Laplace Beltrami Based Formulation of Corpus Callosum to Ventricle Ratio for the Analysis of Alzheimer’s Condition in T1-Weighted MR Images

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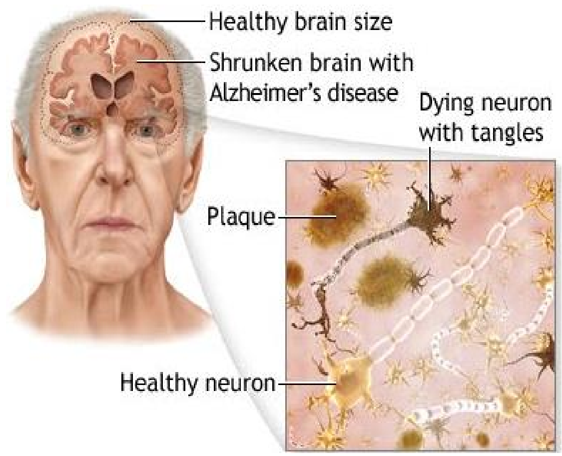
Introduction: Alzheimer's Disease

- Alzheimer's Disease (AD) is characterized by the occurrence of neurofibrillary tangles and amyloid plaques
- It affects 10 % of the people above age 65 and 50% of the people over the age 85



Stages

MCI
- Memory Loss, Language Problems
- Difficulties in thinking

Moderate AD
- Behavioral ,personality changes
- Misinterpretation of spatial relationships

Severe AD
- Gait inconsistence
- Unable to perform daily activities

Neuropsychological Tests
- Mini-Mental State Examination
- Clinical Dementia Rating

Invasive Tests
- Cerebro spinal fluid biomarker
- Plasma Biomarkers
- Genetic Tests
- Brain Biopsy

Non-Invasive Tests
- Imaging techniques such as MRI, DTI, and PET
- Electroencephalogram

Clinical Significance and Challenges in the early diagnosis of Alzheimer's disease

T1-weighted MR images → Atrophy analysis → Precise extraction of brain regions → Classification of normal, MCI and AD subjects

Challenges

- Structural changes are subtle in brain sub-anatomic structures
- Structural alterations that take place at specific locations of brain regions are not adequately reflected in the volume measurements
- Need for the development of methods to measure regional atrophy

Clinical Significance

- Early diagnostics is necessary to identify and treat at risk individuals before irreversible neuronal loss occurs
- Lack of biomarkers for early stage of disease in the absence of clinical symptoms
- Quantify the changes in brain as disease progresses

Literature Review: Ventricle enlargement and Callosal atrophy

- The ventricles are cavities situated in the center of the brain and are filled with Cerebrospinal fluid
- Regional measures of ventricular enlargement and callosal atrophy are reported to be significant morphometric measurements in the AD diagnosis
- Enlargement of ventricles captures considerable variations between elderly normal and subjects with MCI, and AD subjects
- Rate of change in ventricle volume is also greatly correlated with the increase in senile plaques and neurofibrillary tangles
- Lateral ventricular volume enhances AD diagnosis compared to psychometric, media temporal lobe and whole brain MR measurements
- Corpus Callosum (CC) is located adjacent and superior to lateral ventricles
- Any change in the shape of the lateral ventricle directly results in the collasal arching and thinning

Literature Review: Ventricle enlargement and Callosal atrophy

- Callosal atrophy may result in functional disability due to reduced interhemispheric integration
- CC atrophy - death of gray matter cells and Wallerian degeneration of axons in the white matter structure
- There exists large overlap in the volume measurements of ventricle and CC for normal, MCI and AD subjects
- Recent research has focused on extracting more meaningful information from the shape of brain structures
- Morphometric changes of the brain structures are subtle but reliable and identifiable in the asymptomatic individuals nearly a decade before dementia
- Accurate segmentation of ventricle and CC is necessary to obtain quantitative measurements of various structures

Motivation

- ✓ Only way of diagnosing AD is by doing a post-mortem examination of brain
- ✓ Large overlap in the volume measurements of control, MCI and AD groups and their subtle morphometric changes are imperceptible
- ✓ Shape differences are feasible to quantify and can act as structural biomarker for the early diagnosis of AD
- ✓ Level Set can represent contours of complex topology and are able to handle topological changes
- ✓ Laplace Beltrami eigen values could provide information on the intrinsic geometry of objects

Aim

To analyse the morphological changes of ventricles and CC in Alzheimer MR images using reaction diffusion level set and Laplace Beltrami eigen values

Objectives

1. To segment ventricles and CC in normal, MCI and AD images
2. To extract LB eigen value features from the segmented regions and analyze
3. To derive CC to Ventricle Ratio (CVR) as morphometric index to quantify the shape changes

METHODOLOGY

Database

Database name	: Open Access Series of Imaging Studies (OASIS) (Subjects have right hand dominance and participated in the MRI studies at the Washington University Alzheimer Disease Research Center (ADRC))
No of Subjects	: T1- weighted MR (Normal=92, MCI=63, AD=29) images
Average Age	: Normal=67.90 ± 13.96 and AD=75.32 ± 8.04 (Young, middle-aged and old-age subjects)
Image Size	: 176 X 208
Slice Selected	: 90th slice
Image Resolution	: 1mm
Sequence	: Magnetization Prepared Rapid Gradient Echo (MPRAGE)
TR (ms)	: 9.7
TE (ms)	: 4.0
Flip angle	: 10^{o}

Segmentation and Feature Extraction

- The segmentation of the ventricle and CC in the T1-weighted MR images is attempted using reaction diffusion level set method
- Level sets are active contour models that have the capability of tracking complex deformations in the brain structures
- In this method, a closed contour has been formulated as a zero-level set of a high dimensional function which undergoes motion dynamically to extract objects in the images
- LB eigenvalue features are obtained from segmented ventricles and CC to quantify the structural variations due to AD
- For the given segmented binary image with foreground , its corresponding Laplace operator is given by

$$\Delta_{\Omega} f \square \sum_{i=1}^{d} \frac{\partial^2 f}{\partial x_i^2}, \forall X \in \Omega,$$

$X = [x_1, \ldots, x_d]$ - spatial coordinates

Segmentation and Feature Extraction

- The eigen values and the eigen functions of are given by the solutions of the Helmholtz equation and is given by

$$\Delta f + \lambda f = 0, \forall X \in \Omega, f(x) = 0, \forall X \in \partial\Omega$$

$\partial\Omega$ denotes boundary of the segmented sub-anatomic structure

$\lambda \in \square$ is a scalar

- The well-ordered collection of a positive eigenvalue series is given by

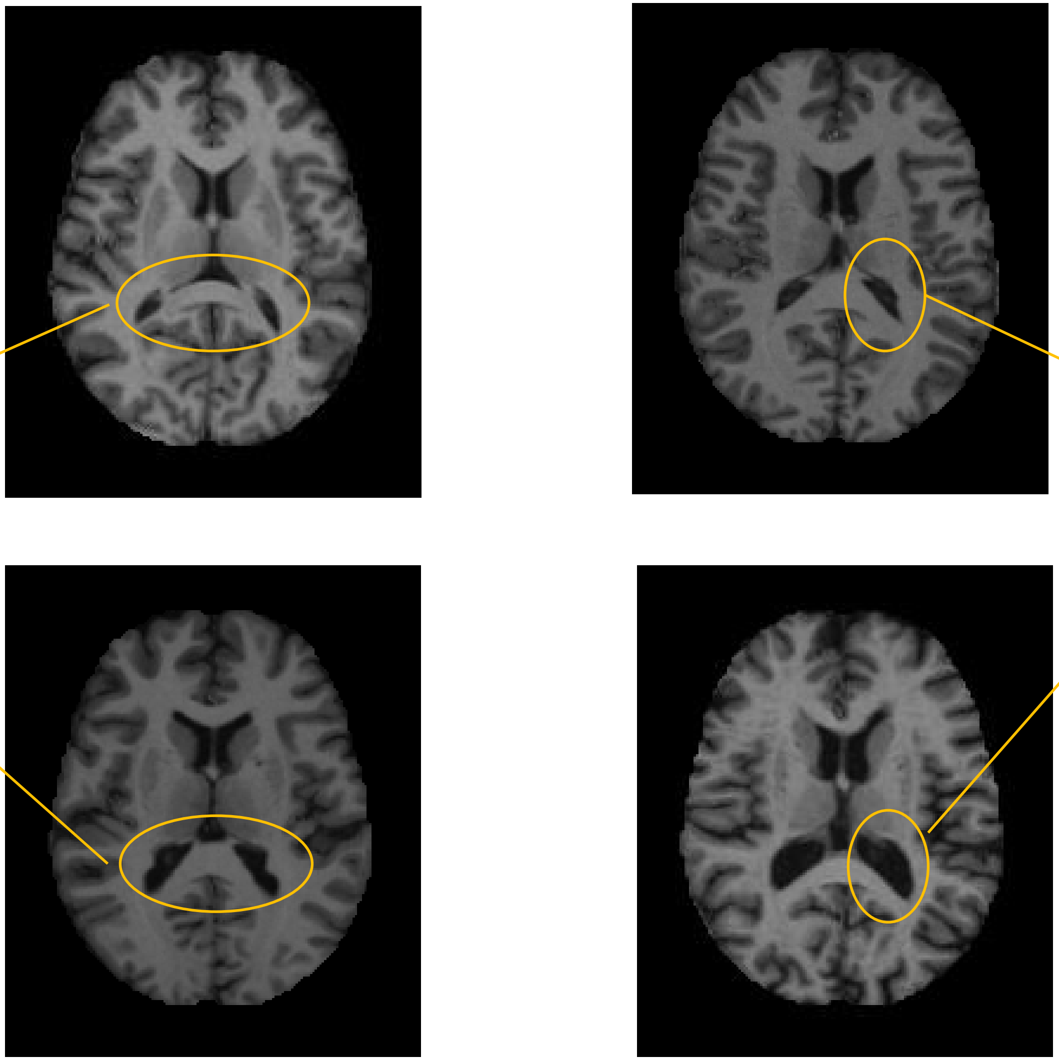
$$0 \leq \lambda_1 \leq \lambda_2 \leq \ldots \uparrow \infty,$$

- The above series represents the continuum of binary images ΔΩ.
- This set of eigenvalues comprise aspects of inherent geometry of segmented (binary) brain sub-anatomic structures
- The shape variations of the lateral ventricle and CC are extracted and analyzed using this LB eigenvalue spectrum

Results

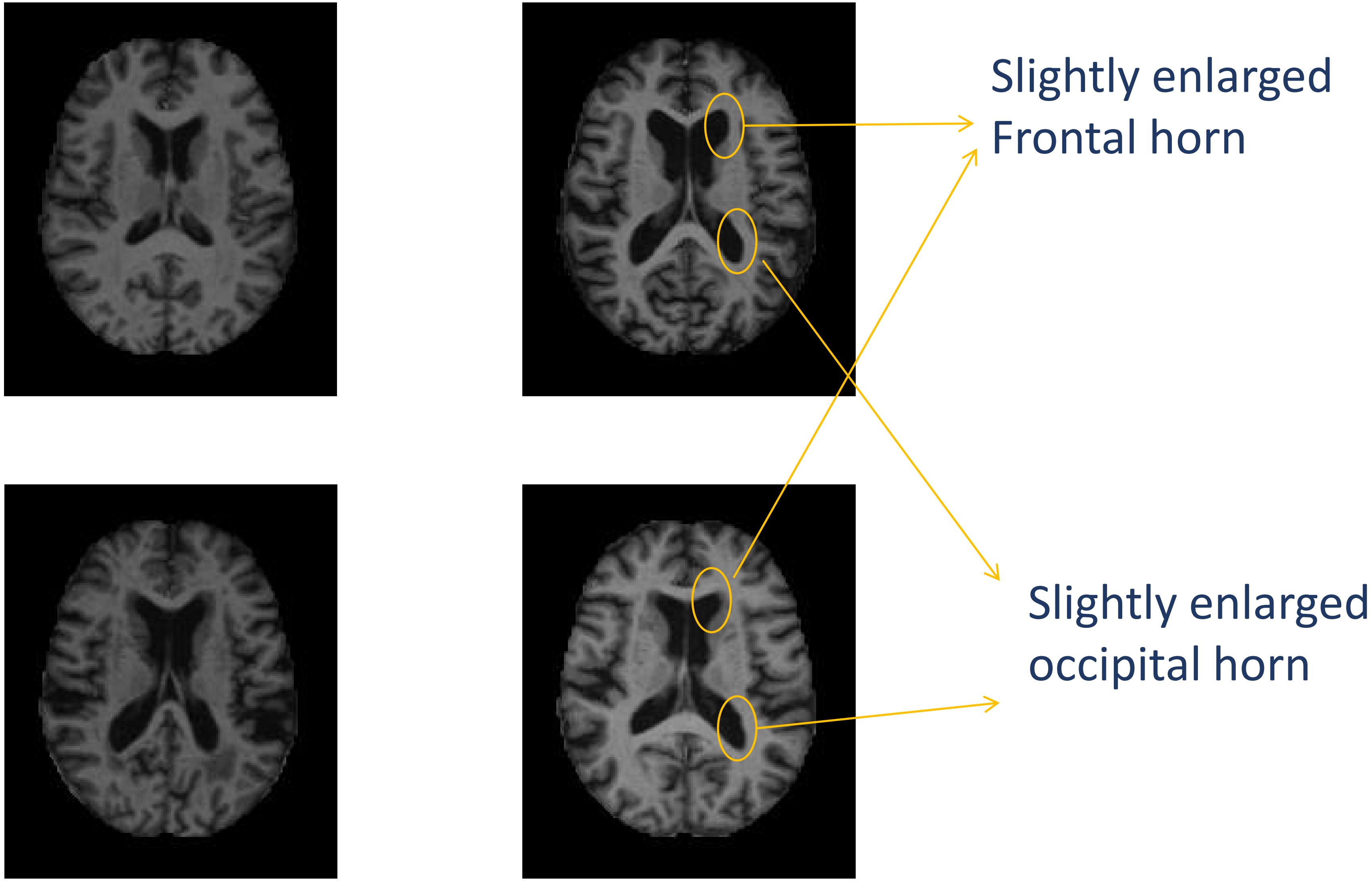
Representative set of typical T1-weighted MR images of normal subjects

Concave and
dissimilar in Shape

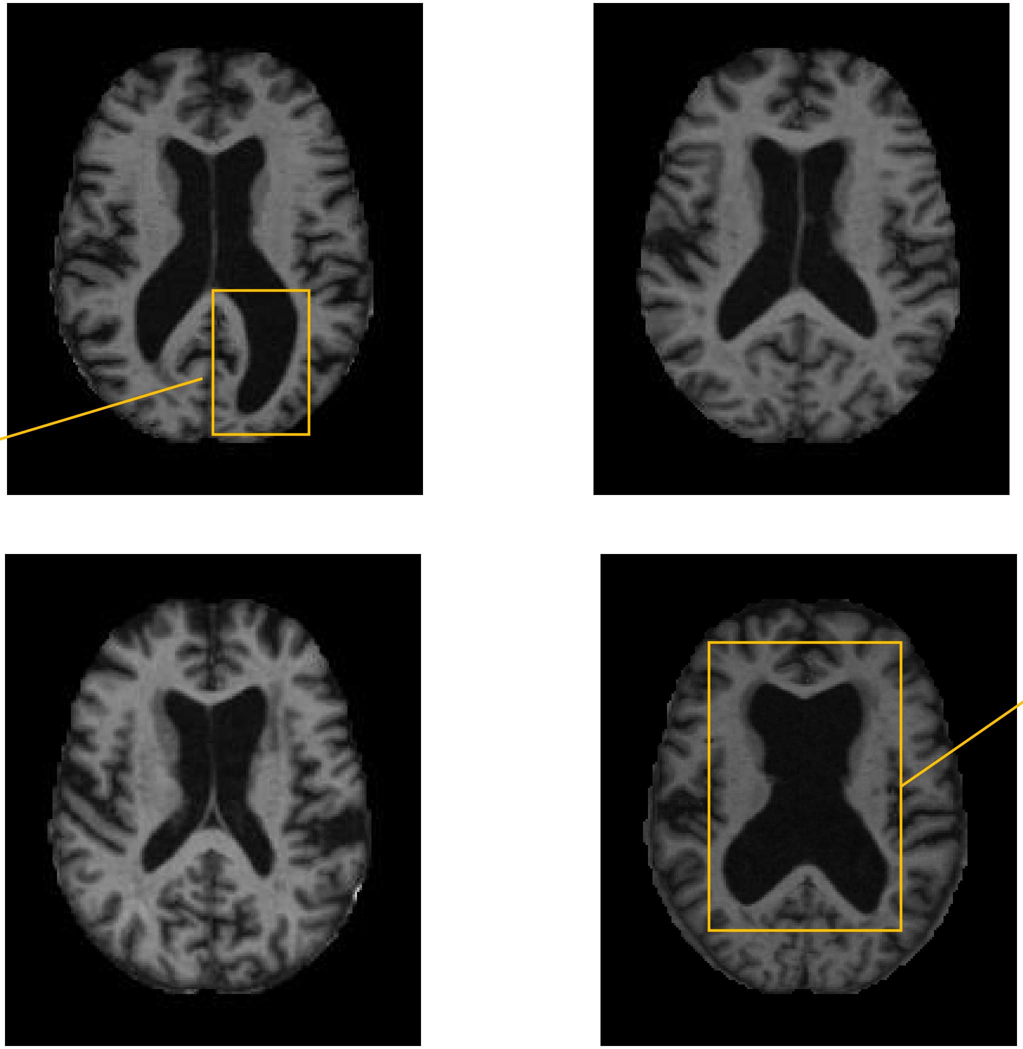


Varying shapes
of Occipital horns

Representative set of typical T1-weighted MR images of MCI subjects



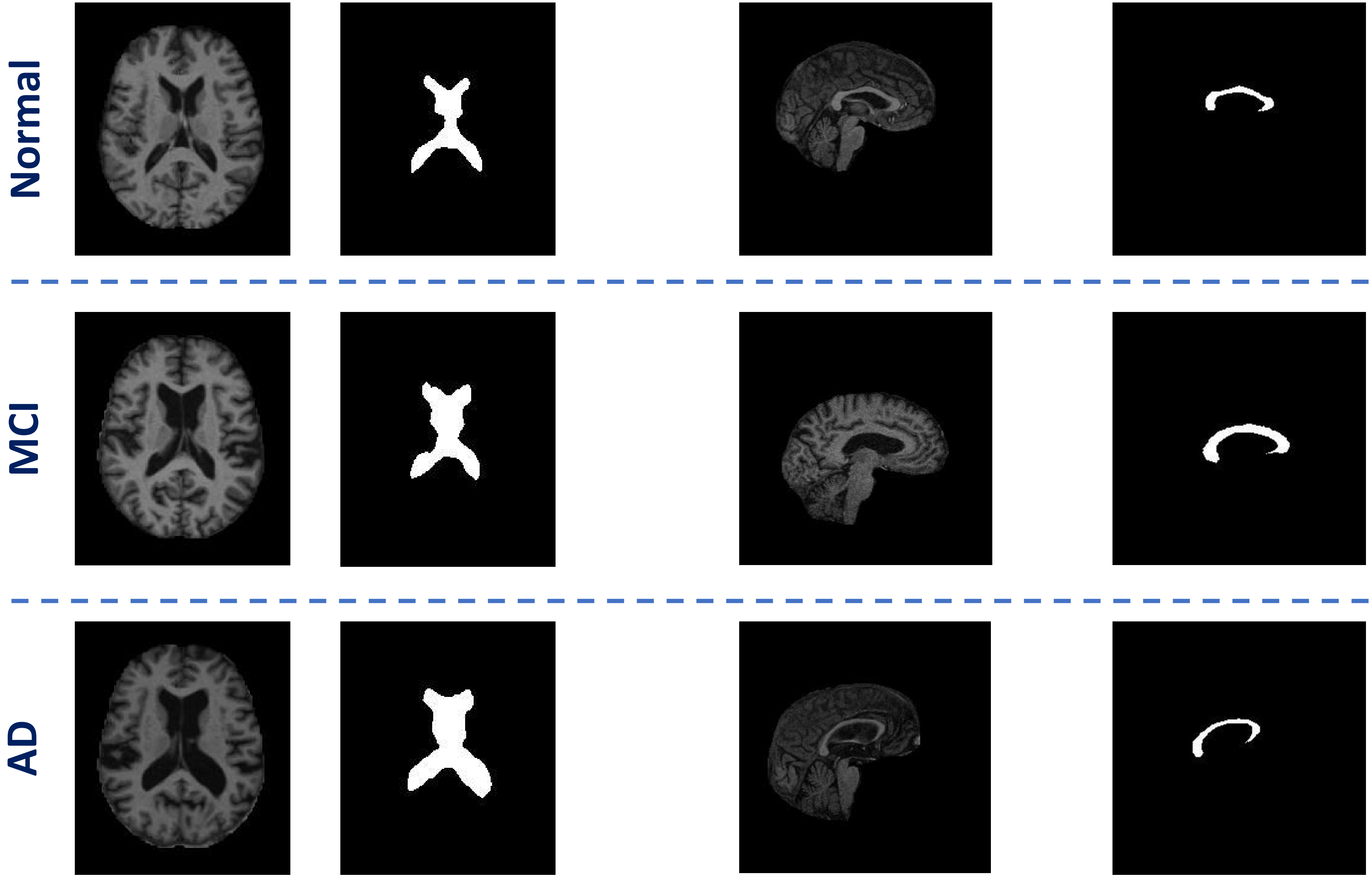
Representative set of typical T1-weighted MR images of AD subjects



Non-uniform enlargement of occipital horn

Completely enlarged lateral ventricles

Segmented Axial and Sagittal Region of Interest



Ventricle enlargement resulted in collosal arching and thinning

LB eigenvalues – Segmented Ventricles

LB eigenvalues	Mean ± Standard deviation		
	Normal	MCI	AD
$\boldsymbol{\lambda_1}$*	0.36 ±0.12	0.40 ± 0.12	0.56 ± 0.50
$\boldsymbol{\lambda_2}$*	0.36 ± 0.14	0.47 ± 0.15	0.59 ± 0.18
$\boldsymbol{\lambda_3}$*	0.45 ± 0.16	0.53 ± 0.16	0.62 ± 0.13
$\boldsymbol{\lambda_4}$*	0.39 ± 0.13	0.48 ± 0.17	0.52 ± 0.12
$\boldsymbol{\lambda_5}$*	0.41 ± 0.15	0.50 ± 0.17	0.62 ± 0.12
λ_6	0.46 ± 0.17	0.55 ± 0.18	0.64 ± 0.14
λ_7	0.45 ± 0.16	0.52 ± 0.17	0.63 ± 0.14
λ_8	0.43 ± 0.15	0.51 ± 0.16	0.60 ± 0.12
λ_9	0.41 ± 0.13	0.51 ± 0.16	0.64 ± 0.13
λ_{10}	0.44 ± 0.16	0.54 ± 0.17	0.66 ± 0.13
* p<0.0001 (Statistically highly significant)			

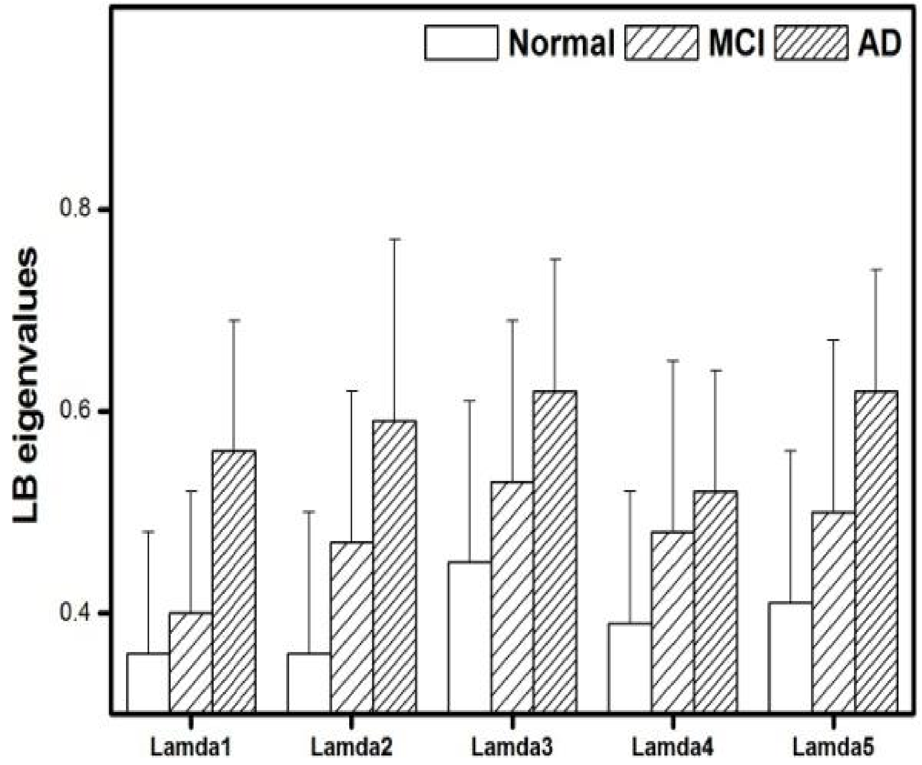
- LB eigenvalues λ1 to λ5 are statistically highly significant
- Mean eigenvalues are high for AD compared to normal and MCI subjects

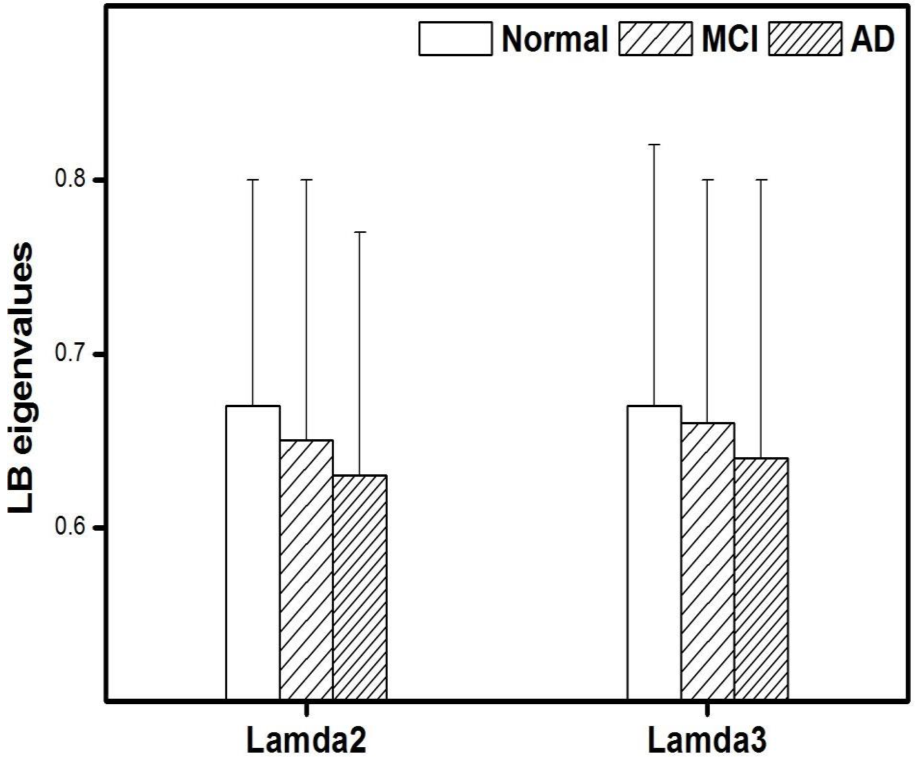
LB eigenvalues – Segmented Corpus Callosum

LB eigenvalues	Mean ± Standard deviation		
	Normal	MCI	AD
λ_1	0.63 ± 0.15	0.63 ± 0.12	0.62 ± 0.14
λ_2*	0.67 ± 0.13	0.65 ± 0.15	0.63 ± 0.14
λ_3*	0.67 ± 0.15	0.66 ± 0.14	0.64 ± 0.16
λ_4	0.65 ± 0.12	0.64 ± 0.12	0.63 ± 0.12
λ_5	0.68 ± 0.14	0.67 ± 0.12	0.67 ± 0.16
λ_6	0.65 ± 0.15	0.65 ± 0.12	0.63 ± 0.17
λ_7	0.61 ± 0.17	0.60 ± 0.11	0.59 ± 0.11
λ_8	0.64 ± 0.13	0.62 ± 0.10	0.62 ± 0.17
λ_9	0.66 ± 0.12	0.66 ± 0.10	0.64 ± 0.17
λ_{10}	0.65 ± 0.13	0.65 ± 0.12	0.64 ± 0.11
* p<0.0001 (Statistically highly significant)			

- λ2 and λ3 are found to be statistically highly significant
- Mean eigenvalues of normal subjects are high in magnitude compared to MCI and AD subjects

LB eigen value based analysis

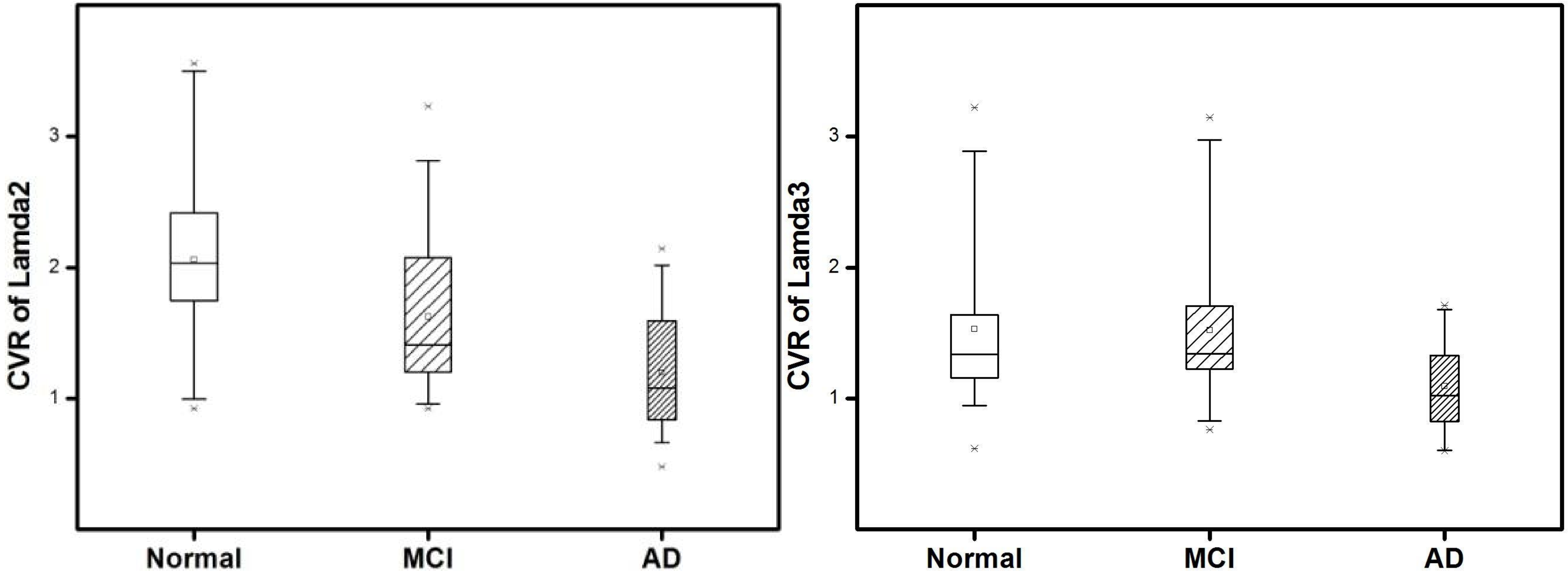




Mean LB eigen values for (a) ventricles and (b) CC of normal, MCI and AD subjects

Lamda2 is able to provide distinct variations in ventricle and CC for normal, MCI and AD subjects

Eigen Value Ratios



Comparison of CC to ventricle ratio for normal, MCI and AD subjects using (a) λ2 and (b) λ3

- CVR illustrates the phenomenal atrophy of CC caused due to the ventricle enlargement
- This ratio also shows the relationship and dependency of ventricle enlargement in the CC atrophy and describes the shape changes
- This is an important ratio in the disease diagnosis as it considers both CC and ventricle in the shape analysis

Conclusions

- Level set is able to segment ventricles and CC in all the normal, MCI and AD subjects
- LB eigen values are able to differentiate normal, MCI and AD subjects
- The newly formulated CVR is able to serve as an index in quantifying the shape changes of ventricle and CC in all the images

Thank you

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