

# Developmental Fractionation of Working Memory and Response Inhibition During Childhood

Satoshi Tsujimoto, Mariko Kuwajima, and Toshiyuki Sawaguchi

Laboratory of Cognitive Neurobiology, Hokkaido Univ. Graduate School of Medicine, Sapporo, Japan

**Abstract.** The lateral prefrontal cortex (LPFC) plays a major role in both working memory (WM) and response inhibition (RI), which are fundamental for various cognitive abilities. We explored the relationship between these LPFC functions during childhood development by examining the performance of two groups of children in visuospatial and auditory WM tasks and a go/no-go RI task. In the younger children (59 5- and 6-year-olds), performance on the visuospatial WM task correlated significantly with that in the auditory WM task. Furthermore, accuracy in these tasks correlated significantly with performance on the RI task, particularly in the no-go trials. In contrast, there were no significant correlations among those tasks in older children (92 8- and 9-year-olds). These results suggest that functional neural systems for visuospatial WM, auditory WM, and RI, especially those in the LPFC, become fractionated during childhood, thereby enabling more efficient processing of these critical cognitive functions.

**Keywords:** executive function, prefrontal cortex, children, preschool-age, school-age

## Introduction

Working memory (WM) refers to the brain mechanism for temporary storage and manipulation of information. It is important for a wide range of cognitive functions, such as language comprehension, reasoning, and learning (Baddeley, 1986). Response inhibition (RI), the ability to withhold behavioral responses that are inappropriate in the current context, is also fundamental to various cognitive abilities and adaptive behaviors (Barkley, 1997; Diamond, 2002). WM has long been a focus of neurophysiological and lesion studies of monkeys (Funahashi, Bruce, & Goldman-Rakic, 1993; Sawaguchi & Iba, 2001; Tsujimoto & Sawaguchi, 2004) and brain-imaging and neuropsychological studies of humans (Freedman & Oscar-Berman, 1986; Jonides et al., 1993; McCarthy et al., 1994; Tsujimoto, Yamamoto, Kawaguchi, Koizumi, & Sawaguchi, 2004). The neural basis of RI has also been extensively studied in neuroimaging studies on human adults, which mainly use variations of a go/no-go task paradigm (Casey et al., 1997; Liddle, Kiehl, & Smith, 2001). These studies have established that the lateral areas of the prefrontal cortex (LPFC) play a critical role in the execution of both WM and RI tasks (for a review, see Fuster, 1997).

The present study focused on the development of WM and RI. This developmental approach to examining cognitive function may not only extend our understanding of cognitive development, but also our understanding of the neural mechanisms underlying these cognitive functions

(Casey, 2001). Studies of brain morphology have shown that the LPFC in humans undergoes considerable maturation during early childhood (between the ages of about 2 and 7 years), including a dramatic reduction in neuronal density (Huttenlocher, 1990), a marked expansion in the dendritic trees of pyramidal cells (Mrzljak, Uylings, van Eden, & Judas, 1990), and an increase in the volume of gray and white matter (Giedd et al., 1999). Therefore, the period from early childhood to school age should be important in the development of the LPFC function. Indeed, behavioral measures of WM systems improve substantially between the ages of 5 and 9 years (Gathercole, Pickering, Ambridge, & Wearing, 2004; Logie & Pearson, 1997; Luciana & Nelson, 1998). However, little is known about the relationship between visual WM, WM for other modalities, and RI during early childhood development.

Recent studies have provided evidence that subsystems for higher cognitive functions, such as WM, are fractionated in the adult human brain (for a review, see Baddeley & Dela Sala, 1998). For example, Bushara et al. (1999) reported that separate, adult, human brain areas were activated during visual and auditory WM tasks even in the same participants. Consistent with this notion, Sweeney, Rosano, Berman, and Luna (2001) suggested that WM and inhibitory control are processed independently in normal elderly participants. The LPFC of young children, however, is still immature (Huttenlocher, 1979), and has the potential to change with learning and practice (Gaillard et al., 2000; Goldman, Rosvold, & Mishkin, 1970; Tucker & Kling, 1967). Therefore, the neural systems in the LPFC

may fractionate through development from early childhood to adolescence or early adulthood. Indeed, Logie and Pearson (1997) suggested that the systems for visuospatial WM are fractionated to a greater extent in children aged 8 to 9 years than in those aged 5 to 6 years, and Gathercole et al. (2004) showed that the modular structure of WM is present from 6 years of age, but is not present in 4-year-olds.

Thus, it is likely that the LPFC functions of WM for different modalities and RI use common neural systems in young childhood, and become fractionated during later development. We therefore hypothesized that performance in visual WM would be more highly correlated with performance in WM for a different modality, and with RI in younger children than in older children. Specifically, young children, but not older children, with higher visual WM performance should also show higher auditory WM and RI performance. To test this hypothesis, we examined the behavioral performance of two age groups, 5- and 6-year-olds and 8- and 9-year-olds, in visuospatial and auditory versions of an n-back task and a go/no-go task. Several neuroimaging studies in children of these ages have reported that the LPFC is actually activated during both WM and RI processing (Casey et al., 1997; Tamm, Menon, & Reiss, 2002; Tsujimoto et al., 2004). The n-back task is a typical WM task involving temporary storage, manipulation, and selection of information. It has been widely used to assess WM function in many neuroimaging studies (Carlson et al., 1998; Cohen et al., 1997; Kwon, Reiss, & Menon, 2002), and in behavioral studies (Steenari et al., 2003; Vuontela et al., 2003). The go/no-go task requires participants to withhold their responses to a designated item in a series of stimuli; it has been extensively used to assess RI function (Casey et al., 1997; Liddle et al., 2001; Tamm et al., 2002).

## Methods

### Participants

Participants of this study were sampled from two age ranges. Younger participants were 59 5- and 6-year-old children (26 boys and 33 girls), ranging in age from 5 years 1 month to 6 years 8 months (mean = 5 years 11 months;  $SD = 5.1$  months). Older participants were 92 8- and 9-year-old children (47 boys and 45 girls), ranging in age from 8 years 9 months to 9 years 8 months (mean = 9 years 3 months;  $SD = 3.4$  months). Younger children were recruited from two preschools in Japan, and the older children were recruited from a public elementary school in Japan. None of the participants had a history of neurological or psychiatric disorders. Before the children participated in the experiment, their parents provided written informed consent.

An additional 31 younger children and six older children participated, but were excluded from the analyses in this report because they either did not complete the three tasks (see below) or did not satisfy the criterion of more than

60% correct in at least one of three tasks. The criterion of 60% correct was adopted because it was possible that the difference in variability between age groups caused the difference in correlation. This resulted in the exclusion of more participants from the younger group than from the older group. However, we note that the major results were similar when using the original sample without exclusion by the 60% criterion ( $N = 72$  for younger children;  $N = 92$  for older children).

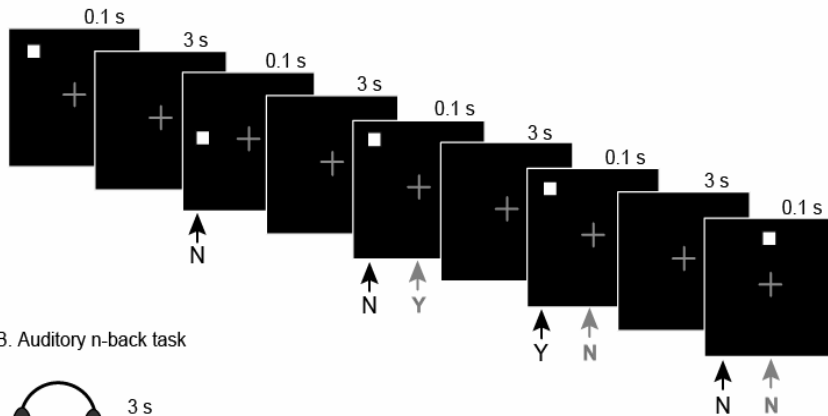
### Behavioral Tasks

We employed three tasks: visuospatial n-back, auditory n-back, and go/no-go tasks to examine visuospatial WM, auditory WM, and RI, respectively. Both visuospatial and auditory n-back tasks had two different conditions, called 1-back task and 2-back task. The 1-back task was used for the younger group, and the 2-back task was used for the older group. The tasks were controlled using a Pentium-based computer running visual C++ software (Microsoft Japan, Tokyo). Visual stimuli were presented on a liquid crystal display, and auditory stimuli were presented using a headphone. Temporal sequences of the three tasks are shown in Figure 1.

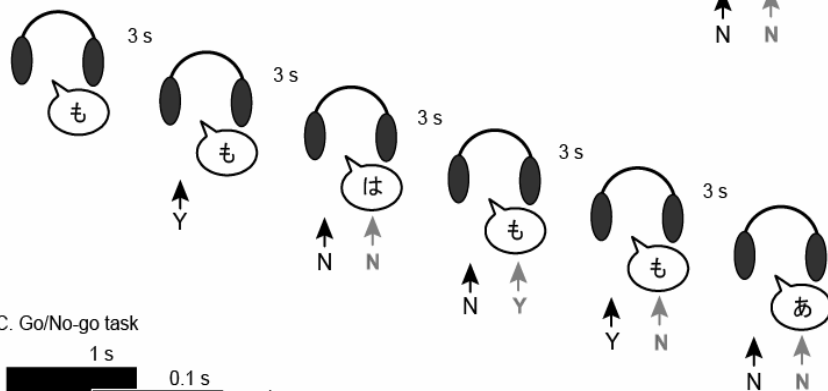
The visuospatial n-back task (Figure 1A) started when a fixation spot (white cross,  $\sim 1^\circ \times 1^\circ$ ) appeared at the center of the display. While the participants fixated on the central cross, white squares ( $\sim 1.5^\circ \times 1.5^\circ$ ) were presented sequentially and pseudo-randomly at one of eight possible locations that were distributed approximately  $6^\circ$  from the central cross. The stimuli were presented for 0.1 s, with an inter-stimulus interval (ISI) of 3 s. Only the central fixation cross was visible on the display during the ISI. In the 1-back task, on presentation of each stimulus except the first, the participants were required to decide whether the stimulus appeared at the same location as the immediately preceding one (see black arrows in Figure 1A). In the 2-back task, the participants were required to decide whether the current stimulus appeared in the same location as the one that had been presented two stimuli previously (see gray arrows in Figure 1A). The participants had 2 s to report their decision by pressing one of two buttons: "yes" was indicated using the right index finger and "no" by the left index finger. "Yes" and "no" trials were pseudorandomized and approximately equal in number.

The auditory n-back task (Figure 1B) had the same temporal sequence as the visuospatial n-back task but with auditory instead of visual stimuli. The auditory stimuli were pseudo-randomly selected from 46 single Japanese hiragana letters. Hiragana are Japanese phonograms, originally kanji but strongly simplified over the centuries: Hence, the auditory stimuli used here did not have any semantic meaning. The auditory stimuli were presented while the participants fixated on the central cross, with an ISI of 3 s. In a similar fashion to the visuospatial n-back task, the participants were required to report by button-press whether the

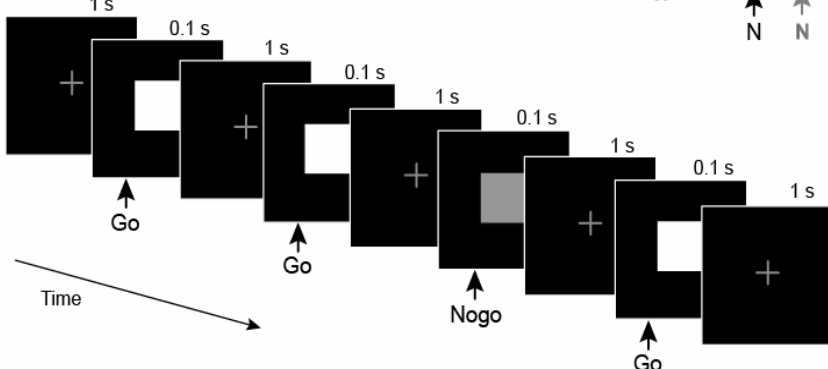
## A. Visuospatial n-back task



## B. Auditory n-back task



## C. Go/No-go task



*Figure 1.* The temporal sequence of behavioral tasks. (A) Visuospatial n-back task. Visual stimuli (white squares) were sequentially presented at one of eight possible locations for 100 ms, with an inter-stimulus interval (ISI) of 3000 ms. In the 1-back task (for the younger children), the participants were required to report whether the location of the stimulus was identical to that of the previous one (black arrows). In the 2-back task (for the older children), the participants were required to decide whether the current stimulus appeared in the same location as the one that had been presented two stimuli previously (gray arrows). Y and N show that the correct response is “yes” and “no,” respectively. (B) Auditory n-back task. Temporal sequence and task requirements were the same as for the visual n-back task, but the stimuli was a Japanese single letter sound presented through a headphone. (C) Go/no-go task. Green or blue (gray or white, respectively, in this figure) squares were sequentially presented at the center of the screen with an ISI of 1000 ms. The participants were required to press a button when the color was blue and withhold the response if the target was green.

stimulus was the same as the immediately preceding one (1-back task; see black arrows in Figure 1B) or the one that had been presented two stimuli previously (2-back task; see gray arrows in Figure 1B).

In the go/no-go task (Figure 1C), participants fixated on the central cross, and blue or green squares ( $\sim 4^\circ \times 4^\circ$ ) were sequentially presented at the center of the display, over the fixation cross. Stimuli were presented for 0.1 s, with an ISI of 1 s. Participants were instructed to push the response button as fast as possible when the blue stimulus was presented (go trial), but not push the button when the stimulus was green (no-go trial). In the go trials, the correct trials were defined as those where the participants pressed the button within 1.1 s or 0.6 s after the onset of the blue stimulus for younger or older participants, respectively. In the no-go trials, the trials were correct when the participants did not press the button before the next stimulus appeared.

Reaction time for this go/no-go task was calculated only for the correct go trials. The go trials were more than three times as frequent as the no-go trials, so that the load of RI would be relatively high.

## Procedure

Oral instructions were given to the participants before each experimental session, using a large screen and video projector. Participants then practiced each task. Once they appeared to understand the tasks and were able to perform them adequately ( $\sim 70\%$  correct response), the experimental session began. Each participant performed 20 trials for each task (i.e., 60 trials in total). The order of sessions was balanced across participants for each group separately.

Table 1. Descriptive statistics and reliabilities

	Visual WM		Auditory WM		Go trials		No-go trials	
	Younger	Older	Younger	Older	Younger	Older	Younger	Older
% correct								
Mean	85	86	86	86	97	94	86	77
SD	12	14	13	12	7	12	16	21
Reliability*	0.74	0.79	0.72	0.80	0.92	0.88	0.79	0.70
Reaction time								
Mean	1076	556	1346	797	570	328	–	–
SD	296	156	313	181	115	52	–	–
Reliability*	0.82	0.86	0.81	0.86	0.90	0.93	–	–

Note: \*Reliability indicates Guttman split-half coefficients.

## Data Analysis

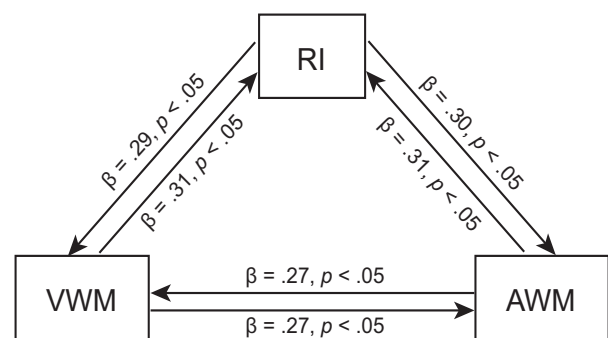
To compare the reliability of the results from each task in each age group, we calculated Guttman split-half coefficients. We also tested the variance between two age groups using the *F*-test. We then examined the correlation between different modalities of WM, and between WM and RI. In this analysis, correct performance rate, reaction time, and age in months were used as variables. Besides the Pearson's simple correlations, we also calculated the partial correlation coefficient in order to factor out the effect of age. To further examine the relationship among the three tasks, we illustrated path diagrams based on the replication of multiple regression analyses, where performance on one task was used as the dependent variable, and performance on the other two tasks, and age (in months), were used as the predictor variables. All the analyses were performed using SPSS 13.0 for Windows (SPSS, Chicago, IL, USA).

## Results

### Descriptive Statistics

A total of 59 5- and 6-year-olds and 92 8- and 9-year-olds performed more than 60% of the three tasks correctly. The descriptive statistics are summarized in Table 1. Both groups showed more than 85% mean correct responses in both visuospatial and auditory WM tasks. In the go/no-go task, both groups showed high performance (> 90%) in go trials, whereas percentage correct was relatively lower in the no-go trials (86% and 77% for younger and older children, respectively). The variance was not significantly different between two age groups for the three tasks ( $F = 0.68$  for visuospatial WM;  $F = 1.18$  for auditory WM; and  $F = 0.68$  for RI;  $p > .05$  for all tasks). The reliability was relatively high (> 0.7) for both percentage correct and reaction time, and there was no clear difference between the two age groups on any measure.

### A. Younger children



### B. Older children

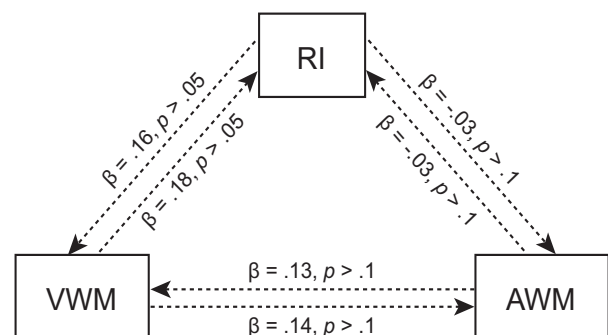


Figure 2. Diagrams show the relationship among three tasks for younger (A) and older age groups (B), based on multiple regression analyses. The standardized partial regression coefficients ( $\beta$ ) and probabilities ( $p$ ) are shown for each pair of structures. Note that the effect of age was also taken into consideration in the regression model, although it is not shown for simplification. VWM, visuospatial working memory; AWM, auditory working memory; RI, response inhibition.

Table 2. Correlation matrices for percentage of correct response

	Age	VWM	AWM	GNG	G	NG
Younger group (5- and 6-year-olds)						
Age	–					
VWM	.26*	–	.38**	.33*	–.04	.40**
AWM	.20	.41**	–	.42**	.17	.41**
GNG	.09	.34**	.43**	–	.62**	.89**
G only	.21	.02	.20	.62**	–	.21
NG only	–.02	.38**	.40**	.88**	.20	–
Older group (8- and 9-year-olds)						
Age	–					
VWM	.27**	–	.13	.10	–.03	.17
AWM	.17	.17	–	.05	.07	–.01
GNG	.17	.14	.08	–	.72**	.55**
G only	.20	.03	.10	.72**	–	–.19
NG only	.00	.17	–.01	.54**	–.19	–

Note: Numbers below the diagonal show Pearson's correlation coefficients, and numbers above the diagonal show standardized partial correlation coefficients (controlled for age). G and NG indicate the results of go and no-go trials of the go/no-go task, respectively.

\* $p < .05$ , \*\* $p < .01$ .

Table 3. Correlation matrices for reaction time

	Age	VWM	AWM	GNG
Younger group (5- and 6-year-olds)				
Age	–			
VWM	–.10	–	.54**	.39**
AWM	–.06	.53**	–	.18
GNG	–.19	.40**	.16	–
Older group (8- and 9-year-olds)				
Age	–			
VWM	–.21*	–	.16	.19
AWM	.14	.13	–	.20
GNG	–.07	.20	.18	–

Note: The format and abbreviations are the same as those used in Table 2. Note that reaction time in go/no-go task was calculated from go trials only.

## Correlations Among Three Tasks

To examine the relationship between each task, we calculated simple correlation coefficients for percentage correct and reaction time separately. This is shown in the area below the diagonal in Tables 2 and 3. In the younger group, all three combinations of the three tasks for percentage correct were significantly correlated at the .01 level, and, when trials of the go/no-go task were divided into go and no-go trials, performance in no-go trials, but not in go trials, was significantly correlated with the other tasks (Table 2). There was a significant correlation in reaction time both between visuospatial and auditory WM tasks, and between visuospatial WM and go/no-go tasks in the younger group (Table 3). In the older group, there were no significant correlations between all three combinations for percentage correct (Table 2) or reaction time (Table 3).

It was possible, however, that these correlations could only reflect the effects of age, rather than the correlation between task performances. To address this point, partial correlation coefficients were calculated with age in months factored out (Tables 2 and 3, above the diagonal). As shown in Tables 2 and 3, however, correlations between each pair of tasks in the younger group, but not in the older group, remained significant in this analysis.

Thus, the correlation analysis showed that correlations between each combination of three tasks were significant in the younger group, but not in the older group. To examine this point further, we applied multiple regression analyses, where performance on one task was used as the dependent variable, and performance on the other two tasks and age (in months) were used as the predictor variables. Specifically, we used the following regression model:

$$TASK_i = \alpha + \beta_1(TASK_j) + \beta_2(TASK_k) + \beta_3(Age)$$



where  $TASK_i$ ,  $TASK_j$ , and  $TASK_k$  are percentage correct in given tasks  $i$ ,  $j$ , and  $k$ , respectively,  $\alpha$  is the constant term, and  $\beta_1$ – $\beta_3$  are standardized partial regression coefficients. Because there were three tasks, this analysis was replicated three times, each of which used performance on a different task as the dependent variable. The results are summarized in Figure 2. In the younger group, performance in every task was significantly predicted by every other task. In the older group, however, each of three tasks was unrelated to the others and formed three independent structures.

## Discussion

We examined the behavioral performance of 59 5- and 6-year-olds and 92 8- and 9-year-olds during behavioral tasks assessing LPFC functions, namely visuospatial and auditory n-back WM tasks, and a go/no-go RI task. In younger participants, there was a significant correlation not only between performance of visuospatial and auditory n-back tasks but also between n-back tasks and go/no-go task, especially in the no-go trials. In contrast, the older participants did not show any significant correlations between any pairs of tasks. Furthermore, multiple regression analyses revealed that each of three components of LPFC functions (visuospatial and auditory WMs, and RI) were significantly related to each other in the younger children, while they were independent in the older children. These findings could not be ascribed to the difference of either sample size or to the variation of age range between two groups because of the following reasons: (1) the participant group with the larger sample size (i.e., the older group) showed weaker correlations between tasks, despite the fact that larger sample size tends to be associated with stronger statistical power; (2) the variances of task performance were not significantly different between age groups for all three measurements; and (3) the results of correlation analyses remained even after the effect of age was partialled out. Thus, these results suggest that, in the LPFC, different modalities of WM and RI share some common system during early childhood (5- and 6-year-olds), whereas, in 8- and 9-year-olds, different modalities of WM and RI recruit different systems.

The findings for independent structures in older children, particularly regarding different WM systems, are consistent with the well-known model of WM developed by Alan Baddeley (for a review, see Baddeley, 1986). This model assumes two independent subsystems, a “visuospatial sketch pad” and a “phonological loop”, which are specialized for processing visuospatial information and speech-based information, respectively. Consistent with this model, Shah and Miyake (1996) suggested domain-specific fractionated systems for spatial and oral executive analysis. The present results imply that 8- and 9-year-old children already have such fractionated systems for WM. The present results also imply that the RI system is separate

from the WM systems in 8- and 9-year-olds. Taken together with the findings of significant correlations between different modalities of WM, and between WM and RI, in 5- and 6-year-olds, we suggest that functional neural systems, especially those in the LPFC for visuospatial WM, auditory WM, and RI, become fractionated during childhood, thereby enabling more efficient processing of these critical cognitive functions.

That there is “developmental fractionation” of the LPFC during childhood is consistent with evidence from several lines of study. During young childhood, the LPFC shows considerable changes in morphology (Giedd et al., 1999; Huttenlocher, 1979). Such changes should provide the structural basis of functional development, including developmental fractionation. In addition, it has been reported that the LPFC shows age-related changes in neural activity during childhood (Kwon et al., 2002; Tamm et al., 2002). Interestingly, this change in LPFC activity includes both an increase in activity in focal, restricted brain-regions, and a decrease in activity when a broader region is included in analysis (Kwon et al., 2002; Tamm et al., 2002). Based on these findings, it has been proposed that, throughout childhood development, neural systems in the LPFC become finely tuned to more specific regions, which play a major role in some specific functions (Casey, Galvan, & Hare, 2005; Tamm et al., 2002). This fine-tuning process could be the neural basis of the developmental fractionation of the LPFC functions.

This study suffers from some limitations, which stem from differences in the tasks used for each group. Because many older children responded correctly to 100% of the 1-back tasks in the preliminary experiment (i.e., ceiling effect), we employed visuospatial and auditory 2-back tasks for the older group. The 2-back tasks have been commonly used as higher load version of the 1-back task in a number of previous studies, which have shown that these two tasks activate the same LPFC region, while the level of activation changes (e.g., Cohen et al., 1997). Although we acknowledge that the 2-back task adds some other features to the 1-back task, the 2-back task still includes the basic characteristics of WM (i.e., short-term retention and manipulation of information) that the 1-back task includes. Therefore, if the processing for each WM were not independent, there would be some correlations in these tasks, though this was not the case with our sample of older children. For the same reason given for the n-back tasks (i.e., ceiling effect), we changed the time limit for the response of go/no-go task. We acknowledge that this could have caused the difference in the strategy used by each group of children, which could have produced the difference in correlation, although the experimenters instructed both groups of children similarly to respond as fast as possible when the “go” stimuli appeared. Ideally, this issue should be addressed further using the same measures.

We should also keep in mind that the presence or absence of correlations in behavioral performance does not need to be associated directly with fractionation in neural

systems. For example, an alternative explanation is that developing executive ability causes the older children to adopt a more diverse range of cognitive strategies. This limitation cannot be overcome in the behavioral experiment only. Nevertheless, developmental change in cognitive ability, including application of different strategies, should be a result of developmental change in neural systems, and our results imply that fractionation is an important feature in such functional neural development. Another possible explanation of the present findings is that the significant correlation in the younger participants might stem from factors unrelated to neural function, such as the degree of participants' comfort with the experimental setup or the environment. However, this possibility is unlikely, because the present experiment was performed in the rooms that were used for everyday classes, and the participants practiced sufficiently with the equipment used for the experiment. Thus, we believe that the present study should contribute substantially to the understanding of cognitive development, although ideally further studies, including those using neuropsychological and neuroimaging techniques, are needed to clarify this issue (Casey, 2001).

In conclusion, the present study suggests that the neural systems underlying visuospatial WM, auditory WM, and RI become fractionated during childhood between preschool age and school age. Such fractionation will enable children to exhibit more complex cognitive abilities. The so-called differentiation theory (or Spearman's law of diminishing returns) states that the correlation between IQ tests decreases as intellectual efficiency increases (Spearman, 1927), and therefore the fractionation of neural systems may be a general principle of brain function to enable more efficient processing. In future studies, the convergence of evidence from different experimental approaches, including psychology and neuroscience should further develop our knowledge.

## Acknowledgments

The authors thank G. Hirano and T. Tanase for their technical and administrative assistance, and D. Tanaka for computer programming. The authors also gratefully acknowledge the cooperation of the children and staff of Shiratori Kindergarten, the Nursery School of Kannami Sakura, and Yamanote-Minami Elementary School. This work was supported by RISTEX, JST, Japan, and in part by a Research Fellowship for Young Scientists (15009927) from JSPS, Japan to S.T., and by a Grant-in-Aid for Exploratory Research (15650124) from MEXT, Japan to T.S.

## References

- Baddeley, A. (1986). *Working memory*. Oxford: Oxford University Press.
- Baddeley, A., & Della Sala, S. (1998). Working memory and executive control. In A.C. Roberts, T.W. Robbins, & L. Weiskrantz (Eds.), *The prefrontal cortex: Executive and cognitive functions* (pp. 9–21). Oxford: Oxford University Press.
- Barkley, R.A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, 121, 65–94.
- Bushara, K.O., Weeks, R.A., Ishii, K., Catalan, M.-J., Tian, B., Rauschecker, J.P. et al. (1999). Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans. *Nature Neuroscience*, 2, 759–766.
- Carlson, S., Martinkauppi, S., Rämä, P., Salli, E., Korvenoja, S., & Aronen, H.J. (1998). Distribution of cortical activation during visuospatial n-back tasks as revealed by functional magnetic resonance imaging. *Cerebral Cortex*, 8, 743–752.
- Casey, B.J. (2001). Bridging the gap between cognition and developmental neuroscience: The example of number representation. In C.A. Nelson & M. Luciana (Eds.), *Handbook of developmental cognitive neuroscience* (pp. 415–432). Cambridge: MIT Press.
- Casey, B.J., Galvan, A., & Hare, T.A. (2005). Changes in cerebral functional organization during cognitive development. *Current Opinion in Neurobiology*, 15, 239–244.
- Casey, B.J., Trainor, R.J., Orendi, J.L., Schubert, A.B., Nystrom, L.E., Giedd, J.N. et al. (1997). A developmental functional MRI study of prefrontal activation during performance of a go/no-go task. *Journal of Cognitive Neuroscience*, 9, 835–847.
- Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J. et al. (1997). Temporal dynamics of brain activation during a working memory task. *Nature*, 386, 604–607.
- Diamond, A. (2002). Normal development of prefrontal cortex from birth to young adulthood: Cognitive functions, anatomy, and biochemistry. In D.T. Stuss & R.T. Knight (Eds.), *Principles of frontal lobe function* (pp. 466–503). Oxford: Oxford University Press.
- Freedman, M., & Oscar-Berman, M. (1986). Bilateral frontal lobe disease and selective delayed response deficits in humans. *Behavioral Neuroscience*, 100, 337–342.
- Funahashi, S., Bruce, C.J., & Goldman-Rakic, P.S. (1993). Dorsolateral prefrontal lesions and oculomotor delayed-response performance: Evidence for mnemonic scotomas. *Journal of Neuroscience*, 13, 1479–1497.
- Fuster, J.M. (1997). *The prefrontal cortex*. Philadelphia: Lippincott-Raven.
- Gaillard, W.D., Hertz-Pannier, L., Mott, S.H., Barnett, A.S., LeBihan, D., & Theodore, W.H. (2000). Functional anatomy of cognitive development: fMRI of verbal fluency in children and adults. *Neurology*, 54, 180–185.
- Gathercole, S.E., Pickering, S.J., Ambridge, B., & Wearing, H. (2004). The structure of working memory from 4 to 15 years of age. *Developmental Psychology*, 40, 177–190.
- Giedd, J.N., Blumenthal, J., Jeffries, N.O., Castellanos, F.X., Liu, H., Zijdenbos, A. et al. (1999). Brain development during childhood and adolescence: A longitudinal MRI study. *Nature Neuroscience*, 2, 861–863.
- Goldman, P.S., Rosvold, E., & Mishkin, M. (1970). Selective sparing of function following prefrontal lobectomy in infant monkeys. *Experimental Neurology*, 29, 221–226.
- Huttenlocher, P.R. (1979). Synaptic density in human frontal cortex – Developmental changes and effects of aging. *Brain Research*, 163, 195–205.

- Huttenlocher, P.R. (1990). Morphometric study of human cerebral cortex development. *Neuropsychologia*, 28, 517–527.
- Jonides, J., Smith, E.E., Koeppe, R.A., Awh, E., Minoshima, S., & Mintun, M.A. (1993). Spatial working memory in humans as revealed by PET. *Nature*, 363, 623–625.
- Kwon, H., Reiss, A.L., & Menon, V. (2002). Neural basis of protracted developmental changes in visuo-spatial working memory. *Proceedings of the National Academy of Sciences USA*, 99, 13336–13341.
- Liddle, P.F., Kiehl, K.A., & Smith, A.M. (2001). Event-related fMRI study of response inhibition. *Human Brain Mapping*, 12, 100–109.
- Logie, R.H., & Pearson, D.G. (1997). The inner eye and the inner scribe of visuo-spatial working memory: Evidence from developmental fractionation. *European Journal of Cognitive Psychology*, 9, 241–257.
- Luciana, M., & Nelson, C.A. (1998). The functional emergence of prefrontally-guided working memory systems in 4- to 8-year-old children. *Neuropsychologia*, 36, 273–293.
- McCarthy, G., Blamire, A.M., Puce, A., Nobre, A.C., Bloch, G., Hyder, F. et al. (1994). Functional magnetic resonance imaging of human prefrontal cortex during a spatial working memory task. *Proceedings of the National Academy of Sciences USA*, 91, 8690–8694.
- Mrzljak, L., Uylings, H.B.M., van Eden, C.G., & Judas, M. (1990). Neuronal development in human prefrontal cortex in prenatal and postnatal states. In H.B.M. Uylings, C.G. van Eden, J.P.C. de Bruin, M.A. Corner, & M.G.P. Feenstra, (Eds.), *The prefrontal cortex: Its structure, function, and pathology*. *Progress in Brain Research* (vol. 85, pp. 185–222). Amsterdam: Elsevier.
- Pickering, S.J., Gathercole, S.E., Hall, M., & Lloyd, S.A. (2001). Development of memory for pattern and path: Further evidence for the fractionation of visuo-spatial memory. *Quarterly Journal of Experimental Psychology*, 54A, 397–420.
- Sawaguchi, T., & Iba, M. (2001). Prefrontal cortical representation of visuospatial working memory in monkeys examined by local inactivation with muscimol. *Journal of Neurophysiology*, 86, 2041–2053.
- Shah, P., & Miyake, A. (1996). The separability of working memory resources for spatial thinking and language processing: An individual differences approach. *Journal of Experimental Psychology: General*, 125, 4–27.
- Sowell, E.R., Thompson, P.M., Holmes, C.J., Batth, R., Jernigan, T.L., & Toga, A.W. (1999). Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping. *Neuroimage*, 9, 587–597.
- Spearman, C.E. (1927). *The abilities of man*. London: Macmillan.
- Steenari, M.-R., Vuontela, V., Paavonen, E.J., Carlson, S., Fjällberg, M., & Aronen, E.T. (2003). Working memory and sleep in 6- to 13-year-old schoolchildren. *Journal of American Academy of Child and Adolescent Psychiatry*, 42, 85–92.
- Sweeney, J.A., Rosano, C., Berman, R.A., & Luna, B. (2001). Inhibitory control of attention declines more than working memory during normal aging. *Neurobiology of Aging*, 22, 39–47.
- Tamm, L., Menon, V., & Reiss, A.L. (2002). Maturation of brain function associated with response inhibition. *Journal of American Academy of Child and Adolescent Psychiatry*, 41, 1231–1238.
- Tsujimoto, S., & Sawaguchi, T. (2004). Properties of delay-period neuronal activity in the primate prefrontal cortex during memory- and sensory-guided saccade tasks. *European Journal of Neuroscience*, 19, 447–457.
- Tsujimoto, S., Yamamoto, T., Kawaguchi, H., Koizumi, H., & Sawaguchi, T. (2004). Prefrontal cortical activation associated with working memory in adults and preschool children: An event-related optical topography study. *Cerebral Cortex*, 14, 703–712.
- Tucker, T.J., & Kling, A. (1967). Differential effects of early and late lesions of frontal granular cortex in the monkey. *Brain Research*, 5, 377–389.
- Vuontela, V., Steenari, M.-R., Carlson, S., Koivisto, J., Fjällberg, M., & Aronen, E.T. (2003). Audiospatial and visuospatial working memory in 6–13 year old school children. *Learning and Memory*, 10, 74–81.

Received October 24, 2005

Revision received February 6, 2006

Accepted February 6, 2006

Satoshi Tsujimoto

Laboratory of Systems Neuroscience  
National Institute of Mental Health  
Bldg. 49, Room B1EE17  
49 Convent Drive, MSC 4401  
Bethesda, MD 20892–4401  
USA  
Tel. +1 301 402-5482  
Fax +1 301 402-5441  
E-mail tsujimotos@mail.nih.gov