



Regional gray matter volume and default mode network connectivity are associated with age relative to parental symptom onset in sporadic Alzheimer's disease

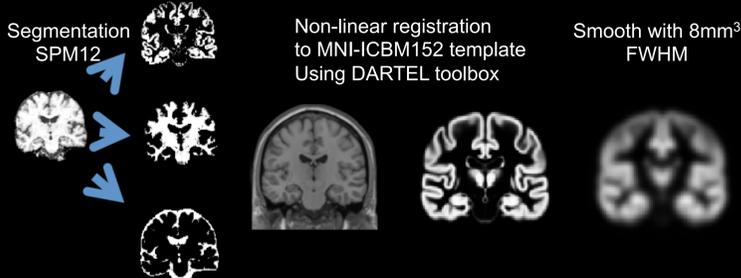
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Background and objectives

- In autosomal dominant Alzheimer's disease (AD) mutations, individuals demonstrate increasing abnormality in AD-related biomarkers as they approach their parent's age of symptom onset. This paradigm has never been tested in sporadic AD.
- AD is characterized by regionally-specific gray matter degeneration, as well as alterations in resting state functional connectivity (rsFC). The default mode network appears especially vulnerable to AD, especially early in the disease process.
- We test whether time till parental symptom onset (tPSO) is associated with abnormality in regional gray matter density (GMD) and rsFC in individuals with a parental history of sporadic AD.

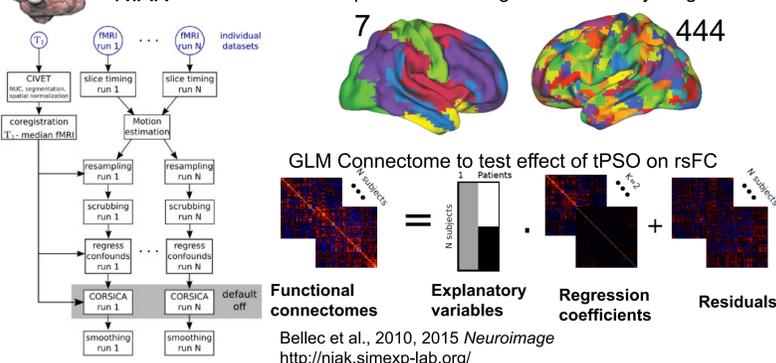
Image Processing

Structural (n=270)

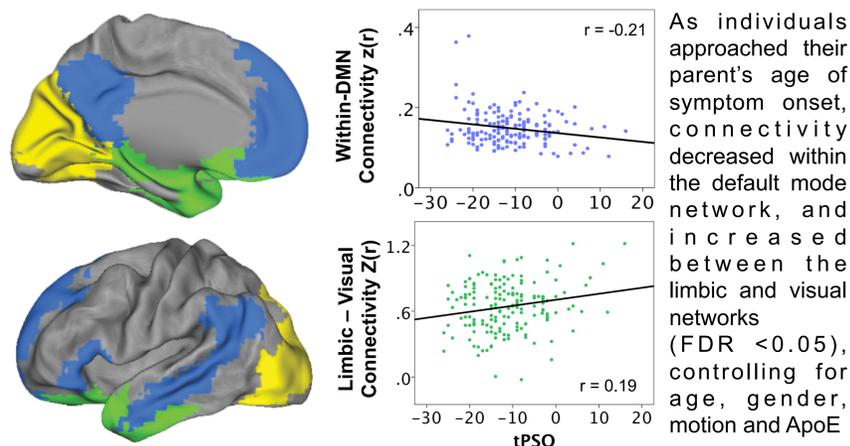


Functional (n=170)

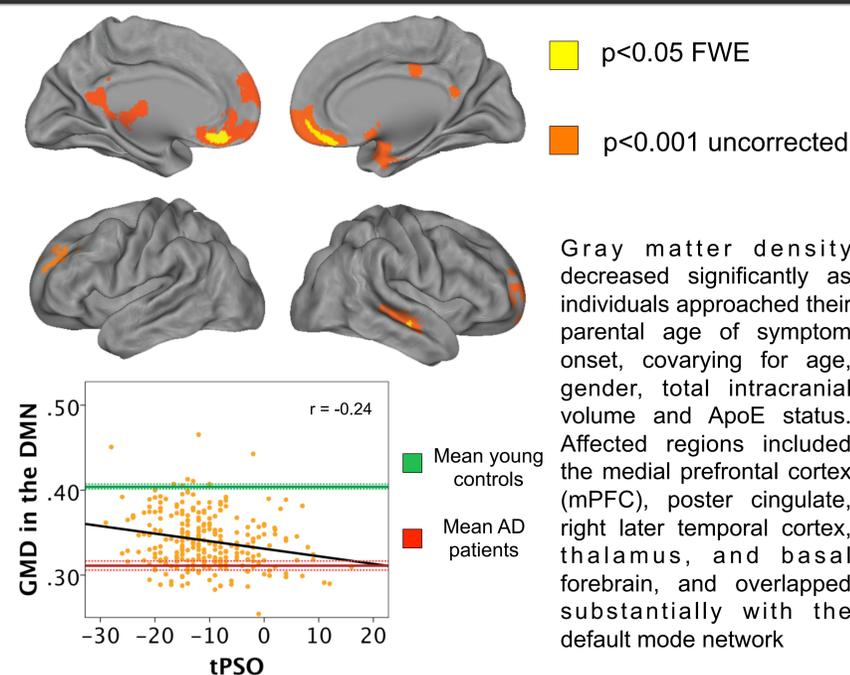
Functional parcellation using BASC on 197 young controls



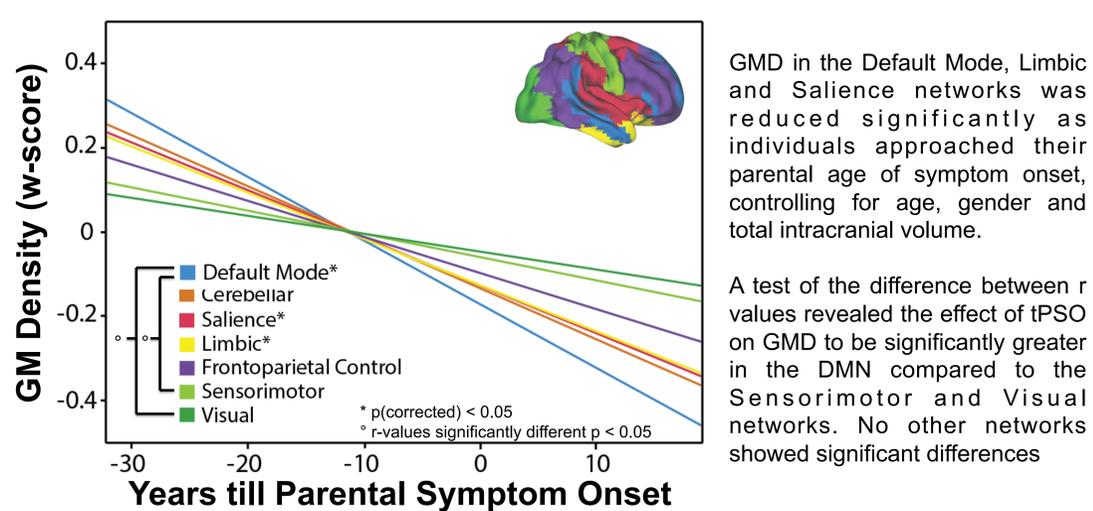
Effect of tPSO on rsFC



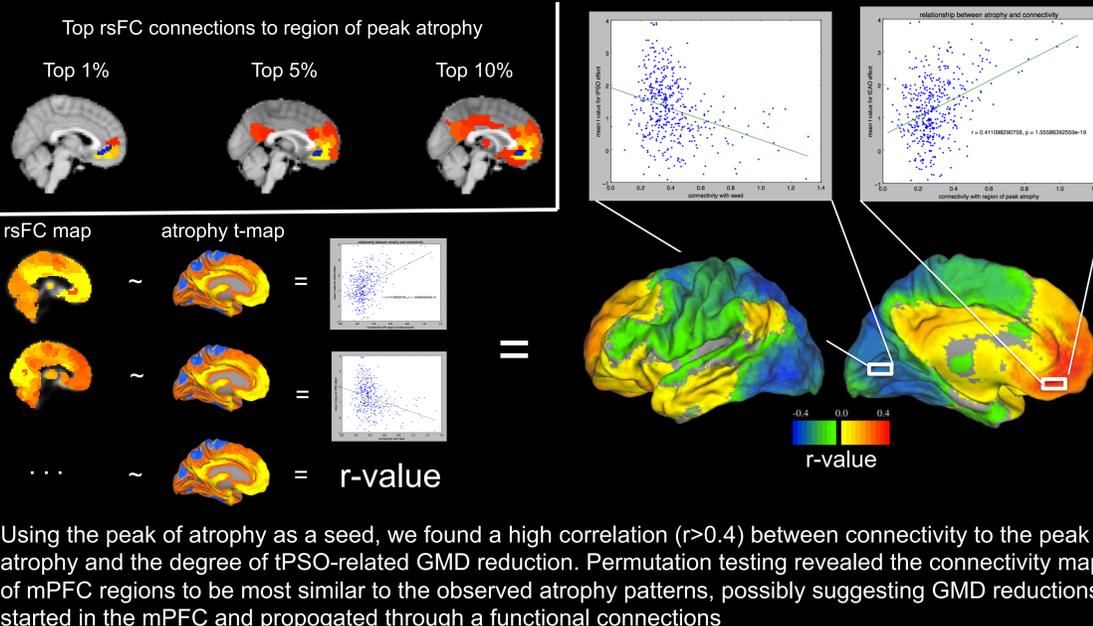
Effect of tPSO on GMD



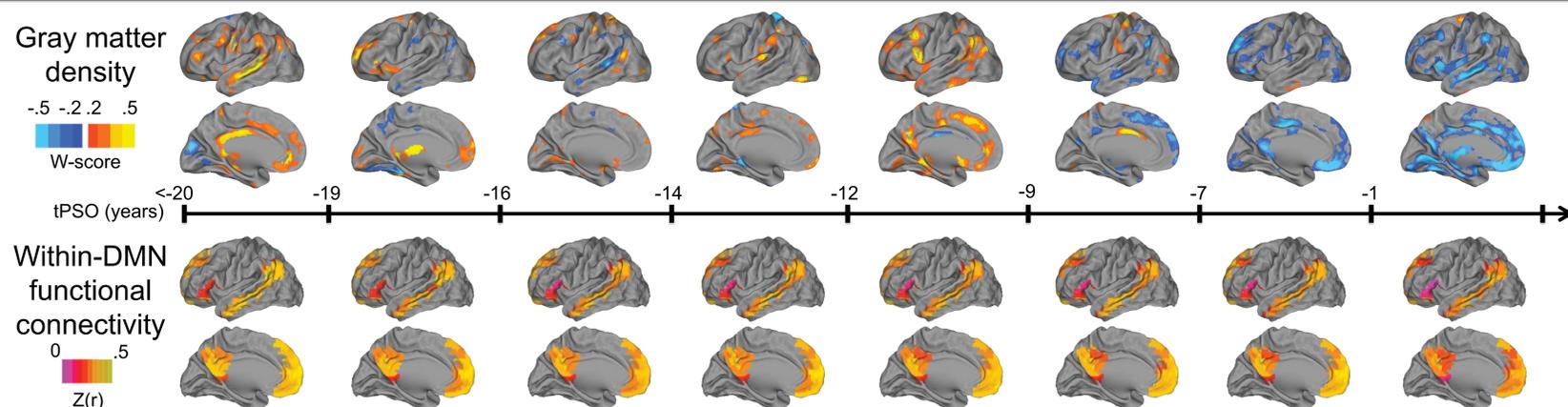
Is the observed pattern of GMD reduction restricted to the DMN?



Is atrophy propagating through functional networks?



GMD and within-DMN rsFC are reduced as individuals approach parental onset age



Summary and Conclusions

- Gray matter density and resting state functional connectivity were found to be more abnormal the closer individuals were to their parent's age of symptom onset. This is the first study to demonstrate this effect in sporadic Alzheimer's disease.
- Consistent with the pathological signature of early Alzheimer's disease, the observed effect was greatest within the default mode network.
- The observed effects were independent of ApoE, suggesting the gene cannot fully explain disease risk conferred by parental history of AD
- The observed similarity between certain resting state connectivity networks and the pattern of atrophy provides further evidence that gray matter degeneration may propagate through functional networks