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Linear width of the medial temporal lobe can discriminate Alzheimer's disease from normal aging: the Sunnybrook Dementia Study

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Abstract

To discriminate Alzheimer's disease (AD) from healthy controls, the thinnest medial temporal lobe (tMTL) width on 3D-MRI was measured according to a newly developed method at the inter-collicular sulcus (ICS) level with scans aligned to the long axis of the hippocampus in 22 mild, 27 moderate probable AD patients and 41 healthy controls. For comparison, MTL width replicating the technique of Jobst et al. (jMTL) as well as hippocampal and parahippocampal volumes, were also measured. Using logistic regression taking into account age, sex, and education, tMTL width classified mild AD from controls with a sensitivity of 86%, specificity of 95% and accuracy of 92%. Similar values were obtained for moderate or total AD group versus controls. By comparison, jMTL width was only useful in distinguishing moderate AD from controls, and volumetric measures were equally sensitive in classifying mild and moderate AD in our sample. This quick, reliable, and standardized measurement of tMTL can be helpful in differentiating even mild AD from controls with reasonable accuracy.

Keywords: Magnetic resonance imaging; Medial temporal lobe; Aging; Alzheimer's disease

1. Introduction

There is a strong need to find user-friendly and reliable in vivo brain measures to assist in the diagnosis and monitoring of dementia patients in the daily clinical setting. It has been suggested that linear measures of medial temporal lobe width on axial computed tomography (CT) can be helpful in diagnosis and for monitoring the progression of Alzheimer's disease (AD) [21,22,34]. These measures reflect parenchymal volume loss from the hippocampus and the parahippocampal gyrus [21,34], which are structures critically affected in AD [2,4]. However, previous studies have shown wide variation in sensitivity ranging from a low of 48% to a high of 92% for distinguishing AD from healthy controls [13,21,34]. This has detracted from using these measures as a neuroimaging marker of AD. Insufficient reproducibility of linear measurements of the medial temporal lobe width has further deterred wider application of this approach.

The angle of scan orientation has been raised as an important issue for reproducibility when using simple linear measures for the medial temporal structures [8–10,21]. The CT technique employs a fixed scan angle of 20° caudal to the orbitomeatal line [21,34], assuming it to be parallel to the long axis of the hippocampus. However, in studies of healthy subjects using magnetic resonance imaging (MRI), marked individual variability of the long axis of the hippocampus has been found [3,15]. Another critical issue is how to determine the vertical level on which to measure the medial temporal lobe width [15,21]. In a MRI study, we demonstrated that the plane parallel to the long axis of the hippocampus is best to achieve a longitudinal view of the medial temporal lobe, and that medial temporal lobe width measured on the slice level of the inter-collicular sulcus (ICS) is highly reproducible [15]. These decision rules allow linear measurement of the medial temporal lobe to be more comparable both within and between subjects.

The objective of this study was to test the ability of this method for measuring medial temporal lobe width on MRI to discriminate AD patients of both mild and moderate severity

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from normal aging, and to compare the classification ability of the linear measurement to volume measurements in the same sample.

2. Methods

2.1. Participants

Forty-nine probable AD patients (age, mean±S.D., 70±8 years; 26 men and 23 women; education, mean±S.D., 14±3 years) were included. All patients were attending the Cognitive Neurology Clinic at a university teaching hospital and had agreed to participate in an ongoing prospective study of aging and dementia. AD participants met criteria for probable AD as defined by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [31]. Using Mini-mental State Examination (MMSE) [11], patients were divided into mild AD (MMSE $>$ 20) and moderate AD (MMSE $>$ 10 and $\leq$20). Four AD participants with MMSE scores less than 10 due to significant language impairment, but who still retained relative independence in self-care activities of daily living, were also included in the moderate group. Forty-one healthy community volunteers free from history of neurological or psychiatric diseases were included as controls. They were matched as a group on age, sex, and years of education (age, 71 ± 6 years; 20 men and 21 women; education, 15 ± 2 years), and performed within normal limits on a detailed neuropsychological battery [27].

2.2. Imaging acquisition

Imaging was performed on a 1.5 T MR unit (Signa, General Electric Medical Systems, Milwaukee, WI). All MR scans were obtained using a standardized protocol with a T1-weighted 3D volumetric spoiled gradient echo sequence, TR/TE/NEX-5/35/1, 35° flip angle, matrix 256 × 192, and 1.2 mm slice thickness, generating 124 axial slices in an imaging time of 10.5 min.

2.3. Image processing

Any rotations of the subject's head were corrected in the sagittal and coronal planes by manually adjusting roll and yaw, respectively. As a standard, scans were reformatted into a plane parallel to a line passing through the anterior and posterior commissures (AC-PC) [39]. Axial slices were generated for each individual at the level of the ICS at an angle parallel to a line drawn through the inferior border of the long axis of the hippocampus (Fig. 1) [15]. The Jobst et al. technique [21] was also carried out with axial slices reconstructed along the plane 20° caudal to orbitomeatal line. Realignment and reformatting of the MR images were conducted using ANALYZE AVW^{TM} Software (Biomedical Imaging Resource, Mayo Foundation, Rochester, MN) on a Sun workstation (Sun Microsystems, Mountain View, CA).

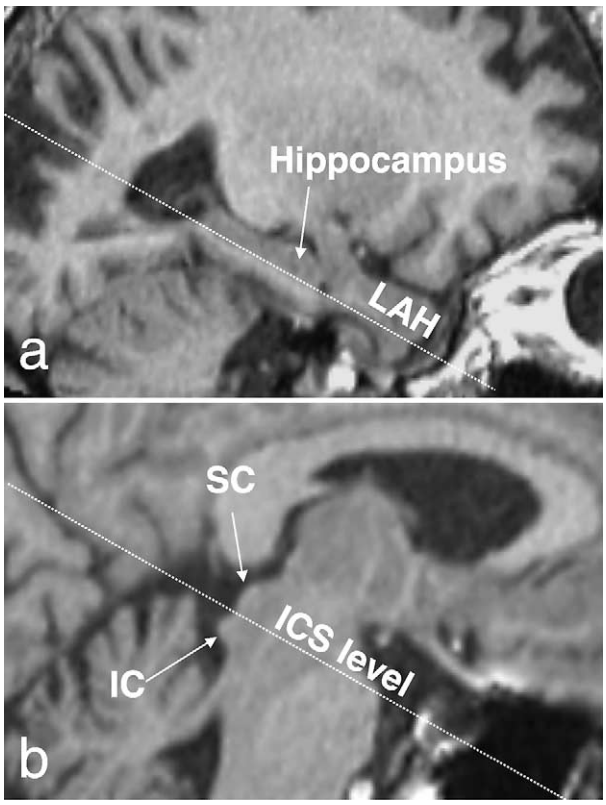

Fig. 1. MR sagittal views demonstrating the long axis of the hippocampus (LAH) (dotted line in (a)) draw through the inferior border of the hippocampus and the level of the ICS (the dotted line in (b)) between the superior colliculus (SC) and inferior colliculus (IC).

2.4. Medial temporal lobe measures

Using our newly developed protocol [15], the thinnest medial temporal lobe (tMTL) width of either hemisphere was measured between the anterior–posterior boundaries of the midbrain at the level of the ICS with scan orientation along the long axis of the hippocampus. Shrout and Fleiss model 3 intraclass correlation coefficients [37] for intra- and inter-rater agreement for this measure were 0.95, based on two blinded raters independently measuring the left and right tMTL width in five AD and five controls (i.e. a total of 20 measurements).

For comparison to previous studies, the tMTL width on an axial slice at approximately mid-height of the medial temporal lobe angled 20° caudal to the orbitomeatal line was measured to replicate the method used by Jobst et al. (jMTL width) [21]. The medial temporal lobe volumes were also generated for comparison according to a published protocol [5]. Hippocampal volumes were obtained by tracing the body of the hippocampus in the sagittal plane and parahippocampal volumes were derived by tracing the parahip-

pocampal cortex in the coronal plane at 2.5 mm intervals [5] (see also www.neurology.org). The volumetric measures were normalized by the individual head-size (total intracranial volume), which is obtained according to a standardized in-house parenchyma and CSF segmentation protocol [35].

All linear measurements were performed by a single trained investigator (F.G.), blinded to clinical information, using the ANALYZE region of interest module. The volumes of the hippocampus and parahippocampal cortex were likewise obtained by a single investigator (D.C.) blinded to clinical status.

2.5. Statistical analysis

We provided descriptive data (means, standard deviations, and ranges) for comparative purposes on all groups (AD versus NC) and subgroups (mild versus moderate AD) for the medial temporal lobe measures, covariates, and MMSE scores. ANOVA was used to examine group differences on age, years of education and MMSE scores. Dunnett's post-hoc comparisons were completed, when appropriate, to investigate AD subgroup differences compared to NC. Independent Chi-square analysis was used to see if the frequencies of men and women were different in the AD groups compared to NC. To illustrate the strength of difference in medial temporal lobe measures between AD and controls, effect sizes were calculated by dividing the difference of the means by the pooled variance [7].

Logistic regression was used to test the ability of the medial temporal lobe measurements to classify AD and controls (model criterion was set at $\alpha = 0.05$). We included the covariates age, sex, and education in our logistic regression models to account for their influence. Specifically, we used tMTL width to classify people as either AD or NC. For comparison purposes, we also performed the same logistic regression model with either jMTL width, hippocampal or parahippocampal volumes along with the same covariates. We did not combine MTL measurements in one model since the purpose of the regression was to compare the ability of individual MTL measures in the classification of AD and NC. Similar individual logistic regression models were calculated for classifying mild AD versus NC and moderate AD versus NC to see how effective the models were in identifying the AD subpopulations.

To be able to compare the effectiveness of our models, we calculated positive likelihood ratios (LR+), defined as (sensitivity/(1 − specificity)) [41]. Positive likelihood ratios reflect the increased likelihood of a positive test (i.e. being below the normal cutoff and classified as AD) being found in a person with clinically diagnosed probable AD as opposed to being considered normal. We also calculated 95% confidence intervals for the positive likelihood ratios. Models whose intervals overlapped were said to be similarly effective.

We also used the positive likelihood ratios calculated above to estimate the increased risk associated with a medial temporal lobe measurement below a specified cutoff threshold (for a given age, sex, and years of education) as compared to published pre-test odds. Post-test probability is the product of pre-test odds for AD (taken as age−appropriate prevalence of AD) × positive likelihood ratio [36,41].

3. Results

3.1. Descriptive data

Demographic data, MMSE scores, and MTL measurements are summarized in Table 1. The ratio of men-to-women was similar for the NC group compared to AD groups ($\chi^2_{(2)} = 0.8$, $P = 0.69$). Similarly, there were no differences in mean age between NC and AD groups on ANOVA ($F_{(2,87)} = 0.1$, $P = 0.9$). ANOVA revealed significant differences across groups on years of education and MMSE scores ($F_{(2,87)} = 4.2$, $P < 0.05$ for YOE; $F_{(2,87)} = 136.3$, $P < 0.0005$ for MMSE). Post-hoc comparisons revealed that only the 'moderate' group (but not the mild group) of AD patients differed from NC for YOE (Dunnett, $P < 0.05$). As expected, both AD subgroups differed from NC on MMSE (Dunnett, $P < 0.0005$). Fig. 2 demonstrates the tMTL width measure in a 76-year-old woman with mild AD, a 76-year-old woman with moderate AD and a sex-matched healthy control. Relative strengths of the differences of the medial temporal lobe measures between AD and controls were examined and revealed that tMTL width was smaller on average than the other atrophy measures and had larger effect sizes (2.4–2.8) in both AD subgroups (Table 1).

3.2. Logistic regression

Logistic regression was utilized in three separate models to test the ability of the tMTL width to distinguish mild AD, moderate AD or all AD patients from healthy controls. We also wanted to account for the possible effects of age, sex, and education, and thus they were also included in the logistic regression models. The model with age, sex, education and the tMTL width was able to classify AD versus healthy controls with a sensitivity of 86%, specificity of 93% and overall accuracy of 89% (model $\chi^2_{(4)} = 1.7$, $P < 0.0005$). The equation from our logistic regression model from our analysis can be used to predict the probability of being classified as AD using the following formula: probability (AD) = $1/(1+e^{-z})$, where $z = 16.20 - \text{age} \times 0.86 - \text{sex} \times 0.89 - \text{years of education} \times 0.118 - \text{tMTL} \times 0.729$.

For comparison, we tested the ability of jMTL width, hippocampal, and parahippocampal volumes to classify AD and healthy controls. Specifically, we investigated the utility of using these measures in differentiating AD from healthy controls by calculating the sensitivity, specificity, and positive likelihood ratios. As can be seen in Table 2, the tMTL

Table 1
Demographic data, MMSE scores, and medial temporal region measurements

Characteristics	Normal control (NC)	Patients with AD		
		Total AD	Mild AD[a]	Moderate AD[b]
Number of subjects	41	49	22	27
Men/women	20/21	26/23	13/9	13/14
Age, mean ± S.D., in years (range)	71.0 ± 6.3 (56–82)	70.2 ± 8.1 (51–86)	70.4 ± 8.8 (54–86)	70.1 ± 7.6 (51–80)
Education, mean ± S.D., in years (range)	14.7 ± 2.5 (10–19)	13.7 ± 3.5 (6–21)	14.9 ± 3.0 (10–20)	12.8 ± 3.6[c] (6–21)
MMSE score, mean ± S.D. (range)	28.4 ± 1.5[c] (24–30)	18.1 ± 6.6[c] (1–29)	23.3 ± 2.1[c] (21–29)	13.8 ± 6.0[c] (1–20)
tMTL width (range) [effect size]	13.2 ± 1.8 (9.4–17.2)	6.2 ± 3.8 (0.9–14.8) [2.4]	6.8 ± 4.8 (1.7–14.8) [2.4]	5.8 ± 3.8 (0.9–14.8) [2.8]
jMTL width (range) [effect size]	10.3 ± 2.5 (6.2–14.6)	8.7 ± 3.2 (1.6–16.3) [0.6]	9.9 ± 3.5 (1.6–16.3) [0.1]	7.7 ± 2.7 (2.6–13.7) [1.0]
Hippocampal volume (range) [effect size]	2947 ± 494 (1963–3965)	2032 ± 551 (356–3316) [1.7]	2154 ± 512 (1100–3316) [1.6]	1933 ± 571 (356–2923) [1.9]
Parahippocampal volume (range) [effect size]	1649 ± 274 (1095–2125)	1274 ± 282 (688–1983) [1.4]	1318 ± 320 (836–1948) [1.1]	1237 ± 247 (688–1983) [1.6]

[a] Mild AD refers to MMSE > 20.

[b] Moderate AD refers to MMSE ≤ 20 and >10.

[c] Groups were examined with ANOVA for differences in age, years of education (YOE) and MMSE scores. YOE and, not surprisingly, MMSE scores were different across the groups ($F_{(2,87)} = 4.2$, $P < 0.05$ for YOE; $F_{(2,87)} = 136.3$, $P < 0.0005$ for MMSE). Post-hoc comparisons revealed that only the 'moderate' group (but not the mild group) of AD patients differed from controls for YOE (Dunnett, $P < 0.05$). As expected, both AD subgroups differed from NC on MMSE (Dunnett, $P < 0.0005$). Results for MTL regions are presented as a mean ± S.D. in mm for the width and mm^3 for the volume. Values in square brackets refer to the effect sizes of the difference between that measurement compared to controls divided by the pooled variance [7]. All measurements were the smallest of either side of left or right. tMTL width: the thinnest medial temporal lobe width using our technique. jMTL width: the thinnest medial temporal lobe width replicating the method by the Jobst et al. [21].

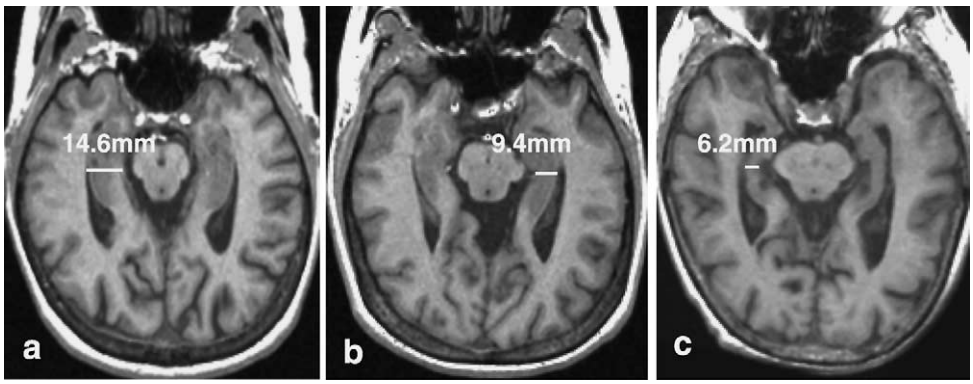

Fig. 2. Comparison of the tMTL width between AD and control at the same level of the ICS with image orientation along the long axis of the hippocampus. MR images show tMTL width in a healthy control (a), a mild AD patient (b) and a moderate AD patient (c).

width performed as well as the volumetric measures and better than jMTL width in classifying our sample.

The tMTL width was similarly good at classifying mild AD versus healthy controls (model $\chi^2_{(4)} = 53.4$, $P < 0.0005$) and moderate AD versus healthy controls (model $\chi^2_{(4)} = 62.6$, $P < 0.0005$) (Table 2 and Fig. 3). By comparison, jMTL width was less successful at classifying moderate AD versus healthy controls (model $\chi^2_{(4)} = 23.1$, $P < 0.0005$), and could not significantly classify mild AD versus healthy controls ($\chi^2_{(4)} = 1.7$, $P > 0.05$). Both volumetric measures were able to discriminate mild and moderate AD from healthy controls, although their models had slightly lower sensitivities (59–82%) and specificities (85–90%). For comparison of the classification abilities of the models, we also calculated 95% confidence intervals. As can be seen from Table 2, the 95% confidence intervals for tMTL width overlapped with those for either volumetric models in all groups and with jMTL width in the model classifying moderate AD versus NC. For example, in classifying AD versus NC the LR+ was 11.7 (95% CI of 3.9–35.0). Since the LR+ for the model using the hippocampus was 4.3 (95% CI of 2.3–8.1) and 4.3 falls within 3.9–35, we can conclude that there is no significant difference between the effectiveness of the two models.

3.3. Post-test probability

To express the odds that a person would or would not be classified as AD based on the tMTL width measurement,

Table 2
Predictive values of the different medial temporal lobe measurements

Measurements	Sensitivity	Specificity	Accuracy	Positive likelihood ratio (LR+)	95% confidence interval
AD vs. NC (n = 90)					
tMTL width	85.7	92.7	88.9	11.7	(3.9–35.0)
jMTL width	71.4	58.5	65.6	1.7	(1.2–2.6)
Hippocampal volume	83.7	80.5	82.2	4.3	(2.3–8.1)
Parahippocampal volume	83.7	75.6	80.0	3.4	(2.0–6.0)
Mild AD vs. NC (n = 63)					
tMTL width	86.4	95.1	92.1	17.7	(4.5–69.1)
jMTL width	9.1	100	68.2	>3.7[a]	(0.4–38.8)
Hippocampal volume	72.7	87.8	82.5	6.0	(2.5–14.1)
Parahippocampal volume	59.1	87.8	77.8	4.8	(2.0–11.8)
Moderate AD vs. NC (n = 68)					
tMTL width	88.9	97.6	94.1	36.4	(5.2–253.7)
jMTL width	63.0	85.4	76.5	4.3	(1.9–9.5)
Hippocampal volume	81.5	90.2	86.8	8.4	(3.2–21.6)
Parahippocampal volume	74.1	85.4	80.9	5.1	(2.3–11.0)

Sensitivities, specificities, and accuracies were obtained from the logistic regression model with the specific MTL measurement along with age, sex, and years of education. Sensitivity: percent of people with probable AD classified as AD. Specificity: percent of people without probable AD classified as not having AD. Accuracy: percent of subjects properly classified. Positive likelihood ratio (LR+): increased likelihood of a positive test to be found in a person deemed clinically to have AD and is calculated as (sensitivity/(1 − specificity)). tMTL width: the medial temporal lobe width using our technique. jMTL width: the medial temporal lobe width replicating the method by the Jobst et al. [21].

[a] The distribution of patients according to jMTL resulted in no normal control being misclassified, and thus LR+ can only be estimated at infinity. However, using a misclassification of one NC as being identified as AD led to a LR+ of 3.7 for comparison purposes.

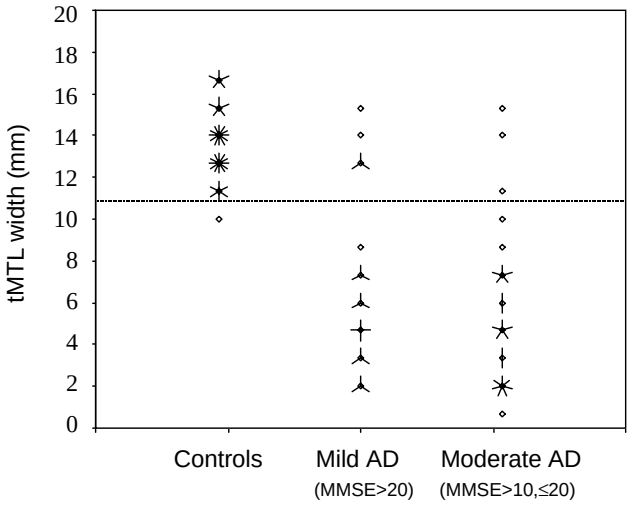

Fig. 3. Scatterplot of the tMTL width: healthy controls and patients with mild and moderate AD. Dotted line is at cutoff value of tMTL width = 11 mm. Each diamond represents one subject and the lines indicate additional subjects.

positive likelihood ratios and post-test probability of having AD for age groups were calculated (Table 3). As described earlier, a logistic regression model with only tMTL width with covariates was used to predict group membership (AD versus NC) in order to be able to calculate the positive likelihood ratio. Using the equation detailed above to predict group membership, sensitivities, and specificities, and thus also positive likelihood ratios, were calculated for the specific age ranges of interest (Table 3). Using these ratios, the increased risk of AD was estimated for a person of a certain age, sex, and years of education, and with a tMTL width measurement below a specified threshold (the cutoff threshold was estimated from a scatterplot of tMTL width versus diagnosis to be 11 mm (see Fig. 3)). To calculate the post-test probability (i.e. the potential impact of the tMTL width on the likelihood ratio for AD), we used a prevalence of 1.0% for AD in the age group 65–74 and 6.9% for ages 75–84 based on results from Canadian Study of Health and Aging [6]. The probability of AD increased ninefold for those aged 65–84 and broken down by age subgroups, 18-fold for those aged 65–74, and sevenfold for ages 75–84.

4. Discussion

This study demonstrated that the tMTL width determined by our recently developed 3D T1-weighted MRI protocol [15] had good diagnostic accuracy in classifying probable AD patients compared to age-, sex- and education-matched healthy controls. tMTL width was useful in distinguishing both mild and moderate AD from healthy aging.

Using an estimated cutoff value of the tMTL width of 11 mm (assuming a 70-year-old man with 14 years of education), we were able to detect 86% of probable AD patients with a specificity of 93% in our sample. The incremental probability for AD was significant using the tMTL measurement, compared to the pre-test probability of 54% (49 out of 90) for a patient being diagnosed with AD by chance in our sample. Although the predictive values were in agreement with previous CT studies [21,34] in which 84–85% of AD subjects were detected with a cutoff value of medial temporal lobe width at 11.5 mm and a specificity of 95%, an advantage of our technique was its sensitivity in discriminating not only moderate AD from healthy controls but also mild AD from healthy controls.

In our logistic regression, we were able to classify mild AD just as effectively as moderate AD in relation to healthy controls. By comparison, using jMTL width (the measure attempting to replicate the previous Jobst CT method [21]), we were only able to accurately distinguish between moderate AD and controls. This difference was also highlighted by the fact that tMTL width was decreased by 54% (of healthy controls) in AD patients, whereas jMTL width was only 16% smaller. However, the decrease in tMTL width was similar to the 44% reduction found by previous CT method of measuring medial temporal lobe width reported by Jobst et al. [21]. Reasons for this discrepancy include: (1) variability in the choice of slice level involved in the Jobst method, (2) variability in the angulation of the hippocampus, which meant it was exposed in an oblique as opposed to longitudinal view in some cases, and (3) the difference in resolution between CT and MRI, which makes the boundaries less clear. Also, in the initial Jobst et al. study [21], more severe cases of AD were investigated (average MMSE reported was (9), whereas our study included mild as well as moderate AD. The ability to differentiate mild AD from healthy controls would certainly be more useful clinically. The effect

Table 3
Increased risk of being classified as AD

	Age group	*n* (AD, NC)	Pre-test probability[a] (%)	LR+	Post-test probability (%)	Increased risk (post-test/pre-test)
Combined age range	65–84	71 (36, 35)	5.0	15.33	45	9×
Age range subgroups	65–74	43 (21, 22)	1.0	22.50	18	18×
	75–84	28 (15, 13)	6.9	11.62	46	7×

[a] Based on Canadian Study of Health and Aging [6]. LR+ refers to the positive likelihood ratio, calculated as (sensitivity/(1 − specificity)) and the values were obtained from a logistic regression model with tMTL along with age, sex, and years of education to predict AD vs. NC. Using this model, sensitivities and specificities were calculated for the specific age groups above.

size of the tMTL measure was 2.4 for mild and 2.8 for moderate disease, which is near the value of 3 required to more completely distinguish disease from controls [7].

Using the equation differentiating AD from healthy controls from our logistic regression model, we were able to estimate the probabilities of being classified as AD for a given age, sex, education, and tMTL width. For example, a 70-year-old woman with 12 years of education and a tMTL width of 8 mm would have an 89% likelihood of being classified as AD. We were also able to show the increased probabilities of AD for those with tMTL <11 mm using age-specific prevalence data from the Canadian Study of Health and Aging [6]. An important caveat, however, is that the likelihood ratios and diagnostic models we used were based on a convenience clinic memory sample and on clinical, not pathological diagnosis. Further, the healthy controls were selected as a group to match our AD subjects. Thus, the values obtained are not necessarily generalizable of the dementia population in the community. Further, the equation is only applicable to those aged 51–86 years, with an education level between 6 and 21 years and with a tMTL width of between 0.9 and 17.2 mm, since the equation is only based on our specific dataset. Replication in a larger, more representative sample would be needed before these equations could be applied clinically. In addition, the ability of this measure to differentiate between other disease states remains to be tested. In our study, there appeared to be a relationship between disease severity and the tMTL width. We are investigating further in a group with mild cognitive impairment, whether it has any prognostic utility, as has been found in some volumetric MTL studies [19,25].

Eleven of 49 AD patients in this series died and six of them underwent autopsy. Four patients were reported to have AD and two met criteria for both AD and Dementia with Lewy's Bodies (DLB). tMTL width was below the cutoff value in all four confirmed AD patients, indicating good association with histopathology. The other two were young patients (age 56 and 60) with the combined AD and DLB and their tMTL widths were above the cutoff value (14.1 and 14.5 mm) at the time of measurement (5 years prior to death for one patient and 3 years prior to death for the other). Their MMSEs were 22. The combined pathology may have given rise to dementia at an earlier stage of hippocampal atrophy that would have been the case with AD pathology alone. Both developed Parkinsonism in later stage and one had hallucinations in his last year. Further autopsy cases and comparative studies in other dementias will be needed to evaluate the role of tMTL width in differential diagnosis of the common dementias, bearing in mind that mixed etiologies have been reported in a third of memory clinic autopsy cases [16]. It is known that medial temporal lobe atrophy is not specific for AD [14,33,40]. Perhaps tMTL width combined with other brain measures or the pattern of the medial temporal lobe atrophy may help to differentiate dementias of different etiologies, a possibility we are currently investigating in our neuroimaging unit.

We compared the ability of tMTL width to volumetric methods with respect to distinguishing mild and moderate AD from elderly controls. Volumetric techniques have been widely used for measuring medial temporal lobe atrophy in aging and dementia [18,20,23–27,32]. Hippocampal volume on MRI has been shown to have sensitivity and specificity in the range of 85–90% in differentiating AD from controls [17,28,32,38], even for very mild AD [18]. An entorhinal cortex volume measure yielded a sensitivity of 80% and specificity of 94% in another series [23,24]. In our study, tMTL width and hippocampal or parahippocampal volumes were equally successful at classifying mild and moderate AD from healthy controls. Thus, the classification ability of tMTL width is comparable with currently accepted volumetric methods but tMTL width required much less time and effort than the volumetric measurements.

The clinical diagnostic accuracy using NINCDS-ADRDA in medical research centers was 85–90% [1,12,31]. However, the clinical experience of the neurobehavioral specialists, the familiarity that they have with the diagnostic criteria and the amount of clinical information provided to them can affect the validity of the clinical diagnostic accuracy [30]. Furthermore, these accuracies are based on research cohorts that are not necessarily generalizable to patients seen in the general medical community. Using the current clinical diagnostic criteria in a large community-based incident dementia case series, the clinical diagnostic accuracy for AD was 75% [29]. The tMTL width is a simple objective neuroimaging marker, and can quickly provide information on the critical medial temporal region. It could assist in diagnostic accuracy of AD for clinicians in medical centers or community-based clinics.

In summary, we found that our measurement of the tMTL width on axial MRI scans had good diagnostic accuracy, especially in distinguishing mild AD from controls. This simple, reliable in vivo measurement could have clinical utility in the diagnosis of AD. If validated in a larger, independent sample and in individuals with different forms of dementia, the technique could provide a useful metric in clinical practice for the health of the medial temporal lobe.

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