Disease Knowledge Transfer across Neurodegenerative Diseases

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Aim

Propose mechanism to infer progression of non-MRI biomarkers in rare neurodegenerative diseases by leveraging larger datasets of common neurodegenerative diseases.

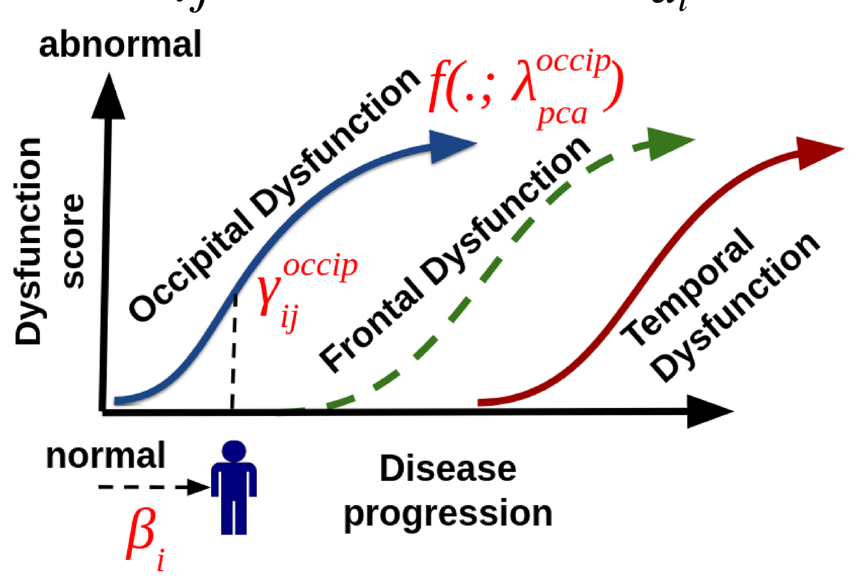
Why

- Datasets on rare neurodegenerative diseases (e.g., Posterior Cortical Atrophy) are unimodal (MRI only), cross-sectional and small.
- The continuous progression of non-MRI markers in rare neurodegenerative diseases is not well understood

Method

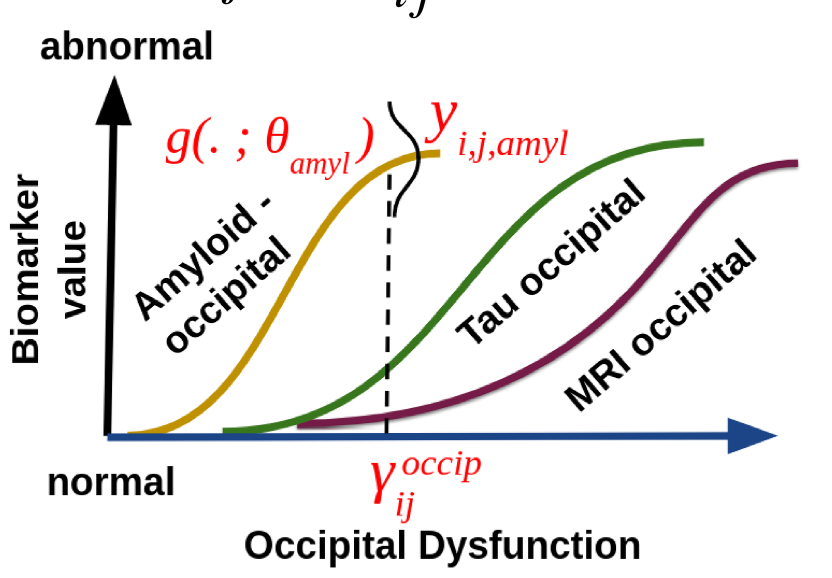
1. Each disease characterised by region-specific dysfunction profile

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



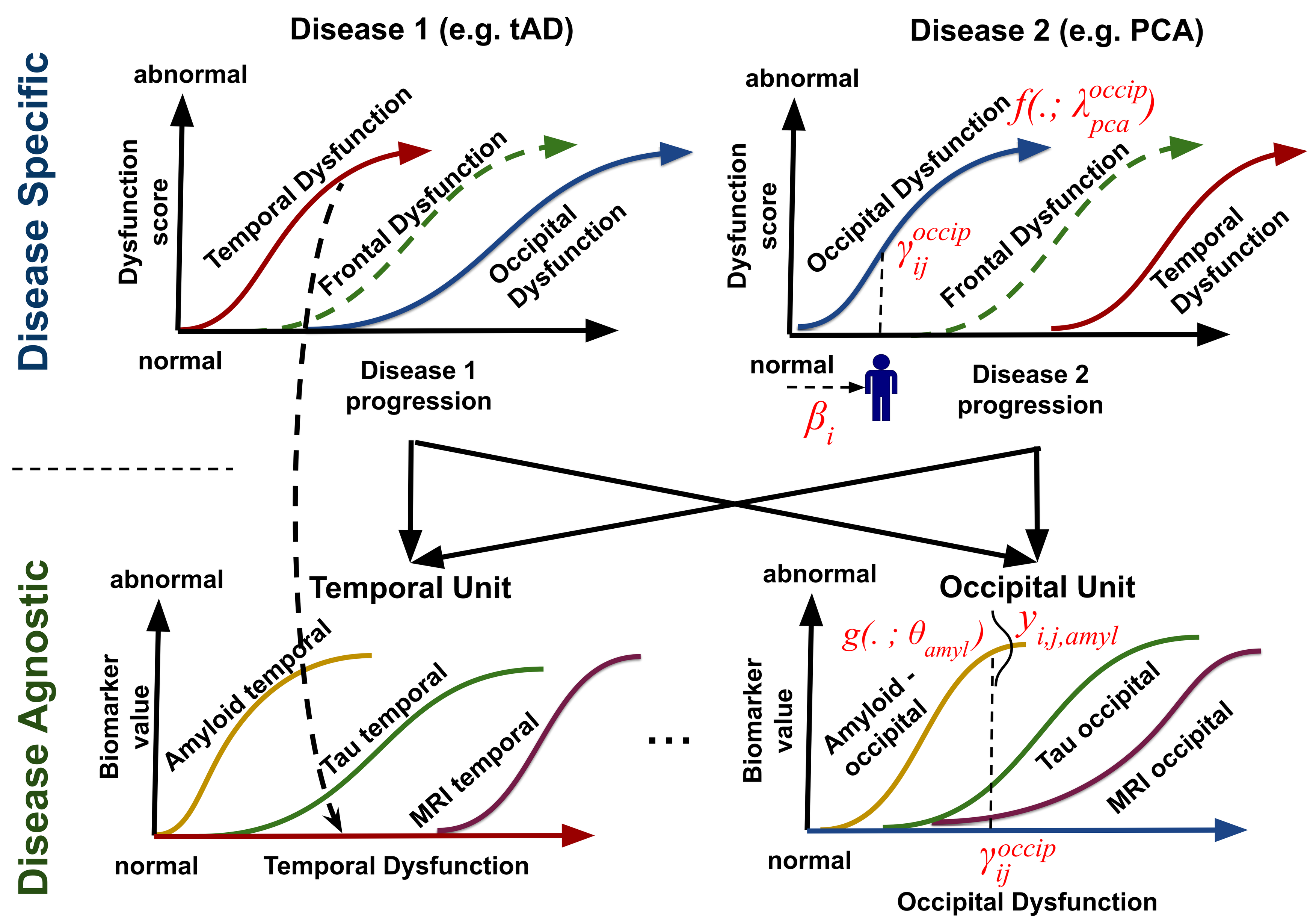
2. Dysfunction score modelled using region-specific biomarkers

$$p(y_{ijk}|\theta_k, \lambda_{d_i}^{\psi(k)}, \beta_i, \epsilon_k) = N(y_{ijk}|g(\gamma_{ij}^{\psi(k)}; \theta_k), \epsilon_k)$$



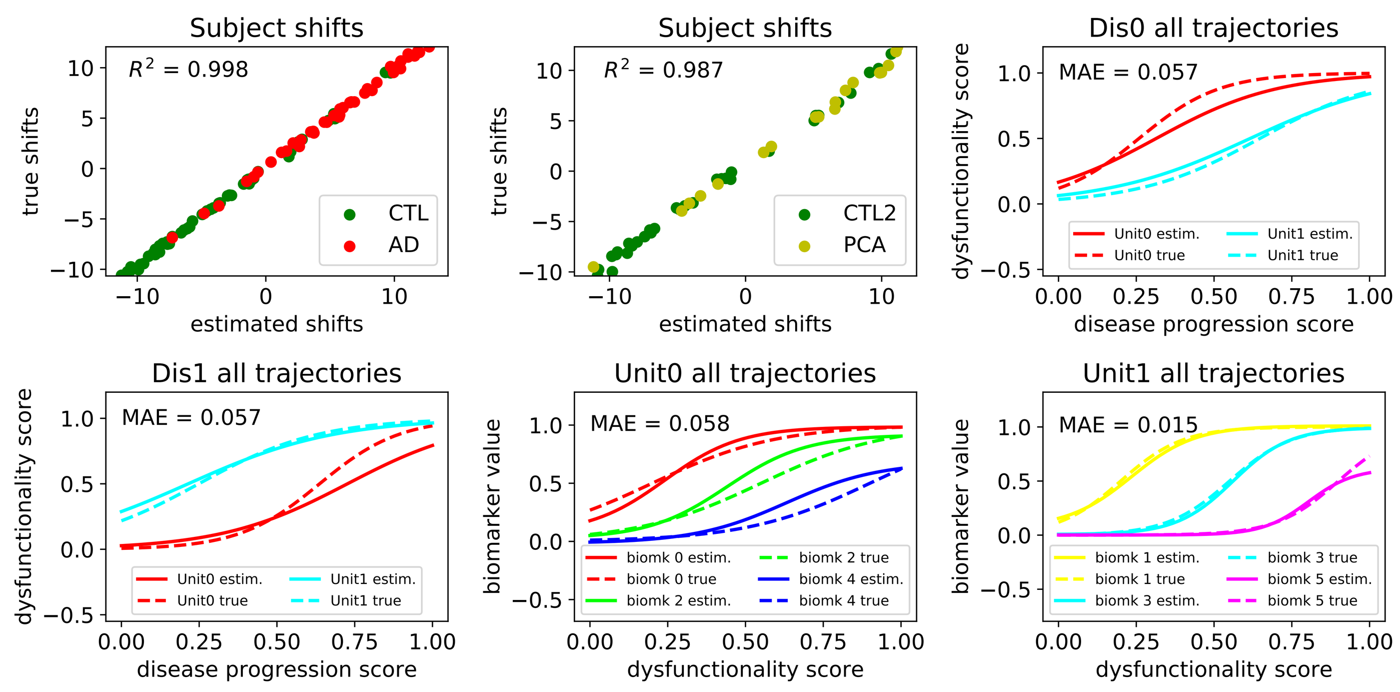
3. Extend to multiple subjects, biomarkers and diseases

$$p(\mathbf{y}|\theta, \lambda, \beta, \epsilon) = \prod_{(i,j,k)\in\Omega} p(y_{ijk}|\theta_k, \lambda_{d_i}^{\psi(k)}, \beta_i)$$

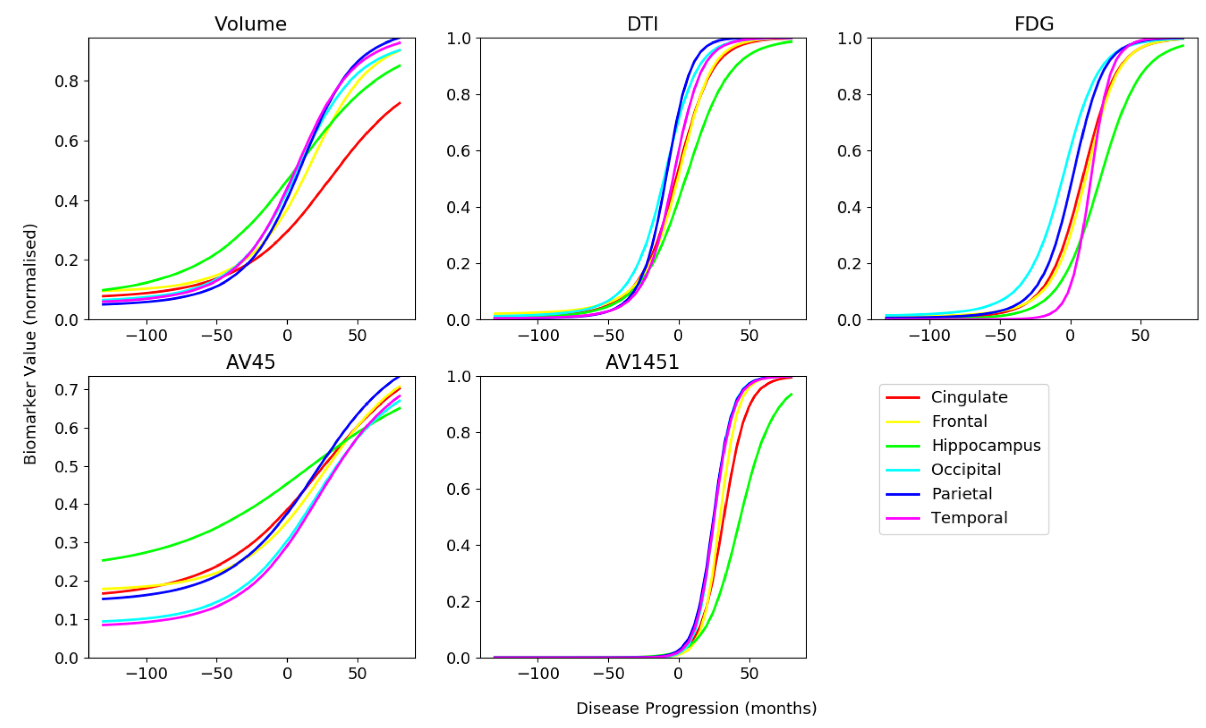


Results

Synthetic experiment shows that the model can recover the underlying parameters



Inferred trajectories for Posterior Cortical Atrophy



Our model has favourable performance compared to other models

Model	Cingulate	Frontal	Hippocam.	Occipital	Parietal	Temporal
	TADPOLE: Hippocampal subgroup to Cortical subgroup					
DKT (ours)	0.56 ± 0.23	**0.35** ± **0.17**	**0.58** ± **0.14**	-0.10 ± 0.29	**0.71** ± **0.11**	**0.34** ± **0.26**
Latent stage	0.44 ± 0.25	0.34 ± 0.21	0.34 ± 0.24*	**-0.07** ± **0.22**	0.64 ± 0.16	0.08 ± 0.24*
Multivariate	**0.60** ± **0.18**	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*
	typical Alzheimer's to Posterior Cortical Atrophy					
DKT (ours)	0.77 ± 0.11	0.39 ± 0.26	0.75 ± 0.09	0.60 ± 0.14	**0.55** ± **0.24**	**0.35** ± **0.22**
Latent stage	**0.80** ± **0.09**	**0.53** ± **0.17**	**0.80** ± **0.12**	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*	**0.64** ± **0.17**	0.54 ± 0.22	0.30 ± 0.21*

Conclusion

References

1. Fontejin et al., Neuroimg., 2012
2. Young et al., Nat. Comms., 2018
3. Villemagne et al., Lancet Neurol., 2013
4. Marinescu et al., IPMI, 2017

Weblinks

- UCL Progression of Neurodegenerative Disease (POND): cmic.cs.ucl.ac.uk/pond/
- UCL Centre for Medical Image Computing: www.ucl.ac.uk/cmic/

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