On-line Supplementary Material

Section 1: Postprocessing Method

Postprocessing of the EPI signal included both spatial smoothing and temporal alignment. Spatial smoothing was applied using a full width at half maximum Gaussian kernel. Eight-mm smoothing was applied to 1.5T datasets that were acquired with 6-mm sections and 1-mm skip. Six-mm smoothing was applied to the 3T data that was acquired with 5-mm section thickness. Temporal alignment was done with the Analysis of Functional NeuroImages (AFNI, Cox, 1996) 3dTshift function that shifts voxel time series from the input dataset so that the separate sections are aligned to the same temporal origin and helped account for differences in temporal acquisition at each section location within the 2-second TR. AFNI 3Dvolreg was used to correct for head motion in the reconstructed time courses. This was done by spatially coregistering all data to the middle time point of the fMRI run. The EPIs were coregistered with structural images. They were manually moved for perceived optimal spatial coregistration with the corresponding 3D anatomy. The AFNI plug-in "nudge dataset" allowed visualization in 3 planes of the anatomy with an overlay showing the EPI volume. This was applied in 6 planes to align the disparate EPI and anatomic datasets into a best fit. Once 1 of the EPI datasets was thus manually aligned, all the other EPI datasets from the same scan session were automatically coregistered using AFNI 3dvolreg.

Cox R. **AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages.** *Comput Biomed Res* 1996;29:162–73

Section 2: Supplemental Results

On-line Fig 1. Example of motor LAD measurement. This illustrates an example of the distance measurement made from tumor margin to periphery of functional activation in a patient with a Grade III, right frontoparietal astrocytoma (t>10). The yellow arrow demarcates the right inferior/lateral primary sensorimotor cortex, while the pink arrow defines the distance of interest (ie LAD).

On-line Fig 2. Kaplan-Meier curves for the motor patient population. (Logrank test, P =.018) Kaplan-Meier curves for the motor data indicates survival time for patients with either preoperative or postoperative motor deficit (blue) was significantly longer (mean = 2233 days, 95% CI = 1958–2508 days) than for patients with both preoperative and postoperative motor deficits (green; mean = 1544 days, 95% CI = 1046 to 2042; Mantel-Cox Logrank test, $\chi^2 = 5.61$, $P = .018$).

On-line Fig 3. Kaplan-Meier curves for the language patient population. (Logrank test, P =.079) Kaplan-Meier analysis indicates that survival time for patients with either preoperative or postoperative deficit (blue) was longer (mean = 2306 days, 95% CI = 2013–2599 days) than for patients with both preoperative and postoperative deficits (green; mean = 1282 days, 95% CI = 847–1718 days), however, this difference only trended towards significance (Mantel-Cox Logrank test, $\chi^2 = 3.08$, $P = .079$).

[1] Note that not all patients underwent breath-holding scans because the database is 10 years old. More recent patients underwent breatholding scans regardless of diagnosis.

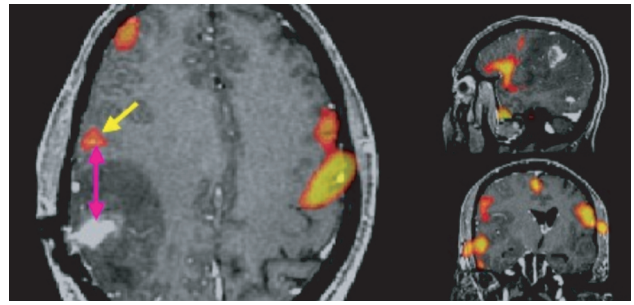

Fig S1. Example of motor LAD measurement. This illustrates an example of the distance measurement made from tumor margin to periphery of functional activation in a patient with a Grade III, right fronto-parietal astrocytoma (t>10). The yellow arrow demarcates the right inferior/lateral primary sensorimotor cortex, while the pink arrow defines the distance of interest (i.e. LAD).

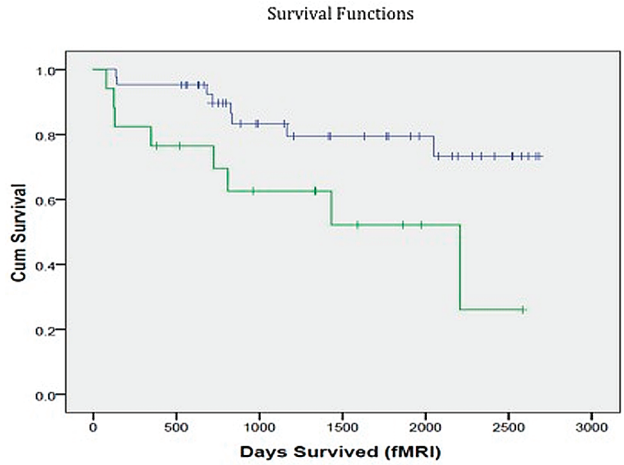

Fig S2. Kaplan-Meier curves for the motor patient population. (Log Rank test, P = .018) Kaplan-Meier curves for the motor data indicates survival time for patients with either preoperative or postoperative motor deficit (blue) was significantly longer (mean = 2233 days, 95% CI = 1958 to 2508 days) than for patients with both preoperative and postoperative motor deficits (green; mean = 1544 days, 95% CI = 1046 to 2042; Mantel-Cox Log-Rank test, $\chi^2 = 5.61$, $P = .018$).

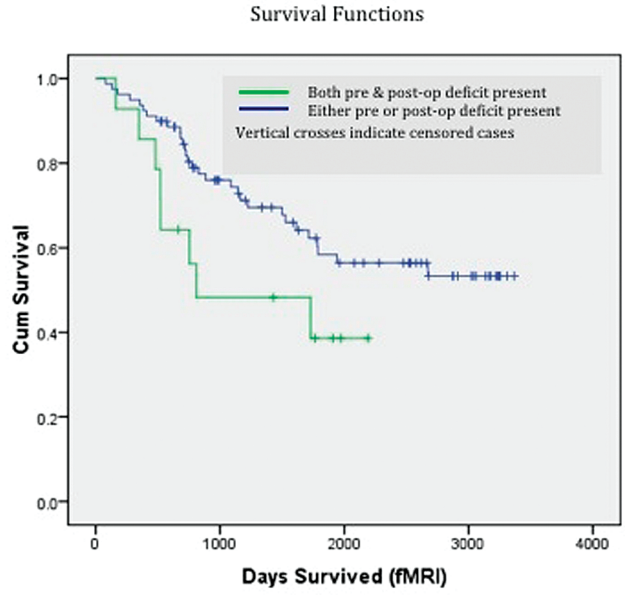

Fig S3. Kaplan-Meier curves for the language patient population. (Log Rank test, P = .079) Kaplan-Meier analysis indicates that survival time for patients with either preoperative or postoperative deficit (blue) was longer (mean = 2306 days, 95% CI = 2013 to 2599 days) than for patients with both preoperative and postoperative deficits (green; mean = 1282 days, 95% CI = 847 to 1718 days), however, this difference only trended towards significance (Mantel-Cox Log-Rank test, $\chi^2 = 3.08$, $P = .079$).

On-line Table 1: Patient clinical data

Patient	Handedness	Age	Sex	Tumor Location	Surgical Pathology Diagnosis	Motor Task	Language Task	Breath-holding[1]
1	R	68	F	R parietal	Metastatic adenocarcinoma	Y	Y	N
2	R	45	F	L frontal	Meningioma	Y	Y	N
3	R	40	M	L frontotemporal	Oligodendroglioma Grade II	Y	Y	N
4	R	6	M	L temporal	Gangliocytoma	Y	Y	N
5	L	31	F	R frontal	Oligodendroglioma Grade III	Y	Y	N
6	L	24	M	L temporal	Oligoastrocytoma Grade II	Y	Y	N
7	R	57	M	R temporal	Gliosis, mild cerebral white matter	Y	Y	N
8	R	41	F	L frontal	Oligodendroglioma Grade II	Y	Y	N
9	L	45	F	R frontal	Oligodendroglioma Grade III	Y	Y	N
10	R	57	M	L temporal	Dysembryoplastic neuroepithelial tumor	N	Y	N
11	R	37	F	L frontal	Oligodendroglioma Grade II	Y	Y	N
12	R	24	F	R frontoparietal	Astrocytoma Grade III	Y	Y	N
13	R	49	M	L temporal	Oligodendroglioma	N	Y	N
14	R	33	M	R frontal	Oligodendroglioma Grade II	Y	Y	N
15	L	64	M	R temporal	Astrocytoma Grade IV	N	Y	N
16	R	60	M	L frontal	Oligodendroglioma Grade II	Y	Y	N
17	R	54	F	L temporal	No biopsy	N	Y	N
18	L	39	M	R parietal	Oligodendroglioma Grade II	Y	Y	N
19	R	41	F	L frontotemporal	Benign meningioma	Y	Y	N
20	R	26	M	L temporal	Astrocytoma Grade IV	N	Y	N
21	R	57	F	L temporal	Astrocytoma Grade IV	N	Y	N
22	R	45	M	R frontal	Oligodendroglioma Grade II	Y	Y	N
23	R	56	M	L frontal	Oligodendroglioma Grade II	Y	Y	N
24	R	69	F	L frontal	Metastatic breast carcinoma	Y	Y	N
25	R	42	F	L frontotemporal	Meningioma	Y	Y	N
26	L	34	F	L frontal	Minimally abnormal/hypercellular cerebral white matter	Y	Y	N
27	R	27	M	L frontal	Astrocytoma Grade III	Y	Y	N
28	R	21	M	L frontal	Astrocytoma Grade II	Y	Y	N
29	R	53	M	L frontal	Oligodendroglioma Grade II	Y	Y	N
30	R	23	M	L frontal	Oligoastrocytoma Grade III	Y	Y	N
31	R	28	M	L frontal	Oligoastrocytoma Grade II	Y	Y	N
32	R	56	M	L frontal	Astrocytoma Grade IV	Y	Y	N
33	R	21	F	R temporal	Dysembryoplastic neuroectodermal tumor	Y	Y	N
34	–	25	M	L temporal	Astrocytoma Grade II	Y	Y	N
35	R	60	M	L temporal	Astrocytoma Grade IV	Y	Y	N
36	L	8	M	L frontal	Primitive neuroectodermal tumor	Y	Y	N
37	R	43	M	L temporal	Astrocytoma Grade IV	Y	Y	N
38	R	76	F	L temporal	No biopsy	Y	Y	N
39	L	51	F	R frontal	Astrocytoma Grade IV	Y	Y	N
40	–	70	M	R frontal	Astrocytoma Grade IV	Y	N	N
41	R	42	F	L frontal	No biopsy	Y	Y	N
42	R	68	F	R frontal	No biopsy	Y	N	N
43	R	52	M	L temporal	Astrocytoma Grade IV	Y	Y	N
44	–	51	M	L frontal	Astrocytoma Grade IV	Y	Y	N
45	R	31	F	R frontal	Astrocytoma Grade III	Y	Y	N
46	R	29	M	L parieto-occipital	Oligodendroglioma Grade III	Y	Y	N
47	R	63	M	L parietal	Metastatic carcinoma	Y	Y	N
48	R	43	F	L parietal	Astrocytoma Grade IV	Y	N	N
49	R	49	M	L temporal	Astrocytoma Grade IV	Y	Y	N
50	R	70	M	L temporal	Astrocytoma Grade IV	N	Y	N
51	R	68	M	L parietal	Astrocytoma Grade IV	Y	Y	N
52	L	46	M	R frontal	Astrocytoma Grade II	Y	Y	N
53	L	76	M	R frontal	Astrocytoma Grade IV	Y	Y	N
54	R	65	F	L frontal	Astrocytoma Grade IV	Y	Y	N
55	R	30	F	L frontal	Astrocytoma Grade III	Y	Y	N
56	R	86	F	L parietal	Meningioma	Y	Y	N
57	R	57	M	L frontal	Astrocytoma Grade IV	Y	Y	N
58	R	70	F	L frontal	Metastatic clear cell carcinoma	Y	N	N
59	A	49	F	R frontal	Meningioma	Y	Y	N
60	R	28	M	R parietal	Astrocytoma Grade IV	Y	N	N

On-line Table 1: Patient clinical data *(Continued)*

Patient	Handedness	Age	Sex	Tumor Location	Surgical Pathology Diagnosis	Motor Task	Language Task	Breath-holding[1]
61	R	46	M	R frontal	Oligodendroglioma Grade II	Y	Y	N
62	R	66	M	L frontal	Astrocytoma Grade III	Y	Y	N
63	R	65	M	L parietal	Astrocytoma Grade IV	Y	Y	N
64	–	49	M	L frontoparietal	Oligoastrocytoma Grade II	Y	Y	N
65	R	32	F	L insula (parietotemporal)	Oligodendroglioma Grade II	Y	Y	N
66	L	36	F	R temporal	Ganglioma	N	Y	N
67	R	54	M	R frontal	Oligoastrocytoma Grade II	Y	Y	N
68	R	53	F	L frontotemporal	Oligodendroglioma Grade III	Y	Y	N
69	L	55	M	R frontal	Oligodendroglioma	Y	Y	N
70	R	65	M	L temporal	Astrocytoma Grade IV	N	Y	N
71	L	48	M	L frontal	Astrocytoma Grade IV	Y	Y	N
72	R	56	M	L parietal	Oligodendroglioma Grade II	Y	Y	N
73	R	28	M	L frontal	Astrocytoma Grade III	Y	Y	N
74	R	43	M	L temporal	Oligodendroglioma Grade II	Y	Y	N
75	R	44	F	L parietal	Astrocytoma Grade IV	Y	Y	N
76	L	29	M	R temporal	Oligoastrocytoma Grade II	N	Y	Y
77	L	48	M	R frontoparietal	Astrocytoma Grade III	Y	Y	N
78	A	51	M	R frontal	Astrocytoma Grade IV	Y	Y	Y
79	L	57	M	R frontal	Metastatic colonic adenocarcinoma	Y	Y	Y
80	R	55	M	L temporal	Astrocytoma Grade IV	N	Y	Y
81	L	59	M	R temporal	No biopsy	Y	Y	Y
82	–	43	M	R frontal	No biopsy	Y	Y	Y
83	R	35	F	L temporal	Dysembryoplastic neuroepithelial tumor	Y	Y	Y
84	L	26	F	L frontal	Astrocytoma Grade IV	Y	Y	N
85	R	28	M	L frontal	Astrocytoma Grade III	Y	Y	N
86	R	51	F	L frontal	Astrocytoma Grade II	Y	Y	Y
87	R	33	F	L occipital	Astrocytoma Grade IV	N	Y	N
88	R	43	F	R frontal	Astrocytoma Grade III	Y	Y	Y
89	R	67	M	L frontal	Astrocytoma Grade IV	Y	Y	Y
90	R	49	M	L temporal	No biopsy	Y	Y	N
91	R	27	M	R frontal	Astrocytoma Grade IV	Y	Y	Y

[1] Note that not all patients underwent breath-holding scans because the data base is 10 years old and standardized protocols had not been established. More recent patients underwent breath-holding scans regardless of diagnosis.R = right-handed; L = left-handed; A = ambidextrous; Y= patient underwent the indicated task during scanning, N= patient did not undergo the indicated task during scanning.

On-line Table 2: Demographics of patients who underwent surgery

Characteristic	<1 cm	1–2 cm	2+ cm	*P* value
Characteristics of patients based on distance between lesion and SMC				
Number of subjects (*n*=64)	26	14	24	0.14
Male (%)	61	57	75	0.14
Handedness (% right)	64	93	82	0.23
Average age (years)	49 +/− 17.0	44 +/− 12.9	40 +/- 15.6	0.15
Grade III or IV tumors (%)	65	50	42	0.23
Characteristics of patients based on distance of lesion from Broca or Wernicke areas				
Number of subjects (*n*=67)	25	12	30	0.01
Male (%)	64	75	60	0.65
Handedness (% right)	84	67	77	0.54
Average age (years)	44 +/− 14	36 +/− 17	50 +/- 16	0.05
Grade III or IV tumors (%)	52	58	50	0.88

On-line Table 3: Univariate analysis: Results for subset of patients who underwent surgery

Characteristic	<1	1–2	2+	*P* value
SMC LAD vs motor deficits				
With pre- or postoperative paresis (%) (*n*=64)	80	50	8	0.0001
Broca and/or Wernicke areas LAD vs language deficits				
With pre- or postoperative aphasia (%) (*n*=67)	68	25	30	0.007

LAD = lesion to activation distance

On-line Table 4: Broca versus Wernicke aphasia

Characteristic	<1	1–2	2+	*P* value
Broca area LAD vs aphasia				
With pre- or postoperative aphasia (%)	71	36	35	0.01
Wernicke area LAD vs aphasia				
With pre- or postoperative aphasia (%)	73	54	44	0.28

LAD = lesion to activation distance

On-line Table 5: Survival analysis using Cox-proportional hazards

Parameter*	*P* value	HR (95.0% CI)
Motor distance (<1 cm, 1–2 cm, >2 cm)		
SMC LAD		
Dist 2 vs 1	0.648	1.281 (0.443–3.705)
Dist 3 vs 1	0.280	0.537 (0.174–1.660)
Dist 3 vs 2	0.155	2.386 (0.721–7.898)
Language Distance (<1 cm, 1–2 cm, >2 cm)		
Broca LAD		
Dist 2 vs 1	0.112	2.779 (0.789–9.783)
Dist 3 vs 1	0.085	2.886 (0.863–9.650)
Dist 3 vs 2	0.913	0.963 (0.487–1.902)
Wernicke LAD		
Dist 2 vs 1	0.384	0.625 (0.217–1.802)
Dist 3 vs 1	0.403	0.709 (0.317–1.587)
Dist 3 vs 2	0.783	0.881 (0.358–2.165)
Either language area LAD		
Dist 2 vs 1	0.991	1.005 (0.426–2.368)
Dist 3 vs 1	0.466	1.335 (0.614–2.903)
Dist 3 vs 2	0.459	0.752 (0.354–1.597)
Motor deficits		
Pre-op deficit present (*no, yes)	0.051	2.624 (0.987–6.978)
Post-op deficit present (*no deficit *n*=34; transient deficits *n*=11; persistent deficits *n*=14)		
Transient	0.404	0.412 (0.051–3.311)
Persistent	0.022	3.159 (1.183–8.435)
Both pre- and post-op deficit present (*no, yes)	0.025	3.100 (1.156–8.308)
Language deficits		
Pre-op deficit present (*no, yes)	0.290	1.523 (0.719–3.224)
Post-op deficit present (*no deficit, transient, persistent)		
Transient	0.597	0.772 (0.295–2.017)
Persistent	0.133	1.908 (0.821–4.437)
Both pre- and post-op deficit present (*no, yes)	0.085	1.993 (0.909–4.370)
Motor tumor characteristics		
Hemisphere (*L, R)	0.861	1.087 (0.427–2.771)
Tumor location by lobes (F–frontal, O–other, P–parietal, T–temporal)		
Temporal vs F	0.332	1.814 (0.545–6.038)
Parietal vs F	0.036	3.172 (1.081–9.310)
Other vs F	0.451	0.448 (.056-3.607)
Parietal vs T	0.326	1.959 (0.512–7.491)
Other vs T	0.168	0.212 (0.023–1.925)
Grade		
Grade 3 vs Grade 1 and 2	0.009	8.791 (1.723–44.858)
Grade 4 vs Grade 1 and 2	<0.001	42.485 (7.684–234.889)
Language tumor characteristics		
Hemisphere (*L, R)	0.423	1.315 (0.673–2.567)
Lobe by lobe (*1-Frontal)		
2–Temporal	0.339	1.458 (0.672–3.163)
3–Parietal	0.121	2.083 (.823–5.270)
4–Other	0.543	0.734 (.272–1.985)
Grade (Grade 1, 2, 3, 4)		
Grade 2 vs Grade 1	0.792	1.246 (0.242–6.425)
Grade 3 vs Grade 1	0.027	5.467 (1.210–24.713)
Grade 4 vs Grade 1	0.001	12.958 (3.011–55.769)
Grade 3 vs Grade 2	0.006	4.367 (1.514–12.590)
Grade 4 vs Grade 2	<0.001	10.327 (3.849–27.709)
Grade 4 vs Grade 3	0.028	2.290 (1.096–4.785)

* reference category; LAD=lesion to activation distance; L = left; R=right; LAD code: LAD <1 cm = Dist1; LAD 1–2 cm = Dist2; LAD >2cm = Dist3

On-line Table 6: Models with interactions

	P value (Overall)
Motor interactions	
Distance X tumor grade (Grades 1 and 2 collapsed)	0.216
LAD X tumor location	0.057
LAD X pre-op deficit	0.119
	0.777
LAD X post-op deficit (no deficit, transient,	0.719
*persistent)	0.803
Language interactions	
LAD X grade	<0.001
LAD X tumor location	0.376
LAD X pre-op deficit	0.438
LAD X post-op deficit	0.624

* reference category; LAD = lesion to activation distance