

Specialization in the Left Prefrontal Cortex for Sentence Comprehension

Ryuichiro Hashimoto¹ and Kuniyoshi L. Sakai^{1,2,3}

¹Department of Cognitive and Behavioral Science
Graduate School of Arts and Sciences
The University of Tokyo, Komaba
3-8-1 Komaba, Meguro-ku
Tokyo 153-8902

²CREST
Japan Science and Technology Corporation
Kawaguchi-shi 332-0012
Japan

Summary

Using functional magnetic resonance imaging (fMRI), we examined cortical activation under syntactic decision tasks and a short-term memory task for sentences, focusing on essential properties of syntactic processing. By comparing activation in these tasks with a short-term memory task for word lists, we found that two regions in the left prefrontal cortex showed selective activation for syntactic processing: the dorsal prefrontal cortex (DPFC) and the inferior frontal gyrus (IFG). Moreover, the left DPFC showed more prominent activation under the short-term memory task for sentences than that for word lists, which cannot be explained by general cognitive factors such as task difficulty and verbal short-term memory. These results support the proposal of specialized systems for sentence comprehension in the left prefrontal cortex.

Introduction

It is a central issue in cognitive neuroscience whether language ability is subserved by a distinct module, separable from other cognitive modules (Shallice, 1988; Smith and Tsimpli, 1995; Sakai et al., 2001). Modularists have proposed such language modules, further claiming the existence of specialized submodules for syntactic processing and other linguistic faculties (Fodor, 1983; Chomsky, 1984; Coltheart, 1999). Syntactic processing in sentence comprehension refers to the mental processes that apply grammatical rules to analyzing sentence meaning. Consistent with the modular view, previous imaging studies have identified cortical regions, which are suggested to be selectively involved in syntactic processing, in the left inferior frontal gyrus (L. IFG; Brodmann's areas [BAs] 44 and 45) (Dapretto and Bookheimer, 1999; Embick et al., 2000), as well as in the left dorsal prefrontal cortex (L. DPFC; BAs 6, 8, and 9) and the left dorsolateral prefrontal cortex (L. DLPFC; BAs 46 and 9) (Kang et al., 1999; Indefrey et al., 2001; Newman et al., 2001).

In contrast, there has been a proposal that does not assume any modularity in language processing, such that syntactic processing is fully carried out by a system of verbal working memory (Just and Carpenter, 1992;

Dick et al., 2001). Verbal working memory refers to a brain system that provides temporal storage and manipulation of verbal information necessary for language comprehension and other cognitive tasks (Baddeley, 1992). Baddeley's model of verbal working memory assumes the phonological store, in which verbal information is registered and maintained by the subvocal rehearsal system. Typical examples of verbal information maintained are word/letter identity (what) and word/letter order (when). As to the "what" aspect, several imaging studies reported activations of the bilateral DLPFC, DPFC, and IFG (Paulesu et al., 1993; Cohen et al., 1994; Fiez et al., 1996; Clark et al., 2000). As to the "when" aspect, neuropsychological studies have suggested that short-term memory for the temporal order of words requires the involvement of L. DLPFC (Milner et al., 1991). This proposal has been supported by recent imaging studies (Cabeza et al., 1997; Marshuetz et al., 2000) in which DPFC was also activated.

In addition to the phonological store and the subvocal rehearsal system, it has been proposed that the central executive is engaged when a verbal task involves demanding mnemonic processes. Previous imaging studies have investigated the neural basis of the central executive by increasing task difficulty stemming from verbal memory load, that is, the number of verbal items to be memorized (Braver et al., 1997; Cohen et al., 1997; Rypma et al., 1999). These studies have consistently reported enhanced activation of DLPFC, DPFC, and IFG. By increasing task difficulty with a dual-task condition, it has been suggested that these prefrontal regions constitute the common neural basis for verbal executive processes, such as sentence comprehension and verbal memorization (Bunge et al., 2000). On the other hand, a previous imaging study reported task difficulty-related modulation in IFG and DPFC (but not in DLPFC), with memory load held constant while manipulating verbal effects of difficulty, such as word length, phonological similarity, and lexicality (Chein and Fiez, 2001). However, it is also possible that activations of IFG and DPFC are modulated by other verbal-specific factors than task difficulty and executive processes.

Given the controversy between the two opposing views on syntactic modularity, a crucial question is whether syntactic processing is dissociable from the verbal working memory system. Indeed, some previous behavioral studies have indicated such a dissociation (Martin, 1993). First, it has been shown that an English sentence of up to 14 words can be understood and immediately recalled with near perfect accuracy when the rate of presentation is as high as 12 words per second, while only 2 or 3 unrelated words can be recalled at the same presentation rate (Potter, 1993). This observation led to the proposal that grammatically structuralized information is immediately transformed into stable representation, while maintenance of memory for unrelated words requires continuous subvocal rehearsal. Second, neuropsychological studies have reported patients with profound verbal short-term memory deficits, whose ability for sentence comprehension is well pre-

³Correspondence: sakai@mind.c.u-tokyo.ac.jp

served (Martin, 1987; Waters et al., 1991). Third, a double dissociation has been shown, such that the span-impaired aphasics were better at repeating sentences (up to five or seven words) than repeating three-word lists, whereas the span-preserved aphasic showed the opposite pattern of performance (McCarthy and Warrington, 1987). Fourth, a previous neuropsychological study investigated the syntactic ability of patients with deficits in the central executive, showing that the effect of syntactic complexity was unaffected by a concurrent verbal memory load (Waters et al., 1995). Based on these findings, it has been claimed that there is a specialized system for assigning the syntactic structure of a sentence and using that structure in determining sentence meaning (Caplan and Waters, 1999). However, its precise neural substrates have not been elucidated.

A possible separation between syntactic processing and verbal working memory has been also examined by event-related brain potential (ERP) studies. One ERP component, the left anterior negativity (LAN), has been associated with grammatical errors (Neville et al., 1991; Münte et al., 1993; Friederici et al., 1993). However, its syntactic specificity has been challenged by the observation that the LAN effect was independent of grammaticality and correlated with working memory required in sentence processing (Kluender and Kutas, 1993; Röslér et al., 1998). Moreover, it has been shown that the amplitude of the LAN was modulated by the combination of syntactic complexity and additional working memory load (Vos et al., 2001). Recent imaging studies have manipulated syntactic complexity (canonical/noncanonical word order) and a maintenance delay interval (the distance of a filler-gap linkage), and reported increased activation of the left BA 44 or BA 47, which was induced by delay intervals but not by complexity alone (Fiebach et al., 2001; Cooke et al., 2002). Delay intervals, however, are necessarily confounded with general task difficulty, because it is more difficult to process a sentence while keeping an item longer in memory. Besides, the memory demands in these studies may not be syntax-specific but domain-independent verbal short-term memory. Therefore, it still remains to be elucidated whether or not syntactic processing is separable from general task difficulty and verbal short-term memory.

The present study addressed whether or not there are specialized neural systems for sentence comprehension. Toward this objective, we focused on two essential properties of syntactic processing that contrast with properties of task difficulty and verbal working memory. First, syntactic processing is based not only on word identities and the linear order of words, but on the structure-dependent rules underlying a sentence as well. In the example shown in Figure 1A, the structure dependency refers to the information that *Taro* is in the main clause, whereas *Saburo* is in the subordinate clause. On the other hand, the linear order of words only provides the information that *Taro* precedes *Saburo*, but offers no structural information. The structure-dependency of rules is one of the unique properties of syntax, universally observed in all known natural languages (Chomsky, 1980; Comrie, 1989; Baker, 2001). Second, in natural reading conditions, syntactic information is processed immediately and automatically as each new word is encountered (Neville et al., 1991; Gunter and

Friederici, 1999). This automaticity clearly contrasts with task difficulty, which involves conscious effort and strategies in control of conflicting or competitive responses.

To identify neural systems reflecting these essential properties of syntactic processing, we contrasted two syntactic decision (SYN) tasks (SYN-1 and SYN-2) with two short-term memory (STM) tasks (STM-S and STM-W) (Figure 1A). In SYN-1 and SYN-2, participants read Japanese sentences, each of which consisted of sequentially presented phrases. After one complete sentence, we presented a pair of words to participants who were instructed to make syntactic judgments on argument-predicate (noun-verb) relations in SYN-1, and on coreference (noun-noun) relations in SYN-2 (see Experimental Procedures). These two tasks explicitly required participants to utilize the structure-dependent rules. In STM-S (an STM task for sentences), participants were presented with the same set of sentences as that used in the SYN tasks but were asked to memorize each phrase. Participants were then presented with a pair of phrases and judged their temporal order in the original sequence (Figure 1A). While this judgment does not require explicit syntactic decisions, reading sentences obligatorily accompanies syntactic processes. In STM-W (an STM task for words), phrases of one sentence were rearranged into separate groups of nouns and verbs, so that they were syntactically unrelated (Figure 1A). Its task requirements including memory encoding and retrieval were the same as those in STM-S, which are commonly involved in standard verbal working memory tasks.

During these four tasks, we measured cortical activity using functional magnetic resonance imaging (fMRI), and performed random effects analyses. Because behavioral studies have indicated that grammatical sentences can be more easily understood and recalled than lists of unrelated words, SYN-1, SYN-2, and STM-S would be easier tasks than STM-W that lacks syntactic relationships among words. Thus, STM-W would activate regions reflecting verbal working memory, together with additional regions due to task difficulty. If syntactic processing is fully carried out by the verbal working memory system, then the regions activated in STM-W would completely include the regions recruited in the other three tasks. If this is not the case, however, it will turn out that syntactic processing cannot be explained by nonmodular views. Our goal in this novel paradigm was to separate syntactic processing from verbal working memory processes by directly comparing syntactic decision tasks and verbal short-term memory tasks.

Results

Behavioral Data

The accuracy in SYN-1, SYN-2, STM-S, and STM-W was $87.7\% \pm 5.4\%$, $84.8\% \pm 7.0\%$, $90.1\% \pm 4.0\%$, and $79.5\% \pm 7.5\%$ (mean \pm SD, $n = 16$), respectively. Reaction times (RTs) for these tasks were 1071 ± 145 ms, 1109 ± 117 ms, 1298 ± 142 ms, and 1354 ± 155 ms, respectively. An ANOVA showed significant main effects of *task*, in both accuracy and RT ($p < 0.0001$). According to a post hoc test, RTs in both STM-W and STM-S were significantly longer than those in the two SYN tasks ($p <$

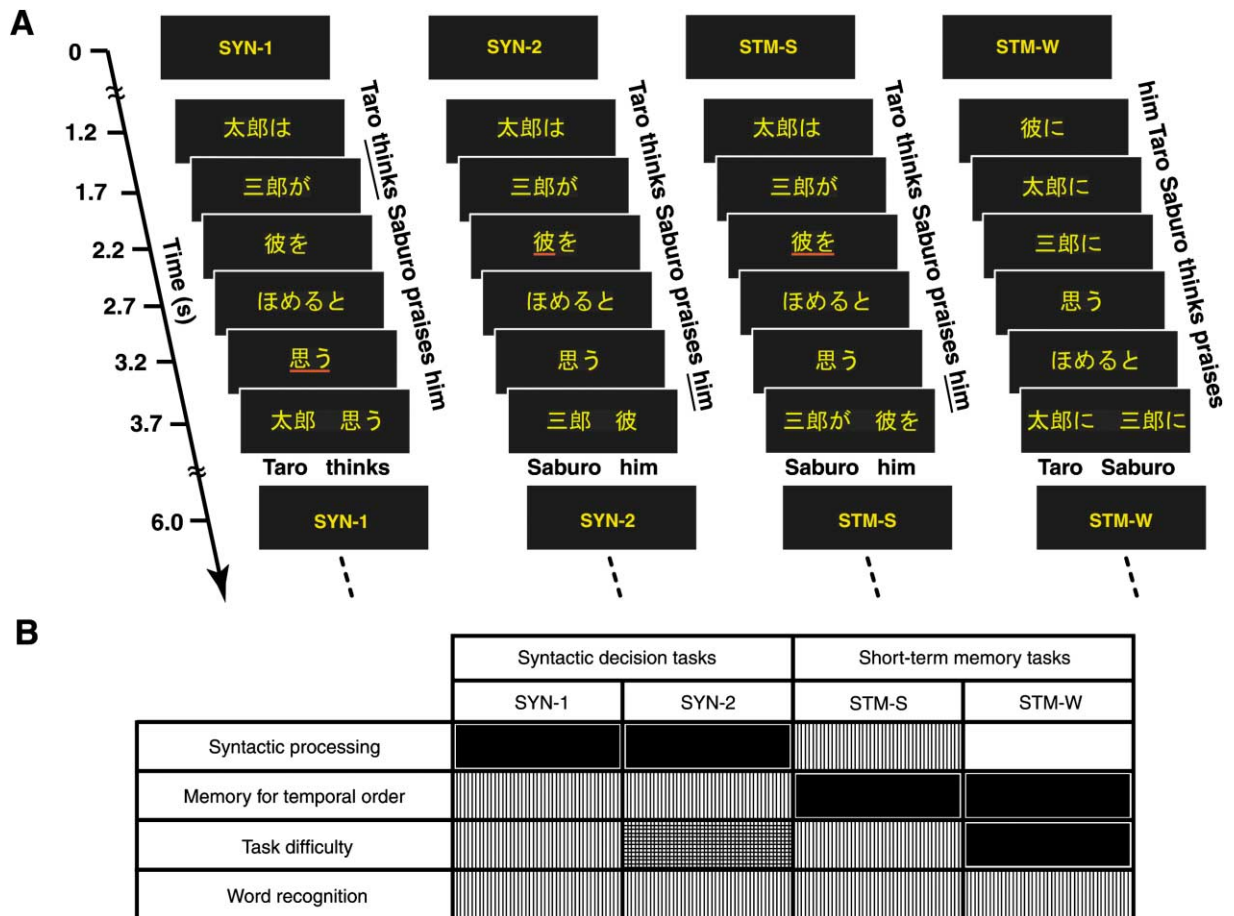


Figure 1. Four Tasks to Identify the Neural Substrates for Syntactic Processing

(A) Examples of stimuli used in the four tasks: two syntactic decision (SYN) tasks (SYN-1 and SYN-2) and two short-term memory (STM) tasks (STM-S [an STM task for sentences] and STM-W [an STM task for words]). In each trial for 6 s, five phrases (0.5 s each) were sequentially presented, followed by paired phrases (2.2 s) for judgment. An example of a Japanese sentence is shown: “*Taro-wa Saburo-ga kare-wo homeru-to omou.*” Its word by word translation is “*Taro-topic Saburo-nominative him praise that think.*” A red cross for fixation was always shown at the center of the screen, but it was omitted from the figure. Note that the task label was presented at the initiation of every trial.

(B) The cognitive components involved in each task, the contributions of which are shown in a black and white scale: black (maximum), crosshatched, hatched, and white (none). Syntactic processing is explicitly required in both SYN tasks, whereas it is implicitly involved in STM-S. Memory for temporal order is explicitly required in both STM tasks, whereas it is implicitly included for syntactic analyses in both SYN tasks. Behavioral data indicated that STM-W was the most difficult among the four tasks, and that SYN-2 was more difficult than STM-S. STM-S and SYN-1 were comparable in task difficulty. Word recognition was commonly involved in the four tasks.

0.0001), and RT in STM-W was marginally longer than that in STM-S ($p = 0.06$). STM-W showed significantly lower accuracy than the other three tasks ($p < 0.01$), and accuracy in SYN-2 was significantly lower than that in STM-S ($p < 0.01$). These results showed that STM-W was the most difficult task (Figure 1B).

Selective Activation for Sentence Processing in L. DPFC and L. IFG

First, we directly compared the STM-S and STM-W tasks (Figure 2A and Table 1). Although the task requirement was the same in these two tasks, STM-S involved syntactic processing at the sentence level, while STM-W required the most demanding mnemonic processes without syntactic relationships among words (Figure 1B). We found that L. DPFC (BAs 6, 8, and 9) showed significantly larger responses to STM-S. In contrast, se-

lective responses to STM-W were observed in the ventral portion of the left precentral gyrus, the left parietal operculum, and the right anterior cingulate cortex. The anterior border of L. DPFC activation was on the superior frontal sulcus, whereas its posterior border was on the precentral sulcus. This result demonstrates the existence of a specialized neural system for sentence comprehension, which is separable from task difficulty and verbal working memory.

In addition to the region activated for sentence processing in STM-S, we further examined whether there are neural substrates that are specifically recruited when employing structure-dependent syntactic rules in sentence comprehension. For this purpose, we contrasted the two SYN tasks (SYN-1 + SYN-2) with STM-W (Figure 2B and Table 1). Selective activation for the SYN tasks was found in the same regions of L. DPFC as those

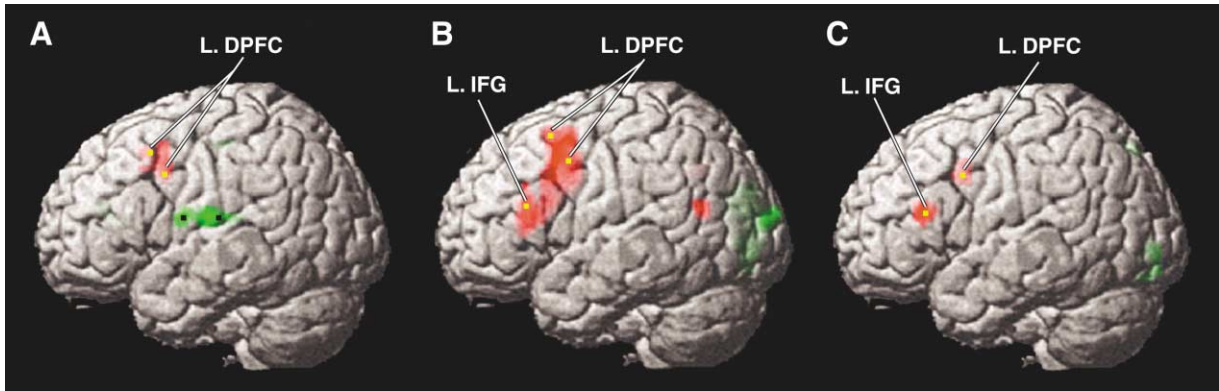


Figure 2. Selective Activation for Syntactic Processing in the Left Prefrontal Cortex

(A) Regions identified by STM-S – STM-W (red) and STM-W – STM-S (green). They were projected together onto a surface-rendered representative brain in MNI space. For display purposes, the threshold is set at uncorrected $p < 0.00005$ with an extent threshold of 16 voxels, but the local maxima of t values (yellow and black dots) reached a threshold of $p < 0.05$, corrected for multiple comparisons.

(B) Regions identified by (SYN-1 + SYN-2) – STM-W (red) and STM-W – (SYN-1 + SYN-2) (green). We found that L. DPFC and L. IFG showed selective activation for the SYN tasks.

(C) Regions identified by (SYN-1 + SYN-2) – STM-S (red) and STM-S – (SYN-1 + SYN-2) (green). The posterior focus of L. DPFC in each of (A), (B), and (C) was located within the left inferior precentral sulcus.

observed by the contrast of STM-S – STM-W, as well as in an additional region of L. IFG, which was mainly localized in the pars triangularis (BA45). In contrast, selective activation for STM-W was found in the bilateral lingual gyrus and the right cuneus.

Finally, we performed the remaining comparison (SYN-1 + SYN-2) versus STM-S (Figure 2C and Table

1). In this comparison, the regions with selective activation for the SYN tasks would include L. IFG for the application of structure-dependent syntactic rules. Moreover, the L. DPFC activation for syntactic processing in STM-S would be enhanced in the SYN tasks because the SYN tasks directed more attention to syntactic processing than STM-S. Indeed, we found that both L. IFG

Table 1. Cortical Regions Identified by Syntactic Decision versus Short-Term Memory Tasks

Brain Region	BA	x	y	z	Z Value
STM-S > STM-W					
L. DPFC	6/8/9	-27	15	48	4.8
		-39	6	36	4.7
STM-W > STM-S					
L. Precentral gyrus	4/6	-63	-3	15	4.9
L. Parietal operculum	43	-51	-15	15	5.4
R. Anterior cingulate cortex	24/32	12	33	21	5.4
(SYN-1 + SYN-2) > STM-W					
L. DPFC	6/8/9	-27	15	57	5.5
		-39	3	42	5.8
L. IFG	45	-54	27	21	4.9
STM-W > (SYN-1 + SYN-2)					
L. Lingual gyrus	18/19	-6	-84	3	5.5
R. Lingual gyrus	18/19	15	-78	0	5.5
R. Cuneus	18/19	9	-66	9	5.4
(SYN-1 + SYN-2) > STM-S					
L. DPFC	6/9	-36	6	36	4.8
L. IFG	45	-39	24	18	5.2
STM-S > (SYN-1 + SYN-2)					
L. Lingual gyrus	18/19	-9	-87	0	4.8
R. Lingual gyrus	18/19	18	-78	-12	5.4
R. Posterior parietal cortex	7/39/40	30	-75	42	5.3

Stereotactic coordinates (x, y, z) in Montreal Neurological Institute (MNI) space are shown for each voxel with a local maximum of Z values in the contrasts indicated ($p < 0.05$, corrected for multiple comparisons). BA, Brodmann's area; L, left; R, right; DPFC, the dorsal prefrontal cortex; IFG, the inferior frontal gyrus.

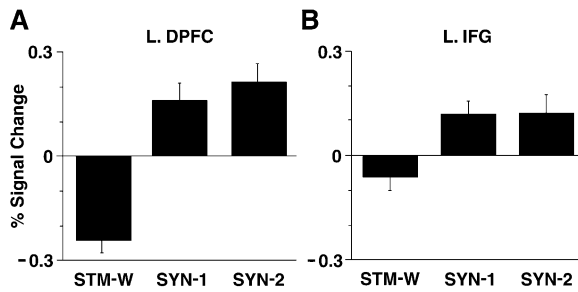


Figure 3. Task-Dependent Activation of L. DPFC and IFG
Taking STM-S as a reference, the percent signal changes (mean \pm SEM of participants) under SYN-1, SYN-2, and STM-W are shown for L. DPFC (A) and L. IFG (B) at the local maxima shown in Figure 2C.

and L. DPFC showed significantly larger activation in the SYN tasks than STM-S. On the other hand, we found selective activation for STM-S in the bilateral lingual gyrus and the right posterior parietal cortex.

Because STM-S was identical with STM-W as to task requirements, while being identical with the SYN tasks as to sentence stimuli, STM-S would serve as an ideal reference task for other tasks. Therefore, we calculated the mean signal changes under SYN-1, SYN-2, and STM-W from STM-S for each participant at the coordinates corresponding to local maxima of *t* values in the contrast of (SYN-1 + SYN-2) – STM-S. We found that L. DPFC (Figure 3A) and L. IFG (Figure 3B) showed a notable difference in signal changes for STM-W – STM-S, whereas signal changes for the SYN tasks were comparable between the two regions. Furthermore, SYN-1 and SYN-2 showed similar activation ($p > 0.1$, *F* test) in each region. A two-way ANOVA (*region* \times *task*) indicated significant interaction effects of *region* and *task* ($p < 0.05$), as well as significant main effects of *task* ($p < 0.0001$). These results indicate selective contributions of L. DPFC and L. IFG to sentence comprehension.

Discussion

In the present study, we identified two regions in the left prefrontal cortex that showed selective activations for syntactic processing involved in sentence comprehension: L. DPFC and L. IFG. Previous imaging studies have reported that L. IFG activation increased with syntactic complexity of a sentence (Stromswold et al., 1996; Just et al., 1996). However, two contrasting positions have been based on these similar findings. While Stromswold et al. (1996) attributed their results to demands made on a specialized working memory system (i.e., a modular interpretation), Just et al. (1996) attributed their results to demands made on a general-purpose verbal working memory system (i.e., a nonmodular interpretation). According to the nonmodular view, activations of L. DPFC and L. IFG have been attributed to the executive processes for working memory or cognitive demands in general (Smith and Jonides, 1999; Duncan and Owen, 2000). In contrast, our previous imaging study showed syntax-selective activation of L. IFG, even

when syntactic complexity (using identical sentences) as well as cognitive demands was approximately equated in each of contrasting tasks (Embick et al., 2000). The present study demonstrates specialization in the prefrontal cortex for sentence comprehension by directly comparing syntactic decision tasks and verbal short-term memory tasks.

A number of previous imaging studies on verbal working memory have interpreted greater activation of the prefrontal regions as reflecting general task difficulty stemming from memory load (Braver et al., 1997; Cohen et al., 1997; Rypma et al., 1999) or delay intervals (Barch et al., 1997). Chein and Fiez (2001) suggested that DLPFC plays a more prominent role in nonverbal (domain-independent) mnemonic factors that affect task difficulty, which is consistent with the absence of its activation in the present study. The prefrontal regions have been also suggested to be involved in effortful mnemonic retrieval of verbal information (Petrides et al., 1995; Buckner et al., 1998). In the present study, L. DPFC (rather than L. DLPFC) showed larger responses to STM-S than STM-W. As to task difficulty as well as employment of the subvocal rehearsal system, STM-S was less demanding than STM-W, as demonstrated by behavioral data. The following cognitive factors were thoroughly equated between STM-S and STM-W: word recognition, mnemonic encoding and retrieval of “what” and “when” information, the verbal memory load (the number of verbal items held in the phonological store), delay intervals (immediate recall after the sequential presentation of five phrases), and recency judgments. Therefore, only remaining factors for explaining selective activation of L. DPFC for STM-S are processes of analyzing syntactic structures as well as the selection and integration of semantic information during sentence comprehension. It is still possible that L. DPFC activation can be modulated by task difficulty in general, but our results clearly established that sentence processing is a much more prominent factor for the activation of L. DPFC.

By the comparisons between the SYN tasks and the STM tasks, we consistently observed that L. IFG was selectively activated when the use of syntactic rules was explicitly required by the SYN tasks. Although the SYN tasks and STM-S involved syntactic processing of the same sentences, only the SYN tasks explicitly required employment of syntactic rules in sentence comprehension. It is possible that structure-dependent computations performed in L. IFG was not fully evoked by STM-S, because the task directed attention to the linear order of words rather than structure-dependent relationships. According to a previous imaging study, it has been proposed that verbal-specific difficulty modulates the activation of the left prefrontal cortex (BAs 44 and 6) (Chein and Fiez, 2001). In the present study, however, the SYN tasks showed larger responses in L. IFG than the most demanding STM-W. Furthermore, SYN-1 and SYN-2 showed comparable responses (Figure 3B), although SYN-2 was a more difficult task than SYN-1. Therefore, we conclude that L. IFG activation in the present study reflects explicit recruitment of syntactic rules rather than verbal executive processes imposed by task difficulty.

Previous imaging studies have proposed that the subregions in the left prefrontal cortex are involved in differ-

ent aspects of language processing. There has been a proposal of anterior (BA 45/47) and posterior (BA 44/45) prefrontal regions as reflecting semantic and phonological/lexical processing, respectively (Poldrack et al., 1999). On the other hand, L. IFG (BA 44/45) has been suggested to be selectively involved in syntactic processing (Dapretto and Bookheimer, 1999; Embick et al., 2000), which is consistent with the L. IFG activation in the present study. It should be noted that L. IFG and L. DPFC (BA 9) are also activated in syntactic tasks independent of lexico-semantics (Friederici et al., 2000; Indefrey et al., 2001; Moro et al., 2001). Recently, we found that the left BA 45/47 is involved in the selection and integration of semantic information during sentence comprehension that are separable from lexico-semantic processing (Homae et al., 2002). Because this region barely overlaps with the extent of activated regions in Figure 2B, we suggest that major roles of L. DPFC and L. IFG in the present study may be also distinct from semantic aspects of sentence comprehension.

Although individual roles of L. DPFC and L. IFG in sentence comprehension remain to be clarified by future studies, selective contributions of these regions to the present tasks are intriguing. Compared with STM-W, L. DPFC was activated not only by the SYN tasks but also by STM-S in which syntactic information is processed without explicit instructions. In contrast, L. IFG was activated only when the explicit use of syntactic rules was required by the SYN tasks. Specific task demands would play a critical role for the present findings, as we have recently demonstrated the impact of syntactic demands on sentence processing (Embick et al., 2000). It may be that L. DPFC is sensitive to the presence of sentence processing in STM-S and that further syntactic demands of the SYN tasks may recruit L. IFG in addition to L. DPFC. As to the requirements of the two STM tasks, one difference lies in the aspect of case marking; noun phrases in STM-S were always case marked correctly in a sentence, whereas all three noun phrases in STM-W were marked with the same case marker. Participants had to encode and retrieve the case marking for each noun phrase in STM-S, while case marking in STM-W can be encoded only once. Thus the activation of L. DPFC in STM-S – STM-W could be due to the conscious encoding and retrieval of either case or thematic information, which is more demanding in STM-S than STM-W. Compared with STM-S, this process may be more demanding for sentence comprehension explicitly required by the SYN tasks.

Linguistic computations based on structure-dependent syntactic rules involve organizing and maintaining transient representations of combinations of words and phrases. Both L. DPFC and L. IFG showed larger activation for the SYN tasks than STM-S (Figure 2C), probably because the SYN tasks required more of such syntactic computations than STM-S. Interestingly, a previous imaging study suggested that the activation of L. DLPFC (BA 9/46, close to our L. DPFC) reflects the creation of an organizational structure (Fletcher et al., 1998). This result is consistent with our study, in that syntactic processing also involves processes for organization, such as combining words into phrases and sentences. Our results further suggest that these organization processes may proceed obligatorily in syntactic pro-

cessing, as involved in STM-S, without intentional efforts to create artificial organizational structures. Furthermore, syntax-selective activation of L. IFG (BA45), which is close to our L. IFG, has been reported in a recent imaging study (Caplan et al., 1999), suggesting that its activation reflects syntactic complexity of sentences. Our hypothesis is consistent with this suggestion, in that the L. IFG activation is attributable to structure-dependent computations of sentences.

We observed several other regions that were involved in nonsyntactic processing. In the contrast of STM-W – STM-S, the left precentral gyrus, the left parietal operculum, and the right anterior cingulate cortex showed selective responses to STM-W. A previous imaging study has indicated that the region implicated in subvocal rehearsal or phonological processing extends into the left precentral gyrus and the left parietal operculum (Paulesu et al., 1993). According to another imaging study, which segregated semantic components and phonological components involved in reading words, phonological processing has been associated with the left precentral gyrus (Price et al., 1997). Thus, activation of these Rolandic operculum regions may reflect involvement of intense articulatory rehearsal in memorizing lists of syntactically unrelated phrases. On the other hand, it has been shown that the anterior cingulate cortex is involved in performance monitoring that is engaged in control of conflicting or competitive responses (Botvinick et al., 1999; Barch et al., 2000). Selective activation of this region for STM-W may reflect such processes induced by task difficulty. In the contrast of STM-W – (SYN-1 + SYN-2), we observed STM-W-selective activation in the bilateral lingual gyrus and the right cuneus. Similarly, in the contrast of STM-S – (SYN-1 + SYN-2), we observed STM-S selective activation in the bilateral lingual gyrus and the right posterior parietal cortex. Some of these regions were shown to be selectively involved in verbal short-term memory tasks with recency judgment (Cabeza et al., 1997; Marshuetz et al., 2000). Therefore, STM-selective activation of these regions is likely to reflect mnemonic processes for temporal order of verbal items, especially required in the STM tasks.

Conclusion

The present study demonstrated that there exist neural systems in the left prefrontal cortex specialized for sentence comprehension: L. DPFC and L. IFG. The activation of these regions is related to processes of analyzing syntactic structures, and it cannot be explained either by task difficulty or by verbal working memory components, such as the phonological store, the subvocal rehearsal system, and the central executive. Moreover, these cortical regions are affected differently by the conditions that are required when one recalls the serial order of words either in a sentence or in a scrambled series of words, and when one makes syntactic judgments on a sentence. We also clarified that there is a further distinction between unconscious, obligatory sentence processing and conscious, controlled sentence processing. Linguists have provided a clear conceptualization of what distinctions need to be made between syntactic processing and other cognitive processes in order

to account for linguistic competence (Chomsky, 1980). We believe that identification of cortical regions responsible for the essential properties of syntactic processing eventually leads to understanding how language is specialized and instantiated in the human brain.

Experimental Procedures

Participants

Sixteen male native Japanese speakers (ages 18–37) participated in the present study. All but one participant showed right handedness. During the study, participants wore prism glasses and earplugs, and were in a supine position in the magnet, while the participant's head was immobilized with padding inside the radio-frequency coil. Informed consent was obtained from each participant after the nature and possible consequences of the studies had been explained. Approval for these experiments was obtained from the institutional review board of the University of Tokyo, Komaba.

Stimuli and Tasks

As shown in Figure 1, we presented each word in yellow letters in *hiragana* and *kanji* against a dark background (maximum visual angle, $1.5^\circ \times 12^\circ$ for a pair of phrases). The visual stimuli were always presented at the center of the screen. Participants read the stimuli covertly through prism glasses. Each sentence was a center-embedded sentence that included two proper nouns (names), two verbs, and one pronoun. The sentence set consisted of six types of grammatical collocations as follows; [N₁-*wa* N₂-*ga* P-*wo* V₁-*to* V₂], [N₁-*ga* N₂-*ni* P-*ga* V₁-*to* V₂], [N₁-*ni* N₂-*ga* P-*wo* V₁-*to* V₂], [N₁-*ga* P-*wo* V₁-*to* N₂-*ni* V₂], [N₁-*ga* P-*wa* N₂-*to* V₁-*to* V₂], and [N₁-*ga* P-*ni* V₁-*to* N₂-*ni* V₂] (N, proper noun; V, verb; P, pronoun; -*ga*, nominative or accusative marker; -*wa*, topic marker; -*ni*, dative marker; -*wo*, accusative marker; N₂-*to*, postposition “with N₂”; and V₁-*to*, complementizer “that V₁”) (Tsujimura, 1996). For each type, we prepared twelve sentences that contained different lexical items. Because -*ga* can mark either nominative or accusative case, participants had to analyze syntactic structures for assigning a thematic role to each noun phrase.

In SYN-1, participants were asked to judge whether the subject of an underlined verb corresponded to the person in paired words. The underlined verb was presented again in the paired words. In SYN-2, participants judged whether an underlined pronoun was able to refer to the person in paired words. The underlined pronoun was presented again in the paired words, and it had only one possible sentence-internal antecedent. Participants responded by pressing yes/no buttons. These tasks were further controlled by the following conditions. With the presence of an embedded clause, the subject and verb were not always adjacent in a sentence as a result of the Japanese word order of subject-object (an embedded clause)-verb. An underlined pronoun was either the pronominal *kare/kanjo* (he/she, him/her in English) or the reflexive *zibunzishin* (himself/herself in English), with the pronominal and reflexive referring to different people when occurring in the same position. In the example shown in Figure 1A, when *him* is replaced with *himself*, the reflexive *himself* refers to *Saburo*, whom the pronominal *him* cannot refer to (Haegeman, 1994; Tsujimura, 1996).

In STM-S, participants were presented with the same set of sentences used in the SYN tasks and were asked to memorize each sentence. Paired phrases including an underlined phrase were presented, and participants judged whether the left phrase preceded the right one in the original sequence or not. The paired phrases were always adjacent in the original sequence. Participants responded by pressing yes/no buttons. In STM-W, participants were presented with nouns and verbs separately that were used in a sentence and were asked to memorize individual phrases within either noun or verb group. We added the Japanese case marker of -*wo* (accusative) or -*ni* (dative) to all of the three nouns, so that one noun had no syntactic relationship with the other nouns and verbs, while the number of phonological units was equated between STM-W and the other three tasks. Paired phrases (no underlined phrase in STM-W) were presented, and participants judged whether the left phrase preceded the right one in the original sequence or not. The

paired phrases were always adjacent in the noun or verb group. To control the serial position effect on memory recall, the randomized positions of paired phrases within the original sequence were equated between STM-S and STM-W. In one out of six trials of the STM tasks, we presented paired phrases with a different case marker for nouns or a different tense for verbs, to which participants were to respond “No.” As a result of this procedure, participants had to memorize whole phrases as well as phrase orders.

Participants underwent practice sessions before scanning so that they were fully familiarized with each task. Furthermore, the task label was presented at the initiation of each trial (see Figure 1A) to exclude the possible ambiguity or conflict caused by task transitions. The four tasks were conducted in a conventional block design of fMRI. One trial with a fixed duration of 6 s was repeated six times in each task block. STM-W served as a baseline task of a single scanning session, in which STM-W and each of SYN-1, SYN-2, and STM-S were alternatively presented (seven blocks per session). All sentences were different within each session. We prepared three types of sessions, each using a different order of tasks: SYN-1, SYN-2, STM-S; SYN-2, STM-S, SYN-1; and STM-S, SYN-1, SYN-2. We tested 12 sessions (four sessions for each type) for each participant, and the order of tasks was counterbalanced within and across participants.

Imaging and Data Analyses

The fMRI scans were conducted using a 1.5 T scanner (Stratus II, Premium, Hitachi Medical Corporation, Tokyo, Japan). We scanned over 15 horizontal slices, each 6 mm thick, covering from $z = -24$ to 66 mm, with a gradient echo echo-planar imaging sequence (repetition time, 3 s; echo time, 50 ms; flip angle, 90°; field of view, 192×192 mm²; resolution, 3×3 mm²). High-resolution structural T1-weighted images were also acquired from all participants in order to permit anatomical localization of activation foci. For analyses of functional data, we used statistical parametric mapping software (SPM99, Wellcome Department of Cognitive Neurology, London, UK). The data were realigned, spatially normalized to the standard brain space, resampled every 3 mm using sinc interpolation, and smoothed with an isotropic Gaussian kernel of 8 mm full width at half maximum. Low-frequency noise and global changes in activity were further removed. Task-specific effects were estimated using a general linear model with a delayed (6 s) boxcar waveform. For random effects analyses, a contrast image between tasks was generated for each participant and used for intersubject comparisons. A statistical threshold was set to $p < 0.05$, corrected for multiple comparisons.

Acknowledgments

This work was supported by a Core Research for Evolutional Science and Technology (CREST) grant from Japan Science and Technology Corporation and by a Young Investigators' Grant from Human Frontier Science Program (HFSP) to K.L.S. We would like to thank Yasushi Miyashita for encouragement; Colin Phillips, Christopher Tancredi, and Noriaki Yahata for critical comments; Alec Marantz, David Poeppel, and David Embick for comments on the earlier draft; David Caplan and Michael W.L. Chee for helpful discussion; Fumitaka Homae, Kei Suzuki, Yasuki Hashimoto, and Yasuki Noguchi for technical assistance; and Hiromi Matsuda for administrative assistance.

Received: December 13, 2001

Revised: May 13, 2002

References

- Baddeley, A. (1992). Working memory. *Science* 255, 556–559.
- Baker, M.C. (2001). *The Atoms of Language* (New York: Basic Books).
- Barch, D.M., Braver, T.S., Nystrom, L.E., Forman, S.D., Noll, D.C., and Cohen, J.D. (1997). Dissociating working memory from task difficulty in human prefrontal cortex. *Neuropsychologia* 35, 1373–1380.
- Barch, D.M., Braver, T.S., Sabb, F.W., and Noll, D.C. (2000). Anterior

- cingulate and the monitoring of response conflict: evidence from an fMRI study of overt verb generation. *J. Cogn. Neurosci.* 12, 298–309.
- Botvinick, M., Nystrom, L.E., Fissell, K., Carter, C.S., and Cohen, J.D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature* 402, 179–181.
- Braver, T.S., Cohen, J.D., Nystrom, L.E., Jonides, J., Smith, E.E., and Noll, D.C. (1997). A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage* 5, 49–62.
- Buckner, R.L., Koutstaal, W., Schacter, D.L., Wagner, A.D., and Rosen, B.R. (1998). Functional-anatomic study of episodic retrieval using fMRI. I. Retrieval effort versus retrieval success. *Neuroimage* 7, 151–162.
- Bunge, S.A., Klingberg, T., Jacobsen, R.B., and Gabrieli, J.D.E. (2000). A resource model of the neural basis of executive working memory. *Proc. Natl. Acad. Sci. USA* 97, 3573–3578.
- Cabeza, R., Mangels, J., Nyberg, L., Habib, R., Houle, S., McIntosh, A.R., and Tulving, E. (1997). Brain regions differentially involved in remembering what and when: a PET study. *Neuron* 19, 863–870.
- Caplan, D., and Waters, G.S. (1999). Verbal working memory and sentence comprehension. *Behav. Brain Sci.* 22, 77–126.
- Caplan, D., Alpert, N., and Waters, G. (1999). PET studies of syntactic processing with auditory sentence presentation. *Neuroimage* 9, 343–351.
- Chen, J.M., and Fiez, J.A. (2001). Dissociation of verbal working memory system components using a delayed serial recall task. *Cereb. Cortex* 11, 1003–1014.
- Chomsky, N. (1980). *Rules and Representations* (New York: Columbia University Press).
- Chomsky, N. (1984). *Modular Approaches to the Study of the Mind* (San Diego, CA: San Diego State University Press).
- Clark, C.R., Egan, G.F., McFarlane, A.C., Morris, P., Weber, D., Sonkikilla, C., Marcina, J., and Tochon-Danguy, H.J. (2000). Updating working memory for words: a PET activation study. *Hum. Brain Mapp.* 9, 42–54.
- Cohen, J.D., Forman, S.D., Braver, T.S., Casey, B.J., Servan-Schreiber, D., and Noll, D.C. (1994). Activation of the prefrontal cortex in a nonspatial working memory task with functional MRI. *Hum. Brain Mapp.* 1, 293–304.
- Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J., and Smith, E.E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature* 386, 604–608.
- Coltheart, M. (1999). Modularity and cognition. *Trends Cogn. Sci.* 3, 115–120.
- Comrie, B. (1989). *Language Universals and Linguistic Typology* (Chicago: The University of Chicago Press).
- Cooke, A., Zurif, E.B., De Vita, C., Alsop, D., Koenig, P., Detre, J., Gee, J., Pinango, M., Balogh, J., and Grossman, M. (2002). Neural basis for sentence comprehension: grammatical and short-term memory components. *Hum. Brain Mapp.* 15, 80–94.
- Dapretto, M., and Bookheimer, S.Y. (1999). Form and content: dissociating syntax and semantics in sentence comprehension. *Neuron* 24, 427–432.
- Dick, F., Bates, E., Wulfeck, B., Utman, J.A., Dronkers, N., and Gernsbacher, M.A. (2001). Language deficits, localization, and grammar: evidence for a distributive model of language breakdown in aphasic patients and neurologically intact individuals. *Psychol. Rev.* 108, 759–788.
- Duncan, J., and Owen, A.M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends Neurosci.* 23, 475–483.
- Embick, D., Marantz, A., Miyashita, Y., O'Neil, W., and Sakai, K.L. (2000). A syntactic specialization for Broca's area. *Proc. Natl. Acad. Sci. USA* 97, 6150–6154.
- Fiebach, C.J., Schlesewsky, M., and Friederici, A.D. (2001). Syntactic working memory and the establishment of filler-gap dependencies: insights from ERPs and fMRI. *J. Psycholinguist. Res.* 30, 321–338.
- Fiez, J.A., Raife, E.A., Balota, D.A., Schwarz, J.P., Raichle, M.E., and Petersen, S.E. (1996). A positron emission tomography study of the short-term maintenance of verbal information. *J. Neurosci.* 16, 808–822.
- Fletcher, P.C., Shallice, T., and Dolan, R.J. (1998). The functional roles of prefrontal cortex in episodic memory. I. Encoding. *Brain* 121, 1239–1248.
- Fodor, J.A. (1983). *The Modularity of Mind* (Cambridge, MA: The MIT Press).
- Friederici, A.D., Pfeifer, E., and Hahne, A. (1993). Event-related brain potentials during natural speech processing: effects of semantic, morphological and syntactic violations. *Cogn. Brain Res.* 1, 183–192.
- Friederici, A.D., Meyer, M., and von Cramon, D.Y. (2000). Auditory language comprehension: an event-related fMRI study on the processing of syntactic and lexical information. *Brain Lang.* 74, 289–300.
- Gunter, T.C., and Friederici, A.D. (1999). Concerning the automaticity of syntactic processing. *Psychophysiology* 36, 126–137.
- Haegeman, L. (1994). *Introduction to Government and Binding Theory* (Oxford: Blackwell Publishers Ltd).
- Homae, F., Hashimoto, R., Nakajima, K., Miyashita, Y., and Sakai, K.L. (2002). From perception to sentence comprehension: the convergence of auditory and visual information of language in the left inferior frontal cortex. *Neuroimage* 16, 883–900.
- Indefrey, P., Hagoort, P., Herzog, H., Seitz, R.J., and Brown, C.M. (2001). Syntactic processing in left prefrontal cortex is independent of lexical meaning. *Neuroimage* 14, 546–555.
- Just, M.A., and Carpenter, P.A. (1992). A capacity theory of comprehension: individual differences in working memory. *Psychol. Rev.* 99, 122–149.
- Just, M.A., Carpenter, P.A., Keller, T.A., Eddy, W.F., and Thulborn, K.R. (1996). Brain activation modulated by sentence comprehension. *Science* 274, 114–116.
- Kang, A.M., Constable, R.T., Gore, J.C., and Avrutin, S. (1999). An event-related fMRI study of implicit phrase-level syntactic and semantic processing. *Neuroimage* 10, 555–561.
- Kluender, R., and Kutas, M. (1993). Bridging the gap: evidence from ERPs on the processing of unbounded dependencies. *J. Cogn. Neurosci.* 5, 196–214.
- Marshuetz, C., Smith, E.E., Jonides, J., DeGutis, J., and Chenevert, T.L. (2000). Order information in working memory: fMRI evidence for parietal and prefrontal mechanisms. *J. Cogn. Neurosci.* 12, 130–144.
- Martin, R.C. (1987). Articulatory and phonological deficits in short-term memory and their relation to syntactic processing. *Brain Lang.* 32, 159–192.
- Martin, R.C. (1993). Short-term memory and sentence processing: Evidence from neuropsychology. *Mem. Cognit.* 21, 176–183.
- McCarthy, R.A., and Warrington, E.K. (1987). The double dissociation of short-term memory for lists and sentences: evidence from aphasia. *Brain* 110, 1545–1563.
- Milner, B., Corsi, P., and Leonard, G. (1991). Frontal-lobe contribution to recency judgements. *Neuropsychologia* 29, 601–618.
- Moro, A., Tettamanti, M., Perani, D., Donati, C., Cappa, S.F., and Fazio, F. (2001). Syntax and the brain: disentangling grammar by selective anomalies. *Neuroimage* 13, 110–118.
- Munte, T.F., Heinze, H.-J., and Mangun, G.R. (1993). Dissociation of brain activity related to syntactic and semantic aspects of language. *J. Cogn. Neurosci.* 5, 335–344.
- Neville, H., Nicol, J.L., Barsz, A., Forster, K.I., and Garrett, M.F. (1991). Syntactically based sentence processing classes: evidence from event-related brain potentials. *J. Cogn. Neurosci.* 3, 151–165.
- Newman, A.J., Pancheva, R., Ozawa, K., Neville, H.J., and Ullman, M.T. (2001). An event-related fMRI study of syntactic and semantic violations. *J. Psycholinguist. Res.* 30, 339–364.
- Paulesu, E., Frith, C.D., and Frackowiak, R.S.J. (1993). The neural correlates of the verbal component of working memory. *Nature* 362, 342–345.
- Petrides, M., Alivisatos, B., and Evans, A.C. (1995). Functional activation of the human ventrolateral frontal cortex during mnemonic retrieval of verbal information. *Proc. Natl. Acad. Sci. USA* 92, 5803–5807.

- Poldrack, R.A., Wagner, A.D., Prull, M.W., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage* 10, 15–35.
- Potter, M.C. (1993). Very short-term conceptual memory. *Mem. Cognit.* 21, 156–161.
- Price, C.J., Moore, C.J., Humphreys, G.W., and Wise, R.J.S. (1997). Segregating semantic from phonological processes during reading. *J. Cogn. Neurosci.* 9, 727–733.
- Rösler, F., Pechmann, T., Streb, J., Röder, B., and Hennighausen, E. (1998). Parsing of sentences in a language with varying word order: word-by-word variations of processing demands are revealed by event-related brain potentials. *J. Mem. Lang.* 38, 150–176.
- Rypma, B., Prabhakaran, V., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1999). Load-dependent roles of frontal brain regions in the maintenance of working memory. *Neuroimage* 9, 216–226.
- Sakai, K.L., Hashimoto, R., and Homae, F. (2001). Sentence processing in the cerebral cortex. *Neurosci. Res.* 39, 1–10.
- Shallice, T. (1988). *From Neuropsychology to Mental Structure* (Cambridge, UK: Cambridge University Press).
- Smith, E.E., and Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science* 283, 1657–1661.
- Smith, N., and Tsimpli, I.-M. (1995). *The Mind of a Savant: Language Learning and Modularity* (Oxford: Blackwell Publishers).
- Stromswold, K., Caplan, D., Alpert, N., and Rauch, S. (1996). Localization of syntactic comprehension by positron emission tomography. *Brain Lang.* 52, 452–473.
- Tsujimura, N. (1996). *An Introduction to Japanese Linguistics* (Cambridge, MA: Blackwell Publishers).
- Vos, S.H., Gunter, T.C., Kolk, H.H.J., and Mulder, G. (2001). Working memory constraints on syntactic processing: an electrophysiological investigation. *Psychophysiology* 38, 41–63.
- Waters, G.S., Caplan, D., and Hildebrandt, N. (1991). On the structure of verbal short-term memory and its functional role in sentence comprehension: evidence from neuropsychology. *Cogn. Neuropsychol.* 8, 81–126.
- Waters, G.S., Caplan, D., and Rochon, E. (1995). Processing capacity and sentence comprehension in patients with Alzheimer's disease. *Cogn. Neuropsychol.* 12, 1–30.