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WMS–III performance in patients with temporal lobe epilepsy: Group differences and individual classification

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Abstract

The utility of the WMS–III in detecting lateralized impairment was examined in a large sample of patients with temporal lobe epilepsy. Methods of analysis included evaluation of group means on the various indexes and subtest scores, the use of ROC curves, and an examination of Auditory–Visual Index discrepancy scores. In addition, performance on immediate and delayed indexes in the auditory and the visual modality was compared within each group. Of the WMS–III scores, the Auditory–Visual Delayed Index difference score appeared most sensitive to side of temporal dysfunction, although patient classification rates were not within an acceptable range to have clinical utility. The ability to predict laterality based on statistically significant index score differences was particularly weak for those with left temporal dysfunction. The use of unusually large discrepancies led to improved prediction, however, the rarity of such scores in this population limits their usefulness. Although the utility of the WMS–III in detecting laterality may be limited in preoperative cases, the WMS–III may still hold considerable promise as a measure of memory in documenting baseline performance and in detecting those that may be at risk following surgery. (*JINS*, 2001, *7*, 881–891.)

Keywords: Memory, Temporal lobe epilepsy, Wechsler Memory Scale–3rd Edition

INTRODUCTION

Memory difficulty in individuals with temporal lobe epilepsy is a phenomenon that has long been recognized and documented (Gowers, 1881; Reynolds, 1861). Patients who have undergone temporal lobectomy tend to display material-specific deficits in the ability to learn new material. Early neuropsychological studies indicated that resection of the left temporal lobe may impair the ability to learn verbal material while right temporal resection can produce a deficit in the ability to learn new nonverbal and visuospatial information (Kimura, 1963; Meyer & Yates, 1955; Milner, 1958, 1968; Taylor, 1969; Weingartner, 1968). Although less pronounced, nonsurgical patients with unilateral temporal lobe seizures exhibit similar impairments (Delaney et al., 1980; Hermann et al., 1987; Loring et al., 1988; Milner, 1975). Despite these reports, other investigators have failed to detect differential impairment on verbal and visuospatial tasks as a function of seizure laterality (Barr et al., 1997; Glowinski, 1973; Loiseau et al., 1983; Mayeux et al., 1980; Naugle et al., 1993, 1994; Schwartz & Dennerll, 1969). Since many patients undergo surgical resection for intractable temporal lobe epilepsy, it is important for neuropsychologists to develop reliable and valid methods for identifying impairment and for identifying individuals who may be at increased risk for cognitive impairment after surgery (Dodrill et al., 1993; Jones-Gotman et al., 1993).

The most common tests used to evaluate learning and memory in individuals with epilepsy have been the Wechsler Memory Scale (Wechsler, 1945) and its second revision, the Wechsler Memory Scale–Revised (Wechsler, 1987). An international survey of 82 epilepsy surgery centers found

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that 84% of centers routinely administer all or part of the WMS or the WMS–R in their pre-operative evaluations of epilepsy patients (Jones-Gotman et al., 1993). Despite its wide usage, a number of conflicting findings have been reported in studies comparing WMS or WMS–R performance levels in nonoperated left and right temporal lobe epilepsy samples. Some studies have found significant group differences on selected scores (Bornstein et al., 1988; Delaney et al., 1980; Ivnik et al., 1987; Jones-Gotman, 1991; Moore & Baker, 1996), particularly when the differences between verbal and visual performance are compared (e.g., Barr, 1997). Nonsignificant group differences between patients with left or right temporal lobe onset have also been reported (Barr et al., 1997; Chelune et al., 1993; Delaney et al., 1980; Glowinski, 1973; Ivnik et al., 1987; Loiseau et al., 1983; Mayeux et al., 1980; Naugle et al., 1993). When group differences occurred, they tended to be predominantly on verbal measures, leading researchers to suggest that the WMS and the WMS–R were sensitive to left but not right temporal lobe dysfunction (Chelune & Bornstein, 1988; Loring, 1989). In an analysis of over 1000 individuals with medically refractory seizures, WMS–R verbal memory deficits tended to occur in the context of left-sided dysfunction, while visual memory was not related to laterality (Strauss et al., 1995).

It has been suggested that within-subject comparisons may provide a better test of the ability of the WMS–R to detect material specific deficits (Naugle et al., 1993). By subtracting the visual memory measures from their verbal counterparts, Chelune and Bornstein (1988) found that, in a mixed group of patients, those with left hemisphere dysfunction were less adept at verbal memory and learning tasks, whereas patients with right hemisphere disturbance showed the opposite pattern. Naugle et al. (1993) however, found no significant differences in pre-operative verbal–visual discrepancy scores between left temporal lobe (LTL) and right temporal lobe (RTL) epilepsy patients. Nonetheless, the clinical utility of this comparison may be important to the practitioner, who typically looks for intraindividual patterns and discrepancies when attempting to infer lateralization effects on a case-by-case basis (Chelune & Bornstein, 1988).

Investigators have also used various magnitudes of discrepancy between verbal and visual indexes to examine the ability of these scores to predict side of temporal dysfunction. Moore and Baker (1996) found that a WMS–R Verbal–Visual Index difference at the .05 level of significance correctly predicted laterality for those people with a left temporal focus but was ineffective for those with right temporal foci, classifying most of them as having a left-sided impairment based on their discrepancy scores. Similar results were obtained in an investigation of patients who had previously undergone temporal lobectomy (Loring et al., 1989).

Barr (1997) used receiver operating characteristic (ROC) curves to determine the diagnostic accuracy of the WMS–R in the classification of epilepsy surgery candidates. Using ROC curves, one can assess the proportion of patients who can be accurately classified into left and right temporal groups based on a given score. Barr concluded that the WMS–R scores provided relatively poor discrimination of patients into left and right temporal groups, yet the highest level of classification accuracy was obtained for a measure of the difference between Verbal and Visual Memory indexes. This supports the contention that within-subject comparisons of WMS–R scores may be relatively better indicators of lateralized effects among seizure patients than index means.

The Wechsler Memory Scale–Third Edition (Wechsler, 1997a) is the most recent revision of the original WMS and the WMS–R. Although the WMS–III has maintained many aspects of its predecessors, significant changes have been made in response to current research and theory. The content and structure of the WMS–III is considerably different from the WMS–R. Due to research suggesting that the WMS–R visual memory subtests were not adequate measures of a hypothetical "pure" visual memory system and were not differentially sensitive to unilateral lesions (Chelune & Bornstein, 1988; Heilbronner, 1992; Loring, 1989; Naugle et al., 1993), new visual memory subtests were developed, and include both immediate and delayed trials.

The WMS–III nomenclature of the index scores has also changed such that now a distinction is made between "auditory" and "visual" memory to reflect the modality of presentation of the subtests, rather than purporting to tap exclusively a hypothetical verbal or visual memory system as the WMS–R labels suggested (The Psychological Corporation, 1997).

The index structure of the WMS–III also differs considerably from that of its predecessors and is formed by summing the scaled scores of the subtests to ensure equal weighting of the components. In addition to an Auditory Immediate Index and a Visual Immediate Index, three modality-specific delayed indexes are calculated: the Auditory Delayed Index, the Visual Delayed Index, and the Auditory Recognition Delayed Index. It has been suggested that performance differences on the immediate and the delayed tasks have some clinical utility (Tulsky et al., 2000a), and that the delayed scores are likely more ecologically valid (The Psychological Corporation, 1997). A Working Memory Index is composed of one auditory and one visual working memory task (see Wechsler, 1997a and The Psychological Corporation, 1997 for additional information about changes in the WMS–III).

The *WAIS–III–WMS–III Technical Manual* provides some preliminary data suggesting that the new measures of auditory and visual memory may be useful in determining laterality of dysfunction among patients who have undergone temporal lobectomies (p. 159), although the sample size was quite small (LTL = 15, RTL = 12).

As with the revision of any widely used instrument, there is an empirical need to establish its utility. This is of particular relevance in the assessment of patients with epilepsy because scores on the WMS–III are assumed to aid in the localization of dysfunction. Accordingly, the purpose of this study was to assess the ability of the WMS–III to detect lateralized temporal impairment in a large sample of pre-operative epilepsy patients. Methods of analysis included evaluation of group means on the various WMS–III indexes and subtest scores, the use of ROC curves to determine the classification accuracy of the WMS–III, and an examination of WMS–III Auditory–Visual Index discrepancy scores to determine if this within-subject comparison could reliably indicate side of temporal dysfunction. In addition, performance on the immediate and delayed indexes in the auditory and visual modalities was compared within each group to determine the utility of this distinction in this population.

METHODS

Research Participants

The study sample was selected from a database of patients with temporal lobe epilepsy and medically refractory seizures from three epilepsy surgery centers participating in the Bozeman Epilepsy Consortium: the Cleveland Clinic Foundation, Cleveland, Ohio, the Medical College of Georgia, Augusta, Georgia, and the University of Alabama at Birmingham Epilepsy Center, Birmingham, Alabama. Patients were considered for inclusion in this study if they met the following criteria: (1) unilateral seizure onset of temporal lobe origin confirmed by EEG/video monitoring; (2) information was available regarding age of onset of recurrent seizures, duration (computed as age at time of examination minus age at seizure onset), sex, hand preference, and Full Scale IQ as measured by the Wechsler Adult Intelligence Scale–Third Edition (Wechsler, 1997b); and (3) they had received neuropsychological evaluation including the Wechsler Memory Scale–Third Edition (Wechsler, 1997a). The Cleveland Clinic and Medical College of Georgia also routinely included the intracarotid sodium amytal procedure (IAP) for language and memory in their evaluation of patients. From this information only those patients with left hemisphere language representation were selected for inclusion in the study. Since speech representation data were not available from the University of Alabama, only those patients who demonstrated a right-hand preference were selected from this center, in order to maximize the probability of left hemisphere dominance for speech.

A total of 102 patients met criteria for inclusion in the study. The characteristics of the patients classified by side of dysfunction and examination center are provided in Table 1. The presence of preexisting differences across centers was examined with separate analyses of variance for age, education level, age of onset, duration, and FSIQ. Chi-square analyses were conducted to evaluate differences in sex and handedness. Center differences were found for age [$F(2,99) = 3.21$, $p < .05$], age of onset [$F(2,99) = 3.16$, $p < .05$], and FSIQ [$F(2,97) = 5.57$, $p < .01$]. In each of these cases, the patients from University of Alabama differed from the other two centers, that is, this patient sample was significantly older, had a later age of onset, and a lower FSIQ than the patients from the other two centers. Sex also differed significantly between the sites [$\chi^2(2, N = 102) = .277$, $p < .05$], with the University of Alabama sample containing a larger proportion of female patients than the other two centers.

To examine the effect of center on the WMS–III variables, a one-way MANOVA was conducted on the WMS–III Primary Indices. The multivariate effect was non-significant [Wilks's Lambda $F(12,176) = 1.73$, n.s.]. Thus, center was not considered when computing statistical analyses.

Procedures

Participants were administered the WMS–III as part of comprehensive neuropsychological evaluations. Analyses of the data were limited to subtasks common to all centers, which included the Primary Index scores and associated subtest scores. Supplementary scores were not included in the analy-

Table 1. Sample characteristics

Center	Group	*n*	Age (years) *M* (*SD*)	Education (years) *M* (*SD*)	Full Scale IQ (WAIS–III) *M* (*SD*)	Age of onset (years) *M* (*SD*)	Duration of epilepsy (years) *M* (*SD*)	Gender M	Gender F	Hand. R	Hand. L
Cleveland Clinic	LTL	25	32.20 (10.38)	12.76 (1.88)	89.08 (13.29)	13.30 (11.60)	19.02 (11.63)	12	13	21	4
Foundation	RTL	29	33.62 (10.78)	12.83 (2.58)	92.62 (12.53)	13.14 (9.19)	20.48 (12.54)	17	12	25	4
Medical College	LTL	9	28.67 (8.26)	12.44 (2.51)	90.67 (13.83)	16.33 (12.74)	12.33 (8.40)	6	3	8	1
of Georgia	RTL	6	32.67 (10.37)	13.50 (2.81)	87.00 (16.20)	12.17 (7.28)	20.50 (12.76)	4	2	6	0
Univ. of Alabama	LTL	21	39.05 (10.98)	12.33 (2.78)	80.10 (14.45)	18.84 (16.63)	21.88 (16.47)	7	14	21	0
Epilepsy Center	RTL	12	35.50 (12.66)	13.17 (3.13)	82.92 (13.01)	21.58 (11.59)	13.42 (11.16)	2	10	12	0
Total Sample	LTL	55	34.24 (10.90)	12.55 (2.32)	86.02 (14.32)	15.91 (13.89)	19.02 (13.48)	25	30	50	5
	RTL	47	33.98 (11.03)	13.00 (2.70)	89.48 (13.45)	15.17 (10.19)	18.68 (12.36)	23	24	43	4

Note. LTL = left temporal lobe; RTL = right temporal lobe; WAIS–III = Wechsler Adult Intelligence Scale–Third Edition; M = male; F = female; hand. = handedness; R = right hand preference; L = left hand preference.

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ses since the specific tasks that were administered differed across sites. In addition, age-corrected scaled and standard scores served as the units of analysis, since raw scores were not available from all centers. Tests were administered and scored by trained personnel according to standardized procedures provided in the WMS–III manual (Wechsler, 1997a).

Statistical Analysis

Data were analyzed in a series of steps designed to evaluate WMS–III performance in individuals with right and left temporal seizure foci. SPSS for Windows, Release 10.0.5 (1999) was used to conduct all statistical analyses. First, a descriptive analysis of the characteristics of the sample was performed. Second, differences in group means for the primary memory indexes and the individual subtests were assessed with a series of independent *t* tests. Third, discrepancy scores, calculated by subtracting the Visual Memory Index from the Auditory Memory Index, were compared between the groups for both immediate and delayed indexes. Fourth, the immediate and delayed indexes in each modality were compared within each group via paired sample *t* tests. Because of the large number of comparisons, we considered applying the Bonferroni correction method to account for Type I error. However, this approach is highly conservative, lacks power to reject an individual hypothesis, and may mask actual differences across groups (e.g., Olejnik et al., 1997; Simes, 1986). Thus, in order to protect against excessive Type I error, while maintaining adequate power and minimizing the risk of Type II error, alpha was set at .025 for statistical significance for all group comparisons.

Fifth, ROC curves were calculated for the WMS–III primary indexes, subtests, and discrepancy scores to evaluate the diagnostic efficiency of the WMS–III. The area under the curve (AUC), the maximal cut-off score, and a suggested cut-off score based on an a priori determination of specificity values greater than 70% (with the highest accompanying level of sensitivity), were calculated using nonparametric analyses (Barr, 1997).

Finally, Auditory–Visual Immediate and Delayed Index difference scores were further evaluated to examine the utility of different magnitudes of discrepancy for patient classification. Discrepancy criteria were obtained from the WMS–III manual and included (1) the .05 level of statistical significance determined from measurement error of the Auditory and Visual Indices, and (2) the difference between the indexes corresponding to a frequency of occurrence of less than 5% in the standardization sample.

RESULTS

Sample Characteristics

The mean age of the sample was 35.0 years ($SD = 11.1$) and the mean educational level was 12.8 years ($SD = 2.3$). Mean WAIS–III FSIQ was 88.7 ($SD = 16.1$). Patient characteristics of the RTL and LTL groups are presented in Table 1. A comparison of groups according to demographic variables revealed no significant differences in group composition for age, education, age at onset or duration, FSIQ, sex, or hand dominance.

Group Differences Among the Primary Indexes and Subtest Scores

The means and standard deviations for the WMS–III primary indexes and subtest scores are provided in Table 2. Univariate *t* tests of the primary index scores indicated that the RTL and LTL group differed significantly from one another only on the Auditory Delayed Index [$t(100) = 2.39$, $p < .025$], with the LTL group obtaining lower Auditory Delayed Index scores than the RTL group. Performance on only one subtest, Verbal Paired Associates II [$t(100) = 2.72$, $p < .01$], differed significantly between the LTL and the RTL groups.

Auditory–Visual Index Discrepancy Comparison

Analyses of the Auditory–Visual Index discrepancy scores revealed differences for the RTL and the LTL groups, for both the Immediate [$t(98) = 2.95$, $p < .01$] and the Delayed scores [$t(97) = 3.82$, $p < .001$]. Furthermore, the net difference scores were in the positive direction for the RTL group indicating that Visual Index scores were lower than Auditory Index scores, whereas the opposite was the case for the LTL group.

Figure 1 shows each group's mean performance on the individual indexes and subtests, with the scores converted to *z* scores for ease of comparison across scales.[1] Examination of the figure reveals that, while the performance of the LTL group was uniformly low, performance of the RTL patients was depressed on the visual subtests only.

Comparison of Immediate and Delayed Index Scores

Performance on the Visual Immediate and Delayed Indexes was compared in each group. This procedure was repeated with the Auditory Index scores. Paired-samples *t* tests revealed that performance differences between immediate and delayed index scores were not statistically significant for either modality, in either group (see Table 3).

ROC Curves

ROC curve analyses were computed and analyzed in a manner similar to those described by Monsch and colleagues

[1]The scores demonstrated in Figure 1 were calculated for each scale by converting individual scaled scores ($M = 10$, $SD = 3$) or standard scores ($M = 100$, $SD = 15$) to *z* scores by subtracting the normative mean (i.e., 10 for subtest scores and100 for index scores) from each participant's score, dividing by the normative standard deviation, and then calculating a mean *z* score for each group.

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Table 2. Mean WMS–III scores for the right and left temporal lobe groups

	LTL			RTL		
WMS–III score	*n*	M	(*SD*)	*n*	M	(*SD*)
Indexes						
General Memory Index	55	82.68	(17.04)	46	86.11	(16.13)
Auditory Immediate Index	55	84.29	(16.58)	47	89.81	(15.87)
Visual Immediate Index	53	85.91	(15.89)	47	81.87	(14.16)
Immediate Memory Index	53	82.19	(16.67)	47	83.15	(16.56)
Auditory Delayed Index*	55	82.64	(17.53)	47	90.91	(17.42)
Visual Delayed Index	55	85.43	(15.92)	46	81.63	(14.67)
Auditory Recognition Index	55	90.55	(16.49)	47	94.15	(15.30)
Working Memory Index	53	87.36	(14.84)	46	91.67	(16.28)
Auditory Immediate–Visual Immediate Index**	53	−1.11	(16.74)	47	7.94	(13.48)
Auditory Delayed Index–Visual Delayed Index***	55	−2.40	(15.25)	46	9.59	(15.90)
Subtests						
Logical Memory I	55	7.38	(3.29)	47	8.36	(3.38)
Logical Memory II	55	7.09	(3.45)	47	8.34	(3.36)
Faces I	55	7.93	(2.61)	47	7.77	(2.15)
Faces II	55	7.96	(2.23)	47	7.66	(2.30)
Verbal Paired Ass. I	55	7.18	(3.01)	47	8.17	(2.67)
Verbal Paired Ass. II**	55	6.87	(3.44)	47	8.64	(3.05)
Family Pictures I	53	7.60	(3.35)	47	6.55	(2.90)
Family Pictures II	55	7.20	(3.63)	45	6.80	(3.09)
Letter–Number Seq.	53	8.13	(3.16)	46	8.39	(3.21)
Spatial Span	54	7.63	(3.14)	47	8.66	(3.49)

Note. *n*s differ due to cases of missing data. LTL = left temporal lobe; RTL = right temporal lobe; WMS–III = Wechsler Memory Scale–Third Edition.
$^*p < .025$. $^{**}p < .01$. $^{***}p < .001$.

(Monsch et al., 1992) and Barr (1997). Each score was treated as a separate cutoff. Measures of sensitivity (Se) and specificity (Sp) were based on the cumulative number of RTL and LTL patients who obtained scores at or below these cutoff values. Se and Sp (1 − Sp) values were plotted graphically to obtain ROC curves for each test.

The results of ROC curve analyses are provided in Table 4. The most common index for describing an ROC curve is the area under the curve (AUC, Swets, 1988). Areas close to .50 indicate that the classification is close to chance level, while areas close to 1.0 indicate perfect discrimination. The total areas for individual subtest scores in this study ranged from a low of .524 (Faces I) to a high of .647 (Verbal Paired Associates II). The largest AUC for any score was observed for the difference between the Auditory and Visual Delayed Memory Indexes (AUC = .702). This ROC curve is provided in Figure 2.

Empirically derived cutting scores can be obtained from ROC curves for use in making diagnostic decisions. Two cutting scores were calculated in this study. First, the maximal cutting score defined as those scores where the sum of Se and Sp reaches a maximum value was calculated. These scores provide maximal separation of groups, irrespective of sensitivity and specificity values. Second, it was determined *a priori* based on Barr (1997) that a suggested cutting score with Sp values exceeding 70% and the highest accompanying level of Se would be most appropriate for making clinical decisions between patients with right and left temporal lobe dysfunction. Maximal and suggested cutting scores and their respective Se and Sp values are included in Table 4.

The most accurate maximal cutting score was obtained from the Auditory–Visual Delayed Memory Index discrepancy. For this measure, a score of 0.5 yielded a sensitivity of .62 and a specificity of .74 (sum = 1.36). This means that 62% of the LTL patients obtained Auditory–Visual Index difference scores of 0.5 or below, whereas 74% of the RTL patients obtained scores exceeding that level. The Auditory Delayed Index (score = 93, Se + Sp = 1.31) and the Verbal Paired Associates II subtest (score = 5.5, Se + Sp = 1.31) yielded cutting scores with the next highest levels of maximal separation. The Delayed Index difference score also provided the best separation of groups when utilizing the suggested cutting score, with an Sp value of .72 and a Se value of .64. The Auditory Immediate Index, Auditory Delayed Index and the Auditory–Visual Immediate Memory Index difference score also exhibited modest discrimination, with Se values exceeding 50%.

Patient Classification Using Significant and Infrequent Index Discrepancies

Auditory–Visual Index discrepancy scores were evaluated further to examine the ability of the WMS–III in predicting

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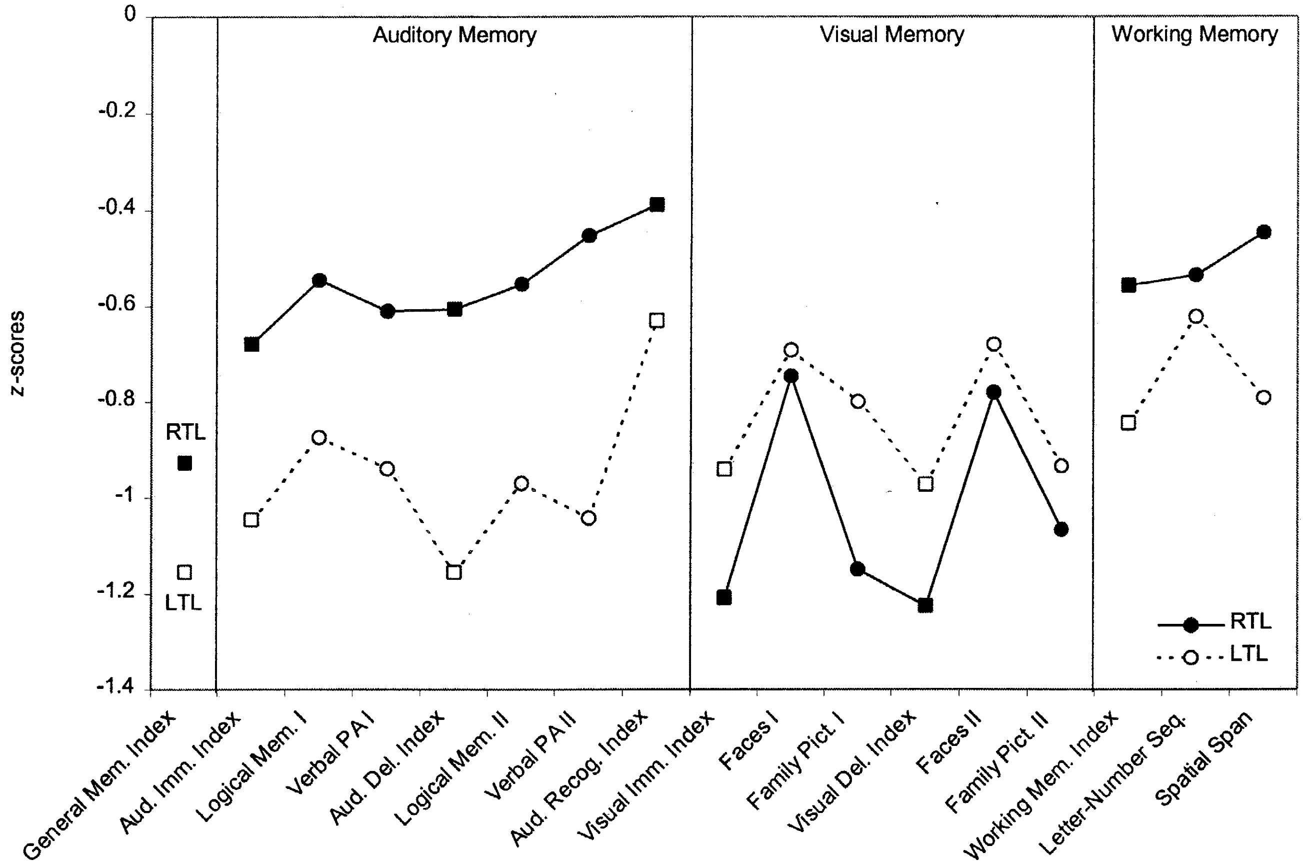

Fig. 1. Mean *Z* scores for the LTL (left temporal lobe) and the RTL (right temporal lobe) groups for performance on the WMS–III indexes and individual subtests. Note that better performance is represented by *Z* values closer to the normative mean of zero. Square markers denote index scores and circle markers denote subtest scores.

side of temporal lobe seizure focus. Two discrepancy criteria were used to classify patient performance. The first represented the .05 level of statistical significance determined from the measurement error of the Auditory and Visual Indices, obtained from the WMS–III manual (Wechsler, 1997a). This resulted in discrepancy scores of 15 points for the immediate indexes, and 17 points for the delayed indexes. The second discrepancy criterion was obtained from the rarity of difference scores in the standardization sample. Tables included in the WMS–III manual report the frequency of discrepancies independent of the directionality of the score. That is, the cumulative percentages listed in Table F.2. (p. 206) combine individuals who obtained an Auditory Index score that was higher than their Visual Index score, and people who showed the reverse pattern. Based on suggestions of Tulsky and colleagues for use with the WAIS–III (Tulsky et al., 2000b), the frequencies reported in Table F.2. should be divided in half to obtain the appro-

Table 3. Immediate-delayed index score differences

Index modality	Group	*n*	Immediate Index score (*M*)	Delayed Index score (*M*)	Difference score (*M*)	Difference score (*SD*)	*t*-test value	*p*
Auditory	LTL	55	84.29	82.64	1.65	(7.19)	1.71	.09
	RTL	47	89.81	90.91	−1.11	(8.44)	−.90	.37
Visual	LTL	53	85.91	85.43	.47	(7.53)	.46	.65
	RTL	46	82.02[a]	81.63	.39	(9.01)	.29	.77

Note. Significance test is two-tailed. Difference score = Immediate Index score–Delayed Index score. RTL = right temporal lobe, LTL = left temporal lobe. *p* = obtained significance level
[a]Index mean differs from value listed in Table 2 due to missing data for 1 participant on the Visual Delayed Index score, and thus for calculation of the difference score.

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Table 4. ROC curve statistics for WMS–III index and subtest scores

WMS–III scale	AUC	Maximal cutting score				Suggested cutting score		
		Score	Se	Sp	Se + Sp	Score	Sep	Sp
Indexes								
General Memory Index	.569	80	.70	.49	1.19	90	.37	.70
Auditory Immediate Index	.617	90.5	.53	.73	1.26	90.5	*.53*	.73
Visual Immediate Index	.596	82.5	.60	.62	1.22	86	.49	.70
Immediate Memory Index	.523	88	.40	.70	1.10	88	.40	.70
Auditory Delayed Index	.657	93	.51	.80	*1.31*	90.5	*.55*	.73
Visual Delayed Index	.589	86	.51	.70	1.21	86	.51	.70
Auditory Recognition Index	.563	87.5	.70	.42	1.12	97.5	.38	.71
Working Memory Index	.586	106.5	.26	.92	1.19	97.5	.43	.74
Subtests								
Logical Memory I	.611	8.5	.66	.64	1.30	9.5	.40	.73
Logical Memory II	.626	7.5	.70	.56	1.27	8.5	.47	.71
Verbal Paired Associates I	.601	9.5	.32	.85	1.17	9.5	.32	.85
Verbal Paired Associates II	.647	5.5	.87	.44	*1.31*	9.5	.45	.76
Faces I	.524	7.5	.58	.51	*1.09*	8.5	.38	.70
Faces II	.546	8.5	.42	.70	1.12	8.5	.42	.70
Family Pictures I	.606	6.5	.60	.60	1.20	8.5	.38	.77
Family Pictures II	.539	9.5	.29	.84	1.14	8.5	.36	.76
Letter–Number Sequencing	.536	8.5	.57	.55	1.11	10.5	.24	.79
Spatial Span	.591	10.5	.40	.78	1.18	9.5	.47	.70
Difference scores								
Auditory–Visual Immediate Index	.655	−0.5	.77	.51	1.28	1.5	*.57*	.70
Auditory–Visual Delayed Index	.702	0.5	.62	.74	*1.36*	1.5	*.64*	.72

Note. Values discussed in text are italicized. AUC = area under the curve; Se = sensitivity; Sp = specificity; WMS–III = Wechsler Memory Scale–Third Edition.

priate base rate when a directional hypothesis is being tested. Thus, to obtain a 95% level of confidence, a 27-point difference was required for the immediate indexes, and a 26-point discrepancy for the delayed indexes (which correspond to cumulative percentages obtained in 10% of the standardization sample as listed in Table F.2.).

Patients were grouped into one of three categories (*left*, *right*, *inconclusive*) on the basis of their Auditory–Visual Memory Index discrepancy scores. If the Auditory Memory Score was significantly below the Visual Memory score, the patient was classified as having probable left temporal dysfunction. Similarly, if the Visual Memory score was significantly lower than the Auditory Memory score, the patient was classified as having probable right temporal dysfunction. Discrepancies not exceeding the criterion were deemed inconclusive for indicating laterality.

Eighteen RTL patients had immediate index discrepancy scores of 15 or more points. In 16 of 18 patients, the Visual Memory Index was the lower value, which is consistent with right temporal lobe dysfunction. There were 22 LTL patients meeting the 15-point difference criterion. However, 12 of these patients had significantly lower Visual Memory Indices, suggesting relative impairment of *right* temporal lobe function. These results are shown in Table 5.

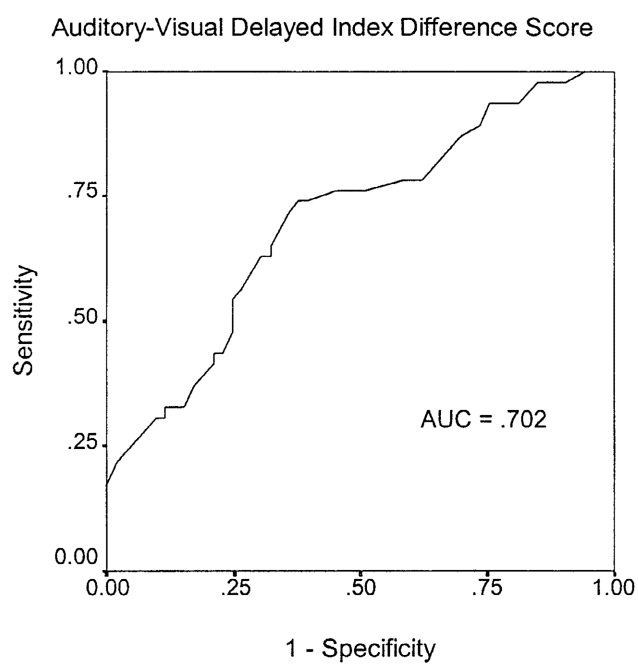

Fig. 2. Receiver operating characteristic (ROC) curve for the WMS–III Auditory–Visual Delayed Index difference score. AUC = area under the curve.

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Table 5. Auditory–Visual Index Difference Scores and Classifications

WMS–III Index difference	Size and direction of difference score	LTL *n*	LTL %	RTL *n*	RTL %
Auditory–Visual Immediate Index	≤−15	10	83.3	*2*	16.7
	≥15	*12*	42.9	16	57.1
	≤−27	5	83.3	*1*	16.7
	≥27	*1*	16.7	5	83.3
Auditory–Visual Delayed Index	≤−17	10	76.9	*3*	23.1
	≥17	*9*	34.6	17	65.4
	≤−26	5	83.3	*1*	16.7
	≥26	*0*	0	8	100

Note. *n* = number of patients in each group with difference scores meeting or exceeding the stated magnitudes; italicized values indicate patients who obtained difference scores in the direction opposite to prediction. % = percent of patients with given difference scores who fall within each group; LTL = left temporal lobe; RTL = right temporal lobe; WMS–III = Wechsler Memory Scale–3rd Edition.

Similar patterns were evident when statistically significant discrepancies between the delayed indices were examined. The majority of the RTL patients meeting the 17-point criterion were correctly classified, but a large proportion of LTL patients exhibited relatively greater impairment on *visual* memory tasks.

Twelve patients (6 RTL, 6 LTL) had discrepancies that exceeded the more conservative 27-point criterion for immediate index differences. In each group, 1 out of 6 patients was incorrectly classified. There were 14 patients (9 RTL, 5 LTL) who met the 26-point criterion for the delayed discrepancy score. Using this stringent criterion, only 1 RTL patient was misclassified.

Alternatively, it is also useful to identify the likelihood of being correct in the classification of laterality when given a certain discrepancy score. As indicated in Table 5, the likelihood of correctly classifying a patient with a large negative discrepancy between Auditory and Visual indexes as having left temporal dysfunction was in the range of 75 to 85% across all given discrepancy criteria. However, positive discrepancies based on difference scores calculated from statistical significance levels led to correct prediction of RTL patients in only 55 to 65% of cases. This is due to the large number of LTL patients who obtained discrepancy scores in the direction opposite to prediction (i.e., significantly better Auditory than Visual Index scores). With very large and infrequent discrepancy scores, improved prediction of patients was obtained. It must be kept in mind, however, that few individuals (less than 15% of the sample) displayed such large discrepancies.

DISCUSSION

The purpose of the present study was to examine the utility of the WMS–III in predicting laterality of impairment in patients with temporal lobe epilepsy. The results suggest that the new WMS–III does not represent a significant improvement over its predecessors in its ability to distinguish patients with left and right temporal dysfunction associated with a unilateral seizure onset. LTL patients tended to perform more poorly on the auditory/verbal tasks than the RTL group, whereas the RTL patients showed the opposite pattern of performance. However, group performance on the WMS–III indexes and subtests was largely insensitive to laterality. Within subject performance as demonstrated by auditory–visual difference scores appeared most sensitive to side of temporal dysfunction. This is consistent with previous research on the WMS–R, which has suggested that discrepancy scores may be most useful at detecting material-specific memory impairments (Bornstein et al., 1988; Chelune & Bornstein, 1988; see Naugle et al., 1993 for negative findings). It is important to note, however, that when considering the performance within each group, material-specific performance was not observed for the LTL group. Thus, the LTL group performed at the same low level on the auditory and the visual subtests. Indeed, the auditory–visual discrepancy scores obtained by the LTL group did not differ significantly from zero. This calls into question the selectivity of verbal memory deficits in LTL patients as measured by the WMS–III. On the other hand, in the RTL group a more specific pattern of performance was demonstrated such that depressed performance of patients with right temporal lobe seizures was relatively specific to the visual tasks.

At the individual subtest level, some tasks appeared more sensitive to laterality of dysfunction than others. Verbal Paired Associates II was the only subtest to differ significantly between the groups, due to the very low mean performance of LTL patients. This finding is consistent with much of the literature on memory functioning in epilepsy demonstrating impairment on verbal tasks in patients with left temporal dysfunction (Chelune & Bornstein, 1988; Hermann et al., 1987; Loring et al., 1988; Moore & Baker, 1996). Of the new visual subtests included in the WMS–III, the Family Pictures subtest appeared most sensitive to right temporal lobe dysfunction, despite the fact that patients are required to visually encode as well as verbally recall the content in this task. The fact that dual encoding and processing is required may account at least in part for the nonsignificant difference between LTL and RTL patients on this task. Note however that such an explanation cannot account for the failure of the Faces subtest to distinguish between groups.

The area under the ROC curve provides a quantitative index of the diagnostic accuracy of a given score. The area values in this study, while somewhat higher than those reported by Barr (1997) using WMS–R scores, were still substantially lower than those reported in other studies using ROC curves and neuropsychological test scores with clinical populations (Drebing et al., 1994; Engelhart et al., 1994; Guilmette & Rasile, 1995; Monsch et al., 1992). As would be expected based on the obtained results of group differences, the highest level of classification accuracy in this study was obtained using the auditory–visual discrepancy scores, a finding also observed by Barr (1997) in his analysis of the WMS–R (see also Loring et al., 2000, with regard to the Memory Assessment Scales). The benefit of using ROC curves is that the analysis provides an empirically derived cutting score to aid in diagnostic classification. Using the cutting score of 0.5 obtained from the Auditory–Visual Delayed Index, which had the highest combined level of sensitivity and specificity (maximal cutting score), 38% of the LTL group and 26% of the RTL group were incorrectly classified. Thus, although diagnostic accuracy was significantly better than chance, the classification rates obtained from this study were not within an acceptable range to have utility for clinical use.

When discrepancy scores were further examined based on the magnitude of difference, classification rates also provided unsatisfactory results. First, the vast majority of patients did not produce results that met the discrepancy criteria, therefore minimizing the utility of this approach. Second, a large proportion of patients were misclassified. Statistically significant discrepancy scores from the WMS–III were more accurate in predicting laterality for people with right temporal focus than for patients with left temporal dysfunction; many of the LTL patients would have been classified as having right temporal dysfunction based on their discrepancy scores. Consequently, the ability to correctly predict right-sided laterality given a positive Auditory–Visual Index difference score was especially poor since more than one-third of patients who obtained statistically significant positive difference scores were LTL patients. The particularly poor classification of LTL patients in this study is contrary to the findings of other researchers examining index score discrepancies using the WMS–R (Loring et al., 1989; Moore & Baker, 1996) who generally found that LTL patients were correctly classified while RTL patients were incorrectly classified. The reason for this difference is unclear. At a group level, index scores are within expectations. Inspection of the individual patients who were misclassified does not suggest any differences in terms of demographic factors, and the WMS–III index scores obtained from these patients spans the range from severely impaired to superior. This finding awaits replication from other researchers, but these preliminary results suggest that the WMS–III may have somewhat different characteristics with respect to laterality than did the WMS–R. Using the more conservative discrepancy criteria of unusually large index differences resulted in improved prediction of laterality; very few individuals were misclassified. However, the rarity of such large discrepancies in this population limits the usefulness of this approach. Specifically, the utility of the WMS–III in characterizing, detecting, and classifying individuals with lateralized temporal dysfunction is put into question by the results of this study.

Another goal of this study was to examine the utility of the immediate *versus* the delayed memory indexes, since it has been suggested that the delayed measures may be more clinically relevant and ecologically valid than the immediate scores. Factor analytic support of the distinction between immediate and delayed memory dimensions is provided in the *WAIS–III–WMS–III Technical Manual* (The Psychological Corporation, 1997, p. 115). In this study, there were no differences between immediate and delayed index performance in either the auditory or the visual modality, in either the LTL or the RTL group. This sheds some doubt on the particular significance of the delayed memory scores and suggests that the immediate and the delayed subtests may be assessing similar functions. Each subtest on the WMS–III requires the retention of material for the immediate task beyond that which would be possible based on models of working memory, and thus it seems likely that to perform adequately on the immediate memory measures, multiple memory components including encoding, storage, and retrieval would be required. The lack of distinction between immediate and delayed measures may be population specific and awaits further research with other neurological patient groups in which a distinction might be expected, such as in patients with Alzheimer's disease or Wernicke–Korsakoff's syndrome.

A number of limitations of the present study must be acknowledged. First, analysis of raw scores may have resulted in additional findings, since scaled scores coincide with ranges of raw scores and thus potentially reduce the variance of results, especially at the extremes. In addition, percent retention scores, which have been shown to differentiate LTL and RTL groups (e.g., Delaney et al., 1980, Jones-Gotman, 1991), were unavailable in this study. While this study illustrated the relative merit of utilizing discrepancy scores over group means, it will be useful in the future to examine discrepancies between the auditory and visual subtests, with respect to absolute differences and percent retention. For example, studies utilizing the WMS–R have often compared performance on Logical Memory to Visual Reproduction (e.g., Chelune & Bornstein, 1988; Naugle et al., 1993).

In addition, it may be that parsing or combining tasks in a different manner results in an increased sensitivity of the WMS–III to laterality effects. For example, Holley and col-

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leagues (Holley et al., 2000) divided the Family Pictures subtest into Character, Location, and Action components, and examined performance in patients who had undergone temporal lobectomies. After statistically removing verbal memory scores, they found that the Location score was sensitive to right temporal lobe dysfunction. Further studies that investigate alternative methods of looking at WMS–III performance will be useful in determining its ability to detect laterality differences.

In addition, this study did not address issues such as the degree of mesial temporal sclerosis and the integrity of the contralateral hippocampus. Memory functioning has been shown to vary according to such indicators (see Bell & Davies, 1998, for review). Thus, future research in patients with and without hippocampal pathology presents an important avenue for further study.

While the purposes of this study were to examine the ability of the WMS–III to detect laterality in a presurgical sample, it is expected that the magnitude of modality-specific differences would be enhanced following temporal lobectomy. The *Technical Manual* provides some preliminary data suggesting that the WMS–III scores are sensitive to laterality in postsurgical epilepsy patients. However, the sample size was quite small and analysis of the data was rather limited. A more comprehensive study of WMS–III in epilepsy patients after temporal lobectomy is needed.

Obviously, considerable research is needed before the utility of the WMS–III in patients with epilepsy is known. The present results indicate that the WMS–III alone is limited in the prediction of laterality in epilepsy patients. In particular, selective verbal memory deficits were not demonstrated for those patients with left temporal foci, as indicated by their poor overall performance and high misclassification rate. Future research and clinical experience with the WMS–III will demonstrate whether the findings from this study are replicable and will assist in establishing its usefulness as a neuropsychological measure in the epilepsy population.

This study also emphasizes the fact that scores from the WMS–III should not be used in isolation. It may be that the combination of the WMS–III with other neuropsychological or diagnostic measures provides an improved rate of classification of epilepsy patients. Furthermore, the limitations of the WMS–III in classifying patients with temporal lobe seizures should not be extended to making predictions regarding the use of the WMS–III in other clinical populations. In addition, it should be recognized that neuropsychological testing of epilepsy surgery candidates serves a number of useful purposes aside from identifying laterality of seizures, such as providing valuable baseline information for evaluating change after surgery and for identifying those who may be at risk for subsequent impairment (Dodrill et al., 1993). Finally, it is important to bear in mind that the utility of the WMS–III lies in its ability to measure memory (that is, its ability to provide an internally and externally valid indication of memory functioning), not only in its ability to differentiate patient groups.

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