Manifold learning reveals anomalies of language and memory processing in patients with temporal lobe epilepsy

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Context and objectives

- Temporal lobe epilepsy (TLE) patients show neural reorganization of language and memory networks[1,2] in addition to alteration of different resting-state networks[3].
- These two functions have mainly been studied separately, but there is growing evidence about their dynamic interaction[4,5,6].
- We aim to explore abnormal patterns of activation within the joint language and episodic memory network in TLE patients during the tasks that engage one or the other function or both simultaneously.

Methods

- 21 right-handed participants (9 females, M_{age} = 21) and 12 left TLE patients (7 females, M_{age} = 35) performed sentence generation (GE), visual recognition (RECO) and recall with sentence generation (RA) tasks of GE2REC protocol[7].
- The ROIs were defined in the Brainnetome atlas[8] as those regions that had more than 40% of the voxels activated (p <.001, uncorrected; k > 20) in the control group during the tasks.
- Mean beta values were extracted using Rex toolbox[9] for each of the ROIs for each participant and patient for each task.

Pipeline

1. Dimension reduction

- By using the Umap[10] a set of standardized ROI beta values was converted into a unique point in a manifold subspace representing one participant during one task.

2. Model estimation

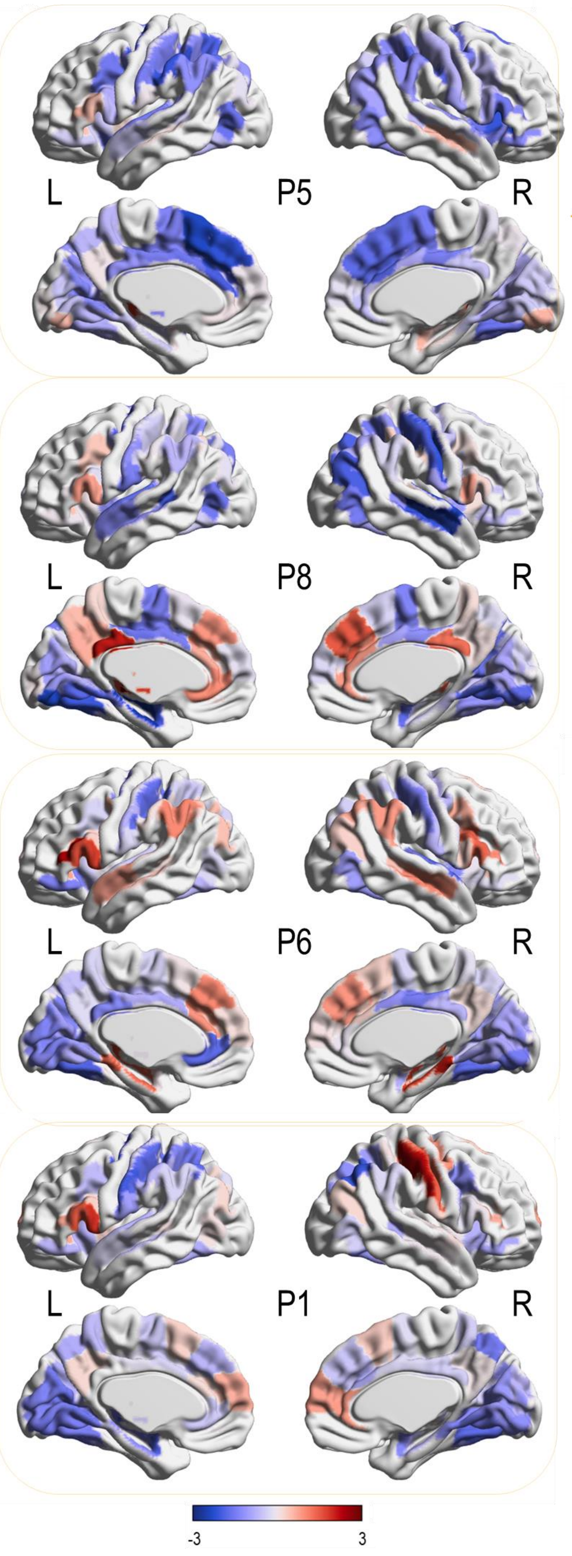
$$Y = f(x) + \varepsilon$$

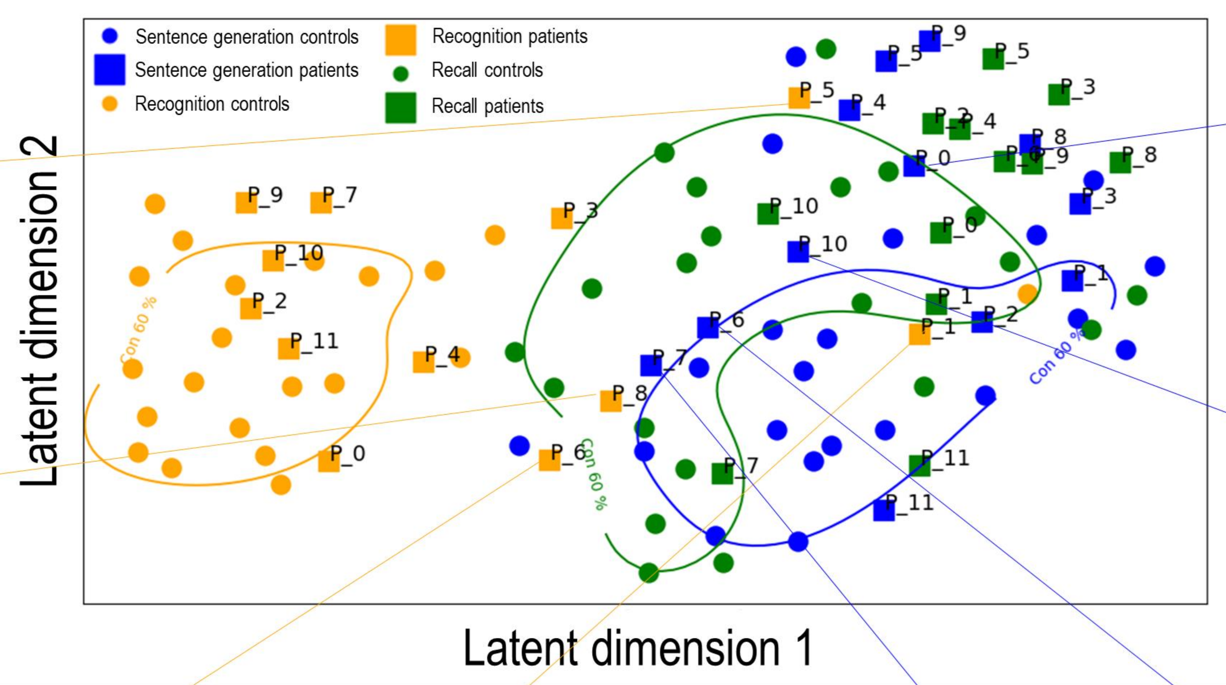
Y – values of all ROIs in real space
x – matching point in the reduced space
f(x) – non-linear kernel regression function

3. TLE patients analysis

- Patients are projected onto the learned manifold space in the point they would hold if they were healthy participants.
- ε depicts the abnormalities in the patient's dataset in the case when it is greater than the model variability obtained by the leave-one-out procedure.

Results





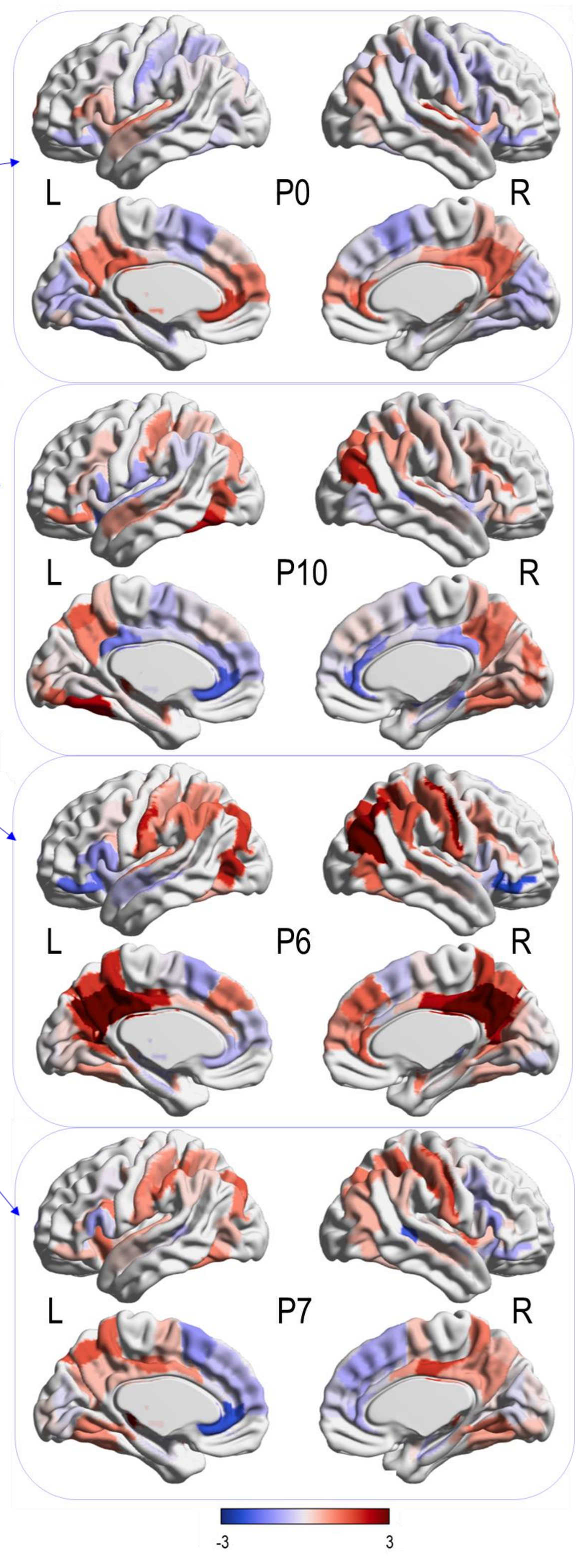


Figure 1. Projection of the patients onto the reconstructed manifold space. For each task the place where 60% of healthy subjects are situated is marked. The reconstructed manifold differentiated the tasks in an expected sense, with mixed task (RA) situated between language (GE) and memory (RECO) tasks. The highest dissimilarity between healthy participants and patients was found for the mixed task (RA) (D_{KL} = 1.37, p < .05). Patients also showed a higher tendency for dispersion and task overlap. The z-scores of patients whose language and memory task patterns shifted towards the mixed (RA) task are illustrated. Those patients whose memory patterns mapped on to the mixed task generally showed a tendency towards lower than expected activation in the hippocampal structures and the fusiform gyrus and some of them tended to have higher activation in the inferior frontal region. While those whose language task patterns mapped on to the mixed task showed a tendency towards less activations in some parts of inferior frontal gyrus and towards more activation in medial and lateral parietal regions.

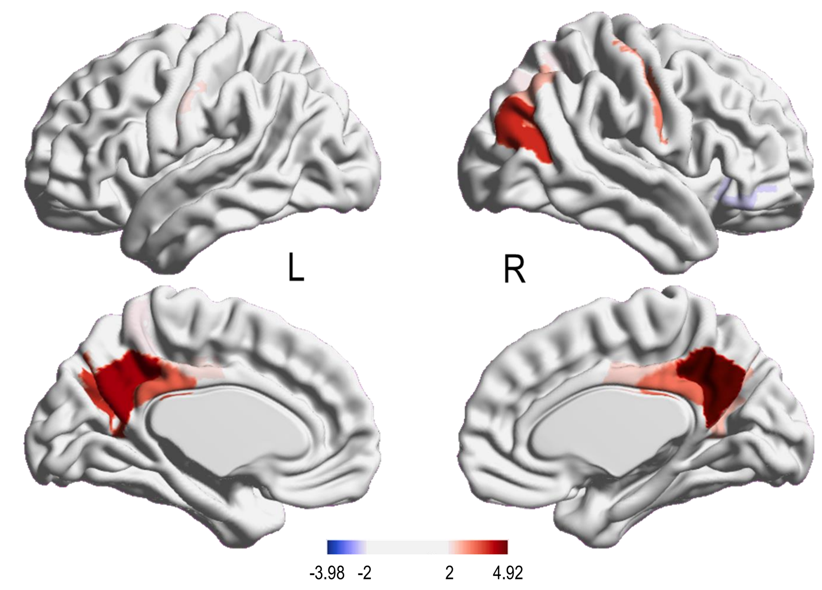


Figure 2. Residual map for the language task (GE) for a patient (P6) with lexical access (DO80[11]). Residuals above/below 2SD were taken as a measure of deviation. Tendency for lower than predicted values was found in the right frontal orbital cortex, while a tendency towards higher values was found in the bilateral precuneus, bilateral middle and posterior cingulum and right angular gyrus.

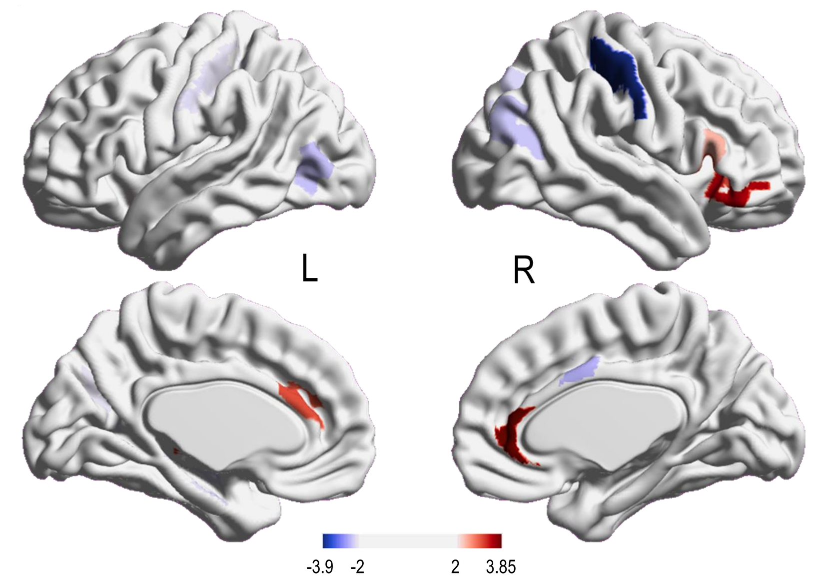


Figure 3. Residual map for memory task for a patient (P0) with difficulties with verbal episodic memory (GB[12]). Residuals above/below 2SD were taken as a measure of deviation. Lower than predicted values are found in the left parahippocampus, bilateral postcentral and bilateral middle occipital, while higher were found in left and right anterior cingulum, right frontal inferior opercularis, triangularis and orbitalis.

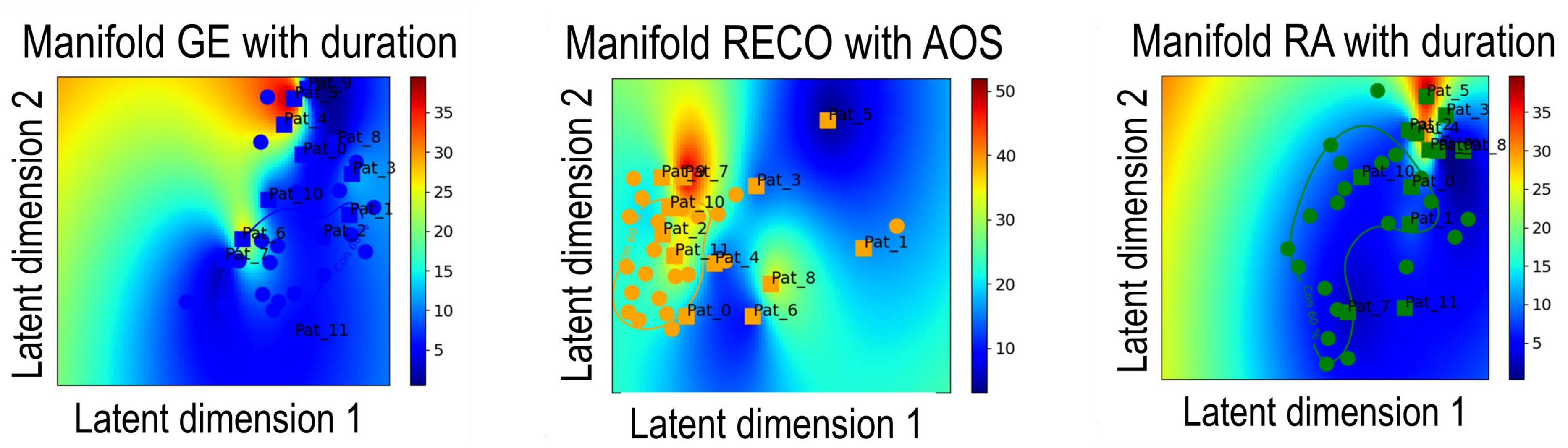


Figure 4. Projection of epilepsy duration and age of onset (ASO) onto the manifold space. The duration of the epilepsy could help to explain the positioning of the patients in the manifold space. TLE patients with longer duration of the illness tended to map further away from the healthy subjects regarding language (GE) and mixed language and memory task (RA). While TLE patients with earlier start of the epilepsy tended to map further from the healthy participants with respect to the recognition task (RECO).

Conclusions

- The non-linear manifold learning for fMRI data dimension reduction can be used as a solution to the problem of high dimensionality of the data.
- This approach enables comparing all the regions of interest simultaneously taking into account their relationship.
- Importantly, using the presented approach we can obtain the measure of deviation.
- The proposed approach is especially relevant for single case and small sample studies.

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