Word fluency in relation to severity of closed head injury, associated frontal brain lesions, and age at injury in children

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Abstract

Effects of closed head injury (CHI) severity, focal brain lesions, and age at injury on word fluency (WF) were studied longitudinally in 122 children (78 severe, 44 mild); 112 CHI patients (68 severe, 44 mild CHI) and 104 uninjured normal controls participated in a cross-sectional study. WF was measured by asking the child to generate as many words as possible beginning with a designated letter within 60 s, repeated for three letters. Intellectual ability, receptive vocabulary, narrative discourse, and word list recall were also measured. Results of the cross-sectional study showed a significant group effect with poorer WF in severe CHI than mild CHI and control groups. Growth curve analysis of longitudinal data revealed an interaction of age, follow-up interval, and CHI severity as WF recovery was slower after severe CHI in younger children as compared to severe CHI in older children or mild CHI in younger children. An interaction of left frontal lesion with age and interval indicated a more adverse effect on WF in older children. Right frontal lesion effect was nonsignificant and did not interact with age. Correlations of WF with receptive vocabulary, word list recall, and narrative discourse were moderate and weak with estimated intellectual ability. Differences in focal lesion effects after traumatic versus nontraumatic brain injury in children, the contribution of diffuse white matter injury, reduced opportunity for language development, and functional commitment of left frontal region at time of CHI were discussed. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Word fluency; Closed head injury; Children; Frontal lesions; Neuroplasticity

1. Introduction

Expressive language impairments are frequent sequelae of severe closed head injury (CHI) in children, involving reduced word fluency (WF), difficulty in naming, reduced spontaneous speech, deficient writing to dictation, and discourse formulation problems [7,17,18,20,25,30,34]. Despite relative recovery of receptive language abilities, expressive language impairments tend to persist after severe CHI in children [17,18]. Factors which could contribute to persistent WF deficit after severe CHI include associated impairments in spontaneity and initiative, attention, verbal productivity under restricted search and retrieval conditions, working memory to monitor words already mentioned and to maintain a word production set, response inhibition to suppress words which are excluded by the rules, and cognitive flexibility to shift from one word to the next and take a novel approach to the task [10,40,44,45]. In a study of WF in healthy adults, Troyer et al. [54] found that clustering ability to produce words within phonetic and semantic subcategories and switching between clusters, were correlated with the number of words generated. Taken together, these processes postulated to be involved in WF performance are widely viewed as executive functions that are subserved by a network dependent on the integrity of the prefron-
tal region. Consistent with this view, reports of WF in adults following focal brain lesions or more diffuse CHI have supported the distinction between a verbal deficit related to left frontal involvement and an executive function impairment which is associated with injury to either frontal lobe [10,44,45]. There is also related evidence that the number of errors might be particularly sensitive to the executive dysfunction component of WF in adults with CHI [10]. Positive correlations of WF scores with verbal intelligence and educational level have also been reported [40].

In contrast to the impaired development of expressive language after severe CHI in infants, non-traumatic focal brain lesions before age 1 year are compatible with relatively normal language development after an initial delay [1,21]. Differences in the linguistic outcomes of severe CHI and nontraumatic vascular lesions are presumably related to distinct pathophysiologic features of these etiologies of brain injury. Severe CHI in young children typically involves diffuse axonal injury (DAI) and multiple ischemic lesions [28] which occur in isolation or concomitant with focal hemorrhagic or ischemic lesions, whereas focal non-traumatic vascular lesions occur relatively free of more widespread brain injury. DAI during a period of rapid white matter development might account for the devastating impact of severe CHI on neurobehavioral functioning in young children relative to older children and adolescents [52], a pattern which is opposite to the apparent sparing of function after early non-traumatic focal vascular lesions. Shearing injury and DAI secondary to excitotoxicity [37] during early childhood could disrupt development of the anterior cerebral circuitry which has been implicated by investigations of WF in adults with left frontal lesions [2,39] and by functional brain imaging studies demonstrating activation of dorsolateral prefrontal cortex, cingulate, and inferior frontal gyrus in normal adults performing WF [11,23,43,47]. Consequently, reorganization of ipsilateral or contralateral homologous frontal cortex which putatively occurs after nontraumatic vascular lesions might be ineffective in compensating for severe, early DAI. However, exceptions to this dissociation between CHI and nontraumatic focal vascular lesions occur. In atypical cases, CHI in infants can produce focal hemispheric lesions associated with mild impairment of consciousness, mild diffuse cerebral insult, and apparent reorganization of function [35].

Cortical development appears to be heterochronous and regionally specific. Postmortem evidence for later maturation of frontal cortex relative to other cortical regions is reflected by synapse elimination extending into midadolescence [31] and later myelination of the frontal lobes than other regions [58]. Recent longitudinal MRI findings [27,49] indicated that frontal lobe gray matter volume increases during pre-adolescence followed by a decline during post-adolescence. Consequently, we postulated that age-related increases in specialization of left frontal cortex for verbal productivity and memory search strategies [26] would result in more adverse and persistent effects of lesions in this region on WF in older children and adolescents as compared with similar lesions sustained by younger children.

The developmental trajectory of WF has been studied [33,46], thus providing a frame of reference for investigating lesion effects in children. Cross-sectional studies [24,33,46] indicate that WF improves with increasing age to at least 13 years, with written WF increasing to 18 years [50]. However, gaps in the developmental CHI literature include the relationship of age at injury to recovery and the relative contributions of focal brain lesions and diffuse cerebral insult. Consequently, we have investigated the effects of CHI severity, associated focal brain lesions, and age on WF in cross-sectional and longitudinal studies. The goals were to address the (1) sensitivity of WF to the severity of CHI in children; (2) relationship of frontal lobe lesions to WF; (3) effects of CHI on development of WF, including an analysis of relationship to age at injury and time since injury; and (4) relationship of WF to intellectual, language, and memory abilities following CHI. Both studies addressed the effects of CHI severity and age at injury, whereas the longitudinal study characterized the process of change based on serial outcome measurements. Administration of the WF test on a single occasion to a sample of uninjured children provided an opportunity to evaluate the performance of mildly injured CHI patients in the cross-sectional study. This goal was important because longitudinal data were collected for the children who sustained mild or severe CHI, whereas participation of the uninjured children was limited to the cross-sectional study.

### 2. Methods

#### 2.1. Subjects

This study was conducted as part of an ongoing, larger project concerning the neurobehavioral outcome of CHI children. Selection criteria for the cross-sectional and longitudinal studies included conscious survival after hospitalization for CHI, an age range of 5–15 years at the time of injury, and resolution of post-traumatic amnesia according to the Children’s Orientation and Amnesia Test [19]. Exclusionary criteria included pre-existing neuropsychiatric disorder, child abuse, or mental deficiency.
2.1.1. Cross-sectional study

The cross-sectional sample was composed of the 112 CHI patients in the longitudinal study who had a 3-month post-injury fluency test, along with 104 non-injured control children who resided in Dallas or Houston and were tested on a single occasion.

2.1.2. Longitudinal study

For the longitudinal study, we selected all 122 subjects in the project who had completed the WF test on at least three occasions. Most participants in the longitudinal study had WF tested on three or four occasions. Of this sample of head injured children, follow-up examinations were completed by 112 patients at 3 months (mean age at test = 9.95 years, S.D. = 3.04); 103 had a 6-month examination (mean age at test = 10.19 years, S.D. = 3.08); 118 had a 12-month (mean of age at test = 10.66 years, S.D. = 3.06) examination; 97 were studied at 21 months (mean age at test = 11.38, S.D. = 3.11); 68 had a 36-month examination (mean age at test = 12.60, S.D. = 3.10); 13 had a 48-month (mean age at test = 14.45, S.D. = 3.60) follow-up assessment; and six had a 60-month evaluation (mean age at test = 12.95, S.D. = 2.17). For those children who missed WF tests at the 3-, 6-, 12-, 21- or 36-month occasions, we documented the reasons for missing data. The reasons included move of family, post-injury interval shorter than 21 or 36 months, and scheduling problems with families on a particular test occasion who returned on the next occasion. Few children were tested at 48 or 60 months after injury due to the closing of one study site and revision of the study protocol. The average age at injury was 9.6 years.

Table 1A and B show the demographic and clinical features of the children included in the cross-sectional and longitudinal studies. There are no differences in age at test, years of parental education, or gender among control, mild and severe groups.

2.2. Characterization of injury severity and MRI acquisition

To address the analysis of CHI severity, the longitudinal study compared WF after severe CHI to findings in children who sustained a mild CHI. Severe CHI was defined by a post-resuscitation score of 8 or less on the Glasgow Coma Scale (GCS) of Teasdale and Jennett [51]. Mild CHI was defined by a GCS score of 13–15, normal findings on computed tomography during the initial hospitalization, and normal magnetic resonance imaging (MRI) results at least 3 months post-injury. Although the MRI protocol evolved during the project to use thinner slices and higher field magnets, T1-weighted sagittal and coronal images, and T2-weighted coronal images have been consistently employed. The protocol used in recently studied patients

Table 1

(A) Demographic and clinical features of the head injured and control groups in a cross-sectional study and (B) of the head injured groups in a longitudinal study

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 104)</th>
<th>Mild CHI (n = 44)</th>
<th>Severe CHI (n = 68)</th>
<th>Statistics</th>
<th>P-value</th>
</tr>
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<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
</tr>
<tr>
<td>Age at study (years)</td>
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<td>3.2</td>
<td>10.1</td>
<td>2.8</td>
<td>9.9</td>
</tr>
<tr>
<td>Age at injury (yrs)</td>
<td>9.8</td>
<td>2.8</td>
<td>9.5</td>
<td>3.2</td>
<td>13.9</td>
</tr>
<tr>
<td>Parental education (years)</td>
<td>14.1</td>
<td>2.5</td>
<td>14.5</td>
<td>2.5</td>
<td>13.9</td>
</tr>
<tr>
<td>GCS score</td>
<td>14.6</td>
<td>0.6</td>
<td>5.8</td>
<td>1.8</td>
<td>6.1</td>
</tr>
<tr>
<td>Right handed (%)</td>
<td>91</td>
<td>98</td>
<td>88</td>
<td>88</td>
<td>3.18</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls (%)</td>
<td>39</td>
<td>48</td>
<td>41</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Boys (%)</td>
<td>61</td>
<td>52</td>
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(B) Longitudinal study

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
<th>F(1,120)</th>
<th>0.09</th>
<th>0.09</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at injury (yrs)</td>
<td>9.8</td>
<td>2.8</td>
<td>9.6</td>
<td>3.2</td>
<td>6.2</td>
<td>1.8</td>
<td>F(1,114)</td>
<td>1.65</td>
<td>0.20</td>
</tr>
<tr>
<td>Parental education (years)</td>
<td>14.5</td>
<td>2.5</td>
<td>13.9</td>
<td>2.4</td>
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<td></td>
<td>F(1,120) = 1035.86</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>GCS score</td>
<td>14.6</td>
<td>0.6</td>
<td>5.7</td>
<td>1.8</td>
<td>6.1</td>
<td>1.5</td>
<td>F(1,120)</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>Right handed (%)</td>
<td>98</td>
<td>90</td>
<td>3.18</td>
<td>0.20</td>
<td></td>
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<tr>
<td>Gender</td>
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<td></td>
</tr>
<tr>
<td>Girls (%)</td>
<td>48</td>
<td>42</td>
<td>3.18</td>
<td>0.20</td>
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<tr>
<td>Boys (%)</td>
<td>52</td>
<td>58</td>
<td>3.18</td>
<td>0.20</td>
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</table>

* Preinjury handedness.
included 5 mm T2 coronal slices without a gap and a 1.5 mm T1 SPGR sequence. A neuroradiologist reviewed all of the scans independent of the cognitive data. The findings were entered on a coding form that specified the anatomic location and pathology of each focal area of abnormal intensity as well as atrophy, including specific frontal lobe gyri [12].

2.3. Neuropsychological procedure

WF was measured by the Controlled Oral Word Association Test [3] which involved asking the child to generate as many words as possible in one minute beginning with a specific letter, excluding proper nouns and the same word repeated with a different suffix. The number of correct words generated was summed across three trials, each using a different initial letter. Errors were also recorded, including intrusions (i.e. words that did not begin with the designated letter), perseverations (i.e. repetitions of a word previously mentioned by the child on the same trial), and other errors (i.e. rule breaks including proper nouns and the same word with a different suffix).

Assessment of intellectual function, other language abilities, and memory, which was performed as part of a broader investigation of outcome, provided an opportunity to study abilities associated with WF in the head injured children and healthy controls. To investigate the relationship of WF to intellectual function, we analyzed data from the cross-sectional study because the healthy control group had also been tested on a single occasion using the Vocabulary and Picture Completion subtests of the Wechsler Intelligence Scale for Children-Revised (WISC-R) [57]. WISC-R subtest scores collected at 3 months post-injury were used for the CHI groups because more children were tested at this interval than at any other endpoint. To estimate Verbal and Performance IQ scores, we multiplied the WISC-R Vocabulary standard score by five to obtain a prorated Verbal IQ and the Picture Completion standard score by five to obtain a prorated Performance IQ for the CHI and control groups.

Associated language measures included a narrative discourse task [8] and the Peabody Picture Vocabulary Test-Revised (PPVT-R) [16] which measured receptive vocabulary. The narrative discourse task [8], which was administered to 67 CHI children in the longitudinal study at 3 and 36 months post-injury, elicited a narrative using eight picture sequence cards that were shown to the child, one at a time, for a minimum of 8 s each without any commentary. After viewing all eight pictures, the child was asked to generate a complete story based on the actions shown. A detailed description of this task is available [8]. Efficiency of narrative discourse production was measured by the number of core propositions produced per minute [8], a measure of spontaneous verbal production which has been used in studies of head injured adults [29]. The California Verbal Learning Test-Children’s Version (CVLT-C) [13] was analyzed to study the relationship between verbal learning and WF. Both the PPVT-R and CVLT-C were administered serially corresponding to the same schedule as the WF test. The numbers of head injured children in the longitudinal study tested on the PPVT-R and CVLT-C at each interval approximated the sample size for the WF test.

2.4. Statistical analysis

In the cross-sectional study, we analyzed word fluency data from 104 control children and 112 mild and severe CHI patients who had a 3-month post-injury evaluation. The corresponding sample sizes with WISC-R data were 101 for control children and 102 mild and severe CHI patients. An analysis of covariance (ANCOVA) model [36] was fit to elucidate age at injury and severity of injury effects in recovery of word fluency, PPVT-R raw score and CVLT-C Monday list total recall as measured at 3, 6, 12, 21, 36, 48 and 60 months post-injury for 122 CHI patients. Using a repeated measures model [6,48] was fit to test the group effect, age at test effect, and their interaction in the cross-sectional study. In the longitudinal study, a growth curve model [15], left and right frontal lesion effects were evaluated in 39 severe CHI patients who completed the 3- and 36-month fluency tests. The discourse data obtained at 3 and 36 months were subjected to a repeated measures analysis. Pearson correlation coefficients among the language and memory measures were also examined.

3. Results

3.1. Cross-sectional study

ANCOVA identified a main effect of Group on WF, \( F(2,208) = 16.65, P < 0.0001 \). Pair-wise comparisons indicated that compared to the severe CHI group, the mild CHI and control groups generated a greater number of total correct words. The age adjusted means for the control, mild, and severe groups were 23, 23 and 17 respectively. Age at the time of testing significantly affected the total number of correct words, \( F(1,208) = 157.42, P < 0.0001 \). There was no significant age x group interaction. Analysis of the three categories of errors on the word fluency test (Table 2) disclosed no significant group differences among control and CHI patients at 3 months post-injury despite a tendency of the severely injured children to produce more errors than the other groups. The mean and standard deviation of the number of errors for the CHI patients at 36 months are also included in Table 2 for comparison.
Comparison of the IQ scores among the severity groups in the cross-sectional study disclosed significant group effects with control and mild TBI groups having higher prorated IQ scores than the severe CHI group. On the Verbal Scale, controls had a mean IQ of 107 (S.D. = 18) and mild CHI patients had a mean IQ of 106 (S.D. = 20) as compared to a mean IQ of 94 (S.D. = 22) for severely injured children, $F(2,194) = 9.28$, $P < 0.0001$. On the Performance Scale controls had a mean IQ of 113 (S.D. = 20) and mild CHI patients had a mean IQ of 112 (S.D. = 19) as compared to a mean IQ of 101 for severely injured children (S.D. = 22), $F(2,196) = 7.13$, $P = 0.001$. Pearson correlation coefficients revealed weak associations between the total correct words on word fluency and prorated Verbal Scale IQ, $r = 0.17$, $P = 0.02$ and Performance Scale IQ, $r = 0.20$, $P = 0.005$.

3.2. Longitudinal study: age, severity, and interval effects on word fluency

We fitted a series of models to identify the covariance structure in the model. By examining Akaike’s information criterion, Schwarz’s Bayesian criterion, and $-2$ log likelihood, it was indicated that a model with random intercept and random slope (interval) fitted the model best. The random intercept and slope showed the baseline measure at 3 months post-injury and the recovery rate for individual head injured children. By including the random effect in the model, we were able to estimate the changes among each individual child more accurately as compared to a marginal repeated measures model. A triple interaction of age at injury × interval × severity of injury was found significant, $F(1,270) = 4.86$, $P = 0.03$, indicating a slower recovery of WF for younger severe CHI children. Fig. 1 shows the mean number of words recalled by 122 mild and severe CHI children from three age at injury groups. Younger severe CHI children exhibited less post-injury improvement in WF as compared to younger mild CHI children and older severe CHI children. The interaction of interval × age at injury was significant, $F(1,270) = 10.95$, $P = 0.001$, indicating that the interval effect was stronger in younger children. Three main effects were significant: (a) CHI severity, $F(1, 270) = 20.46$, $P < 0.0001$; (b) interval, $F(1,118) = 27.71$, $P < 0.0001$, and (c) age at injury, $F(1,270) = 80.69$, $P < 0.0001$. We also found a significant second order interval effect, indicating the curvature of interval and number of correct word associations.

3.3. Longitudinal study: growth curve model of receptive vocabulary and word list recall

Using a growth curve model to analyze the PPVT-R raw scores, we found a significant interval effect, $F(1,116) = 102.64$, $P < 0.0001$ and an interval x interval effect, $F(1,116) = 10.43$, $P = 0.002$. There was also a significant group effect, $F(1,123) = 11.75$, $P = 0.0007$ and a significant age at injury effect, $F(1,123) = 205.49$, $P < 0.0001$. The interval x age at injury interaction was significant, $F(1,123) = 28.58$, $P < 0.0001$, indicating that the receptive vocabulary of young children increased more rapidly after injury as compared to older children.

![Fig. 1. Mean total number of words recalled by mild and severe CHI children from three age at injury groups in longitudinal study. Growth curves show that younger children exhibit less improvement in word fluency after severe CHI as compared to younger children who sustained mild CHI and older children following severe CHI.](image-url)
who sustained a CHI (Fig. 2). Consistent with the lack of a three-way interaction of group, age at injury, and interval, the growth curves in Fig. 2 show parallel improvement over time in receptive vocabulary for the mild and severe CHI groups at various intervals since injury. Despite a tendency for the difference between the mild and severe injury PPVT-R curves to widen with increasing age, there was no interaction between group and age at injury.

Recall of the CVLT-C Monday list was also analyzed in a growth curve model. The main effects of interval \( (F(1,118) = 45.52, P < 0.0001) \), group \( (F(1,268) = 39.35, P < 0.0001) \), and age at injury \( (F(1,268) = 41.99, P < 0.0001) \) were significant. There were also a significant interval \( \times \) interval effect, \( F(1,118) = 14.23, P = 0.0003 \); and a significant age at injury \( \times \) interval interaction, \( F(1,268) = 30.50, P < 0.0001 \), reflecting greater improvement in verbal recall over time since injury in younger children relative to older children. The interval \( \times \) group interaction was significant, \( F(1,268) = 15.88, P < 0.0001 \), reflecting a decrease over time since injury in the difference in word list recall between mild and severe CHI children. Similar to the PPVT-R, there was no triple interaction of group, interval, and age at injury despite a tendency for the difference in scores between mild and severe CHI groups to increase with age.

### Table 3
A repeated measures of discourse measures at 3- and 36-month post-injury

<table>
<thead>
<tr>
<th></th>
<th>3 month</th>
<th>36 month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Severe</td>
</tr>
<tr>
<td>Core</td>
<td>12.1 (4.91)</td>
<td>8.33 (4.73)</td>
</tr>
<tr>
<td>proposition per minute</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3.4. Longitudinal study: repeated measures analysis of discourse data

A repeated measures model was used to analyze the number of core propositions per minute for the 3- and 36-month data because the narrative discourse task was administered at fewer endpoints than the PPVT-R and CVLT-C. Mild CHI children produced more core propositions per minute as compared to severe CHI children, \( F(1,114) = 23.79, P < 0.0001 \) (Table 3). The occasion effect was also significant for core propositions, \( F(1,23) = 7.79, P = 0.01 \), but there was no interaction with group.

### 3.5. Longitudinal study: intercorrelations among word fluency and ancillary measures

Table 4 displays Pearson correlation coefficients of word fluency, PPVT-R, number of core propositions per minute, and total recall of Monday list words on the CVLT-C averaged across the 3- and 36-month data. Receptive vocabulary and total recall of the Monday list on the CVLT-C were moderately correlated with the total number of words generated on WF.

### 3.6. Longitudinal study: focal brain lesion effects on word fluency

We analyzed the effects of left frontal and right
frontal lesions (Table 5) in comparison with the performance of other severely injured children who did not have lesions in these sites (though lesions in other locations might have been present). We categorized 39 severe CHI patients in the longitudinal study who completed both 3- and 36-month fluency tests into two lesion groups: left frontal lesion group (23 patients) and without left frontal lesion group (16 patients). These groups did not differ in demographic features, GCS score or total lesion size. Table 5 shows that children with a left or right frontal lesion frequently had associated lesions in the contralateral frontal lobe, the temporal or parietal lobes, and/or the corpus callosum.

We fitted a regression model that included age at injury, occasion of testing, lesion group, and their interactions. There was a significant age at injury x lesion group interaction, $F(1,35) = 4.36, P = 0.04$. Fig. 3 shows that the difference between two lesion groups increases as age at injury increases, indicating that a left frontal lesion had a larger effect on the older children as compared with younger patients. The main effect of age at injury was also found to be significant, $F(1,35) = 29.25, P < 0.0001$, as was occasion of testing, $F(1,38) = 40.74, P < 0.0001$. Following the same method, we analyzed the right frontal lesion effect. However, no significant contribution of right frontal lesions to verbal fluency was found. Examples of left frontal and right frontal lesions are shown in Fig. 4.

4. Discussion

We found a dissociation between the relationship of age at injury to CHI severity and the effects of left frontal lesions on WF. Severe CHI sustained at a young age more adversely affected WF development than an injury of comparable severity in older children. In view of evidence for growth of cerebral white matter during infancy and early childhood and its prolonged maturational stage [42], shearing and secondary DAI from excitotoxicity [37] might produce disconnections of the neural circuitry engaged in WF. Functional brain imaging studies [11,43,47] in adults have shown that while dorsolateral prefrontal cortex is activated during WF performance, other sites (e.g., cingulate, inferior frontal gyrus) are also involved. Consequently, early DAI and white matter degeneration [4,28,32] could perturb development of an anterior neural network with persisting effects on WF. An alternative interpretation of the age-related dissociation in WF deficit is that brain injury at a young age shortens the period of normal brain function during which children can consolidate their linguistic system through age-appropriate reading acquisition and increases in vocabulary, with the result of reduced lexical knowledge to support efficient word generation under timed conditions. Consistent with this view, WF in children has been shown to load on factors involving reading, writing, and sentence construction [50].

In the present study, left frontal lesions in older children more adversely affected WF as compared with the outcome in young children with similar lesion sites on MRI. This age-related dissociation in the effect of left frontal lesions on WF is in accord with findings reported in adults sustaining lesions in this region.

Fig. 3. Histogram showing left frontal effect on mean total number of words recalled in longitudinal study, reflecting a greater lesion effect on word fluency in older children than in younger children.
Fig. 4. An 11-year-old right-handed boy sustained a severe CHI (GCS score = 7) when he was struck by a golf cart two years prior to the study and was found to have a left orbitofrontal lesion (A) on MRI performed 3 months post-injury. A 6-year-old, right-handed boy sustained a severe CHI (GCS score = 3) when he was struck by a car. MRI 3 months post-injury demonstrated a right frontal lesion (B) involving the gyrus rectus, orbitofrontal frontal gyrus, and inferior frontal gyrus with associated bifrontal white matter lesions and an ipsilateral anterior temporal lobe lesion.

We suggest that the left frontal lesion effect on WF can be interpreted as representing the combined influences of an expressive language deficit and executive dysfunction. Studies of adults [3,38] have also reported that a lesion of either frontal lobe can disrupt WF, possibly reflecting more general impairment in cognitive flexibility, inhibition, initiative, and working memory [44,45,54].

We attribute the left frontal lesion effect in older children and adolescents to the more established functional commitment of this region to expressive language and WF in particular as compared to a similar lesion in young children. This interpretation is supported by the finding of synaptic elimination in the middle frontal gyrus which continues into midadolescence [31] beyond the period of pruning in other cortical regions and a recent fMRI study [26] using a WF task in children and adults which found an age-related increase in a left frontal localization of activation. Consistent with functional brain imaging studies of linguistic recovery after nontraumatic left hemisphere lesions [5,41,55,56], we postulate that homotopic areas of the right hemisphere are recruited to subserve language in at least a subgroup of children sustaining early left frontal lesions.

PET scanning showing a peak of cortical glucose metabolism between ages 4 and 9 years has been interpreted as evidence for a window of cerebral plasticity which facilitates interhemispheric transfer of language [9]. Confirmation of this postulated mechanism of recovery from left frontal lesions associated with CHI would involve language activation studies using fMRI or PET. In addition, frontal lesions could compromise WF through diminished spontaneity, initiative, verbal productivity, cognitive flexibility, working memory, and inhibition [10,40,44,45,54].

Caution is advised in the interpretation of the longitudinal data due to variation in the number of follow-up assessments and unavailability of serial test data from uninjured children. However, availability of patients for follow-up testing at 48 or 60 months was unrelated to WF performance or the recovery status of CHI. There was no association between missing data process and the unobserved WF data. The proportions of missing data of mild and severe CHI were similar (85 and 82%) between 3 and 36 months. The mechanism of missing data appears not to be informative, or missing not at random [14]. According to Troxel et al. [53], the likelihood based analyses provide unbiased estimates using all observed data when the missing data process is not informative. The growth curve models we used, which included all the observed WF data, gave us valid results.

Notwithstanding these limitations of our study, we suggest that the adverse effects of severe CHI on WF in children persist for at least 5 years without evidence of recovery to an age-appropriate level. Although severely
injured children exhibited improved WF over time, their rate of WF development did not increase sufficiently to approximate the performance by children who had sustained mild CHI. In contrast to the persistent effects of severe CHI on WF, the cross-sectional study disclosed no difference in performance between children who had sustained a mild CHI and the scores of uninjured children who were recruited from the same community and did not differ from the patients in demographic features.

Analysis of ancillary tests disclosed that severely injured children had an intellectual impairment relative to mild CHI and uninjured comparison groups in the cross-sectional study. However, the correlations between estimated Verbal and Performance IQs and WF were weaker than expected as compared with previous reports in adults [40]. Of the ancillary measures given in the longitudinal study, WF had moderate correlations with receptive vocabulary and word list recall. Although the correlation of WF with rate of core propositions on a narrative discourse task was weaker, it is difficult to explain the stronger correlation of WF with PPVT-R as compared to estimated Verbal IQ which was based on the vocabulary subtest score. It is conceivable that the forced-choice format of PPVT-R provided a more reliable measure of lexical ability in brain injured children than the WISC-R question and answer format.

Finally, our findings support the utility of growth curve analysis [22] to characterize the measures which depicted effects of brain injury on development. The longitudinal language data reflect a slower rate of development after severe CHI in young children relative to severe injury in older children or mild CHI in either age range [52]. This impact of severe brain injury on development would not have been disclosed by the cross-sectional data.

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References


