Classification between Early Onset Alzheimer's Disease and Frontotemporal Dementia using a single neuroimaging feature

Agnès Pérez-Millan

Alzheimer's Disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Fundació Clínic per a la Recerca Biomèdica, Universitat de Barcelona, Barcelona, 08036, Spain.
Institute of Neurosciences. Department of Biomedicine, Faculty of Medicine, University of Barcelona, Barcelona, 08036, Spain.

agperez@recerca.clinic.cat @agnesperezmi

INTRODUCTION: Early Onset Dementia

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- Early Onset Alzheimer's Disease (EOAD) and Frontotemporal Dementia (FTD) are common forms of early-onset dementia.
- Alzheimer's Disease (AD) is characterized by progressive memory loss accompanied with language, executive and visuospatial problems.
- FTD is characterized by progressive behavioural, executive and language problems.

INTRODUCTION: Challenging Diagnosis

❖ In the clinical practice the overlapping symptoms and brain signatures makes the diagnosis challenging.

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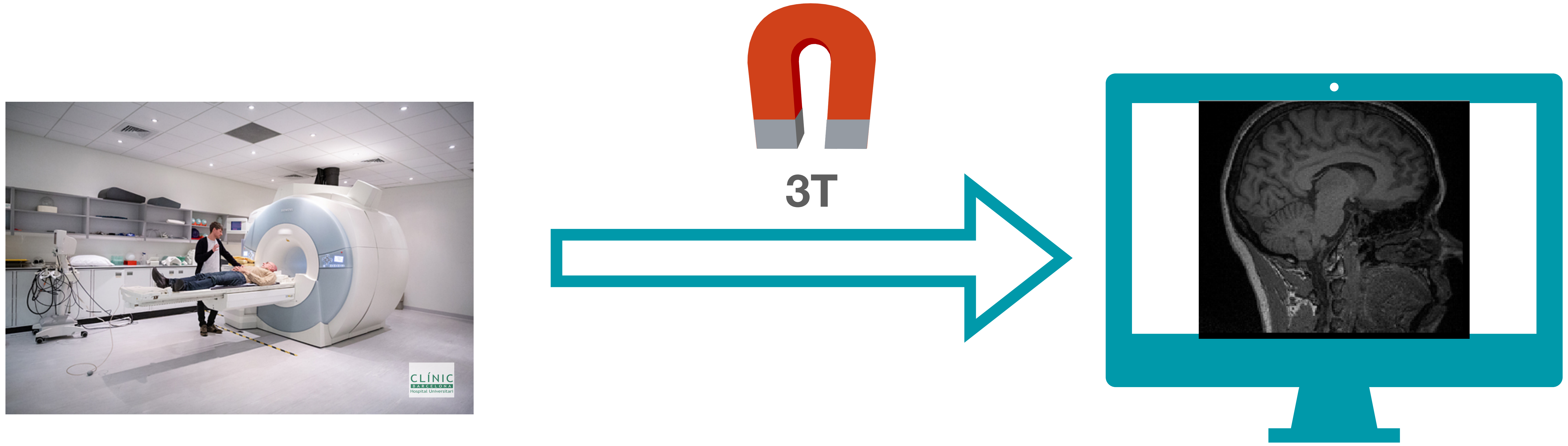

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- Distinct brain atrophy patterns could potentially help in differentiating EOAD and FTD.

INTRODUCTION: Challenging Diagnosis

- ❖In the clinical practice the overlapping symptoms and brain signatures makes the diagnosis challenging.

- ❖Magnetic Resonance Imaging (MRI) has been widely used to detect disease-specific brain changes across these disorders.

- ❖Distinct brain atrophy patterns could potentially help in differentiating EOAD and FTD.

- ❖Unsupervised and supervised machine learning were combined to discriminate between EOAD, FTD and healthy controls (CTR).

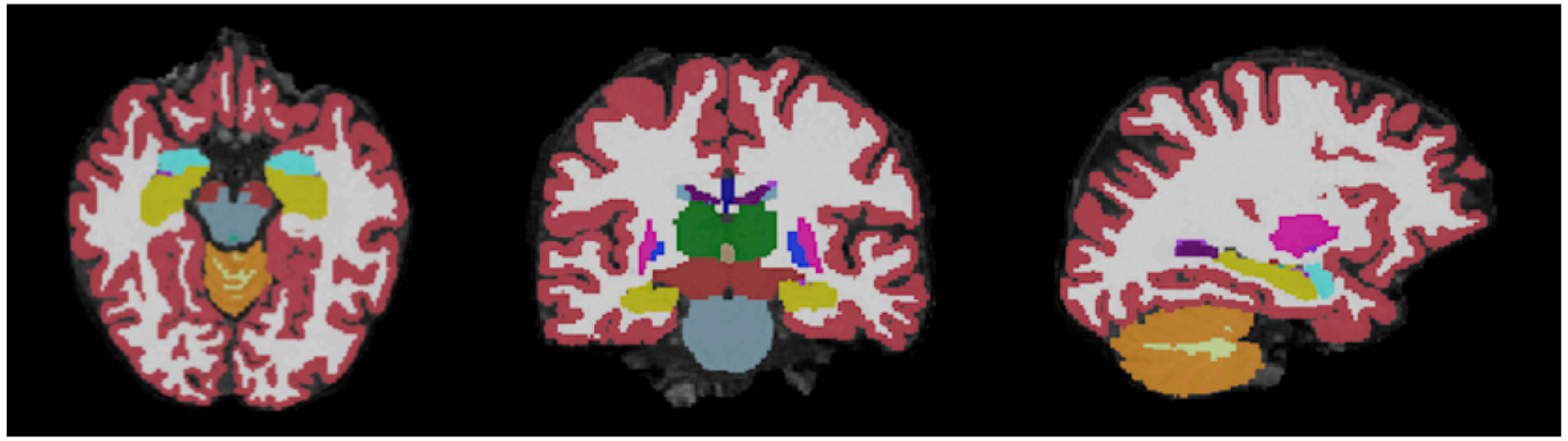
AIM

To develop a classification algorithm using MRI data including EOAD and FTD, while providing interpretability of the results.

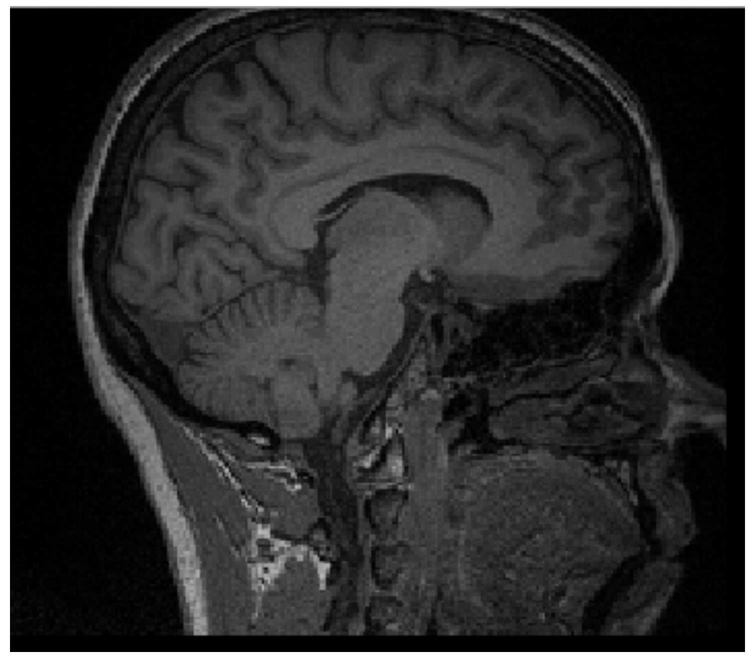
SAMPLE DEMOGRAPHICS

Table 1. Group summaries given as the mean and the standard deviation of each measure. Differences between groups are calculated using Fisher exact Test for sex and ANOVA test for age at MRI.

	CTR	EOAD	FTD	CTR-EOAD p-value	CTR-FTD p-value	EOAD-FTD p-value
Number of participants	66	85	52	——	——	——
Sex (Men/Women)	18/48	35/50	30/22	0.087	**0.0038**	0.087
Age at MRI, years (SD)	54.95 (8.40)	57.29 (6.13)	57.89 (4.85)	0.052	0.052	0.061



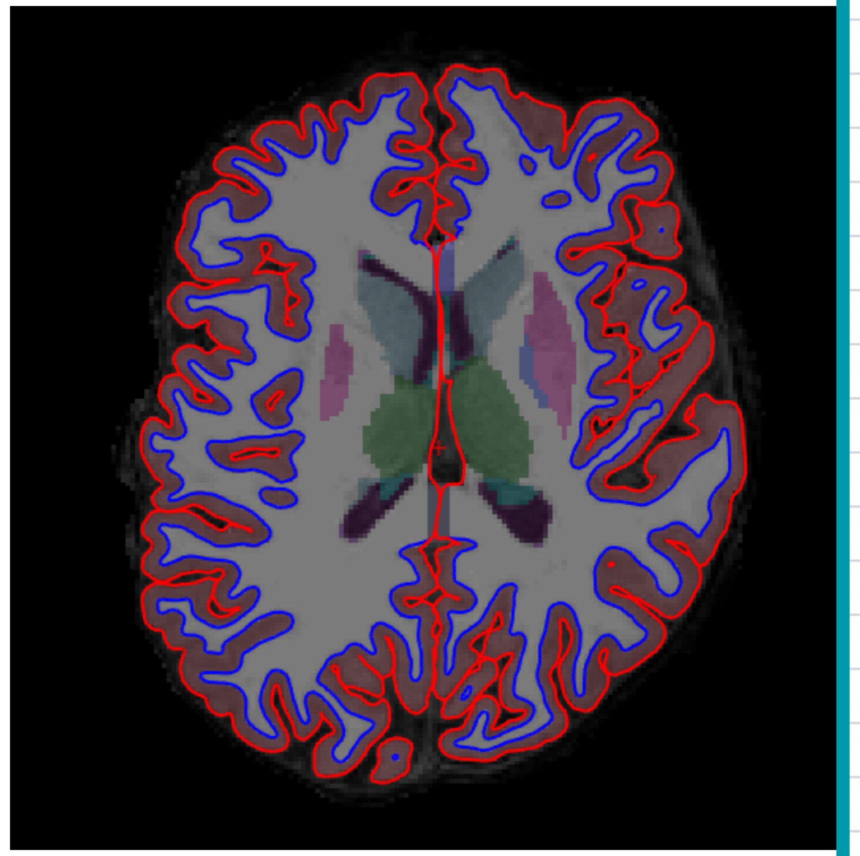
ALGORITHM



FreeSurfer

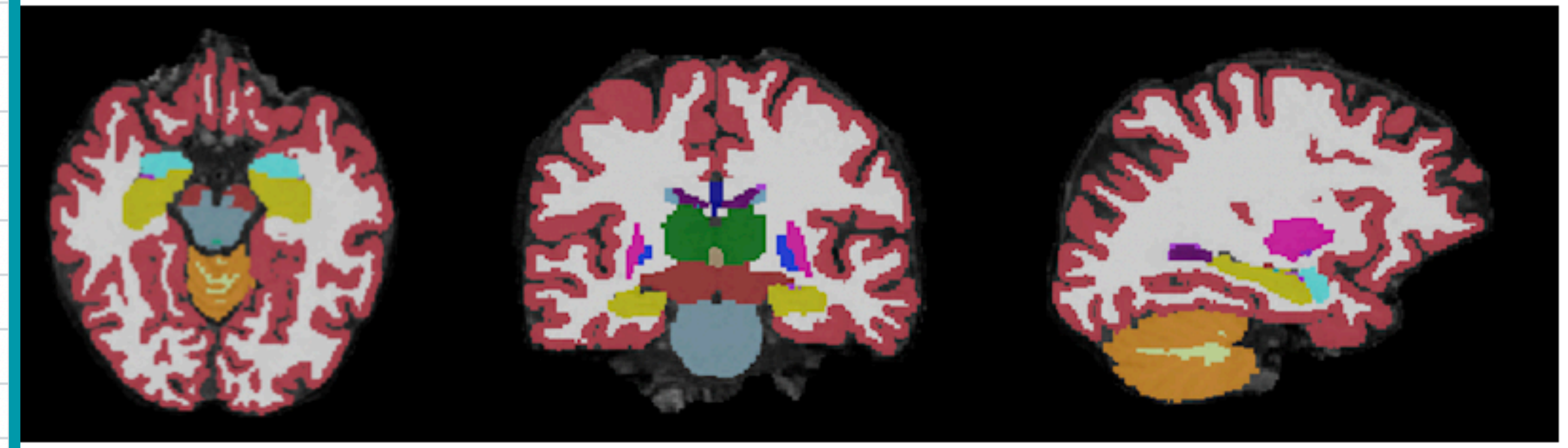
INPUT:

Subcortical gray matter volumes and cortical thickness



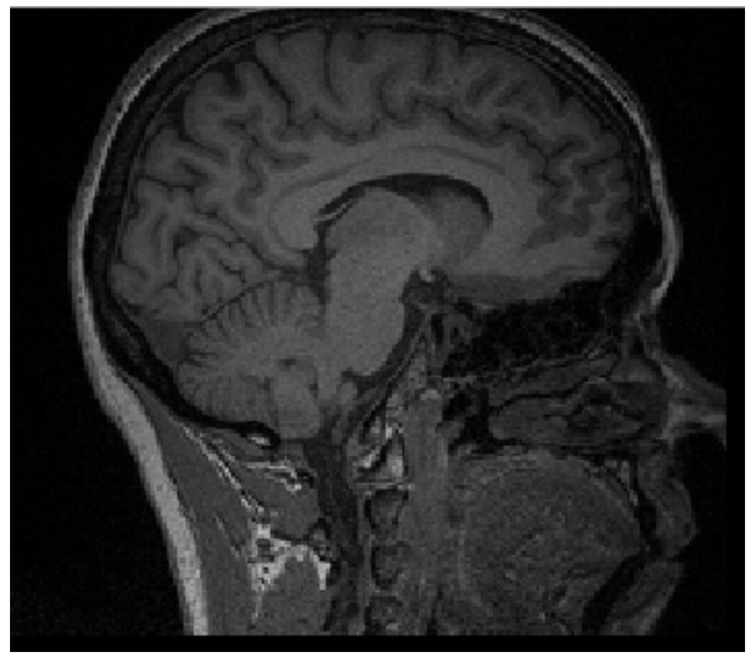
rh_caudalanteriorcingulate_thickness	rh_caudalmiddlefrontal_thickness	rh_cuneus_thickness	rh_entorhinal_thickness	rh_fusiform_thickness
2.523	2.474	1.824	3.608	2.722
2.245	2.417	1.897	3.093	2.788
2.782	2.296	2.043	4.120	2.738
2.222	2.029	2.057	3.581	2.754
2.451	2.230	1.876	2.692	2.339
2.235	2.421	1.900	3.391	2.847
2.332	2.346	1.762	2.890	2.604
2.534	2.383	1.767	3.202	2.308
2.744	2.315	1.943	3.416	2.457
2.398	2.181	1.960	3.853	2.565
2.396	2.310	1.944	3.363	2.921
2.386	2.344	1.809	3.340	2.666
2.516	2.339	1.498	3.455	2.391
2.342	2.350	1.823	3.215	2.617
2.731	2.121	1.815	3.186	2.471
2.773	2.482	1.775	3.192	2.790
2.235	2.132	1.933	2.343	2.147
2.652	2.157	1.919	3.170	2.799
2.280	2.464	2.078	2.987	2.753
2.027	2.266	1.932	3.274	2.374

Left.Thalamus.Proper	Left.Caudate	Left.Putamen	Left.Pallidum
6048.0	3038.4	3935.0	1710.0
7435.4	3268.5	4772.1	2105.6
5559.7	2087.7	3661.5	1429.3
6396.7	2756.8	4411.9	1909.6
5126.6	2344.7	3169.7	1729.3
7240.5	2889.3	3333.4	1805.7
7143.6	3296.8	4073.7	1897.8
7364.9	3430.2	4414.5	2030.1
6240.1	3553.8	3877.7	1819.2
7290.9	3187.6	4667.2	2215.5
7533.0	3141.6	4452.9	2283.9



We used FreeSurfer to obtain subcortical gray matter volumes and cortical thickness from T1w MRI images to train our algorithm.

ALGORITHM



FreeSurfer

TRAIN SET

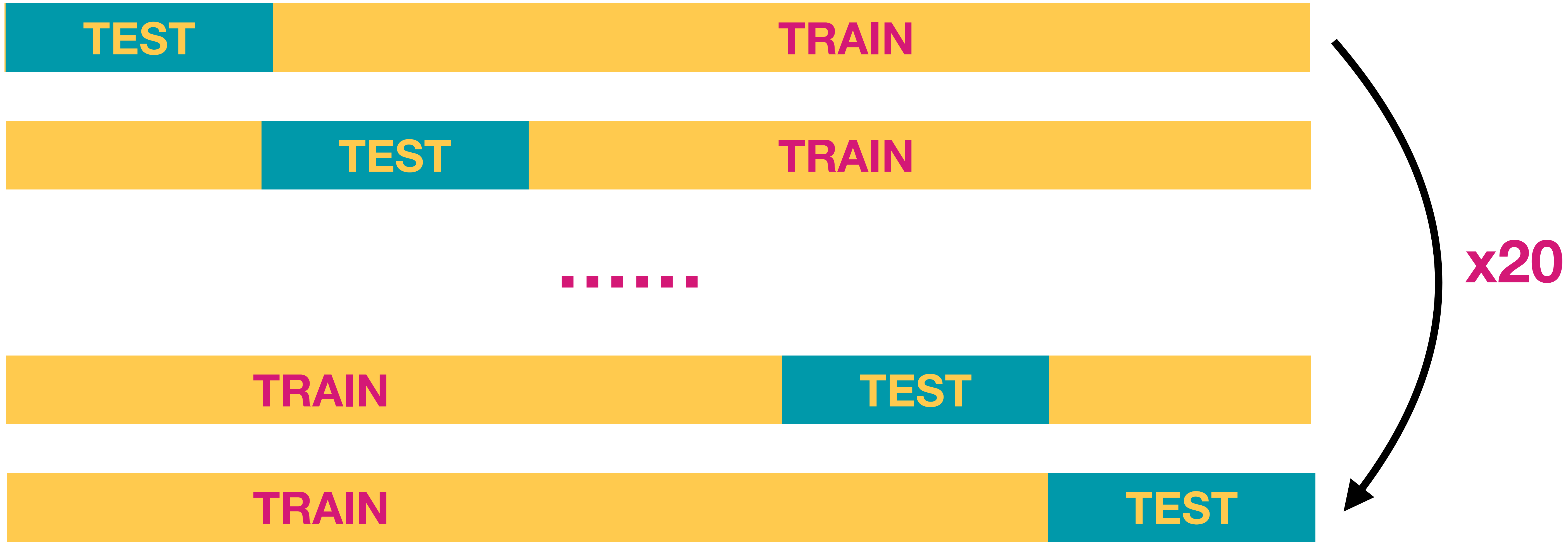
TEST SET

INPUT:

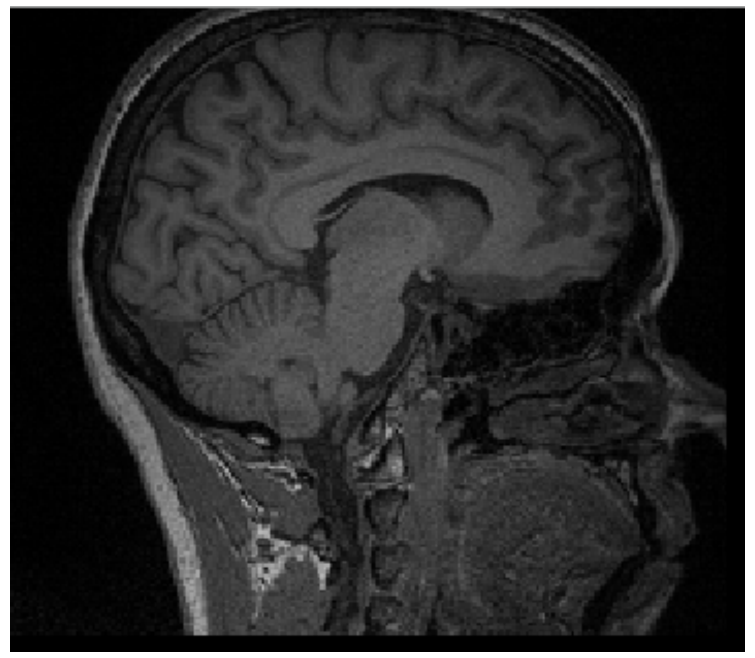
Subcortical gray matter volumes and cortical thickness

k-fold cross-validation

We splitted the data into train and test datasets with a k-fold cross-validation.



ALGORITHM



FreeSurfer

INPUT:
Subcortical gray matter volumes and cortical thickness

TRAIN SET

TEST SET

k-fold cross-validation

Dimensionality reduction:
1 Principal Component (PC)

Principal Component Analysis (PCA)

TRANSFORMED TRAIN SET

OUTPUT:
Weights given to each region

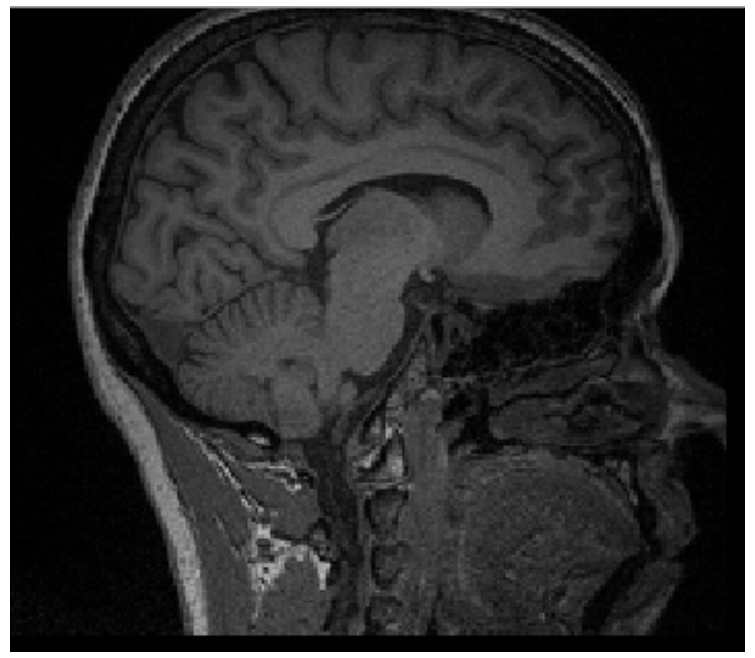
Index	Age_at_MRI	eral.\	Inf.Lat.'	bellu	.eft.Thalamus.Prope	Left.Caudate	Left.Putamen	Left.Pallidum	.eft.Hippocampus	Left.Amygdala	cumbe	oroid	ateral.V	.Inf.Lat	'ebellu	Right.Thalamus.Prope	Right.Caudate
0	-1.20879	-0…	-1.14…	0.0…	-0.596999	-0.106093	-0.282156	-0.793601	0.241611	1.00379	0.75…	-1.…	-0.71…	-0.9…	-0.1…	-1.04795	-0.311487
1	0.0832456	-0…	-1.00…	0.2…	-0.314294	-0.0774216	-0.213605	-0.585758	-0.263446	-0.209823	0.21…	-0.…	-0.02…	-0.9…	-0.1…	-1.38358	-0.33936
2	0.209896	-0…	0.127…	0.8…	0.182785	-0.228444	-0.203529	0.487253	-0.997618	-1.52422	-0.2…	-0.…	-0.57…	-0.1…	1.26…	0.173688	-0.0049531
3	0.334584	1.…	1.851…	-1.…	-1.06111	0.0262218	-0.498637	-0.631365	-1.3831	-1.72891	-1.4…	0.0…	1.457…	-0.1…	-1.0…	-0.599923	0.563366
4	0.408218	1.…	4.033…	-1.…	-1.17751	-1.69441	-2.24398	-1.54868	-2.19693	-1.38496	-0.4…	-0.…	2.447…	4.86…	-1.5…	-2.04065	-1.54436
5	1.4175	0.…	1.539…	-0.…	-1.89348	-1.40693	-1.52225	-0.243069	-0.534128	-1.36953	-1.8…	-0.…	0.662…	1.02…	-1.4…	-1.61707	-0.747341
6	1.45088	1.…	1.687…	-0.…	-1.52725	-1.37354	-1.61841	-1.72411	-2.25535	-2.03689	-0.6…	1.1…	2.181…	2.90…	-0.4…	-1.68142	-0.668878
7	0.946238	1.…	2.100…	0.0…	-1.71526	-0.408582	-1.38296	1.27475	-0.844835	-1.36974	-0.6…	1.8…	1.096…	0.73…	0.49…	-0.805792	-0.621221
8	1.40964	0.…	0.270…	0.7…	-1.16826	-1.00434	-0.375499	-0.569332	-1.0279	0.157696	-1.6…	0.7…	-0.06…	0.00…	0.04…	-2.17336	-0.602281
9	0.920712	-0…	-0.86…	-1.…	0.127395	0.442631	0.245403	0.441244	-1.6176	-0.958503	-0.0…	-1.…	-0.27…	-0.8…	-0.6…	0.32038	1.06763

PCA

	0
0	-0.180822
1	0.0626757
2	0.124022
3	0.110981
4	0.691609
5	0.467265
6	0.851905
7	0.426191
8	0.254307
9	-0.177468
10	0.192423
11	0.263028
12	-0.0625034
13	0.179495
14	-0.167746
15	0.475608

We applied a dimensionality reduction using PCA. We only kept the first PC. We obtained the transformed dataset and the weights of all the features which give us the first PC.

ALGORITHM



FreeSurfer

INPUT:
Subcortical gray matter volumes and cortical thickness

TRAIN SET

TEST SET

k-fold cross-validation

Dimensionality reduction:
1 Principal Component (PC)

Principal Component Analysis (PCA)

OUTPUT:
Weights given to each region

TRANSFORMED TRAIN SET

We trained a SVM with a single feature obtained with the PCA.

Support Vector Machine (SVM)

	0
0	-0.180822
1	0.0626757
2	0.124022
3	0.110981
4	0.691609
5	0.467265
6	0.851905
7	0.426191
8	0.254307
9	-0.177468
10	0.192423
11	0.263028
12	-0.0625034
13	0.179495
14	-0.167746
15	0.475608

+

	0
0	EOAD
1	EOAD
2	FTD
3	CTR
4	CTR
5	EOAD
6	FTD
7	EOAD
8	FTD
9	EOAD
10	CTR
11	EOAD
12	FTD
13	EOAD
14	CTR
15	FTD

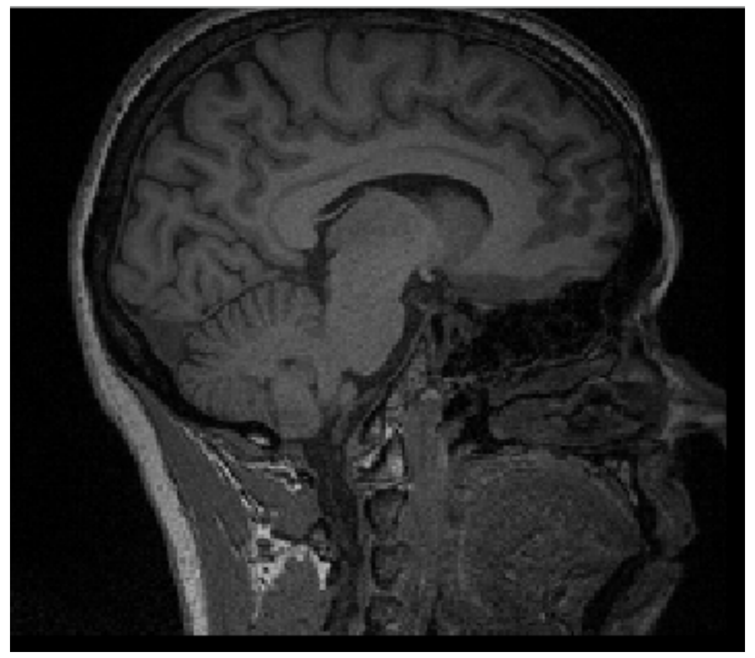
SVM

EOAD

FTD

ALGORITHM

We used the test dataset to obtained the performance evaluation of the algorithm. First, we applied the same PCA to the test data and then applied the trained SVM with a single feature of the test data.



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1 Principal Component (PC)

Principal Component Analysis (PCA)

OUTPUT:
Weights given to each region

TRANSFORMED TRAIN SET

TRANSFORMED TEST SET

Support Vector Machine (SVM)

OUTPUT:
Performance evaluation

	0
0	−0.180822
1	0.0626757
2	0.124022
3	0.110981
4	0.691609
5	0.467265
6	0.851905
7	0.426191
8	0.254307
9	−0.177468
10	0.192423
11	0.263028
12	−0.0625034
13	0.179495
14	−0.167746
15	0.475608

EOAD ✓
FTD ✓
EOAD ✗

RESULTS: Classification

Classification:

- 87.2 ± 14.2 % CTR vs EOAD
- 80.8 ± 20.4 % CTR vs FTD
- 66.5 ± 12.9 % EOAD vs FTD
- 65.2 ± 10.6 % CTR vs EOAD vs FTD

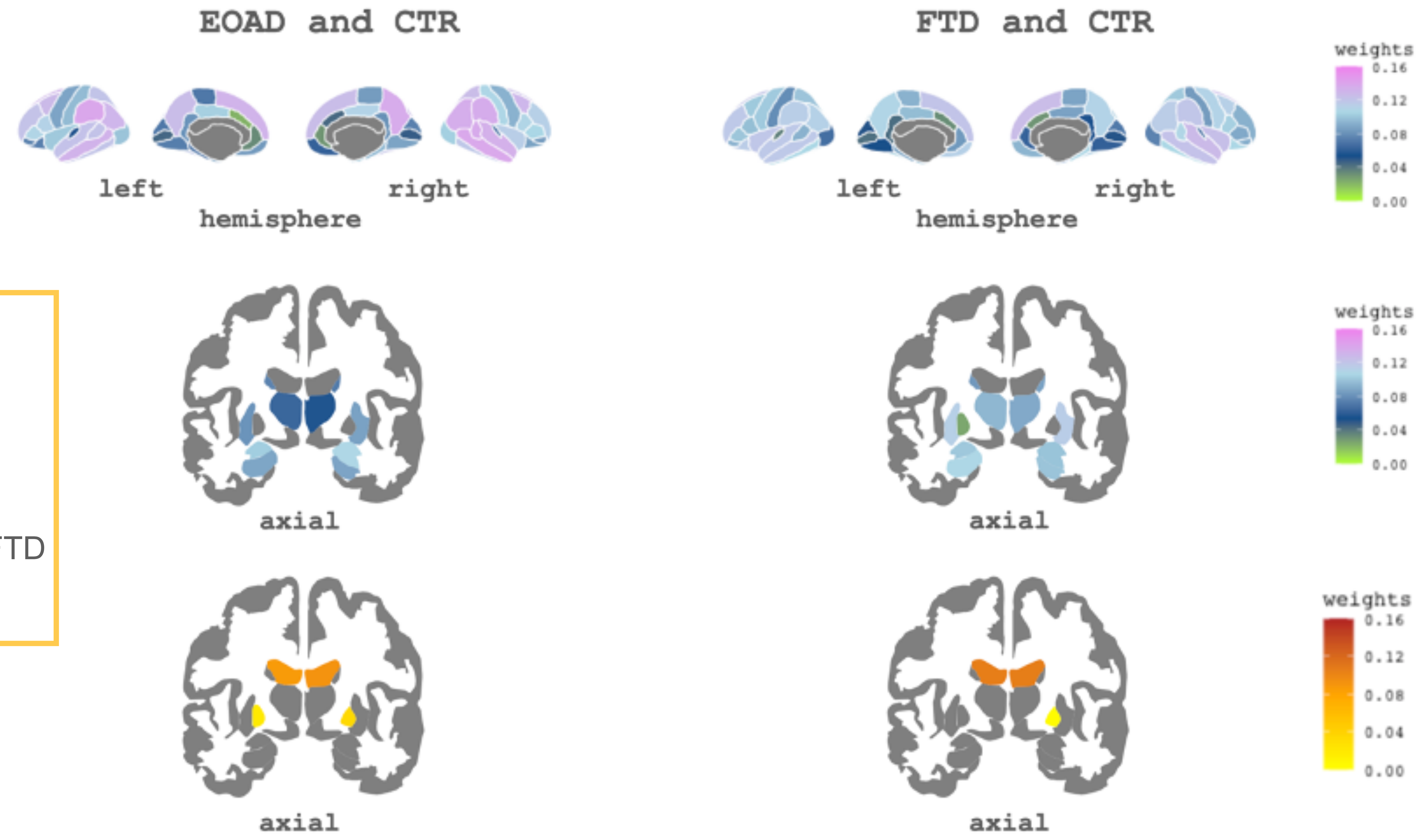
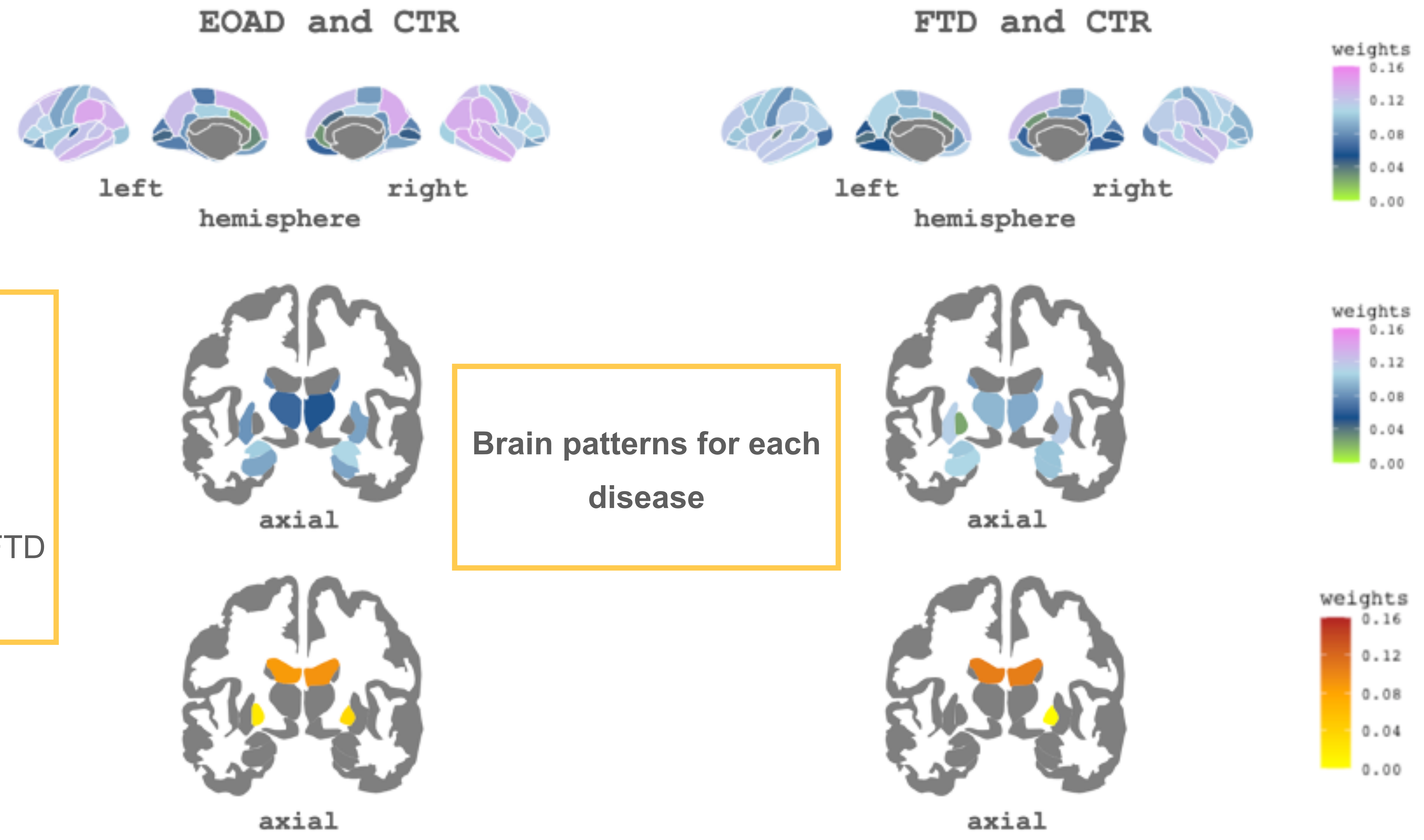


Figure 1. Subcortical and cortical patterns of the first PC's weights associated with EOAD and FTD. Top: Cortical ROIs included in the component. Bottom: subcortical ROIs of the component. Cool color scale represents negative weights and warm scale represents positive weights within the component.

RESULTS: Patterns



Classification:

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- **80.8 ± 20.4 % CTR vs FTD**
- 66.5 ± 12.9 % EOAD vs FTD
- 65.2 ± 10.6 % CTR vs EOAD vs FTD

Brain patterns for each disease

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DISCUSSION: Classification

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87.2 ± 14.2 % CTR vs EOAD

80.8 ± 20.4 % CTR vs FTD

66.5 ± 12.9 % EOAD vs FTD

65.2 ± 10.6 % CTR vs EOAD vs FTD

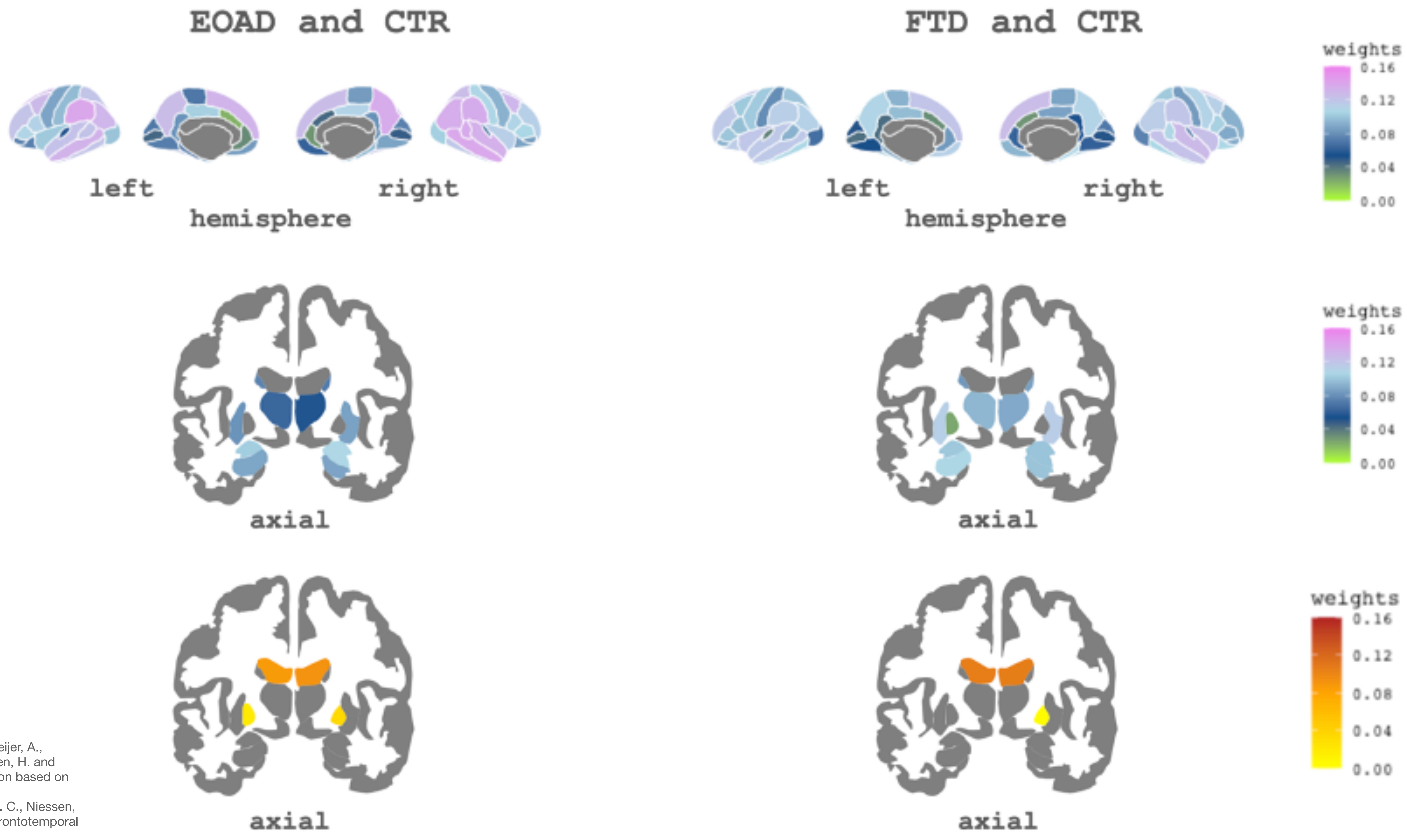
Published Papers[1,2,3,4]:

80-95 % CTR vs EOAD (or AD)

72-88 % CTR vs FTD

69-89 % EOAD (or AD) vs FTD

70 % CTR vs AD vs FTD



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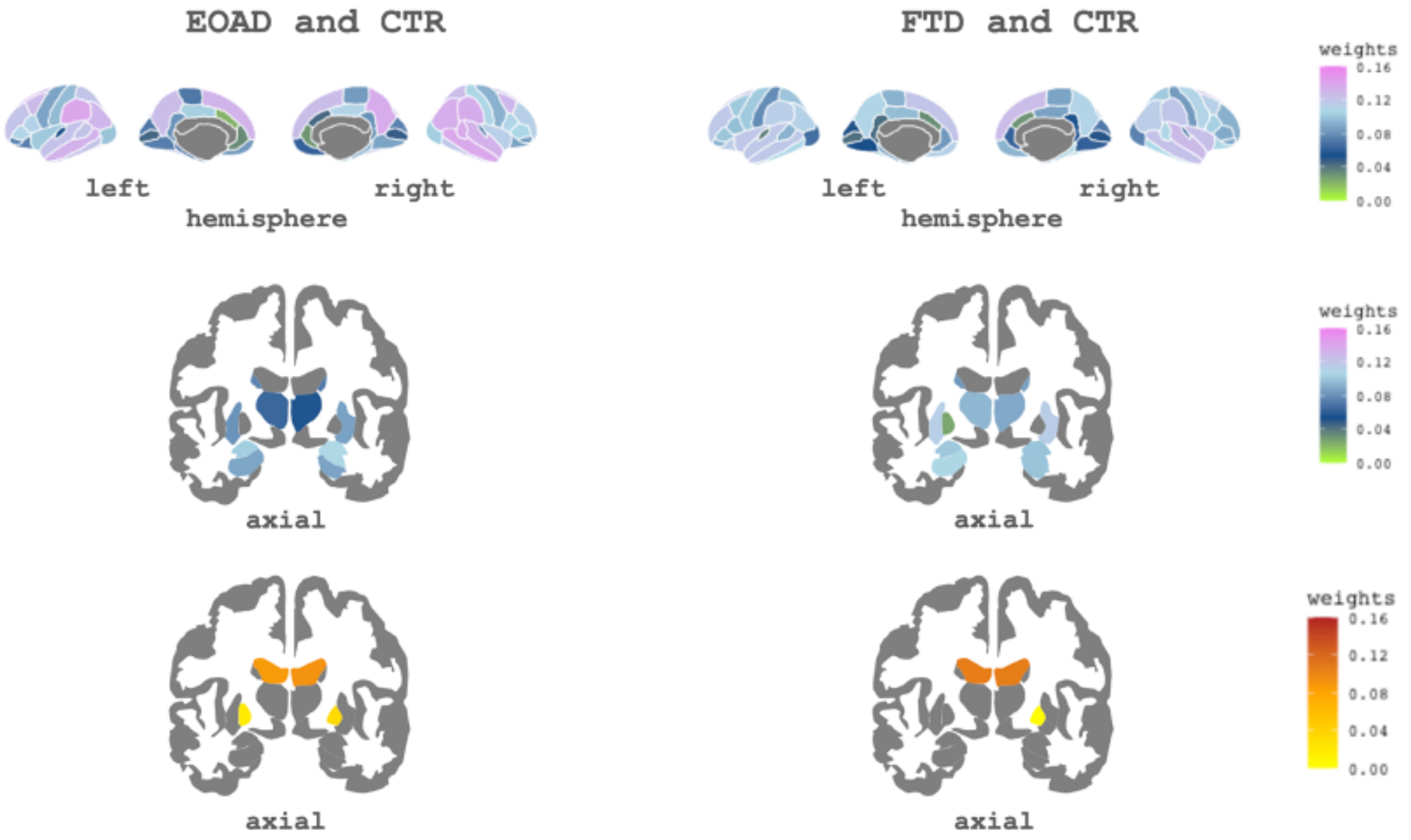
Brain patterns for each disease

↓

Interpretability of the results



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CONCLUSIONS

The combination of unsupervised and supervised techniques of machine learning provided the opportunity of:

1. Reducing all subcortical gray matter volumes and cortical thickness measures into a single feature.
2. Obtaining good accuracy classifying EOAD, FTD and CTR.
3. Giving interpretability of the results with the atrophy patterns.

Thanks!

José Contador, Mircea Balasa, Albert Lladó & Raquel Sánchez-Valle

Laia Borrell & Roser Sala-Llonch

agperez@recerca.clinic.cat @agnesperezmi

CLÍNIC BARCELONA Hospital Universitari · IDIBAPS · Universitat de Barcelona, Facultat de Medicina i Ciències de la Salut · Institut de Neurociències, Universitat de Barcelona · Generalitat de Catalunya, Departament de Salut

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