SUPPLEMENTARY MATERIAL**:**

Methods:

1) Gray matter and white matter segmentation

In order to obtain probabilistic gray and white matter maps, we employed an extension of the software Statistical Parametric Mapping (SPM) entitled "Clinical Toolbox". The Clinical Toolbox was developed by our group [1], with the intent to optimize the segmentation and registration of brains with distorted anatomy due to large lesions (e.g., post ischemic necrosis after stroke). It utilizes a cost-function approach [2] to normalize the brain into the standard stereotaxic space (MNI space), which signifies that a manually defined mask of the stroke necrosis site (drawn by one of the authors - Bonilha) is used to weigh tissue influence on normalization.

The Clinical Toolbox employs SPM's unified normalization-segmentation subroutines to yield probabilistic gray and white matter tissue maps [3], which are subsequently used to guide subsequent connectivity assessment steps. The gray and white matter regions corresponding to the location of the stroke lesion were excluded from the resulting probabilistic tissue maps.

Linear and non-linear normalization parameters were applied to a Brodmann Areas (BA) ROI Atlas in standard space - distributed with MRIcro [4], and the probabilistic map of gray matter (in native T1 space) was segmented into a map of cortical BA ROIs.

To enable the registration of the tissue maps (including the ROI segmented gray matter map) into DTI space, native volumetric T2 weighted image was linearly co-registered onto the native T1 image. Since tissue contrast is comparable between B0 and T2 images, 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 DWI space.

2) Fiber tracking and connectome reconstruction.

Probabilistic tractography was used to define the number of white matter streamlines connecting cortical regions, which were separately defined according to an anatomical atlas. This

step was iteratively performed until the connectivity between all possible pairs of cortical regions was determined. The connectivity information was then compiled in a connectivity matrix, providing a two-dimensional representation of the brain connectome. These steps are explained in detail below.

Structural connectivity was obtained by applying FDT's probabilistic method for fiber tracking [5-7]. Probabilistic tractography was performed on diffusion data after voxel-wise calculation of the diffusion tensor. FDT's BEDPOST was used to build default distributions of diffusion parameters at each voxel. Probabilistic tractography was obtained using FDT's probtrackx with 5000 individual streamlines drawn through the probability distributions on principal fiber direction. We chose to employ probabilistic tractography in this study, since it is theoretically capable of accommodating intra-voxel fiber crossings [5, 8].

The cortical ROIs corresponding to the BA were used as seed regions for tractography. For each subject, we calculated the connectivity between cortical ROIs i and j defined as the number of probabilistic white matter streamlines arriving at j when i was seeded, averaged with the number of probabilistic streamlines arriving at i when j was seeded. The step was iteratively repeated to ensure that all BAs were used as seed regions. Once all iterations were completed, a connectivity matrix A was constructed, where each entry A_{ij} corresponded to the weighted connectivity between structures i and j, also referred to as the link between nodes i and j. Since the number of streamlines between i to j, and j to i were averaged, the connectivity matrix was symmetrical with respect to its main diagonal.

References

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Legends for Supplementary Materials

Supplementary Table 1- demographic information and language performance for all subjects included in this study.

Supplementary Table 2- summary of linear regression models.

Supplementary Figure 1- this figure demonstrates the structural connectomes from all subjects. The rows and columns of each matrix correspond to Brodmann Areas (BA). The left quadrant of each matrix illustrates connections within the left hemisphere, while connections within the right hemisphere are illustrated in lower right quadrant. The scale bar demonstrates the link-wise strength, which corresponds to the log of the number of streamlines connecting the ROIs (corrected based on ROI volume and distance travelled by the streamlines).

Supplementary Figure 2- two-dimensional circular diagrams demonstrating the brain network configurations from all subjects. Each node corresponds to a different Brodmann Area (BA) (as indicated by the adjacent number). Only links above the 95% link-weight percentile are shown. The color of the node represents the percentage of the ROI that was damaged by the stroke (in accordance with the colorbar).

Supplementary Table 1

Demographics							**Aphasia classification**	
Subject Number	Gender	Race	Handedness	Age at testing	Age at stroke	Months since stroke	WAB-AQ	Aphasia type
1	F	W	RH	45	39	40	79.1	Anomic
2	F	W	RH	76	70	72	83.6	Anomic
3	F	W	RH	36	31	24	31.8	Broca
4	M	B	RH	56	48	56	83.2	Anomic
5	M	W	RH	74	71	28	30.9	Broca
6	F	B	RH	66	55	92	21.3	Broca
7	M	B	RH	62	58	11	79.6	Conduction
8	F	W	RH	73	67	38	92	Anomic
9	M	W	RH	60	56	11	86	Anomic
10	M	W	RH	67	55	88	50.7	Broca
11	F	W	RH	47	39	37	43.4	Broca
12	F	W	RH	83	80	12	68.7	Anomic
13	M	W	RH	55	50	22	30.6	Wernicke
14	F	W	RH	71	66	35	95.2	Anomic
15	M	W	RH	61	56	24	92.1	Anomic
16	F	W	RH	57	54	15	22.9	Global
17	F	W	RH	50	47	10	31.3	Broca
18	M	W	RH	54	50	29	70.7	Broca
19	F	W	RH	80	78	9	69.5	Conduction
20	M	W	RH	44	43	18	25.7	Broca
21	M	W	RH	59	54	48	47.6	Broca
22	M	W	RH	58	56	6	31.2	Wernicke
23	F	W	RH	60	59	9	17.2	Global
24	M	W	RH	50	49	6	32.7	Broca

Subject Number	**PNT before treatment (average of 2 sessions)**			**PNT after treatment (average of 2 sessions)**			**Treatment related changes**	
	Correct items	SP	PP	Correct items	SP	PP	New	Improvement (%)
1	138	8	1.5	155.5	5.5	2.5	17.5	0.47
2	143	5	12	150.5	5	7	7.5	0.23
3	4.5	17	60.5	11	28.5	55.5	6.5	0.04
4	136.5	7	15.5	146.5	1	17.5	10	0.26
5	3	0.5	0.5	5	2	0.5	2	0.01
6	0	0	0	0	0	15	0	0.00
7	77	9.5	9	101	6.5	2.5	24	0.24
8	149	10	0	161.5	3.5	0	12.5	0.48
9	144.5	8.5	0.5	154	7	1	9.5	0.31
10	42.5	25	2	42	29.5	1.5	-0.5	0.00
11	45.5	11	7	57	14	10.5	11.5	0.09
12	55	25.5	9	60.5	20	9	5.5	0.05
13	1.5	2.5	0.5	1	2.5	0.5	-0.5	0.00
14	154	2	1.5	161.5	0	0.5	7.5	0.36
15	139	8	0.5	144.5	1.5	0	5.5	0.15
16	1	1	1	0	0	1	-1	-0.01
17	4	19.5	19.5	8.5	36	29	4.5	0.03

18	100.5	12	37	96	6.5	24.5	-4.5	-0.06
19	46	5	19.5	53.5	10.5	37	7.5	0.06
20	3	10.5	10.5	17	13.5	11.5	14	0.08
21	12	16.5	27	16.5	17.5	28.5	4.5	0.03
22	0.5	11.5	11	1	8	17	0.5	0.00
23	0	0.5	0	0	0	2	0	0.00
24	23	14.5	25.5	43.5	11.5	44.5	20.5	0.13

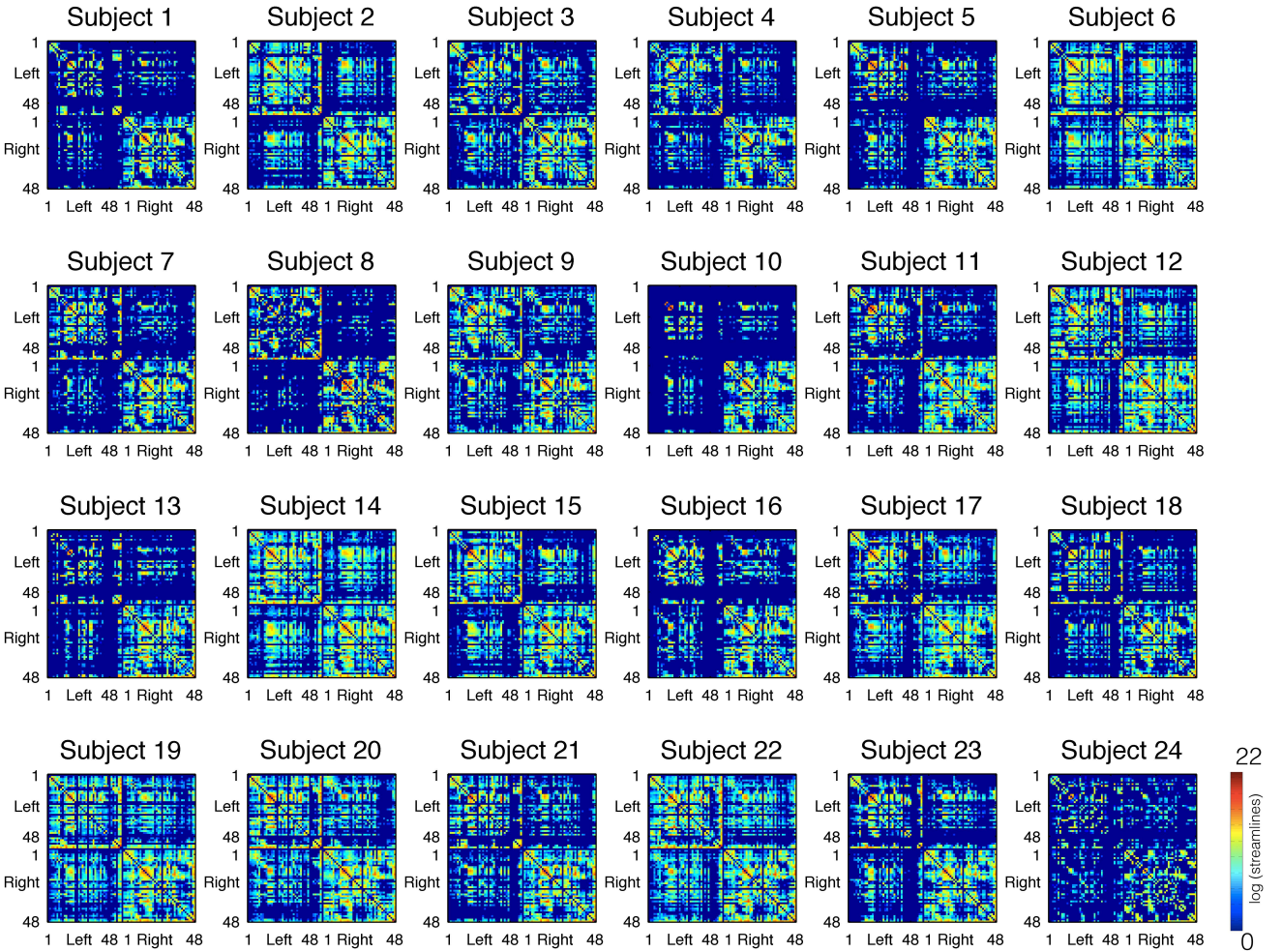
Legend: F=female; M=male; W=white; B=black; WAB-AQ= Western Aphasia Battery Aphasia Quotient; SP = Semantic Paraphasias; PP= Phonemic Paraphasias; New = New items correctly named after treatment.

Supplementary Table 2

Dependent Variable = WAB – AQ (upper row on Figure 4)				
Independent Variables	Estimate	SE	T	p
(Intercept)	-0.8452	27.6310	-0.03	0.9760
Age	0.8090	0.4397	1.84	0.0833
Time after Stroke	-0.0923	0.1042	-0.89	0.3884
Lesion size	-0.0001	0.0001	-0.99	0.3338
Frontal BC	-0.0819	0.0513	-1.60	0.1290
Parietal BC	0.0217	0.0542	0.40	0.6939
Temporal BC	0.2177	0.0642	3.39	0.0035
Number of observations: 24, Error degrees of freedom: 17				
Root Mean Squared Error: 20.6				
R-squared: 0.584, Adjusted R-Squared 0.437				
F-statistic vs. constant model: 3.97, p-value = 0.0114				
Dependent Variable = WAB - AQ				
Independent Variables	Estimate	SE	T	p
(Intercept)	-22.9680	38.2850	-0.60	0.5557
Age	1.0962	0.4587	2.39	0.0274
Time after Stroke	-0.1227	0.1194	-1.03	0.3171
Lesion size	-0.0001	0.0001	-1.37	0.1858
NSW	11.9470	7.7794	1.54	0.1411
Number of observations: 24, Error degrees of freedom: 19				
Root Mean Squared Error: 24.2				
R-squared: 0.358, Adjusted R-Squared 0.223				
F-statistic vs. constant model: 2.65, p-value = 0.0655				
Dependent Variable = PNT improvement (middle row on Figure 4)				
Independent Variables	Estimate	SE	T	p
(Intercept)	-0.0623	0.1266	-0.49	0.6295
Age	-0.0013	0.0022	-0.58	0.5718
Time after Stroke	0.0004	0.0005	0.87	0.3970
Lesion size	0.0000	0.0000	-0.31	0.7638
WAB-AQ	0.0027	0.0011	2.45	0.0261
Frontal BC	-0.0001	0.0003	-0.38	0.7083
Parietal BC	0.0000	0.0002	-0.05	0.9606

Temporal BC	0.0011	0.0004	2.85	0.0116
Number of observations: 24, Error degrees of freedom: 16				
Root Mean Squared Error: 0.0944				
R-squared: 0.74, Adjusted R-Squared 0.638				
F-statistic vs. constant model: 6.79, p-value = 0.000765				
Dependent Variable = PNT improvement (bottom row on Figure 4)				
Independent Variables	Estimate	SE	T	p
(Intercept)	-0.2173	0.1524	-1.43	0.1711
Age	-0.0018	0.0020	-0.86	0.3976
Time after Stroke	0.0003	0.0005	0.66	0.5178
Lesion size	0.0000	0.0000	-0.27	0.7859
WAB-AQ	0.0039	0.0009	4.47	0.0003
NSW	0.0915	0.0332	2.76	0.0129
Number of observations: 24, Error degrees of freedom: 18				
Root Mean Squared Error: 0.0952				
R-squared: 0.712, Adjusted R-Squared 0.632				
F-statistic vs. constant model: 8.89, p-value = 0.0002				

Legend: PNT improvement = treatment-related improvement in the naming; WAB-AQ= Western Aphasia Battery Aphasia Quotient; NSW= Normalized small worldness; SE = Standard Error; T= T-statistic; p= p value.


Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
Subject 9
Subject 10
Subject 11
Subject 12
Subject 13
Subject 14
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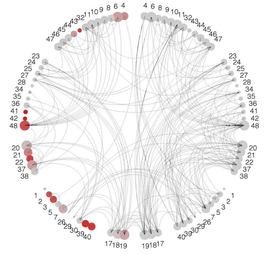
Subject 16
Subject 17
Subject 18
Subject 19
Subject 20
Subject 21
Subject 22
Subject 23
Subject 24
1
Left
48
1
Right
48
1 Left 48 1 Right 48
22
log (streamlines)
0

Subject 1
NSW = 3.4091 LT BC = 211.4
PNT improvement = 47.30%



Subject 2
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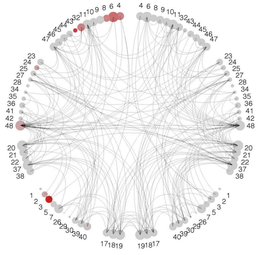
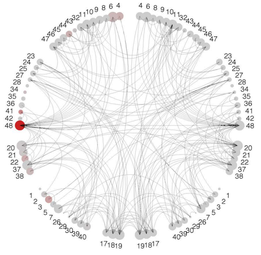
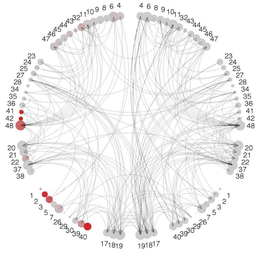
PNT improvement = 23.44%



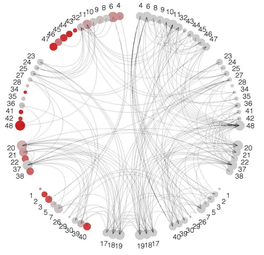
Subject 3
NSW = 2.4977 LT BC = 184.6
PNT improvement = 3.81%



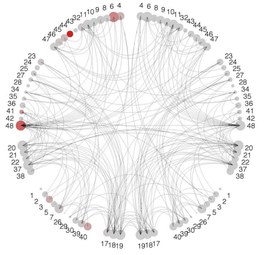
Subject 4
NSW = 2.7946 LT BC = 234.6
PNT improvement = 25.97%



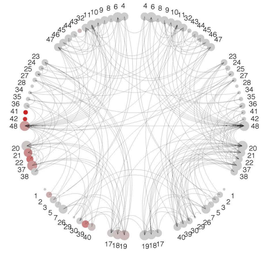
Subject 5
NSW = 2.4357 LT BC = 27.4
PNT improvement = 1.16%



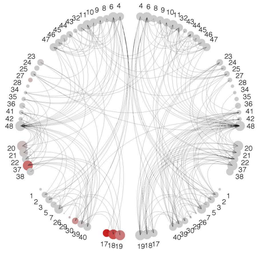
Subject 6
NSW = 1.8585 LT BC = 43.4
PNT improvement = 0.00%



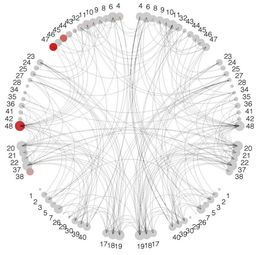
Subject 7
NSW = 2.9315 LT BC = 188.3333
PNT improvement = 24.49%



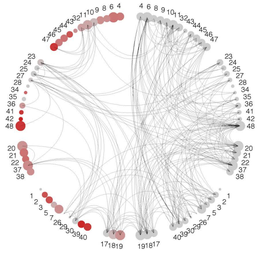
Subject 8
NSW = 4.5241 LT BC = 346.2
PNT improvement = 48.08%



Subject 9
NSW = 2.6373 LT BC = 134.8
PNT improvement = 31.15%



Subject 10
NSW = 2.1312 LT BC = 74.8
PNT improvement = -0.38%



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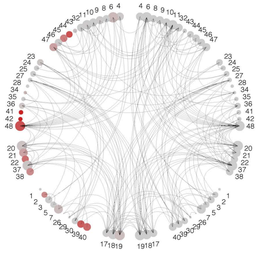
NSW = 2.8749 LT BC = 94
PNT improvement = 8.88%



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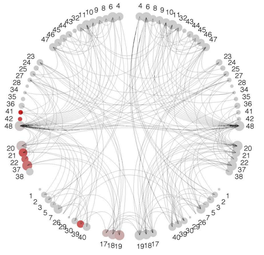
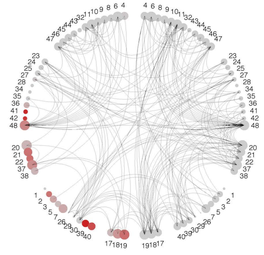
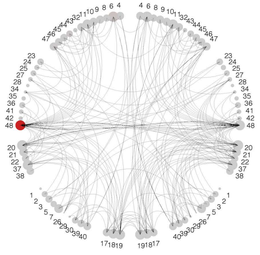
NSW = 1.9328 LT BC = 115.4
PNT improvement = 4.58%



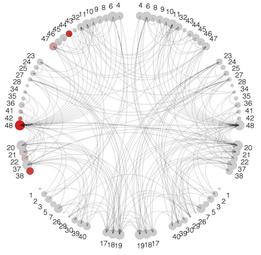
Subject 13
NSW = 2.4309 LT BC = 81.4
PNT improvement = -0.29%



Subject 14
NSW = 1.6929 LT BC = 111.4
PNT improvement = 35.71%



Subject 15
NSW = 2.223 LT BC = 123.6
PNT improvement = 15.28%



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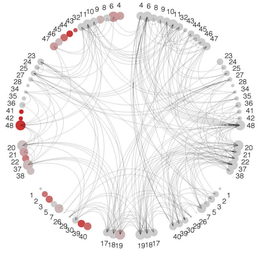
NSW = 2.4988 LT BC = 30
PNT improvement = -0.57%



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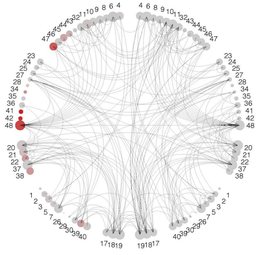
NSW = 2.1393 LT BC = 104.2
PNT improvement = 2.63%



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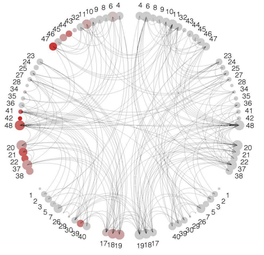
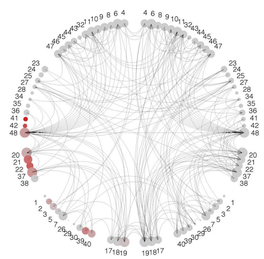
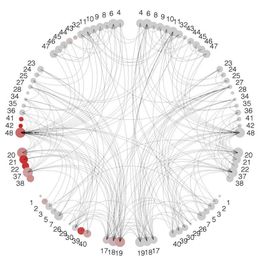
NSW = 2.1985 LT BC = 39.4
PNT improvement = -6.04%



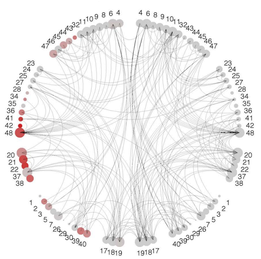
Subject 19
NSW = 1.9068 LT BC = 67.4
PNT improvement = 5.81%



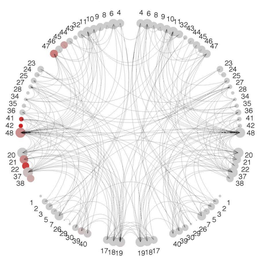
Subject 20
NSW = 2.1115 LT BC = 82.2
PNT improvement = 8.14%



Subject 21
NSW = 2.6147 LT BC = 8.4
PNT improvement = 2.76%



Subject 22
NSW = 1.7172 LT BC = 128.4
PNT improvement = 0.29%



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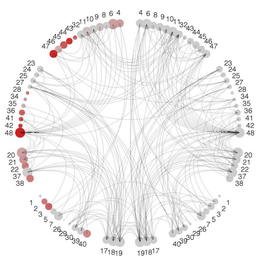
NSW = 2.3664 LT BC = 46.2
PNT improvement = 0.00%



Subject 24
NSW = 3.8159 LT BC = 106
PNT improvement = 13.49%