



The neural substrates associated with attentional resources and difficulty of concurrent processing of the two verbal tasks

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ABSTRACT

The kana pick-out test has been widely used in Japan to evaluate the ability to divide attention in both adult and pediatric patients. However, the neural substrates underlying the ability to divide attention using the kana pick-out test, which requires participants to pick out individual letters (vowels) in a story while also reading for comprehension, thus requiring simultaneous allocation of attention to both activities, are still unclear. Moreover, outside of the clinical area, neuroimaging studies focused on the mechanisms of divided attention during complex story comprehension are rare. Thus, the purpose of the present study, to clarify the neural substrates of kana pick-out test, improves our current understanding of the basic neural mechanisms of dual task performance in verbal memory function. We compared patterns of activation in the brain obtained during performance of the individual tasks of vowel identification and story comprehension, to levels of activation when participants performed the two tasks simultaneously during the kana pick-out test. We found that activations of the left dorsal inferior frontal gyrus and superior parietal lobule increase in functional connectivity to a greater extent during the dual task condition compared to the two single task conditions. In contrast, activations of the left fusiform gyrus and middle temporal gyrus, which are significantly involved in picking out letters and complex sentences during story comprehension, respectively, were reduced in the dual task condition compared to during the two single task conditions. These results suggest that increased activations of the dorsal inferior frontal gyrus and superior parietal lobule during dual task performance may be associated with the capacity for attentional resources, and reduced activations of the left fusiform gyrus and middle temporal gyrus may reflect the difficulty of concurrent processing of the two tasks. In addition, the increase in synchronization between the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition may induce effective communication between these brain regions and contribute to more attentional processing than in the single task condition, due to greater and more complex demands on voluntary attentional resources.

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1. Introduction

People are often required to perform multiple tasks simultaneously, such as conversing while driving and writing down dictated information (Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999). The ability to divide one's attention is necessary to successfully perform multiple tasks in parallel. This ability to divide attention for multitasking decreases with age and is impaired in patients suffering from disorders such as Alzheimer's disease, Korsakoff's disease, Parkinson's disease and chronic fatigue syndrome (Bokura, Yamaguchi, & Kobayashi, 2005; Lezak,

1995; Ross, Fantie, Straus, & Grafman, 2001). Thus, a divided attention task, the kana pick-out task (KPT) was designed to clinically evaluate patients' higher cognitive abilities, specifically, the ability to perform two tasks simultaneously.

The KPT demands performance of parallel processing during a reading task. Participants must pick out a subset of letters contained within a story while reading the story for comprehension. The task requires appropriate allocation of attentional resources to the two activities (Yamamoto, 1992). It has been widely used to evaluate the extent of dementia in older participants, and is an established method for screening persons with signs of mild dementia (Kaneko, 1996). The KPT has also been used for detecting cognitive dysfunction in patients with Parkinson's disease (Bokura et al., 2005). In addition, its utility has been demonstrated in pediatric disorders; deficits in the ability to divide attention in the KPT have been associated with childhood

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chronic fatigue syndrome (CCFS), a disorder characterized by profound disabling fatigue that persists for at least six months (Fukuda et al., 1994; Tomoda et al., 2007). It can also assess the development of the ability to divide attention in healthy children and adolescents (Mizuno et al., 2011a). In addition, the ability to divide attention across tasks in the KPT is affected by fatigue (Mizuno, Tanaka, Fukuda, Imai-Matsumura, & Watanabe, 2011b) and motivation for learning (Mizuno, Tanaka, Fukuda, Imai-Matsumura, & Watanabe, 2011c). Thus, the KPT has been widely used in Japan to evaluate the ability to divide attention in adult and pediatric patients and in healthy children and adolescents. However, the neural substrates underlying the ability to divide attention across tasks in the KPT are still unclear. In addition, neuroimaging studies focused on mechanisms of divided attention during a complex story comprehension task are rare outside of the clinical arena. Therefore, the investigation of the neural substrates of KPT improves our current understanding of the basic neural mechanisms of dual task performance in verbal memory function.

For the KPT letter task, participants are required to pick out vowel symbols included in Japanese kana (syllabogram) words. Thuy et al. (2004) demonstrated that perception of the Japanese kana word is processed by the lateral occipital complex, in the visual cortex and fusiform gyrus. During detection of the target letters, these brain regions were more active than when only reading the word (Murray & He, 2006) and are thus thought to be associated with the process of picking out letters in the KPT.

A number of neuroimaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have demonstrated that sentence comprehension is processed by the left inferior frontal gyrus along Broca's area [Brodmann's area (BA) 44/45, Caplan, Alpert, & Waters, 1998; Dapretto & Bookheimer, 1999; Ikuta et al., 2006]. The left inferior frontal gyrus has been implicated in syntactic processing (Bradley, Garrett, & Zurif, 1980; Caramazza & Zurif, 1976; Grodzinsky, 1984, 2000), but is also thought to play a role in verbal working memory for sentence comprehension (Caplan, Alpert, & Waters, 1999; Just & Carpenter, 1992; Martin, 2003). Several neuroimaging studies using a sentence-processing task have implicated the left inferior frontal gyrus, particularly in the comprehension of complex structures (Caplan et al., 1998; Caplan et al., 1999; Dapretto & Bookheimer, 1999; Just, Carpenter, Keller, Eddy, & Thulborn, 1996; Stromswold, Caplan, Alpert, & Rauch, 1996). Comprehension of complex sentences appears to necessitate that verbal information be stored in something like Baddeley's phonological loop (Baddeley, 1986; Baddeley & Hitch, 1974). Previous studies of verbal working memory have regularly implicated the inferior frontal gyrus, premotor area, and supplementary motor area in the phonological loop (Smith, Jonides, Marshuetz, & Koeppe, 1998; Zatorre, Evans, Meyer, & Gjedde, 1992). In addition, the left parietal lobule mediates the pure storage component of verbal working memory (Paulesu, Frith, & Frackowiak, 1993). The left middle temporal gyrus also relates to processing the complex sentence structure necessary for story comprehension (Grossman et al., 2002; Stowe et al., 1998). Thus, these brain regions are associated with the process of complex sentence comprehension.

The results from neuroimaging studies of dual task performance to date will be considered in relation to two potential mechanisms of dual task performance (Klingberg, 1998): (i) that there is a specific region of the brain activated during dual task performance; and (ii) greater activations of the stimulated brain regions will occur during dual task overlap, compared to activation during single task performance. In a neuroimaging study of the concurrent performance of two tasks with different input modalities (a word classification task and an object rotation task),

D'Esposito et al. (1995) reported significant activation of the dorsolateral prefrontal cortex during dual task performance but no activation of the dorsolateral prefrontal cortex during single task performance. In contrast, recent studies using modality independent dual tasks revealed that the no novel regions were engaged under the dual task condition relative to the single task condition and that there was increased activity in one or more regions involved in single task condition (Dux, Ivanoff, Asplund, & Marois, 2006; Dux et al., 2009; Sigman & Dehaene, 2008; Tombu et al., 2011). Likewise, when neuroimaging was used to examine the concurrent performance of two tasks with the same input modalities, increased activation of the stimulated brain regions during the dual task performance overlapped with stimulated brain regions during performance of each single task (Hahn et al., 2008; Nebel et al., 2005). In these studies, the lateral prefrontal cortex was activated even during the single task condition. These results suggest that increases in activations of the brain regions involved in single tasks without relation to input modalities during dual task performance are associated with more attentional processing when the lateral prefrontal cortex is already activated during single task performance. The lateral prefrontal cortex is associated with processing for sentence comprehension (Prat, Keller, & Just, 2007), which is one of the single tasks of the KPT. Therefore, we hypothesized that the brain regions activated during dual and single task performance would overlap. Moreover, the level of activation of brain regions stimulated during dual task performance is expected to be greater than during performance of each single task.

Although previous fMRI studies of dual tasks have focused on the intensity of activation of brain regions, a recent study focused on the functional connectivity between brain regions related to the dual task processing (Buchweitz, Keller, Meyler, & Just, in press). Functional connectivity analysis measures the degree of synchronization among activated brain regions. Thus, this analysis can evaluate the differences in internode synchronization of brain activation during dual task as opposed to single task performance. An increase in synchronization may indicate an attempt to establish more effective communication among the brain regions of the task-dependent network and hence attain a high level of performance in the dual task (Buchweitz et al., in press).

A greater understanding of the neural substrates of the KPT might help the evaluation of impairments of neural processing during divided attention with age, and in patients suffering from dementia-related disorders. In addition, studies identifying the neural substrates of KPT have improved our current understanding of the basic neural mechanisms of dual task performance in verbal memory function (Buchweitz et al., in press; Just et al., 2001; Just, Keller, & Cynkar, 2008; Newman, Keller, & Just, 2007). Therefore, in the present study, we aimed to define the neural substrates associated with the KPT by using fMRI to localize the brain regions activated and evaluate the functional connectivity among these brain regions during dual and single task performance.

2. Materials and methods

2.1. Participants

A total of 19 healthy volunteers participated in the present study, comprising 11 women and 8 men with an average age of 22.8 ± 3.4 years (mean \pm SD). Participants had normal or corrected-to-normal visual acuity, no history of medical illness, and were right-handed according to the Edinburgh handedness inventory (Oldfield, 1971). The protocol was approved by the Ethics Committee of the National Institute for Physiological Sciences, and all participants gave written informed consent for participation in the study. The experiments were undertaken

in compliance with national legislation and the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association (Declaration of Helsinki).

2.2. *Experimental paradigms for functional imaging*

The fMRI experimental design is shown in Fig. 1. The participants performed the modified version of the KPT, which included single and dual task conditions presented on a computer screen for use with fMRI. Single tasks comprised the conditions of picking out vowels (PV) and story comprehension (SC), and the dual task required participants to perform PV and SC tasks concurrently (PV+SC). In addition, to control for the normal activation of brain areas due to visual and motor processing, the participants performed a test under control (CL) conditions.

Hereafter, this part of the KPT is referred to as the PV and/or SC session. In the PV condition, participants judged whether vowels included in the words were presented in the center of the screen. If the target letters were presented in the center of the screen, participants were instructed to press the right button. If the target letters did not appear in the center of the screen, participants were instructed to press the left button.

In the SC condition, participants read silently each presented word as it appeared in sequence on the screen. An example sentence was “Takashi gazed at the blue sea and Mariko gazed at the blue mountain.” The participants pressed the right and left buttons alternately for each word presented.

In the PV + SC condition, the participants were required to simultaneously pick out vowels and understand the story. Thus, when the target letters (vowels) were presented in the center of the screen, the participants pressed the right button. If target letters did not appear in the center of the screen the participants were instructed to press the left button. These judgments about the individual vowels and the direction of the button press were performed while reading the story for comprehension.

In the CL condition, the participants were not required to perform either task and were instructed to simply press the right and left buttons alternately when presented with the word “press” on every trial.

Each condition consisted of 20 trials; 20 word stimuli, displayed for 1 s followed by a blank screen displayed for 1 s, for a total of 40 s per condition for the PV and/or SC session. Before the first word stimulus was presented, the name of the stimulus condition appeared on the screen for 5 s (“PV”, “SC”, “PV + SC” or “CL”) to instruct the participants. The probability of a target letter appearing in the PV and PV+SC conditions was 50%. The sequence of presented words was

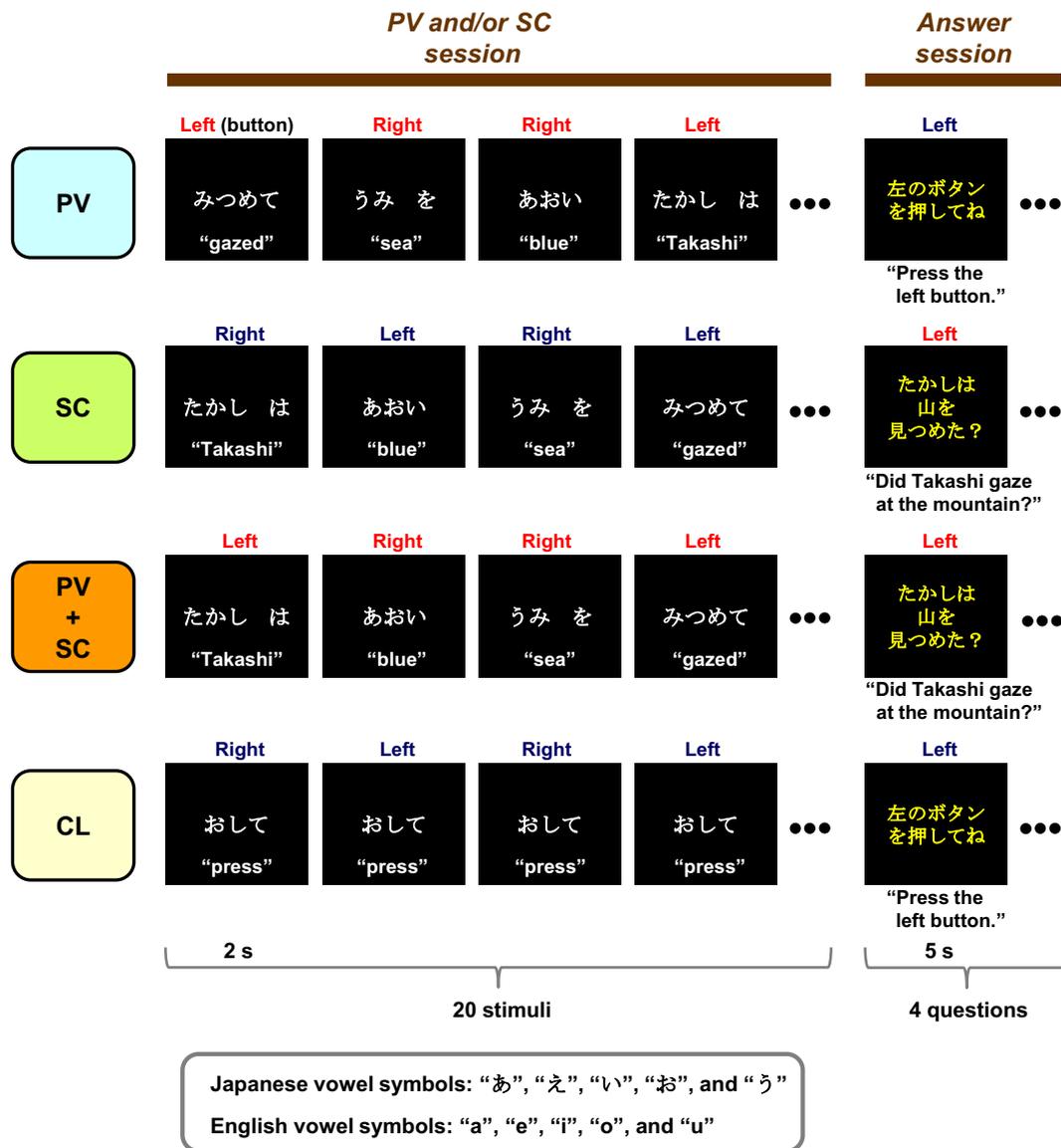


Fig. 1. Time course of stimulus display sequences of the PV and/or SC session and answer session. The PV and/or SC session involved picking out vowels (PV), story comprehension (SC), the concurrent processes of both PV and SC (PV+SC) and control (CL) conditions. During the PV and/or SC session, in the PV condition, participants judged whether a target word included vowels (/a/,/e/,/i/,/o/, and/u/). In the SC condition, the participants read each word presented in sequence on the screen and were later tested for comprehension of the short story. In the PV+SC condition, the participants concurrently performed both picking out vowels and story comprehension. In the CL condition, the participants pressed either the right or left button in alternate trials. The word “press” appeared on the screen for every control trial. After the PV and/or SC session, the participants performed an answer session. In the SC and PV+SC conditions, the participants answered four questions, designed to require “yes” or “no” answers. In the PV and CL conditions, participants did not answer questions and only pressed the indicated right or left button in the answer session. The role of the button press (Left or Right) in each condition is described in the materials and methods section of the text.

pseudorandom in the PV condition, and the presented words were chosen from those used in the SC and PV+SC conditions. In order to control the difficulty of the comprehension of the story between the SC and PV+SC conditions, sentences from the SC condition were replaced with sentences from the PV+SC condition for each participant alternately.

After all conditions, the participants completed an answer session. In the SC and PV+SC conditions, this comprised a series of four “yes” or “no” questions to assess story comprehension. Example questions were “Did Takashi gaze at the mountain?” or “Did Mariko gaze at the mountain?”. Participants were instructed to press the right button if the answer was “yes” and the left button if the answer was “no”.

In the PV and CL conditions, participants were not required to answer questions and were simply directed to press the right or left button (e.g., “Press the left button.”). The questions for each condition consisted of four trials, which each lasted 4 s followed by a blank, which lasted 1 s, for a total of 20 s in the answer session.

The probability of a “yes” question appearing in the SC and PV+SC conditions was 50%. The total time for each condition, including the answer session, was 60 s. Each condition was repeated twice per run, in counter-balanced order and the time interval between conditions was 20 s. The participants were instructed to perform each task as quickly and accurately as possible. The direction of the button press was inverted for half of the participants. Before scanning, participants practiced a series of CL, PV, SC and PV+SC conditions for approximately 15 min, to ensure that all participants understood the task. The visual stimuli and the duration of each stimulus presentation were developed and presented using Presentation software (Neurobehavioral Systems, Albany, CA).

2.3. Functional imaging

All images were obtained using a 3-Tesla MR scanner (Allegra; Siemens, Erlangen, Germany) located at National Institute for Physiological Sciences. For functional imaging, a series of 272 volumes (136 volumes per run) were acquired using T2-weighted, gradient echo, echo planar imaging (EPI) sequences. Each volume consisted of 34 transaxial slices, each having a thickness of 3.0 mm with a 0.5 mm gap between slices to include the entire cerebrum and cerebellum [repetition time (TR), 2500 ms; echo time, 30 ms; flip angle (FA), 75°; field of view (FoV), 19.2 cm; in-plane matrix size, 64 × 64 pixels, voxel dimensions, 3.0 × 3.0 × 3.0 mm]. Oblique scanning was used to exclude the eyeballs from the images. Tight but comfortable foam padding was placed around the participant's head to minimize head movement. To acquire a fine structural whole-brain image, magnetization-prepared rapid-acquisition gradient-echo (MP-RAGE) images were obtained [repetition time (TR), 2500 ms; echo time (TE), 4.38 ms; flip angle=8°; FoV, 230 mm; one slab; number of slices per slab=192; voxel dimensions=0.9 × 0.9 × 1.0 mm].

The first 2 volumes acquired in each MRI run were discarded due to unsteady magnetization, and the remaining 134 volumes per run were used for analyses. Data were analyzed using Statistical Parametric Mapping 5 (The Wellcome Trust Centre for Neuroimaging, London, UK; <http://www.fil.ion.ucl.ac.uk/spm>) implemented in MATLAB 7.7.0 (Mathworks, Natick, MA). Following realignment for motion correction of all EPI images, high-resolution whole-brain T1-weighted image was co-registered with the first volume of EPI images. The whole-head MP-RAGE images were then normalized to the Montréal Neurological Institute (MNI) T1 image template. These parameters were applied to all EPI images. The EPI images were spatially smoothed in 3 dimensions using an 8 mm full-width half-maximum Gaussian kernel.

2.4. Statistical analyses

In the present experimental design, it was not possible to exclude the error trials from the analyses for the SC and PV+SC conditions because these conditions required integrative understanding of sequentially presented words for the story comprehension in contrast to the PV and CL conditions. In each MRI run, as all participants' accuracies for each task condition of the PV and/or SC session were higher than 80%, we did not exclude any data from the analyses.

Statistical analyses were performed at 2 levels. First, individual task-related activation was evaluated. Expected signal changes caused by the tasks were modeled with a delta function convolved with a hemodynamic response function which combines two gamma functions (as described by Friston et al. (1998a), Friston, Josephs, Rees, and Turner, (1998b)) without a temporal derivative for each participant. The data were high-pass filtered with a cut-off period of 160 s to remove low-frequency signal drifts. An autoregressive model was used for whitening the residuals so as to meet the assumptions for application of a general linear model (GLM). The effect of each condition was evaluated with GLM. The weighted sum of the parameters estimated in the individual analyses consisted of “contrast” images. Second, the contrast images corresponding to each condition in each participant were used for group analyses with a random-effects model to obtain population inferences (Friston, Holmes, & Worsley, 1999). The resulting set of voxel values for each comparison constituted a statistical parametric map of t statistics [SPM(t)]. Significant signal changes for each contrast were assessed by means of t statistics on a voxel-by-voxel basis. The threshold for the SPM(t) of

group analyses was set at $p < .005$ at voxel level and $p < .05$ with a correction for multiple comparisons at the cluster level for the entire brain (Friston, Holmes, Poline, Price, & Frith, 1996).

Comparisons of PV, SC, and PV+SC conditions with the CL condition (PV, SC, or PV+SC *minus* CL) were performed in order to obtain the activation pattern of the two types of single task processing and the dual task processing. To specify the brain areas involved in the processing of PV, we used the contrast of (PV *minus* SC) masked by the contrast of (PV *minus* CL). Likewise, to identify the brain areas involved in the processing of SC, we used the contrast of (SC *minus* PV) masked by the contrast of (SC *minus* CL). In addition, to specify the brain areas involved in the processing of PV+SC, we used the contrast of [2 (PV+SC) *minus* (SC plus PV)] and conjunction analysis between contrasts of (PV+SC *minus* PV) and (PV+SC *minus* SC) masked by the contrast of (PV+SC *minus* CL). Anatomic localization of significant voxels within clusters was done using the Wake Forest University (WFU) Pick-Atlas (Maldjian, Laurienti, Kraft, & Burdette, 2003) and a probabilistic cytoarchitectonic map (Eickhoff et al., 2005). The effects of task condition on activation of brain region in single and dual trials were analyzed using one-way repeated-measures analysis of variance (ANOVA). When statistically significant effects were found, intergroup differences between the three conditions (PV *minus* CL, SC *minus* CL, and PV+SC *minus* CL) were evaluated using the paired t -test with Bonferroni correction.

For the functional connectivity analysis, to address anatomical variability and allow for more accurate estimation of interregional coupling, the regions of interest were determined on an individual basis using the normalized and smoothed images that had been low-pass filtered and had the linear trend removed. After each group coordinate was defined using the above statistical threshold ($p < .005$ at the voxel level and $p < .05$ with a correction for multiple comparisons at the cluster level), the nearest local maximum for each participant was determined for each of the group-level coordinates. Each of these participant-specific local maxima was required to be within a 12 mm radius from each group coordinate and to survive a threshold of $p < .005$ or $.05$ at the voxel level. In cases where participant-specific local maxima within a 12 mm radius were not identified, group coordinates were used as the individual coordinate for that participant. Participant-specific time courses of activation were summarized with principal eigenvariate over voxels within a radius of 6 mm around the individually determined coordinates using the volume-of-interest tool in the SPM5. The correlation between the time courses for each pair of functional regions of interest was computed on the images belonging to the PV, SC, and PV+SC conditions in the PV and/or SC session. Therefore, the correlation reflects the relation between the activation in the two brain regions while the participant was performing the task. Fisher's r -to- z transformation was applied to the correlation coefficients for each participant before statistical analysis using a paired t -test.

Behavioral performance was assessed as time to respond (reaction time) and percentage of correct responses (accuracy). The only meaningful analysis in the PV and/or SC session was between the PV and PV+SC conditions, whereas that in the answer session was between the SC and PV+SC conditions. Thus, we analyzed the intergroup differences between the single and dual tasks were evaluated using the paired t -test. All p values were two-tailed, and p values less than .05 were considered statistically significant. Behavioral analyses were performed with SPSS 17.0 software package (SPSS Inc., Chicago, IL).

3. Results

3.1. Behavioral results

The results for task performance are summarized in Fig. 2. In the PV and/or SC session, the reaction time of the PV+SC condition was longer than that of the PV condition ($p < .001$) (Fig. 2A). The accuracies of the PV and PV+SC conditions in this session were similar ($p = .559$) (Fig. 2B). In the answer session, although the reaction time of the PV+SC condition was also longer than that of the SC condition ($p = .024$) (Fig. 2C), the accuracies of the SC and PV+SC conditions were similar ($p = .142$) (Fig. 2D).

3.2. Imaging results

Imaging results for each condition in the PV and/or SC session using the contrast of (PV, SC, or PV+SC *minus* CL) are shown in Fig. 3A and Table 1. In the PV condition, activations of the left inferior frontal gyrus, left superior frontal gyrus, left insula, left inferior parietal lobule, bilateral superior parietal lobules, pre-cuneus, left fusiform gyrus, and left middle and inferior occipital gyri were observed. Aside from the left inferior occipital gyrus, these brain regions were also activated in the SC condition.

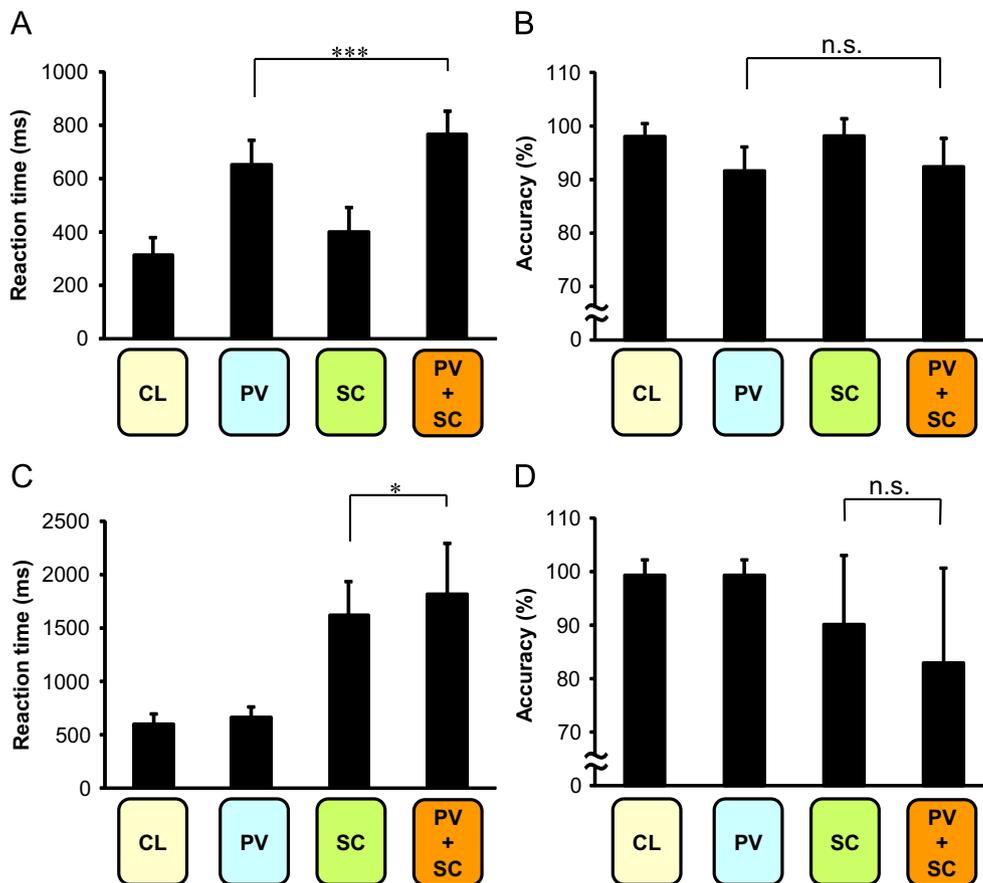


Fig. 2. Reaction time and accuracy. (A) Reaction time and (B) accuracy of the control (CL), picking out vowels (PV), story comprehension (SC), and concurrent processes of both PV and SC (PV+SC) conditions in the PV and/or SC session. (C) Reaction time and (D) accuracy of the CL, PV, SC, and PV+SC conditions in the answer session. n.s., not significant, * $p < .05$, *** $p < .001$ (two-tailed paired t -test). Values are the mean and SD.

Additional activations of the left middle frontal gyrus, right superior frontal gyrus, bilateral supplementary motor areas, right insula and cingulate gyrus, bilateral middle temporal gyri, and cerebellum were observed in the SC condition. Activated brain regions in the PV+SC condition almost overlapped with those in the PV or SC condition. However, additional activated regions were not observed.

Unique or greater activated brain regions during single tasks in the PV and/or SC session were identified using the contrast of (PV *minus* SC) masked by the contrast of (PV *minus* CL) or contrast of (SC *minus* PV) masked by the contrast of (SC *minus* CL). Although the activations of the left fusiform gyrus in the PV and SC condition were commonly observed (Table 1), the activation of the left fusiform gyrus in the PV condition tended to be higher than that in the SC condition (Table 2 and Fig. 4A). In the SC condition, unique activations of the left middle frontal gyrus, supplementary motor area, middle temporal gyrus, and cerebellum, and greater activations of the left inferior frontal gyrus and superior frontal gyrus were observed (Table 2 and Fig. 4B) in comparison with the PV condition. In addition, we found that activation of the left fusiform gyrus in the PV condition tended to be greater than that in the PV+SC condition using the contrast of (PV *minus* PV+SC) masked by the contrast of (PV *minus* CL) (Table 2 and Fig. 4A). The activation of the left middle temporal gyrus in the SC condition was also greater than that in the PV+SC condition using the contrast of (SC *minus* PV+SC) masked by the contrast of (SC *minus* CL) (Table 2 and Fig. 4B). Furthermore, the activated areas of the left fusiform gyrus between the contrasts of (PV *minus* SC) and (PV *minus* PV+SC) masked by the contrast of (PV *minus* CL) were overlapped (Fig. 4A). Likewise, the activated areas of the middle temporal gyrus between the contrasts

of (SC *minus* PV) and (SC *minus* PV+SC) masked by the contrast of (SC *minus* CL) were also overlapped (Fig. 4B). We compared the extent of activations of voxel (left fusiform gyrus, $x = -44$, $y = -68$, $z = -6$; left middle frontal gyrus, $x = -58$, $y = -32$, $z = -2$) in these overlapped regions among PV, SC, and PV+SC conditions. One-way repeated-measures ANOVA in the left fusiform gyrus [$F(2, 36) = 4.07$, $p = .025$] and the middle temporal gyrus [$F(2, 36) = 23.06$, $p < .001$] revealed a significant main effect of task condition. A paired t -test with Bonferroni correction revealed that the activation of the left fusiform gyrus in the PV condition was greater than that in the SC condition ($p = .007$) or PV+SC condition ($p = .049$) (Fig. 4C). The activations of the left fusiform gyrus between the SC and PV+SC conditions were similar ($p > .05$). The activation of the left middle temporal gyrus in the SC condition was higher than in the PV condition ($p < .001$) or PV+SC condition ($p < .001$) (Fig. 4D). The activations of the left middle temporal gyrus between the PV and PV+SC conditions were not different ($p > .05$). Time courses of activations of the left fusiform gyrus and middle temporal gyrus are shown in Figs. 4E and 4F, respectively. During the PV and/or SC session, activations of the left fusiform gyrus and middle temporal gyrus in the PV+SC condition were continuously lower than those in the PV and SC conditions, respectively.

Unique or greater activated brain regions during dual tasks in the PV and/or SC session were identified using the contrast of [(PV+SC) *minus* (SC plus PV)] masked by the contrast of (PV+SC *minus* CL). Although the left dorsal inferior frontal gyrus and superior parietal lobule were commonly activated in the PV, SC and PV+SC conditions (Table 1), the activations of these regions in the PV+SC condition were higher than those in the PV or SC conditions (Fig. 5A, top). No unique activated regions were

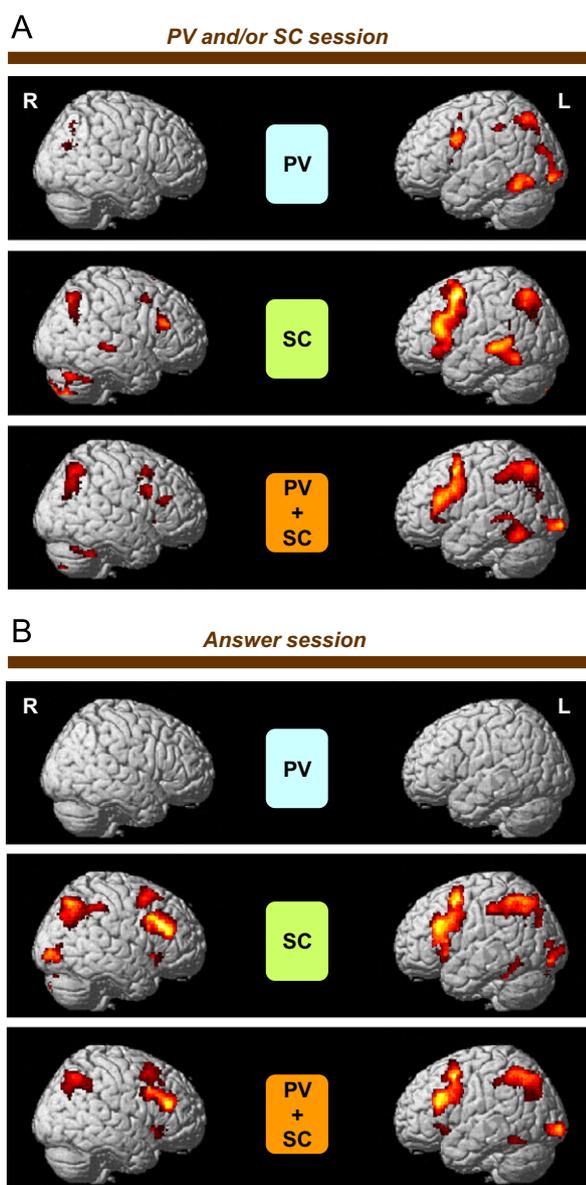


Fig. 3. Activation patterns of PV, SC and PV+SC conditions. Statistical parametric maps of picking out vowels (PV *minus* CL), story comprehension (SC *minus* CL) and concurrent processes both of PV and SC (PV+SC *minus* CL) in (A) the PV and/or SC session and (B) the answer session are shown. The extent threshold was set at $p=.05$ with a correction for multiple comparisons at the cluster level for the entire brain. The height threshold was set at $p=.005$ (uncorrected) at the voxel level. Statistical parametric maps are superimposed on surface-rendered high-resolution MRIs. Right (R) and left (L) sides are indicated.

observed in the PV+SC condition. Conjunction analysis between the contrasts of (PV+SC *minus* PV) and (PV+SC *minus* SC) also revealed that the greater activations of the left dorsal inferior frontal gyrus and left superior parietal lobule in the PV+SC condition compared with the PV or SC condition when no other highly activated regions were observed (Fig. 5A, bottom). We compared the extent of activations of peak voxel (left dorsal inferior frontal gyrus, $x=-46$, $y=4$, $z=32$; left superior parietal lobule, $x=-30$, $y=-58$, $z=48$) among PV, SC, and PV+SC conditions. One-way repeated-measures ANOVA in the left dorsal inferior frontal gyrus [$F(2, 36)=6.13$, $p=.005$] and superior parietal lobule [$F(2, 36)=6.72$, $p=.003$] revealed a significant main effect of task condition. A paired *t*-test with Bonferroni correction revealed that the activation of the left dorsal inferior frontal gyrus in the PV+SC condition were greater than those in

the PV condition ($p=.039$) or SC condition ($p=.009$) (Fig. 5B) and that of superior parietal lobule in the PV+SC condition were also greater than those in the PV condition ($p=.002$) or SC condition ($p=.037$) (Fig. 5C). Time courses of activations of the left dorsal inferior frontal gyrus and superior parietal lobule were shown in Fig. 5D and E, respectively. During the PV and/or SC session, activations of the left dorsal inferior frontal gyrus and superior parietal lobule in the PV+SC condition were continuously higher than those in the PV or SC condition.

In the PV, SC, and PV+SC conditions during the PV and/or SC session, we compared the intensities of synchronizations of the activations among higher activated regions (left dorsal inferior frontal gyrus and superior parietal lobule) and lower activated brain regions (left fusiform gyrus and middle temporal gyrus) under the PV+SC condition relative to the PV or SC condition using the functional connectivity analysis. The synchronization between the left dorsal inferior frontal gyrus and superior parietal lobule in the PV+SC condition was higher and tended to be higher than that in the PV condition ($p=.031$) and SC condition ($p=.089$), respectively (Fig. 6). The extents of synchronizations between other regions in the PV+SC condition were similar to those in the PV or SC condition ($p > .05$).

Imaging results for each condition in the answer session using the contrast of (PV, SC, or PV+SC *minus* CL) are shown in Fig. 3B and Table 3. No activated regions were observed in the PV condition. In the SC condition, the bilateral middle frontal gyri, left inferior and right superior frontal gyri, left supplementary motor area, bilateral inferior and superior parietal lobules, precuneus, left fusiform gyrus, bilateral middle and left inferior occipital gyri, and cerebellum were activated. Aside from the right middle occipital gyrus and cerebellum, these brain regions were also activated in the PV+SC condition. However, unique or more highly activated regions were not observed in the PV+SC condition using the contrast (PV+SC *minus* SC) masked by the contrast of (PV+SC *minus* CL). In the SC condition, no unique or greater activated regions were observed using the contrast (SC *minus* PV+SC) masked by the contrast of (SC *minus* CL).

4. Discussion

In the present study, our principal finding is that activations of the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition were more highly activated than in the two-single task conditions. In contrast, activations of the left fusiform gyrus and middle temporal gyrus, which are primary regions for processing of the picking out vowels and story comprehension tasks, respectively, were lower in the dual task condition than in the two single task conditions. In addition, we observed higher synchronization between the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition than in the two single task conditions.

Perception of Japanese kana words in the PV condition has previously been associated with activation of the lateral occipital complex, which includes the visual cortex and the fusiform gyrus (Murray & He, 2006; Thuy et al., 2004). In addition, sentence comprehension in the SC condition has been associated with activation of the left inferior frontal gyrus along Broca's area (Caplan et al., 1998; Dapretto & Bookheimer, 1999; Ikuta et al., 2006), the supplementary motor area as the phonological loop (Smith et al., 1998; Zatorre et al., 1992), and the left posterior parietal lobule, which mediates the pure storage component of verbal working memory (Paulesu et al., 1993). Furthermore, increased activation of the left middle temporal gyrus, which relates to processing the complex sentence structure necessary

Table 1
Activated brain regions associated with picking out vowels (PV), story comprehension (SC) and the concurrent processes of PV and SC (PV+SC) during the PV and/or SC session.

Brain region	Side	BA	PV				SC				PV+SC			
			MNI coordinates		Z value	MNI coordinates		Z value	MNI coordinates		Z value			
Inferior frontal gyrus	L	44/45	-40	12	10	3.29	-44	22	10	4.99	-46	26	14	4.91
	L	9/44	-46	6	30	4.31	-40	6	32	4.95	-46	8	30	5.40
Middle frontal gyrus	L	9	-	-	-	-	-44	26	30	4.35	-54	28	24	3.64
Superior frontal gyrus	L	6	-20	0	56	3.99	-14	18	54	4.26	-22	4	54	4.01
	R	6	-	-	-	-	14	24	44	3.91	-	-	-	-
Supplementary motor area	L	6	-	-	-	-	-4	12	58	4.60	-4	14	54	4.79
	R	6	-	-	-	-	10	16	50	3.90	6	16	52	3.15
Insula	L	13	-40	12	10	3.29	-32	24	4	3.66	-32	22	2	4.25
	R	13	-	-	-	-	32	-2	24	4.15	28	24	20	4.28
Cingulate gyrus	R	24	-	-	-	-	18	2	32	4.76	18	4	34	4.93
Inferior parietal lobule	L	40	-42	-36	44	4.31	-36	-46	42	3.67	-42	-38	42	4.55
Superior parietal lobule	L	7	-30	-60	48	4.78	-34	-60	46	5.30	-30	-60	46	5.47
	R	7	30	-66	46	3.49	34	-66	48	3.98	32	-66	48	4.79
Precuneus	L	7	-24	-74	40	4.25	-26	-72	38	3.58	-24	-72	40	3.92
	R	7	30	-64	38	3.69	30	-64	36	3.80	30	-62	36	4.20
Middle temporal gyrus	L	21	-	-	-	-	-58	-32	-2	4.99	-58	-48	2	3.67
	R	21	-	-	-	-	52	-34	-2	4.05	-	-	-	-
Fusiform gyrus	L	37	-46	-52	-16	4.83	-48	-52	-16	4.29	-46	-54	-18	5.03
Middle occipital gyrus	L	19	-30	-78	20	4.19	-30	-74	20	3.25	-28	-74	24	4.05
Inferior occipital gyrus	L	18	-26	-92	-10	3.90	-	-	-	-	-22	-96	-6	4.36
Cerebellum	L	-	-	-	-	-	-8	-78	-26	4.01	-6	-82	-40	4.53
	R	-	-	-	-	-	12	-86	-42	5.47	8	-84	-40	4.47

L, left; R, right; BA, Brodmann's area; MNI, Montréal Neurological Institute. The extent threshold was set at $p=.05$ with a correction for multiple comparisons at the cluster level for the entire brain. The height threshold was set at $p=.005$ (uncorrected) at voxel level.

Table 2

More highly activated brain regions associated with picking out vowels (PV) and story comprehension (SC) during the PV and/or SC session.

Brain regions	Cluster size	Side	BA	MNI coordinates			Z value
PV minus SC							
Fusiform gyrus	25	L	37	-44	-68	-6	3.05
PV minus PV+SC							
Fusiform gyrus	22	L	37	-44	-64	-10	2.76
SC minus PV							
Inferior frontal gyrus	1044	L	44/45	-40	12	12	4.25
Middle frontal gyrus		L	9	-44	30	36	4.48
Superior frontal gyrus		L	8	-30	20	54	4.48
Supplementary motor area	129	L	6	-4	18	60	3.41
Middle temporal gyrus	627	L	21	-64	-38	-2	4.23
Cerebellum	209	R		22	-76	30	4.64
SC minus PV+SC							
Middle temporal gyrus	185	L	21	-66	-40	4	3.83

L, left; R, right; BA, Brodmann's area; MNI, Montréal Neurological Institute. Results of (PV minus SC) and (PV minus PV+SC) were conducted that the extent threshold was set at more than 10 voxels at the cluster level and the height threshold was set at $p=.005$ (uncorrected) at voxel level. Results of (SC minus PV) and (SC minus PV+SC) were conducted that the extent threshold was set at $p=.05$ with a correction for multiple comparisons at the cluster level and the height threshold was set at $p=.005$ (uncorrected) at voxel level.

for story comprehension (Grossman et al., 2002; Stowe et al., 1998), was also observed in the present study.

Although uniquely activated brain regions were not observed in the dual task (PV+SC) condition, unlike in the two single task conditions, overall activations of the left dorsal inferior frontal gyrus and superior parietal lobule were higher in the dual than in the single task conditions. This finding that dual task performance results in greater activity in regions activated by component tasks, rather than recruitment of novel regions, is consistent with previous studies (Adcock, Constable, Gore, & Goldman-Rakic, 2000; Klingberg, 1998). Data from previous neuroimaging studies suggests that concurrent performance of two tasks with different input modalities (e.g., a word classification task and an object rotation task), results in specific activation of the dorsolateral prefrontal cortex in the dual task processing but not in the single

task processing (D'Esposito et al., 1995). In contrast, recent studies using modality independent dual tasks revealed that no novel regions were engaged under the dual task condition relative to the single task condition and that there was increased activity in one or more regions involved in the single task condition (Dux et al., 2006; Dux et al., 2009; Sigman & Dehaene, 2008; Tombu et al., 2011). Likewise, data from neuroimaging studies examining the concurrent performance of two tasks with the same input modality demonstrated that brain regions activated during performance of the dual task overlapped with brain regions activated during the single task (Hahn et al., 2008; Nebel et al., 2005). In these studies, the lateral prefrontal cortex was activated even under the single task condition. We also found the activation of the left middle frontal gyrus (BA 9) under the single task (SC) condition and in the present study (Table 1). These results suggest

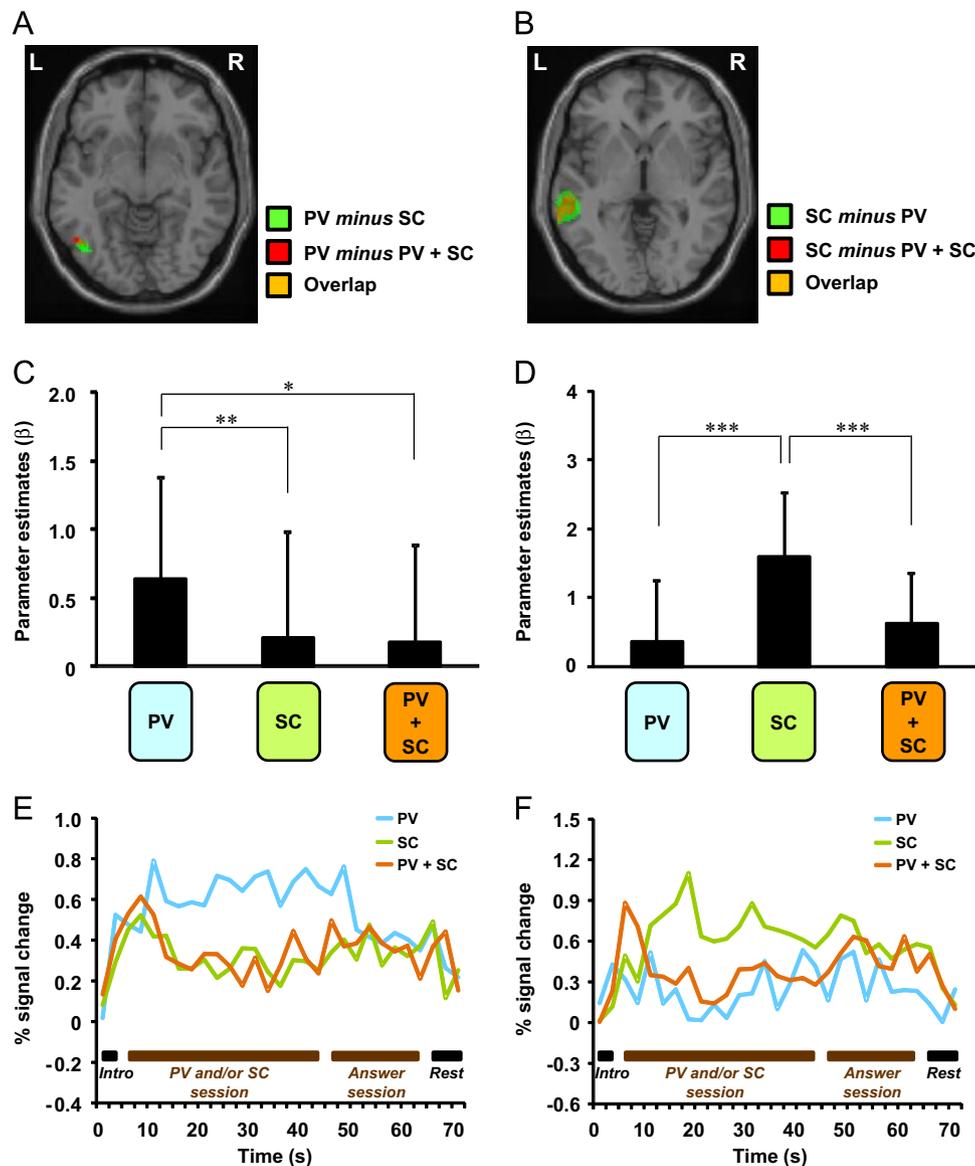


Fig. 4. Unique activated regions in PV and SC (single task) conditions. Statistical parametric maps of higher activations of the (A) left fusiform gyrus in the condition of picking out vowels [PV minus SC or PV minus PV+SC; The extent threshold was set at more than 10 voxels and the height threshold was set at $p=.005$ (uncorrected) at the voxel level] and (B) left middle temporal gyrus in the condition of story comprehension [SC minus PV or SC minus PV+SC; The extent threshold was set at $p=.05$ with a correction for multiple comparisons at the cluster level. The height threshold was set at $p=.005$ (uncorrected) at the voxel level] during the PV and/or SC session are shown. Right (R) and left (L) sides are indicated. Comparisons of the extent of activation of (C) left fusiform gyrus ($x=-44, y=-68, z=-6$) and (D) left middle temporal gyrus ($x=-58, y=-32, z=-2$) among the PV, SC, and PV+SC conditions (PV minus CL, SC minus CL, and PV+SC minus CL). Time course of activation of (E) left fusiform gyrus and (F) left middle temporal gyrus in the PV, SC, and PV+SC conditions. The % signal change was obtained by signal of each scan divided by the mean of the first scan of the introduction stimulus (Intro), which is the name of the stimulus condition that appeared on the screen for 5 s, in the PV, SC, and PV+SC conditions. * $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed paired t -test with Bonferroni correction). Values are the mean and SD.

that the lateral prefrontal cortex, especially; the dorsal part of this region, engages in processing for task coordination or shifting attention during dual task performance when recruitment of activation of the lateral prefrontal cortex during single task performance is not necessary. However, increases in activations of the brain regions involved in the single tasks, without relation to input modalities during dual task performance, are associated with more attentional processing when the lateral prefrontal cortex is already activated during the single task performance.

In the present study, although greater activation of the left dorsal inferior frontal gyrus and superior parietal lobule were observed during performance of the dual task, activation of the middle and ventral inferior frontal gyrus was not observed. Based on previous studies, the left inferior frontal gyrus can be divided into the following areas involved in different aspects of linguistic

processing: semantic ventral, syntax middle and phonological dorsal inferior frontal gyrus (Bookheimer, 2002; Haller, Klarhoefer, Schwarzbach, Radue, & Indefrey, 2007). Several studies have reported that the left dorsal inferior frontal gyrus and superior parietal lobule are associated with phonological loop processing (Li et al., 2003; McDermott, Petersen, Watson, & Ojemann, 2003) and that these regions form part of verbal working memory (Smith et al., 1998; Zatorre et al., 1992). The present findings demonstrate a longer reaction time to answer the question of story comprehension in the dual task condition compared to that in the single task condition. Therefore, although the activation level of the left dorsal inferior frontal gyrus or superior parietal lobule was not correlated with the reaction time to answer the question of sentence comprehension in the dual task condition (data not shown), the greater activation of the left

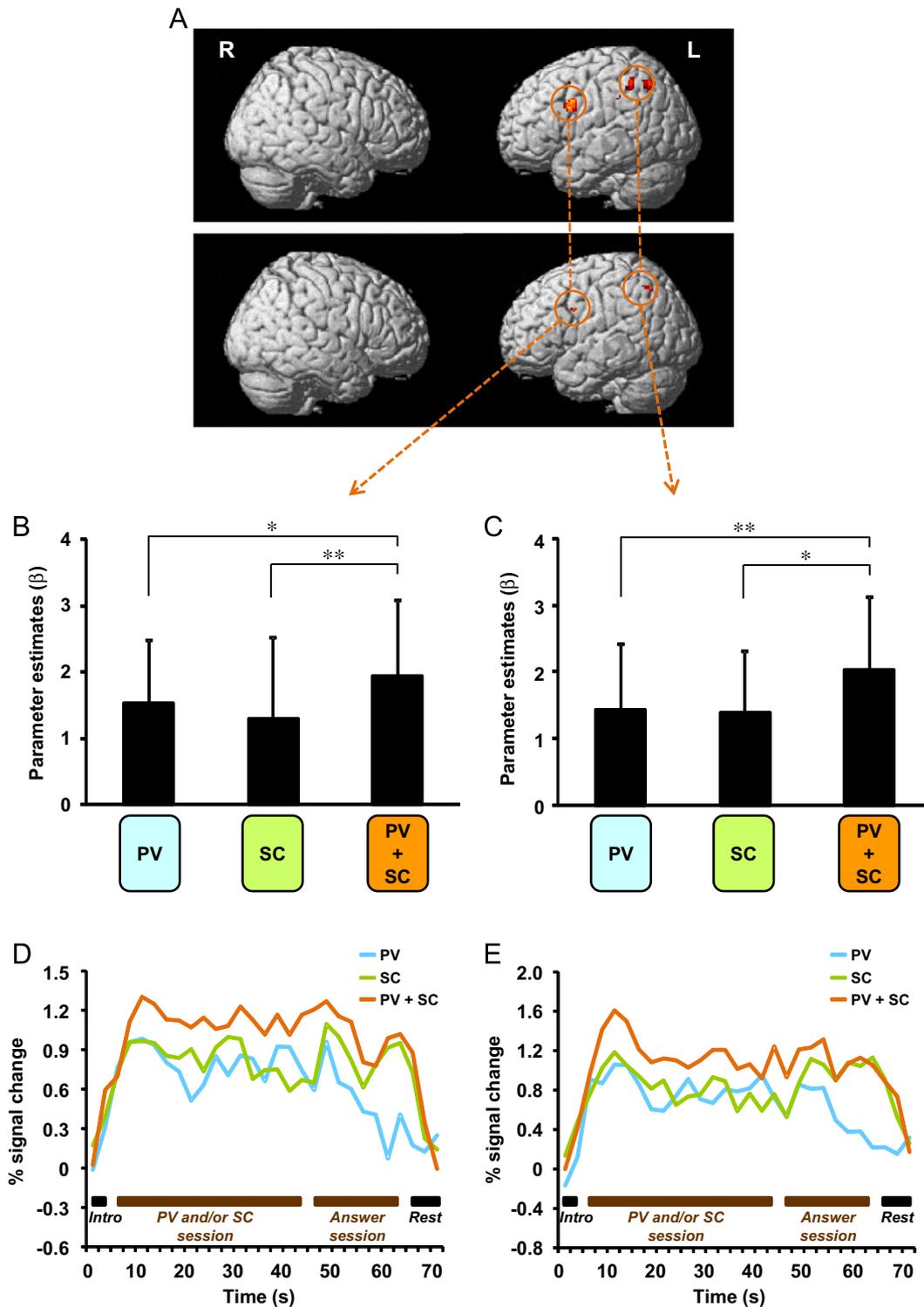


Fig. 5. Unique activated regions in the dual task, PV+SC, condition. Statistical parametric maps of greater activations of the left dorsal inferior frontal gyrus and superior parietal lobule in the condition of concurrent processes both of PV and SC in comparison with the single task conditions of the PV and SC [2 (PV+SC) minus (SC plus PV)] (A, top) and [(PV+SC) minus PV] and [(PV+SC) minus SC] (A, bottom) using a conjunction analysis during the PV and/or SC session are shown. The extent threshold was set at $p=.05$ with a correction for multiple comparisons at the cluster level and the height threshold was set at $p=.005$ (uncorrected) at the voxel level. Right (R) and left (L) sides are indicated. Comparison of the extent of activation of the (B) left dorsal inferior frontal gyrus ($x=-46, y=4, z=32$) and the (C) left superior parietal lobule ($x=-30, y=-58, z=48$) among the PV, SC, and PV+SC conditions (PV minus CL, SC minus CL, and PV+SC minus CL). The time course of activation of the (D) left dorsal inferior frontal gyrus and (E) left superior parietal lobule in the PV, SC, and PV+SC conditions. The % signal change was obtained by dividing the signal from each scan by the mean of the first scan of the introduction stimulus (Intro), which appeared on the screen for 5 s, in the PV, SC, and PV+SC conditions. * $p < .05$, ** $p < .01$ (two-tailed paired t -test with Bonferroni correction). Values are the mean and SD.

dorsal inferior frontal gyrus and superior parietal lobule during dual task performance may reflect the enhancement of working memory processing necessary for fast comprehension.

Fronto-parietal areas, including the left dorsal inferior frontal gyrus and superior parietal lobule, are engaged by visual attentional processes (Corbetta & Shulman, 2002; Kanwisher & Wojculik, 2000).

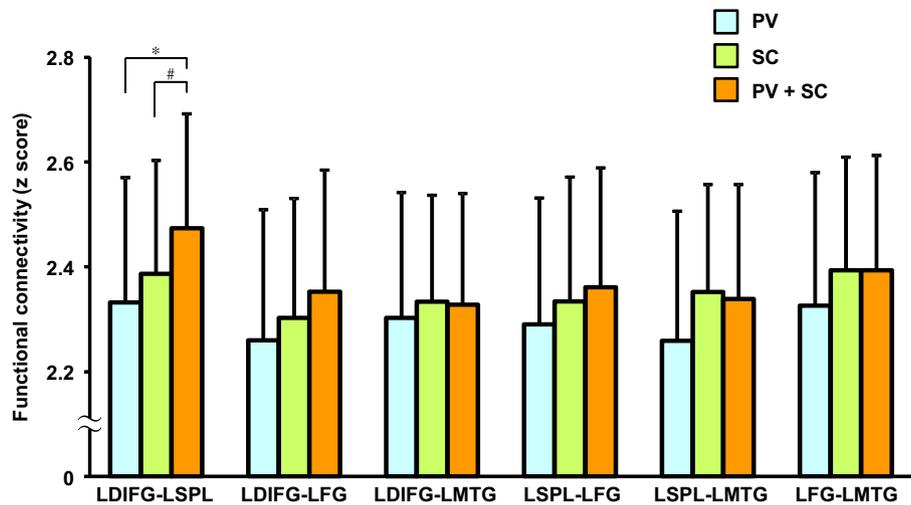


Fig. 6. Functional connectivity among the left dorsal inferior frontal gyrus (LDIFG), left superior parietal lobule (LSPL), left fusiform gyrus (LFG), and left middle temporal gyrus (LMTG) under PV, SC, and PV+SC conditions in the PV and/or SC session. Analytical methods for the functional connectivity are described in the Materials and methods section in detail. * $p < .1$, # $p < .05$ (two-tailed paired t -test). Values are the mean and SEM.

Table 3

Activated brain regions associated with the single process of story comprehension (SC) and the concurrent processes of picking out vowels (PV) and SC (PV+SC) during the answer session.

Brain region	Side	BA	SC				PV+SC			
			MNI coordinates		Z value	MNI coordinates		Z value		
Middle frontal gyrus	L	9/46	-58	28	32	5.16	-50	26	32	5.19
	R	9/46	56	26	32	4.76	44	34	18	5.19
Inferior frontal gyrus	L	44/45	-44	22	10	4.22	-50	22	24	4.96
	L	9/44	-52	10	36	3.83	-50	8	40	4.01
Superior frontal gyrus	R	6	24	14	42	3.38	24	14	40	3.31
Supplementary motor area	L	6	-4	12	54	3.82	-4	18	52	3.70
Inferior parietal lobule	L	40	-42	-34	42	4.17	-46	-36	44	3.87
	R	40	48	-40	44	4.11	38	-48	34	4.47
Superior parietal lobule	L	7	-34	-60	50	5.23	-34	-58	48	5.53
	R	7	38	-62	46	4.82	36	-62	46	4.71
Precuneus	L	7	-12	-78	56	3.61	-12	-62	46	3.23
	R	7	6	-60	44	4.17	-	-	-	-
Fusiform gyrus	L	37	-40	-42	-26	3.77	-46	-64	-20	3.31
Middle occipital gyrus	L	19	-26	-74	28	4.12	-34	-68	30	4.25
	R	19	36	-70	34	4.40	-	-	-	-
Inferior occipital gyrus	L	18	-24	-90	-10	3.56	-26	-90	-4	4.51
Cerebellum	L	-	-8	-78	-30	4.74	-	-	-	-
	R	-	10	-80	-30	4.30	-	-	-	-

L, left; R, right; BA, Brodmann's area; MNI, Montréal Neurological Institute. The extent threshold was set at $p = .05$ with a correction for multiple comparisons at the cluster level for the entire brain. The height threshold was set at $p = .005$ (uncorrected) at voxel level.

Bookheimer (2002) noted that increased activation of the left dorsal inferior frontal gyrus may reflect an increased need for attention to verbal memory processing. In addition, the left parietal lobule displays greater activation during higher short-term memory load associated with attentional resources (Magen, Emmanouil, McMains, Kastner, & Treisman, 2009). When two arithmetic tasks are performed concurrently, the tasks compete for limited resources (Just et al., 2001; Wickens, Kramer, Vanasse, & Donchin, 1983), especially when these tasks entail activation in the same parts of the cortex (Klingberg, 1998; Klingberg & Roland, 1997), which correspond to the left dorsal inferior frontal gyrus and superior parietal lobule in the present study. Therefore, enhanced activation of the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition may engage more attentional processing than the single task conditions, due to greater and more complex demands on voluntary attentional resources. Tombu et al. (2011) reported that

when using a dual task with different input modalities (an auditory–vocal task and a visual–manual task), activations of the left inferior frontal junction and inferior parietal lobule, which are close to the identified regions involved in dual task performance in our study, were more highly activated in the dual task condition relative to the single task condition. Hence, the inferior frontal cortex and posterior parietal lobule during the dual task performance, without relation to input modalities, may be involved with the primary brain regions when additional attentional processing is required, relative to that in the single task condition.

The functional connectivity analysis measures the degree of synchronization among activated brain regions. Thus, this analysis can evaluate the differences in internode synchronization of brain activation during dual task opposed to single task performance. An increase in synchronization may indicate an attempt to establish more effective communication among the brain regions

of the task-dependent network and hence attain a high level of performance in the dual task (Buchweitz et al., in press). Therefore, higher levels of synchronization between the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition than in the single task condition may lead to more effective communication between these regions and contribute more attentional processing than in the single task condition.

Consistent with our findings, decreased activation was reported for the primary brain regions for single task processing during dual task performance compared with activation during single task performance (Just et al., 2008; Newman et al., 2007). The left middle temporal gyrus is generally thought to play a dominant role in story comprehension (Grossman et al., 2002; Stowe et al., 1998). The result of greater activation of the left middle temporal gyrus in the SC condition in comparison with the PV condition is consistent with previous evidence. Activation of the left middle temporal gyrus in the PV+SC condition was reduced compared to the SC condition. Newman et al. (2007) reported that language related activation in the temporal regions was much lower during the “attend-both” condition than during the “attend-sentence” condition, equivalent to the dual and single task processing investigated in the present study. Therefore, the reduced activation of the left middle temporal gyrus during dual task performance may be related to the increased difficulty of maintaining story comprehension while picking out individual letters simultaneously. During detection of the target letters, the left fusiform gyrus was more active than when only reading the word (Murray & He, 2006) and are thus associated with the process of picking out letters in the KPT. In fact, activation of the left fusiform gyrus in the PV condition was higher than that in the SC condition in the present study. Activation of the left fusiform gyrus in the PV+SC condition was reduced in comparison with the PV condition. Since the reaction time for picking out vowels in the PV+SC condition was longer than that in the PV condition, the reduced activation of the left fusiform gyrus during dual task performance may be related to the increased difficulty of the task or lower priority being assigned to picking out vowels relative to comprehending the story, which is being done simultaneously. Therefore, the KPT is characterized by a decrease in the activation of the domain regions associated with picking out vowels and sentence comprehension by concurrent processing of the two tasks.

The KPT is useful for detection of deficits in cognitive function in persons with mild or slight dementia (Kaneko, 1996) and Parkinson's disease (Bokura et al., 2005). In addition, the ability to divide attentional resources, as measured by the KPT, plays a crucial role not only in patients with dementia but also in children suffering from CCFS (Tomoda et al., 2007). Based on the present findings, we might be able to evaluate impairments of the neural substrates associated with the KPT in these patients.

In conclusion, the left dorsal inferior frontal gyrus, superior parietal lobule, fusiform gyrus, and middle temporal gyrus appear to play a crucial role in processing during dual task performance as measured by the KPT. Increased activation of the dorsal inferior frontal gyrus and superior parietal lobule during dual task performance may be associated with the capacity of attentional resources. In contrast, reduced activation of the left fusiform gyrus and middle temporal gyrus, which relate to the processes of picking out letters and story comprehension, respectively, may reflect the difficulty of concurrent processing of the two tasks. In addition, the increase in synchronization between the left dorsal inferior frontal gyrus and superior parietal lobule in the dual task condition may lead to more effective communication between these brain regions and contribute more attentional processing than the single task condition, due to greater and more complex demands on voluntary attentional resources. Our findings

improve our current understanding of the neural mechanisms of dual task performance involved in verbal memory function, a critical ability in everyday life.

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References

- Adcock, R. A., Constable, R. T., Gore, J. C., & Goldman-Rakic, P. S. (2000). Functional neuroanatomy of executive processes involved in dual-task performance. *Proceedings of the National Academy of Sciences of the United States of America*, 97, 3567–3572.
- Baddeley, A. D. (1986). *Working Memory*. Oxford: Clarendon Press.
- Baddeley, A. D., & Hitch, G. J. (1974). Working memory. In: G. A. Bower (Ed.), *The Psychology of Learning and Motivation, Vol. 8, Advances in Research and Theory* (pp. 47–89). New York: Academic Press.
- Bokura, H., Yamaguchi, S., & Kobayashi, S. (2005). Event-related potentials for response inhibition in Parkinson's disease. *Neuropsychologia*, 43, 967–975.
- Bookheimer, S. (2002). Functional MRI of language: new approaches to understanding the cortical organization of semantic processing. *Annual Review of Neuroscience*, 25, 151–188.
- Bradley, D. C., Garrett, M. E., & Zurif, E. B. (1980). Syntactic deficits in Broca's aphasia. In: D. Caplan (Ed.), *Biological Studies of Mental Processes* (pp. 269–286). Cambridge, MA: MIT Press.
- Buchweitz, A., Keller, T.A., Meyler, A., & Just, M.A. (in press). Brain activation for language dual-tasking: Listening to two people speak at the same time and a change in network timing. *Human Brain Mapping* <<http://www.ncbi.nlm.nih.gov/pubmed?term=Brain%20activation%20for%20language%20dual-tasking%3AListening%20to%20two%20people%20speak%20at%20the%20same%20time%20and%20a>>.
- Caplan, D., Alpert, N., & Waters, G. (1998). Effects of syntactic structure and propositional number on patterns of regional cerebral blood flow. *Journal of Cognitive Neuroscience*, 10, 541–552.
- Caplan, D., Alpert, N., & Waters, G. (1999). PET studies of syntactic comprehension with auditory sentence presentation. *NeuroImage*, 9, 343–351.
- Caramazza, A., & Zurif, E. B. (1976). Dissociation of algorithmic and heuristic processes in language comprehension: evidence from aphasia. *Brain and Language*, 3, 572–582.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, 3, 201–215.
- Dapretto, M., & Bookheimer, S. Y. (1999). Form and content: dissociating syntax and semantics in sentence comprehension. *Neuron*, 24, 427–432.
- D'Esposito, M., Detre, J. A., Alsop, D. C., Shin, R. K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature*, 378, 279–281.
- Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. *Neuron*, 52, 1109–1120.
- Dux, P. E., Tombu, M. N., Harrison, S., Rogers, B. P., Tong, F., & Marois, R. (2009). Training improves multitasking performance by increasing the speed of information processing in human prefrontal cortex. *Neuron*, 63, 127–138.
- Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., et al. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage*, 25, 1325–1335.
- Friston, K. J., Holmes, A., Poline, J. B., Price, C. J., & Frith, C. D. (1996). Detecting activations in PET and fMRI: levels of inference and power. *NeuroImage*, 4, 223–235.
- Friston, K. J., Fletcher, P., Josephs, O., Holmes, A., Rugg, M. D., & Turner, R. (1998a). Event-related fMRI: characterizing differential responses. *NeuroImage*, 7, 30–40.
- Friston, K. J., Josephs, O., Rees, G., & Turner, R. (1998b). Nonlinear event-related responses in fMRI. *Magnetic Resonance in Medicine*, 39, 41–52.
- Friston, K. J., Holmes, A. P., & Worsley, K. J. (1999). How many subjects constitute a study? *NeuroImage*, 10, 1–5.
- Fukuda, K., Straus, S. E., Hickie, I., Sharpe, M. C., Dobbins, J. G., & Komaroff, A. (1994). The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Annals of Internal Medicine*, 121, 953–959.
- Grodzinsky, Y. (1984). The syntactic characterization of agrammatism. *Cognition*, 16, 99–120.
- Grodzinsky, Y. (2000). The neurology of syntax: language use without Broca's area. *Behavioral and Brain Sciences*, 23, 1–71.

- Grossman, M., Cooke, A., DeVita, C., Chen, W., Moore, P., Detre, J., et al. (2002). Sentence processing strategies in healthy seniors with poor comprehension: an fMRI study. *Brain and Language*, 80, 296–313.
- Hahn, B., Wolkenberg, F. A., Ross, T. J., Myers, C. S., Heishman, S. J., Stein, D. J., et al. (2008). Divided versus selective attention: evidence for common processing mechanisms. *Brain Research*, 1215, 137–146.
- Haller, S., Klarhoefer, M., Schwarzbach, J., Radue, E. W., & Indefrey, P. (2007). Spatial and temporal analysis of fMRI data on word and sentence reading. *European Journal of Neuroscience*, 26, 2074–2084.
- Ikuta, N., Sugiura, M., Sassa, Y., Watanabe, J., Akitsuki, Y., Iwata, K., et al. (2006). Brain activation during the course of sentence comprehension. *Brain and Language*, 97, 154–161.
- Just, M. A., & Carpenter, P. A. (1992). A capacity theory of comprehension: individual differences in working memory. *Psychological Review*, 99, 122–149.
- Just, M. A., Carpenter, P. A., Keller, T. A., Eddy, W. F., & Thulborn, K. R. (1996). Brain activation modulated by sentence comprehension. *Science*, 274, 114–116.
- Just, M. A., Carpenter, P. A., Keller, T. A., Emery, L., Zajac, H., & Thulborn, K. R. (2001). Interdependence of nonoverlapping cortical systems in dual cognitive tasks. *NeuroImage*, 14, 417–426.
- Just, M. A., Keller, T. A., & Cynkar, J. (2008). A decrease in brain activation associated with driving when listening to someone speak. *Brain Research*, 1205, 70–80.
- Kaneko, M. (1996). A neuropsychological index of aging data from 9000 elderly people. *Nippon Ronen Igakkai Zasshi*, 33, 811–815.
- Kanwisher, N., & Wojciulik, E. (2000). Visual attention: insights from brain imaging. *Nature Reviews Neuroscience*, 1, 91–100.
- Klingberg, T., & Roland, P. (1997). Interference between two concurrent tasks is associated with activation of overlapping field in the cortex. *Cognitive Brain Research*, 6, 1–8.
- Klingberg, T. (1998). Concurrent performance of two working memory tasks: potential mechanisms of interference. *Cerebral Cortex*, 8, 593–601.
- Koechlin, E., Basso, G., Pietrini, P., Panzer, S., & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature*, 399, 148–151.
- Lezak, M. (1995). *Neuropsychological Assessment* (3rd edn.). New York: Oxford University Press.
- Li, X., Gandour, J., Talavage, T., Wong, D., Dziedzic, M., Lowe, M., et al. (2003). Selective attention to lexical tones recruits left dorsal frontoparietal network. *Neuroreport*, 14, 2263–2266.
- Magen, H., Emmanouil, T. A., McMains, S. A., Kastner, S., & Treisman, A. (2009). Attentional demands predict short-term memory load response in posterior parietal cortex. *Neuropsychologia*, 47, 1790–1798.
- Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage*, 19, 1233–1239.
- Martin, R. C. (2003). Language processing: functional organization and neuroanatomical basis. *Annual Reviews of Psychology*, 54, 55–89.
- McDermott, K. B., Petersen, S. E., Watson, J. M., & Ojemann, J. G. (2003). A procedure for identifying regions preferentially activated by attention to semantic and phonological relations using functional magnetic resonance imaging. *Neuropsychologia*, 41, 293–303.
- Mizuno, K., Tanaka, M., Fukuda, S., Sasabe, T., Imai-Matsumura, K., & Watanabe, Y. (2011a). Changes in cognitive functions of students in the transitional period from elementary school to junior high school. *Brain and Development*, 33, 412–420.
- Mizuno, K., Tanaka, M., Fukuda, S., Imai-Matsumura, K., & Watanabe, Y. (2011b). Relationship between cognitive functions and prevalence of fatigue in elementary and junior high school students. *Brain and Development*, 33, 470–479.
- Mizuno, K., Tanaka, M., Fukuda, S., Imai-Matsumura, K., & Watanabe, Y. (2011c). Relationship between cognitive function and prevalence of decrease in intrinsic academic motivation in adolescents. *Behavioral and Brain Functions*, 7, 4.
- Murray, S. O., & He, S. (2006). Contrast invariance in the human lateral occipital complex depends on attention. *Current Biology*, 16, 606–611.
- Nebel, K., Wiese, H., Stude, P., de Greiff, A., Diener, H. C., & Keidel, M. (2005). On the neural basis of focused and divided attention. *Brain Research Cognitive Brain Research*, 25, 760–776.
- Newman, S. D., Keller, T. A., & Just, M. A. (2007). Volitional control of attention and brain activation in dual task performance. *Human Brain Mapping*, 28, 109–117.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, 9, 97–113.
- Paulesu, E., Frith, C. D., & Frackowiak, R. S. (1993). The neural correlates of the verbal component of working memory. *Nature*, 363, 583–584.
- Prat, C. S., Keller, T. A., & Just, M. A. (2007). Individual differences in sentence comprehension: a functional magnetic resonance imaging investigation of syntactic and lexical processing demands. *Journal of Cognitive Neuroscience*, 19, 1950–1963.
- Ross, S., Fantie, B., Straus, S. F., & Grafman, J. (2001). Divided attention deficits in patients with chronic fatigue syndrome. *Applied Neuropsychology*, 8, 4–11.
- Sigman, M., & Dehaene, S. (2008). Brain mechanisms of serial and parallel processing during dual-task performance. *Journal of Neuroscience*, 28, 7585–7598.
- Smith, E. E., Jonides, J., Marshuetz, C., & Koeppel, R. A. (1998). Components of verbal working memory: evidence from neuroimaging. *Proceedings of the National Academy of Sciences of the United States of America*, 95, 876–882.
- Stowe, L. A., Broere, C. A., Paans, A. M., Wijers, A. A., Mulder, G., Vaalburg, W., et al. (1998). Localizing components of a complex task: sentence processing and working memory. *Neuroreport*, 9, 2995–2999.
- Stromswold, K., Caplan, D., Alpert, N., & Rauch, S. (1996). Localization of syntactic comprehension by positron emission tomography. *Brain and Language*, 52, 452–473.
- Thuy, D. H., Matsuo, K., Nakamura, K., Toma, K., Oga, T., Nakai, T., et al. (2004). Implicit and explicit processing of kanji and kana words and nonwords studied with fMRI. *NeuroImage*, 23, 878–889.
- Tombu, M. N., Asplund, C. L., Dux, P. E., Godwin, D., Martin, J. W., & Marois, R. (2011). A Unified attentional bottleneck in the human brain. *Proceedings of the National Academy of Sciences of the United States of America*, 108, 13426–13431.
- Tomoda, A., Mizuno, K., Murayama, N., Joudoi, T., Igasaki, T., Miyazaki, M., et al. (2007). Event-related potentials in Japanese childhood chronic fatigue syndrome. *Journal of Pediatric Neurology*, 5, 199–208.
- Wickens, C., Kramer, A., Vanasse, L., & Donchin, E. (1983). Performance of concurrent tasks: a psychophysiological analysis of the reciprocity of information-processing resources. *Science*, 221, 1080–1082.
- Yamamoto, K. (1992). Analysis of cognitive function and regional cerebral blood flow in Parkinson's disease by 123I-IMP SPECT. *Rinsho Shinkeigaku*, 32, 1–7.
- Zatorre, R. J., Evans, A. C., Meyer, E., & Gjedde, A. (1992). Lateralization of phonetic and pitch discrimination in speech processing. *Science*, 256, 846–849.