Differential Effects of Left Versus Right Mesial Temporal Lobe Epilepsy on Wechsler Intelligence Factors

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This study investigates the effects of left versus right mesial temporal lobe epilepsy (MTLE) on Wechsler intelligence factors. In the left MTLE group, the Verbal Comprehension (VC) factor score was significantly lower than the Perceptual Organization (PO) factor score, whereas in the right MTLE group, the PO factor score was significantly lower than the VC factor score. The VC factor score was significantly lower for the left than the right MTLE group, whereas the PO factor score was significantly lower for the right than the left MTLE group. Thus, left versus right MTLE was associated with relative deficits in verbal versus nonverbal intelligence, respectively. These findings indicate that lateralized cognitive deficits in unilateral MTLE patients are not limited to the learning–memory domain but include more global intelligence functions.

Mesial temporal lobe epilepsy (MTLE) may be the most common form of human epileptogenic disorders (Engel, 1996). Pre- and postsurgical neuropsychological studies of MTLE patients have greatly contributed to the current understanding of human brain–behavior relationship. MTLE is frequently associated with memory impairments reflecting epileptogenic lesions in the mesial temporal lobe, a region known to be critical for consolidating new memory. A notable characteristic of the memory deficits in MTLE is the significant relationship between side of seizure onset and material-specific memory capacity: Patients with left MTLE tend to show more severe verbal than nonverbal memory deficits, whereas patients with right MTLE tend to show more severe nonverbal than verbal memory impairments (e.g., Delaney, Rosen, Mattson, & Novelty, 1980; Fedio & Mirsky, 1969; Helmstaedter, Pohl, & Elger, 1995; Hermann, Wyler, Richey, & Rea, 1987; Kim, Yi, Son, & Kim, 2003; Ladavas, Umlàt, & Provinciali, 1979). Although the link between right MTLE and nonverbal memory deficits has not been always supported, some well-controlled prior studies (e.g., Abrahams, Pickering, Polkey, & Morris, 1997; Baxendale, Thompson, & van Paesschen, 1998) have provided convincing evidence for the link. These selective verbal or nonverbal memory deficits that are dependent on side of seizure onset provide evidence that the left and the right mesial temporal regions are specialized for verbal versus nonverbal memory processing, respectively (Milner, 1975).

The aim of the present study was to investigate possible differential effects of left versus right MTLE on material-specific intelligence. Although neuropsychological studies of MTLE have emphasized memory deficits, neuropsychological deficits in MTLE are not limited to the learning–memory domain but extend into more global intelligence functions (Hermann, Seidenberg, Schoenfeld, & Davies, 1997). For example, the IQ level of MTLE patients is as low as their memory quotient level (Chelune, Naugle, Lüders, & Awad, 1991; Gold et al., 1995; Ivnik, Sharbrough, & Laws, 1987; Mayeux, Brandt, Rosen, & Benson, 1980; Selwa et al., 1994). Consistent with global intelligence deficits, there is a growing body of evidence that brain abnormalities in MTLE, even in well-defined cases of unilateral MTLE, are not limited to the epileptogenic region but extend into widespread areas of extrahippocampal temporal and extratemporal regions. This evidence is known from position emission tomography (PET; e.g., Arnold et al., 1996; Henry, Mazziotta, & Engel, 1993; Henry et al., 1990; Jokeit et al., 1997; Van Bogaert et al., 2000), single photon emission computed tomography (SPECT; e.g., Avery et al., 2001; Duncan, Patterson, Hadley, Roberts, & Bone, 1996; Yune et al., 1998), quantitative magnetic resonance imaging (MRI; e.g., Briellmann, Jackson, Kalnis, & Berkovic, 1998; DeCarli et al., 1998; Jutila et al., 2001; Kuzniecky et al., 1999; Lee et al., 1998; Marsh et al., 1997; Moran, Lemieux, Kitchen, Fish, & Shorvon, 2001; Sisodiya et al., 1997; Specht et al., 1997), and postmortem pathological studies of MTLE patients (Margerson & Corsellis, 1966). The abnormal extratemporal regions, although variable...
across MTLE patients, can be extremely widespread, including the frontal and parietal lobes, the temporal neocortex, the basal ganglia, the thalamus, the limbic system, and the cerebellum. Important for the present purpose, the extratemporal abnormalities are usually more severe on the ipsilateral than the contralateral side of the epileptogenic region. For example, using high-resolution MRI, Lee et al. (1998) found that the mean relative reduction in the temporal lobe volume (excluding the hippocampal formation and the parahippocampal gyrus) was about 15% in the ipsilateral temporal lobe and about 7% in the contralateral temporal lobe. The more severe ipsilateral abnormalities presumably reflect an asymmetric disease process associated with unilateral MTLE.

Thus, the working hypothesis for the present study was that left MTLE is associated with relative verbal intelligence deficits, whereas right MTLE is associated with relative nonverbal intelligence impairments. A review of the literature concerning this lateralized intelligence deficits hypothesis reveals that most of the research has used the Wechsler intelligence scales; research using other intelligence instruments is virtually nonexistent. Moreover, with few exceptions, these studies used verbal IQ (VIQ) and performance IQ (PIQ) as dependent measures. Some of these studies reported significantly lower VIQ for left than for right MTLE patients but no significant difference in PIQ between the two groups (Blakemore, Ettlinger, & Falconer, 1966; Kneebone, Chelune, & Lüders, 1997; Loring, Lee, & Meador, 1988). Others found significantly lower PIQ as well as VIQ for left than for right MTLE patients (Moore & Baker, 1996; Selwa et al., 1994). However, in the great majority of these studies, neither VIQ nor PIQ was significantly different between left versus right MTLE patients (Abrahams et al., 1997; Bornstein, Pakalnis, & Drake, 1988; Breier et al., 1997; Fedio & Mirsky, 1969; Hermann et al., 1995; Hermann et al., 1987; Loring, Lee, Martin, & Meador, 1988; Mayeux et al., 1980). Thus, extant literature provides poor support for the lateralized intelligence deficits hypothesis.

However, the poor support is rather puzzling in view of the fact that MTLE is associated with widespread extratemporal (and extrahippocampal temporal) lesions that are more severe on the ipsilateral than the contralateral side of the epileptogenic region. Thus, the prior failures to support the lateralized intelligence deficits hypothesis may reflect, at least in part, methodological inadequacy rather than true absence of lateralized intelligence deficits in MTLE. For example, in studies that have used a relatively small sample size (Abrahams et al., 1997; Blakemore et al., 1966; Bornstein, Pakalnis, & Drake, 1988; Fedio & Mirsky, 1969; Hermann et al., 1987; Loring, Lee, Martin, & Meador, 1988; Loring, Lee, & Meador, 1988; Mayeux et al., 1980), a weak statistical power may have contributed to the failures. More relevant for the present purpose, VIQ and PIQ, which were used as dependent measures in most prior studies, may not be ideal measures of verbal and nonverbal intelligence. Numerous factor-analytic studies of the Wechsler intelligence scales indicate that a three-factor structure, consisting of a Verbal Comprehension (VC) factor, a Perceptual Organization (PO) factor, and a Freedom From Distractibility (FD)/Working Memory (WM) factor, best fits the data (e.g., Dai, Gong, & Zhong, 1990; Waller & Waldman, 1990; Ward, Ryan, & Axelrod, 2000). This is found not only for Wechsler intelligence data obtained from nonclinical control subjects but also from various clinical groups (e.g., Bornstein, Drake, & Pakalnis, 1988; Burgess, Flint, & Adhead, 1992; Choi & Kim, 1990; Fowler, Richards, & Boll, 1980; Hermann et al., 1995; Lansdell, 1968; Ryan & Schneider, 1986). It is generally recognized that VC and PO factor scores (or index scores) are better measures of verbal and nonverbal intelligence than VIQ and PIQ, respectively (for a review, see Kaufman, 1990). Nevertheless, few prior studies (Hermann et al., 1995; Ivnik et al., 1987) have addressed the lateralized intelligence deficits hypothesis using VC and PO factor scores as dependent measures. Thus, in the present study, VC and PO factor scores were used as dependent measures, with the expectation that these scores might reveal certain lateralized material-specific intelligence deficits that are not apparent with VIQ and PIQ as dependent measures.

Subjects

The subjects were 71 patients who had ultimately undergone surgery of the left or right mesial temporal lobe for treatment of medically intractable epilepsy of unilateral mesial temporal origin. They were selected from a consecutive series of patients undergoing mesial temporal lobe surgery in an epilepsy surgery center in Korea who met the following criteria: (a) completion of the K-WAIS (Yeom, Park, Oh, Kim, & Lee, 1992), the Korean version of the Wechsler Adult Intelligence Scale—Revised (WAIS–R; Wechsler, 1981) as part of presurgical workup, (b) age greater than 15 years, (c) left hemisphere language dominance as determined by intracarotid amobarbital procedure (IAP), (d) full scale IQ greater than 64, (e) no evidence of space-occupying structural lesions on MRI scanning other than hippocampal atrophy, and (f) seizure-free (Class I) or near seizure-free (Class II) status (Engel, Van Ness, Rasmussen, & Ojemann, 1993) at 1-year postsurgery follow-up. The presurgical evaluation included seizure semiology, prolonged interictal and ictal video electroencephalograph (EEG) from scalp/sphenoidal electrodes, MRI scanning, interictal SPECT, IAP, neuropsychological testing, and if necessary, EEG from chronically implanted bilateral subdural strip electrodes. Thirty-four subjects had epileptogenic discharges localized in the left mesial temporal lobe, and 37 in the right mesial temporal lobe. Forty-seven were male, and 24 were female. The mean age (±SD) at the time of study was 29.3 ± 6.8 years. The mean age at recurrent seizure onset was 15.0 ± 6.6 years, and the mean seizure duration was 14.8 ± 7.4 years. Sixty-nine were right-handed and 2 were left-handed, as determined by a 13-item questionnaire (Chapman & Chapman, 1987). The average full scale IQ on the K-WAIS was 86.9 ± 11.0. Five subjects had a history of pure complex partial seizures (CPS), and 66 subjects had a history of CPS frequently or occasionally followed by generalized tonic-clonic seizures.

1 In some of these studies, the VIQ and PIQ scores were reported as part of clinical characteristics of the sample and were not related to the main hypotheses of the studies.
Procedures

Intelligence assessment. The K-WAIS (Yeom et al., 1992) was administered to each patient in the context of a comprehensive presurgical neuropsychological evaluation. The structure and pattern of the K-WAIS are the same as those of the WAIS-R (Wechsler, 1981), although some items (e.g., What are the colors in the American flag?) were changed to make them suitable for Korean subjects. The K-WAIS standardization sample included a total of 1,396 healthy adult men and women, ranging in age from 16 to 64 years. Only 9 of 11 subscales of the K-WAIS, excluding the Vocabulary and Picture Arrangement subscales, were administered to shorten the testing time. The decision to exclude the Vocabulary subscale was based on the fact that its administration time is the longest among the Wechsler subscales and that it is highly correlated with other VC subscales (Kaufman, 1990). The decision to exclude the Picture Arrangement subscale reflected the fact that its administration time is relatively long and that the strength of its loading on the PO factor is comparatively modest (Kaufman, 1990).

IAP. All patients underwent IAP as part of presurgical evaluation. The IAP was conducted, with the patient supine, immediately following angiography. Amobarbital 125 mg in a 10% solution was injected into the internal carotid artery using a transfemoral catheter over a 4–5-s interval. In most patients, the side considered for resection was injected first. Left and right hemisphere injections were done on the same day, with a minimum of 40 min between the two injections. Following demonstration of hemiplegia, the patient was presented with a series of language tasks that lasted approximately 60–90 s. Assessment of language functions during the course of the IAP have varied slightly over the years but always included both receptive and expressive language tasks. The core tasks included following a simple command (e.g., “close your eyes”), reading a short sentence, naming a picture, and repeating a phrase spoken by the examiner. Only patients with left hemisphere language dominance, as determined by the IAP, were included to avoid possible confounding effects associated with a shift of language dominance.

Analyses

To test the hypothesis that left and right MTLE have differential effects on material-specific intelligence, we conducted three separate analyses, one involving the VIQ and PIQ, one involving the VC and PO index scores, and one involving the VC and PO factor scores. In the analyses involving the VIQ and PIQ, the VIQ was computed on the basis of the protated sum of scaled scores of the four verbal subscales, and the PIQ was computed on the basis of the protated sum of scaled scores of the four performance subscales. In the analyses involving the VC and PO index scores, the VC index score was derived from Information, Comprehension, and Similarities subscale scores, and the PO index score was derived from Picture Completion, Block Design, and Object Assembly subscale scores. Each derivation involved converting the sum of scaled scores of the three subscales into its index score equivalent on the basis of the conversion tables provided by Kim (2002). Each index score had a normative mean of 100 and a standard deviation of 15. In the analyses involving the VC and PO factor scores, the correlation matrix for the nine subscale raw scores were first subject to a factor analysis, and resulting factor scores were then subject to analyses. The factor-analytic procedure involved a principal component analysis, followed by extraction of three factors with varimax rotation. The factor scores were z scores with a mean of 0 and a standard deviation of 1, and they were mutually uncorrelated, reflecting use of an orthogonal rotation method. Finally, we also performed analyses of individual subscale scores to explore possible source differences in the results obtained with various summary measures.

Results

Demographic and Clinical Variables

The demographic and clinical characteristics of the left and right MTLE groups are presented in Table 1. Group differences were examined by F tests for continuous variables and by 2 × 2 Fisher exact tests for categorical variables. Statistical analyses revealed no significant differences between the left and right MTLE groups in terms of age, education, gender ratio, handedness, onset age of recurrent seizures, duration of seizures, incidence of febrile convulsions, 1-year postsurgery outcome (% Class I), or full scale IQ (ps > .10). Thus, these demographic and clinical variables may not account for any differences in material-specific intelligence between the left and right MTLE groups.

VIQ and PIQ

The VIQ and PIQ scores on the K-WAIS were analyzed using a 2 × 2 (Intelligence Type × Seizure Laterality) analysis of variance (ANOVA). The mean VIQ and PIQ scores of the left and right MTLE groups are depicted in Figure 1. In this ANOVA, no main or interaction effects reached statistical significance (ps > .10). Within the left MTLE group, the VIQ and PIQ scores were not significantly different, F(1, 33) < 1. However, within the right MTLE group, the PIQ score was significantly lower than the VIQ score, F(1, 36) = 4.24, p < .05. The left versus right MTLE groups were not significantly different in the VIQ score, F(1, 69) < 1, or the PIQ score, F(1, 69) = 2.22, p > .10. Thus, with the VIQ and PIQ scores as dependent variables, there is little support for the hypothesis that left and right MTLE are associated with relative verbal and nonverbal intelligence impairments, respectively.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Left MTLE (n = 34)</th>
<th>Right MTLE (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29.9 (SD: 6.1)</td>
<td>28.7 (SD: 7.4)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11.8 (SD: 2.9)</td>
<td>11.5 (SD: 3.2)</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>74.0 (SD: 60.0)</td>
<td></td>
</tr>
<tr>
<td>Handedness (% right-handed)</td>
<td>97.0 (SD: 97.0)</td>
<td></td>
</tr>
<tr>
<td>Onset age of recurrent seizures (years)</td>
<td>15.2 (SD: 6.2)</td>
<td>14.9 (SD: 7.1)</td>
</tr>
<tr>
<td>Duration of seizures (years)</td>
<td>15.4 (SD: 7.5)</td>
<td>14.2 (SD: 7.4)</td>
</tr>
<tr>
<td>Febrile convulsions (%)</td>
<td>41.0 (SD: 41.0)</td>
<td></td>
</tr>
<tr>
<td>1-year postsurgery outcome (% Class I)</td>
<td>68.0 (SD: 84.0)</td>
<td></td>
</tr>
<tr>
<td>Full scale IQ (K-WAIS)</td>
<td>87.8 (SD: 12.2)</td>
<td>86.0 (SD: 10.0)</td>
</tr>
</tbody>
</table>

Note. MTLE = mesial temporal lobe epilepsy; K-WAIS = K-Wechsler Adult Intelligence Scale (Yeom, Park, Oh, Kim, & Lee, 1992).
VC and PO Indices

We analyzed the VC and PO index scores using a 2 × 2 (Intelligence Type × Seizure Laterality) ANOVA. The derivation of the VC and PO index scores is described above. The mean VC and PO index scores of the left and right MTLE groups are depicted in Figure 2. The only significant effect in this ANOVA was an Intelligence Type × Seizure Laterality interaction, F(1, 69) = 10.98, p < .005. Within the left MTLE group, the VC index score was significantly lower relative to the PO index score, F(1, 33) = 4.63, p < .05, whereas within the right MTLE group, the PO index score was significantly lower compared with the VC index score, F(1, 36) = 6.72, p < .05. Between-groups comparisons showed that the right MTLE group had a significantly lower PO index score than the left MTLE group, F(1, 69) = 5.81, p < .05. The left MTLE group had a lower VC index score than the right MTLE group, but this difference was not statistically significant, F(1, 69) = 1.07, p > .30. Thus, with the VC and PO index scores as dependent variables, the results indicate that left and right MTLE are associated with relative verbal and nonverbal intelligence impairments, respectively.

VC, PO, and WM Factors

The correlation matrix for the nine subscales were first subject to a factor analysis. Details of this factor-analytic procedure are presented in the Method section. The varimax-rotated factor loadings of the three-factor solution are shown in Table 2. Factor loadings greater than .50 were considered significant. With this criterion, the first factor was a familiar VC factor (i.e., Information, Comprehension, Similarities), and the second factor was a PO factor (i.e., Picture Completion, Block Design, Object Assembly). On the third factor, the Digit Span and Arithmetic subscales loaded strongly, at .86 and .66, respectively, whereas the Digit Symbol subscale loaded comparatively weakly, at .32. Thus, the third factor was considered as a WM factor. The percent of the total variance attributed to each of the factors was 29.6 for VC, 22.8 for PO, and 18.5 for WM.

The VC and PO factor scores derived from the factor analysis were subject to a 2 × 2 (Intelligence Type × Figure 1. Mean verbal IQ and performance IQ for the left and the right mesial temporal lobe epilepsy (MTLE) groups. Error bars represent ±1 standard error of the mean.

Figure 2. Mean Verbal Comprehension (VC) and Perceptual Organization (PO) index scores for the left and the right mesial temporal lobe epilepsy (MTLE) groups. Error bars represent ±1 standard error of the mean.

Table 2

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Factor loading 1</th>
<th>Factor loading 2</th>
<th>Factor loading 3</th>
<th>Communality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information</td>
<td>.85</td>
<td>.14</td>
<td>.15</td>
<td>.77</td>
</tr>
<tr>
<td>Comprehension</td>
<td>.80</td>
<td>.26</td>
<td>.21</td>
<td>.76</td>
</tr>
<tr>
<td>Similarities</td>
<td>.80</td>
<td>.02</td>
<td>.33</td>
<td>.75</td>
</tr>
<tr>
<td>Picture Completion</td>
<td>.43</td>
<td>.68</td>
<td>–.17</td>
<td>.68</td>
</tr>
<tr>
<td>Block Design</td>
<td>.01</td>
<td>.80</td>
<td>.41</td>
<td>.81</td>
</tr>
<tr>
<td>Object Assembly</td>
<td>.16</td>
<td>.85</td>
<td>.14</td>
<td>.77</td>
</tr>
<tr>
<td>Digit Span</td>
<td>.26</td>
<td>.04</td>
<td>.86</td>
<td>.81</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>.38</td>
<td>.28</td>
<td>.66</td>
<td>.65</td>
</tr>
<tr>
<td>Digit Symbol</td>
<td>.48</td>
<td>.23</td>
<td>.32</td>
<td>.39</td>
</tr>
<tr>
<td>Eigenvalue</td>
<td>2.67</td>
<td>2.05</td>
<td>1.66</td>
<td></td>
</tr>
<tr>
<td>% of variance</td>
<td>29.64</td>
<td>22.81</td>
<td>18.49</td>
<td></td>
</tr>
</tbody>
</table>

Note. Boldface indicates factor loadings greater than .50.
Seizure Laterality) ANOVA. The mean VC, PO, and WM factor scores of the left and right MTLE groups are depicted in Figure 3. In this ANOVA, the Intelligence Type × Seizure Laterality interaction was significant, $F(1, 69) = 11.07, p < .05$, and no other effects reached statistical significance ($ps > .80$). Within the left MTLE group, the VC factor score was significantly lower than the PO factor score, $F(1, 33) = 4.63, p < .05$, whereas within the right MTLE group, the PO factor score was significantly lower than the VC factor score, $F(1, 36) = 6.84, p < .05$. Between-groups comparisons showed that the left MTLE group had a significantly lower VC factor score than the right MTLE group, $F(1, 69) = 4.48, p < .05$, whereas the right MTLE group had a significantly lower PO factor score than the left MTLE group, $F(1, 69) = 5.82, p < .05$. Thus, with the VC and PO factor scores as dependent variables, there is clear evidence that left and right MTLE are associated with relative verbal and nonverbal intelligence impairments, respectively.

With respect to the WM factor, the right MTLE group had a significantly lower WM factor score than the left MTLE group, $F(1, 69) = 5.19, p < .05$ (see Figure 3). Within the left MTLE group, the WM factor score was significantly higher than the VC factor score, $F(1, 33) = 4.77, p < .05$, whereas within the right MTLE group, the WM factor score was significantly lower than the VC factor score, $F(1, 36) = 5.67, p < .05$. The WM factor score was not significantly different from the PO factor score within the left MTLE group, $F(1, 33) < 1$, or within the right MTLE group, $F(1, 36) < 1$. These results indicate that WM factor performance is more adversely affected by right than left MTLE. Thus, when VC, PO, and WM factors were considered simultaneously, left MTLE was associated with lowered VC factor but relatively preserved PO and WM factors, whereas right MTLE was associated with depressed PO and WM factors but relatively preserved VC factor.

**Subscale Scores**

We performed analyses of subscale scores twice, first with the raw scores and second with the age-corrected scaled scores. General trends and significant differences were similar for the two sets of analyses. Therefore, only results obtained with the age-corrected scaled scores are presented in detail. The mean subscale scores for the left and right MTLE groups are shown in Table 3. The left and right MTLE groups were significantly different in only one subscale, Block Design, $F(1, 69) = 6.57, p < .05$, reflecting lower performance by the right MTLE group. Statistical significance aside, the group means of all nine subscales were in the direction consistent with the group differences found with summary measures. Thus, all three VC subscales were performed less well by the left MTLE group, whereas all three PO subscales were performed less well by the right MTLE group. In addition, both WM subscales (i.e., Digit Span and Arithmetic) were performed less well by the right MTLE group. These results suggest that the group differences found with various summary measures reflect the differences of most subscales rather than a small number of particular subscales.

**Individual Patient Prediction**

The group results described above indicate a significant association between seizure laterality and patterns of VC versus PO discrepancy. However, the group data do not speak directly to the issue of the clinical utility of VC versus PO discrepancy as a predictor of seizure laterality. To address this issue, we performed three separate classification studies, using 15-, 23-, and 28-point discrepancies between VC index and PO index as the cut-off criteria. The 15-, 23-, and 28-point discrepancies represent the 25th, 10th, and 5th percentiles in Kim’s (2002) normative study.

Table 3

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Left MTLE $(n = 34)$</th>
<th>Right MTLE $(n = 37)$</th>
<th>$F(1, 69)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information</td>
<td>7.09 2.61</td>
<td>7.92 2.34</td>
<td>2.00</td>
</tr>
<tr>
<td>Comprehension</td>
<td>8.59 3.34</td>
<td>8.68 3.13</td>
<td>0.01</td>
</tr>
<tr>
<td>Similarities</td>
<td>7.47 2.54</td>
<td>8.35 2.29</td>
<td>2.37</td>
</tr>
<tr>
<td>Picture Completion</td>
<td>8.03 2.56</td>
<td>7.57 2.51</td>
<td>0.59</td>
</tr>
<tr>
<td>Block Design</td>
<td>8.79 3.05</td>
<td>7.08 2.58</td>
<td>6.57*</td>
</tr>
<tr>
<td>Object Assembly</td>
<td>8.65 2.14</td>
<td>7.92 2.19</td>
<td>2.00</td>
</tr>
<tr>
<td>Digit Span</td>
<td>8.21 2.40</td>
<td>7.38 2.53</td>
<td>1.99</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>8.21 2.73</td>
<td>7.19 2.22</td>
<td>2.99</td>
</tr>
<tr>
<td>Digit Symbol</td>
<td>7.85 2.39</td>
<td>7.81 2.11</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Note.* MTLE = mesial temporal lobe epilepsy.

*$p < .05$. 

![Figure 3. Mean Verbal Comprehension (VC) and Perceptual Organization (PO) factor scores for the left and the right mesial temporal lobe epilepsy (MTLE) groups. Error bars represent ±1 standard error of the mean. WM = Working Memory.](image-url)
In each classification, those patients who had a magnitude of discrepancies less than the cut-off criterion were left unclassified (i.e., indeterminate). The classification results are shown in Table 4. In each classification, a large number of patients failed to meet the criterion and were left unclassified. Nonetheless, each classification produced an assignment of patients that significantly differed from chance (all \( p < .05 \)). Using the criterion representing the 25th percentile, a lateralizing or determinate result was obtained in 32% of patients. In 78% of these, the prediction was correct, and in 22% it was false. Using the criterion representing the 10th percentile, a lateralizing result was obtained in 13% of patients. In 78% of these, the prediction was correct, and in 22% it was false. Using the criterion representing the 5th percentile, a lateralizing result was obtained in 7% of patients, and in 100% of these, the prediction was correct.

### Effects of Surgical Outcome

One of the subject selection criteria required that patients have a favorable surgical outcome (i.e., Class I or II). This selection criterion may have inadvertently limited our sample to patients with more focal and perhaps ipsilateral neuropathology, reflected in the VC versus PO findings. Thus, there is the possibility that our lateralized VC versus PO findings may reflect the surgical outcome selection criterion. With this possibility in mind, we examined VC and PO factor scores for all MTLE patients who met the same selection criteria outlined in the Method section, with the exception of the surgical outcome criterion. This analysis involved 80 patients: 71 with a favorable surgical outcome, 8 with a nonfavorable surgical outcome (i.e., Class III or IV), and 1 with no follow-up data because of loss of contact. The VC and PO factor scores derived from 80 patients were analyzed using a 2 \( \times \) 2 (Intelligence Type \( \times \) Seizure Laterality) ANOVA. The Intelligence Type \( \times \) Seizure Laterality interaction was again significant, \( F(1, 78) = 9.87, p < .05 \). Within the left MTLE group, the VC factor score was significantly lower than the PO factor score, \( F(1, 41) = 4.23, p < .05 \), whereas within the right MTLE group, the PO factor score was significantly lower than the VC factor score, \( F(1, 37) = 8.07, p < .01 \). Between-groups comparisons showed that the left MTLE group had a significantly lower VC factor score than the right MTLE group, \( F(1, 78) = 6.63, p < .05 \), whereas the right MTLE group had a significantly lower PO factor score than the left MTLE group, \( F(1, 78) = 3.96, p < .05 \). Thus, the lateralized VC versus PO findings were apparent even when the surgical outcome selection criterion was dropped. These findings indicate that the selection criterion is not critical for the present lateralized VC versus PO findings.\(^2\)

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\(^2\) An anonymous reviewer raised the possibility that a congruent VC versus PO discrepancy might be a favorable prognostic sign for surgical outcome. We have addressed this possibility by examining the relationship between the lateralization of VC versus PO difference (correctly lateralized, falsely lateralized, nonlateralized) and the surgical outcome (favorable, nonfavorable). The lateralization of VC versus PO difference was derived from prediction of seizure laterality using the clinical criterion of a 15-point or greater difference between the VC index and PO index. This analysis involved 71 patients with a favorable outcome and 8 with a nonfavorable outcome. The proportion of patients with a favorable outcome was .95, .83, and .89 for the correctly lateralized, falsely lateralized, and nonlateralized groups, respectively. These differences were not statistically significant, \( \chi^2(2, N = 79) < 1, p > .50 \), indicating no association between lateralization of VC versus PO difference and surgical outcome.
Discussion

Neuropsychological studies of MTLE have concentrated largely on memory functioning, as recently noted by Hermann et al. (1997). A major finding in this literature is that left MTLE is associated with relative verbal memory deficits, whereas right MTLE is associated with relative nonverbal memory impairments (Delaney et al., 1980; Fedio & Mirsky, 1969; Helmstaedter et al., 1995; Hermann et al., 1987; Kim et al., 2003; Lådavas et al., 1979). This finding is thought to reflect the fact that the left mesial temporal region is more important for verbal learning, whereas the right mesial temporal lobe is more important for nonverbal learning. However, less is known about whether material-specific cognitive deficits in MTLE are confined to the learning–memory domain or extend into more general intelligence functions. Thus, the present study investigated whether left versus right MTLE has differential effects on material-specific intelligence, as determined by VC and PO factor scores derived from K-WAIS. The results show that within the left MTLE group, the VC factor score was significantly lower relative to the PO factor score, whereas within the right MTLE group, the PO factor score was significantly lower compared with the VC factor score. Between-groups comparisons showed that the left MTLE group had a significantly lower VC factor score than the right MTLE group, whereas the right MTLE group had a significantly lower PO factor score than the left MTLE group. These findings provide strong evidence that left and right MTLE are associated with relative verbal and nonverbal intelligence deficits, respectively.

Factor scores are, by nature, hypothetical. Thus, the group differences found with the factor scores might be criticized for lack of actuality. However, the differential effects of left versus right MTLE on material-specific intelligence were also apparent with the VC and PO index scores as dependent measures. Thus, within the left MTLE group, the VC index score was significantly lower relative to the PO index score, whereas within the right MTLE group, the PO index score was significantly lower compared with the VC index score. Thus, both analyses involving actualistic and hypothetical measures of verbal and nonverbal intelligence supported the lateralized intelligence deficits hypothesis. In striking contrast to the present results, virtually all prior relevant studies (Abrahams et al., 1997; Blakemore et al., 1966; Bornstein, Pakalnis, et al., 1988; Breier et al., 1997; Fedio & Mirsky, 1969; Hermann et al., 1995; Hermann et al., 1997; Kneebone et al., 1997; Mayeux et al., 1980; Moore & Baker, 1996; Selwa et al., 1994) failed to find supporting evidence for the lateralized intelligence deficits hypothesis. However, the great majority of these studies have used VIQ and PIQ as dependent measures. Even in our data, the material-specific intelligence deficits were not apparent with VIQ and PIQ as dependent measures. Thus, neither VIQ nor PIQ was significantly different between the left and right MTLE groups. This finding as well as prior failures to support the lateralized intelligence deficits hypothesis presumably reflects, at least in part, the fact that VIQ and PIQ are relatively poor measures of verbal and nonverbal intelligence. Thus, the present results underscore the importance of using sensitive measures of verbal and nonverbal intelligence in addressing the lateralized intelligence deficits hypothesis.

The neural substrates underlying the material-specific intelligence deficits in MTLE may be widespread extratemporal (and extra-hippocampal temporal) lesions that are more severe on the ipsilateral than the contralateral side of the epileptogenic region, as indicated by numerous reports of quantitative MRI (e.g., Briellmann et al., 1998; DeCarli et al., 1998; Jutila et al., 2001; Kuzniecky et al., 1999; Marsh et al., 1997; Moran et al., 2001; Sisodiya et al., 1997) and functional brain-imaging studies (e.g., Arnold et al., 1996; Avery et al., 2001; Duncan et al., 1996; Henry et al., 1990, 1993; Jokeit et al., 1997; Van Bogaert et al., 2000; Yune et al., 1998). Consistent with this view, some studies have found a significant relation between extratemporal abnormalities in MTLE patients and their intellectual impairments (e.g., Arnold et al., 1996; Jokeit et al., 1997; Martin et al., 2000; Rausch, Henry, Ary, Engel, & Mazzotta, 1994). For example, Rausch et al. (1994) reported that relative reductions in glucose metabolism of the left hemisphere and left lateral temporal lobe in MTLE patients correlated with a lower VIQ score. However, not all aspects of the material-specific intelligence deficits in MTLE patients may be a direct result of neurological lesions but secondary to their material-specific memory impairments. For example, the verbal memory deficits associated with left MTLE may interfere more with acquisition of verbal than nonverbal knowledge. Thus, the relatively depressed verbal intelligence in left MTLE patients could be, at least in part, secondary to their relatively low verbal memory.

Right MTLE was also associated with relative deficits in the WM factor compared with left MTLE. This finding was somewhat surprising because the Digit Span and Arithmetic subscales are at least partially verbal. However, the present pattern of findings is not without precedence. Hermann et al. (1995) authored one of the few studies that has compared the Wechsler subscale scores of left and right MTLE patients. The data reported in this study indicate that the Digit Span and Arithmetic subscale scores are nonsignificantly lower for right than for left MTLE patients. Testing postsurgical temporal lobe epilepsy patients, Lansdell (1968) reported that the right temporal group showed poorer freedom-from-distractibility (FD) performance relative to the left temporal group. This postsurgical group difference reported by Lansdell may also have been present presurgically, although to a lesser extent. The greater impairment on WM tasks in right than left MTLE may be related to right hemisphere dominance for certain attentional functions (Heilman & Van Den Abell, 1980; Roy, Reuter-Lorenz, Roy, Copland, & Moscovitch, 1987). However, in brain lesions other than MTLE, such as cerebral vascular accidents and tumors, the Digit Span and Arithmetic subscales tend to be performed less well by patients with left-brain damage than by patients with right-brain damage (e.g., Black, 1986; De Renzi & Nichelli, 1975; Russell, 1979; Warrington, James, & Maciejewski, 1986; Zillmer, Waechtl, Harris, Khan, & Fowler, 1992). For example,
testing patients with unilateral brain damage of various etiologies, De Renzi and Nichelli (1975) found that digit repetition was impaired in patients with left-brain damage but not in patients with right-brain damage. Thus, the hypothesis that WM performance is more adversely affected by left than right hemisphere lesions may be limited to pathological processes associated with unilateral MTLE. Clearly, a larger study including MTLE as well as other brain lesion groups, with both cognitive and brain abnormality measures, is needed to fully address these complex but potentially important issues.

The present results indicate that left MTLE is associated with lower VC than PO scores, whereas right MTLE is associated with lower PO than VC scores. These results suggest the possible use of VC versus PO difference to predict the side of seizure onset. However, the mean differences in VC versus PO scores were of relatively small magnitude for either the left or right MTLE group, suggesting their limited clinical utility. Thus, for example, applying the clinical criterion of a 15-point difference (i.e., the 25th percentile) between VC index and PO index to the present sample provided correct lateralization in only 18 of 71 patients (25%), with false lateralization in 5 patients (7%). Forty-eight patients (68%) were considered indeterminate patients (25%), with false lateralization in 5 patients (7%).

The present results indicate that left MTLE is associated with lower VC than PO scores, whereas right MTLE is associated with lower PO than VC scores. These results suggest the possible use of VC versus PO difference to predict the side of seizure onset. However, the mean differences in VC versus PO scores were of relatively small magnitude for either the left or right MTLE group, suggesting their limited clinical utility. Thus, for example, applying the clinical criterion of a 15-point difference (i.e., the 25th percentile) between VC index and PO index to the present sample provided correct lateralization in only 18 of 71 patients (25%), with false lateralization in 5 patients (7%).

In summary, previous studies have established that cognitive deficits in MTLE patients are not limited to the learning–memory domain but include more global intelligence functions. The present study extends the findings by showing that material-specific cognitive deficits in MTLE patients are also not limited to the learning–memory domain but include more global intelligence functions. Thus, left MTLE was associated with a depressed VC factor but a relatively spared PO factor, whereas right MTLE was associated with lowered PO factor but a relatively preserved VC factor. The neural substrates underlying these material-specific intelligence impairments may be widespread extratemporal (and extrahippocampal temporal) lesions that are more severe on the ipsilateral than the contralateral side of the epileptogenic region. Prior multiple failures to find evidence for the lateralized intelligence deficits hypothesis may reflect, at least in part, use of VIQ and PIQ scores, which are relatively poor indices of verbal and nonverbal intelligence. Consistent with this view, even in our data, lateralized material-specific intelligence deficits were not apparent with VIQ and PIQ as dependent measures. However, there are previous investigations (e.g., Hermann et al., 1995) that used VC and PO scores but that failed to find lateralized intelligence effects. Thus, certain factors other than choice of dependent measures, such as certain patient characteristics, may also have significant effects on whether laterality findings are obtained or not. Considering these factors would be more likely to further elucidate the link between MTLE and material-specific intelligence deficits.

References


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