



Just be you?

# Degeneration of Social Cognition



# 1. Frontotemporal dementia

Clinical picture, incidence, pathways

# 2. Neurodegeneration

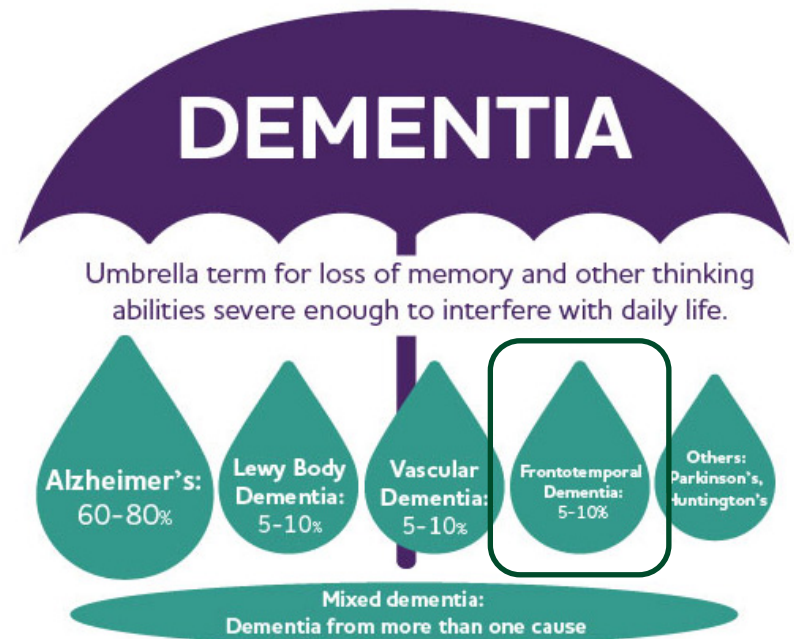
Atrophy, progression

# 3. Socioemotional deficits

Empathy, coherent concepts

## Clinical picture

- FTD, originally called Pick's disease (1892)
- Present day: heterogeneous disorder, associated with changes in personality, social conduct, and linguistic abilities, multiple causes and courses
- Challenging to diagnose:
  - Detailed history
  - Neuropsychological tests
  - Blood tests
  - Brain scans (MRI, PET)





**FTD may cause changes in personality, social conduct, and linguistic abilities**

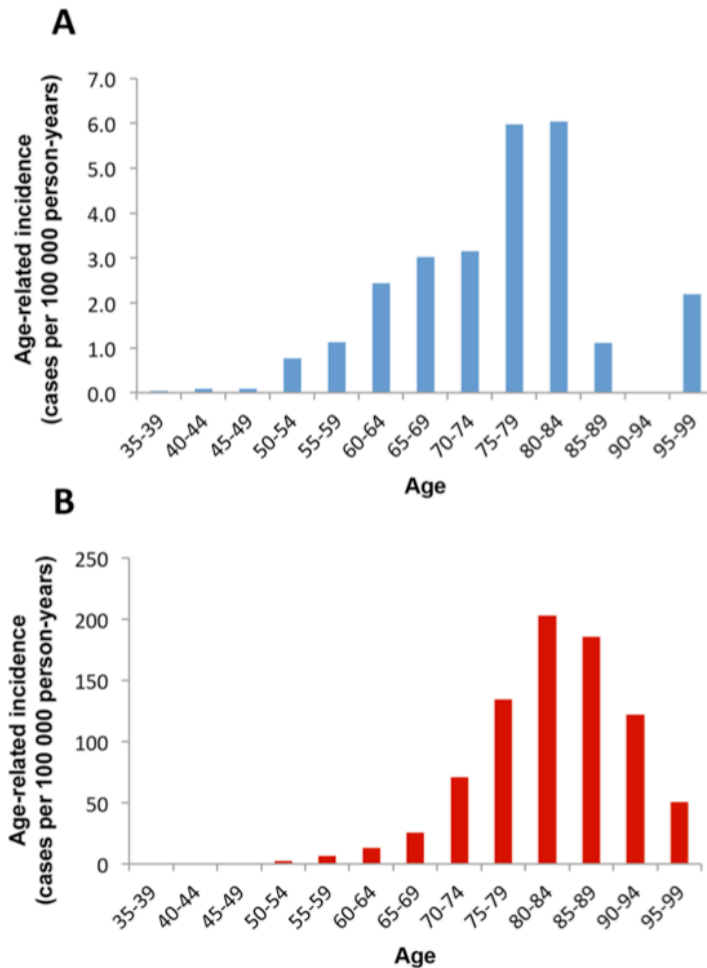
Her doctor referred her to our center at the insistence of the patient's husband, who upon learning of bvFTD thought his wife may have the disease. ... She made several racial comments about a restaurant server. ... She repeatedly interrupted her son's graduation ceremony by initiating conversation with guests during the ceremony. She also attempted to take a bouquet of flowers from another family to give it to her son. ... Her brain MRI revealed marked bilateral frontal and anterior temporal lobar atrophy. She died at age 59 years, approximately 8 years after onset. Brain autopsy confirmed frontotemporal lobar degeneration (FTLD).

The behavioural variant frontotemporal dementia (bvFTD) syndrome in psychiatry

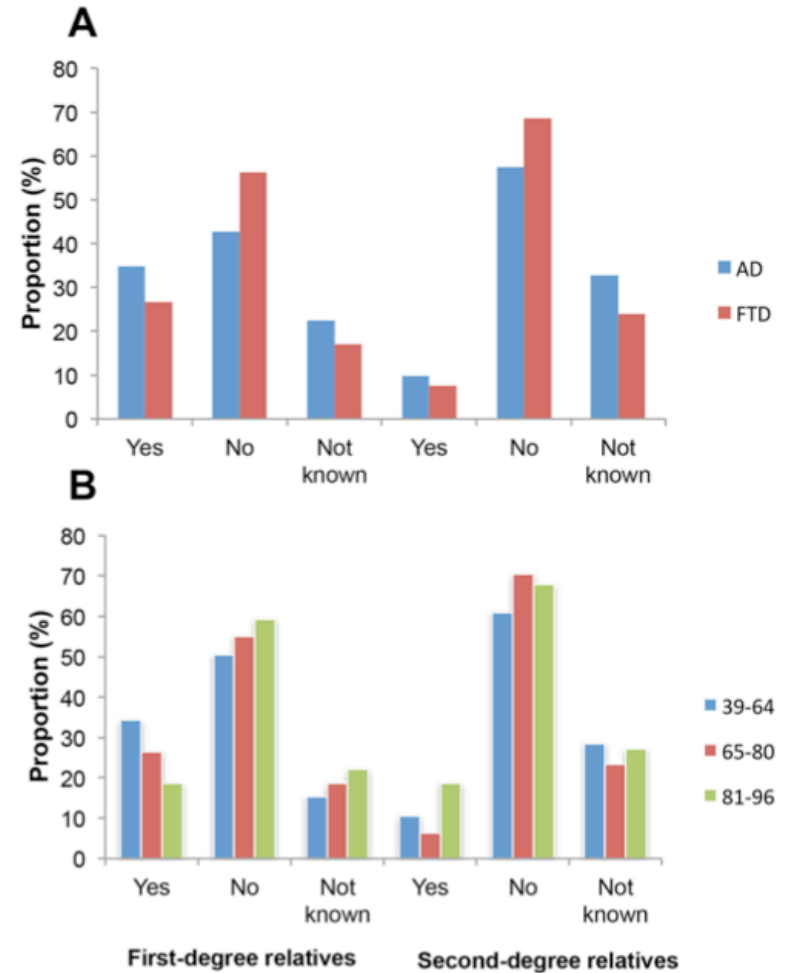
Serggio C. Lanata, Bruce L. Miller

**FTD may cause changes in personality, social conduct, and linguistic abilities**

## Incidence



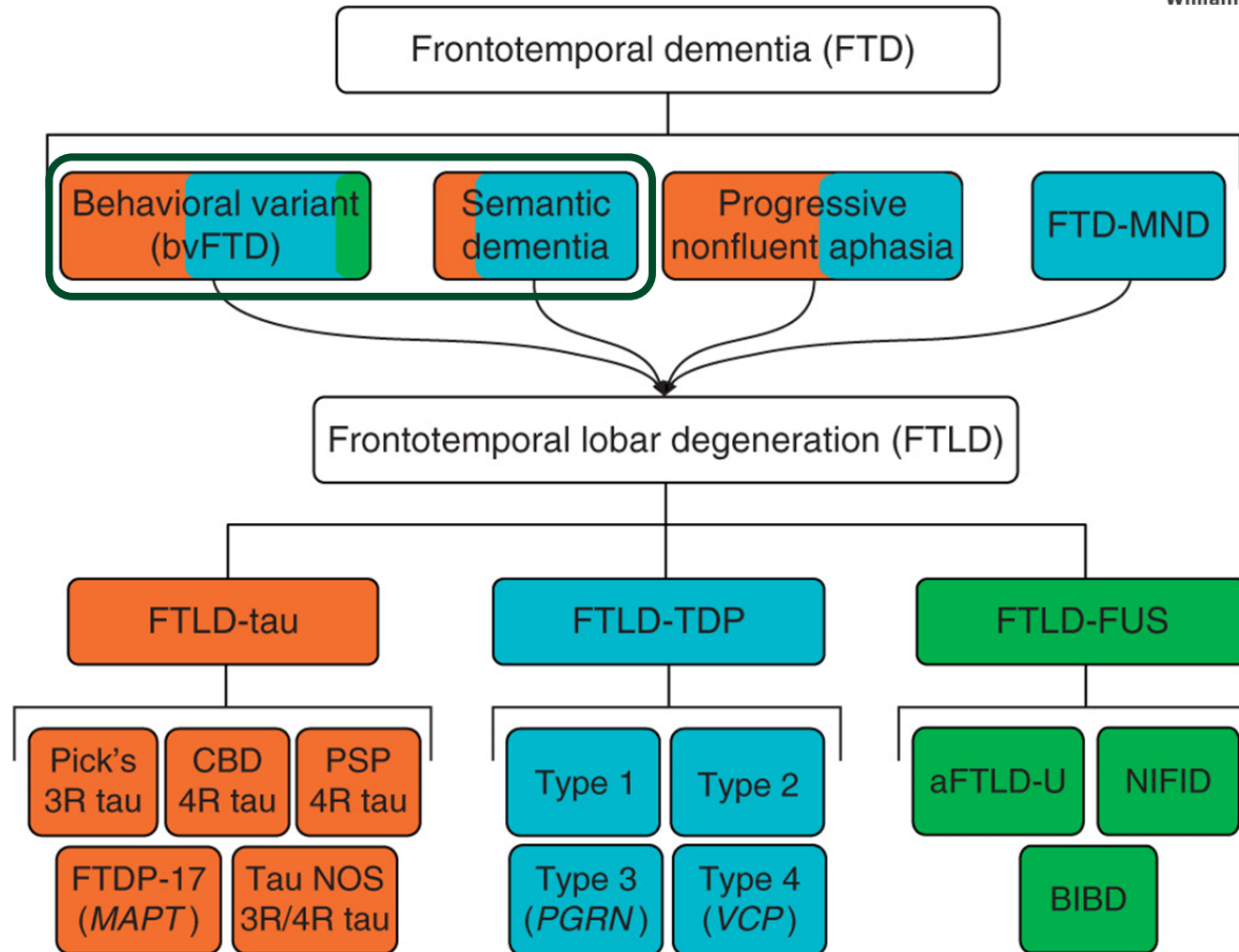
**Figure 2. Age-related incidence in FTD and AD.**



**Figure 3. Family history in FTD and AD.**

# Syndromes and pathways

Harrison's Neurology in Clinical Medicine, 3rd Edition  
CHAPTER 29. ALZHEIMER'S DISEASE AND OTHER DEMENTIAS  
William W. Seeley ■ Bruce L. Miller



Neuroinflammation due to toxic levels of protein accumulation



# 1. Frontotemporal dementia

Clinical picture, incidence, pathways

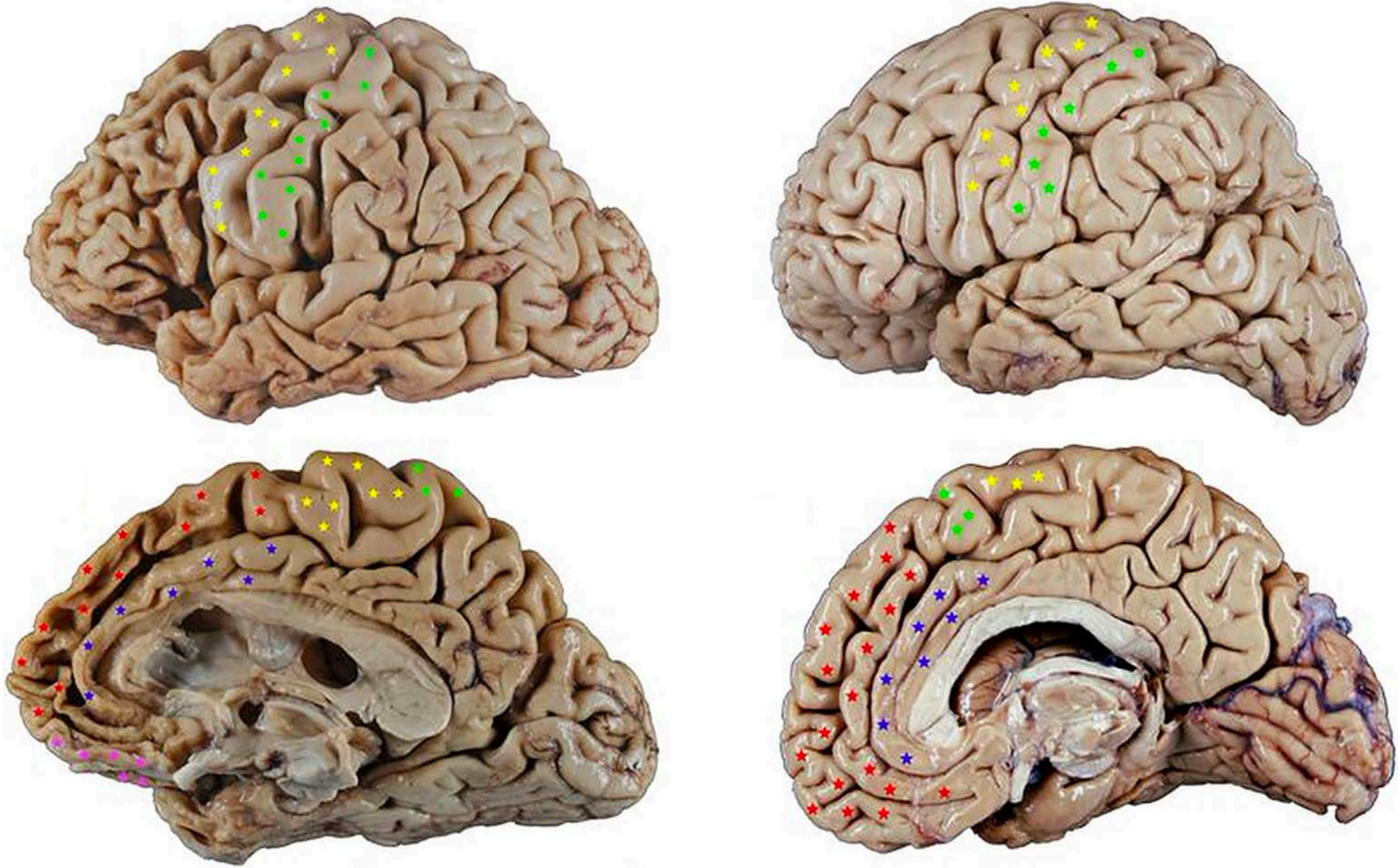
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# Brain autopsy

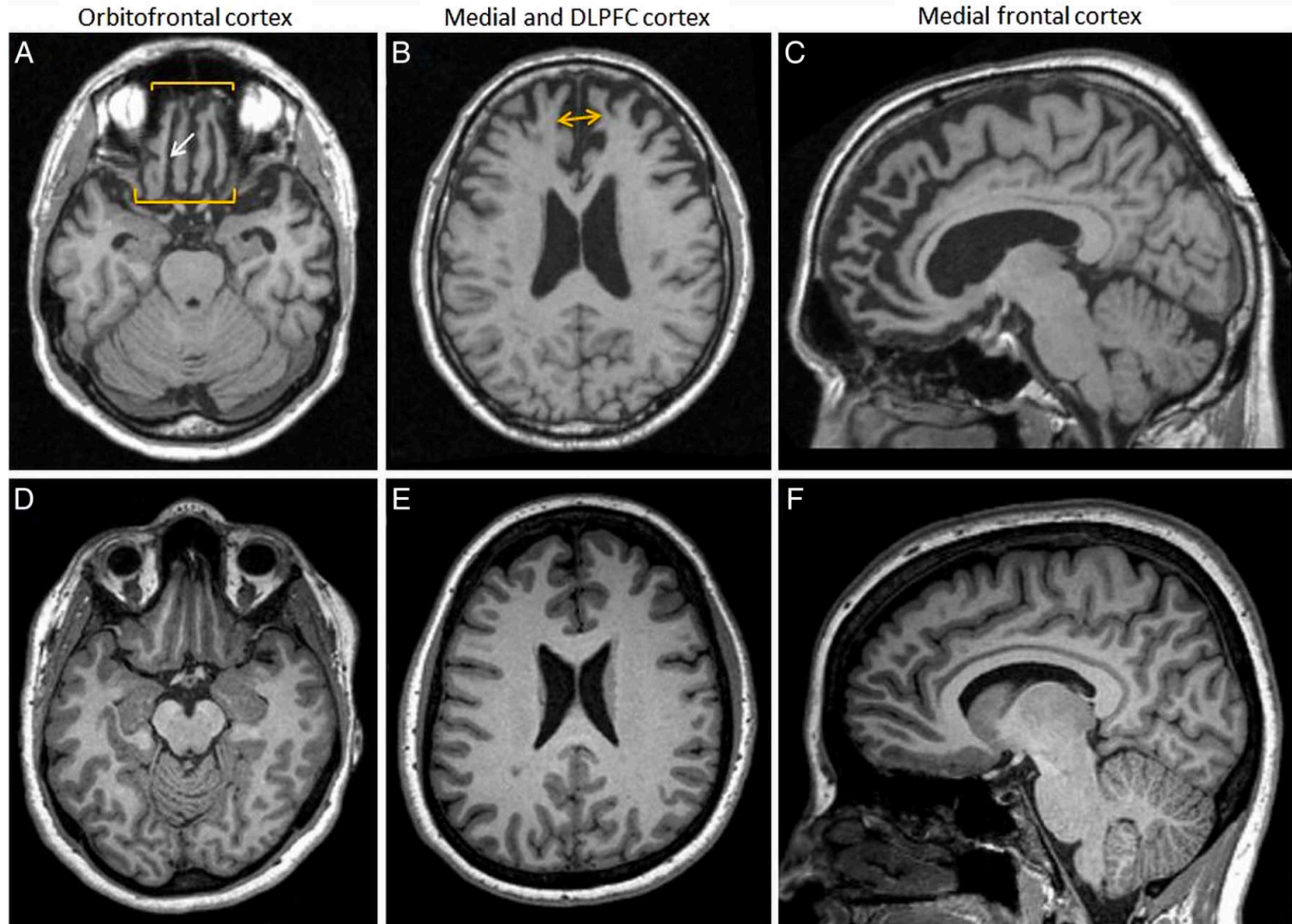


The behavioural variant frontotemporal dementia (bvFTD) syndrome in psychiatry

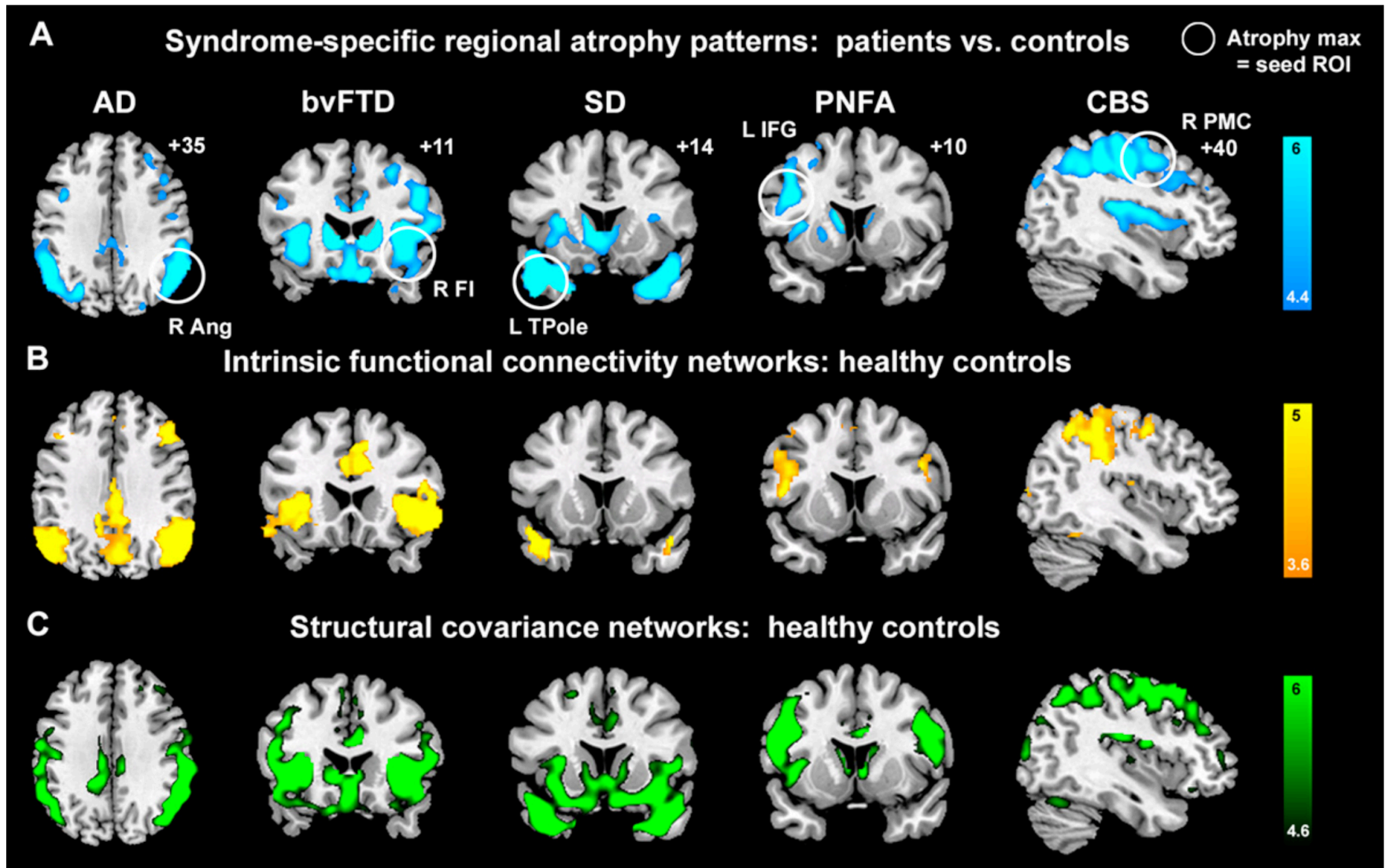
Sergio C Lanata, Bruce L Miller

**Atrophy of ACC, superior frontal gyrus, and OFC**

# MRI scan 7 years before death



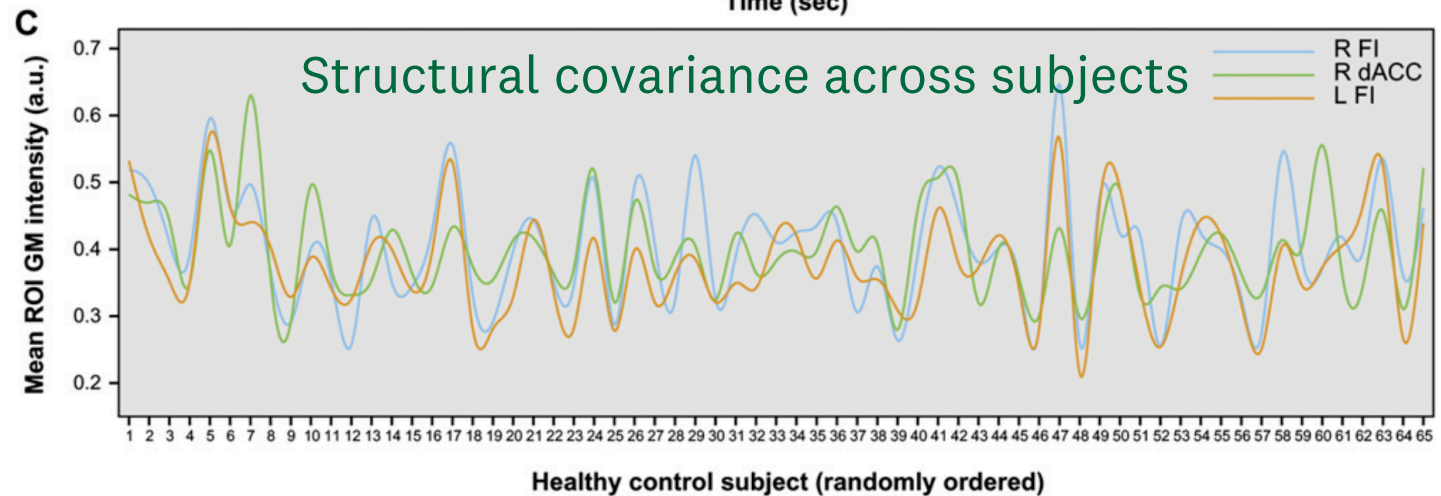
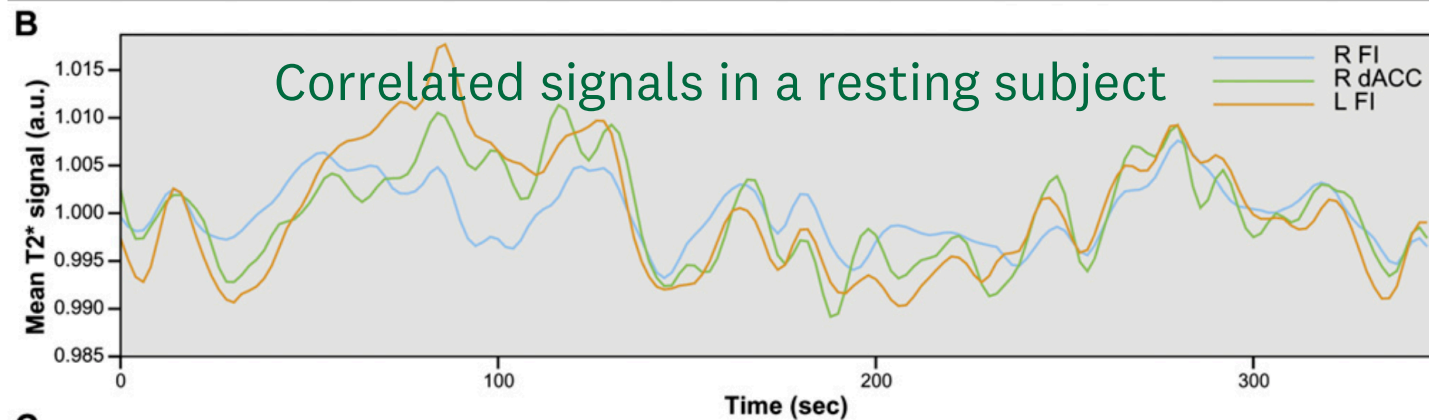
Atrophy of ACC, superior frontal gyrus, and OFC



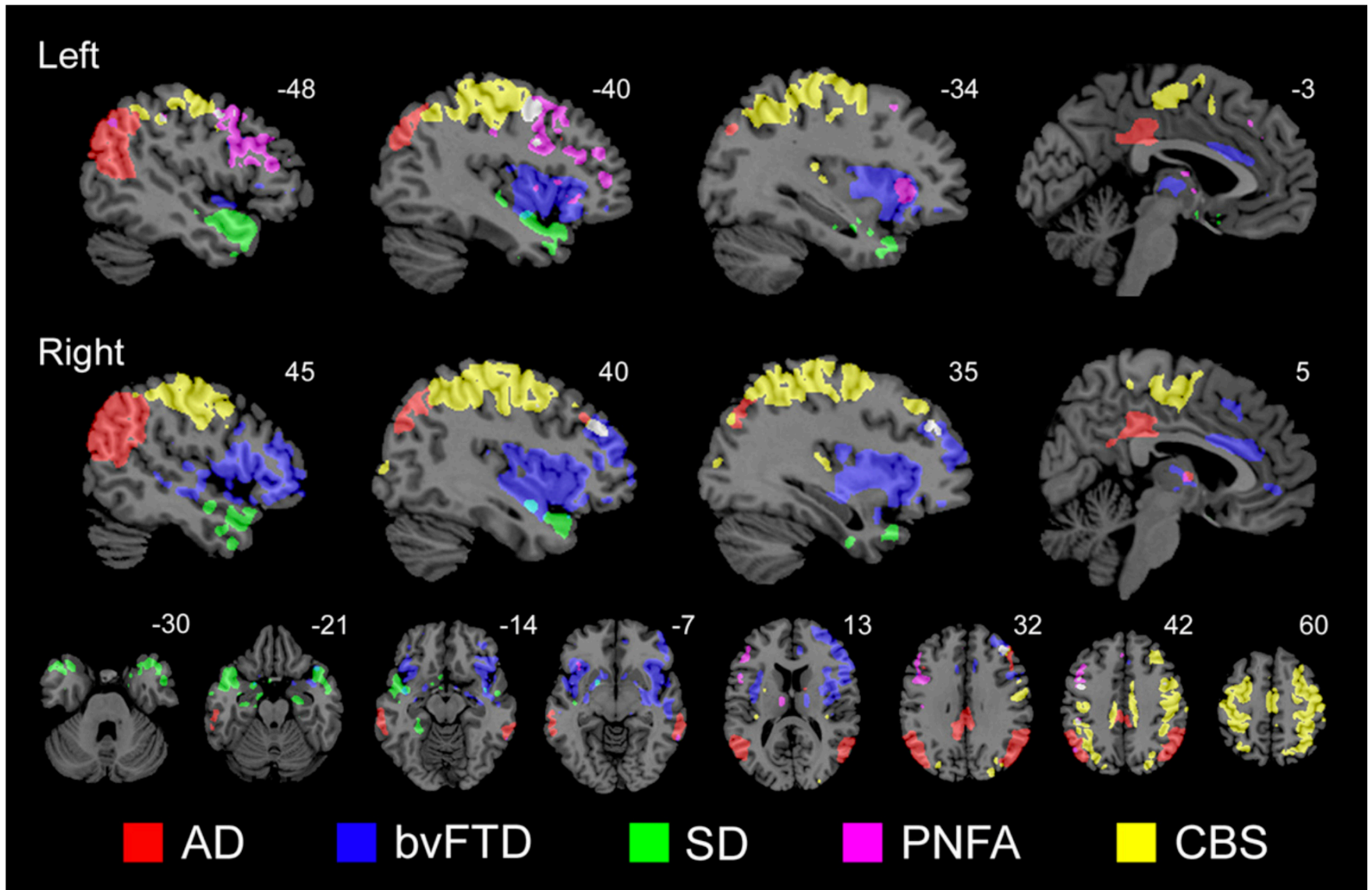
Neurodegenerative Diseases Target  
Large-Scale Human Brain Networks

William W. Seeley,<sup>1\*</sup> Richard K. Crawford,<sup>1</sup> Juan Zhou,<sup>1</sup> Bruce L. Miller,<sup>1</sup> and Michael D. Greicus<sup>2</sup>

Neurodegeneration spreads through intrinsically connected networks

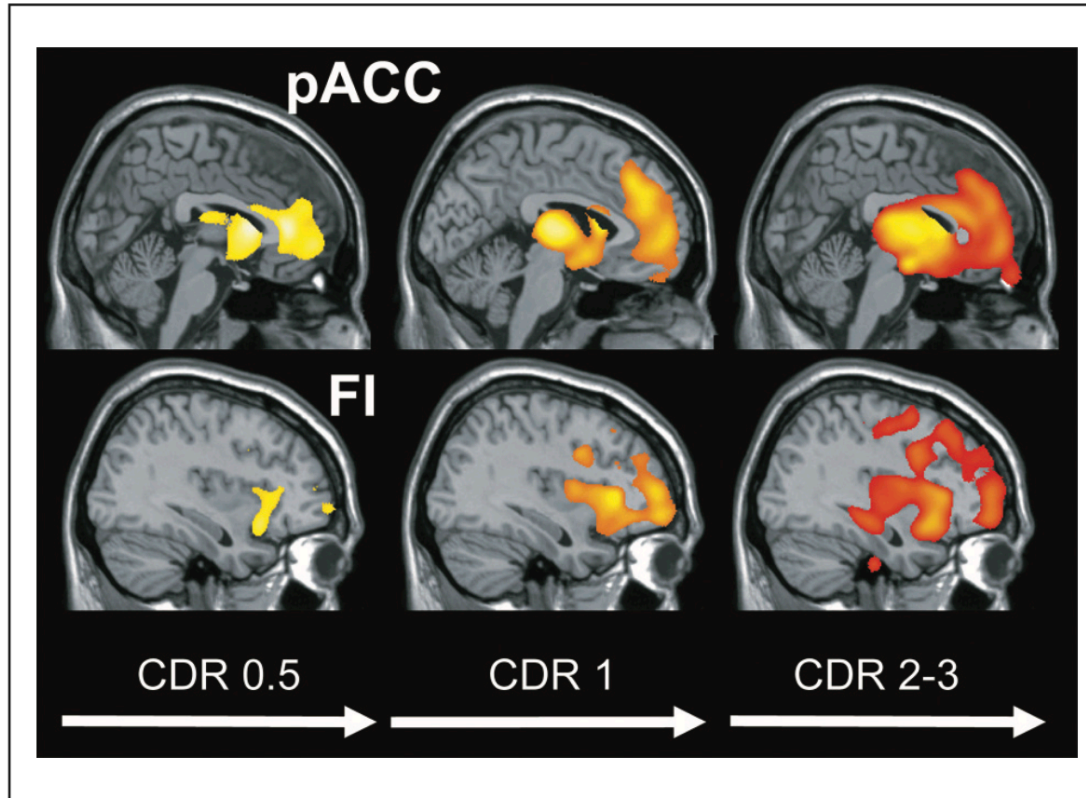


Neurodegeneration spreads through intrinsically connected networks



Neurodegeneration spreads through intrinsically connected networks

## Brain-behavior relationships



**Frontotemporal Dementia: What Can the Behavioral Variant Teach Us about Human Brain Organization?**

William W. Seeley<sup>1</sup>, Juan Zhou<sup>1</sup>, and Eun-Joo Kim<sup>2</sup>

**Figure 1.** Anatomical progression of the behavioral variant of frontotemporal dementia (bvFTD). Patients with bvFTD were categorized as having very mild, mild, or moderate to severe functional severity, as assessed using the Clinical Dementia Rating (CDR) scale. Each group (n = 15) was compared to a group of 45 age-matched controls using voxel-based morphometry.

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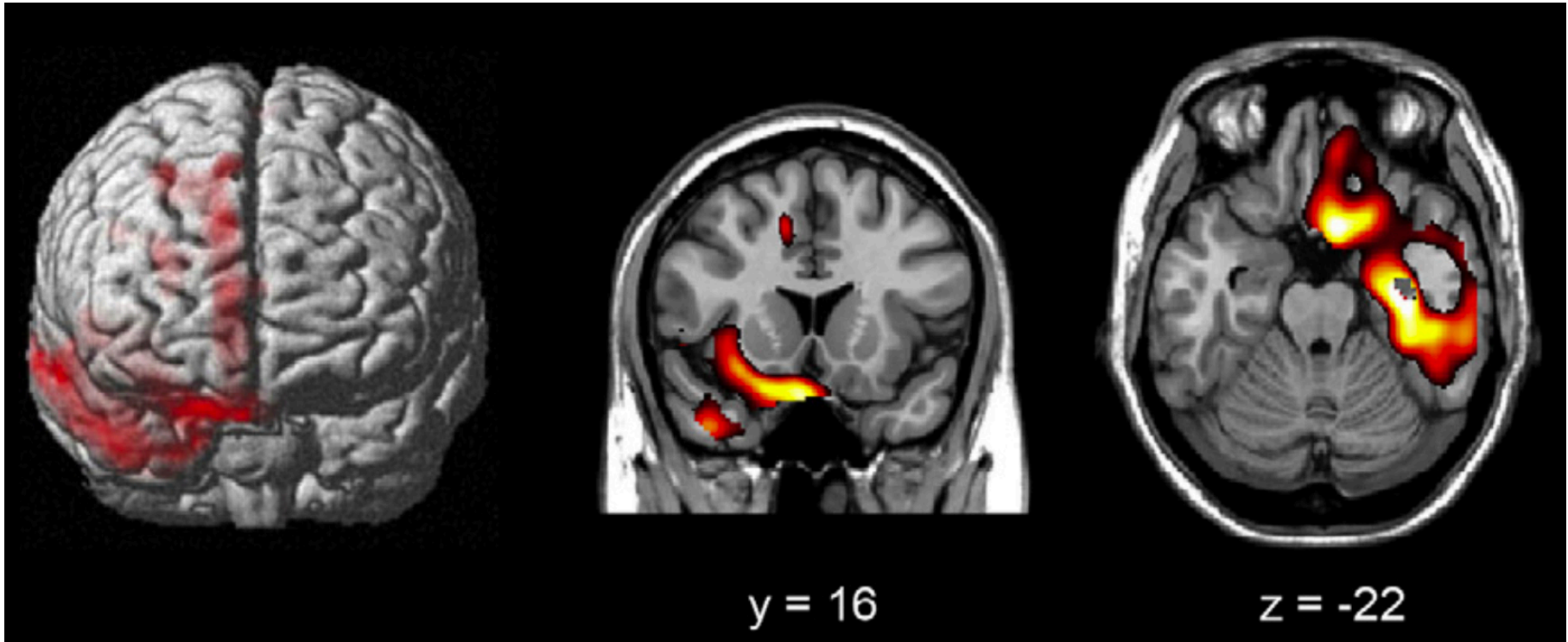




## Regional correlates

Deficit	Imaging	Patients Included	Regional Correlates	Reference
Emotional empathy (empathic concern)	MRI	bvFTD, svPPA, nfvPPA, CBS, PSP,AD	<u>Right ATL</u> , FI, sACC, pACC, striatum	Rankin and others (2006)
Cognitive empathy (perspective taking)	MRI	bvFTD, svPPA, nfvPPA	dmPFC, pACC	Eslinger and others (2011)
	MRI	bvFTD, svPPA, nfvPPA, CBS, PSP,AD	<u>Right ATL</u> , fusiform gyrus, dmPFC, sACC, striatum	Rankin and others (2006)
Interpersonal warmth	MRI	bvFTD, svPPA, nfvPPA	FP, dmPFC, dIPFC, ATL, lateral parietal	Eslinger and others (2011)
	MRI	bvFTD, svPPA, nfvPPA, CBS, AD	<u>Right FI</u> , mOFC > ATL	Sollberger and others (2009)
Emotion recognition: faces (negative emotion)	MRI	bvFTD, svPPA, nfvPPA, PSP, MCI,AD, HC	<u>Right ITG</u> , lat OFC	Rosen and others (2006)
	MRI	bvFTD, svPPA	Bilateral AI, lat OFC	Omar and others (2011)
Emotion recognition: music	MRI	bvFTD, svPPA	Bilateral pACC, sACC, AI, OFC, dmPFC, ATL, amygdala, striatum	Omar and others (2011)
Emotional moral judgment	SPECT	bvFTD,AD, HC	<u>Right frontotemporal</u> <sup>a</sup>	Mendez and Shapira (2009)
Prosocial sentiments (guilt, pity, embarrassment)	PET	bvFTD	<u>Right FP</u> , septum	Moll and others (2011)
Other critical sentiments (anger, disgust)	PET	bvFTD	dmPFC, right amygdala	Moll and others (2011)
Embarrassment	NA	bvFTD, svPPA, nfvPPA, HC	Not studied	Sturm and others (2006)
Autonomic response to embarrassment	MRI	bvFTD, svPPA, nfvPPA, HC	pACC	Sturm and others (2008), Sturm and others (2011)
Mutual gaze during dyadic interaction	NA	bvFTD, svPPA,AD, HC	Not studied	Sturm and others (2010)

## Interpersonal warmth

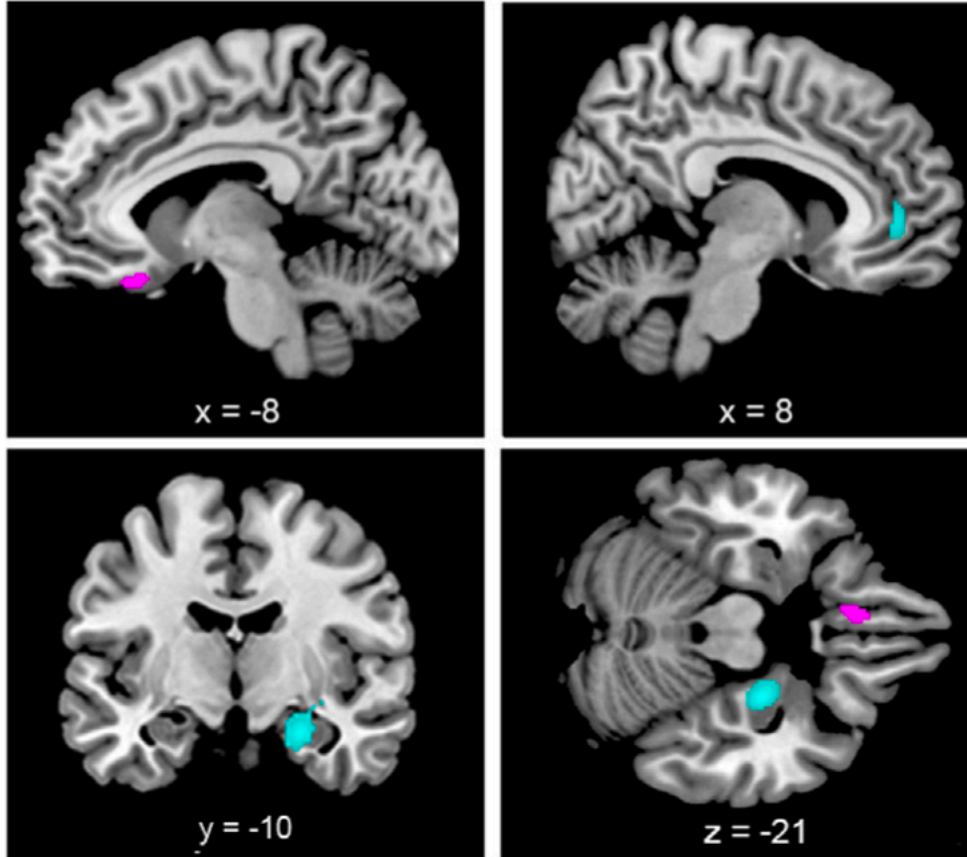


Neural basis of interpersonal traits in neurodegenerative diseases

Marc Sollberger<sup>a,b</sup>, Christine M. Stanley<sup>a,b</sup>, Stephen M. Wilson<sup>a,b</sup>, Anett Gyurak<sup>e</sup>,  
Victoria Beckman<sup>a,b</sup>, Matthew Growdon<sup>a,b</sup>, Jung Jang<sup>a,b</sup>, Michael W. Weiner<sup>c,d</sup>,  
Bruce L. Miller<sup>a,b</sup>, Katherine P. Rankin<sup>a,b,\*</sup>

Patients with damage to right frontotemporal regions are considered less warm

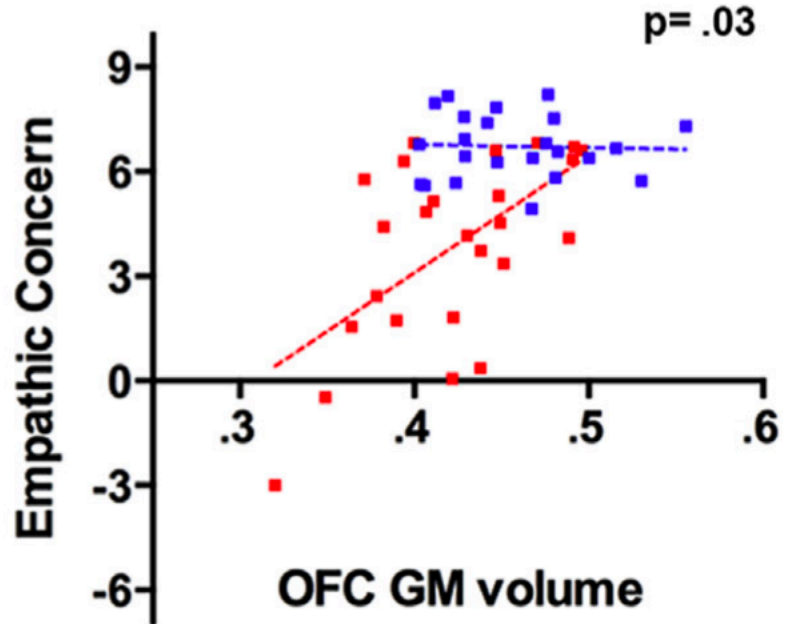
# Empathic concern



■ Empathic concern  
■ Intentionality

Orbitofrontal and limbic signatures of empathic concern and intentional harm in the behavioral variant frontotemporal dementia

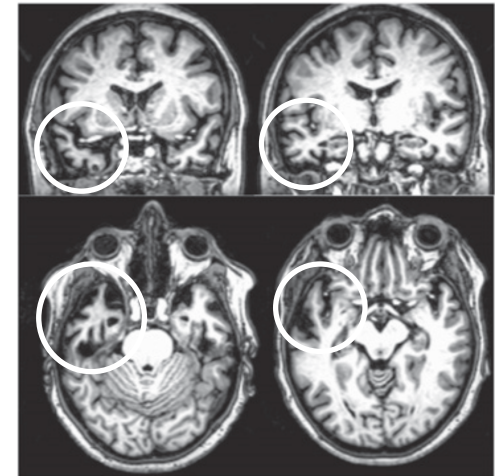
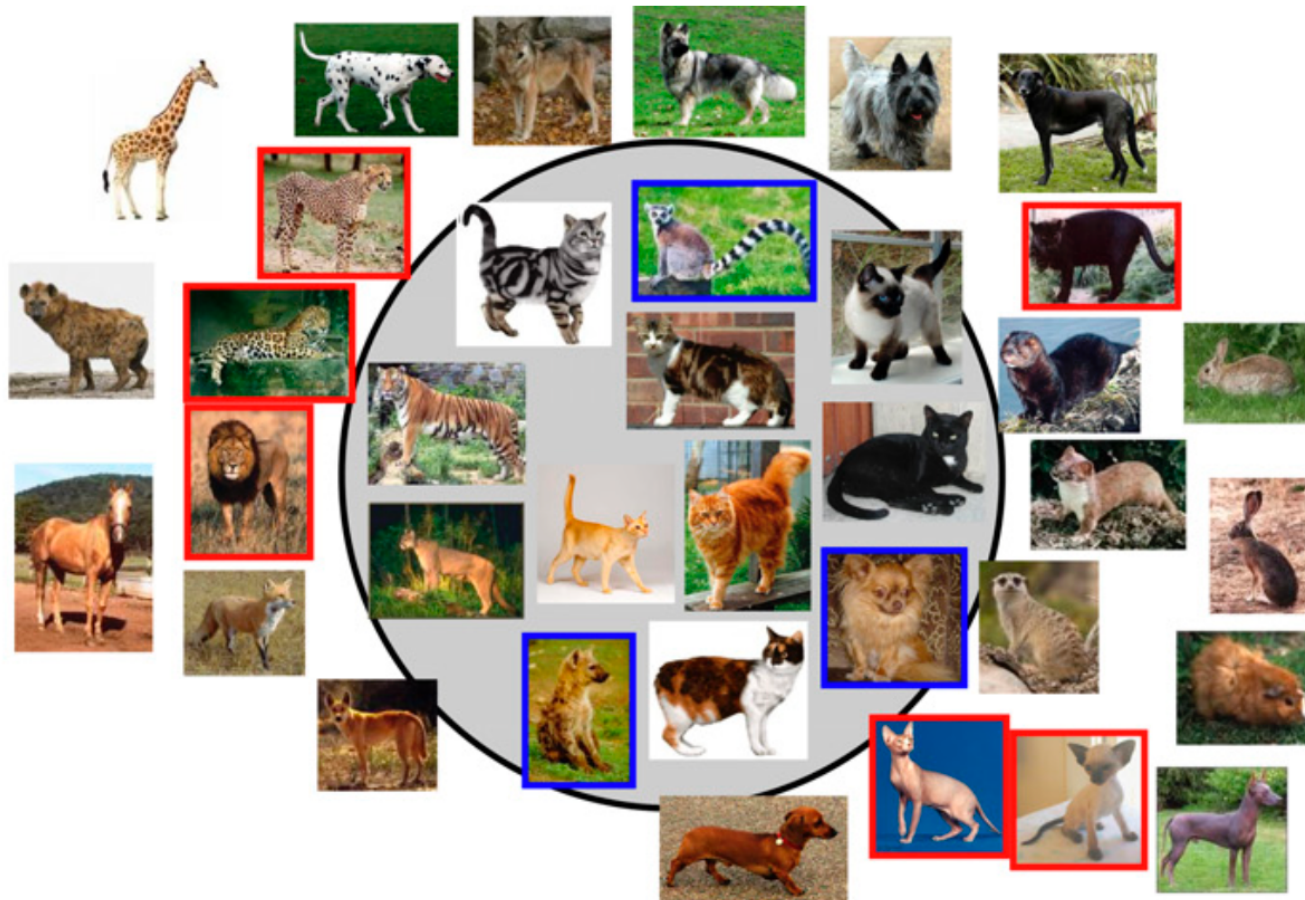
Sandra Baez <sup>a,b,c</sup>, Juan P. Morales <sup>b</sup>, Andrea Slachevsky <sup>b,c,d,e</sup>,  
 Teresa Torralva <sup>a,b</sup>, Cristian Matus <sup>f,g</sup>, Facundo Manes <sup>a,b,c,e,f</sup> and  
 Agustín Ibanez <sup>a,b,c,d,e,f,g</sup>



- - - Controls  
- - - Patients

OFC damage affects empathic concern

# Coherent concepts

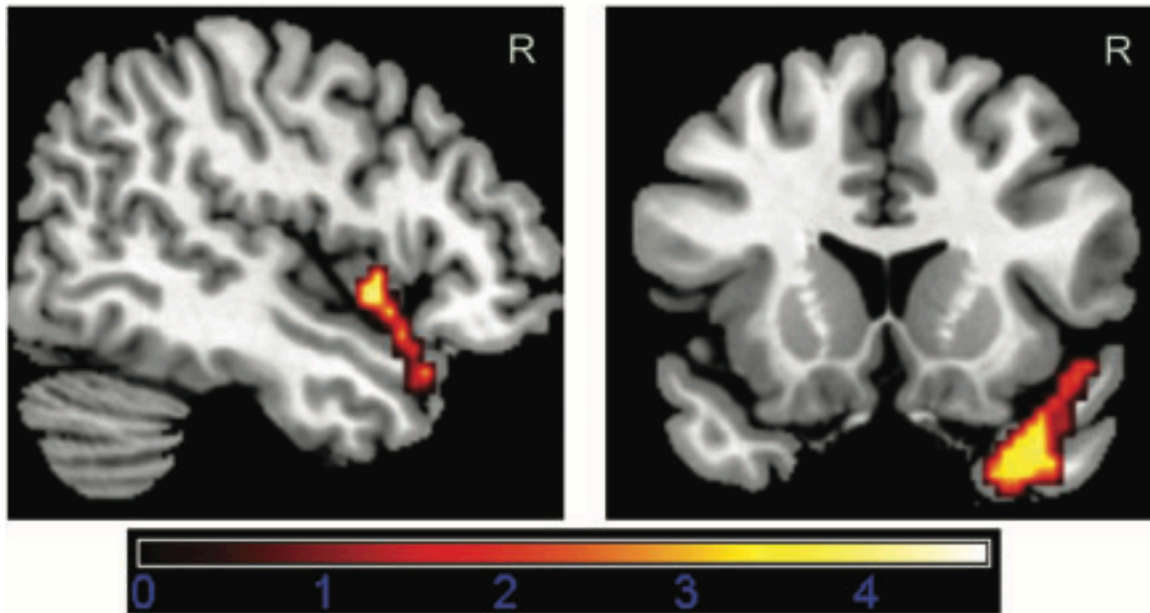


Coherent concepts are computed in the anterior temporal lobes

Matthew A. Lambon Ralph<sup>a,\*</sup>, Karen Sage<sup>a</sup>, Roy W. Jones<sup>b</sup>, and Emily J. Mayberry<sup>a</sup>

Semantic concepts are supported by the left anterior temporal lobe

## Coherent concepts



Social conceptual impairments in frontotemporal lobar degeneration with right anterior temporal hypometabolism

Roland Zahn,<sup>1,2</sup> Jorge Moll,<sup>1,3</sup> Vijeth Iyengar,<sup>1</sup> Edward D. Huey,<sup>1,4</sup> Michael Tierney,<sup>1</sup> Frank Krueger<sup>1</sup> and Jordan Grafman<sup>1</sup>

- ‘polite’
- ‘stingy’
- ‘ambitious’
- ‘tactless’
- ‘adventurous’

Social concepts are supported by the right anterior temporal lobe

- FTD is a neurodegenerative disorder altering personality, social conduct, and linguistic abilities
- The anterior temporal lobes support the processing of coherent concepts

- Neurology of Social Cognition