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Consistent functional connectivity pattern associated with Alzheimer's disease genetic risk factor APOE4

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BACKGROUND

- Alzheimer's disease (AD) is the most common cause of dementia in older adults and an effective treatment needs to be administered as early as possible [1].
- Advanced fMRI technics characterize brain change at earliest disease stages of AD [2].
- A genetic risk factor for late-onset sporadic AD is having at least one ApolipoproteinE4 (ApoE4) allele [3].

AIMS

The **aim** of our study is to provide a better understanding of brain functional connectivity (FC) in individuals having the genetic risk factor.
Our principal **hypothesis** are that (1) individuals with at least one ApoE4 allele present a **different** brain FC compared to non-carriers.
(2) **consistent** ApoE4 associated differences in brain connectivity can be observed at **all stages of AD**.

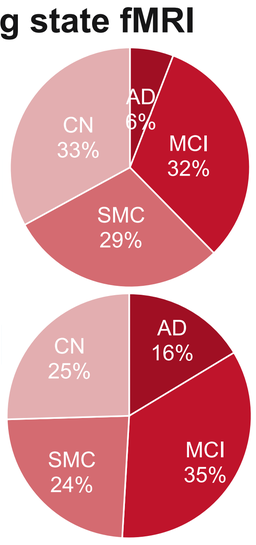
METHODS

ADNI database – 10 min resting state fMRI

Total 138 subjects

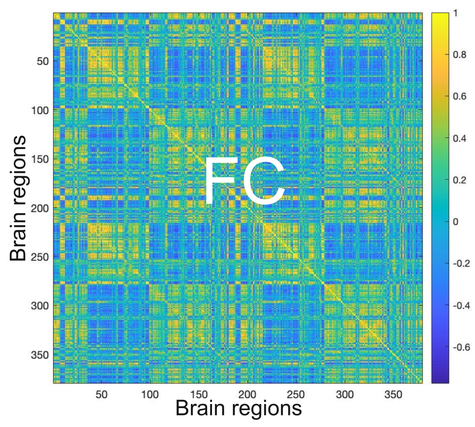
42 CN
38 SMC
45 MCI
13 AD

84 non-ApoE4



54 ApoE4

Cognitive Normal: **CN**
Significant (subjective) memory complaints: **SMC**
Mild cognitive impairement: **MCI**
Alzheimer's disease: **AD**



Functional connectivity (FC) for each subject

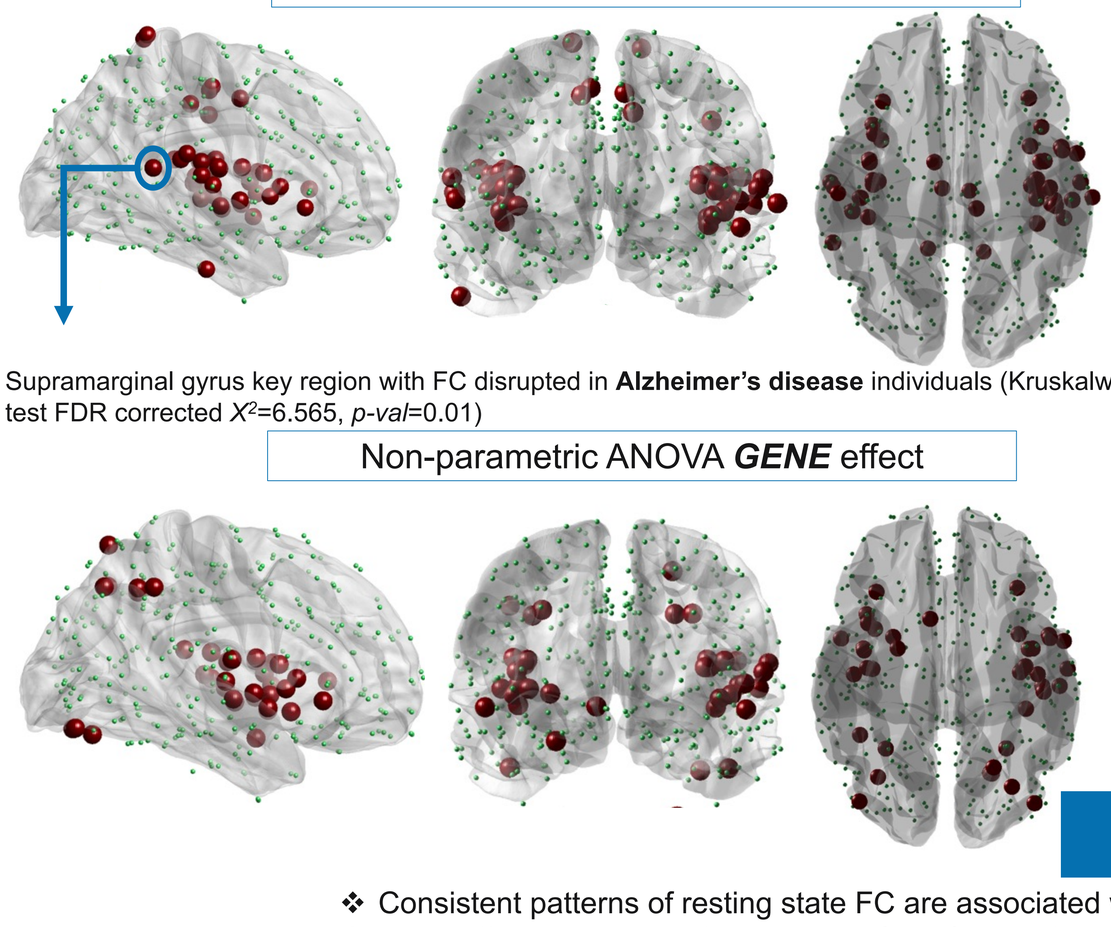
Regional functional properties :
Centrality measure
(1st eigenvector of FC)

Regional functional properties : Connectivity strength
(sum of absolute value of FC)

Group comparison
ApoE4 vs non-ApoE4

RESULTS

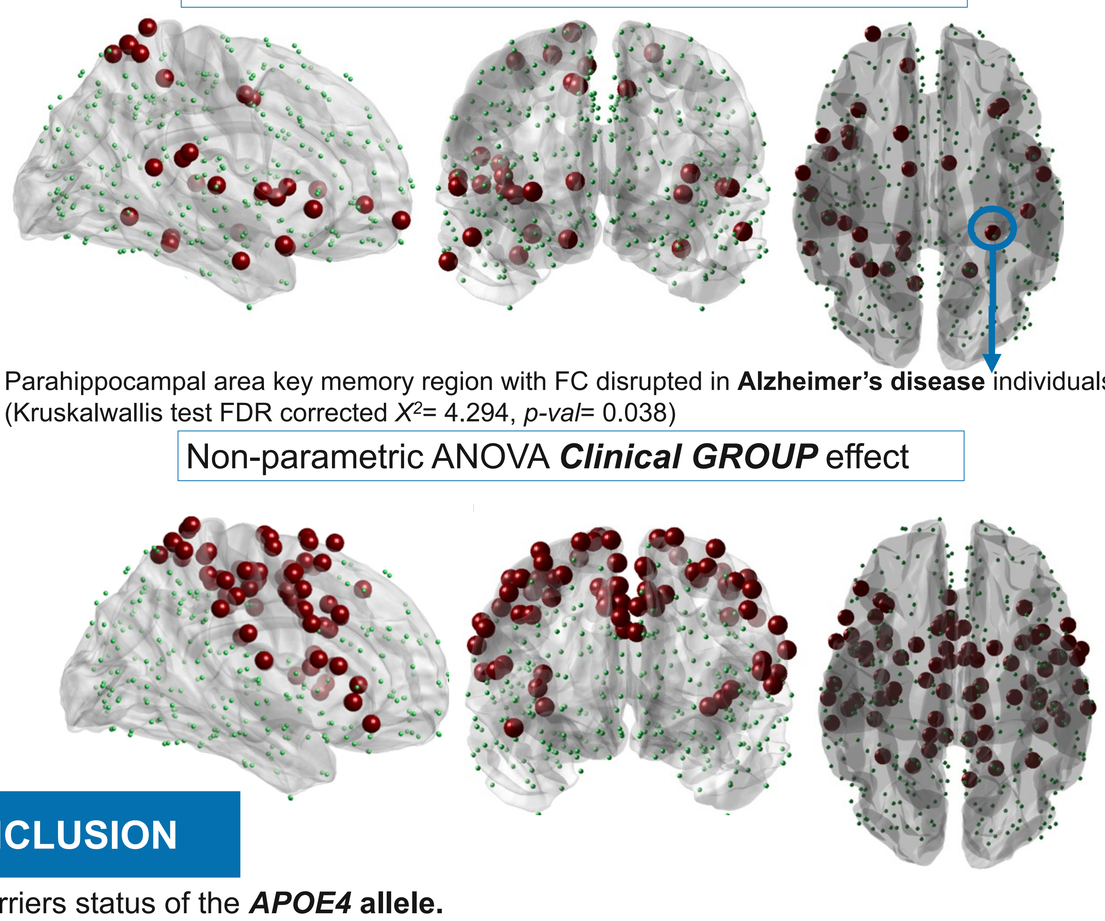
Centrality differences
APOE4 carriers < *APOE4* non-carriers



Supramarginal gyrus key region with FC disrupted in **Alzheimer's disease** individuals (Kruskalwallis test FDR corrected X^2=6.565, *p-val*=0.01)

Non-parametric ANOVA ***GENE*** effect

Connectivity strength differences
APOE4 carriers < *APOE4* non-carriers



Parahippocampal area key memory region with FC disrupted in **Alzheimer's disease** individuals (Kruskalwallis test FDR corrected X^2= 4.294, *p-val*= 0.038)

Non-parametric ANOVA ***Clinical GROUP*** effect

CONCLUSION

- Consistent patterns of resting state FC are associated with carriers status of the ***APOE4*** **allele.**
- This pattern was present in **various** clinical phenotypes, which may be associated with increased risk and progression of AD: CN, SMC, MCI, AD.
- Additional longitudinal studies are needed to characterize relevance for individual risk profiling and early therapeutical intervention.

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