SUPPLEMENT

The supplement includes:

1.1. Neuropsychological assessments

1.1.1. Executive

Set shifting or mental flexibility was assessed by modified Trail Making test (Delis *et al.*, 2004; Ranasinghe *et al.*, 2016). The modified Trail Making test requires the patient to draw lines linking items marked on paper and serially alternate between numbers and days of the week for a period of 120 seconds. The number of correct connections and time taken for the task were recorded. To adjust for the fact that some patients do not complete the task within the required time window of 120 seconds, the dependent measure was calculated as the number of correct connections made per second. Cognitive control was assessed by the Stroop tests (Golden, 1978, 2002). lexical fluency, was assessed with 'D-words', in which patients generate as many words as possible that are not proper nouns within 60 seconds beginning with the letter 'D'(Spreen and Benton, 1977; Benton *et al.*, 1994). A nonverbal counterpart of fluency comprises design fluency (Delis *et al.*, 2004), in which patients are required to use 4 lines to connect the dots within boxes each containing five dots, creating a unique pattern each time. We recorded the number of D-words, animals and patterns patients generated, within 60 seconds. Phonological short term memory was assessed by digit span forward, and verbal working memory was assessed by digit span backward.

1.1.2. Visuospatial

Subjects were asked to copy a complex figure (Benson figure) as the object of visual construction and the accuracy was scored on a 17 point scale (Possin *et al.*, 2011). The Number Location subtest of the Visual Object Space Perception (VOSP)(Warrington and James, 1991) test required the participant to precisely locate a stimulus on a two-dimensional plane, requiring dorsal-stream ("where") visual processing and scored out of 10. The face matching subtest of the Comprehensive Affect Testing System (CATS)(Froming *et al.*, 2006) is a ventral-stream task involving 12 trials where the participant determined whether two faces are the same or different.

1.1.3. Memory:

Verbal episodic memory was evaluated with the California Verbal Learning Test–Short Form (CVLT), which includes a list of 9-item words, presented over 4 learning trials (Delis *et al.*, 2000). Immediate (30 seconds) and delayed (10 minutes) CVLT were assessed by free recall of the list at 30-seconds and 10-minutes intervals respectively. The correct number of items recalled, out of 9 were recorded. Visual memory was assessed by asking the patients to draw the Benson figure2 from memory after a 10-minute delay, and scored on a 17 point scale (Possin *et al.*, 2011).

1.1.4. Language:

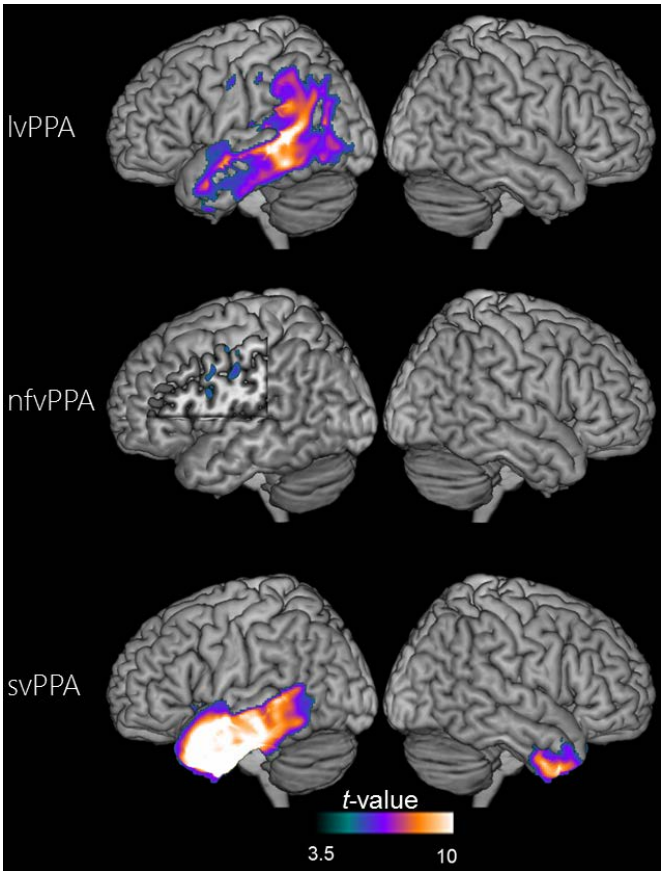
Speech and syntactic production were evaluated using the Western Aphasia Battery (WAB)(Kertesz, 1980). The spontaneous speech section of WAB was analyzed to derive specific

measures reflecting fluency according to previously described methods (Wilson *et al.*, 2010). Repetition was assessed based on WAB-repetition and scored out of 100. Sentence and syntactic comprehension abilities were tested using the Sequential Command subtest of the WAB. Motor speech was evaluated using the Motor Speech Evaluation (MSE) (Wertz, 1984). Videotaped MSEs were reviewed by a certified speech pathologist to rate apraxia of speech and dysarthria in each patient. Speech apraxia rating is defined as impaired articulatory planning resulting in slow speech rate, effortful articulation, sequencing errors and frequent consonant distortions. Dysarthria is defined as a primary motor deficit of the musculature involved in speech and is characterized mostly by consistent and predictable errors. Confrontation naming was assessed with a 15-item short form of the Boston Naming Test (Mack *et al.*, 1992; Kaplan *et al.*, 2001). The number of correctly named items was recorded out of a total score of 15. Word comprehension was tested with a subset of 16 items of the Peabody Picture Vocabulary Test (PPVT; 4 items in each: verbs, descriptive, animate and inanimate), in which each item required the patient to match a word representing object or action and attribute to one of four picture choices (Dunn and Dunn, 2007). Category fluency, was assessed with the ability to generate a list of items within a given category, in which patients generated as many as possible names of animals within 60 seconds (Spreen and Benton, 1977; Benton *et al.*, 1994). Syntax comprehension was measured using a series of sentences, which the examiner read aloud and the participant had to select among 2 options the picture that best matched the sentence. The final score of syntax comprehension was estimated as the correct percentage.

1.2. Voxel based morphometry (VBM) analysis

Image processing was performed using the unified segmentation procedures of VBM toolbox of SPM8 and DARTEL toolbox. After tissue segmentation, gray matter probabilistic maps were transformed onto the standard MNI space. The modulated images were smoothed with an 8 mm full-width-at-half-maximum isotropic Gaussian kernel to be used in the subsequent analyses. We generated gray matter atrophy maps for each PPA subgroup, compared to a separate large group of age-matched healthy controls (n=50 healthy participants evaluated at the NIC using the same unified MRI acquisition protocol as patients, on 1.5, 3, or 4 Tesla scanners). When comparing between each subgroup and controls, age, gender, scan-strength and total intracranial volume were included into the model as covariates.

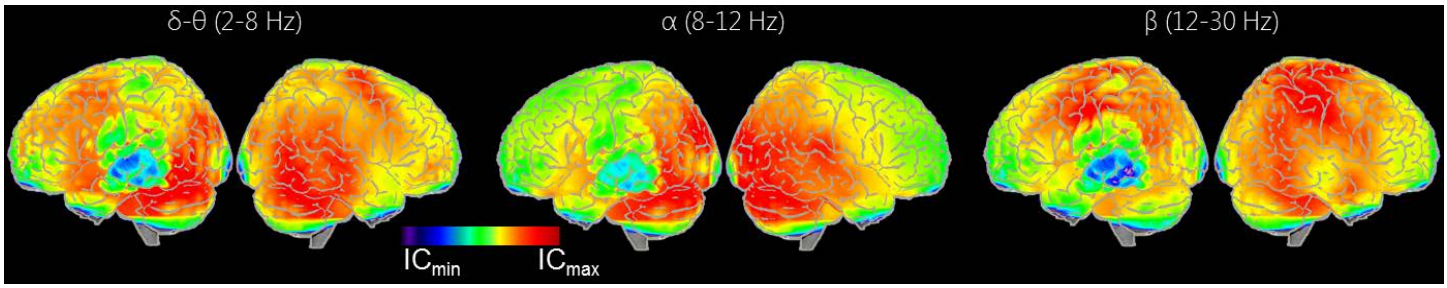
2. Supplementary Figure 1



Cortical grey matter atrophy maps of the PPA variants. Voxel based morphometry-derived atrophy maps of each PPA subgroup from top to bottom lvPPA, nfvPPA and svPPA. T maps show the atrophy patterns compared to a cohort of age matched controls (n = 50), and are superimposed onto whole-brain template. Each variant showed a characteristic pattern of atrophy and all three variants showed stronger effects in the left hemisphere compared to the right. nfvPPA patients showed minimal cortical atrophy and a cutout is shown to illustrate the distribution of neuronal loss. Effects are corrected for age, gender and total intracranial volume of each individual. Corrections for multiple comparisons are performed corrected using family-wise error at the whole brain level at $P<0.05$.

Abbreviations: lvPPA=logopenic variant; nfvPPA = non-fluent variant; PPA = primary progressive aphasia; svPPA = semantic variant.

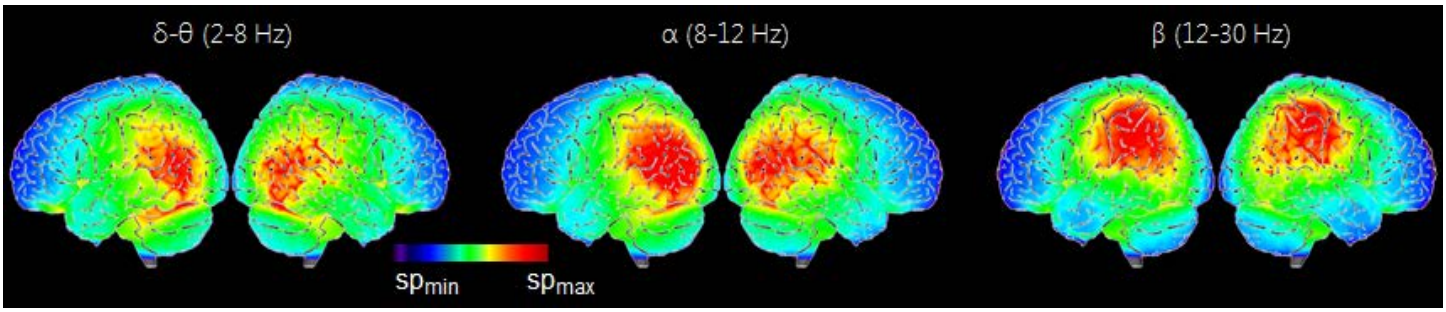
3. Supplementary Figure 2



Spatiotemporal patterns of resting state functional connectivity in age-matched controls. Global functional connectivity is estimated using imaginary coherence (IC) for each frequency band (from left to right: delta-theta, alpha, and beta), in age-matched healthy control cohort (n=20). The color gradient indicates the strength of connectivity. For clarity of illustration, images are thresholded to the minimum and maximum IC values under each band. IC values are superimposed onto a rendering of Montreal Neurological Institute (MNI) template brain image.

Abbreviations: δ-θ = delta-theta; α = alpha; β = beta; lvPPA = logopenic variant; nfvPPA = non-fluent variant; PPA = primary progressive aphasia; svPPA = semantic variant.

4. Supplementary Figure 3



Spatiotemporal patterns of spectral power in age-matched controls. Spectral power values from MEG source space analysis in age-matched healthy control cohort (n=20), for each frequency band is shown from left to right: delta-theta, alpha, and beta. The color gradient corresponds to the degree of spectral power. For clarity of illustration, images are thresholded to the minimum and maximum power values under each band, and are superimposed onto a rendering of Montreal Neurological Institute (MNI) template brain image.

Abbreviations: δ-θ = delta-theta; α = alpha; β = beta; lvPPA = logopenic variant; nfvPPA = non-fluent variant; PPA = primary progressive aphasia; svPPA = semantic variant.

5. Supplementary Table 1

Anatomic areas showing significant functional connectivity changes in each PPA variant

	Cluster size (voxels)	Anatomic area and MNI coordinates (*x, y, z*)	
		Left hemisphere	**Right hemisphere**
lvPPA			
Delta-theta (2 - 8 Hz)	319	Superior-medial frontal gyrus (Left BA10; -10, 55, 25) Supra marginal gyrus (Left BA 39; -60,-55, 25)	Superior-medial frontal gyrus (Right BA10; 0, 65, 15) Supra marginal gyrus (Right BA 40; 40, -35, 45)
Alpha (8 - 12 Hz)	23	Inferior temporal gyrus (Left BA 37; -60, -55, -5)	-
Beta (12 - 30 Hz)	338	Inferior frontal gyrus (Left BA 44; -50, 25, 25) Primary sensory region (-50, -15, 35) Superior temporal gyrus (Left BA39; -50, -55, 10) Inferior temporal gyrus (Left BA 20; -60, -35, -25)	Primary sensory region (50, -25, 45) Para-hippocampus (30, -25, -15) Inferior temporal gyrus (Right BA 20; 40, -5, -35) Fusiform (Right BA37; 50, -45, -15)
nfvPPA			
Delta-theta (2 - 8 Hz)	319	Superior-medial frontal gyrus (Left BA8; -10, 45, 45)	Superior medial frontal gyrus (Right BA8; 0, 35, 45)
Alpha (8 - 12 Hz)	63	Inferior frontal gyrus (-50, 45, 5)	Superior temporal gyrus (Right BA22; 60, 5, -5)
Beta (12 - 30 Hz)	305	Inferior frontal gyrus (Left BA47; -40, 35, -15)	Inferior frontal gyrus (Right BA47; 50, 35, -5) Fusiform (BA 37; 65, -45, -15) Inferior temporal gyrus (60, -45, -5)
svPPA			
Delta-theta (2 - 8 Hz)*	262	Middle occipital lobe (-40, -85, 5)	Temporal pole (50, 15, -35)
Alpha (8 - 12 Hz)	23	Post central gyrus (-65, -15, 25) Superior temporal gyrus (-70, -25, 5)	-
Beta (12 - 30 Hz)	139	Pre central gyrus (Left BA 6; -50, -5, 25) Superior temporal gyrus (-70, -25, 5)	Superior frontal gyrus (Right BA 9; 15, 55, 35) Primary sensory (50, -25, 45) Inferior occipital (Right BA 19; 45, -70, -15)

Abbreviations: BA = Brodmann area; lvPPA = logopenic variant; MNI coordinates = Montreal Neurological Institute brain coordinates; nfvPPA = non-fluent variant; PPA = primary progressive aphasia; svPPA = semantic variant.

* = Delta-theta level differences in svPPA patients were not significant after controlling for cortical atrophy (Figure 2).

The table shows the anatomical labels (with the Brodmann Area labels when available) of each voxel cluster in left and right hemispheres. The MNI coordinates indicate the local maxima depicting the most distinct imaginary coherence difference compared to age-matched controls within the identified cluster. The complete regions are shown in Figure 1.

6. Supplementary Table 3

Anatomic areas showing significant spectral power changes in each PPA variant

	Cluster size (voxels)	**Anatomic area and MNI coordinates (*x, y, z*)**	
		Left hemisphere	**Right hemisphere**
lvPPA			
Delta-theta (2 - 8 Hz)	671	Left superior frontal gyrus (Left BA9; -20, 35, 25)	Right superior frontal gyrus (Right BA9; 10, 35, 25)
Alpha (8 - 12 Hz)	184	Left cuneus (-10, -85, -5)	Right cuneus (0, -85, 5)
Beta (12 - 30 Hz)	581	Left superior temporal gyrus (-4, -35, 5)	Right middle temporal gyrus (40, -45, 5)
nfvPPA			
Delta-theta (2 - 8 Hz)	87	Left temporal pole (Left BA 38; -20, 35, 25)	Right inferior frontal gyrus (Right BA 44; 60, 15, 5)
Alpha (8 - 12 Hz)	137	-	Right inferior frontal gyrus (Right BA 44; 50, 15, 15)
Beta (12 - 30 Hz)	183	Left precentral gyrus (Left BA 44; -50, 5, 15)	Right inferior frontal (Right BA 45; 40, 25, 5)
svPPA			
Delta-theta (2 - 8 Hz)*	202	Left inferior temporal lobe (Left BA 20; -40, -5, -35)	Right inferior temporal lobe (Right BA 20; 50, -5, -35)
Alpha (8 - 12 Hz)	189	Left inferior temporal lobe (Left BA 20; -40, -5, -35)	Right superior temporal lobe (Right BA 22; 50, -5, -15)
Beta (12 - 30 Hz)	62	Left temporal pole (Left BA 38; -40, 15, -15)	-

Abbreviations: BA = Brodmann area; lvPPA = logopenic variant; MNI coordinates = Montreal Neurological Institute brain coordinates; nfvPPA = non-fluent variant; PPA = primary progressive aphasia; svPPA = semantic variant.

* = spectral power differences are not significant after controlling for cortical atrophy (Figure 4).

The table shows the anatomical labels (with the Brodmann Area labels when available) of each voxel cluster in left and right hemispheres. The MNI coordinates indicate the local maxima depicting the most distinct spectral power density difference compared to age-matched controls within the identified cluster. The complete regions are shown in Figure 3.

7. REFERENCES

Benton AL, Hamsher Kd, Sivan AB. Multilingual Aphasia Examination : Third Edition. San Antonio, TX: The Psychological Corporation; 1994.

Delis DC, Kramer JH, Kaplan E, Holdnack J. Reliability and validity of the Delis-Kaplan Executive Function System: an update. J Int Neuropsychol Soc 2004; 10(2): 301-3.

Delis DC, Kramer JH, Kaplan E, Ober BA. California Verbal Learning Test - Second Edition, Adult Version. San Antonio, TX: The Psychological Corporation; 2000.

Dunn LM, Dunn DM. Peabody picture vocabulary test. 4 ed. Minneapolis, MN: Pearson Assessents; 2007.

Froming K, Levy M, Schaffer S, Ekman P. The comprehensive affect testing system: psychology software, Inc; 2006.

Golden CJ. Stroop Color and Word Test: A manual for clinical and experimental uses. Chicago, IL: Stoelting Co; 1978.

Golden CJ. Stroop Color and Word Test: Revised examiner's manual. Wood Dale, IL: Stoelting Co; 2002.

Kaplan EF, Goodglass H, Weintraub S. The Boston Naming Test : Second Edition. Philadelphia: Lippincott Williams and Wilkins; 2001.

Kertesz A. Western aphasia battery. Ontario: University of Western Ontario Press; 1980.

Mack WJ, Freed DM, Williams BW, Henderson VW. Boston Naming Test: shortened versions for use in Alzheimer's disease. J Gerontol 1992; 47(3): P154-8.

Possin KL, Laluz VR, Alcantar OZ, Miller BL, Kramer JH. Distinct neuroanatomical substrates and cognitive mechanisms of figure copy performance in Alzheimer's disease and behavioral variant frontotemporal dementia. Neuropsychologia 2011; 49(1): 43-8.

Ranasinghe KG, Rankin KP, Lobach IV, Kramer JH, Sturm VE, Bettcher BM, *et al.* Cognition and neuropsychiatry in behavioral variant frontotemporal dementia by disease stage. Neurology 2016; 86(7): 600-10.

Spreen O, Benton AL. Neurosensory Center Comprehensive Examination for Aphasia. Victoria, BC: Neuropsychology Laboratory, University of Victoria; 1977.

Warrington EK, James M. The Visual Object and Space Perception Battery. Bury St. Edmunds, Suffolk, England: Thames Valley Test Company; 1991.

Wertz RT. Apraxia of speech in adults: The disorder and its management: Pearson Allyn & Bacon; 1984.

Wilson SM, Henry ML, Besbris M, Ogar JM, Dronkers NF, Jarrold W, *et al.* Connected speech production in three variants of primary progressive aphasia. Brain 2010; 133(Pt 7): 2069-88.