

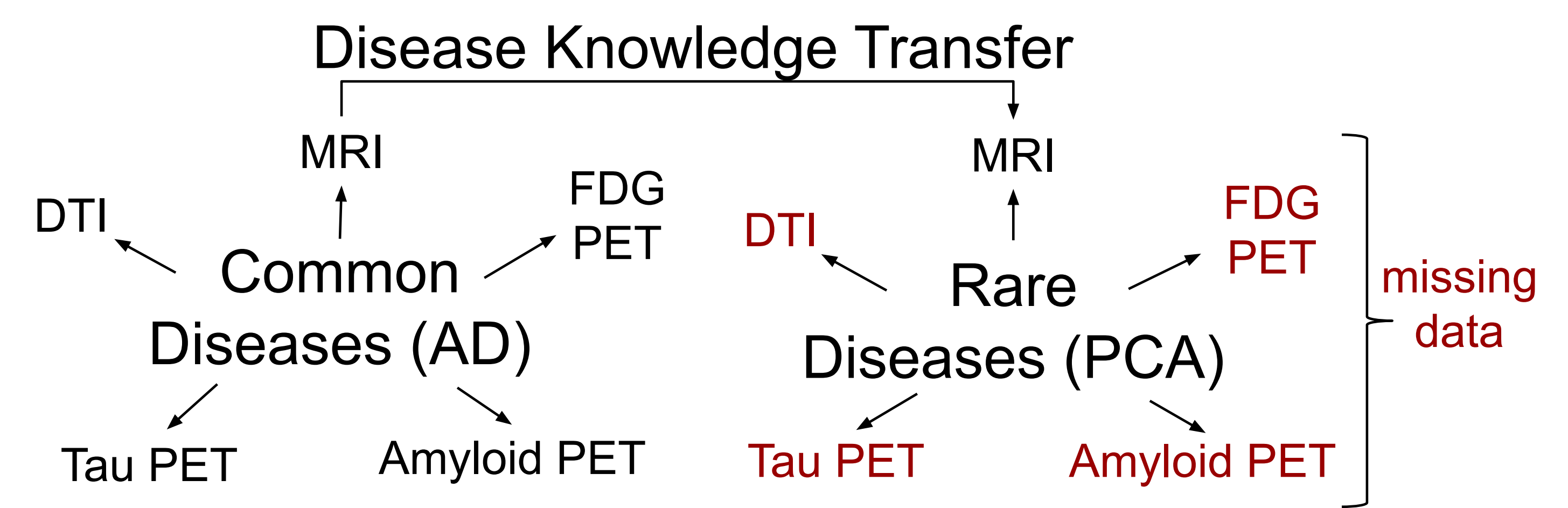
# Disease Knowledge Transfer across Neurodegenerative Diseases



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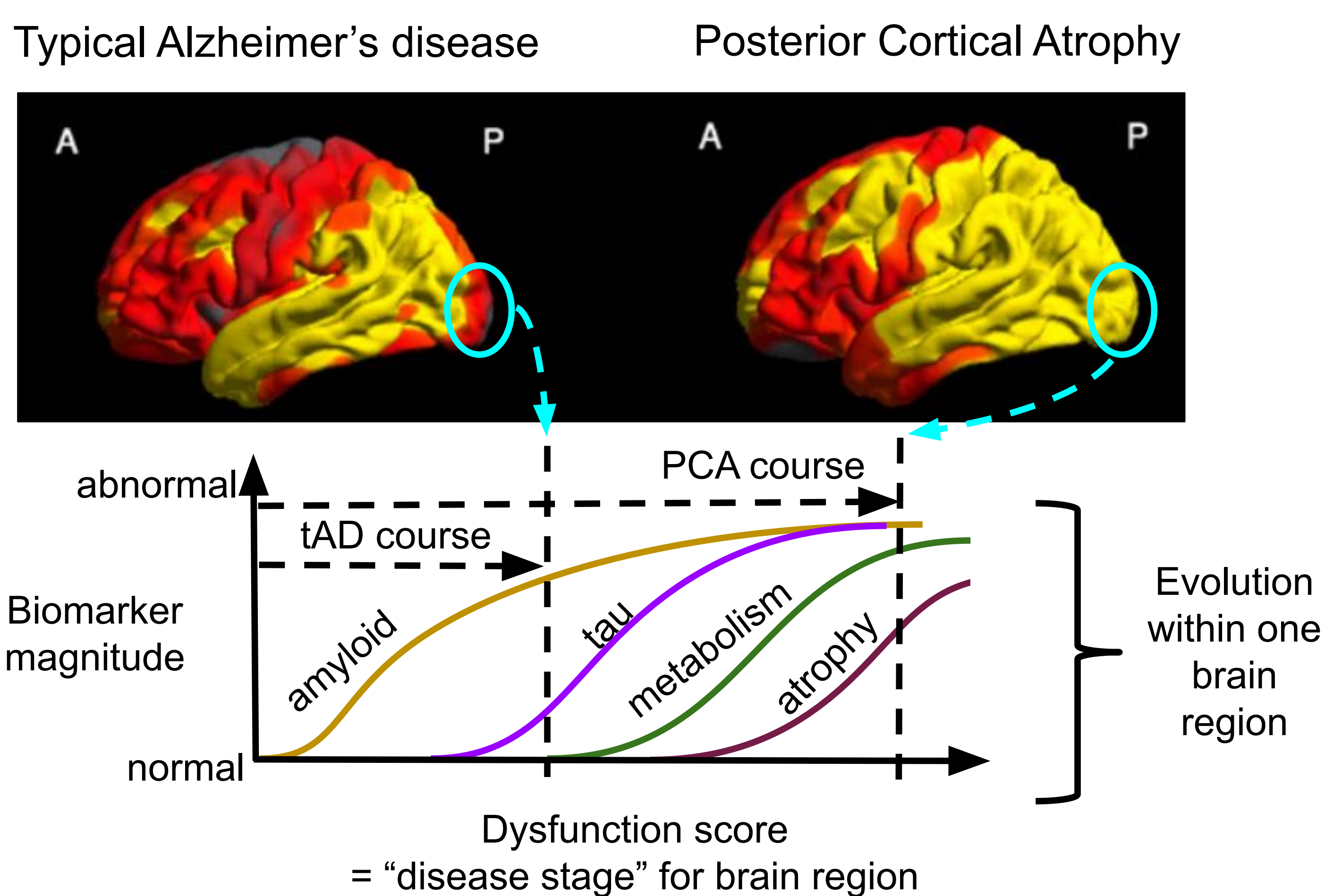
**Aim:** Infer progression of multimodal biomarkers in rare neurodegenerative diseases (NDs) by leveraging larger datasets of common NDs.

**Why:** Posterior Cortical Atrophy (PCA): progression of multimodal biomarkers not known → Identify outcome measures and suitable subjects for PCA clinical trials.



## 1. Intuition

- Diseases affect different brain regions un-equally, but underlying mechanisms are the same (amyloid cascade).
- **Idea:** each brain region follows “its own disease course”, common across diseases.

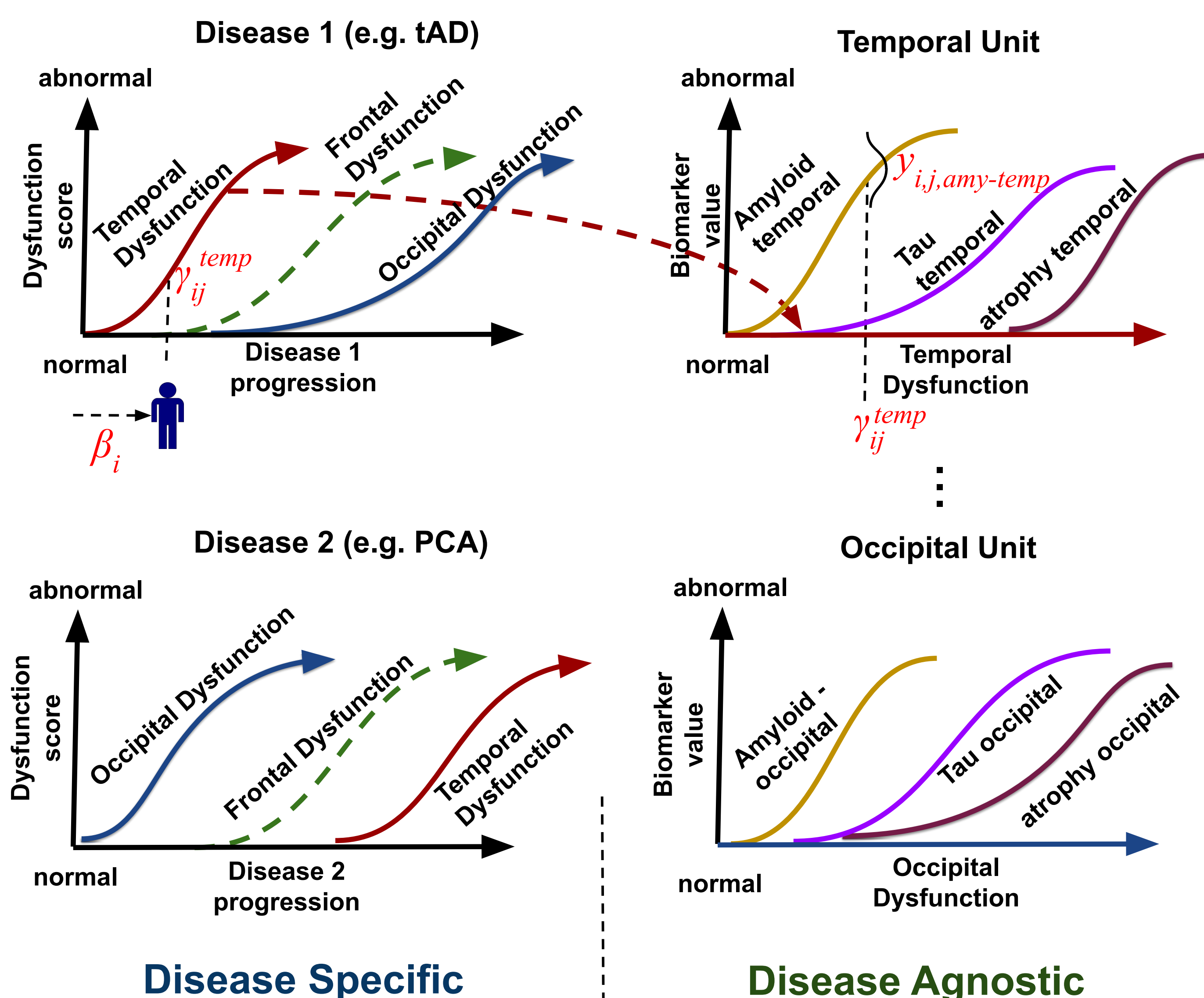


## 2. Method

1. Each disease characterised by region-specific dysfunction trajectories
2. Dysfunction trajectory modelled using region-specific biomarkers

$$\gamma_{ij}^l = f(\beta_i + m_{ij}; \lambda_{d_i}^l)$$

$$y_{ijk} = g(\gamma_{ij}^k; \theta_k) + N(0, \epsilon_k)$$



## 3. Inference with belief propagation

while  $\theta, \lambda, \beta$  not converged do

; // Estimate biomarker trajectories (disease agnostic)

$$\theta_k^{(u)} = \arg \min_{\theta_k} \sum_{(i,j) \in \Omega_k} \left[ y_{ijk} - g \left( f(\beta_i^{(u-1)} + m_{ij}; \lambda_{d_i}^{k,(u-1)}); \theta_k \right) \right]^2$$

; // Estimate dysfunction trajectories (disease specific)

$$\lambda_d^{l,(u)} = \arg \min_{\lambda_d^l} \sum_{(i,j,k) \in \Omega_{d,l}} \left[ y_{ijk} - g \left( f(\beta_i^{(u-1)} + m_{ij}; \lambda_d^l); \theta_k^{(u)} \right) \right]^2$$

; // Estimate subject-specific time shifts

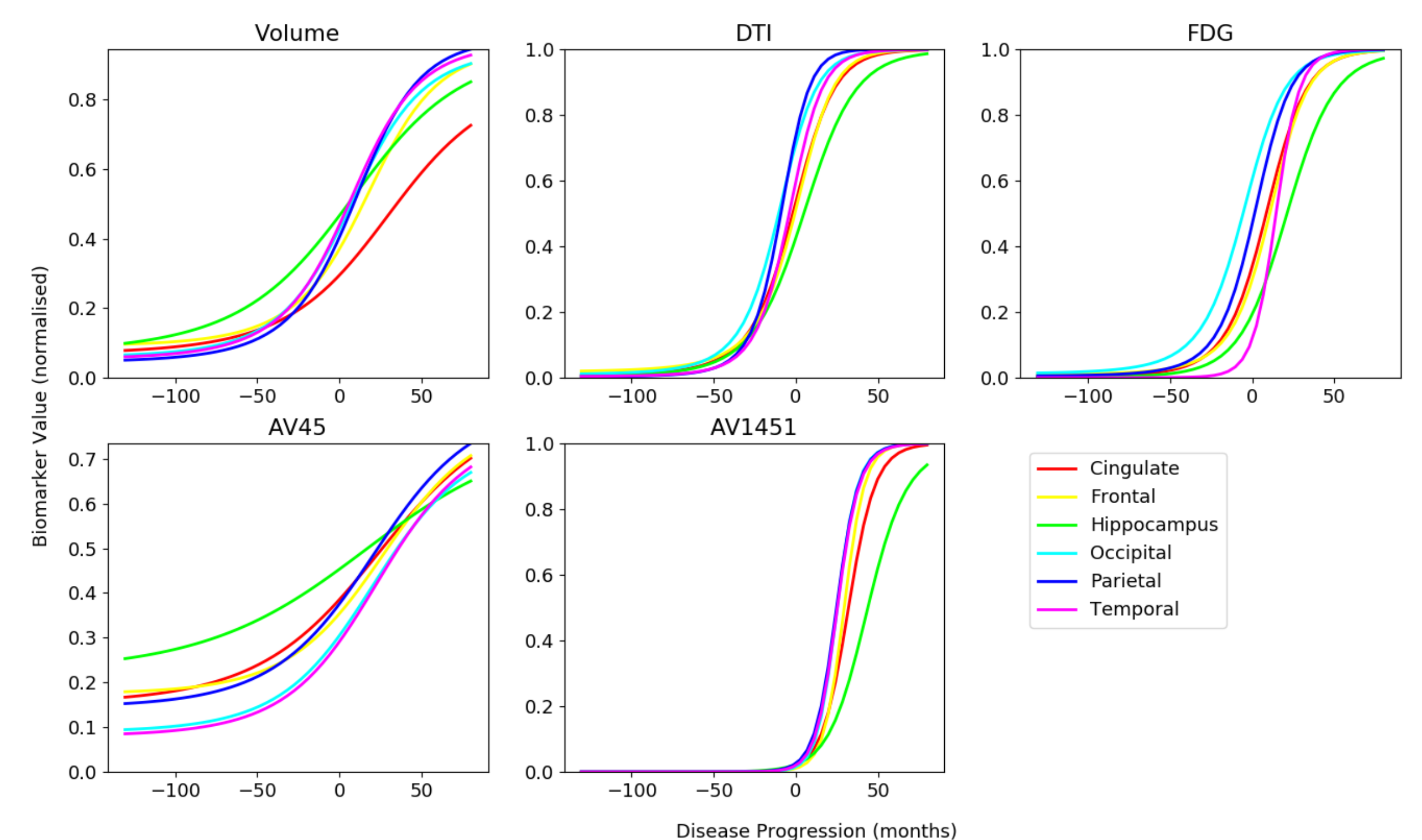
$$\beta_i^{(u)} = \arg \min_{\beta_i} \sum_{(j,k) \in \Omega_i} \left[ y_{ijk} - g \left( f(\beta_i + m_{ij}; \lambda_{d_i}^{k,(u)}); \theta_k^{(u)} \right) \right]^2$$

## 4. Datasets

- Dementia Research Center cohort: MRI scans from 76 PCA, 67 tAD, 87 controls for training, 10 PCA with DTI for validation.
- TADPOLE dataset (ADNI) split into three subgroups with different progressions: 21 hippocampal, 35 cortical, 27 subcortical.

## 5. Results

- Inferred multimodal trajectories for PCA in lack of such data.
- Results are plausible, suggesting late-stage posterior damage.



- Our model has favourable performance compared to other models, on two different datasets.

Model	Cingulate	Frontal	Hippocam.	Occipital	Parietal	Temporal
<b>TADPOLE: Hippocampal subgroup to Cortical subgroup</b>						
DKT (ours)	0.56 ± 0.23	<b>0.35 ± 0.17</b>	<b>0.58 ± 0.14</b>	-0.10 ± 0.29	<b>0.71 ± 0.11</b>	<b>0.34 ± 0.26</b>
AD model	0.44 ± 0.25	0.34 ± 0.21	0.34 ± 0.24*	<b>-0.07 ± 0.22</b>	0.64 ± 0.16	0.08 ± 0.24*
Multivariate	<b>0.60 ± 0.18</b>	0.11 ± 0.22*	0.12 ± 0.29*	-0.22 ± 0.22	-0.44 ± 0.14*	-0.32 ± 0.29*
Spline	-0.24 ± 0.25*	-0.06 ± 0.27*	0.58 ± 0.17	-0.16 ± 0.27	0.23 ± 0.25*	0.10 ± 0.25*
Linear	-0.24 ± 0.25*	0.20 ± 0.25*	0.58 ± 0.17	-0.16 ± 0.27	0.23 ± 0.25*	0.13 ± 0.23*
<b>typical Alzheimer's to Posterior Cortical Atrophy</b>						
DKT (ours)	0.77 ± 0.11	0.39 ± 0.26	0.75 ± 0.09	0.60 ± 0.14	<b>0.55 ± 0.24</b>	<b>0.35 ± 0.22</b>
AD model	<b>0.80 ± 0.09</b>	<b>0.53 ± 0.17</b>	<b>0.80 ± 0.12</b>	0.56 ± 0.18	0.50 ± 0.21	0.32 ± 0.24
Multivariate	0.73 ± 0.09	0.45 ± 0.22	0.71 ± 0.08	-0.28 ± 0.21*	0.53 ± 0.22	0.25 ± 0.23*
Spline	0.52 ± 0.20*	-0.03 ± 0.35*	0.66 ± 0.11*	0.09 ± 0.25*	0.53 ± 0.20	0.30 ± 0.21*
Linear	0.52 ± 0.20*	0.34 ± 0.27	0.66 ± 0.11*	<b>0.64 ± 0.17</b>	0.54 ± 0.22	0.30 ± 0.21*

## 6. Conclusion

- Developed a novel methodology and model for transfer learning across different diseases
- Inferred multimodal trajectories for Posterior Cortical Atrophy

### Weblinks

- Source code: <https://github.com/mrazvan22/dkt>
- Website: <https://people.csail.mit.edu/razvan/>

### Funders

