Hemispheric asymmetry in patients with Alzheimer's Disease as feature for pathogenesis and prediction

Laura Broderius[1,2], Shammi More[1,2], & Kaustubh Patil[1,2] , Kathrin Reetz[1,3,4] Patrick Friedrich[1,2] Felix Hoffstaedter[1,2]

[1]Institute of Neuroscience and Medicine (INM-1 & INM-7), Research Center Juelich, Juelich, Germany,
[2]Institute of Systems Neuroscience, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany,
[3]Department of Neurology, University Hospital Rheinisch-Westfälische Technische Hochschule [RWTH],
[4]JARA-Translational Brain Medicine, Jülich and Aachen, Germany

Introduction

- **Hemispheric asymmetry is different in Alzheimer brains than in normally aging brains. [1,2] This could help to understand the structural changes in Alzheimer's disease better.**

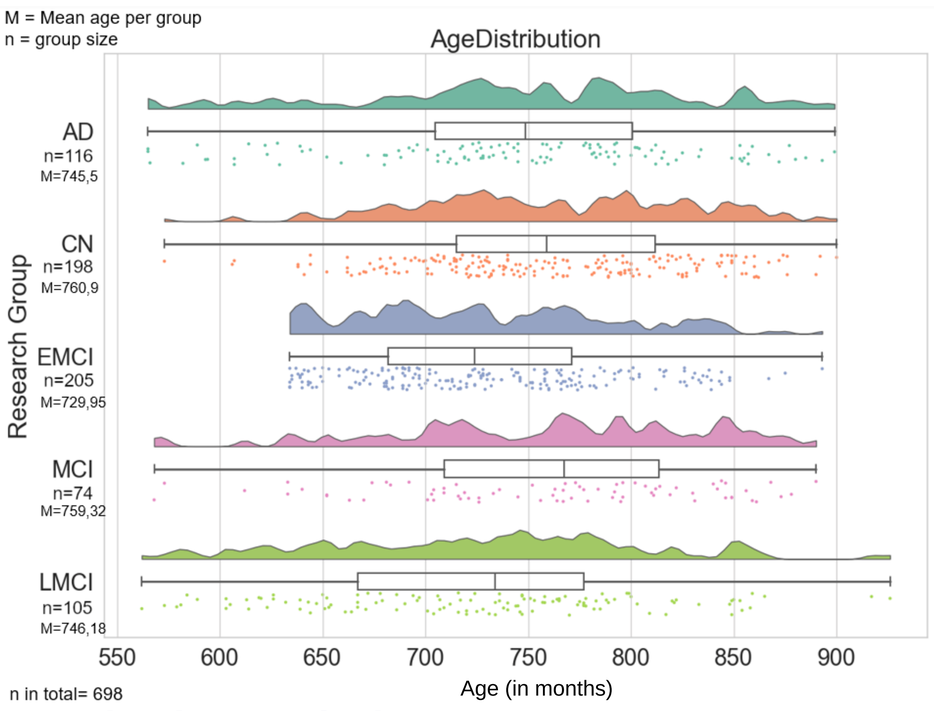
- **Alzheimer's disease is still often diagnosed at a late stage → Early detection markers are important. [3] Classical biomarkers are measured with amyloid PET and CSF. Hemispheric asymmetry could help to find additional structural early detection markers. These would be initially available to more patients.**

Hypotheses:

- **Hemispheric asymmetry will differ between the groups.**
- **These differences will enable a diagnosis prediction.**

Methods

- **Images: T1 weighted structural mri images**
- **Symmetrical template: built with IXI sample with CAT 12.8.**
- **Preprocessing of ADNI sample with CAT 12.8 → five matched groups:**

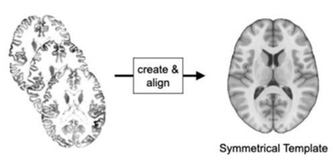


n in total= 698

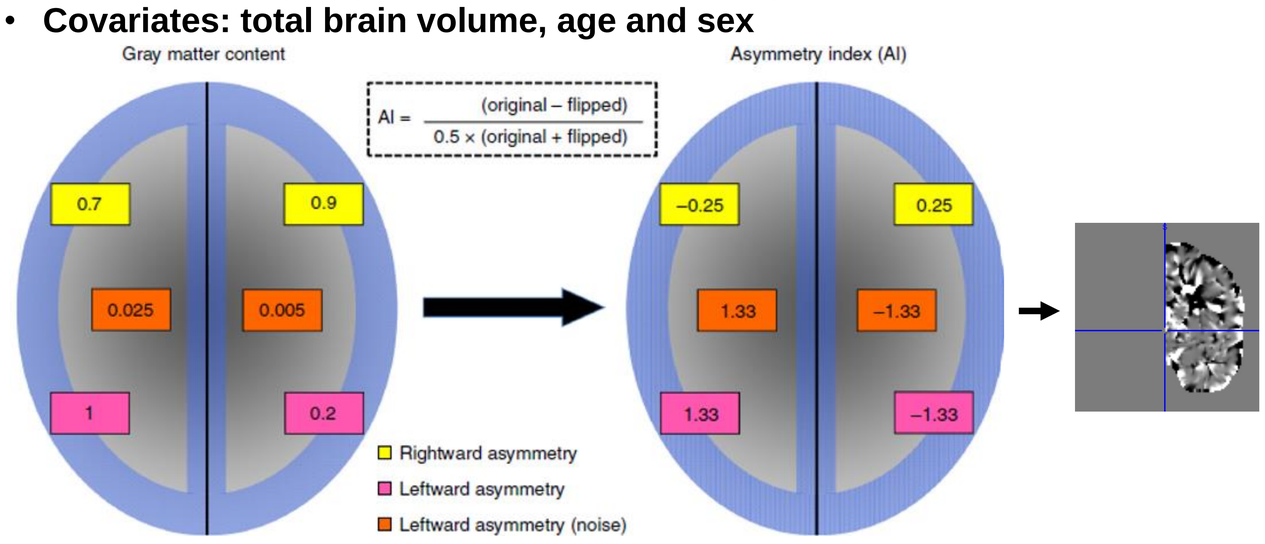
Group abbreviations:
AD = Alzheimer's disease
CN = Cognitively normal
MCI = Mild Cognitive Impairment
EMCI = Early MCI
LMCI = Late MCI

Sex distribution:

	M	F
AD	60	56
CN	95	103
EMCI	114	91
MCI	45	29
LMCI	53	52



- **Univariate analysis:**
- **whole brain calculation of asymmetry index images [4]**
- **GLM between groups with TFCE correction, p=0.05**
- **Covariates: total brain volume, age and sex**



- **Multivariate analysis:**
- **RandomForest Classification of the hemispheres per group and Boruta feature selection of the relevant voxels [5]**

- **Diagnosis classifications with Julearn [6] between the groups with the GMV (gray matter volume) and the asymmetry index as features**
  - **Model: support vector machine (svm), Confounds: age & sex**

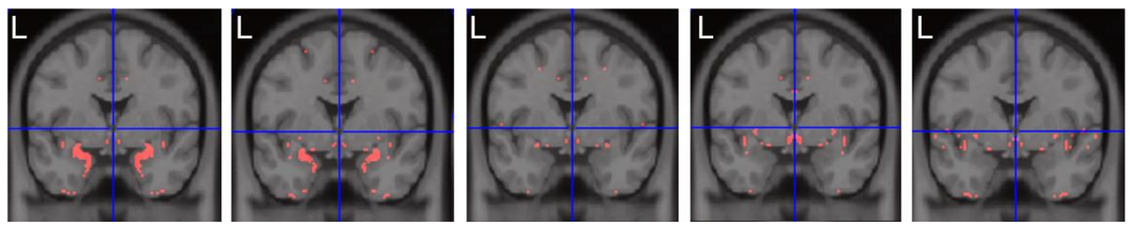
Results

- **Univariate analysis:**
- **no differences between the groups**

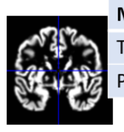
- **Multivariate analysis:**
- **Relevant clusters for hemispheric classification found → Biggest clusters of the Boruta feature selection per group:**

Cluster	CN (2490 Vox.)	EMCI (2614 Vox.)	MCI (1734 Vox.)	LMCI (2334 Vox.)	AD (2142 Vox.)
1	Entorhinal cortex, Amygdala (832 Vox.)	Entorhinal cortex, Amygdala (780 Vox.)	Thalamus (478 Vox.)	Thalamus (294 Vox.)	Thalamus (288 Vox.)
2	Thalamus (318 Vox.)	Thalamus (406 Vox.)	Insula, Parietal Operculum (406 Vox.)	Amygdala, Putamen (136 Vox.)	Parietal operculum, Insula, Heschl's Gyrus (242 Vox.)
3	Hippocampus, Amygdala (174 Vox.)	Hippocampus, Amygdala (140 Vox.)	Amygdala, Putamen (140 Vox.)	Middle Temporal Gyrus, superior temporal gyrus (136 Vox.)	Amygdala, Putamen (184 Vox.)
4	motor cortex, primary somatosensory cortex (140 Vox.)	Pallidum (64 Vox.)	Inferior Parietal Cortex (66 Vox.)	Insula (118 Vox.)	Insula, Frontal Orbital Cortex (58 Vox.)

- **In AD more clusters and smaller clusters compared to CN → they spread more globally from CN to AD**



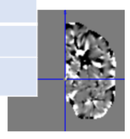
- **Results of the diagnosis classifications of CN and AD**
  - GMV
  - Whole brain GMV (Features 15907)



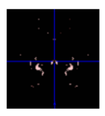
Mean Test Score	**0.86**
Test Accuracy:	0.86
Precision Score (AD):	0.88

  - AI
  - Whole brain AI (Features 8156)

Mean Test Score	**0.63**
Test Accuracy:	0.59
Precision Score (AD):	0.25



  - Boruta regions GMV (Features 223)

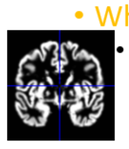


Mean Test Score	**0.85**
Test Accuracy:	0.84
Precision Score (AD):	0.76

  - Boruta regions AI (Features 111)

Mean Test Score	**0.64**
Test Accuracy:	0.57
Precision Score (AD):	0.23

- **Results of the diagnosis classifications of CN and MCI**
  - GMV
  - Whole brain GMV (Features 15907)



    - CN vs EMCI

Mean Test Score	**0.57**
Test Accuracy:	0.58
Precision Score EMCI:	0.64

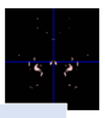
    - CN vs MCI

Mean Test Score	**0.82**
Test Accuracy:	0.75
Precision Score MCI:	0.70

    - CN vs LMCI

Mean Test Score	**0.71**
Test Accuracy	0.69
Precision Score LMCI	0.64

  - GMV
  - Boruta regions GMV



    - CN vs. EMCI (Features 191)

Mean Test Score	**0.56**
Test Accuracy	0.54
Precision Score EMCI	0.46

    - CN vs. MCI (Features 239)

Mean Test Score	**0.78**
Test Accuracy	0.72
Precision Score MCI	0.66

    - CN vs. LMCI (Features 203)

Mean Test Score	**0.62**
Test Accuracy	0.69
Precision Score LMCI	0.42

Discussion

- **No group differences in the univariate analysis could mean:**
  - **There are no differences.**
  - **The differences are too subtle to be detected with VBM after correction for multiple comparisons.**

- **The multivariate analysis shows several clusters that are relevant for the left vs. right decision. These are related to hemispheric asymmetry which seems to differ between the groups of the AD continuum.**

- **The performance of those clusters in diagnosis classifications was very similar to the whole brain → Only <1.5% of the features of the whole brain was sufficient. This shows potential for AD as well as MCI prediction in the ADNI dataset.**

References:

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