Sentence comprehension in multiple sclerosis


Introduction – Explanations of sentence processing difficulty in aphasia have implicated slowed information processing speed. We tested this hypothesis by evaluating sentence comprehension in multiple sclerosis (MS), and relating comprehension performance to measures of information processing speed. Material & methods – Twenty right-handed, high school-educated, non-demented, native English speakers with clinically definite MS and 16 age- and education-matched control subjects were examined on 3 different sentence comprehension measures that stress grammatical appreciation. Performance was related to quantitative assessments of mental information processing speed. Results – Group-wide analyses demonstrated a trend toward sentence comprehension difficulty in MS. Analyses of individual patient profiles identified a subgroup of MS patients who were consistently impaired to a significant extent across all sentence comprehension tasks. Their sentence comprehension difficulty was associated with selectively compromised mental information processing speed. This finding supports the claim that information processing speed contributes to sentence processing. Conclusion – Sentence comprehension difficulty in MS is associated with slowed information processing speed. This finding supports the claim that information processing speed contributes to sentence processing.

Language deficits have been studied only rarely in multiple sclerosis (MS) (1, 2). Single cases of aphasia have been reported during disease exacerbations (3-5), but persistent linguistic deficits during periods of disease stability have not been well documented. One study of language functioning found significant impairments in MS (6), but this was attributed to the patients' sensori-motor difficulties. The purpose of this study was to investigate sentence comprehension in MS.

There is an important theoretical reason to investigate sentence processing in MS. Slowed speed of mental information processing is said to be a major feature of the cognitive profile of MS. For example, compromised information processing speed has been proposed to account for certain aspects of their impaired verbal memory (7,8). Several investigators recently have proposed that the sentence comprehension deficit of Broca's aphasia is due in part to compromised information processing speed that has resulted in grammar-concept mismatching during the temporal course of sentence processing (9-13). A strong test of this hypothesis involves investigating sentence comprehension difficulty in MS, since this disease generally is not associated with impaired sentence comprehension but does result in slowed speed of mental information processing. We also assessed other cognitive factors such as memory and executive functioning that may contribute to sentence comprehension in MS.

Material and methods

We evaluated sentence comprehension in 20 right-handed, consecutively-presenting, non-demented native English speakers with clinically definite MS (14). These patients were recruited from the Comprehensive Multiple Sclerosis Center in the Department of Neurology at the Hospital of the University of Pennsylvania. The MS cohort included 17 patients with a relapsing-remitting pattern characterized by transient decrements in neurologic functioning which resolved over a short time period during the 24 months prior to evaluation. None of the patients demonstrated an exacerbation during the time of testing. The remaining 3 patients had a chronic-progressive pattern involving a progressive deterioration in their neurologic status not punctuated by acute decrements, and without a return to baseline. Patients were stable clinically at the time of testing. Neuro-
logical examination and Kurtzke's Extended Disability Severity Scale (EDSS) (15) were performed within two weeks of testing by experienced neurologists who were blinded to the nature of this study. In order to control for the possibility that the MS patients had progressed clinically during the course of the study, EDSS scores were obtained at each testing session. EDSS scores changed minimally and did not approach a statistically significant change. Statistical analyses involving EDSS scores used an average for each patient across sessions. Age and disease duration were those at the completion of the study. Exclusionary criteria included the presence of a dementia, hydrocephalus, head trauma, or some other central neurologic process, a primary psychiatric diagnosis such as major depression, another medical problem that could have interfered with performance on the neuropsychological tasks, or visual or auditory difficulties that could have interfered with task performance. All MS patients thus had visual acuity better than 20/50 and did not have an oculomotor abnormality. None of the patients were taking psychoactive medications at the time of testing. The MS patients were compared with 16 age-matched [t(34) = 1.05; ns] and education-matched [t(34) = 0.53; ns] control subjects who were recruited from among patients’ spouses and the local community. Clinical and demographic data are summarized in Table 1.

Language materials

We evaluated sentence processing performance on three comprehension tasks: 1) Sentence-Picture Matching; 2) Written Sentence Comprehension; 3) Oral Sentence Comprehension. These tasks were administered in a randomly ordered fashion at 3 different sessions separated by 2 monthso that there was no interference across tasks.

Sentence-picture matching – Subjects were asked to match an orally presented sentence with one picture from among four choices. Forty trials were presented. Each sentence stimulus contained a simple transitive verb with a semantically reversible subject and object, and the duration of sentence was between 2 and 3 s. Among the 40 sentences, grammatical phrase structure and grammatical voice were systematically varied. Thus, 8 target sentences were simply declarative in form (such as ‘The cat chased the dog’); 16 target sentences contained a relative clause at the end of a simple sentence (so-called terminal subordinate items, such as ‘The cat chased the dog that was fast’); and 16 target sentences contained a relative clause in the middle of a simple sentence (so-called center-embedded subordinate items, such as ‘The cat that chased the dog was fast’). Grammatical voice was manipulated by casting half of each sentence type in an active voice or with an object-relative center-embedded phrase (as in the examples above), and half of each sentence type in the passive voice (e.g., ‘The dog was chased by the cat’) or a subject-relative center-embedded phrase. The three incorrect picture foils were designed specifically to illustrate either an incorrect agent error (e.g., a person chasing a dog), an incorrect verb error (e.g., a cat and a dog sitting next to each other), or a subject-object reversal error (e.g., a dog chasing a cat). The items were arranged in random order and read twice in a naturalistic manner that provided no cues as to the correct response. Responses were untimed; all subjects responded to all items. A practice session preceded the administration of the task. The practice items were ordered so that they became progressively more difficult, eventually approximating all types of sentences used in the task. Patients were given feedback during the practice session. All patients appeared to understand the nature of the task.

Written sentence comprehension – Subjects were asked to answer a simple probe question about a target written sentence. There were 40 target sentences, each of which was followed by a simple probe (such as, ‘The eagle was chased by the hawk that was fast. Which bird was chased?’). Phrase structure was manipulated by including 8 simple sentences, 16 terminal subordinate sentences, and 16 center-embedded sentences. Grammatical voice was manipulated in the target sentences as in the sentence-picture matching task. As a control feature, half of each type of item featured a probe question in the same grammatical voice as the target sentence, as in the example provided above. In the remaining items, the voice of the probe question did not correspond to the voice of the target sentence (such as ‘The eagle chased the hawk. Which bird was chased?’). Semantic constraint was manipulated by using a semantically reversible subject and object, as in the above examples. The remaining half of the sentences used a non-reversible subject and object that could change places only by violating commonly held semantic

Table 1. Means (SD) clinical characteristics of control subjects and MS patients

<table>
<thead>
<tr>
<th></th>
<th>Control subjects</th>
<th>All MS patients</th>
<th>MS preserved sentence comprehension</th>
<th>MS impaired sentence comprehension</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>16</td>
<td>20</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38.06 (4.39)</td>
<td>36.10 (6.32)</td>
<td>35.93 (6.30)</td>
<td>36.87 (7.10)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.69 (1.99)</td>
<td>15.25 (2.81)</td>
<td>15.90 (2.80)</td>
<td>13.20 (1.79)</td>
</tr>
<tr>
<td>Severity (EDSS)</td>
<td>3.03 (1.68)</td>
<td>2.72 (1.66)</td>
<td>3.28 (1.69)</td>
<td></td>
</tr>
<tr>
<td>Duration (months)</td>
<td>81.75 (52.36)</td>
<td>77.99 (67.30)</td>
<td>91.21 (39.07)</td>
<td></td>
</tr>
</tbody>
</table>
notions (such as ‘The worm was chased by the eagle’). The items were arranged in random order, and presented visually in block capital letters printed in black against a white background. Responses were untimed, the sentences remained in view until subjects responded, and subjects responded to all items. A practice session was administered prior to the experimental session. The items were discussed with patients, and they appeared to understand the nature of the task.

**Oral sentence comprehension** – This 40-item task was similar to the written sentence comprehension task, except that the target sentences were presented orally. Grammatical phrase structure, grammatical voice, and semantic constraint were manipulated, as above. The sentences created for this task differed in content from the written sentences. Each item was read twice to the subjects in a naturalistic manner, and the duration of each sentence presentation was between 2 and 3 s. Responses were untimed and all subjects responded to all items. A practice session preceded the task.

**Other neuropsychological materials**

All MS patients performed several neuropsychological tasks to determine the basis for their difficulty. With two exceptions noted below, these tasks were administered at each session, and were then averaged to obtain a performance score on each task. Performance did not differ statistically across sessions for any of the tasks.

**Speed of information processing** – a) Digit-Symbol Decoding – decoding a random series of digits listed on a sheet of paper according to a written template of corresponding visual symbols. We measured the number of correctly decoded pairs in 90 s (16); b) Paced Auditory Serial Addition Test (PASAT) – serial addition of numbers that are presented aurally at set speeds. The 2.4-s pacing speed was used here, and a ratio of the time required to complete the 60-items divided by the proportion of correct responses is reported (17).

**Verbal memory** – The free recall portion of the Rey Auditory Verbal Learning Test (RAVLT) was used as a measure of verbal memory. This required order-free recall of an aurally presented list of 15 semantically unrelated nouns over five consecutive learning trials. The subject was asked to recall as many words as possible after each presentation. We report the number of words learned on trial 5 minus the number learned on trial 1 (18).

**Executive functioning** – a) Controlled Oral Word Association Test (phonemic fluency) – spontaneous oral production of words beginning with a given letter, ‘f’ or ‘a’ or ‘s’, over one minute for each letter target. We report the cumulative number of correct targets produced over three minutes (19); b) Wis-
Wisconsin Card Sorting Test (WCST) – card sorting according to a rule that must be discovered by the patient in a trial-and-error fashion on the basis of feedback from the examiner. After 10 accurate sorts, the rule for card sorting is shifted covertly. The number of categories achieved (or progressive number of rules successively discovered) is reported here (20). This task was administered only once during the course of the study.

Language – The Western Aphasia Battery (WAB) – This battery was administered once during the study in order to characterize language deficits according to traditional aphasia syndromes (21). The reported measures include: spontaneous speech production (information content, fluency); auditory verbal comprehension (yes-no questions, word recognition, sequential commands); repetition (simple words, phrases, sentences); and naming (object naming, word fluency, sentence completion, responsive speech). The WAB does not include a measure of sentence comprehension that stresses grammatical processing, and thus differs critically from the tasks devised for this study.

Statistical Analyses

Group data were analyzed using non-parametric analyses of variance (ANOVAs), including Kruskal-Wallis one-way ANOVA by rank and Friedman two-way ANOVA by rank. This was necessary since control subjects' mean group performance at times approached ceiling levels. Individual patient analyses were performed by the conversion of critical variables to standard z-scores, based on control subjects' performance. Individual patient performance profiles on the three sentence comprehension tasks could then be compared across tasks independently of task difficulty. A z-score of less than –1.65, differing from control subjects' performance at the \( P < 0.05 \) level of significance, was used as the criterion for impaired performance.

![Fig. 2. Mean (SD) performance on particular sentence features of sentence-picture matching, written sentence comprehension, and oral sentence comprehension tasks in all MS patients and control subjects.](image-url)
Grossman et al.

Results

Between-group analyses

Sentence-picture matching – Overall performance in comparison to controls is illustrated in Fig. 1. Friedman two-way ANOVAs demonstrated interaction effects that approached significance for group × grammatical phrase structure \( F(2) = 5.59; P < 0.06 \). MS patients and controls did not differ in their performance on active voice or simple declarative sentences, but Fig. 2 shows that MS patients were somewhat worse as a group than controls in their appreciation of sentences with subordinate phrase structures and sentences cast in the passive voice. An analysis of picture pointing errors revealed a significant group × error type effect \( F(2) = 16.83; P < 0.0002 \). MS patients erred by selecting the subject-object reversal foil (7.50% of responses) more often than controls (4.55% of responses), and more often than MS patients’ own selection of other types of errors.

Written sentence comprehension – Overall performance in comparison to controls is summarized in Fig. 1. Friedman two-way ANOVAs demonstrated significant interaction effects for group × semantic constraint \( F(1) = 6.25; P < 0.01 \), and for group × grammatical voice \( F(1) = 4.00; P < 0.05 \). Thus, MS patients and controls did not differ in their comprehension of semantically constrained sentences or sentences in the active voice, but Fig. 2 shows that MS patients encountered relatively more difficulty as a group than controls in appreciating semantically reversible sentences and passive voice sentences. Significant interaction effects were not observed for group × grammatical phrase structure \( F(2) = 1.06; \text{ns} \).

Oral sentence comprehension – Overall MS performance is illustrated in Figure 1. Friedman two-way ANOVAs found a significant interaction effect for group × semantic constraint \( F(1) = 11.3; P < 0.0008 \). MS patients did not differ from controls in their comprehension of semantically constrained sentences, but Fig. 2 shows that they were more impaired as a group than controls at appreciating semantically reversible sentences. Significant interaction effects were not observed for group × grammatical phrase structure \( F(2) = 1.01; \text{ns} \), or group × grammatical voice \( F(1) = 1.26; \text{ns} \).

Western aphasia battery – As a group, MS patients demonstrated a normal Aphasia Quotient (98.98 (S.D. = 1.38; range = 95.60-100)). Scores for each of the four major language skills measured by this instrument were normal as well.

Table 2. Individual patient profiles on three sentence comprehension tasks

<table>
<thead>
<tr>
<th>Case #</th>
<th>Overall accuracy</th>
<th>Subordinate phrase</th>
<th>Passive voice</th>
<th>Overall accuracy</th>
<th>Subordinate phrase</th>
<th>Passive voice</th>
<th>Semantically reversible</th>
<th>Overall accuracy</th>
<th>Subordinate phrase</th>
<th>Passive voice</th>
<th>Semantically reversible</th>
</tr>
</thead>
</table>
| Impaired subgroup
| 12213 | -                | -                  | -              | -                | -                 | -             | -                       | -               | -                 | -             | -                     |
| 12110 | -                | -                  | -              | -                | -                 | -             | +                       | +               | +                 | +             | -                     |
| 12115 | -                | -                  | -              | -                | -                 | -             | -                       | -               | -                 | -             | +                     |
| 12205 | -                | -                  | -              | -                | -                 | -             | -                       | -               | -                 | -             | +                     |
| 12217 | -                | -                  | -              | -                | -                 | -             | -                       | -               | -                 | -             | -                     |
| Preserved subgroup
| 12204 | +                | +                  | +              | +                | +                 | +             | -                       | -               | -                 | -             | +                     |
| 12100 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12106 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12107 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12109 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12112 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12117 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12118 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12119 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12120 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12123 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12124 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12200 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12210 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |
| 12223 | +                | +                  | +              | +                | +                 | +             | +                       | +               | +                 | +             | +                     |

1. = impaired (z ≤ -1.65); + = intact (z > -1.65)
Within-group analyses

It is possible that all MS patients were marginally impaired on sentence processing measures. Alternatively, overall group performance may have reflected an averaging across individual patients with different levels of performance, obscuring the detection of individual MS patients who are significantly compromised in their sentence processing. To assess these possibilities, we converted patient performance on the sentence comprehension tasks to z-scores. As can be seen in Table 2, five MS patients were impaired on most aspects of sentence comprehension across the 3 tasks.

On the basis of these findings, we partitioned the MS patients into two performance subgroups: those with relatively impaired sentence comprehension, and those with preserved sentence comprehension. Table 1 indicates that these subgroups did not differ in terms of clinical or demographic features. Overall performance of these MS subgroups on the three sentence comprehension tasks, summarized in Fig. 3, confirmed our hypothesis that a subgroup of MS patients is significantly impaired on sentence comprehension measures.

In order to examine the basis for the sentence comprehension impairment in MS, we compared the impaired and preserved MS subgroups on other neuropsychological variables. As summarized in Table 3, these comparisons demonstrated significantly impaired performance only on PASAT and Symbol-Digit Decoding for the subgroup of MS patients with sentence comprehension difficulty. Differences were not observed on the RAVLT, phonemic fluency, or the WCST.

Discussion

Previous group studies of cognitive function in MS rarely have reported language deficits (6, 22-27). Single case studies have reported occasional language difficulties (3-5). Standard aphasia batteries such as the WAB do not include a measure of grammatical comprehension, and may not be sensitive to
detecting language problems in MS. Group-wide analyses similarly demonstrated only marginal sentence comprehension impairments in MS patients when compared to age- and education-matched control subjects. However, our preliminary analyses of individual patient profiles revealed that a subgroup of MS patients – 25% of the patients in this survey – is consistently impaired to a significant extent in their sentence comprehension. Group averaging may have obscured the detection of language difficulty in some MS patients.

Several possible accounts may be offered to explain these sentence comprehension deficits. Clinical variables reported to influence cognitive functioning in MS (22, 25), such as age, education, disease duration and disease severity, did not distinguish between MS subgroups and were unrelated to sentence comprehension performance. Jennekins-Schinkel et al (6) attributed language deficits in MS specifically to their sensori-motor abnormalities, including impaired phonatory apparatus, oculomotor weakness, or weakness of color vision. We excluded patients with these abnormalities from our study, and we failed to observe a relationship between EDSS score and sentence comprehension performance in MS. Sentence comprehension of auditory material may depend in part on verbal memory, since information must be stored temporarily for accurate comprehension to occur (28-30). An auditory-verbal memory impairment could not explain the difficulty we found understanding written sentences, and differences in verbal memory were not observed between MS subgroups. A central executive component of short-term memory may play a special role in organizing and selectively attending to material such as complex syntactic structures (31, 32), but we failed to find a correlation between executive functioning and sentence comprehension performance. Indeed, the absence of verbal memory differences and the comparable performance on measures of executive functioning in the MS subgroups emphasize that a global cognitive impairment or a dementia can not fully explain these findings.

It is important to point out that specific aspects of sentences appeared to be particularly difficult for MS patients. Thus, little difficulty was encountered in their attempts to understand grammatically simple sentences cast in an active voice. MS patients also were able to interpret sentences that were semantically constrained. Deficits did become apparent, however, when the MS patients were attempting to understand semantically non-constrained sentences with subordinate phrases or sentences in the passive voice. One possibility is that the sentence comprehension deficit in MS is due to the loss of certain aspects of grammatical knowledge, analogous to some hypotheses forwarded to account for sentence comprehension difficulty in Broca’s aphasics (33, 34). While our data can not address this issue directly, the results of the WAB demonstrated that MS patients do not resemble Broca’s aphasics clinically.

An alternative account for their comprehension difficulty stems from the observation that the comprehension-impaired MS subgroup also had deficits on neuropsychological measures said to reflect mental information processing speed. To be sure, these are crude measures, and additional work is needed to confirm this association. Nevertheless, it can be speculated that slowed neural processing associated with demyelination contributes to these processing speed limitations. Several investigators have hypothesized that deranged information processing speed may contribute to compromised grammatical comprehension in Broca’s aphasics (9-13). This hypothesis assumes that grammatical knowledge is preserved, but that grammatical and semantic information can not be integrated efficiently to support accurate sentence comprehension. Specifically, deranged information processing speed may result in a temporal mismatch of grammatical structures and representations of meaning. Compromised speed of information processing has been proposed to undermine performance in other cognitive domains such as verbal memory in MS (7, 8). We speculate that slowed information processing speed may also account for the sentence processing deficits of some MS patients. If confirmed by additional studies, these findings would provide additional support for the claim that speed of information processing plays a crucial role in sentence processing.

Several caveats must be kept in mind when interpreting our preliminary results. We studied a small group of consecutively seen MS patients at a university medical center, and these results require verification in a larger MS population that is community-based. We focused on one specific aspect of linguistic functioning, and our findings cannot be generalized to other aspects of language processing. We used multiple off-line sentence comprehension tasks that presented materials in both auditory and visual modalities, but convincing support for the hypothesized relationship between sentence comprehension and information processing speed requires further investigation with on-line measures. Neuropsychological tasks such a PASAT and Symbol-Digit are quite complex, involving multiple processing components, and it is necessary to confirm the role of information processing speed in the sentence comprehension of MS patients with other measures of mental processing speed such as the Sternberg Memory Scanning Task. It would be important in future studies to establish the physiological basis for sentence comprehension difficulty through correlative MRI investigations of plaque burden in MS. With these cave-
ats in mind, our preliminary findings indicate that a subgroup of MS patients has consistent difficulty understanding sentences. These deficits appear to be associated with compromised speed of mental information processing.

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References