

Specific Right Temporal Contributions to Distinct Behavioral Subcomponents of Empathy in Neurodegenerative Disease

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INTRODUCTION

Patients with neurodegenerative diseases often lose their ability to accurately read socioemotional signals and make empathic choices in real-life situations. Socioemotional sensitivity requires skills in several domains, such as the ability to identify emotional expressions from face and voice, the ability to infer another's perspective in a situation, capacity to automatically sense and react to another's socioemotional expression, as well as the capacity to respond appropriately by altering behavior. Localizing the distinct anatomic contributions of these subcomponents of empathic behavior provides valuable insight into the function of the frontal and temporal lobe circuits mediating these social behaviors.

While advances in social cognitive neuroscience have revealed the functional anatomy of many aspects of empathy in healthy individuals, the relationship to structural anatomy, particularly in disease models, is not well understood. In addition to providing a clear lesion model of brain-behavior relationships, quantifying empathic behavior in neurodegenerative disease patients can improve differential diagnosis by more precisely localizing neurodegeneration.

Aim: To determine the specific anatomic contributions of the frontal and temporal lobe structures associated with different dimensions of empathic behavior in neurodegenerative disease patients.

METHODS

- Participants:** 235 patients with neurodegenerative disease
- Neuroimaging Analysis:** Each patient had a structural MRI scan within 3 months of behavioral evaluation. Each measure was analyzed using voxel-based morphometric (VBM) of gray matter structural maps, controlling for age, sex, Mini Mental State Exam (MMSE), and total intracranial vol (TIV).
- Measures:** Patients were tested on their ability to correctly read emotions and understand social interactions from videos, and participants' informants reported on three subcomponents of empathy:

Description of Measures

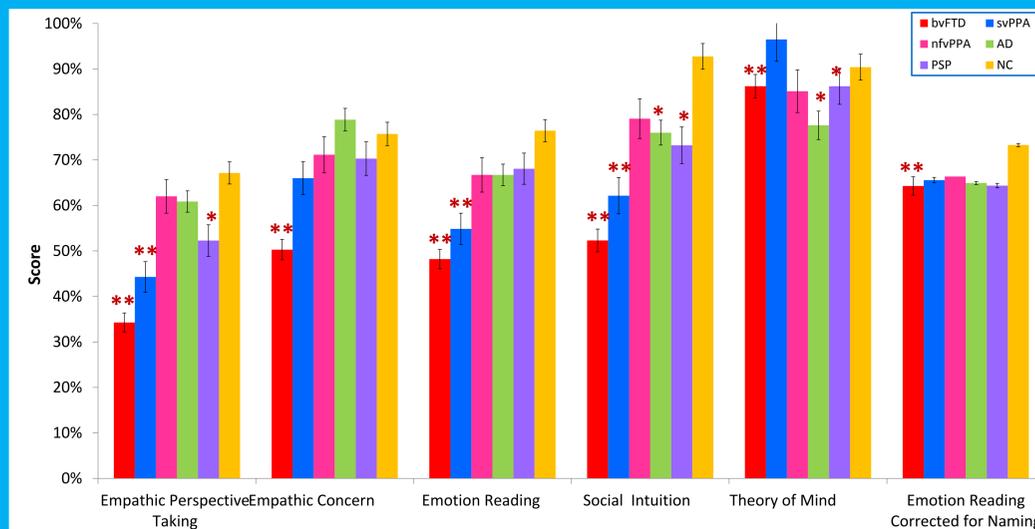
Measure Name	Abbrev	Construct Measured
Face-to-face Measures:		
UCSF Cognitive Theory of Mind	cToM	Visual perspective taking/cognitive theory of mind
The Awareness of Social Inference Test – Emotion Evaluation Test	TASIT-EET	Ability to accurately read emotions in short video vignettes
Informant Measures:		
Interpersonal Reactivity Index - Perspective Taking	IRI-PT	Tendency to spontaneously imagine others' perspective
Interpersonal Reactivity Index - Empathic Concern	IRI-EC	Tendency to enact an other-centered prosocial response
Revised Self-Monitoring scale	RSMS	Intuitive sensitivity/responsiveness to others' subtle social cues

Sample characteristics

	M (SD)	bvFTD ¹	svPPA	nvfPPA	AD	PSP	NC	F/ χ^2	p-value
N		59	22	18	56	22	58	-	-
Gender (M/F)		35/24	13/9	8/10	25/31	7/15	27/31	$\chi^2=6.89$	-
Age		60.8* (9.19)	63.0* (6.35)	68.0 (8.81)	62.4* (8.25)	68.7 (6.29)	69.5 (6.38)	8.93	<0.0001
Education		16.7 (2.87)	16.6 (2.66)	17.2 (3.93)	15.9* (3.12)	15.2* (2.61)	17.7 (2.13)	3.08	0.0065
CDR		1.12* (0.59)	0.80* (0.45)	0.53* (0.27)	0.81* (0.40)	0.70* (0.30)	0.00 (0.07)	47.62	<0.0001
CDR Sum of boxes		6.56* (2.89)	3.82* (2.19)	2.25* (1.70)	4.26* (2.34)	4.41* (2.52)	0.04 (0.22)	49.35	<0.0001
MMSE (max=30)		23.9** (4.47)	21.7** (7.33)	24.5* (5.88)	19.9** (6.21)	25.9 (2.96)	29.3 (0.89)	21.83	<0.0001
GDS (max=30)		7.49** (5.94)	10.2** (6.09)	6.53* (4.63)	8.28** (6.01)	12.8** (5.90)	1.71 (2.31)	11.59	<0.0001

¹ bvFTD = behavioral variant frontotemporal dementia, svPPA = semantic variant primary progressive aphasia, nvfPPA = non-fluent variant PPA, AD = Alzheimer's disease, PSP = progressive supranuclear palsy, NC = healthy older controls
* Differs from NCs at p<0.05

BEHAVIORAL RESULTS



F-statistics and p-values are for overall diagnostic group differences controlling for age, gender, and MMSE. Post hoc pair-wise group differences were performed comparing each patient group with the control group using a Dunnett-Hsu test.
* Group differs from NC at p<.05, ** Group differs from NC at p<.001

Socioemotional Sub-processes Involved in Empathy					
Measure	Visceral emotional experience	Online thinking about own/other's emotions	Non-emotional perspective taking	Basic emotion reading	Higher-order integration of emotions & behavior
Revised Self-Monitoring Scale	X	X		X	X
Empathic Perspective Taking	X	X			
Empathic Concern	X				X
Emotion Reading	X			X	
Cognitive Theory of Mind			X		
	Medial temporal/limbic	Anterior lateral temporal	Posterior Lateral Temporal	Bilateral	Right lateralized
Specific Regional Contributions/Associated Brain Organization					

DISCUSSION

Hemispheric lateralization and empathy

- Measures involving **basic emotion reading** (e.g., TASIT-EET, RSMS) were more likely to be mediated by bilateral circuits, particularly in the temporal lobe
- However, when tasks required **higher-order integration of emotions and behaviors** (e.g., empathic concern (IRI-EC), which often is evoked by complex social or situational cues without a direct emotional display by the other) was almost entirely right lateralized

Medial versus lateral temporal lobe gradient in empathy

- The ability to **experience automatic visceral emotional responses**, an ability required for most of the measures used in this study, was mediated by right medial temporal and limbic regions common across all tests involving emotion
- However, the ability to think/perform online metacognition about one's own or others' emotions (e.g., empathic perspective taking, IRI-PT, and the ability to change one's behavior on the basis of social intuition, RSMS) corresponded with right lateral temporal regions.

Anterior-posterior temporal lobe gradient in empathy

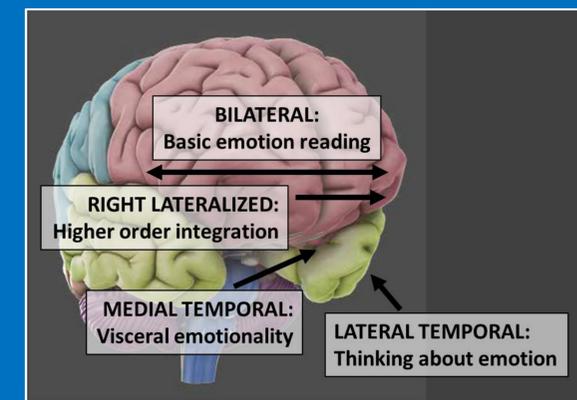
- Though most socioemotional processes reflected by these measures involved anterior temporal cortex, the task reflecting non-emotional social cognition (i.e., cToM) corresponded to a more posterior lateral temporal anatomy, as well as right frontal regions related to sustained attention and executive functioning

STRUCTURAL VBM RESULTS

Regions where loss of gray matter volume predicts diminished socioemotional function

Measure	Brain regions
Revised Self-Monitoring Scale (RSMS)	anterior insula (R>L) basal ganglia (R) medial temporal (R) inferior temporal gyrus (R/L) medial orbitofrontal (R>L) inferior frontal gyrus (R) thalamus (R)
Perspective Taking (IRI-PT)	anterior insula (R>L) basal ganglia (R/L) medial temporal (R) inferior temporal gyrus (R) middle temporal gyrus (R) thalamus (R)
Emotion Reading (TASIT-EET) Corrected for Boston Naming test	anterior insula (R>L) basal ganglia (R) medial temporal (R) inferior frontal gyrus (R/L) medial orbitofrontal (R/L) anterior cingulate (R) thalamus (R)
Empathic Concern (IRI-EC)	anterior insula (R) basal ganglia (R) medial temporal (R) medial orbitofrontal (R) thalamus (R)
Cognitive Theory of Mind (UCSF cToM)	middle frontal gyrus (R) posterior middle temp gyrus (R)

T values: 4.33 to 6.33. All figures min pFWE<0.05, T > 4.33



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