Effects of Age and Speed of Processing on rCBF Correlates of Syntactic Processing in Sentence Comprehension

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Abstract: Positron emission tomography (PET) was used to determine the effect of age on regional cerebral blood flow (rCBF) during syntactic processing in sentence comprehension. PET activity associated with making plausibility judgments about syntactically more complex subject object (SO) sentences (e.g., *The juice that the child spilled stained the rug*) was compared to that associated with making judgments about synonymous syntactically simpler object subject (OS) sentences (e.g., *The child spilled the juice that stained the rug*). In the first study, 13 elderly (70–80-year-old) subjects showed increased rCBF in the left inferior parietal lobe. This result contrasted with previous studies, which have shown activation in Broca's area in this task in young subjects. Elderly subjects were noted to have longer reaction times than young subjects previously tested. A second study found that young subjects whose reaction times were as long as those of the elderly subjects tested in Experiment 1 activated left superior parietal, and not left inferior frontal, structures. A third experiment found that elderly subjects with reaction times as fast as previously tested young subjects activated left inferior frontal structures. The results suggest that the speed of syntactic processing, but not age per se is related to the neural location where one aspect of syntactic processing is carried out. *Hum. Brain Mapping 19:112–131, 2003.* © 2003 Wiley-Liss, Inc.

Key words: speed of processing; age; syntactic comprehension; rCBF

INTRODUCTION

The ability to determine the semantic relationships between the words in a sentence (the sentence's propositional content) is central to normal comprehension of language. The syntactic structure of a sentence is the principal determinant of how the meanings of the words in a sentence are related to each other [Chomsky, 1965, 1981, 1986, 1995], and there is near universal agreement that, when normal language users understand sentences, they construct syntactic structures as part of this process [Frazier and Clifton, 1996; Just and Carpenter, 1992; MacDonald et al., 1994]. The process

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whereby syntactic structures are constructed is a distinctly human, abstract, cognitive function and, as such, its neural basis is of interest.

There is very strong evidence from both the effects of lesions on syntactic processing and from correlations between metabolic and electrophysiological brain activity with syntactic processing that the assignment of syntactic form and its use in determining meaning is largely carried out in the dominant perisylvian association cortex [for review see Caplan, 2002]. There is disagreement about how the perisylvian association cortex is organized to support syntactic comprehension. Different researchers endorse strongly localizationist models [Grodzinsky, 1990, 1995, 2000; Swinney and Zurif, 1995; Zurif et al., 1993], distributed models [Bates and Goodman, 1997; Damasio, 1992; Dick et al., 2001; Mesulam, 1990] and models that postulate individual variability in the neural substrate for this function [Caplan, 1987, 1994; Caplan et al., 1985, 1996]. Localizationist models have focused on Broca's area as the locus of all or part of syntactic processing. Distributed models have argued that the entire perisylvian association cortex constitutes a neural net in which this function takes place. In some versions of distributed models [e.g., Mesulam, 1990], one region within this area, Broca's area, is thought to play a more important role than other parts of this area in this function. Other versions of distributed models [e.g., Dick et al., 2001] claim that syntactic processing takes place throughout this area. Researchers who postulate individual variability maintain that different individuals use different parts of this cortex to process syntax, or different parts of syntax.

Deficit-lesion correlational studies have provided data regarding these models. Deficits in syntactic comprehension occur in all aphasic syndromes [Berndt et al., 1996; Caplan et al., 1985, 1997] and following lesions throughout the perisylvian cortex [Caplan et al., 1996]. Conversely, patients of all types and with all lesion locations have been described with normal syntactic comprehension [Caplan et al., 1985; Caplan, 1987]. The fact that lesions throughout the perisylvian cortex are associated with syntactic processing deficits and that there is no clear relationship between these lesions or aphasic syndromes and these deficits is incompatible with localizationist models. The finding of spared comprehension after strokes in all parts of the perisylvian association cortex is also hard to reconcile with distributed models, since these models predict that there should be some degree of syntactic impairment after any perisylvian lesion. The data are most compatible with an individual variability model, and constitute the main reason that such a model has been postulated [Caplan, 1987, 1994; Caplan et al., 1985, 1996].

Despite this evidence for variability in the localization of syntactic processing in comprehension, advocates of localizationist models have argued that the deficit-lesion correlational data are consistent with the localization of one syntactic operation in and around Broca's area [Grodzinsky, 2000; Swinney and Zurif, 1995; Swinney et al., 1996; Zurif et al., 1993]. This operation connects noun phrases to distant grammatical positions that determine their thematic roles. For instance, the head noun of a relative clause is related to a grammatical position in the relative clause that determines the role it plays around the verb of the relative clause. This is illustrated in sentence 1, in which *the boy* is related to the position of the object of the verb *chased* (marked by ***t***, standing for "trace," in Chomsky's [1981, 1986, 1995] syntactic theory) and plays the thematic role of theme of *chased.*

1. The boy who the girl chased ***t*** fell down

The claim that this operation connecting noun phrases to distant syntactic positions, called "the co-indexation of traces," only occurs in Broca's area is hotly contested. In our view, the evidence from deficit-lesion correlations does not support this hypothesis [for discussion, see Caplan, 1995, 2000, 2001, 2002].

Functional neuroimaging results using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have begun to provide evidence regarding the neural basis for sentence comprehension and, more specifically, regarding the organization of the perisylvian cortex for syntactic processing.

Several functional neuroimaging studies have compared sentences to fixation, a list of words, or another type of non-sentential stimulus [e.g., Bavelier et al., 1997; Chee et al., 1999; Grossman et al., 2002; Mazoyer et al., 1993; Stowe et al., 1994, 1998]. Overall, these studies indicate that sentence comprehension involves the dominant hemisphere, and suggest that areas both within and outside the perisylvian cortex may be involved in this function. However, these experiments do not isolate syntactic processing and their implications for the functional neuroanatomy of syntactic processing are, therefore, limited.

A number of controlled experiments have focused more narrowly on syntactic processing. Using PET, Stromswold et al., [1996] reported an increase in rCBF in Broca's area when eight right-handed young male subjects made plausibility judgments about written sentences with complex subject object (SO) relative clauses (e.g., *The juice that the child spilled stained the rug*) compared to sentences with simpler object subject (OS) relative clauses (e.g., *The child spilled the juice that stained the rug*). Caplan et al. [1998] replicated this result in eight right-handed young females, and Caplan et al. [1999] found a similar result with auditory presentation comparing cleft object (CO) sentences (e.g., *It was the juice that the child spilled*) with cleft subject (CS) sentences (e.g., *It was the child that spilled the juice*). Caplan et al. [2000] reported that the increase in rCBF in Broca's area with visually presented SO and OS sentences was not eliminated by concurrent articulation, suggesting that the role of Broca's area is not simply to rehearse the complex sentences more than the simple ones but is likely to be related to abstract aspects of syntactic processing of the more complex sentences. Using fMRI, Just et al. [1996] had subjects read simple conjoined (CON), more complex subject–subject (SS), and most complex subject–object (SO) sentences, and then verify assertions about these sentences. They found that BOLD signal increased in Broca's area when the sentences contained complex relative clauses. Dapretto and Bookheimer [1999] found an increase in BOLD signal in Broca's area in a synonymity judgment task in which subjects were to say that the sentences were the "same" if the thematic roles (agent of the verb, theme of the verb, theme of a preposition) did not differ between an active and a passive sentence (e.g., *The policeman arrested the thief, The thief was arrested by the policeman*) compared to a baseline in which active and passive sentences were evaluated for synonymous words. Cooke et al. [2001] found increases in BOLD signal in left inferior frontal lobe when subjects made judgments regarding the gender of the agent in object relativized (SO) sentences in which an appositive phrase occurred after the embedded subject compared to subject relativized (SS) sentences without such phrases. All these studies reported increases in rCBF or BOLD signal in Broca's area in association with processing sentences in which syntactic processing, in particular the co-indexation of traces, is more demanding.

However, not all experiments have produced activation in Broca's area, or exclusively in Broca's area, in association with syntactic processing and sentences in which the co-indexation of traces is more demanding. In the Just et al. [1996] study, there was also an increase in BOLD signal in Wernicke's area of the left hemisphere, as well as smaller but reliable increases in rCBF in the homologous regions of the right hemisphere, when subjects were presented with the more complex sentences (SO and SS compared to Conjoined sentences). Using event-related fMRI and a plausibility judgment task with word-by-word visual sentence presentation, Caplan et al. [2001] found increased BOLD signal in the left inferior parietal lobe in association with presentation of the relative clause in SO compared to SS sentences. Cooke et al. [2001] found increases in BOLD signal in left and right inferior temporal lobe in the gender-judgment task for object relativized (SO) sentences compared to subject relativized (SS) sentences when appositive phrases did not occur in the sentences. Overall, the activation literature provides more convincing support for localization in Broca's area of one aspect of syntactic processing—one or more operations and/or a memory system related to processing traces—than the deficit-lesion correlational literature does, but still shows some degree of variability in patterns of activation.

There are many possible reasons for differences between the results of different studies. Focusing on the functional neuroimaging literature, differences in task demands may have affected patterns of vascular responsivity to syntactic processing [for discussion see Caplan et al., 2001]. Comparing the deficit-lesion correlational and functional neuroimaging literatures, a major difference is the populations that have been studied. Activation studies have been carried out exclusively in young subjects, while lesion studies have recruited stroke victims who are considerably older. Age-related changes have been documented in a variety of tasks [Cabeza et al., 1997; Grady et al., 1995] and may affect the linguistic disturbances seen after lesions [Joanette et al., 1983]. A mechanism that has been suggested whereby age could affect the neural basis of function is that age-related changes in a region that supports a function may lead to that function being taken over by another location [Cabeza et al., 1997]. Since age-related changes occur at different rates in different brain regions in different individuals, this type of re-organization would be expected to occur to different degrees in different subjects. In addition, individual differences in age-related changes in the brain would lead to differences in the ability of other brain regions to support a function. The end result of these factors would be a more variable pattern of localization of function in an elderly than in a younger population, consistent with the degree to which the functional neuroimaging literature in young subjects and the deficit-lesion literature in elderly subjects have shown different degrees of variability in the localization of one aspect of syntactic processing.

Another factor that might affect the neural basis of syntactic processing is the level of proficiency of a subject. King and Kutas [1995] reported differences in electrophysiological responses (ERP components) to sentences with object relativized clauses in subjects who differed in the accuracy of their comprehension. Kutas and King [1999] suggested that the level of performance of their subjects may be related to working memory, and some studies have demonstrated differences in ERPs in syntactic processing as a function of working memory [Vos et al., 2001]. In turn, working memory capacity may reflect subjects' speed of processing information [Verhaeghen and Salthouse, 1997]. Both working memory and speed of processing show greater variability in older than in young subjects [Salthouse, 1996], suggesting that the larger variability seen in deficit-lesion correlational studies than in activation studies may be related to greater differences in these functional operational capacities in older individuals.

The studies undertaken here were initially directed at the question of whether the localization of syntactic processing differed in young and elderly subjects. In the course of the studies, the factor of speed of processing emerged as potentially relevant to the interpretation of the results that were obtained, and was subsequently explored. We report the series of studies in the order in which they were undertaken, beginning with the investigation of the effects of age.

EXPERIMENT 1

Experiment 1 was designed to determine whether the materials and methods used in previous PET studies with young subjects [Caplan et al., 1998, 2000, Stromswold et al., 1996], would yield the same rCBF results in an elderly population.

Methods

Subjects

Thirteen subjects (seven males and six females) participated after giving informed consent. Their mean age was 73.4 years (range: 70–79). Their mean number of years of education was 14.3 (range: 12–18), All subjects were native, monolingual English-speaking subjects, and were strongly right-handed with no first degree left-handed relatives. All had normal vision and hearing, and no positive neurological or psychiatric history.

Materials

The materials were those used in previous experiments [Caplan et al, 1998, 2000; Stromswold et al., 1996]. Subjects were scanned during two experimental conditions. Condition 1 contained sentences with subject object (SO) relative clauses (e.g., *The juice that the child spilled stained the rug*) and condition 2 contained sentences with object subject (OS) relative clauses (e.g., *The child spilled the juice that stained the rug*). All sentences contained verbs that required that a noun in either subject or object position be either animate or inanimate. Half of the sentences in each condition were semantically plausible sentences that obeyed this restriction, and half were semantically implausible sentences that violated this restriction (e.g., the SO sentence **The child that the juice spilled stained the rug* or the OS sentence **The juice spilled the child that stained the rug*). Subjects were required to read each sentence and indicate whether it was plausible or not.

These sentence types were chosen as stimuli for PET experiments on syntactic processing for both theoretical and empirical reasons. Theoretically, the differences between SO and OS sentences that make for the increased complexity of the former are related to the co-indexation of the trace in the relative clause, and the contrast between these two sentence types is, therefore, relevant to a specific claim that has been articulated regarding the localization of one aspect of syntactic processing. There are a number of specific models that account for the increased processing load associated with SO compared to OS sentences in different ways [see Gibson, 1998]; this study was not designed to choose between these different explanations of the difficulty associated with structuring and understanding SO sentences, but rather capitalized on the existence of well-developed theories of the increased complexity associated with these sentences to create materials in which the demands of syntactic processing could be manipulated. Empirically, psycholinguistic research has indicated that normal subjects reliably make more errors and take longer to process SO sentences than OS sentences [Waters et al., 1987], and that they have longer reading and listening times at points in SO compared to SS and OS sentences at the points where parsing theories predict greater processing load [King and Just, 1991; Waters and Caplan, 2001]. These empirical results provide support for the theoretical models that have been proposed regarding processing these sentences.

A number of controls and counterbalances were introduced to ensure that the two conditions differed only on the syntactic dimension(s) outlined above, and that subjects did not adopt alternative strategies for judging the sentences.

1. Sentences were based on scenarios. There were a total of 144 scenarios (such as the scenario involving a child staining a rug by spilling juice onto it). Each scenario appeared once as an SO and once as an OS sentence, and the same words were used in each syntactic form of the scenario. The two versions of a scenario appeared in different PET blocks, and the order in which subjects saw the two versions of each scenario was counterbalanced across subjects. Because of this aspect of the design, differences in semantic goodness of scenarios, frequency of words, word choice, and order of presentation of scenarios could not be responsible for any differences in rCBF between the conditions.
2. The animacy of subject and object noun phrases and the plausibility of the sentences were systematically varied within block by sentence type. Thus, for example, the semantically plausible sentence *The patient that the drug cured thanked the doctor* and the semantically implausible sentence **The girl that the miniskirt wore horrified the nun* both contained an animate noun phrase, followed by an inanimate noun phrase, followed by an animate noun phase, and both appeared in a single block. This feature of the design was included to ensure that subjects could not make plausibility judgments on the basis of the sequence of animacy of the nouns.
3. All noun phrases were singular, common, and definite. This feature of the design was included to ensure that subjects would not be influenced by discourse effects (the referential assumptions made by the noun phrases in a sentence) in different ways in the two conditions.
4. Sentences became implausible at various points in the relative clauses and the main clauses. This feature was included to ensure that subjects had to read each sentence in its entirety before they could decide that it was plausible. Overall, the point at which SO sentences became implausible was earlier than the point at which OS sentences became implausible. This feature was included to eliminate the possibility that subjects could decide that an OS sentence was plausible at an earlier point than was possible in a SO sentence.

Behavioral testing procedure

The studies were carried out in the MGH PET imaging suite that has been designed to provide for control of ambient light, temperature, and noise level. PET scans were taken as subjects read and judged the plausibility of sentences presented visually in whole sentence format on a Macintosh Powerbook G3 computer screen. The computer screen rested on a shelf approximately 12 inches from the subject's eyes. After a 300-msec fixation point, a whole sentence appeared on a single line, subtending a visual angle of 20–25 degrees. This sentence remained on the computer screen until the subject responded. Subjects were instructed to indicate whether the sentence was plausible or not via key presses with two fingers of the left hand. Subjects were instructed to make plausibility judgments as quickly as possible without making errors. After a response, the screen was blank for 700 msec, followed first by the 300-msec fixation point, and then by the next sentence to be judged. Reaction time and error rate data were collected during PET scanning.

The two conditions were presented in blocked format, with each subject being presented each condition three times. Each block contained 48 items. Each subject saw three blocks of each sentence type. The order of presentation of blocks was counterbalanced across subjects in order to eliminate any effect of order of presentation on behavioral or PET data. At the beginning of the experiment, subjects were given six practice trials judging simple active sentences for semantic plausibility (e.g., *The child licks the lollipop*, **The lollipop licks the child*).

Image collection

Image collection began 15 sec into each experimental block, at a point when subjects were making judgments about the sentence types presented in that block. Subjects performed the judgment task throughout the period in which PET data was acquired, and for about 90 sec thereafter.

A General Electric Scanditronix PC4096 15 slice whole body tomograph was used in its stationary mode to acquire PET data. Data were acquired in 10 contiguous slices covering the forebrain with a center-to-center distance of 6.5 mm (axial field = 97.5 mm) and an axial resolution of 6.0-mm full width half maximum (FWHM), with a Hanning-weighted reconstruction filter set to yield 8.0-mm in-plane spatial resolution (FWHM). Subjects' heads were restrained in a custom-molded thermoplastic face mask, and aligned relative to the cantho-meatal line, using horizontal and vertical projected laser lines. Subjects inhaled ^{15}O-CO_2 gas by nasal cannulae within a face mask for 90 sec, reaching terminal count rates of 100,000 to 200,000 events per second. Previous work in our laboratory has demonstrated that the integrated counts over inhalation periods up to 90 sec are a linear function over the flow range 0 to 130 ml/min/100 g.

Image reconstruction

Each PET data acquisition block consisted of 20 measurements, the first three with 10-sec duration and the remaining 17 with 5-sec duration each. Scans 4–16 were summed after reconstruction to form images of relative blood flow. To minimize the effect of head movement during the experiment, the summed images from each subject were realigned using the first scan as the reference. Realignment parameters (translation and rotation) were determined using a least-squares fitting technique [Alpert et al, 1996]. Spatial normalization to the coordinate system of Talairach and Tournoux [1988] was performed by deforming the contour of the 10-mm parasagittal PET slice to match the corresponding slice of the reference brain [Alpert et al., 1993].

Statistical analyses

Following spatial normalization, scans were filtered with a two-dimensional Gaussian filter, full width at half maximum set to 20 mm. Statistical analysis followed the theory of Gaussian Random Fields for assigning *P* values to a *t* and z score that is implemented in statistical parametric mapping (SPM) software [Friston et al., 1991, 1995; Worsley et al., 1992, 1996]. Data were analyzed with SPM99 (from the Wellcome Dept. of Cognitive Neurology, London, UK). The PET data at each voxel (the unit volume of PET image resolution) was normalized by the global mean and fit to a linear statistical model with cognitive state (i.e., scan condition) considered as a main effect. Hypothesis testing was performed using the method of planned contrasts at each voxel. The resulting *t* values were converted to z scores, as is standard in the SPM approach. A z score was considered significant if it exceeded the z score significance threshold for a region of interest calculated by Worsley et al., [1996]. Random effects analyses of the z scores were used to identify regions in which rCBF was greater for one sentence type than for another, making no a priori assumptions about the location or direction of rCBF differences. Fixed effects analysis was used to identify regions in which rCBF was greater for one sentence type than for another, making the a priori assumption that rCBF was expected to be greater for SO than for OS sentences in left perisylvian and midline frontal ROIs. These a priori predictions were based upon the results of deficit–lesion correlational studies and functional neuroimaging studies reviewed above. As in previous studies, we report all z scores for the SO–OS contrast that were higher than z scores in these predicted ROIs. SO–OS differences in ROIs identified in these analyses were examined for direction for each scan for each subject. SO–OS differences in these ROIs were also correlated with reaction times on the plausibility judgments.

Results

Behavioral results

RTs for incorrect responses were discarded and RTs greater than 3 SD above and below the resulting condition means for each subject were replaced by that subject's condition means. The resulting data are shown in Figure 1. These data were analyzed in ANOVAs for the effects of block, which did not emerge as a main effect or in interaction with other variables. The reaction time (RT) and error (E) data were then analyzed in 2 (syntactic structure: SO vs. OS) × 2 (semantic plausibility: plausible vs. implausible) ANOVAs by subjects (F_1) and items (F_2). There was a main effect of sentence structure (F_{1RT} (1, 12) = 20.7, $P < .001$; F_{2RT} (1,284) = 9.0, $P < 0.01$; F_{1E} (1, 12) = 7.1, $P = 0.02$; F_{2E} (1, 284) = 9.6, $P < 0.01$). Responses were longer and less accurate for subject–object than for object–subject sentences. There was an interaction between sentence type and plausibility in the accuracy data (F_{1E} (1, 12) = 6.1, $P = 0.03$; F_{2E} (1, 284) = 9.7, $P < 0.01$). Subjects made more errors on implausible SO sentences than on the other sentence types.

rCBF results

Differences in rCBF between the SO and OS conditions were not significant in the random effects analysis. Table I and Figure 2 show the location of increases in rCBF associated with z scores that exceeded the threshold for significance in the fixed effect analysis for the SO–OS contrast. A significant increase in rCBF occurred in the left inferior parietal lobe (Brodmann's area 40). There was also an increase in rCBF in the superior frontal gyrus (Brodmann's area 10) just to the left of the midline. There were no areas in which rCBF decreased in the SO condition compared to the OS condition.

Nine of the 13 subjects showed rCBF effects in the expected direction in the left inferior parietal region, and nine in the superior frontal gyrus (six subjects showed effects in both). Correlations between reaction time for plausibility judgments and PET counts were not significant in these or other regions.

Discussion: Experiment 1

As expected, the behavioral results show that subject–object sentences were more difficult to understand than object–subject sentences for this group of elderly subjects. Reaction times for subject–object sentences were longer than for object–subject sentences. The accuracy data showed that the subjects had the greatest difficulty with implausible SO sentences.

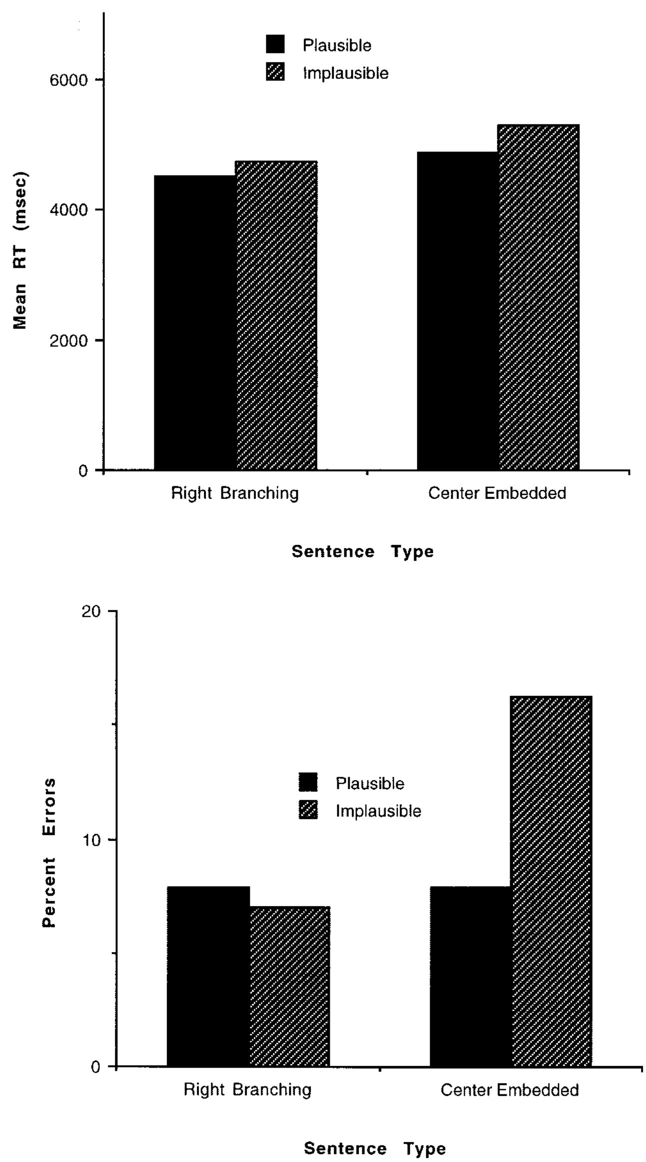

Figure 1.
Experiment 1: Reaction times and error rates to sentences.

TABLE I. Areas of increased rCBF for subtraction of PET activity associated with object–subject sentences from subject–object sentences: Experiment 1: 13 elderly subjects, slow responders

Location	Max z-score	Number of pixels	Location {x, y, z}
Inferior parietal lobe (Area 40)	3.77	127	−54, −32, 32
Superior frontal gyrus (Area 10)	3.10	73	−22, 56, 8

The results of this study reveal localized increases in rCBF in the midline anterior frontal cortex and in the left inferior parietal lobe in elderly subjects when they made plausibility judgments about the syntactically more complex sentences compared to the syntactically less complex sentences. These effects are small, but significant if a priori assumptions are made that syntactic processing and related cognitive functions recruit perisylvian and midline regions. We discuss the magnitude of these effects in the General Discussion.

The frontal region activated in the present study, Brodmann's area 10, may be involved in syntactic processing, but other plausible accounts of the functions it supports exist. This region has shown increased rCBF in the Stroop task, visual object decision, delayed matching to sample, and word-paired associate learning, as well as reading and verbal retrieval tasks [for review, see Cabeza and Nyberg, 2000]. It is possible that its roles in control of attention and response selection are responsible for its activation in the more complex condition in the present experiment. Activation in other midline frontal structures—the anterior cingulate and surrounding cortex—has been related to deploying attention and processing resources when subjects process more complex stimuli in many cognitive domains [Posner et al., 1987, 1988], and area 10 may be part of a midline frontal system involved in these functions.

The activation found in the left inferior parietal lobe is more likely to be related to sentence processing per se. The inferior parietal lobe is part of the perisylvian association cortex that is associated with language processing in general and syntactic comprehension in particular [Caplan et al., 1996].

In previous experiments in young adults using the materials and experimental paradigm employed here, the inferior parietal lobe has not been reported as a site at which rCBF increased in association with processing more complex relative clauses, whereas Broca's

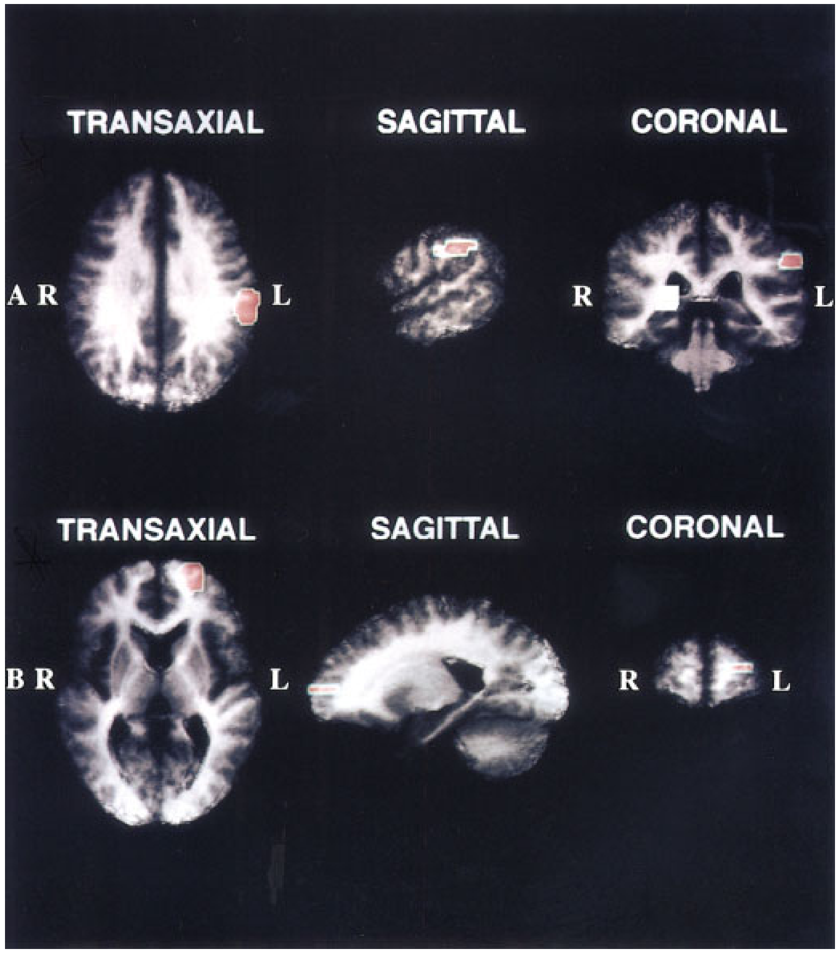

Figure 2.

A: SPM image of the brain showing increased blood flow in the left inferior parietal lobe when slow-responding elderly subjects processed subject–object compared to object–subject sentences. **B:** SPM image of the brain showing increased blood flow in the anterior frontal lobe when slow-responding elderly subjects processed subject–object compared to object–subject sentences.

area has been activated consistently. The results obtained here suggest that the left inferior parietal lobe might be more involved in one aspect of syntactic processing, or a related process, in elderly subjects than in young subjects. We return to the issue of what cognitive processes underlie this activation in the General Discussion. Before taking up that issue, however, we note that the difference between the subjects studied in this experiment and those reported in previous studies may not be their ages. The level of performance and the educational level of the elderly subjects studied here also differed from those of the young subjects in previous studies.

In the present experiment, error rates were 7.4% for OS sentences and 12% for SO sentences. In the Caplan et al. [1998] study with college students, error rates were 5.6% for OS sentences and 9.5% for SO sentences, and the overall error rate was 3.8% in the Stromwold et al. [1996] study (and was not further analyzed). In this experiment, mean RTs for correct responses were 4,600 msec for OS sentences and 5,078 msec for SO sentences. For the subjects in Caplan et al. [1998], they were 3,173 msec for OS sentences and 3,663 msec for SO sentences, and for the subjects in Stromswold et al. [1996], they were 3,719 msec for OS sentences and 4,230 msec for SO sentences. A 2 (Group) $\times$ 2 (Sentence Type) ANOVA showed that RTs for subjects in this experiment were longer than those in the study by Caplan et al. [1998] ($F(1,19) = 4.6$, $P < 0.05$). It is possible that differences in the speed of processing may have been the source of differences in rCBF between this and previous studies.

A related factor is years of education. The participants studies here had an average of 14 years of education, about 2 years less than the average number of years of education of participants in previous studies. Years of education could have an indirect effect on rCBF patterns through an effect on proficiency of syntactic processing. Individuals with more years of formal education may have more experience with studying and retaining the content of passages that contain syntactically complex sentences, or, conversely, individuals with greater verbal skills, including the ability to structure and understand syntactically complex sentences, may obtain more formal education. Thus, it is possible that differences in the extent of formal education of participants in this and previous studies may be related to syntactic processing differences in study participants, and thereby to differences in rCBF in different studies.

We therefore undertook two more experiments to attempt to distinguish between effects of age per se and effects of level of performance and education on rCBF patterns using these materials.

EXPERIMENT 2

Experiment 2 studied young subjects with fewer years of education than those in previous studies, in an effort to match the level of performance of the elderly subjects in Experiment 1.

Subjects

Eight subjects (four men and four women) participated in Experiment 2 after giving informed consent. Their mean age was 24.3 years (range: 19–28), and their mean years of education 14.5 (range: 13–16). All subjects were native, monolingual English-speaking subjects, and were strongly right-handed with no first-degree left-handed relatives. All had normal vision and hearing, and no positive neurological or psychiatric history.

Materials and procedures

Experimental procedures and data analyses were the same as in Experiment 1.

RESULTS

Behavioral results

Reaction time and accuracy data were analyzed as in Experiment 1. Behavioral results are shown in Figure 3. There was an main effect of sentence type (F_{1RT} (1, 7) = 10.9, $P < 0.01$; F_{2RT} (1, 284) = 27.9, $P < 0.001$;

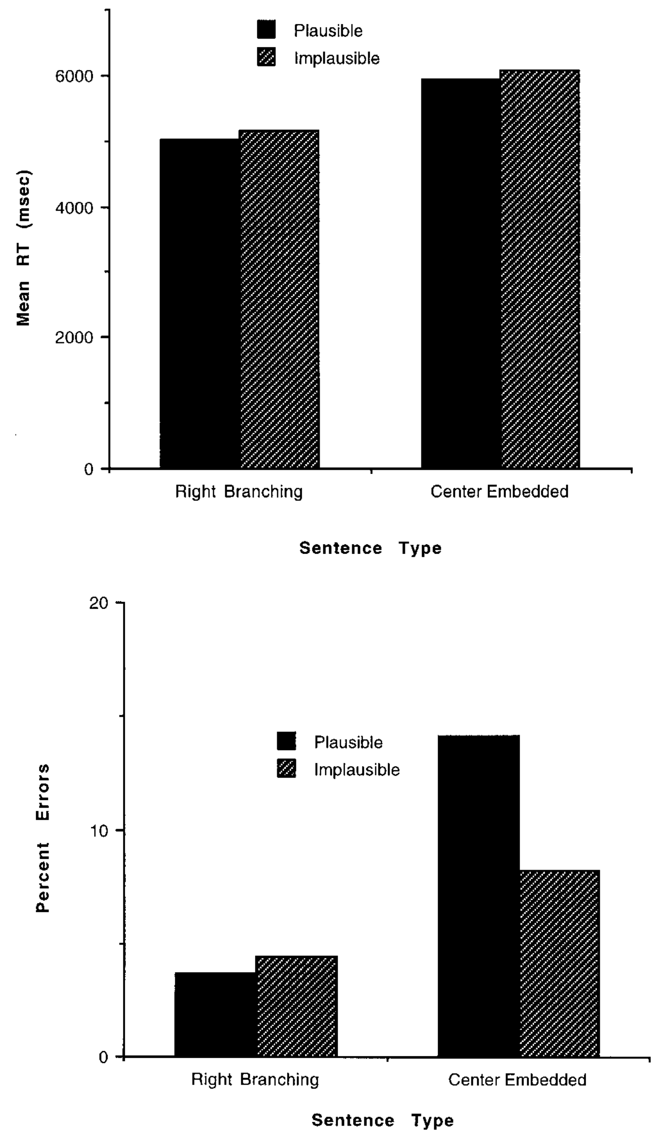

Figure 3.
Experiment 2: Reaction times and error rates to sentences.

F_{1E} (1, 7) = 8.7, $P = 0.02$; F_{2E} (1, 284) = 18.5, $P < 0.001$). Subject–object sentences were responded to more slowly and less accurately than object-subject sentences. There was a significant interaction of sentence type and plausibility in the error data only (F_{1E} (1, 7) = 7.8, $P = 0.02$; F_{2E} (1, 284) = 4.2, $P = 0.04$). Subjects made more errors on plausible SO sentences than on any other sentence type.

The performance of the younger subjects tested in this experiment was compared with that of the elderly subjects tested in Experiment 1 and young subjects tested in previous studies to ensure that matching subjects for years of education resulted in selecting young subjects who performed comparably to the older subjects in Experiment 1 and worse than young subjects in previous studies.

The performance of the younger subjects tested in this experiment was compared with that of the elderly subjects tested in Experiment 1 in mixed model analyses of variance, with the factors of group, sentence type, and plausibility. There was an effect of sentence type (F_{1RT} (1, 19) = 30.3, $P < 0.001$; F_{2RT} (1, 284) = 25.8, $P < 0.001$; F_{1E} (1, 19) = 16.2, $P < 0.001$; F_{2E} (1, 284) = 16.3, $P < 0.001$). SO sentences resulted in longer RTs and more errors than OS sentences. There was an effect of group in the analyses by items (F_{1RT} (1, 19) = 0.45, NS; F_{2RT} (1, 284) = 78.8, $P < 0.001$; F_{1E} (1, 19) = 0.9, NS; F_{2E} (1, 284) = 70.1, $P < 0.001$). Younger subjects had longer RTs and made fewer errors than older subjects. No other main effects or interactions were significant. Thus, the young subjects in Experiment 2 performed comparably to, if not somewhat worse than, the elderly subjects in Experiment 1.

Subjects in this study were then compared to young subjects who activated Broca's area in a previous study [Caplan et al., 1998] using similar analyses. There was an effect of sentence type (F_{1RT} (1, 14) = 16.2, $P < 0.001$; F_{2RT} (1, 284) = 37.2, $P < 0.001$; F_{1E} (1, 14) = 14.0, $P < 0.01$; F_{2E} (1,284) = 20.0, $P < 0.001$). SO sentences produced longer RTs and more errors than OS sentences. There was an effect of group in the RT data (F_{1RT} (1, 14) = 3.4, P = 0.08; F_{2RT} (1, 284) = 618.9, $P < 0.001$). The subjects tested in the Caplan et al. [1998] study responded to the sentences faster than those studied in this experiment. No interactions were significant. Thus, the young subjects in Experiment 2 performed worse than young subjects in previous studies.

rCBF results

Differences in rCBF between the SO and OS conditions were not significant in the random effects analysis. Table II and Figure 4 show the location of increases in rCBF associated with z scores that exceeded the threshold for significance in the fixed effect analysis for the SO–OS contrast. There was an increase in rCBF in the superior frontal lobe (Brodmann's area 6). The increase in rCBF in the precuneal region of the superior parietal lobe (Brodmann's area 7) was greater than that in the superior frontal lobe. There were no areas in which rCBF decreased in the SO condition compared to the OS condition. Comparisons of rCBF patterns across the groups in Experiments 1 and 2 showed greater rCBF in the left inferior parietal area in Experiment 1 than in Experiment 2 (z = 3.6).

TABLE II. Areas of increased rCBF for subtraction of PET activity associated with object–subject sentences from subject–object sentences: Experiment 2: eight young subjects, slow responders

Location	Max z-score	Number of pixels	Location {*x*, *y*, *z*}
Superior parietal lobe (Area 7)	3.84	345	−4, −56, 48
Superior frontal gyrus (Area 6)	3.41	88	8, 16, 48

All subjects showed rCBF effects in the expected direction (greater rCBF for SO than for OS sentences) in the left superior parietal region, and five in the superior frontal lobe. Correlations between reaction time for plausibility judgments and PET counts were not significant in these or other regions.

Discussion: Experiment 2

The behavioral results show that the young less-well educated subjects tested here showed the same effect of sentence type as previous groups. Reaction times for SO sentences were longer than for OS sentences and error rates were higher. Subjects made the most errors on plausible SO sentences.

The behavioral results show that the subjects tested here performed very similarly to the elderly subjects in Experiment 1. In the analyses by subjects, the two groups did not differ with respect to either their RTs or accuracy levels. The analyses by items showed that the young subjects tested in Experiment 2 took longer to make their responses and made fewer errors than the older subjects in Experiment 1. This pattern suggests that the subjects in the two experiments may have traded off on speed and accuracy in different ways, with the younger subjects in Experiment 2 taking longer to respond and achieving greater accuracy levels and the older subjects in Experiment 1 responding faster at the cost of more errors. The subjects in this experiment were slower on this task than young subjects tested in previous studies.

The subjects tested in Experiment 2 showed small focal increases in rCBF when making judgments about the more complex sentences in the superior portion of the frontal lobe and in the precuneal region of the superior parietal lobe. The rCBF effect that had been found in Broca's area in previous studies with young subjects was not seen here.

In our discussion of Experiment 1, we suggested that the increased rCBF in the anterior medial frontal

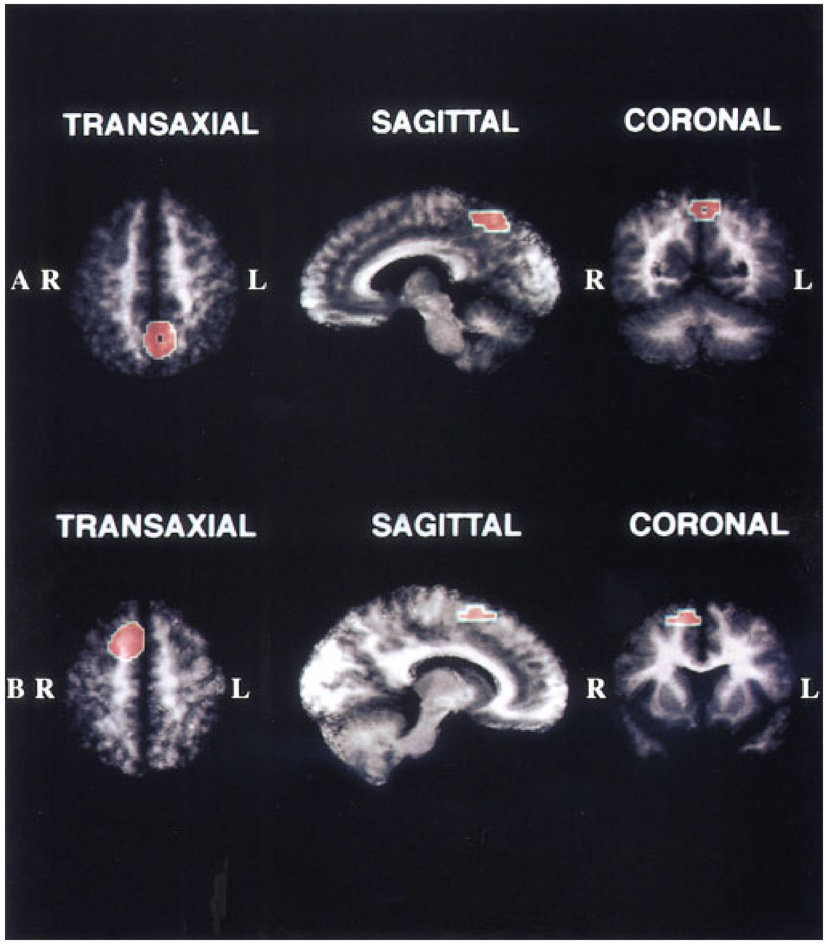

Figure 4.

A: SPM image of the brain showing increased blood flow in the left superior parietal lobe when slow-responding young subjects processed subject–object compared to object–subject sentences. **B:** SPM image of the brain showing increased blood flow in the right superior frontal lobe when slow-responding young subjects processed subject–object compared to object–subject sentences.

lobe could reflect greater deployment of attention in the more complex condition. The frontal lobe area in which rCBF increased in Experiment 2—Brodmann's area 6—is rostral to the midline frontal lobe activation in Brodmann's area 10 in Experiment 1. Area 6 is a motor-planning region [Wise and Strick, 1996]; one plausible explanation for the increase in rCBF in this region in the SO condition is that eye movements may have differed in the SO and OS structures, due to different patterns of visual fixation in the two sentence types. However, the mechanism that we suggested for the increase in activation in area 10 in Experiment 1, that the increased rCBF reflects deployment of attention, may also account for the increased rCBF in area 6 in this study. It is also possible that this activity reflects a role for this region in some aspect of syntactic processing.

It is possible that the activity in the superior parietal lobe is due to its participation in language processing. The superior parietal lobe is not a region in which lesions are known to affect language to the point of causing overt aphasia. However, patients with lesions in this region have not been studied for deficits in syntactic comprehension. These deficits are subtle and are not detectable on routine clinical evaluation, but require specially designed protocols to exhibit, which have not been administered to patients with lesions in this region. It is therefore possible that such deficits might exist in such patients. One evoked potential associated with detecting syntactic anomalies, the P600, has a posterior scalp distribution that suggests a possible high parietal source [Osterhout and Holcomb, 1992]. The activation of the superior parietal lobe in two studies of syntactic processing (this experiment) [Caplan et al., 1999] suggests that a role for this region in this process should be considered. Other functions could also be responsible for the increased rCBF in the superior parietal lobe, in particular, differences in the deployment of visual attention in inspecting visual mental images in the two conditions. We defer discussion of the processes that affected rCBF results to the General Discussion.

The results of Experiments 1 and 2 suggest that processing speed (possibly related to years of education), not age, affects patterns of rCBF on this task. To investigate this question more fully, we carried out a final study in which we repeated the experiment in a group of elderly subjects who were highly educated, and whose behavioral performances proved to be matched to the proficient young adults previously tested.

EXPERIMENT 3

Experiment 3 studied older subjects whose level of performance was intended to match those of young subjects studied previously.

Subjects

Nine subjects (four men and five women) participated after giving informed consent. Their mean age was 75.2 (range: 71–81 years) and the average education was 18.6 years (range: 17–22 years). All subjects were native, monolingual English-speaking subjects, and were strongly right-handed with no first-degree left-handed relatives. All had normal vision and hearing, and no positive neurological or psychiatric history.

Materials and Procedures

Experimental procedures and data analyses were the same as in Experiments 1 and 2.

RESULTS

Behavioral results

Reaction time and accuracy data were analyzed as in Experiment 1. Behavioral results are shown in Figure 5. There was a main effect of sentence type (F_{1RT} (1, 8) = 12.5, $P < 0.01$; F_{2RT} (1, 276) = 24.4, $P < 0.001$; F_{1E} (1, 8) = 10.9, $P = 0.01$; F_{2E} (1, 282) = 12.7, $P < 0.001$). SO sentences were responded to more slowly and less accurately than OS sentences. There was an effect of plausibility in the RT data only (F_{1RT} (1, 8) = 7.5, $P < 0.01$; F_{2RT} (1, 276) = 5.2, $P < 0.05$). Subjects responded more slowly to implausible sentences. There was an interaction of sentence type and plausibility in the RT data and in the analysis of the accuracy data by subjects (F_{1RT} (1, 8) = 6.5, $P < 0.05$; F_{2RT} (1, 276) = 7.7, $P < 0.001$; F_{1E} (1, 8) = 5.9; $P = 0.04$; F_{2E} (1, 284) = 2.0, ns). Subjects responded more slowly to implausible SO sentences than to any other sentence type.

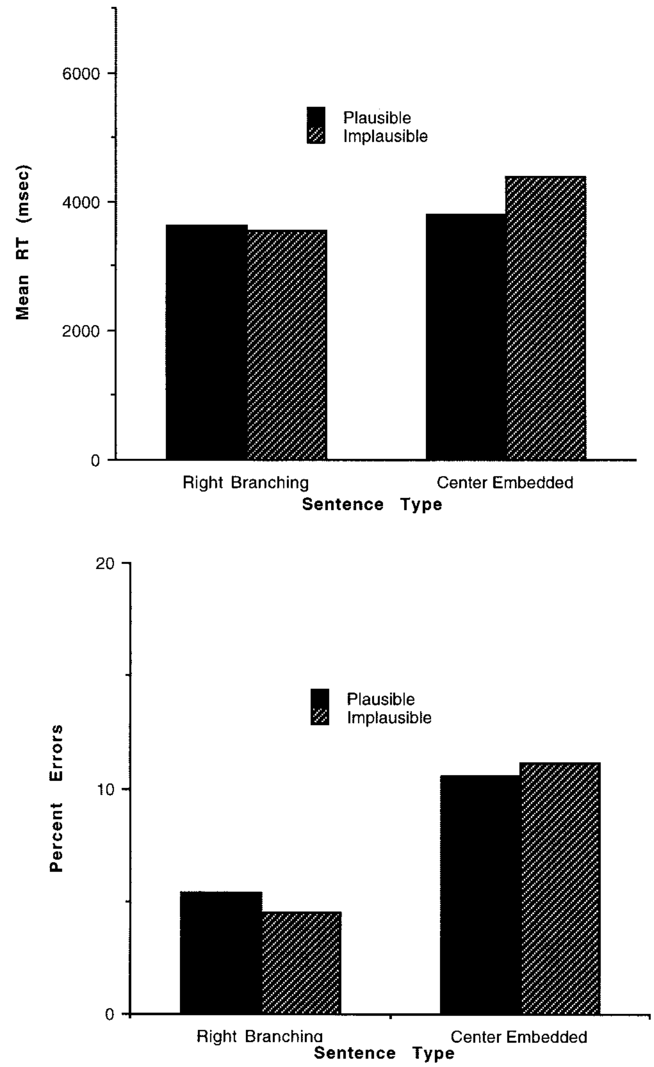

Figure 5.
Experiment 3: Reaction times and error rates to sentences.

The performance of the younger subjects tested in this experiment was compared with that of the less well-educated elderly subjects tested in Experiment 1, that of the less well-educated young subjects tested in Experiment 2, and that of better-educated young subjects tested in previous studies to ensure that matching subjects for years of education resulted in selecting young subjects who performed better than the less well-educated tested subjects in Experiments 1 and 2 and comparably to more highly educated young subjects tested in previous studies.

The performance of the elderly subjects tested in this experiment was compared with that of the less well-educated elderly subjects tested in Experiment 1 in mixed model analyses of variance. There was an effect of sentence type (F_{1RT} (1, 20) = 31.0, $P < 0.001$; F_{2RT} (1, 284) = 17.6, $P < 0.001$; F_{1E} (1, 20) = 16.3, $P < 0.001$; F_{2E} (1, 284) = 48.9, $P < 0.001$). SO sentences were responded to more slowly and less accurately than OS sentences. There was an effect of plausibility in the RT data (F_{1RT} (1, 20) = 7.5, $P < 0.01$; F_{2RT} (1, 284) = 5.2, $P < 0.05$). RTs were faster for plausible sentences. There was a main effect of group in the item analyses (F_{2RT} (1, 284) = 470, $P < 0.001$; F_{2E} (1, 284) = 48.9, $P < 0.001$). The highly educated older subjects in Experiment 3 responded more quickly and more accurately than the less well-educated older subjects in Experiment 1. There were no significant interactions involving the group factor.

The performance of the subjects tested in this experiment was compared with that of the less well-educated young subjects tested in Experiment 2 in similar analyses. There was an effect of sentence type (F_{1RT} (1, 15) = 21.6, $P < 0.001$; F_{2RT} (1, 284) = 34.5, $P < 0.001$; F_{1E} (1, 15) = 19.3, $P < 0.001$; F_{2E} (1, 284) = 19.3, $P < 0.001$). SO sentences were responded to more slowly and less accurately than OS sentences. There was a main effect of group in the RT data in the item analyses (F_{1RT} (1, 15) = 2.3, $P = 0.15$; F_{2RT} (1, 284) = 423.2, $P < 0.001$). The highly educated older subjects in Experiment 3 responded more quickly than the less well-educated young subjects in Experiment 2. There was a three-way interaction of group, sentence type, and plausibility in the RT data (F_{1RT} (1, 15) = 4.4, $P < 0.05$; F_{2RT} (1, 284) = 4.7, $P < 0.05$). Analysis of the terms of the interaction showed that the highly educated older subjects in Experiment 3 responded more quickly and more accurately to each sentence type than the less well-educated young subjects in Experiment 2.

The performance of the subjects tested in this experiment was compared with that of the highly educated younger subjects previously tested by Caplan et al. [1998] in similar analyses. There was an effect of sentence type (F_{1RT} (1, 15) = 15.1, $P < 0.001$; F_{2RT} (1, 284) = 61.1, $P < 0.001$; F_{1E} (1, 15) = 15.1, $P < 0.001$; F_{2E} (1, 284) = 17.5, $P < 0.001$). SO sentences were responded to more slowly and less accurately than OS sentences. There was a significant main effect of plausibility (F_{1RT} (1, 15) = 11.5, $P < 0.01$; F_{2RT} (1, 284) = 4.7, $P < 0.05$; F_{1E} (1, 15) = 1.6, ns; F_{2E} (1, 284) = 3.7, $P < 0.05$). RTs were faster to plausible than to implausible sentences, but subjects tended to make fewer errors on implausible sentences. There was a significant interaction of sentence type and plausibility in the RT data (F_{1RT} (1, 15) = 7.6, $P < 0.01$; F_{2RT} (1, 284) = 4.5, $P < 0.05$). RTs were significantly faster for plausible than for implausible SO sentences, but the difference between plausible and implausible OS sentences was not significant. There were no effects of group and no interactions with the group factor.

TABLE III. Areas of increased rCBF for subtraction of PET activity associated with object–subject sentences from subject–object sentences: Experiment 3: nine elderly subjects, fast responders

Location	Max z-score	Number of pixels	Location {x, y, z}
Inferior frontal lobe (Area 46)	3.09	62	−34, 42, 8

Together, these analyses provide evidence that the subjects in Experiment 3 performed better than the less well-educated subjects in Experiments 1 and 2, and at a comparable level to well-educated young subjects tested in previous studies.

rCBF results

Differences in rCBF between the SO and OS conditions were not significant in the random effects analysis. Table III and Figure 6 show the location of increases in rCBF associated with z scores that exceeded the threshold for significance in the fixed effect analysis for the SO–OS contrast. There was an increase in rCBF in the left inferior frontal lobe (Brodmann's area 46), just below the inferior frontal sulcus. There were no areas in which rCBF decreased in the SO condition compared to the OS condition. Comparisons of rCBF patterns across the groups in Experiments 3 and 1 and those in Experiments 3 and 2 showed no significant differences.

Five of the eight subjects showed rCBF effects in the expected direction in the left inferior frontal region. Correlations between reaction time for plausibility judgments and PET counts were not significant in this or other regions.

Discussion: Experiment 3

The behavioral results of Experiment 3 show the expected effect of sentence type. They also indicate

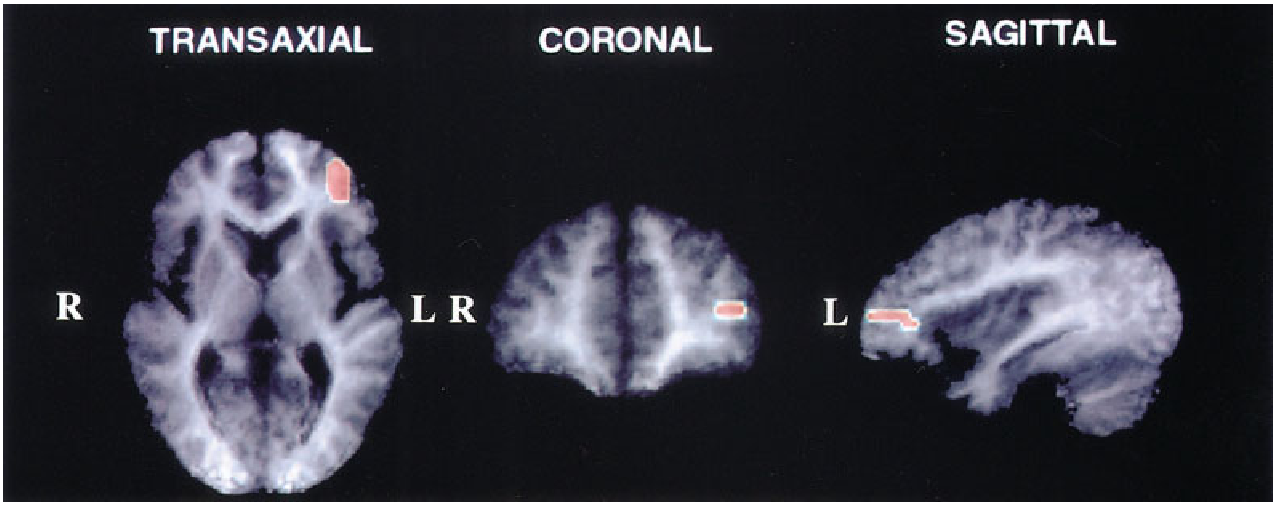

Figure 6.
SPM image of the brain showing increased blood flow in the left inferior frontal lobe when fast-responding elderly subjects processed subject–object compared to object–subject sentences.

that subjects in this study performed at the same level of accuracy and with the same RTs as the young, well-educated subjects previously tested in this experimental paradigm [reported in Caplan et al., 1998]. The subjects tested here responded more quickly than the age-matched subjects with lower educational levels tested in Experiment 1. The difference in RTs between the two groups was on the order of 1,000 msec and was significant in the analyses by items; it was not significant in the analysis by subjects, probably because of the small number of subjects studied. The subjects tested here also had shorter RTs than the young subjects with lower educational levels tested in Experiment 2. The difference in RTs between the the two groups was substantial (~1,700 msec). It was only significant in the analysis by items, again probably because of the small number of subjects tested and the variance across subjects.

The results of Experiment 3 reveal an increase in rCBF in the left inferior frontal lobe in the comparison of SO and OS sentences in these elderly, good-performing subjects. This area of activation is very similar in location to that seen in younger subjects whose level of performance was indistinguishable behaviorally from those tested here. This region was not activated in either the young or elderly subjects tested in Experiments 1 and 2, whose performance speeds were significantly lower. This pattern of results suggests that the left inferior frontal region is activated in this task in subjects who are proficient at syntactic processing. Age per se does not appear to affect this rCBF pattern.

Conjunction analysis

The data from all subjects were analyzed to test for voxels that were commonly activated in the CE-RB contrast. We used SPM99 with a multi-subject condition-by-subject interaction model. Conjunction analysis did not detect any voxels that violated the null hypothesis.

GENERAL DISCUSSION

Our discussion will focus on two related topics: the possible functions of the areas that were activated in these studies, and what determined the variability in these activated areas. We will close with a discussion of a model of the functional neuroanatomy of syntactic processing that emerges from these studies. Before taking up these interpretive issues, we will comment on the magnitude of the rCBF effects found in these studies.

Magnitude of rCBF effects

The rCBF effects of sentence type reported here are significant in fixed effects analyses based upon criteria for significance in specific regions [Worsley et al., 1996]. These analyses are appropriate when a priori hypotheses identify regions in which effects are expected, and the results can be considered as reasonable evidence for the localization of a process if they are found in a series of studies. We have also reported all z scores that are higher than those retained on the basis of the fixed effect regional analyses.

The magnitude of the effects reported here is typical of those reported in the literature for comparisons across sentence types [e.g., Caplan et al., 1998, 1999, 2000; Cooke et al., 2001; Just et al., 1996; Stromswold et al., 1996]. Comparisons of sentences vs. non-sentential baselines, which are driven by many differences between the baseline and experimental condition, produce greater regional activation [Bavalier et al., 1997; Caplan et al., 2001; Cooke et al., 2001; Dapretto and Bookheimer., 1999; Grossman et al., 2002]. It is not surprising that comparisons of conditions that differ minimally with respect to their cognitive processing produce small differences in vascular responses, compared to subtractions that involve a larger number of cognitive operations.

It may be useful to review the consequences of applying this approach to our data. Stromswold et al. [1996] found left inferior frontal activity in the comparison of SO and OS sentences, which was expected on the basis of a priori hypotheses, and this result has been replicated in several studies. We suggest that it is a real effect, and have proposed that it is related to an aspect of syntactic processing. Caplan et al. [1998] found midline frontal activity in the comparison of SO and OS sentences, which was not expected on the basis of a priori hypotheses, but the z score in this region was higher than those that were significant in regions where activity was expected a priori. We therefore reported this activity. It was subsequently found in other studies [Caplan et al., 1999, 2000]. We consider that it occurs reliably in this experimental paradigm and requires an explanation in terms of cognitive operations. We have suggested that it reflects general arousal and attentional deployment. We believe that this region now should be considered one for which an a priori hypothesis exists regarding activation in this and similar experiments. Another example of a region that has been retained is the left superior parietal lobe, in which activation was found in Caplan et al. [1999] and again in Experiment 2 reported here. Whether it is reliably found in studies using these and similar materials, and what operations drive it, remain to be determined.

Areas of activation and their possible functional roles in this experimental paradigm

Using the approach outlined above, we identified four regions in which rCBF increases were associated with the processing of the more complex SO sentences: medial frontal structures, the left inferior parietal lobe (Experiment 1), the left superior parietal lobe (Experiment 2), and the left inferior frontal lobe (Experiment 3).

Medial frontal structures have been activated in many previous experiments using these materials. We have previously suggested that the increase in rCBF in these regions may reflect deployment of attentional resources that occurs when subjects undertake demanding tasks. As noted above, activation in midline frontal structures, especially the anterior cingulate, has been seen on many paradigms under these conditions [Posner et al., 1987, 1988; for review, see Cabeza and Nyberg, 2000]. It is possible that these areas participate in specific operations in many tasks, but the possibility that they become active because of a more general alerting function seems more likely. The connections of these areas to non-specific thalamic nuclei involved in arousal [Fuster, 1997] make this role plausible. In addition, lesions in these areas tend to lead to difficulties regulating alertness, not to specific cognitive impairments in multiple domains of function. While a role for these areas in syntactic processing per se cannot be ruled out, it seems unlikely. Studies of the effects of midline frontal lesions on syntactic processing in sentence comprehension would provide additional data relevant to this question.

We next consider the left inferior frontal region, which has been activated in all previously published functional neuroimaging studies using materials similar to those used here. Lesions in this area are associated with syntactic disorders in comprehension. This region is very likely to be involved in the assignment of syntactic structure and associated aspects of meaning in this task.

Though the left inferior frontal lobe is implicated in syntactic processing, the exact location of the rCBF effects in this area of the brain has not been the same in all studies. The area activated in Experiment 3, Brodmann area 46, is more anterior than the regions in which rCBF and BOLD signal effects have previously been reported (Brodmann areas 44 and 45). Area 46 lies at the junction of the posterior and anterior parts of the dorsolateral frontal lobe. Both the lesion and activation literature provide evidence that there is a difference in the functions supported by these parts of the frontal cortex. More anterior frontal areas (the "dorsolateral prefrontal cortex," DLPFC) are associated with "executive" functions, such as shifting attention from one category to another, working memory, planning, etc. More posterior areas ("Broca's area") are associated with language functions, especially speech production and syntactic processing. The exact boundary of the posterior and anterior portions of the left inferior frontal area is not clear. Brodmann areas 44 and 45 are widely thought to be in the language-devoted posterior portion, and Brodmann areas 47 and 9 in the dorso-lateral, more anterior, region involved in executive functions. Area 46 is not classically included in either. The results of Experiment 3 provide evidence that it is part of the posterior portion of the left inferior frontal lobe, and is involved in at least one language process. Lesion data are consistent with this conclusion. Published reports indicate that many strokes involving Broca's area that are associated with syntactic processing impairments affecting the comprehension of relative clauses are quite large, and include area 46.

The functional and anatomical distinction between the anterior and posterior portions of the left inferior frontal lobe may not be completely sharp. Functionally, these different parts of the left frontal lobe may have some operations in common. For instance, one formulation, associated with the thought of A. R. Luria, is that the frontal lobes are involved in "sequencing." Luria [1966] suggested that, in Broca's area, sequencing operations were applied to the *form-based* elements of language, and, in more superior and anterior frontal areas, they applied to *semantic* and *conceptual* categories. Lesions in and around Broca's area thus affected motor sequences underlying speech (leading to articulation disorders) and syntactic dependencies (leading to agrammatism), and lesions in more rostral areas affected planning, reasoning, switching from one mental set to another, initiation of cognitive activity, and other similar higher-order cognitive functions. The functional difference between the regions may consist primarily in which linguistic categories are operated upon, not the nature of the processing that occurs in each. If there are similarities in the functions of the different parts of the left inferior frontal lobe, the boundary between cortex devoted to "executive" functions and cortex devoted to "language" functions may not be sharp; instead, there may be cortex at the interface between these regions, which is involved in operating on both conceptual representations and linguistic elements. Brodmann's area 46 may be such a region.

We must also consider what specific aspects of sentence comprehension are related to these rCBF effects. One consideration is that, since the left inferior frontal lobe is involved in rehearsal [Smith et al., 1998], increased rehearsal in the SO compared to the OS sentences may be responsible for the rCBF effects in this paradigm in this region. However, as noted in the introduction to this study, previous research has provided evidence against this possibility. Caplan et al., [2000] found that this rCBF effect was not eliminated by concurrent articulation, which renders it very difficult, or perhaps impossible, to rehearse [Baddeley et al., 1975]. This finding makes it likely that the activation in this region is not entirely due to increased rehearsal in the more complex condition.

It is likely that some aspect of syntactic processing is responsible for the left inferior frontal rCBF effect. A model of the factors that make SO sentences more difficult to structure and understand than OS sentences was presented by Gibson [1998]. According to this model, there are two differences between these sentence types. One difference is the number of integration operations that occur at the verb of the relative clause: in SO sentences, the verb of the relative clause can assign a thematic role to both its subject and its object, whereas it can only assign a thematic role to its subject in OS sentences. Second, SO sentences have greater "storage" costs than OS sentences, because more predicted syntactic categories must be maintained between the relative pronoun and the verb in the SO than in the OS sentences. One or both of these features may be responsible for the increased rCBF found in these studies. Cooke et al. [2001] proposed that left inferior frontal activation is only seen in the comparison of object vs. subject-relativized sentences when heavy demands are made on a more general STM store (one whose deployment is not limited to sentence processing). The specific aspect(s) of processing that occurs in object- compared to subject-relativized sentences that makes for increased vascular responses in this region remains to be clearly delineated.

The third region we turn to in which there was increased rCBF is the left inferior parietal lobe (Experiment 1). This region is a part of the perisylvian cortex in which lesions have led to syntactic comprehension deficits [Caplan et al., 1996]. It may also be involved in some aspect of syntactic processing. However, this region's activation may be related to its involvement in a more general short-term memory system, of the sort that Cooke et al. [2001] suggested underlies activation in the left inferior frontal lobe. The left inferior parietal lobe is involved in phonological storage in general verbal short-term memory [Smith et al., 1998; Vallar and Shallice, 1990] and it and the contiguous left posterior superior temporal lobe have been activated by complex syntactic structures in experiments that impose a high "extrinsic" memory load, above and beyond the "syntactic" memory load associated with processing more complex syntactic structures [Caplan et al., 2001; Just et al, 1996; Stowe et al, 1998]. We suggest that the vascular responses seen in this region in these studies may reflect increased verbatim retention of complex sentences in general STM for purposes of review and re-analysis triggered by the demands of specific experimental tasks [for discussion, see Caplan et al., 2001].[†]

The final area in which there was increased rCBF is the superior parietal lobe (Experiment 2). Experiment 2 is the second study in which activation has been found in association with syntactic processing: Caplan et al. [1999] reported increased rCBF in this region in an auditory version of this task using similar sentence types (cleft object and cleft subject sentences). One ERP component associated with syntactic processing, the P600, has a scalp distribution consistent with a cerebral source in this region [Osterhout and Holcomb, 1992], although the cerebral location of ERP sources is hard to determine. Thus, this area may also support some aspect of syntactic processing. However, as with the medial frontal area, lesions in this region have not been associated with disturbances in syntactic comprehension, leading us to consider other possibilities. The precuneal region of the superior parietal lobe is involved in spatially directed attention [Posner et al., 1987]. Increases in vascular responses have been reported in more superior portions of the parietal lobe in a sentence–picture verification task when subjects use a visual as opposed to verbal strategy [Reichle et al., 2000]. One possibility is that the precuneal activation found in Experiment 2 reflects greater use of visual imagery in the SO than in the OS sentences.

In summary, the experiments reported here were designed to highlight syntactic operations required to understand more complex relative clauses. The activation in Broca's area in Experiment 3 is plausibly related to these operations. Additional research is needed to be more specific about exactly which syntactic operation or process is responsible for these rCBF effects and about the exact part of this area that is related to more specific syntactic operations. Other regions that were activated may also support syntactic processing, but may have become activated because they play a role in other functions that were engaged to different extents in the complex and simple conditions in these tasks. The most likely such functions are regulation of arousal and deployment of attention in the midline frontal areas, storage of phonological representations in the left inferior parietal lobe, and generation and inspection of visual mental images in the left superior parietal lobe.

[†]We disagree with Cooke et al. [2001] about the roles of the left frontal and left temporoparietal cortex in syntactic processing and general short-term memory. Cooke et al.'s conclusions are based on stimuli in which increases in STM demand were confounded with increases in syntactic complexity. Their "long" object relative sentences have either appositive prepositional phrases or nonrestrictive relative clauses not found in any other sentence type. The presence of these structures, rather than the simple increase in the number of words in the "long" OR sentences, may have lead to increased BOLD signal in this condition.

Variability in localization of rCBF effects and the factors that determine it

We have already discussed the variability in the left inferior frontal lobe across this and other studies. Whether areas 44, 45, and 46 are a functionally homogeneous region for the aspects of syntactic processing highlighted in this paradigm or whether specific syntactic operations activate different parts of this region, this region is strongly implicated as being involved in syntactic functions. The more striking aspect of variability in rCBF effects in the studies reported here is the activation of the left inferior and superior parietal lobe. We begin our consideration of this feature of the data with a discussion of what factors may underlie this variability.

As we indicated in the introduction to this study, age-related changes in cortical regions could have led to variability in the location of syntactic processing. However, the results of the studies reported here suggest that this is not the case. Rather, this variability was related to the speed with which subjects performed the plausibility judgment task. As noted in the Introduction, differences in speed of processing may be related to differences in working memory, which in turn may be related to differences in sentence processing proficiency, which has previously been shown to be related to different neural responses to syntactic processing [King and Kutas; 1995; Kutas and King, 1999; Vos et al., 2001]. It is also possible that faster processing is due to greater experience with syntactic processing [MacDonald and Christiansen, 2002]; experience has been shown to be related to differences in neural responses to tasks [Raichle et al., 1994]. It is possible that subjects' overall speed of processing is the feature that determined the different rCBF patterns found in these studies, perhaps through such chains of effects.

On the other hand, as opposed to differing with respect to operational capacities that affect a very wide range of cognitive functions, such as speed of processing or general verbal working memory, the subjects in these studies may have differed only with respect to much more circumscribed functions, such as their proficiency in syntactic processing and other closely related aspects of unconscious language comprehension (Caplan and Waters, 1999). More extensive testing of subjects in experiments in which the neural correlates of syntactic processing are measured will be needed to determine whether the differences reported here are related to operating characteristics that apply to a wide range of cognitive processes or to more cognitively isolated differences, such as proficiency of syntactic processing per se.

Implications for the functional neuroanatomy of syntactic processing

The results reported here add to previous studies that have shown activation in the left inferior frontal region in association with one aspect of syntactic processing. They provide evidence that this region is activated by this process in subjects who are proficient at sentence processing. The slow-responding subjects present more of a challenge.

Before considering the neural regions involved in syntactic processing in the slow-responding subjects, one point to note is that the behavioral data provide evidence that all the subjects, fast and slow performers alike, did in fact assign complex syntactic structures in this task. Non-linguistic mechanisms such as verbal short-term memory and mental imagery can only help retain the form of the presented sentence or its interpretation in an accessible state; they cannot generate the meaning of a sentence. Nor can simple heuristics that have been proposed in sentence comprehension [Townsend and Bever, 2001] lead to the correct assignment of the thematic roles in the subject-—object sentences used in these studies. Recently, neural net models have been developed that can predict the occurrence of words in sentences based upon previously presented words, without constructing syntactic representations [MacDonald and Christiansen, 2002; Rohde and Plaut, 1999]. These models, however, have so far operated with tiny vocabularies and have not been applied to the problem of comprehension, and it is not clear that this approach will prove successful in modeling comprehension of SO sentences [for discussion, see Caplan and Waters, 2002]. Given the high rate of correct responses to these structures in all groups of subjects, we would argue that all subjects must have used a syntactic analysis to determine sentence meaning.

It is possible that all subject groups used the left inferior frontal region to support the aspects of syntactic processing that differ between SO and OS sentences in this paradigm. Slow subjects may have allocated more resources to syntactic analysis and interpretation in the simple sentence condition than fast responders, thereby reducing the difference between PET activity in the complex and simple conditions. Alternatively, slow responders may have a lower limit on the amount of resources they can allocate to syntactic processing [for a simulation with this effect, see Just and Carpenter, 1992], also leading to smaller differences in PET activity between the complex and simple conditions.

The parietal activations in the subjects who performed more slowly could be related to their greater utilization of non-syntactic mechanisms in this task. Subjects who responded more slowly are less proficient at sentence processing and could engage additional cognitive mechanisms to help them accomplish the plausibility judgment task. These mechanisms could be used more when complex sentences are presented. Conversely, reliance on cognitive mechanisms such as short-term memory and visual mental imagery may be time-consuming and greater reliance on them could lead to longer response times in sentence comprehension tasks. In either case, parietal activation could be seen in subjects with slower response times.

The suggestion that a region that shows no activation in a paradigm designed to activate a function is nonetheless involved in that function is, of course, speculative, possibly dangerously so. We can defend our offering it here on the grounds that it would save a simple localizationist model, according to which one aspect of syntactic processing invariably involves the left inferior frontal lobe and use of STM and imagery involves the parietal lobe. We note that this account is consistent with the findings that high-performing subjects show activity in parietal regions when sentence comprehension tasks have high "external" STM demands or encourage the use of visual mechanisms, and that it is testable in other ways. If it is correct, slow-responding subjects should show activity in the inferior frontal region if baseline sentences whose processing demands are lower than those of OS sentences are compared with SO sentences, and parietal activation should disappear if these subjects undertake syntactic comprehension tasks under interference conditions that occupy phonological storage and visual mental imagery (e.g., maintenance of a digit load or judgment of identity of rotated nonsense shapes).

Regardless of whether the slow-performing subjects used frontal or parietal structures for syntactic processing, the results of these studies provide evidence that processing of the syntactic structure and meaning of complex relative clauses proceeds most efficiently when these sentences activate the left inferior frontal lobe "optimally." If slow performers utilize this region at all when assigning and interpreting these syntactic structures, they do so in a way that is behaviorally inefficient. If they did not utilize this region for syntactic processing in this task, utilization of other brain regions for this function appears to be behaviorally inefficient.

Overall, this study provides additional evidence that the left inferior frontal lobe plays a critical role in one aspect of syntactic processing. It points to effects of individual differences in either the way this region operates or in its involvement in this process. The results provide evidence that these differences are related to subjects' speed of processing. Pre-morbid differences in this factor could account for individual variability in the relationship between lesions and deficits of syntactic processing. Whether the critical subject feature is a general slowing of cognitive processing, a lowered general verbal working memory capacity, or a lower degree of proficiency in syntactic processing alone, remains to be studied.

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