 3 key was used to indicate an incorrect sum. Subjects' responses were

Table 1 Test performance of subjects

Subject	Percentage of correct responses
1	76%
2	85%
3	88%
4	75%
5	80%
6	82%
7	82%
8	78%
	mean 80.8%

stored in the personal computer, and the number of correct responses was determined after the examination. The presentation speed was controlled by software and could be adjusted. We examined the performance of each subject at four different presentation speeds (1000 ± 80, 1350 ± 70, 1790 ±100, 2160 ± 120 [msec/item]), and we used the speed at which the subject achieved about 80% accuracy.

Functional data acquisition

All experiments were performed with a 1.5 Tesla MR imaging scanner and the use of a head coil (SIEMENS). A single-shot echo-planar image sequence was used. The field of view was 256 mm, matrix size was 64×64, repetition time was 5000 msec, flip angle was 90 degrees, and time to echo was 55.24 msec. Thirty axial slices were collected in each volume. Each slice was 4 mm thick without separation and parallel to the intercommissural plane. Forty-four volumes were acquired per scan, and the first two images of each scan were discarded.

Data analysis

The functional MR imaging data were analyzed with the SPM-96 module included in the MEDx 3.3 software package (Sensor Systems). The images were not aligned with the SPM realign module because the head motion of each subject was less than 0.4 mm (less than 10% of the voxel size). The images were smoothed and normalized by the SPM-96 module according to Montreal Neurological Institute (MNI) coordinates. Statistical analysis was performed with SPM-96 on pooled data with multi-subject analysis; the MR imaging signal data of all 8 subjects were analyzed as a whole. The resulting z-maps were thresholded by the z score height ($z > 6$).

Results were given using the MNI brain and then transformed into the Talairach atlas.[21] The transformation was done with the following formula for translating between two coordinates: $X' = 0.88\ X - 0.8$, $Y' = 0.97\ Y - 3.32$, $Z' = 0.05\ Y +$

Table 2 Significant activated areas on the MNI brain

	X	Y	Z	Z value
Frontal lobe				
Lt. cingulate gyrus	−12	4	48	7.92
Lt. insula	−44	0	20	7.91
Lt. inferior frontal gyrus	−48	16	20	7.60
Lt. precentral gyrus	−44	−8	52	7.60
Lt. middle frontal gyrus	−48	4	48	7.57
Lt. medial frontal gyrus	−8	0	56	7.83
Rt. precentral gyrus	48	−4	48	7.14
Rt. insula	40	12	−4	6.25
Parietal lobe				
Lt. superior parietal lobule	−32	−68	60	7.62
Lt. inferior parietal lobule	−48	−44	36	6.95
Cerebellum				
Rt. cerebellum	24	−76	−28	7.65

Lt., left side; Rt., side; XYZ, MNI coordinates.

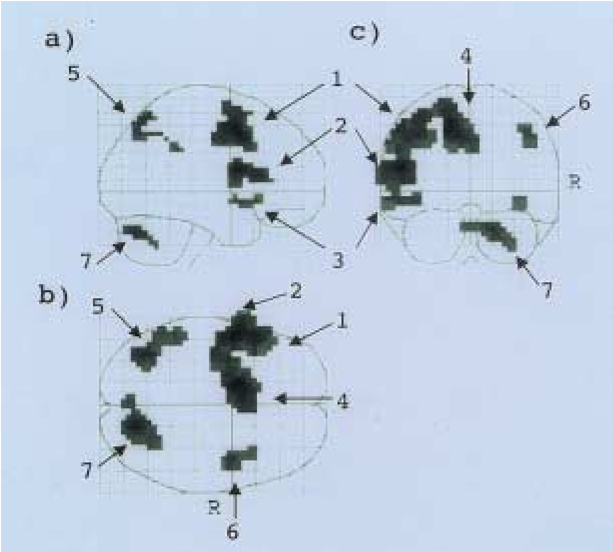

Fig. 1 Activated areas are superimposed on the glass brain. Maximum intensity projections are shown.
a); Ieft side view, b); top view, c); front view
1.; Left precentral gyrus
2.; Left insula and middle frontal gyrus
3.; Left inferior frontal gyrus
4.; Left medial frontal gyrus and cingulate gyrus
5.; Left superior and inferior parietal lobuli
6.; Right precentral gyrus and insula
7.; Right cerebellum

0.88 Z - 0.44. (X', Y', Z'; Talairach atlas, X, Y, Z; MNI brain). We defined the activated areas using the Talairach atlas.

Results

The performance of each subject is shown on Table 1. Subjects responded correctly to >75% and <88% of problems (mean 80.8%).

Regional brain activation is shown on Table 2. The left medial frontal gyrus, left cingulate gyrus, bilateral precentral gyri, left middle and inferior frontal gyri, bilateral insulae, left superior and inferior parietal lobuli, and right cerebellum were activated. Images of the activated areas were superimposed on a glass brain (Fig. 1) and also on the MNI brain (Fig. 2).

Discussion

Mental calculation is one of the most common higher cognitive functions. Many processes are involved, i.e. verbal processing mechanisms, perception and recognition of numerical orthography and/or number-symbol representation, visual-spatial discrimination, short-term memory, long-term memory, syntactic/algorithmic reasoning, and sustained attention.[22] Recent studies have shown that working memory is also associated with mental calculation.[23,24] Therefore, many areas of the brain likely are activated by mental calculation tasks. Although Dehaene et al. reported that in some countries (France and Japan, for example), simple single-digit addition and multiplication are rote verbal tasks, not real mathematical calculations [4], our use of the double-digit addition task activated most areas shown to be activated in complex mathematical tasks. The left medial frontal gyrus, left cingulate gyrus, bilateral precentral gyri, left middle and inferior frontal gyri, bilateral insulae, left superior and inferior parietal lobuli, and right cerebellum were activated in our study. It is difficult to simply compare our results with the results of other mathematical activation studies because the results are influenced by differences in the task and control conditions. What is interesting, however, is that the mental addition task we used in this study activated so many areas associated with mental calculation.

In general, the parietal lobe is believed to be an important area for mathematical calculation.[22,25,26] There have been some reports of bilateral parietal lobe activation and some of left parietal lobe activation [3,19,20], and a parietal lesion was reported to cause selective impairment of addition in a patient.[5] Using complex tasks, Gruber et al. showed that the parietal area plays only a supportive role in mental arithmetic.[14] In our study, the left parietal lobe was activated. Our results suggest that the left parietal lobe is related to mental addition.

The bilateral precentral gyri and the left medial frontal gyrus were activated in our study. The left side precentral gyrus and the medial frontal gyrus were activated by simple addition in previous PET studies.[19] Another simple addition task study showed the left precentral gyrus, left medial frontal gyrus, and left parietal lobe to be associated with the spatial aspects of mental calculation and sequential manipulation of numbers within internal space.[20] We asked our subjects just after the experiment whether they used a verbal or visual strategy in the simple addition task, and all reported they used a visual strategy. Cognitive strategies have been reported to influence patterns of cortical activation during mental calculations.[12] We speculate that the bilateral precentral gyri and left medial frontal gyrus were activated in our subjects because they used a visual strategy for the spatial aspects of mental calculation and sequential manipulation of numbers within internal space.

The insular cortex was activated bilaterally in our study. The insular cortex is associated with many cognitive functions and is connected to many areas.[27] Nagai et al. suggested that the insular cortex is implicated in the translation and integration of different sensations.[27] In our study,

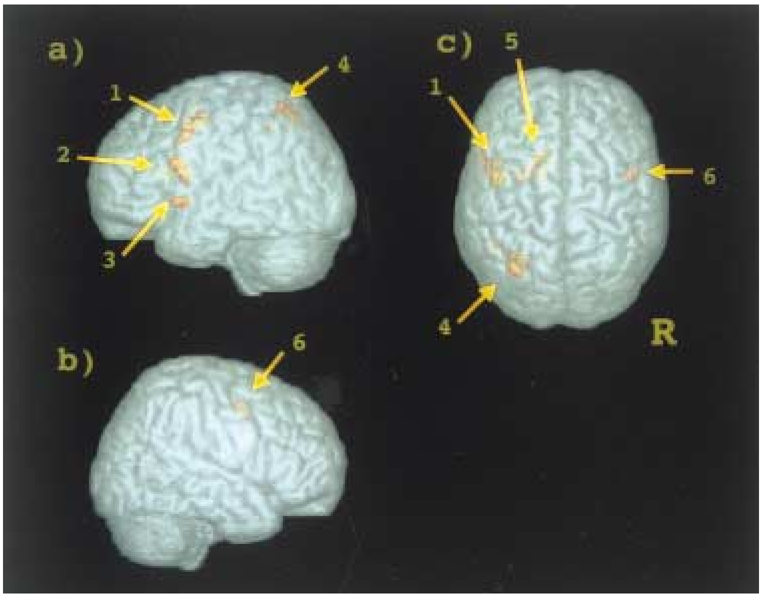

Fig. 2 Activated areas are superimposed on the MNI brain.
a); Ieft side view, b); right side view, c); top view
1.; Left precentral gyrus
2.; Left middle frontal gyrus
3.; Left inferior frontal gyrus
4.; Left superior and inferior parietal lobuli
5.; Left medial frontal gyrus
6.; Right precentral gyrus

subjects approached the auditorily-presented problems with a visual strategy. The insular cortex may be associated with the translation and integration of auditory and visual functions.

The right cerebellum was activated in a few previous mental calculation studies [2,11,19,28], but its function related to calculation is unclear. Because the right cerebellum is activated by many different tasks[28,29] and cerebellar disorders do not cause dyscalculia[22,26,30–34], the cerebellum is believed to play only a supportive role in mental addition.[28] Recent investigations have shown, however, that the cerebellum is associated with working memory and connected to the prefrontal lobe in primates.[33,35] The task used in our study loads the working memory, which may in turn cause the cerebellar activation.

Despite use of the auditory task, no changes were seen in the primary auditory or Broca and Wernicke language-associated areas. This fact may reflect the masking effect of the control task.

Task performance is very important in the investigation of cognitive function such as that used in mental calculation because each participant has a different arithmetic ability and different ability to attend to the mathematical questions. Arithmetic ability and attention are associated with working memory.[23,24] Working memory plays an important role in cognitive function, and attempts have been made to define working memory. Baddeley suggested working memory to be the system that provides temporary storage and manipulation of information necessary for such complex cognitive tasks as language comprehension, learning, and reasoning.[36] One study suggested that the amounts of working memory vary between individuals [37]; another indicated that working memory is made up of separate components .[24] In other words, it is very difficult to control the working memory independently. The subjects in our study were asked to use maximum effort for the mental calculations. Problems were of different degrees of difficulty and were applied on an individual basis. We defined the appropriate task presentation speed as that at which achievement is about 80%. At this speed, subjects concentrated only on the mental addition task, and they could spend their working memory resources on the task. A previous study showed that figures, carrying a number, and the speed at which problems are presented determines the difficulty of the mental addition task .[38] Accordingly, we controlled the level of difficulty by the speed at which questions were asked and thus equalized the influence of working memory for each subject. Working memory is associated with many areas in the brain, especially the prefrontal lobe.[39] In our study, we thought that activation of a part of the prefrontal lobe; the left middle and inferior frontal gyri, spent the resources of working memory.

Individual differences in working memory available for calculation were not considered in earlier mental arithmetic activation studies. In some studies, only the ability of each subject to perform the task was checked. In clinical situations, patients have various mathematical abilities and this must be addressed. Thus, we adjusted the level of difficulty on a per subject basis, and we believe we achieved a more appropriate tool for the investigation of mental calculation. It is important to consider individual mathematical ability in activation studies. Using simple mental addition tasks we can get about the same MR imaging results, obtained by the use of complex mathematical tasks. This method has potential for advancing the investigation of mathematical function in patients with brain damage.

Acknowledgements

I am grateful to Messrs. H. Mizuhara, M. Kitazawa, and J.L. Wu for development of the task presentation software used in this study. And I gratefully thank Prof. M. Morimatsu, associate Prof. K. Negoro, and Prof. N. Matsunaga for helpful discussions, advices and technical supports on this study.

References

1) Ingvar M, Peterssen KM (2000) Functional maps and brain networks In: Toga AW, Mazziotta JC (eds) Brain mapping: the systems. Academic Press, *San Diego,* pp 111-139
2) Zago L, Pesenti M, Mellet E, Crivello F, Mazoyer B, Tzourio-Mazoyer N (2001) Neural correlates of simple and complex mental calculation. *Neuroimage* 13: 314-327
3) Cosson S R, Pinel P, Mortele PF (2000) Understanding dissociations in dyscalculia. A brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation. *Brain* 123: 2240-2255
4) Dehaene S, Cohen L (1997) Cerebral pathways for calculation: double dissociation between rote and quantitative knowledge of arithmetic. *Cortex* 33: 219-250
5) van Harskamp NJ, Cipolotti L (2001) Selective impairments for addition, subtraction and multiplication. Implications for the organization of arithmetical facts. *Cortex* 37: 363-388
6) Lampl Y, Eshel Y, Gilad R, Sarova-Pinhas I (1994) Selective acalculia with sparing the subtraction process in a patient with left parietotemporal hemorrhage. *Neurology* 44: 1759-1761
7) Dixon J, Deets J, Bangert A (2001) The representations of the arithmetic operations include functional relationships. *Mem Cognit* 29: 462-477
8) Cohen L, Dehaene S, Chochon F, Lehericy S, Naccache L (2000) Language and calculation within the parietal lobe: a combined cognitive, anatomical and fMRI study. *Neuropsychologia* 38: 1426-1440
9) Burbaud P, Degreze P, Lafon P, Franconi JM, Bouligand B, Bioulac B, Caille JM, Allard M (1995) Lateralization of prefrontal activation during internal mental calculation: a functional magnetic resonance imaging study. *J Neurophysiol* 74: 2194-2200
10) Rueckert L, Lange N, Partiot A, Appollonio I, Litvan I, Le Bihan D, Grafman J (1996) Visualizing cortical activation during mental calculation with functional MRI. *Neuroimage* 3: 97-103
11) Menson V, Rivera SM, White CD, Eliez S, Glover GH, Reiss AL (2000) Functional optimization of arithmetic processing in perfect performers. *Brain Res Cogn Brain Res* 9: 343-345
12) Burbaud P, Caumus O, Guehl D, Bioulac B, Caille JM, Allard M (2000) Influence of cognitive strategies on the pattern of cortical activation during mental subtraction. A functional imaging study in human subjects. *Neurosci Lett* **287**: 76-80
13) Lee KM (2000) Cortical areas differentially involved in multiplication and subtraction: a functional magnetic resonance imaging study and correlation with a case of selective acalculia. *Ann Neurol* **48**: 657-661
14) Gruber O, Indefrey P, Steinmets H, Kleinschmidt A (2001) Dissociating neural correlates of cognitive components in mental calculation. *Cereb Cortex* **11**: 350-359
15) Hayashi N, Ishii K, Kitagaki H, Kazui H (2000) Regional differences in cerebral blood flow during recitation of the multiplication table and actual calculation: a positron emission tomography study. *J Neurol* Sci **176**: 102-108
16) Cowell SF, Egan GF, Code C, Harasty J, Watson JD (2000) The functional neuroanatomy of simple calculation and number repetition: a parametric PET activation study. *Neuroimage* **12**: 565-573
17) Pesenti M, Zago L, Crivello F, Mellet E, Samson D, Duroux B, Seron X, Mazoyer B, Tzourio-Mazoyer N (2001) Mental calculation in a prodigy is sustained by right prefrontal and medial temporal areas. *Nat Neurosci* **4**:103-107
18) Sakurai Y, Momose T, Iwata M, Sasaki Y, Kanazawa I (1996) Activation of prefrontal and posterior superior temporal areas in visual calculation. *J Neurol Sci* **139**: 89-94
19) Pesenti M, Thioux M, Seron X, Volder AD (2000) Neuroanatomical substrates of Arabic number processing, numerical comparison, and simple addition: a

PET study. *J Cogn Neurosci* **12**: 461-479

20) de Jong BM, von Zomeren AH, Willemsen ATM, Paans AMJ (1996) Brain activity related to serial cognitive performance resembles circuitry of higher order motor cortex. *Exp Brain Res* **109**: 136-140

21) Talairach J, Tournoux P (eds) (1988), Co-planar stereotaxic atlas of the human brain, 3-dimensional proportional system. An approach to cerebral imaging. Thieme Medical Publishers, *New York*, pp 73-113

22) Boller F, Grafman J (1985) Acalculia. In: Frederiks JAM (ed) Handbook of clinical neurology, vol 45. Elsevire, *Amsterdam*, pp 473-481

23) Logie RH, Gilhooly KJ, Wynn V (1994) Counting on working memory in arithmetic problem solving. *Mem Cognit* **22**: 395-410

24) Furust AJ, Hitch GJ (2000) Separate roles for executive and phonological components of working memory in mental arithmetic. *Mem Cognit* **28**: 774-782

25) Botez MI, Botez T, Oliver M (1985) Parietal lobe syndromes. In: Frederiks JAM (ed) Handbook of clinical neurology, vol 45. Elsevire, *Amsterdam*, pp 63-85

26) Grewel F (1969) The acalculias. In: Vinken PJ, Bruyn G (eds) Handbook of clinical neurology, vol 3. Elsevire, *Amsterdam*, pp 181-194

27) Nagai M, Kishi K, Katou S (2002) Structure and functions of the insular cortex. A review of the recent researches. Shinkei Kenkyu no Shinpo *(Adv Neurol Sci)* **46**: 157-174

28) Yamaguchi S (2000) Contributions of cerebellum to higher cognitive function. Shinkei Kenkyu no Shinpo *(Adv Neurol Sci)* **44**: 810-819

29) Cabeza R, Nyberg L (1997) Imaging cognition: an empirical review of PET studies with normal subjects. *J Cogn Neurosci* **9**: 1-26

30) Neau JP, Arroyo A, Bonnaud V, Ingrand P, Gil R (2000) Neurophysiological disturbances in cerebellar infarcts. *Acta Neurol Scand* **102**: 363-370

31) Daum L, Ackermann H, Schugens MM, Reimold C, Dichgans J, Birbaumer N (1993) The cerebellum and cognitive function in humans. *Behav Neurosci* **107**: 411-419

32) Middleton FA, Strick PL (1994) Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science* **266**: 458-461

33) Schmahmann JD, Sherman JC (1998) The cerebellar cognitive affective syndrome. *Brain* **121**: 561-579

34) Feiz JA (1996) Cerebellar contributions to cognition. *Neuron* **16**: 13-15

35) Middleton FA, Strick PL (2001) Cerebellar projections to the prefrontal cortex of the primate. *J Neurosci* **21**: 700-712

36) Baddeley A (1992) Working memory. *Science* **255**: 556-559

37) Just MA, Carpenter PA (1992) A capacity theory of comprehension: individual differences in working memory. *Psychol Rev* **99**: 122-149

38) Wu JL, Mizuhara H, Nishizawa Y (2001) Characteristics of reaction time in parallel information processing of human visual and auditory system. *Systems, Control and Information* **14**: 18-25

39) D'Esposito M (2001) Functional neuroimaging of working memory. In: Cabeza R, Kingstone A (eds) Handbook of functional neuroimaging of cognition. The MIT Press, *Cambridge Massachusetts*, pp 292-327