Exploring multivariate associations between brain grey matter and clinical phenotype in autoimmune limbic encephalitis

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Brain & Behaviour

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Autoimmune Limbic Encephalitis (ALE)

- Temporal lobe seizures

- Grey Matter Alterations

- Heterogenous spectrum of behavioral symptoms including memory deficits and psychiatric symptoms

-> relations between brain structure (measured at MRI) and clinical phenotypes ?

-> can we disentangle different neurocognitive profiles/phenotypes within ALE population ?

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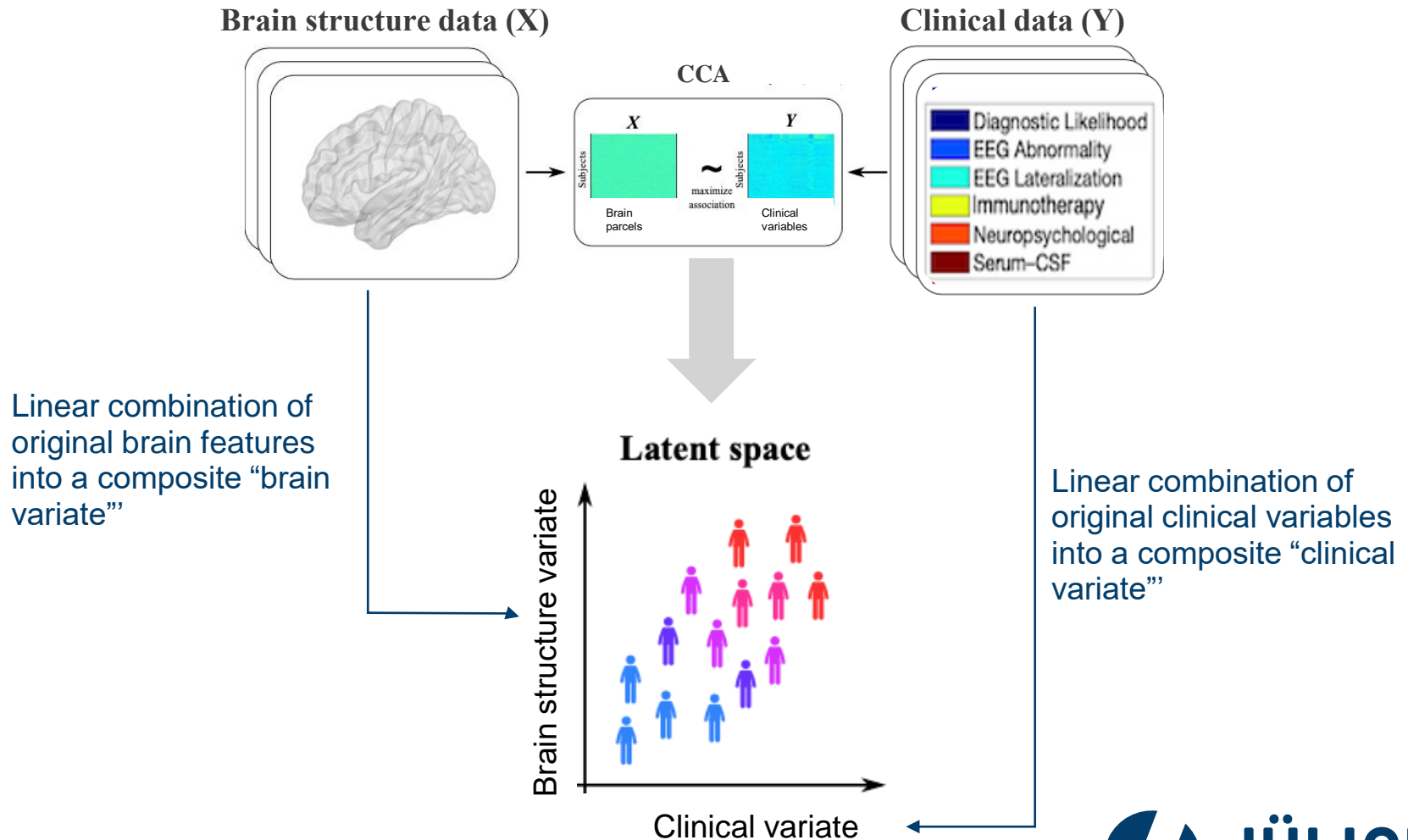
ALE multicentric dataset

- N = 125 (female = 65)

- 6 German Clinical Centers

- Patients with both brain structural imaging and other clinical measurements

- Age (mean (SD)) = 50.65 ± 16.5
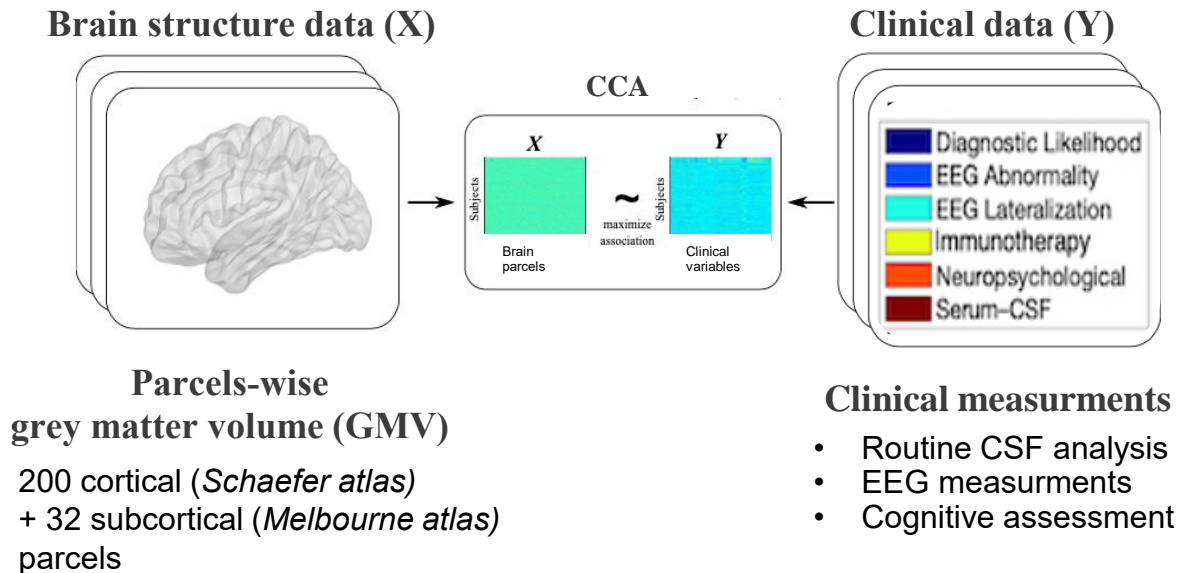
Age Distribution
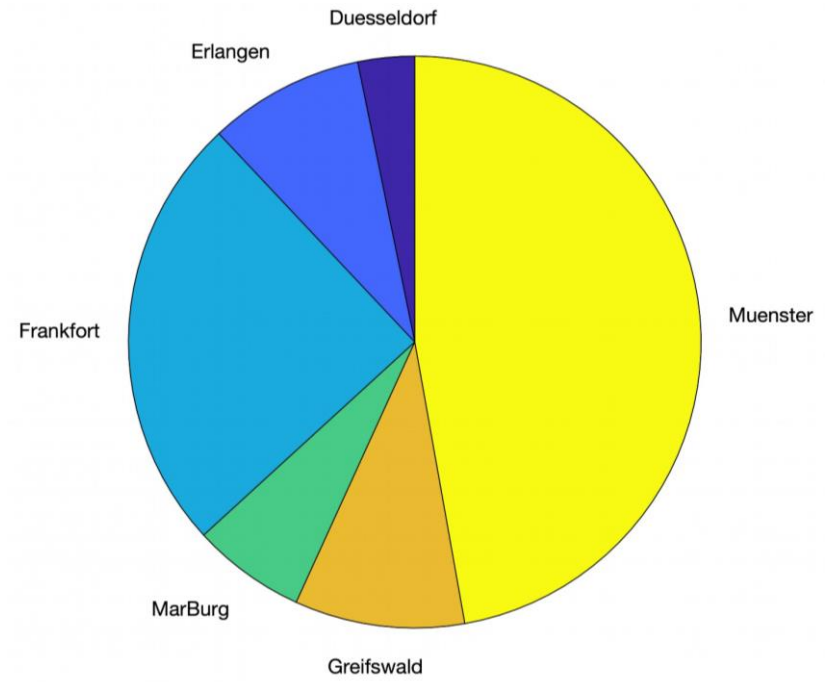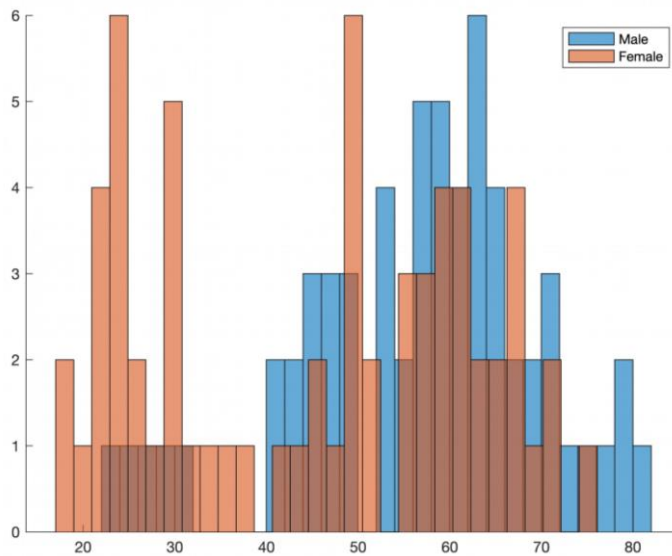
Data Distribution (Clinical Centers)

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Multivariate associations between brain structure and clinical measurements:
Canonical Correlation Analysis (CCA)

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Brain structure data (X)

CCA

Clinical data (Y)

Parcels-wise grey matter volume (GMV)

200 cortical (*Schaefer atlas*)
+ 32 subcortical (*Melbourne atlas*) parcels

Clinical measurments

- Routine CSF analysis
- EEG measurments
- Cognitive assessment

Confounds: Age, age^2, sex, education, TIV, $\sqrt[3]{\text{TIV}}$

Machine Learning Framework: HoLDOUT

We ran the CCA 50 times with 3-inner and 3-outer sample splits
Averaged results across significant splits

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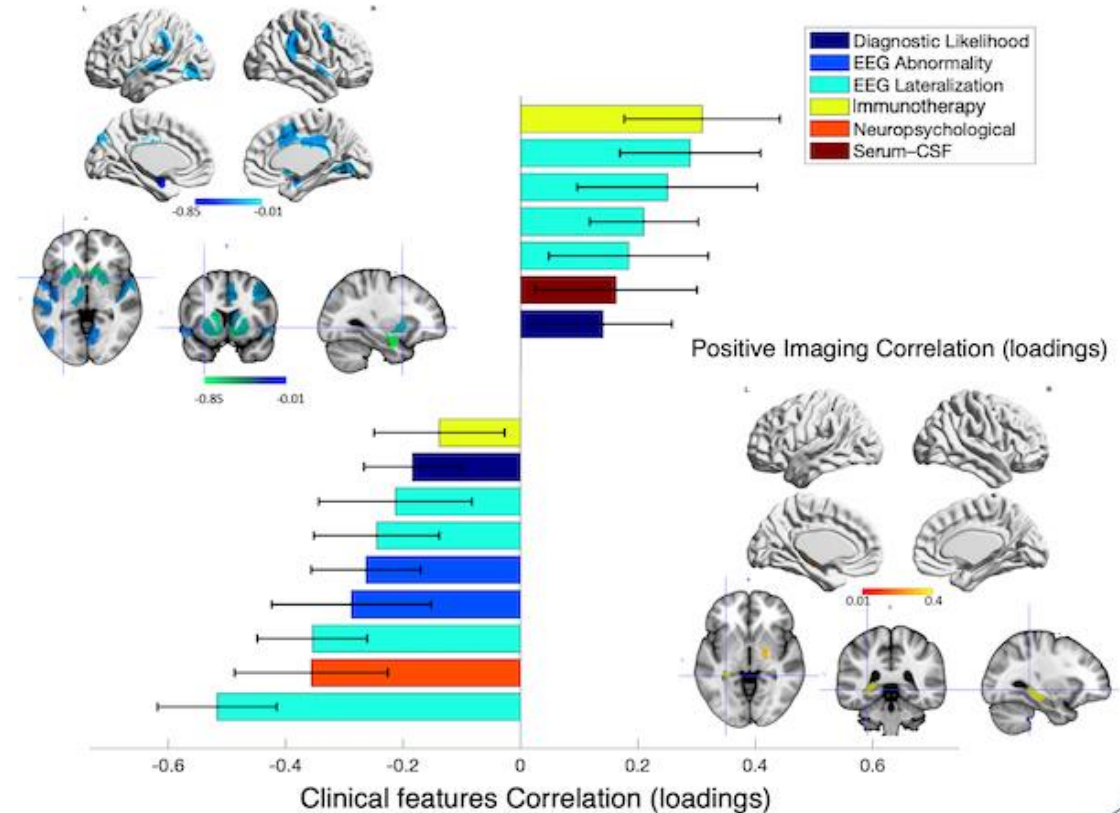
Multivariate associations between brain structure and clinical measurements:
Canonical Correlation Analysis (CCA)

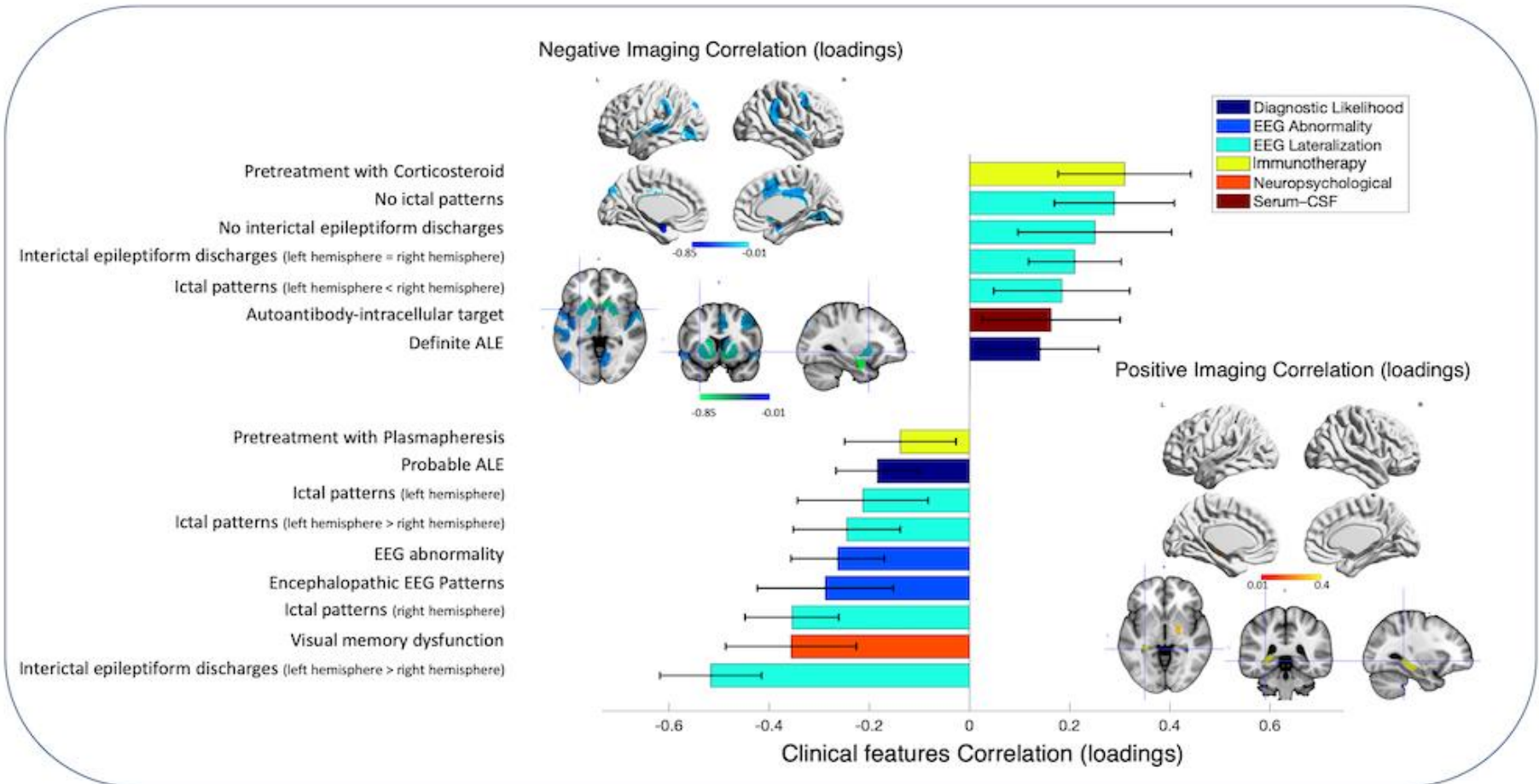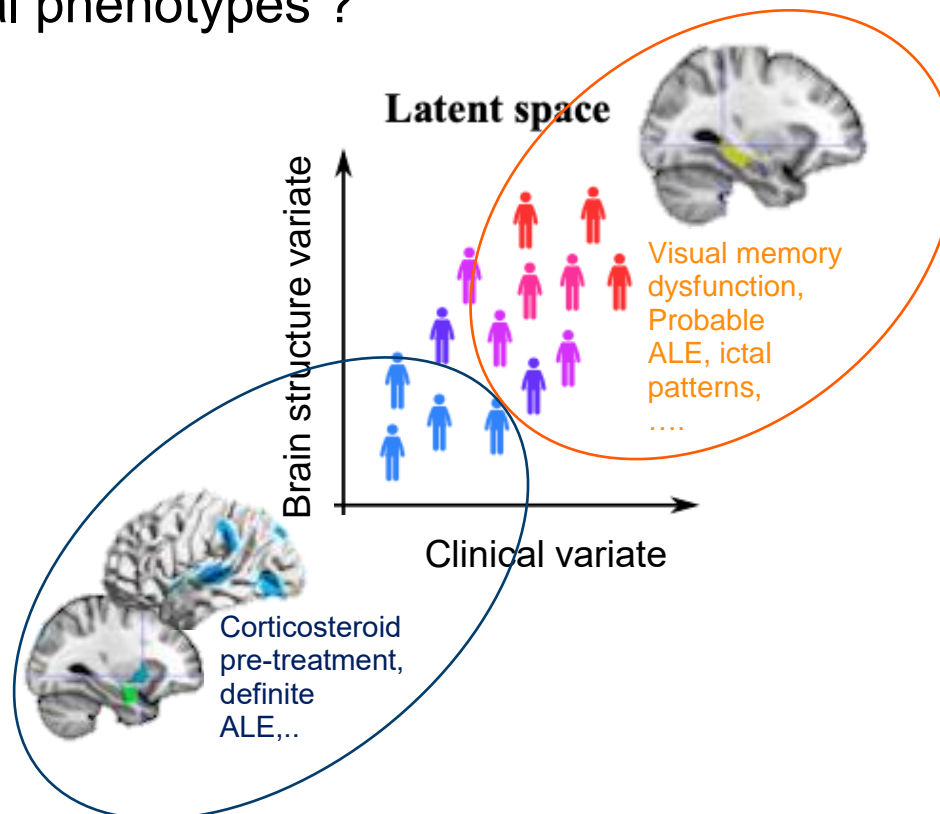# Multivariate associations between brain structure and clinical measurements:
# Canonical Correlation Analysis (CCA)

- Two structural brain patterns that differently relate to clinical variables

-> Different alterations of medial temporal lobe structure associated to different clinical phenotypes ?

Latent space

Brain structure variate

Clinical variate

Visual memory dysfunction, Probable ALE, ictal patterns, ...

Corticosteroid pre-treatment, definite ALE,..

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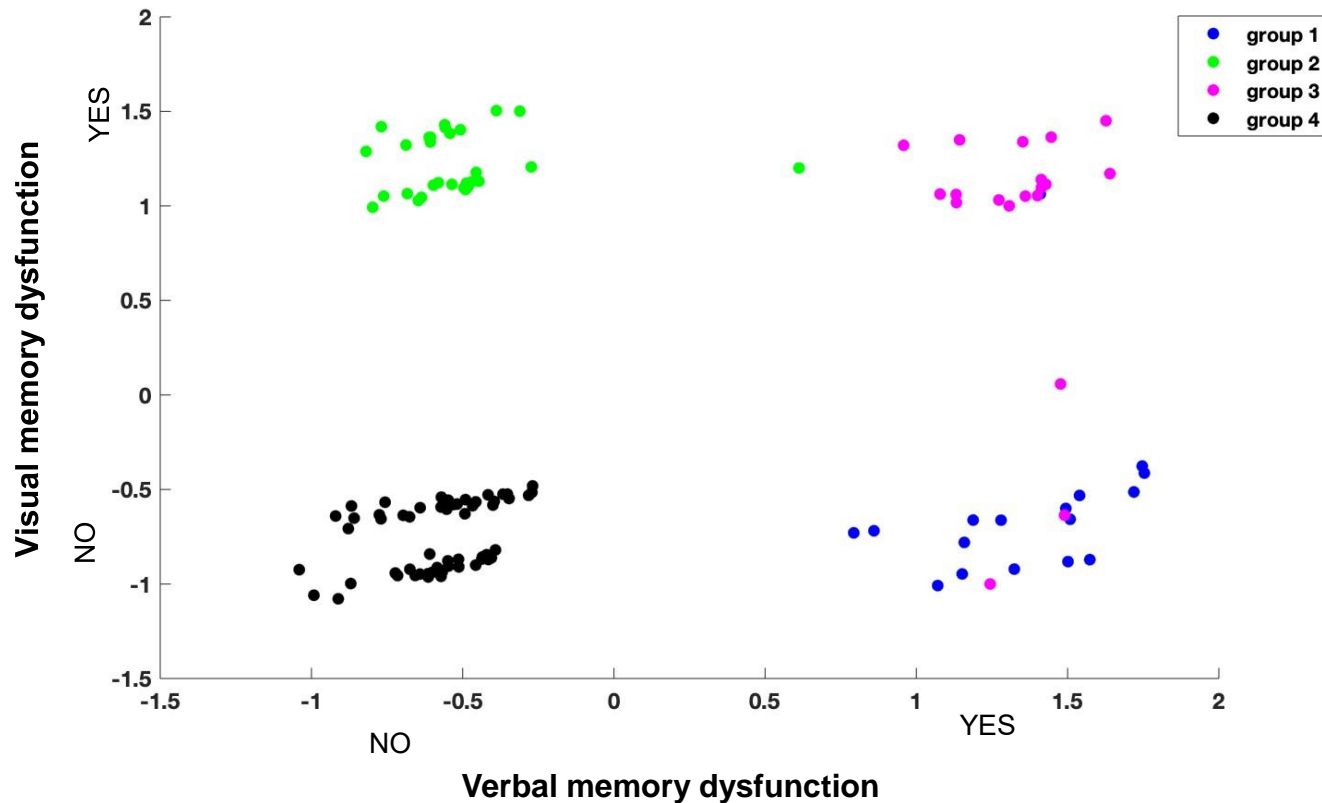# Data-driven clustering of ALE patients based on their scores on clinical measurments

Data-driven clustering of ALE patients based on their scores on clinical measurments

4 groups were identified
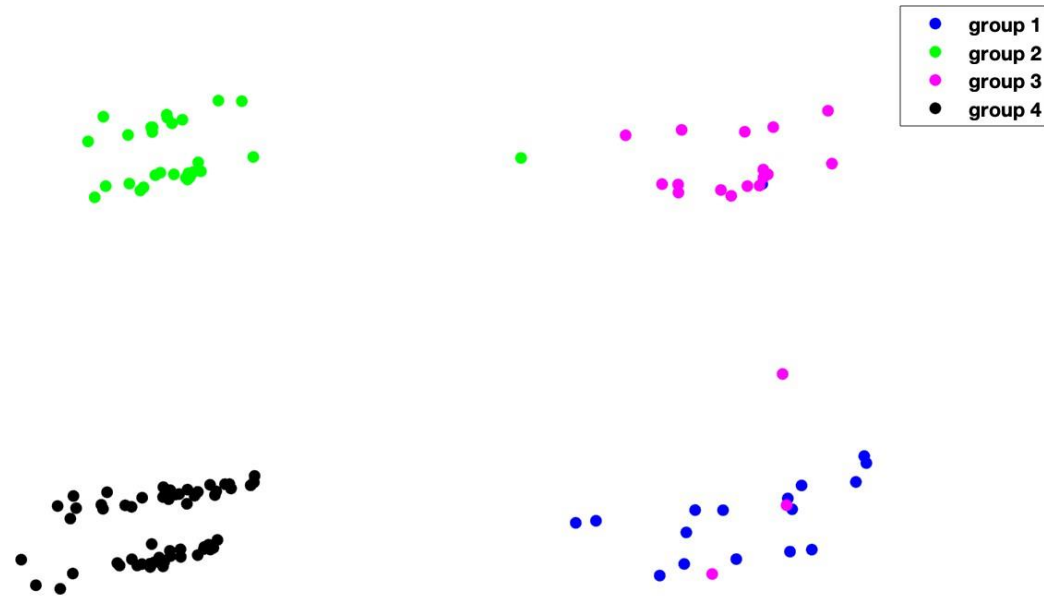
Data-driven clustering of ALE patients based on their scores on clinical measurments

4 groups were identified which mainly differ on their memory profile

Group 1: Patients with only Verbal memory dysfunction (n = 17)
Group 2: Patients with only Visual memory dysfunction (n = 29)
Group 3: Patients with both Verbal &Visual memory dysfunction (n = 19)
Group 4: Patients with No Verbal &Visual memory dysfunction (n = 57)

How do these groups differ in grey matter volume ?: General Linear Model Analysis

- Main effect of memory deficits (G4 > G1,G2,G3 or G4>G3):

- Only visual memory deficit vs. only verbal memory deficit (Group 2>Group 1):

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How do these groups differ in grey matter volume ?: General Linear Model Analysis
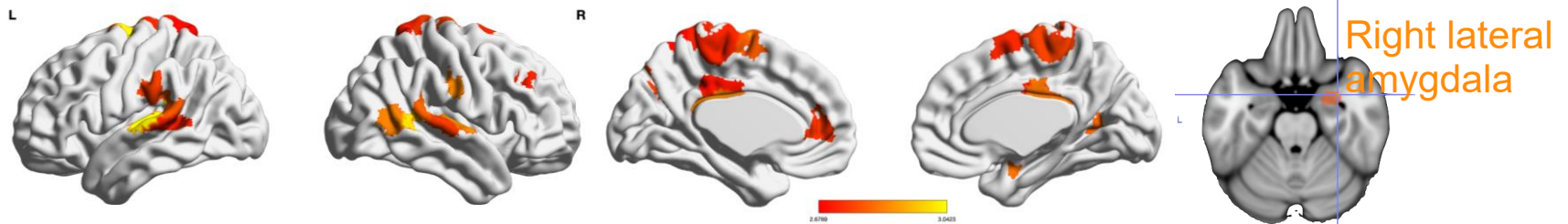
- Main effect of memory deficits (G4 > G1,G2,G3 or G4>G3):

Right posterior hippocampus

Left anterior and posterior hippocampus

- Only visual memory deficit vs. only verbal memory deficit (Group 2>Group 1):

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How do these groups differ in grey matter volume ?: General Linear Model Analysis

- Main effect of memory deficits (G4 > G1,G2,G3 or G4>G3):

Right posterior hippocampus

Left anterior and <mark>posterior</mark> hippocampus

- Only visual memory deficit vs. only verbal memory deficit (Group 2>Group 1):

Right lateral amygdala

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Conclusions and perspectives

- CCA summarizes variability in ALE patients population along a dimension

  - On which amygdala-cortical pattern represents a different pole than a posterior hippocampal atrophy pattern

  - In which MLT ictal patterns and EEG global abnormality load on a different pole than definite diagnosis and corticosteroid treatment

- Data-driven group comparison show that patients groups that differ in memory function profile also differ on posterior hippocampus vs. amygdala-cortical atrophy pattern

- Deeper clinical phenotyping (including socio-affective functions) of ALE patients is needed to better characterize different neurocognitive phenotypes

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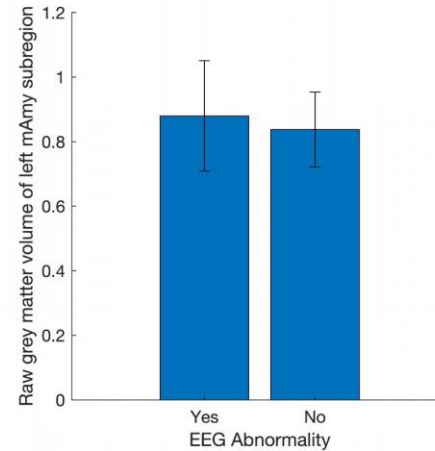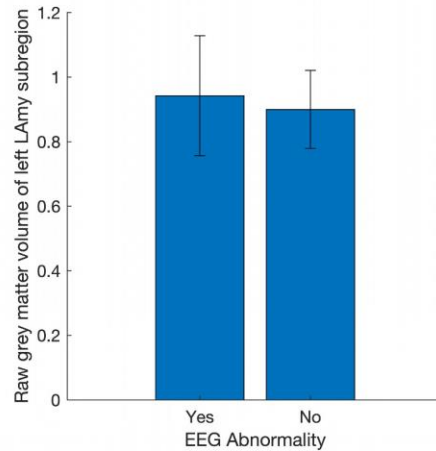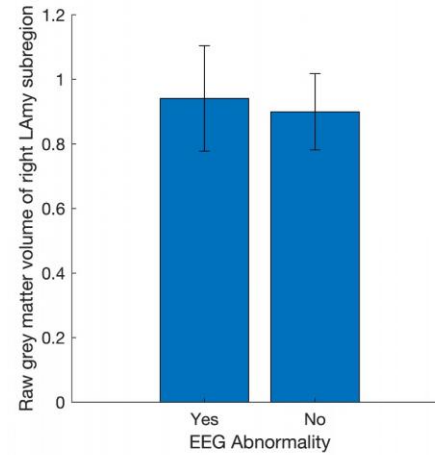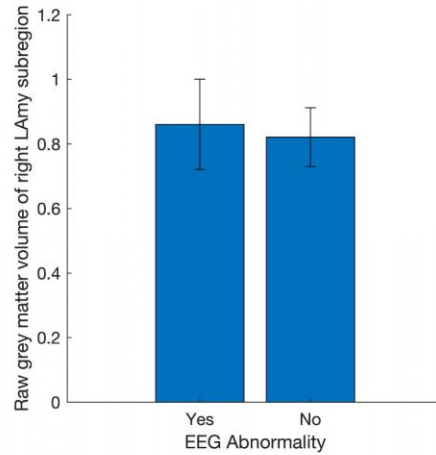
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EEG abnormality is not directly associated with amygdala GMV

Patients who do **not** have asymetric left epileptiform discharges are those with lower amygdala GMV