

# Functional Connectomes in Sporadic and Genetic FTD: Principle Gradient Mapping

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## INTRODUCTION

A brain **network hierarchy** is thought to emerge during neurodevelopment. It is assumed this organisation allows information encoding and integration, **from sensation to cognition** (Mesulam, 1998).

Recent work has applied a **novel decomposition framework** to represent connectomes in low-dimensional space; **gradient mapping**. The principle gradient, which explains the most variance in connectivity, **separates immediate environment sensory processes from transmodal integration processes** (Fig 1).

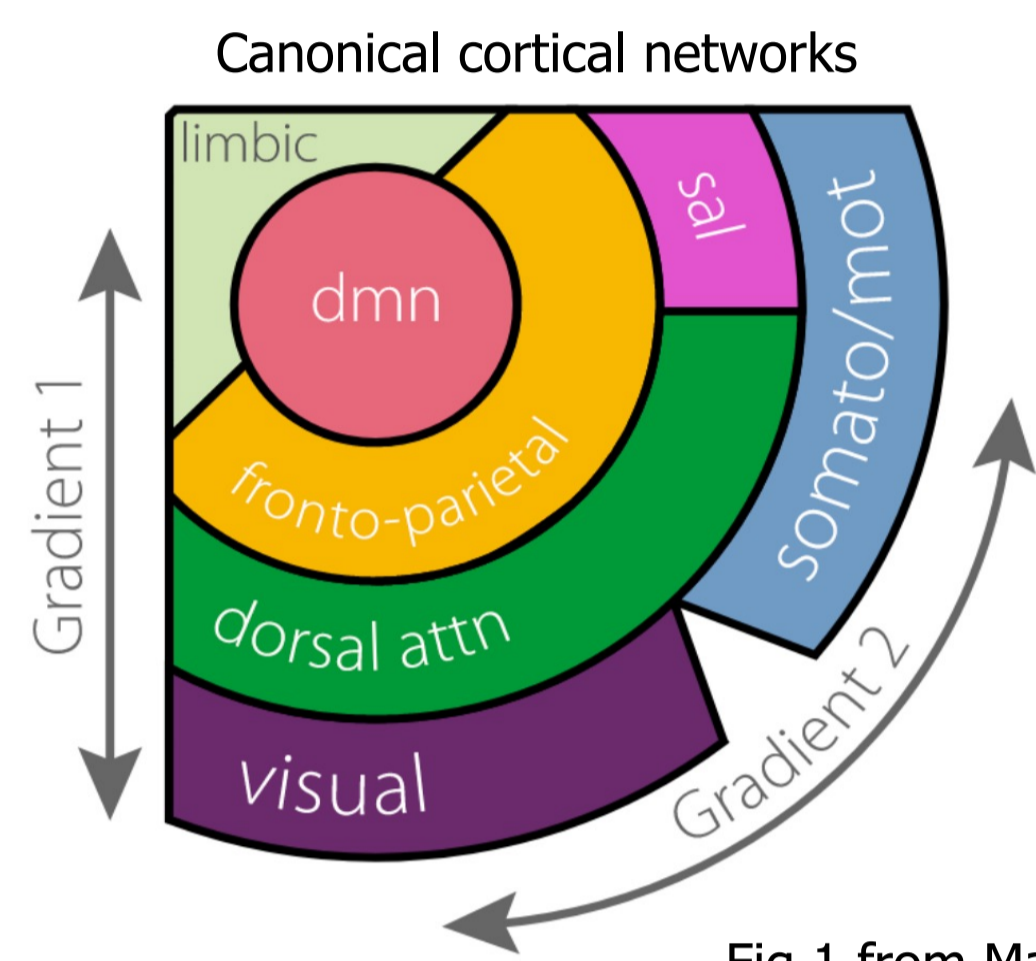


Fig 1 from Margulies et al., 2016

→ This project investigated connectome gradients in sporadic and genetic frontotemporal dementia (FTD).

## METHODS

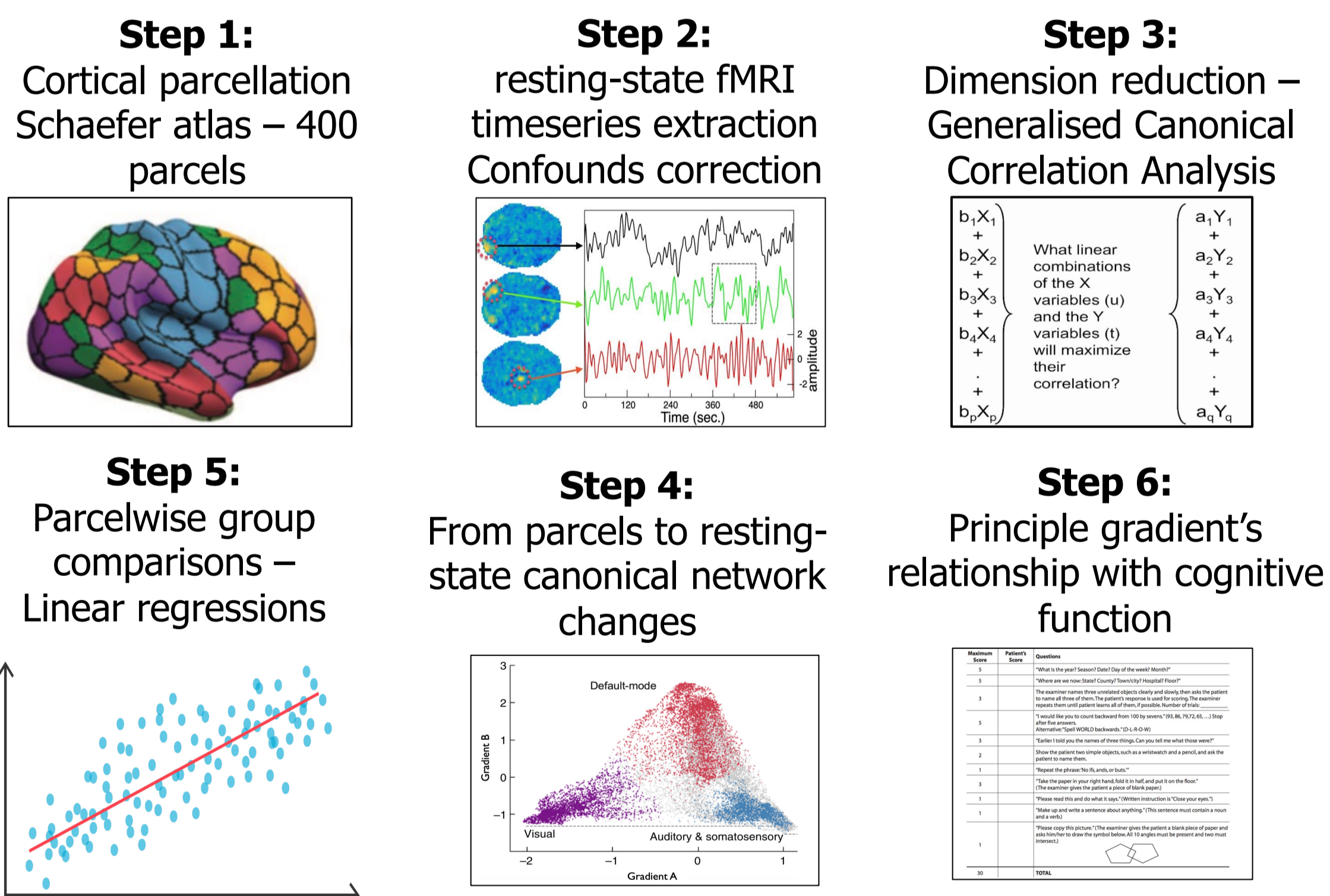
	N	Protocol	Age	Sex	EYO	MMSE
Controls	52	1 & 2	63.6±6.4	27:25	-	29.4±0.8
bvFTD	42	1 & 2	65.9±7.7	12:30	4.2±2.1	23.2±4.0
svFTD	17	2	64.0±6.7	5:12	4.5±1.7	22.8±7.9
nvFTD	18	2	70.6±8.5	9:9	3.6±1.5	20.9±9.3
Non-carriers	25	3	43.6±12.2	11:14	-	29.4±0.7
PS MAPT	23	3	39.6±9.5	15:8	12.2±6.1	29.5±2.3
Symp MAPT	15	3	57.2±8.2	4:11	5.1±3.4	25.6±4.6

**Recruitment:**  
- 2 sporadic studies  
- 1 international genetic study

**Age, EYO, MMSE:**  
group mean ± SD

**Sex:**  
(females:males)

## Whole-brain connectome gradient mapping pipeline



## CONCLUSIONS

**Segregation** of unimodal and transmodal networks is essential for **normal cognitive function**.

**Increased segregation** was observed in **presymptomatic MAPT** mutation carriers.

A **decreased segregation** was found in **patients** with bvFTD and nvFTD  
→ significant shift of cognitive networks towards primary function networks

**svFTD** patients showed **preservation of network segregation**  
→ evolutionarily derived characteristics of networks seems preserved in highly **focal presentation**

Such networks underlie **complex cognitive and behavioural phenotypes** observed in FTD.

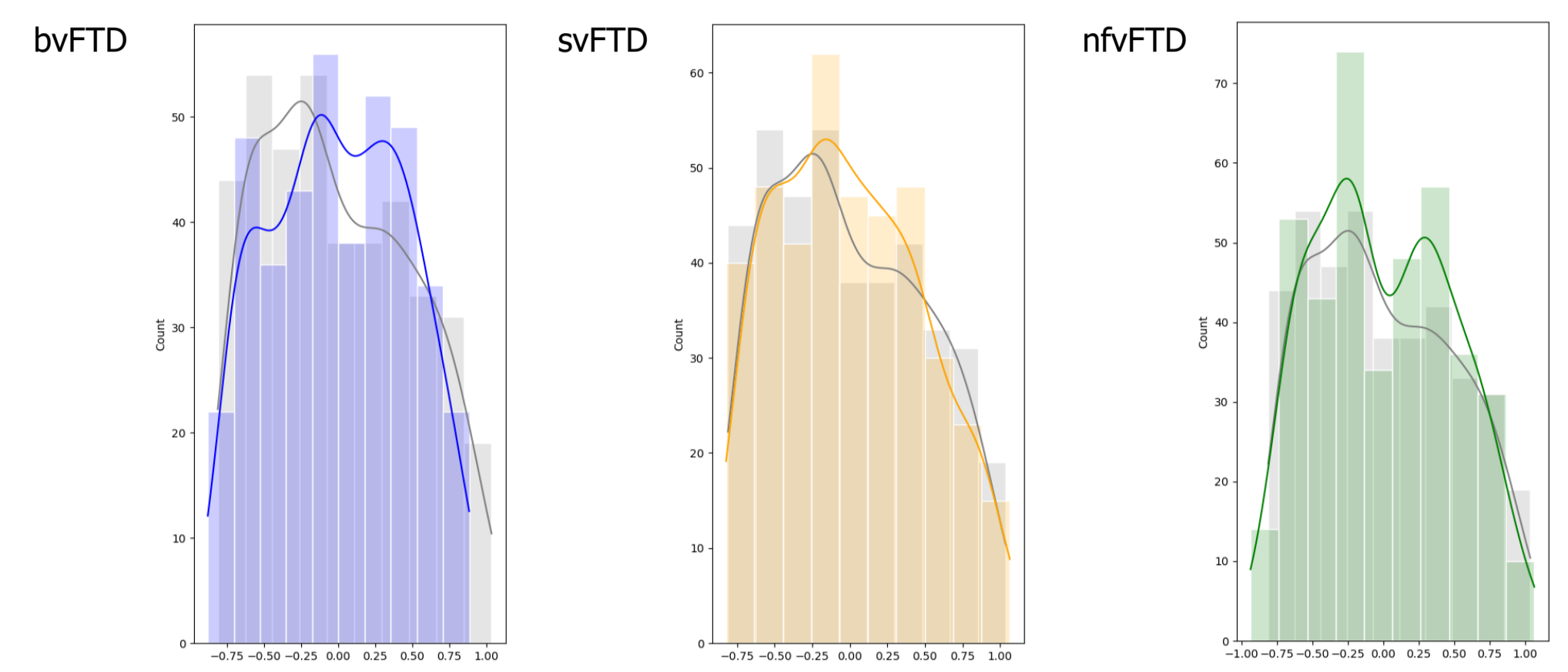
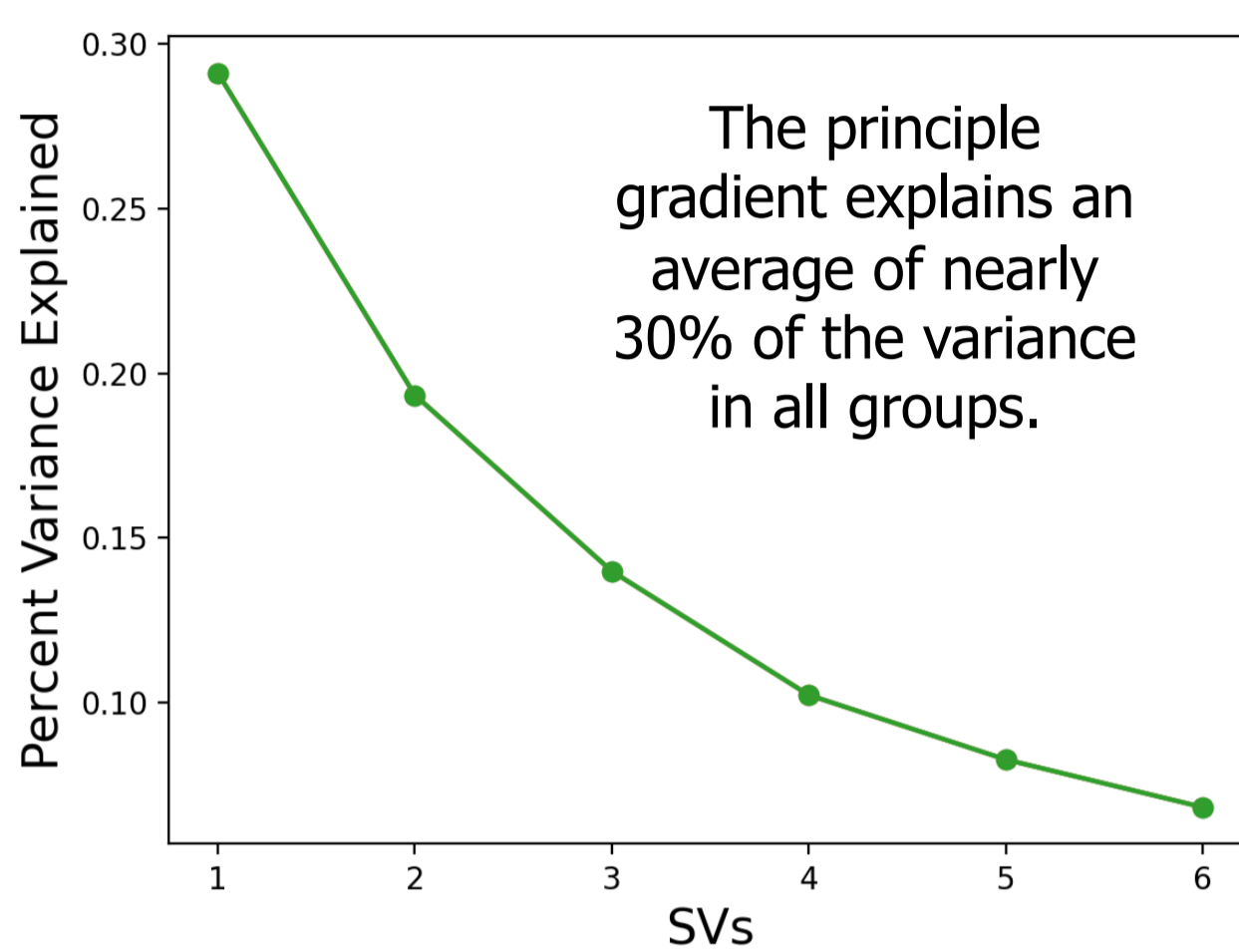
## PERSPECTIVES

Usefulness for **early disease identification and predicting treatment outcomes**.

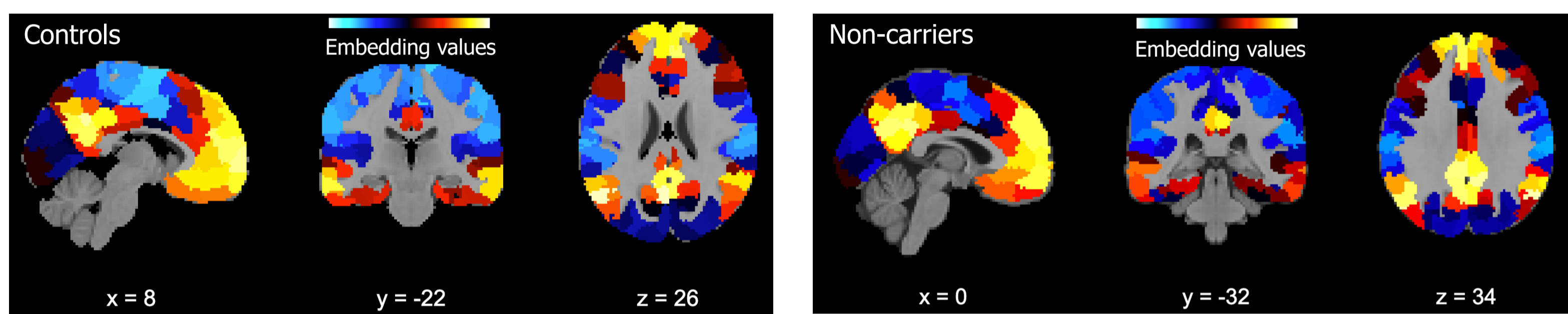
**Potential in therapeutic studies** requires further investigation: longitudinal, larger samples, other genetic groups...

## RESULTS

### 1. Principle gradient group differences



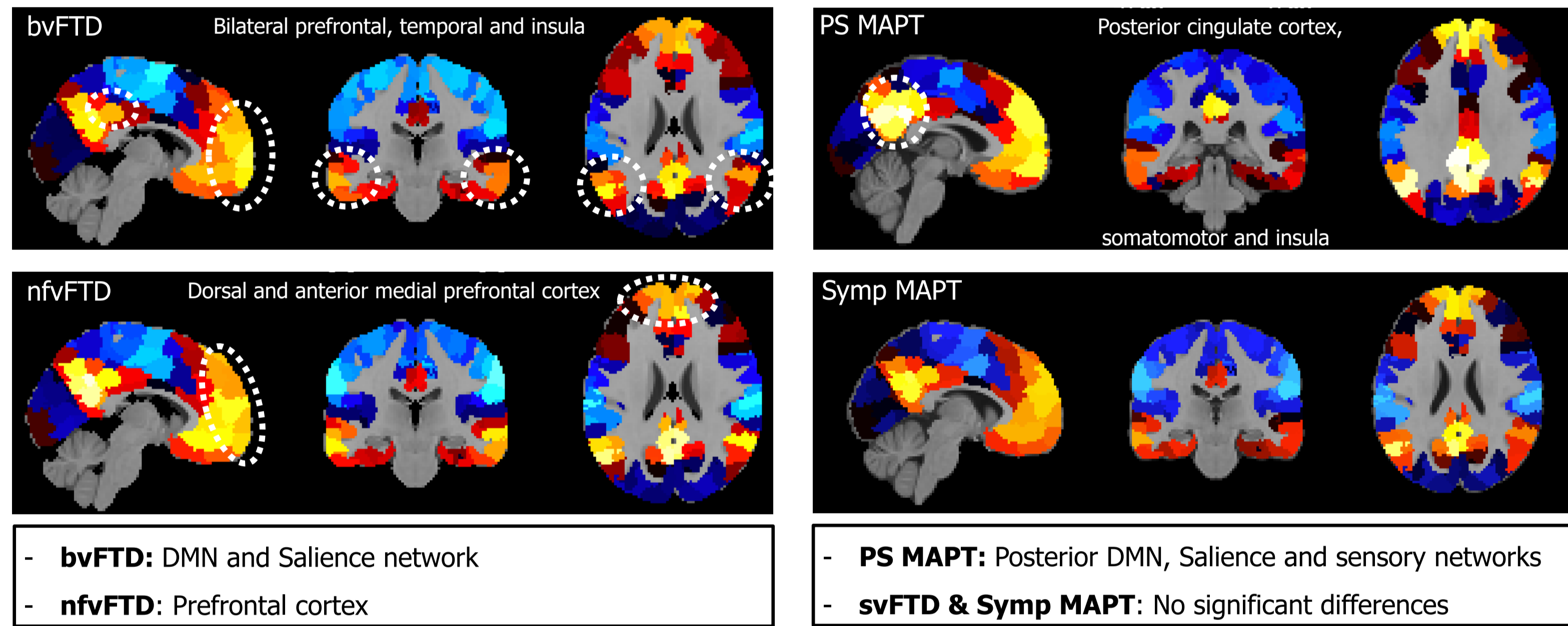
**In controls and non-carriers**, the principle gradient describes connectivity space along a spectrum including the **default-mode** at one extreme and **somatomotor** network on the other.



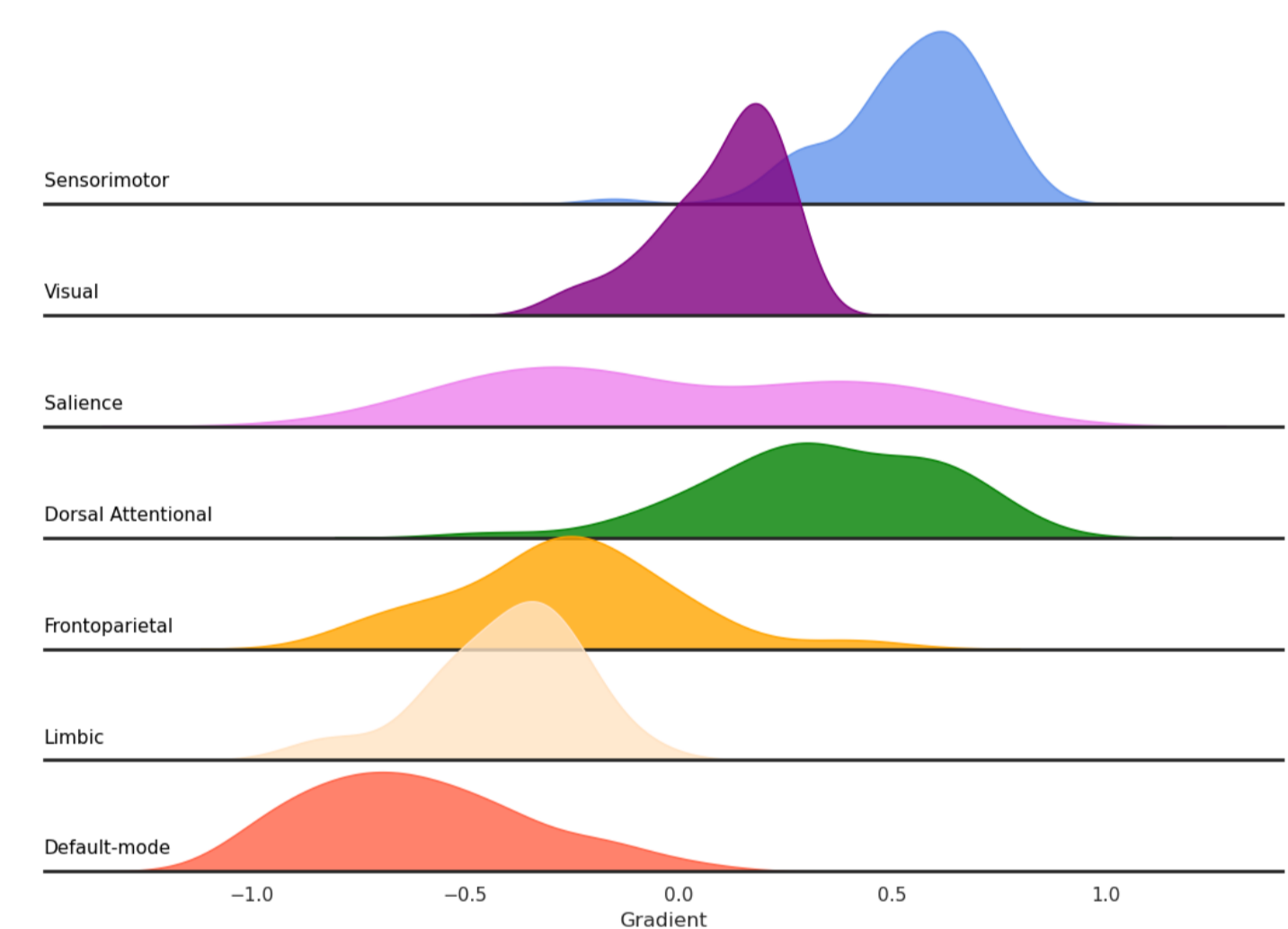
### Parcelwise linear regressions comparing patients with controls.

Models included age, sex and protocol as covariates.

Significantly different parcel principle gradient values are identified by dotted circles, adjusted for 400 multiple comparisons (Benjamini & Hochberg).

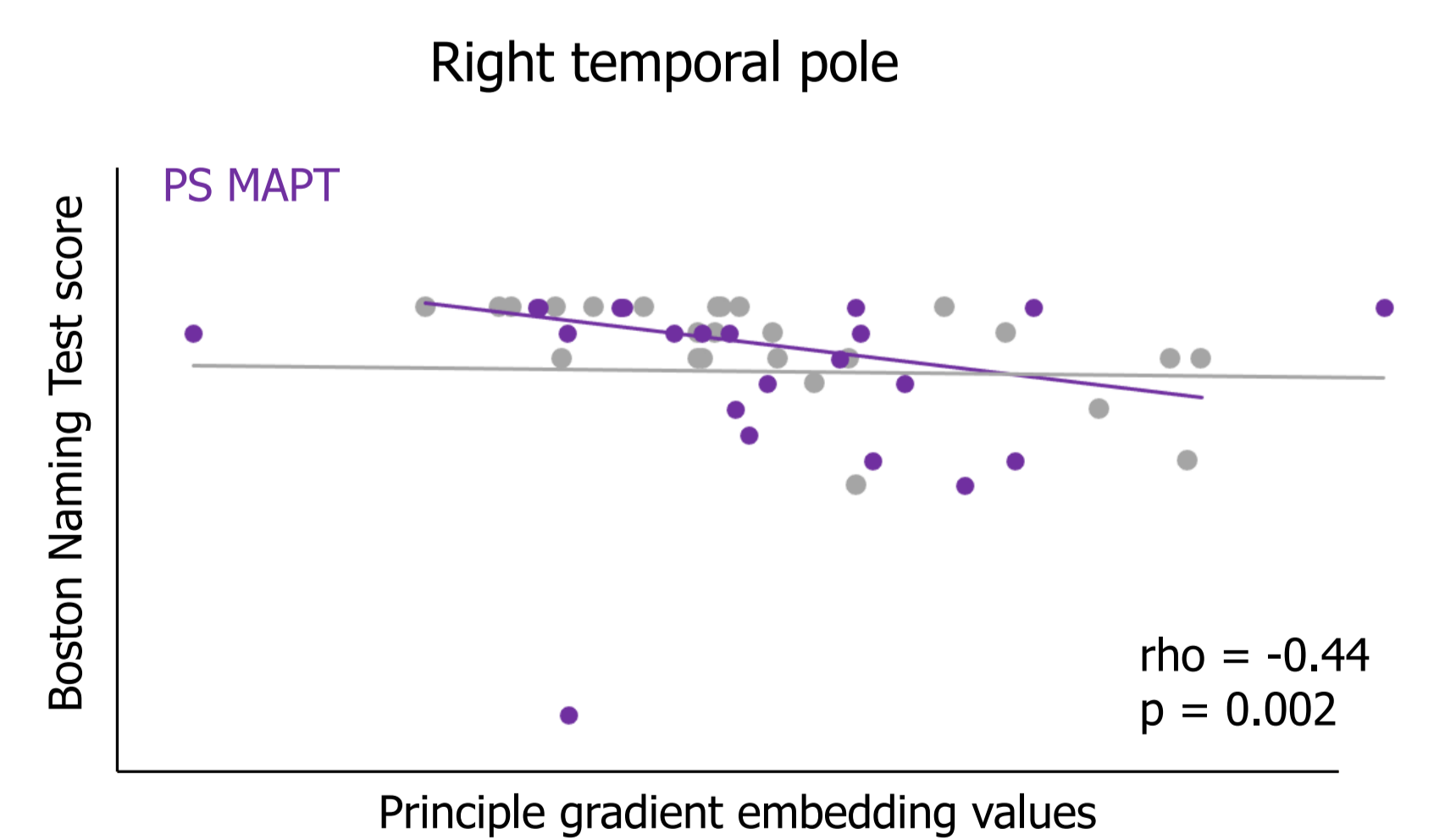
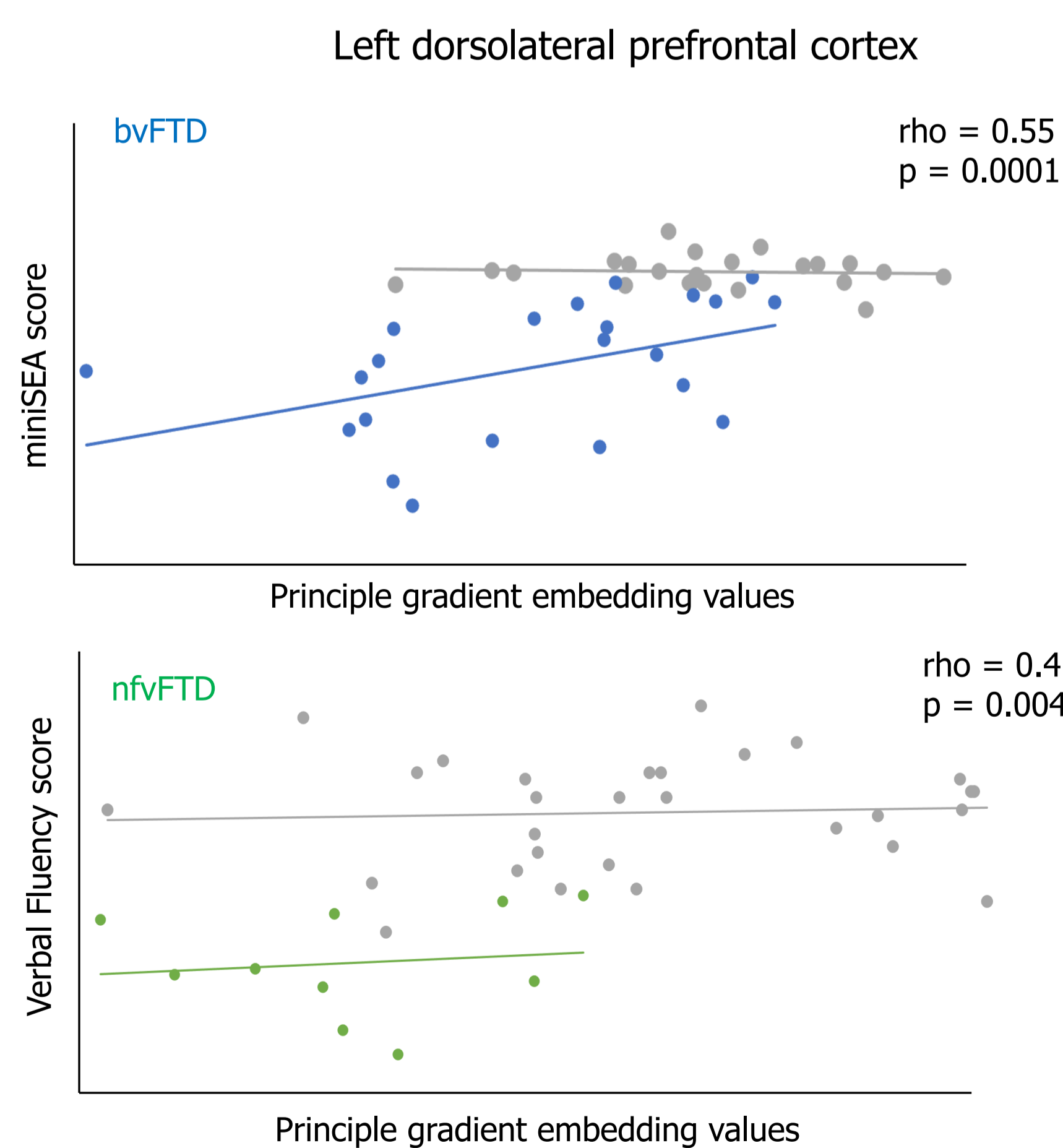


### 2. Principle gradient network changes



Permutation t-tests adjusted for 7 comparisons showed significant differences between mean gradient embedding values within networks for the 3 sporadic patient groups.

### 3. Principle gradient and cognition



Spearman correlations between parcel principle gradient embedding values and relevant cognitive tests revealed significant relationships.

## REFERENCES

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