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Significant Discrepancies between Immediate and Delayed WMS-III Indices Are Rare in Temporal Lobe Epilepsy Patients

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Abstract

Initial factor analysis of Wechsler Memory Scale-Third Edition (WMS-III) standardization data resulted in a five-factor model that included separate immediate (IMM) and delayed (DEL) memory factors for auditory (AUD) and visual (VIS) memory. However, recent factor analyses that revealed three factors—AUD, VIS, and working memory—were discovered to be more accurate. Continued use of separate WMS-III IMM and DEL indices has been recommended because future studies with clinical groups might support this distinction. Data from this investigation of 88 temporal lobe epilepsy (TLE) patients suggested separate IMM and DEL WMS-III indices are not necessary in this population. Results were as follows: 1) There was no significant difference between the IMM and DEL indices for AUD or VIS memory. 2) The percentage of individuals with a significant difference between the IMM and DEL indices (IMM minus DEL > 11 or < -12) was similar for our TLE group and the standardization sample. 3) The mean percent retention standard score (SS) was at the average level for the four memory subtests, and for each subtest only about 10% of the TLE patients had impaired scores. 4) Hippocampal volumes correlated significantly with both IMM and DEL indices. These data suggest that combining the appropriate WMS-III IMM and DEL memory subtest scores to form AUD and VIS memory indices is appropriate for TLE patients.

Keywords

Memory; Hippocampus; Temporal Lobe Epilepsy; Neuropsychological tests

Initial factor analysis of Wechsler Memory Scale-Third Edition (WMS-III) standardization data revealed a five-factor model that included separate immediate (IMM) and delayed (DEL) factors for both auditory (AUD) and visual (VIS) memory (Psychological Corporation, 1997, p. 115). However, this solution was subsequently rejected when model specification errors were recognized (Millis, Malina, Bowers, & Ricker, 1999; Price, Tulsky, Millis, & Weiss, 2002; Psychological Corporation, 2002, pp. 96–102; Tulsky et al., 2003). More recent factor analyses of the standardization data revealed a three-factor solution that consisted of AUD memory, VIS memory, and working memory. IMM and DEL AUD memory scores formed the AUD factor and IMM and DEL VIS memory scores formed the VIS factor (Millis, et al., 1999; Price, et al., 2002; Psychological Corporation, 2002; Tulsky, Ivnik, Price, and Wilkins, 2003). Tulsky et al. (2003) describe how these recent factor analytic findings led to the creation of new WMS-III AUD and VIS memory indices for clinical use. The new AUD and VIS indices require summing the IMM and DEL memory standard scores (SS) from the appropriate subtests.

Although the three-factor model of the WMS-III best fit the data obtained from the healthy individuals in the standardization sample, continued clinical use of separate IMM and DEL AUD and VIS memory indices has been recommended by WMS-III researchers up to this point (Heaton, Taylor, & Manly, 2003; Millis et al., 1999; Price et al., 2002; Psychological Corporation, 2002; Tulsky et al., 2003; see also Delis, Jacobson, Bondi, Hamilton, & Salmon, 2003). This recommendation has been made because of the possibility that future studies with clinical groups might support the validity of the IMM versus DEL memory distinction.

Hippocampal atrophy is common in patients with mesial temporal lobe epilepsy (Babb & Brown, 1987; Davies et al., 1996; Trenerry, Westerveld, & Meador, 1995). In addition, it has been reported that mesial temporal lobe integrity in TLE patients is more closely associated with delayed memory than immediate memory (Griffith et al., 2003; Helmstaedter, Grunwald, Lehnertz, Gleissner, & Elger, 1997). Therefore, it might be predicted that WMS-III DEL memory scores would be lower than IMM memory scores in TLE patients. That is, the IMM versus DEL memory distinction might indeed have utility among TLE patients. However, other TLE studies have reported a relationship between hippocampal integrity and both immediate and delayed memory on various memory measures (Baxendale et al., 1998; Kilpatrick et al., 1997; Kalviainen et al., 1997; Rausch & Babb, 1993). Moreover, Wilde et al. (2001) reported no difference between WMS-III IMM and DEL memory index scores in the AUD or VIS modality for left ($n = 55$) and right ($n = 47$) TLE patients. And a factor analysis of WMS-III data from a larger group of TLE patients ($N = 254$) did not result in separate IMM and DEL memory factors (Wilde et al., 2003).

Notably, the WMS-III IMM versus DEL memory index comparison has not been performed at the individual level. It is possible that a significant minority of TLE patients would show a discrepancy between IMM and DEL memory using the traditional indices for AUD and VIS memory. In addition, percent retention scores, which are less dependent on the amount of initial learning compared to WMS-III DEL memory scores, have not been compared to IMM memory in TLE patients. WMS-III percent retention scores could possibly diverge more than DEL scores from IMM memory performance.

This study examined WMS-III data from TLE patients and controls. In particular, we sought to determine whether the distinction between WMS-III IMM and DEL memory indices can be abandoned in the TLE population, a possibility suggested by recent factor analyses of standardization sample data. We maintain the AUD versus VIS memory distinction in this study. The memory index data first were analyzed at the group level. Then, for each modality, the percentage of patients who demonstrated 1) a significantly higher IMM versus DEL memory index or 2) a significantly higher DEL versus IMM memory index was compared to the percentage of the standardization sample who demonstrated the same pattern of performance.

IMM memory and percent retention SS for the four core memory subtests also were examined. Percent retention scores might provide important information about memory performance after the 30-minute delay. Cumulative frequency data for the difference between IMM memory and percent retention SS are not available in the WMS-III technical manual. Therefore, we compared the TLE patients' subtest scores to a control group of 49 healthy controls. Finally, we examined the correlation between WMS-III scores and hippocampal volumes in the TLE group. Because lateral temporal lobe regions contribute to memory (Griffith et al., 2003; Helmstaedter et al., 1997; Ojemann, Schoenfield-McNeill, & Corina, 2002; Perrine, Devinsky, Uysal, Luciano, & Dogali, 1994; Weintrob, Saling, Berkovic, Berlangieri, & Reutens, 2002) and can be atrophied (Hermann et al., 2003) in TLE patients, we also examined the correlation between lateral temporal lobe gray and white matter volumes and WMS-III scores.

METHODS AND MATERIALS

Participants

All 88 TLE patients were administered the WMS-III between 1998 and 2002 as part of a neuropsychological and MRI study of TLE approved by the Human Subjects Committee of the University of Wisconsin at Madison. These patients were between 16 and 63 years old, had a Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Psychological Corporation, 1997) seven-subtest short form (Pilgrim, Meyers, Bayless, & Whetstone 2000; Ward, 1990) full scale IQ > 69, and had no MRI abnormalities other than atrophy. None of the patients had undergone epilepsy surgery at the time of the neuropsychological assessment.

Patients were recruited after their medical records were reviewed by at least one board certified neurologist with expertise in epilepsy. This review included information pertaining to seizure semiology, previous EEGs and neuroimaging, and clinical history and course. Based on this review, each patient was classified as having seizures of definite, probable, or possible temporal lobe origin. Definite TLE was defined by video/EEG monitoring demonstrating temporal lobe seizure onset. Probable TLE was defined by clinical semiology reported to reliably identify complex partial seizures of temporal lobe origin versus onset in other regions, in conjunction with interictal EEGs, neuroimaging findings, and developmental and clinical history. Only those patients meeting criteria for definite or probable TLE were recruited for study participation. Fifty-two of the 88 patients in this study had undergone ictal EEG monitoring, with 50 having definite TLE (23 right, 19 left, 8 bilateral, 2 indeterminate). For the group as a whole, on the basis of previously acquired ictal or interictal EEG data, 31 of the patients in this study had a right temporal EEG focus, 28 had a left temporal focus, 15 had a bilateral temporal focus, and in 14 the laterality of the temporal lobe focus was indeterminate or unknown. During the study, additional information about medical and demographic history was acquired by means of an interview with each patient and/or a spouse or relative and from additional medical records, where possible. See Table 1 for the patients' demographic and epilepsy data.

For an individual level analysis of the difference between WMS-III subtest immediate memory and percent retention SS, we compared a subset of patients to 49 healthy controls (see Table 1). These controls were friends, relatives, or co-workers of the patients, met WMS-III criteria for healthy controls (Psychological Corporation, 1997), and were administered the same test battery as the patients for the 1998–2002 study. There were no significant differences between the patient and control groups in age, education, or gender ratio. Only controls who had an IMM memory SS < 15 on all four WMS-III subtests were included for the purposes of this study (see “Subtest scaled scores: IMM memory versus percent retention” heading in the Results section for an explanation). The mean volumetric *z* scores in Table 1 are not precisely equal to zero for the control group because the *z* score data were derived from a larger control sample.

Brain Imaging—The majority of the patients and controls underwent brain MRI. Because some participants in the study had claustrophobia, were too large for the MRI apparatus, or moved excessively during MRI, volumetric data were available for approximately 80% of the patients and controls. MRI usually took place on the same day as the neuropsychological assessment. Images were obtained on a 1.5T GE Signa MR scanner. MR images were acquired at the University of Wisconsin in Madison and transferred to the Image Processing Laboratory of the Mental Health Clinical Research Center at the University of Iowa in Iowa City, where they were processed using BRAINS (Brain Research: Analysis of Images, Networks, and Systems), a semi-automated software package (Andreasen et al., 1996). Hippocampal tracing was performed manually, using guidelines also developed at the University of Iowa (Pantel et al., 2000).

Tissue volumes were adjusted for height, gender, and age using multiple regression analyses based on our healthy controls. The regression equations were then applied to the TLE patient volumes and the predicted variance was removed from the observed volume values of the TLE patients. The result represents a residual score that removes variance due to body size and aging. The z score transformations of the adjusted volumes were computed on the basis of the control group's mean adjusted volumes.

Memory Assessment—The WMS-III was administered in the standard manner. All analyses used WMS-III SS. We examined immediate and delayed scores at the index and subtest levels for auditory memory and for visual memory.

Raw savings or percent retention scores are derived by dividing the quantity of information recalled initially by the quantity recalled after the 30-minute delay and then are converted to SS, as described in the WMS-III manual. For the VPA percent retention score, the IMM memory score in this context was the number of word pairs recalled on the fourth and final learning trial. To determine the number of participants in each group with impaired percent retention scores for each subtest, memory impairment was defined as a $SS < 6$.

RESULTS

Memory Indices: IMM versus DEL Memory

Table 2 shows the WMS-III indices for the TLE patients. Paired sample t tests indicated there was no significant difference between IMM and DEL memory indices for the AUD modality ($t = .86, df = 87, p = .39$). There was a trend toward a significant difference between the IMM and DEL memory indices for the VIS modality ($t = -2.0, df = 87, p = .05$). However, that trend was in the unexpected direction; the DEL VIS memory index was slightly *higher* than the IMM VIS memory index. In addition, there were no significant IMM versus DEL memory index differences for the patients with right or left TLE as determined by ictal EEG. Therefore, all patients were treated as a single group in the following analyses.

Five percent of the WMS-III standardization sample had an AUD IMM minus AUD DEL index difference score that was > 11 (Psychological Corporation, 2002, Table D.7.). In our TLE group, 13% ($n = 11$) showed a directional difference score of this magnitude for AUD memory, $z = 3.13, p < .01$ (Bruning & Kintz, 1977). There were no significant differences on demographic, cognitive or seizure variables between the 11 patients who showed a large positive IMM-DEL memory discrepancy and the 77 patients who did not. Thus, although the percentage of patients with a relatively low DEL versus IMM AUD memory index was significantly higher than the percentage in the standardization sample, only a small minority of the patients showed this pattern of performance. And this subgroup had no evident consistent characteristics. Moreover, for VIS memory, only 3% of the patients versus 5% of the standardization sample showed a > 11 point difference score, $z = .83, p > .05$.

Five percent of the WMS-III standardization sample had an AUD IMM minus AUD DEL or VIS IMM minus VIS DEL index difference score that was < -12 . In our TLE group, 3% ($n = 3$) showed a directional difference score of this magnitude for AUD memory and for VIS memory, $z = .83, p > .05$.

Subtest Scaled Scores: IMM Memory versus Percent Retention

As evident in Table 3, the percent retention SS was *higher* than the IMM memory SS for all four core WMS-III subtests (Logical Memory, Verbal Paired Associates, Faces, and Family Pictures). For the two AUD memory subtests, the difference between the IMM memory and percent retention SS was not significant, Logical Memory: $t = -.40, df = 87, p = .69$; Verbal

Paired Associates: $t = -1.4$, $df = 87$, $p = .17$. For each of the two VIS memory subtests, the mean percent retention SS was significantly *higher* than the IMM memory SS, Faces: $t = -3.8$, $df = 87$, $p < .01$; Family Pictures: $t = -3.6$, $df = 87$, $p < .01$.

At the individual level, only about 10% of patients had a percent retention SS in the impaired range ($SS < 6$) for each test (Logical Memory = 9%, Verbal Paired Associates = 10%, Faces = 10%, and Family Pictures = 14%). IMM memory versus percent retention SS data is not available for the standardization sample in the WMS-III technical manual. In addition, for three of the four memory subtests under discussion (Verbal Paired Associates, Faces, and Family Pictures), 12 is the maximum possible percent retention SS for individuals within the age range of the participants in this study. Therefore, in order to determine the percentage of patients who showed a percent retention SS that was more than one standard deviation (> 3 points) lower than the IMM scaled score, for each subtest we selected the subset of patients whose IMM SS was < 15 (Logical Memory, $N = 84$; Verbal Paired Associates, $N = 81$; Faces and Family Pictures, $N = 88$). These patients were compared to a group of 49 controls (see Table 1) who had an IMM memory SS < 15 on all four subtests. We used this criterion, scores no greater than the high average level of performance, because 1) if all IMM memory SS were used in this analysis, the percentage of participants with a percent retention SS > 3 points below the IMM SS would be inflated artificially by the restricted range of the percent retention SS and 2) it insured that the control group's mean WMS-III scores were within the average range. The percentage of participants with a percent retention SS > 3 points below the IMM memory SS ranged from 7 to 18% for the patients and 0% to 22% for the controls (Logical Memory = 12% of patients versus 16% of controls, $Chi\ square = .52$, $df = 1$, $p = .47$; Verbal Paired Associates = 7% versus 0%, $Chi\ square = 3.8$, $df = 1$, $p = .05$; Faces = 16% versus 22%, $Chi\ square = .90$, $df = 1$, $p = .34$; and Family Pictures = 18% versus 18%, $Chi\ square = .001$, $df = 1$, $p = .98$). Thus, for three of the four subtests there clearly was no difference in the percentage of patients and controls showing this pattern of performance. For Verbal Paired Associates, there was a trend ($p = .05$) for a higher percentage of patients to have a percent retention SS that was lower than the IMM SS by at least 3 points. Nonetheless, only a very small minority of the patients (7%) showed this pattern of performance on that particular subtest.

Correlations between WMS-III Scores and Hippocampal and Lateral Temporal Lobe Volumes

When there was a significant relation between hippocampal volume and memory, hippocampal volume correlated significantly with both the IMM and DEL indices (see Table 4). These correlations were slightly, but not significantly, higher for the DEL indices. Results from tests for the difference between correlations (Bruning & Kintz, 1977) were as follows: left hippocampus and AUD IMM and DEL: $t = 1.29$, $df = 66$, $p > .05$; left hippocampus and VIS IMM and DEL: $t = 1.45$, $df = 66$, $p > .05$; right hippocampus and VIS IMM and DEL: $t = 1.0$, $df = 66$, $p > .05$. Interestingly, the AUD IMM and DEL indices correlated with left, but not right, hippocampal volume, whereas the VIS IMM and DEL indices correlated significantly with both left and right hippocampal volumes.

At the subtest level, the volume of the left hippocampus correlated significantly with two of the IMM scores, all the DEL scores, and one of the four percent retention scores. Right hippocampal volume correlated at a significant level only with the DEL memory score on the Faces subtest.

Right temporal gray matter volume correlated only with the Verbal Paired Associates DEL SS. Neither right temporal lobe white matter volume nor left temporal lobe gray matter volume correlated significantly with any of the memory indices or subtest scores. Left temporal lobe white volume correlated with the IMM and DEL Family Picture subtest SS and with the IMM and DEL VIS memory indices. Because the right lateral temporal lobe measures and left lateral temporal lobe gray matter volume did not correlate at all consistently with memory scores,

only the correlations between left lateral temporal lobe white matter volume and the memory scores are shown in Table 4.

DISCUSSION

In recent analyses of WMS-III data from the standardization sample (Millis, et al., 1999) and TLE patients (Wilde et al., 2001,2003), IMM and DEL memory indices did not provide unique information when considered separately. Results from this TLE study are in agreement with those reports. The mean DEL memory index was not significantly lower than the mean IMM memory index for the AUD or VIS modality. Consistent with this finding, analyses at the individual level showed that, in each modality, very few members of the TLE group performed considerably worse on the DEL memory index compared to the IMM memory index. More specifically, although a higher percentage of TLE patients in this study, compared to the standardization sample, had an AUD DEL index that was > 11 points lower than the AUD IMM index, only 13% of the patients showed a discrepancy of this magnitude. Moreover, only 3% of the TLE patients had a significantly higher IMM versus DEL index in the VIS modality. Notably, only 3% of patients demonstrated a significantly lower IMM compared to DEL index (i.e., discrepancy scores < -12) in the AUD and VIS modalities. In addition, for the four memory subtests, there was no difference between the percentage of patients versus controls from our study who had a percent retention SS > 3 points lower than the IMM memory SS. The infrequency of large IMM versus DEL memory index discrepancies and IMM memory versus percent retention SS discrepancies at the subtest level supports the idea that WMS-III immediate memory and 30-minute delay scores typically provide over-lapping information in TLE patients.

Hippocampal volumes in this study correlated significantly with both IMM and DEL indices. Wilde et al. (2001) reported that left TLE patients as a group perform poorly on both AUD and VIS WMS-III indices, whereas the memory deficit in right TLE patients tends to be specific to the VIS memory index. Their data is consistent with our finding that AUD IMM and DEL indices correlated only with left hippocampal volume, whereas the VIS IMM and DEL indices correlated significantly with left and right hippocampal volumes. That is, there was no significant relationship between right hippocampal volume and auditory memory. Our findings also are consistent with past TLE reports that both immediate and delayed memory scores have correlated with left hippocampal volume or T2 relaxometry on MRI (Kilpatrick et al., 1997; Kalviainen, et al., 1997) or hippocampal pathology ratings performed after anterior temporal lobectomy (Baxendale, et al, 1998; Rausch & Babb, 1993).

At the WMS-III subtest level, the volume of the left hippocampus correlated most consistently with the DEL scores, but two of the four IMM scores also were significantly associated with left hippocampal volume. Right hippocampal volume correlated at a significant level only with the DEL score on the Faces subtest. In a recent study (Griffith et al., 2003), we reported a stronger relationship between the left hippocampus and DEL memory compared to IMM memory, especially for AUD memory scores. However, that study examined WMS-III subtest scores, not index scores, and included other memory tests in the analyses.

Considering the lateral temporal lobes, only left temporal white matter had a reasonably strong relationship with memory scores. Left temporal lobe white matter correlated with both the IMM and DEL VIS memory indices and, at the subtest level, with both IMM and DEL Family Pictures SS. Thus, the volumetric data from this study do not provide persuasive support for maintaining separate WMS-III IMM and DEL indices.

TLE patients with early onset epilepsy are more likely to have hippocampal sclerosis and cognitive deficits (Davies et al., 1996; Glosser et al., 1997; Hermann et al., 1997), and

conceivably might show a particular deficit in delayed memory. However, when we conducted the same statistical analyses for the 47 patients who had had an onset of seizures at age 14 or before, the WMS-III results were quite similar. In addition the memory test results were essentially the same for the patients with left or right hippocampal volume z scores <-1.5 ($n = 18$, $n = 10$, respectively).

In a factor analysis of TLE data (Wilde et al., 2003), a two-factor model explained the underlying structure of the WMS-III. The two factors were general memory and working memory, with no separate IMM and DEL or AUD and VIS factors evident. The limited clinical usefulness of comparing AUD and VIS WMS-III scores in an attempt to predict TLE laterality at the individual level has already been described (Wilde et al., 2001) and such an analysis was beyond the scope of this article.

In conclusion, our findings provide additional evidence that combining the relevant IMM and DEL WMS-III subtest scores to form AUD and VIS indices can be considered appropriate for TLE patients. Tulsky et al. (2003) provide tables that allow computation of these composite indices ("i.e., not subdivided into immediate or delayed elements" [p. 155]) from subtest SS.

The possibility should be investigated that, even though rare, the finding of a significant IMM-DEL discrepancy on the WMS-III could have prognostic significance for TLE patients undergoing anterior temporal lobectomy. It also is possible that significant IMM-DEL index discrepancies might be more common in TLE patients with space occupying temporal lobe lesions. In addition, consideration of the separate IMM and DEL WMS-III scores might prove to be more useful in other clinical populations (Delis et al., 2003; Tulsky et al., 2003).

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Table 1

TLE and Control Group Characteristics.

	Group	
	TLE	Control
<i>N</i>	88	49
Age	37 (11)	34 (13)
Education	13.2 (2.3)	13.6 (2.0)
WAIS-III full scale IQ	94 (15)	104 (15)*
WMS-III General Memory	94 (15)	107 (11)**
%Female	65	53
L hippocampus volume <i>z</i> score	-.64 (1.5) ^a	-.05 (1.0) ^{b*}
R hippocampus volume <i>z</i> score	-.88 (1.7) ^a	-.12 (1.1) ^{b**}
L temporal lobe white matter <i>z</i> score	-.79 (.96) ^c	.07 (.93) ^{d**}
Age of epilepsy onset (yrs)	15 (11)	
Epilepsy duration (yrs)	22 (12)	
Number anti-epilepsy drugs (median)	2	
Seizure frequency in past year (median)	monthly	

^a Note. *n* = 69^b *n* = 38^c = 71^d = 39.* *p* < .05.** *p* < .01.

Table 2

WMS-III Indexes for the TLE Group.

Auditory Memory	
Immediate	98.5(15.2)
Delayed	97.7(14.8)
Visual Memory	
Immediate	89.0(13.2)
Delayed	90.3(15.0)

Table 3
WMS-III Subtest Standard Scores for the TLE Group.

Variable	Auditory memory		Visual memory	
	Logical memory	Verbal paired associates	Faces	Family pictures
Immediate	9.8 (2.9)	9.7 (3.2)	8.4 (2.4)	8.1 (3.0)
Delayed	9.5 (2.9)	9.8 (2.9)	8.7 (2.6)	8.2 (3.1)
Percent retention	9.9 (3.1)	10.2 (2.9)	10.2 (3.0)	9.8 (3.3)

Table 4
Correlations between MRL Volumes and WMS-III Scores in the TLE Group.

	L-hipp	R-hipp	L-TL WM
<i>Indexes</i>			
Auditory			
Immediate	.30	.14	.12
Delayed	.38	.17	.16
Visual			
Immediate	.28	.25	.27
Delayed	.35	.30	.27
<i>Subtests</i>			
Immediate SS			
Logical Memory	.14	.11	.18
Verbal Paired Associates	.39	.12	.01
Faces	.11	.20	.15
Family Pictures	.31	.18	.26
Delayed SS			
Logical Memory	.27	.16	.23
Verbal Paired Associates	.39	.12	.05
Faces	.27	.30	.18
Family Pictures	.32	.18	.28
%retention SS			
Logical Memory	.23	.00	.15
Verbal Paired Associates	.37	.14	.17
Faces	.16	.16	-.09
Family Pictures	.07	.13	-.03

Note. Bold print = $p < .05$; L-hipp = left hippocampal volume; R-hipp = right hippocampal volume; L-TL WM = left lateral temporal lobe white matter volume; SS = standard score.