SUPPLEMENTAL MATERIAL**:**

Methods:

1) MRI acquisition parameters

A) T1-weighted images (3D MP-RAGE, TR = 2250ms, TE = 4.15ms, 256×256matrix, 256×256mm FOV, parallel imaging GRAPPA=2, 80 reference lines, TA=377s);

B) Diffusion EPI scan (30-directions with b=1000 s/mm2 and b=2000 s/mm2, TR = 6100ms, TE = 101ms, 82×82 matrix, 222x222mm FOV, parallel imaging GRAPPA=2, 80 45 contiguous 2.7mm axial slices, TA=390s).

2) Cortical segmentation and spatial registration of T1 weighted images.

We employed an extension of the software Statistical Parametric Mapping (SPM) entitled "Clinical Toolbox" developed by our group[1]. The Clinical Toolbox utilizes a cost-function approach[2] to normalize the brain into the standard stereotaxic space (MNI space). This step employs a manually-defined map of the stroke lesion, drawn by one of the authors (Bonilha) to weigh tissue influence on normalization. Notably, the Clinical Toolbox exploits SPM's unified normalization-segmentation subroutines to yield probabilistic gray and white matter tissue maps[3]. These were essential to guide subsequent connectivity assessment steps. Linear and non-linear normalization parameters obtained from the normalization of the brain to standard space were inverted and applied to a BA ROI Atlas in standard space (distributed with MRIcro[4]). The probabilistic map of gray matter in native T1 space was segmented into a map of cortical BA ROIs. Importantly, the areas originally involved in the hand-drawn lesion were excluded from this step in order to eliminate the erroneous segmentation of the necrotic tissue into viable cortical regions. These steps are demonstrated in Figure 1.

3) Transforming white matter map and cortical ROIs onto DTI space.

To improve registration between T1 and DTI spaces, the native volumetric T2 weighted image was linearly co-registered onto the native T1 image using mutual information algorithms in SPM. This step generated a T2 weighted image matched to the native T1 image (the "registered T2 image"). The registered T2 image was linearly

co-registered onto the B0 image using FMRIB's Linear Image Registration Tool (FLIRT). The transformation matrices were then applied to the map of segmented cortical ROIs and to the white matter probabilistic tissue map, yielding cortical ROIs and white matter maps in DTI space.

4) Fiber tracking and connectome reconstruction.

Whole brain tractography was reconstructed in DTI space using the software Diffusion Toolkit (DTK)[5]. Acquisition geometry and gradients were updated using the tool dcm2nii, as part of the software MRIcron. Tractography was reconstructed using a maximal angle threshold of 45 degrees, in accordance with the Fiber Assignment by Continuous Tracking (FACT) algorithm[6]. Two restriction maps were applied. The first one was a dynamic contrast range based on the diffusion-weighted image (DWI), as part of default DTK parameters. Importantly, the second restriction mask was the probabilistic white matter map transformed into DTI space. By applying a white matter restriction mask, we ensured that important quality benchmarks were met, namely: 1) tractography did not attempt to reconstruct fibers in the location of the necrotic lesion, where random diffusion can lead to erroneous fiber tracking and misrepresentation of connectivity; 2) the termination boundaries overlapped and extended into the cortical ROI map, thereby ensuring an accurate end point calculation for each white matter fiber. Once cortical ROIs and white matter maps were registered into DTI space, each and every white matter fiber was evaluated regarding its origin and termination. For each possible pair of BAs, the number of fibers connecting the pair was computed and recorded in a connectivity matrix. These steps were performed through in-house scripts written in MATLAB.

5) Cortical connectivity.

In order to assess connectivity, we computed the weighted sum of all connections to four cortical areas that are typically implicated in language processing: BAs 22, 37, 44, and 45. Certainly, other regions play a role in language processing. **However, we chose** to focus on these four areas to highlight the potential importance of disconnection in functional impairment. Finally, to assess fiber reduction, the

percentage of fibers compared with the homologous BA in the right hemisphere is calculated (yielding the “percentage number of fibers”, as referred to in the sections below). These steps are performed through in-house scripts written in MATLAB. Importantly, this step aimed to eliminate the effect of bias caused by subjects having been scanned in different scanners or with different DTI sequences. Since each patient’s connectivity measures were adjusted based on the patient’s contralateral hemisphere, the final connectivity measure was normalized based on each subject’s imaging properties and therefore comparable across all subjects.

6) Necrotic lesion burden.

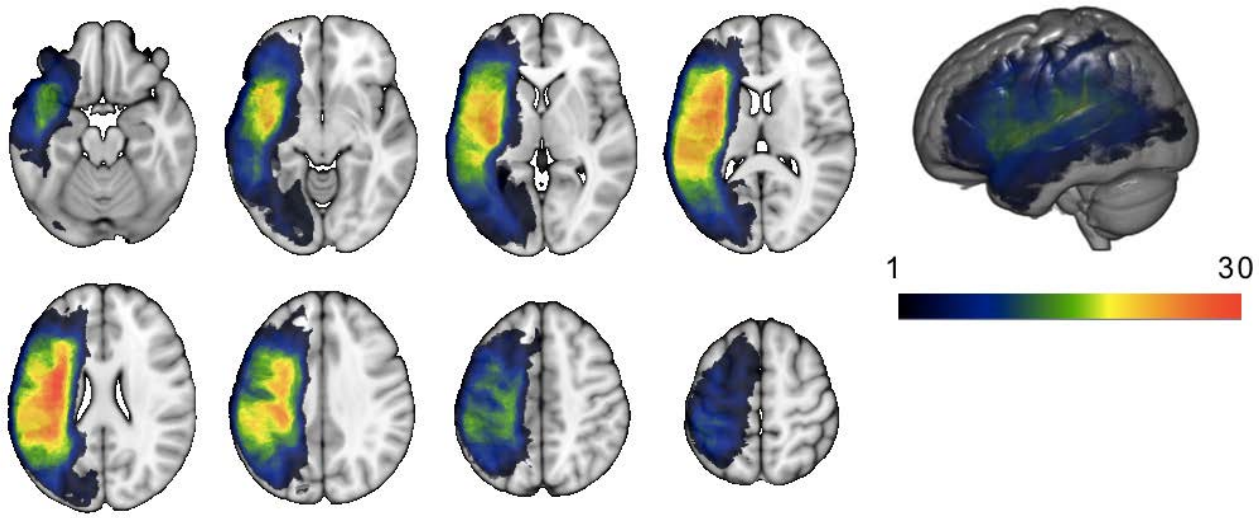
The percentage of damage to each cortical ROI is calculated by overlaying the hand drawn lesion map onto the parcellated cortical map in native T1 space, where the percentage of damage to each BA is calculated. These steps are performed through in-house scripts written in MATLAB.

Online Table I- Demographic and language information. Language performance was assessed through the Western Aphasia Battery (WAB) and Philadelphia Naming Test (PNT). Legends: RH=right handed; LH=left handed; M=male, F=female; W=white; AA= African-American; SD=standard deviation; AQ= aphasia quotient (WAB); Comp=comprehension (WAB); Flu=fluency (WAB); Repet=repetition (WAB); NamingSub=Naming Subscore (WAB); Naming=fraction of correctly named items (PNT).

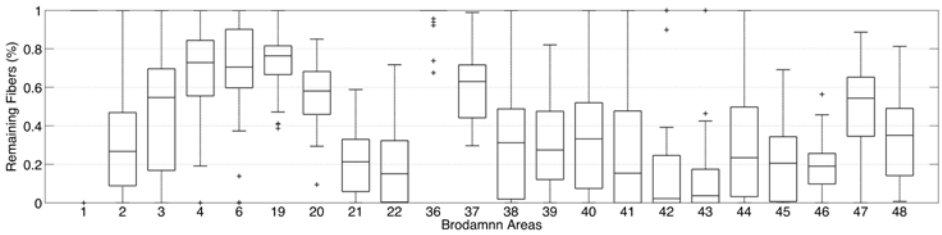
Subject	Handedness	Age	Gender	Race	Aphasia Type	AQ	Comp	Flu	Repet	NamingSub (WAB)	Naming (PNT)
1	RH	77	M	W	Anomic	87.8	8	9	9.2	8.7	0.65
2	RH	71	M	W	Broca	62.7	9.35	4	3.4	7.6	0.32
3	RH	69	M	W	Broca	87.2	8.9	9	8.2	8.5	0.73
4	RH	38	M	W	Broca	41.8	7.5	4	2.8	3.6	0.42
5	RH	67	M	W	Anomic	77.8	9	4	9.4	8.5	0.5
6	RH	50	M	AA	Anomic	80.8	9.8	8	8.3	8.3	0.4
7	RH	48	F	W	Anomic	79	9	6	8.2	8.6	0.06
8	RH	65	M	W	Anomic	96	10	9	9.2	10	0.91
9	RH	39	F	W	Broca	32	8	1	2.5	2.7	0.04
10	RH	58	M	B	Anomic	83.2	9.3	7	9	9.3	0.78
11	RH	77	M	W	Broca	21	4	1	2		1
12	RH	68	F	B	Broca	21	10	1	0	0	0.9
13	RH	64	M	B	Conduction	80	9	9	6.1	7	0.54
14	RH	75	F	W	Anomic	92	9	9	9.6	9	0.83
15	RH	62	M	W	Anomic	86	10	8	9.4		.
16	RH	70	M	W	Broca	51	7	2	7.6	3.7	0.51
17	RH	49	F	W	Broca	43	7	4	1.2	2.5	0.63
18	RH	86	F	W	Anomic	68.7	7.25	7	7.4	6.7	0.38
19	RH	57	M	W	Wernicke	31	6	8	0.6	0.8	0.84
20	RH	60	F	W	Anomic	86	9	8	9.6	8.6	0.82
21	RH	57	F	W	Anomic	95	9	10	9.6	9.2	0.85
22	RH	63	M	W	Anomic	92.1	9.85	9	9.8	8.4	0.81
23	RH	60	F	W	Global	23	6	0	1.7		0.04
24	RH	52	F	W	Broca	31	7	2	2.6	2.9	0.05
25	RH	57	M	W	Broca	71	7	5	7.4	8.5	0.05
26	RH	82	F	W	Conduction	70	7	7	6	6.6	0.37
27	RH	47	M	W	Broca	26	5	1	1.4		.
28	RH	62	M	W	Broca	48	6	4	5.6	1.9	0.08
29	RH	60	M	W	Wernicke	31	5	5	0.3	0.6	0.92
30	RH	62	F	W	Global	17	6	1	0.5	1	0.88
31	RH	76	M	W	Wernicke	31	4	8	0.8	0.6	0.01
32	RH	80	F	W	Global	25	5	1	1.5		.
33	RH	43	F	W	Anomic	82	8	8	8.2	9.1	0.87

34	RH	71	M	W	Broca	26	10	0	0.9	2	0.01
35	RH	77	M	W	Anomic	95	10	9	10	9.5	0.93
36	RH	37	M	B	Global	6	3	0	0		0.38
37	RH	71	F	W	Wernicke	47	6	5	2.4		0.23
38	RH	48	M	W	Broca	44	8	2	2.4	4.3	0.43
39	RH	78	F	W	Anomic	90	10	9	10		.
Average (±SD)	**.**	**62±12.7**	**.**	**.**	**.**	**57.9±27.9**	**7.7±1.9**	**5.2±3.3**	**5.3±3.7**	**5.8±3.4**	**0.51±0.33**

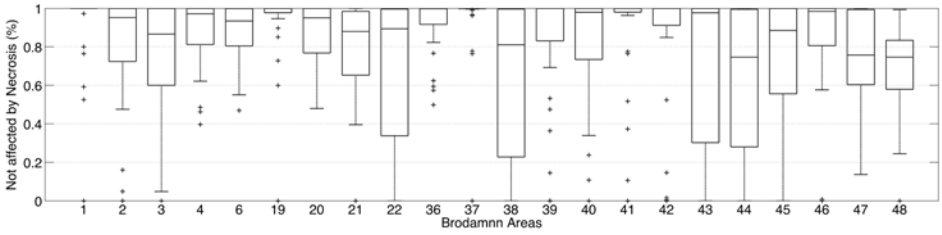
Online Figure I- The spatial distribution of necrotic lesion masks (transformed into standard MNI stereotaxic space) from all subjects included in this study is demonstrated by overlaying the lesion masks onto a T1-weighted atlas. Voxels are color-coded in accordance with the number of individuals with a lesion affecting each specific that specific voxel.



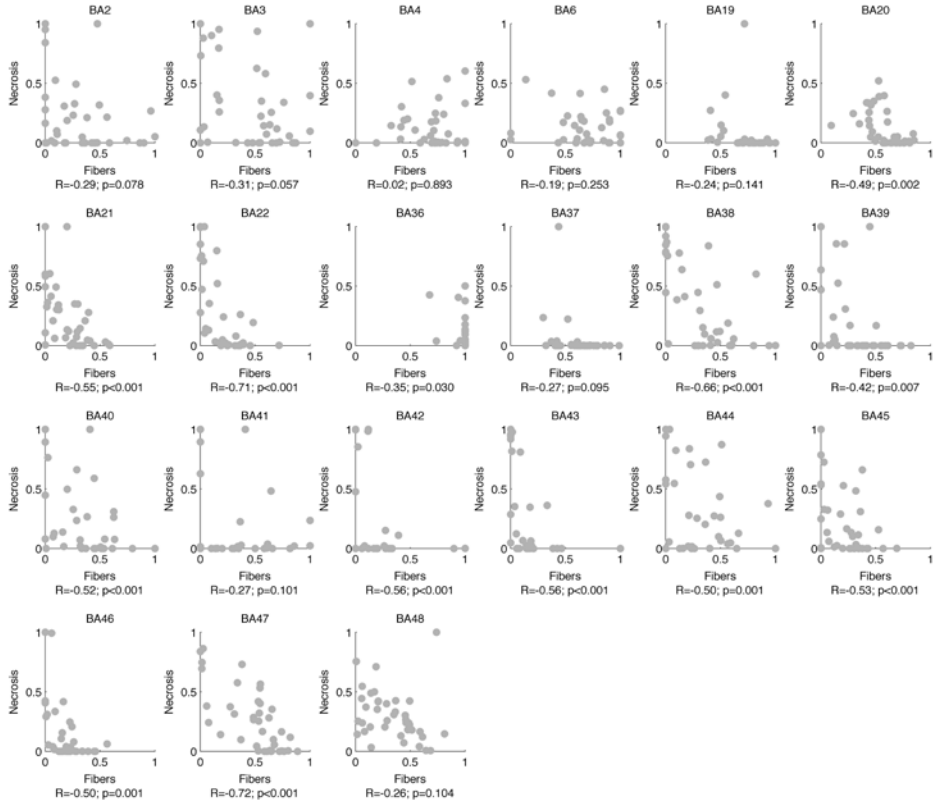
Online Figure II- The relative number of fibers in representative BA ROIs in the left hemisphere, compared with the homologue BA in the right hemisphere (0= no remaining fibers, 1= left hemisphere fibers are at least equal in number to right hemisphere fibers). The box plots demonstrated the distributions across all subjects per each ROI.



Online Figure III- The degree of sparing from necrosis of representative BA ROIs (ranging from 1- the ROI was completely spared, to 0 – completely included by the necrosis). The box plots demonstrated the distributions across all subjects per each ROI.



Online Figure IV- The relationship between necrosis and disconnection for representative Bas. The scatter plots demonstrate percentage of necrosis (y-axis, 0= no necrosis; 1= complete necrosis) and percentage of remaining fibers compared with the right hemisphere (0= no remaining fibers, 1= left hemisphere fibers are at least equal in number to right hemisphere fibers). The correlation coefficient for each ROI is also demonstrated underlying each scatter plot. subjects per each ROI.



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