Fingerprinting Functional Connectivity Of Individuals at Risk Of Developing Alzheimer's Disease

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1. INTRODUCTION

Functional connectome fingerprinting uses patterns of brain connectivity to create a "brain signature" that can accurately identify individuals from a large group. Previous work has shown that individual fingerprinting is stable over time and across resting state and task functional magnetic resonance imaging (fMRI).[1]

Alzheimer's disease (AD) is known to affect brain integrity early during the disease. AD-related functional brain changes, particularly in the default mode network (DMN) and in the limbic network, have been associated with amyloid and tau, the pathological hallmarks of AD, and these changes are hypothesized to be detectable in the asymptomatic phase of the disease.

Unstable fingerprints could be a **proxy of underlying pathological processes destabilizing normal functional networks.**[2,3]

2. OBJECTIVES

Obj. 1 To measure fingerprinting stability between **baseline [BL]** and **follow-up [FU]** visits using whole-brain and DMN/limbic sub-networks resting state (rs)fMRI **fingerprinting correlation coefficient (FPCC)** .

Hyp. 1 The whole-brain and sub-networks fingerprint (i.e. ability to identify an individual) should be stable over time

Obj. 2 To explore the relationship between AD pathology (**amyloid and tau**) and **FPCC** between BL and FU at 12 months. DMN/limbic FPCC will be assessed.

Hyp. 2 FPCC in DMN/limbic networks should be lower in individuals with higher levels of AD pathology when compared to individuals with low pathology

3. METHODS *(Participants and MRI/PET preprocessing)*

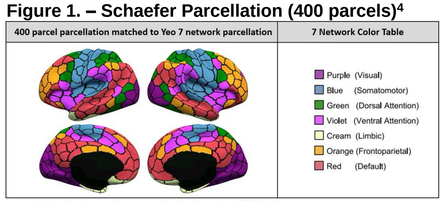
- Recruited from the PREVENT-AD study (n=385)
- First degree familial risk of AD
- Cognitively normal on tests, 50% with subjective cognitive decline

Obj. 1 We included 217 participants that had **BL** and **at least one FU** quality controlled (QC) rsfMRI scan.

Obj. 2 We included 81 participants with **BL** and **FU12 rsfMRI** scans passing QC **AND** an **amyloid and tau scan**

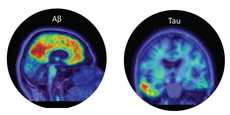
Yearly MRI were performed (from BL to a maximum of 4 years FU

Figure 1. – Schaefer Parcellation (400 parcels)[4]



- We derived one whole-brain FPCC
- We derived one FPCC restricted to DMN and limbic parcels.

One Amyloid PET-scan
One Tau PET-scan



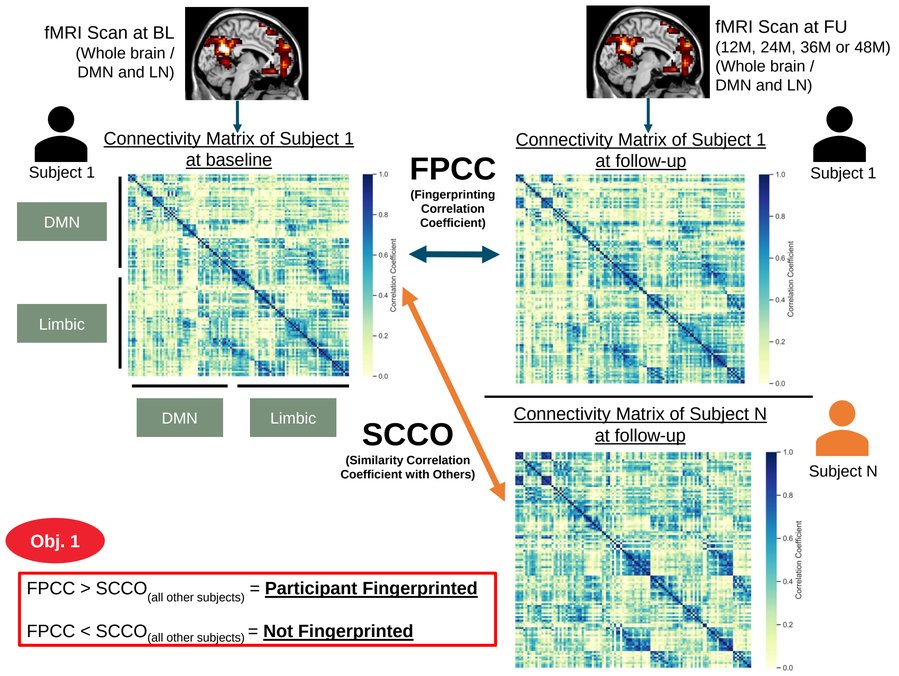
Tau pathology	Amyloid pathology
Temporal meta region of interest[5]	Global amyloid burden[6]
[18F]AV-1451 80-100 min post-injection	[18F]NAV4694 40-70 min post-injection

3. METHODS *(Fingerprinting)*

The **connectivity matrix** represents how the BOLD signal of the rsfMRI in individual brain regions correlate with one another at a single timepoint.

The **FPCC** is calculated using Pearson's correlation between the connectivity matrix at BL and the connectivity matrix of the same individual at a second timepoint.

The **Similarity Correlation Coefficient with Others (SCCO)** refers to the correlation between a subject's connectivity matrix at BL and the connectivity matrix of a different individual at a second timepoint.

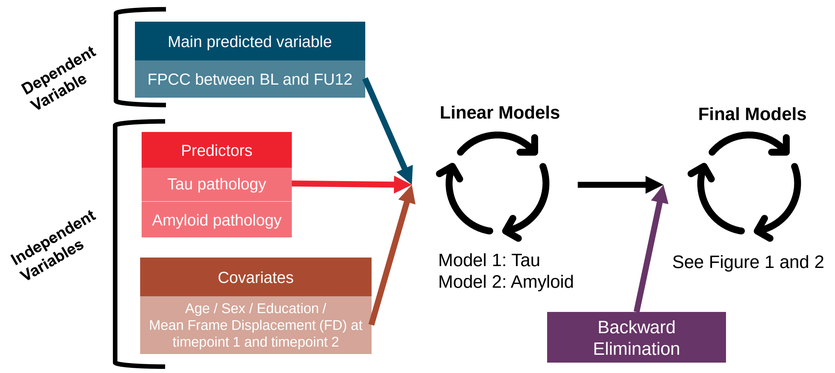


Obj. 1

FPCC > $SCCO_{(all\ other\ subjects)}$ = **Participant Fingerprinted**

FPCC < $SCCO_{(all\ other\ subjects)}$ = **Not Fingerprinted**

Obj. 2 To study the relationship between **FPCC** generated from BL and FU12 data and AD pathology, we used multiple linear regression models (one for tau and one for amyloid)



This poster is made publicly available on the website of the Villeneuve Lab @ www.villeneuvelab.com

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Acknowledgements: The authors would like to thank Hazal Özlen, Jonathan Groff and Porpong Boonmak for reviewing this poster.

References: 1. Finn et al. 2015, Nature Neuroscience. 2. Buckley et al. 2017, Neurology. 3. de Lange et al., Nature 2019. 4. Schaefer et al., Cereb Cortex 2018. 5. Ossenkoppele et al. 2018, JAMA Neurology. 6. Villeneuve et al. 2015, Brain.

Project funded by: CIHR IRSC, Fonds de recherche Santé Québec, Alzheimer Society Canada, MITACS

4. RESULTS

Obj. 1

Table 1. – Demographic information of participants included in Objective 1 (n = 217 to 73)

First / Second Timepoint	Sex (M/F)	Age (Mean ± SD, [Range])	Education (Mean ± SD, [Range])	Age of Expected Onset (Mean ± SD, [Range])
BL / FU12 (n = 198)	51/147	63.3 ± 4.81 [55.3-78.7]	15.4 ± 3.64 [7-29]	73.4 ± 7.87 [50-90]
BL / FU24 (n = 156)	38/118	63.4 ± 4.72 [55.3-77.0]	15.4 ± 3.67 [7-29]	73.9 ± 7.88 [48-90]
BL / FU36 (n = 118)	31/87	63.9 ± 4.81 [55.3-78.7]	15.6 ± 3.72 [7-29]	73.9 ± 8.03 [48-90]
BL / FU48 (n = 66)	23/43	64.8 ± 4.87 [55.3-78.7]	15.5 ± 3.76 [7-24]	75.9 ± 7.66 [53-90]

Only participants with full values are presented in this table.

Table 2. – Stability of the FPCC and differences between fingerprinted and non-fingerprinted individuals

First / Second Timepoint	Fingerprinted / Non-fingerprinted		Variables Differing Between Groups (Whole brain and DMN-LN, significant differences, Mann-Whitney U p <0.05)
	Whole brain	DMN-Limbic	
BL / FU12	210 / 7 (96.8%)	210 / 7 (96.8%)	Mean FD 12 months; Amyloid; Tau
BL / FU24	157 / 11 (93.5%)	154 / 14 (91.7%)	---
BL / FU36	112 / 16 (87.5%)	112 / 16 (87.5%)	Mean FD Baseline and 36 months
BL / FU48	70 / 3 (95.9%)	70 / 3 (95.9%)	Tau

Variables compared: Age, sex, education, FD at both timepoints, global amyloid load measured by PET, global tau load measured by PET.

Obj. 2

Table 3. – Demographic information of participants included in Objective 2 (n = 81)

Sex (M/F)	Age (Mean ± SD, [Range])	Education (Mean ± SD, [Range])	Age of Expected Onset (Mean ± SD, [Range])	Amyloid positivity (+/-) (SUVR ≥ 1.37[5])	Tau positivity (+/-) (SUVR ≥ 1.34[4])
21 / 60	63.7 ± 4.58 [55.3-78.7]	15.3 ± 3.60 [7.00-24.0]	73.7 ± 7.82 [50-90]	13/68	3/78

Figure 2. – Final Tau Model

Only significantly contributing predictors after backward elimination are kept

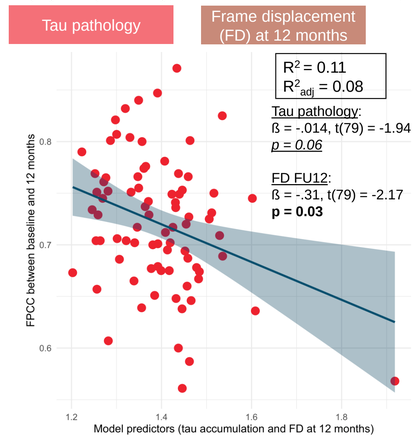
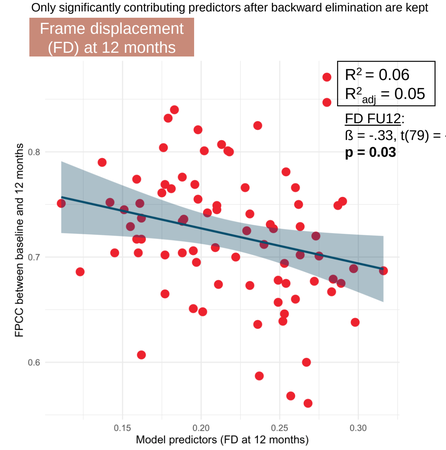


Figure 3. – Final Amyloid Model

Only significantly contributing predictors after backward elimination are kept



5. DISCUSSION

Obj. 1 PREVENT-AD older adult participants' **FPCC is very stable** over time with the fingerprinting **able to recognize a BL individual** at 12-, 24-, 36- and 48-month follow-up for **88-96% of cases both at the whole brain and network level**. "Fingerprintable" individuals **differ from "non-fingerprintable" individuals**, mainly on **FD, amyloid and tau**.

Obj. 2 Using DMN-Limbic parcellation, **only frame displacement at 12 months** appeared significant in both models, while **tau appeared to be trending in the first model**. The **variance explained is relatively low** in both models. This suggests **other factors than AD pathology** and movement in the MRI are at play. However **few subjects have significant levels of amyloid or tau** in their brain.