

# Neuroanatomical Correlates of Expressive Prosody Impairment in Behavior Variant Frontotemporal Dementia

Darren Ha<sup>4</sup>, Joseph Barsuglia<sup>1,2</sup>, Grace Lee<sup>1</sup>, Po Lu<sup>1</sup>, Hemali Panchal<sup>4</sup>, Noosheen Javadi<sup>4</sup>, Aditi Joshi<sup>1,2</sup>, Elvira Jimenez<sup>1,2</sup>, Michelle Mather<sup>1,2</sup>, Mario F. Mendez<sup>1,2,3</sup>  
Departments of Neurology<sup>1</sup> and Psychiatry & Biobehavioral Sciences,<sup>3</sup> Department of Physiological Science, University of California, Los Angeles<sup>4</sup>  
David Geffen School of Medicine, University of California at Los Angeles; and Section of Neurology,<sup>2</sup> V.A. Greater Los Angeles Healthcare Center, Los Angeles, California.

## Background

Expressive prosody output is essential in conveying emotion and establishing interpersonal connectivity with others in an interaction. Examples of expressive prosody include variation of pitch during speech, eye contact, and appropriate variation in facial expressions. Patients with dementia have been shown to exhibit a lack of pitch modulation, mutual eye contact, and facial expressivity during social interactions.<sup>1,2,3</sup> However, the neural correlates for these behaviors have yet to be identified or investigated. In this study, we used tensor-based morphometry (TBM) to characterize regions of the brain correlated with clinical assessment of decreased or atypical expressive prosody (i.e., eye movements, facial expression, and voice variations) in patients with behavioral variant frontotemporal dementia (bvFTD) and early onset Alzheimer's disease (EOAD).

## Methods

Fifteen bvFTD patients and 16 EOAD patients, matched on key demographic variables, were included in the study. We used a novel clinician rating scale of behavioral features called the Frontotemporal Observational Inventory. The scale includes 3 subdomains: voice and pragmatics, eye findings, and face findings. Clinicians rate behaviors as 'abnormal' or 'normal'. Individual item scores are summed for a total score in each domain. Statistical analyses were performed using SPSS software. Mann-Whitney test was used to compare domain scores (e.g., eye findings). \*Chi-square test was used for gender.

**Table 1. Patient Demographics**

	bvFTD (n=15)	EOAD (n=16)	p-value
Age (years)	61.9 (±10.4)	58.3 (±5.76)	n.s.
Gender (males/females)	8M / 7F	7M / 9F	n.s.*
Est. age of onset (years)	57.8 (±10.2)	54.6 (±6.91)	n.s.
Years since onset	4.07 (±3.26)	3.75 (±2.27)	n.s.
Education (years)	15.4 (±2.23)	16.3 (±2.21)	n.s.
Mini-Mental State Exam	24.8 (±4.38)	22.9 (±4.92)	n.s.

### MRI Protocol:

All participants underwent MRI using a standardized protocol on the same 1.5T Siemens Avanto MRI scanner. High-resolution T1-weighted 3D MRI scans were acquired in the coronal plane using an MPRAGE sequence with the following acquisition parameters: TR=2000 ms, TE=2.49 ms, TI = 900ms, flip angle = 8°, slice thickness = 1mm, 25.6 cm field of view, and final voxel size of 1.0 mm<sup>3</sup>.

### Image Processing:

An automated Brain Surface Algorithm (BSE) was applied, along with manual editing to generate a de-skulled brain volume with the scalp, dura, and meninges removed.

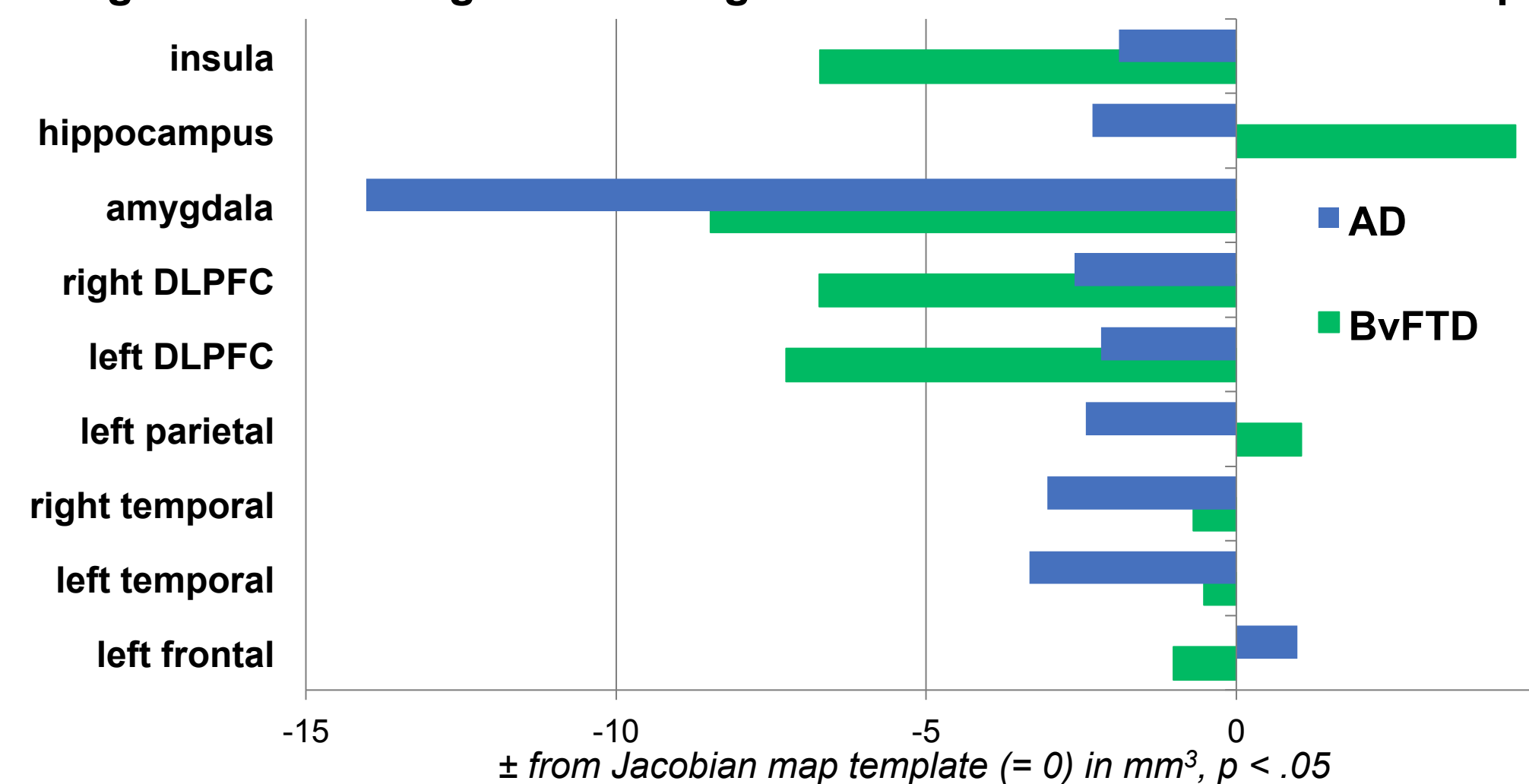
To adjust for global differences in brain positioning and scale across individuals, all scans were linearly registered to the stereotaxic space defined by the International Consortium for Brain Mapping (ICBM) with a 9-parameter transformation. Globally aligned images were resampled in an isotropic space of 230 voxels for each axis (x, y, and z) with a final voxel size of 1 mm<sup>3</sup>. To quantify 3D patterns of volumetric brain differences for each subject, an individual change map, or Jacobian map, was computed by non-linearly registering each individual scan to a template brain.

## Results

**Table 2. Expressive Prosody Scores and Percentage of Sample rated as "abnormal" on the Frontotemporal Observational Inventory**

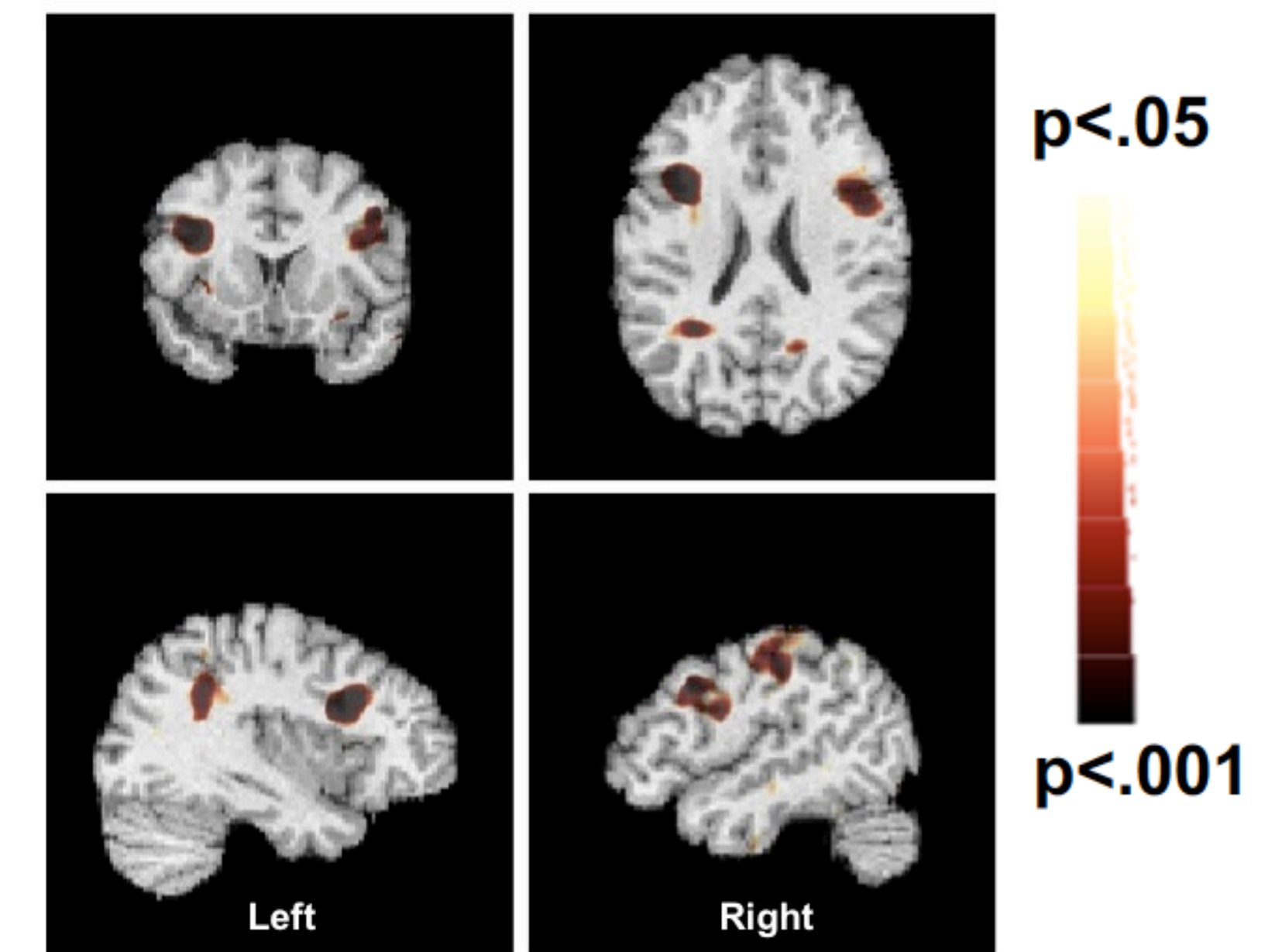
FTD Observational Inventory	bvFTD (m/sd)	EOAD (m/sd)	p-value
<b>Voice and Pragmatics</b> (range 0-3 items)	<b>1.07 (0.96)</b>	<b>0.06 (0.25)</b>	<b>.002</b>
Volume, tone, style of speech (% abnormal)	33.3%	0%	0.012
Turn-taking in conversations	26.7%	6.3%	0.122
Timing or bluntness of responses	53.3%	0%	0.001
<b>Eye Findings</b> (range 0-3 items)	<b>1.20 (1.15)</b>	<b>0.0 (0.0)</b>	<b>.001</b>
Frequency of eye blinks (% abnormal)	20%	0%	0.060
Eye contact or direction of gaze	40%	0%	0.005
Length of eye contact	40%	0%	0.005
<b>Face Findings</b> (range 0-2 items)	<b>0.80 (0.86)</b>	<b>0.0 (0.0)</b>	<b>.011</b>
Expression context-appropriate (% abnormal)	21.4%	0%	0.051
Variability of facial expressions	46.7%	0%	0.002
<b>Total Sum Score</b>	<b>3.07 (2.67)</b>	<b>0.6 (0.25)</b>	<b>.001</b>

**Figure 1. Brain Regions with Sig. Difference in Volume Across Groups**



In a partial correlation (group and age controlled) correlations were found between lower volume in the bilateral dorsolateral prefrontal cortex (DLPFC) and abnormal voice /pragmatics ( $r = -.50$ ,  $p = 0.02$ ), greater on the right DLPFC ( $r = -.56$ ,  $p = .007$ ). Trends were noted for lower bilateral DLPFC volume and eye ( $r = -.39$ ,  $p = .07$ ) and face findings ( $r = -.32$ ,  $p = .14$ ). A higher mean total sum score of prosody items correlated with DLPFC bilaterally ( $r = -.45$ ,  $p = .04$ ) greater on the right ( $r = -.43$ ,  $p = .04$ ) than left ( $r = -.16$ ,  $p = .49$ ) (See Figure 2).

**Figure 2. Abnormal Prosody Item Sum Score Correlates with lower volume in the dorsolateral prefrontal cortex (right > left).**



## Discussion

Patients with bvFTD exhibited greater atypical expressive prosody in all domains compared to EOAD patients. Lower brain volume in the right frontal lobe and DLPFC was associated with specific domains of expressive prosody as identified in Table 2. These results are consistent with studies correlating bvFTD with decreases in right hemispheric cortical activity, as well as a previous case study done by Ghacibeh and Heilman where right frontal lobe atrophy was associated with a patient's inability to convey emotional prosody, specifically facial emotions, as well as a deficiency in detecting pitch.<sup>4</sup> This study advances our knowledge of the neural underpinnings of socioemotional deficits in bvFTD. Future studies can focus more on quantifying the degree of output in subcomponents of emotional prosody as a way to further characterize brain disease and aid the diagnosis of bvFTD.

## References

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