Neuron, volume *61*

Supplemental Data

Lesion Mapping of Cognitive Abilities Linked to Intelligence

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Supplementary Table

Supplementary Table 1. Correlation of index scores with demographic covariates.

Index Score	Age	Gender	Education	Handedness	Lesion Volume
POI	-0.11	0.15 *	0.38 ***	0.005	-0.30 ***
VCI	0.15 *	0.08	0.49 ***	-0.05	-0.09
WMI	-0.04	0.11 $^{+}$	0.45 ***	-0.11 $^{+}$	-0.13 *
PSI	-0.12	-0.12 $^{+}$	0.34 ***	-0.07	-0.28 ***

$^{+}$ $p < 0.1$ (trend), * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

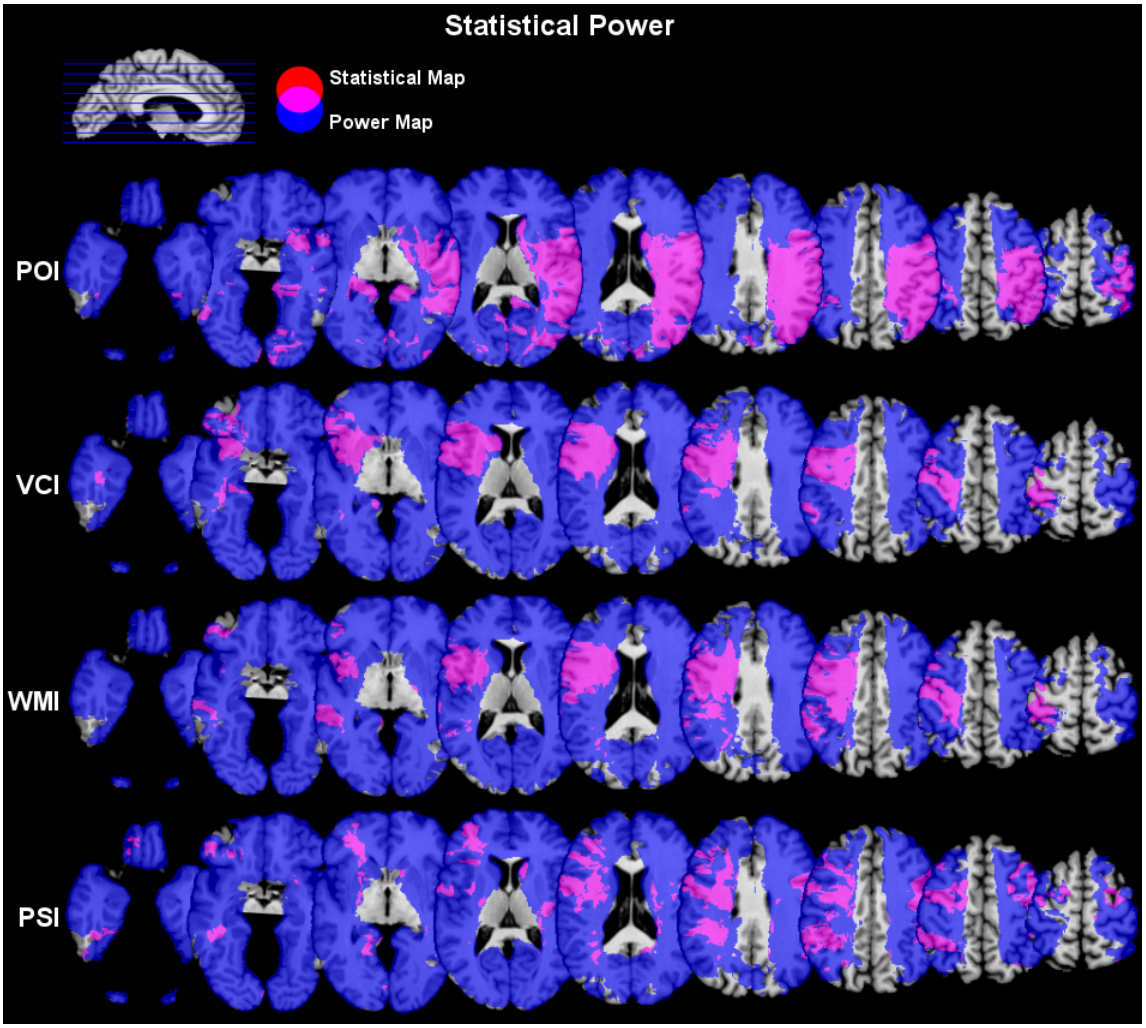
Correlation matrix of WAIS index scores

Index Score	POI	VCI	WMI	PSI
POI		0.47	0.50	0.54
VCI			0.55	0.54
WMI				0.45

all correlations significant at $p < 0.0001$

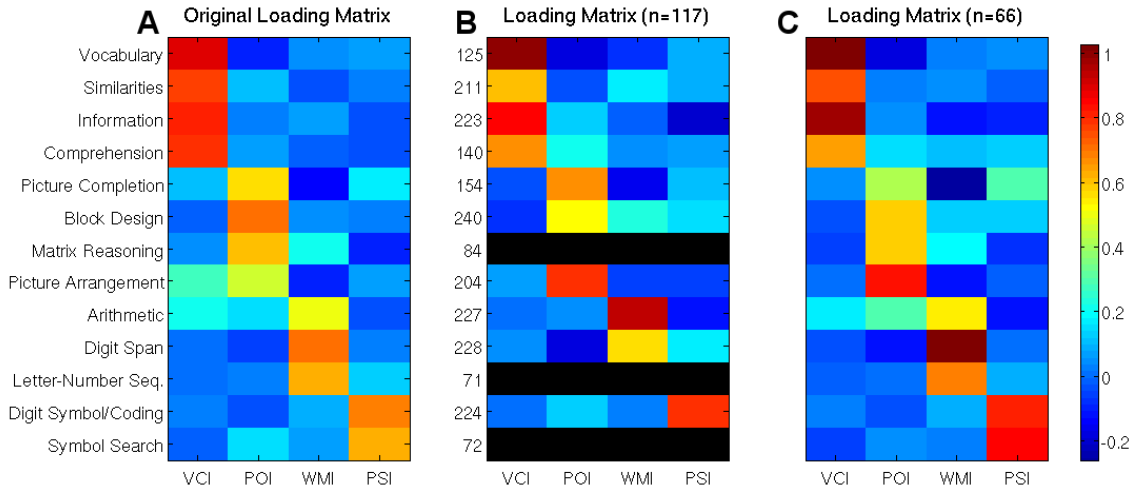
Supplementary Figures

Supplementary Figure 1



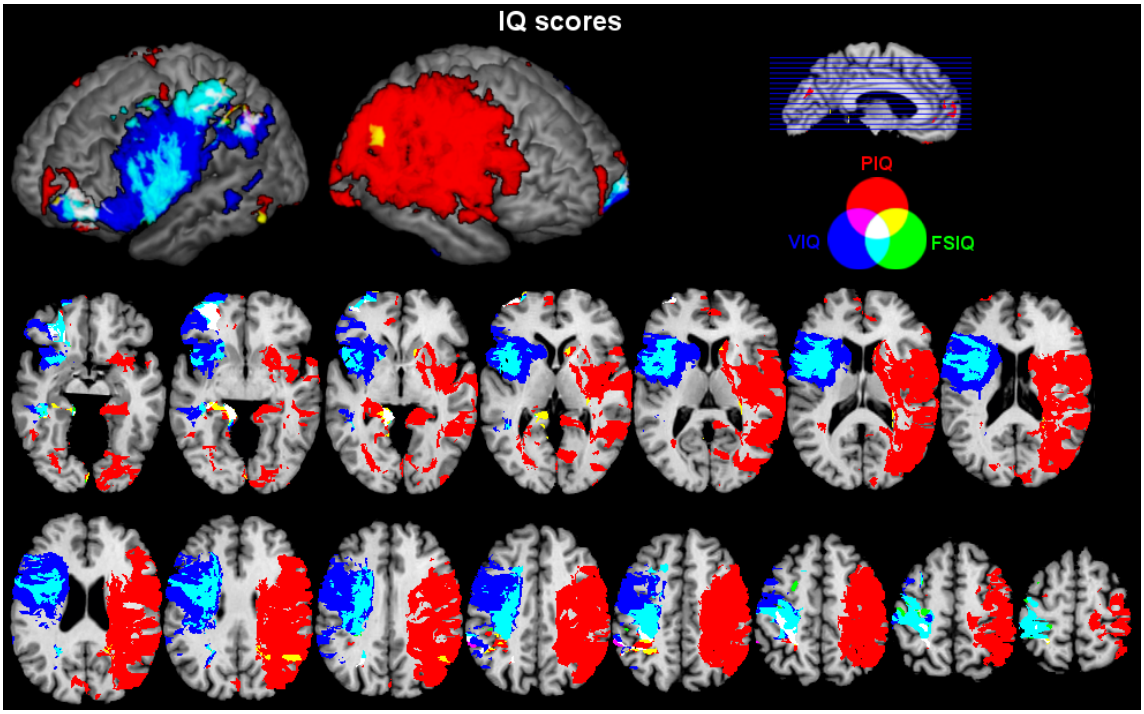
Supplementary Figure 1. Statistical power maps. The slice overlays show the statistically significant voxels from the voxelwise statistical analysis (see Figure 2), uniformly thresholded at 1% FDR and a minimum cluster size of 100 (red). Voxels with sufficient statistical power to detect an effect at this threshold are shown in blue (overlap in magenta). We utilized the implementation available in the MRIcron/NPM software package (Rorden et al., 2007).

Supplementary Figure 2



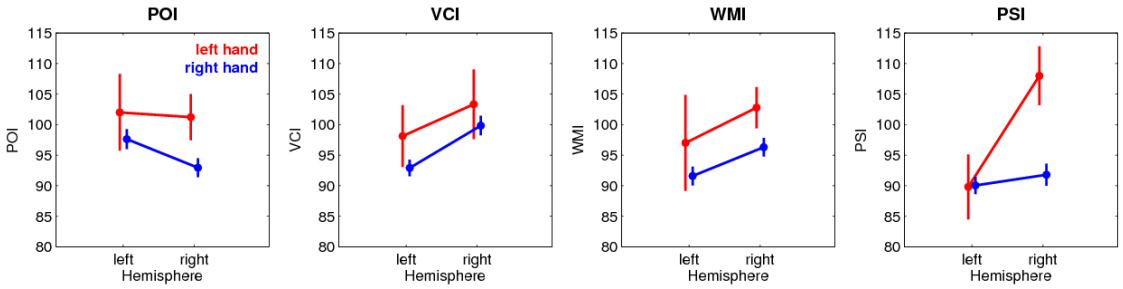
Supplementary Figure 2. Factor loadings of the WAIS subtests. We conducted two promax-rotated factor analyses on the WAIS-III data from our patient sample. The available sample sizes for each subtest are given as row entries for the second matrix. In the first one, we excluded the 3 subtests with the smallest sample sizes (B). These subtests are shown in black in the loading matrix. This resulted in a sample size of 117 patients. In the second factor analysis, we included only patients with complete data sets (n=66) (C). All three factor analyses resulted in highly significant similarity coefficients (Abdi, 2007), thus replicating the original loading matrix (A).

Supplementary Figure 3



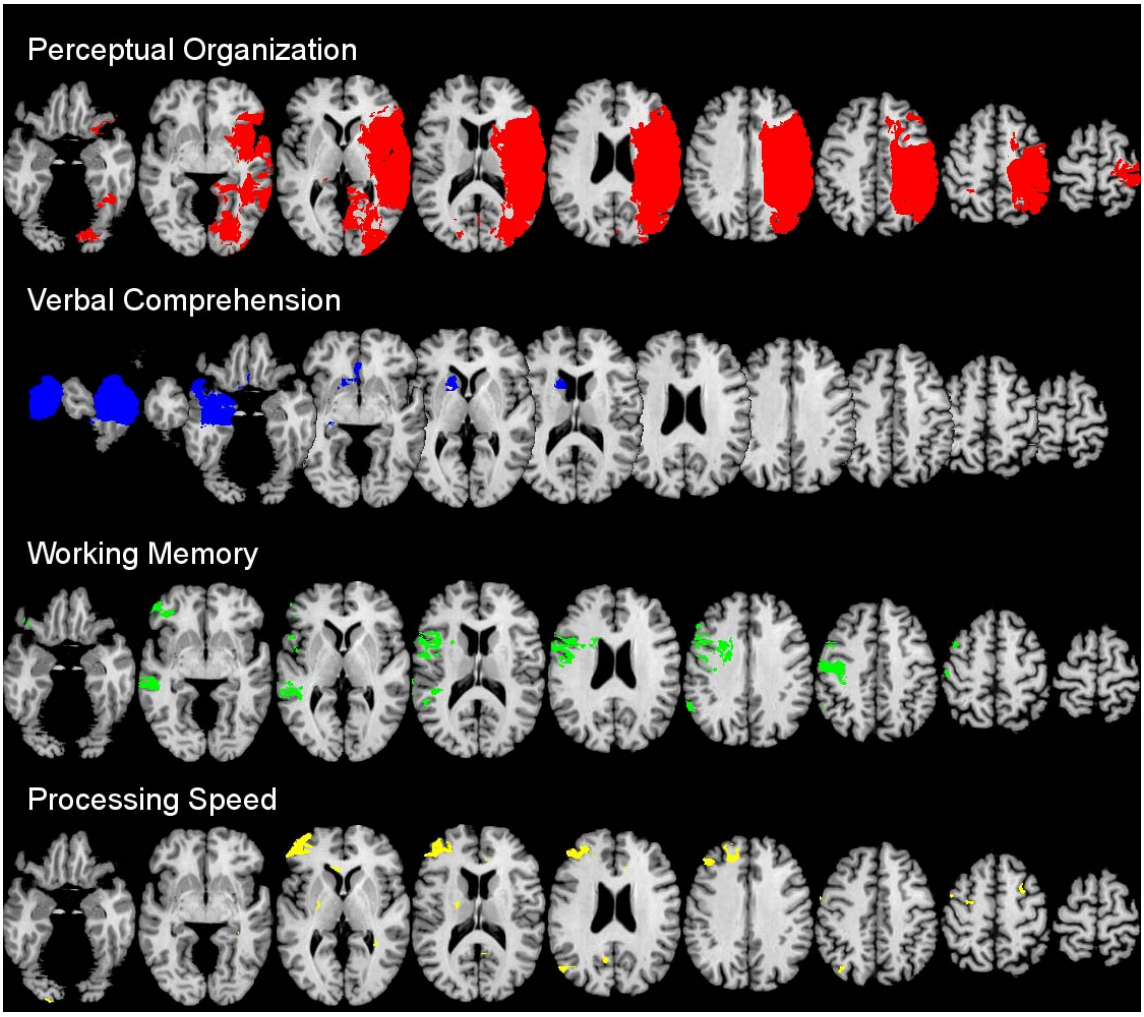
Supplementary Figure 3. Voxel-based lesion symptom mapping (VLSM) analysis for verbal, performance, and full-scale IQ. This analysis compares the IQ scores for patients with a lesion against those without a lesion at each and every voxel in the brain (see Methods for details). Statistical maps are thresholded at 1% False Discovery Rate.

Supplementary Figure 4



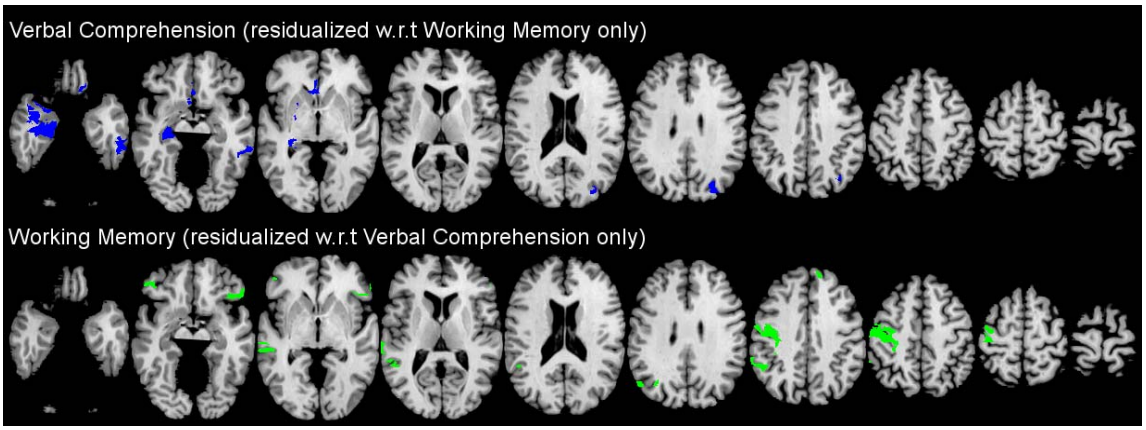
Supplementary Figure 4. Index scores split by hemispheric side of lesion (left and right hemisphere lesion only) and handedness. Data are means (±s.e.m.). A 2-way ANOVA for PSI revealed significant main and interaction effects.

Supplementary Figure 5



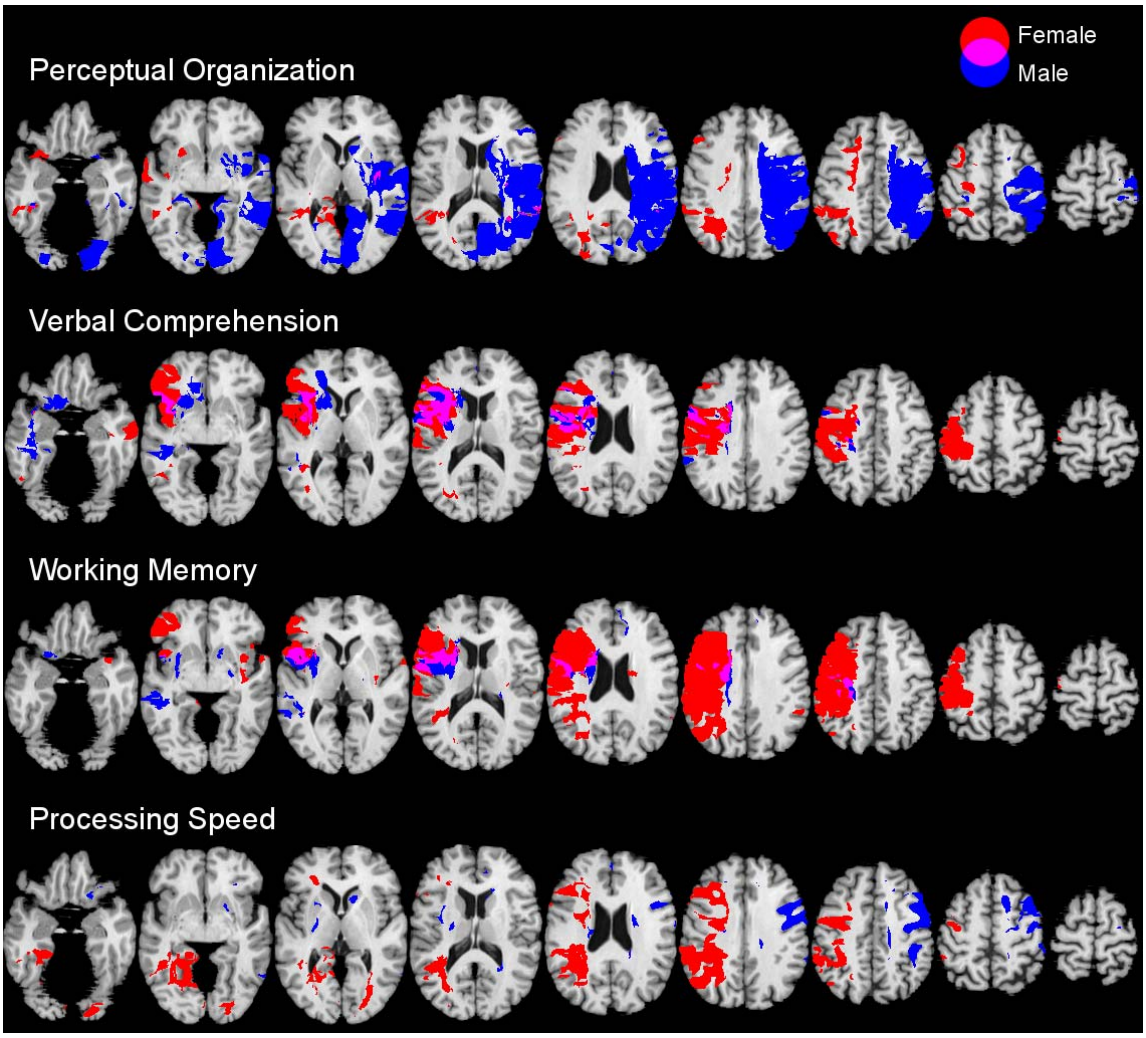
Supplementary Figure 5. Overlap of the results of VLSM analyses of each WAIS index scores after the variance of all other index scores has been removed, i.e. the residualized index scores. The correlation coefficients of the residualized scores with the original scores are: r_{VCI} = 0.56, r_{POI} = 0.69, r_{PSI} = 0.65, r_{WMI} = 0.66. Statistical maps are thresholded at 1% False Discovery Rate.

Supplementary Figure 6



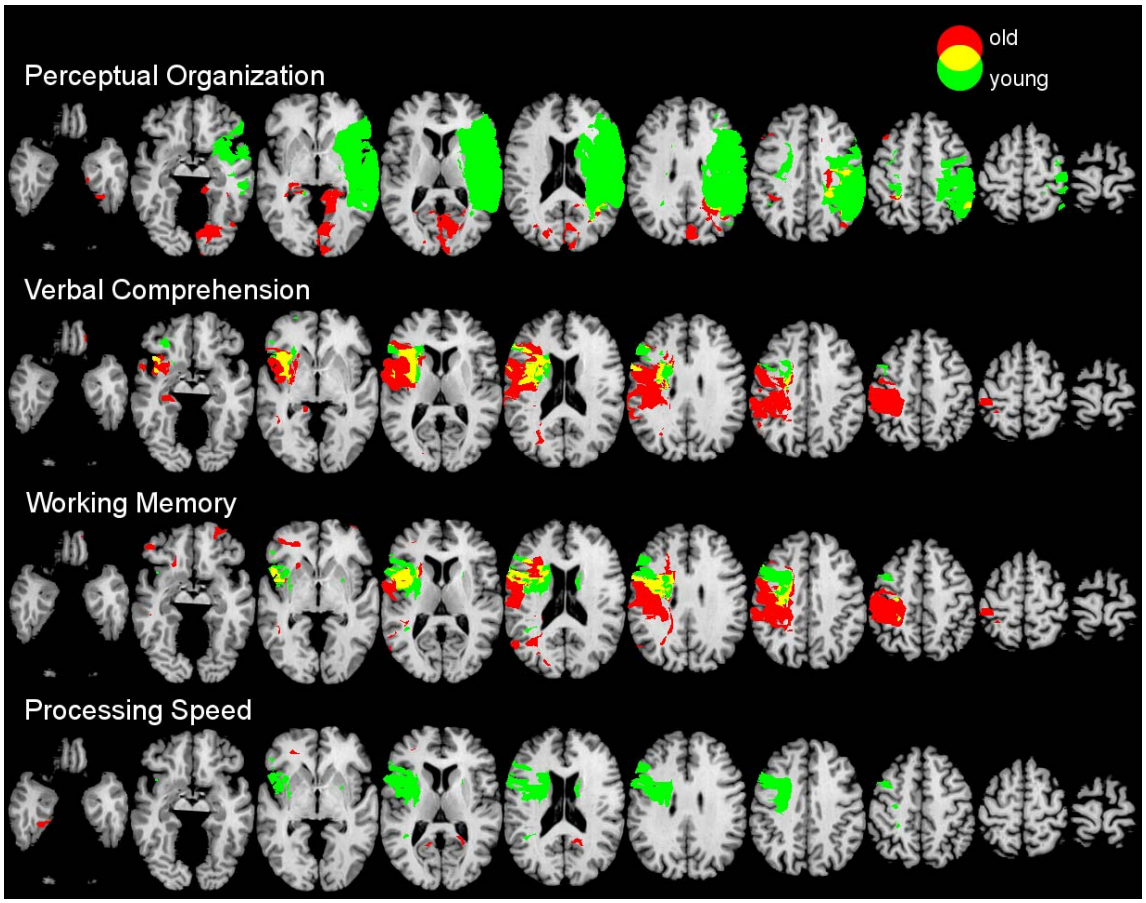
Supplementary Figure 6. Overlap of the results of VLSM analyses of VCI and WMI scores after the variance of the respective other index scores has been removed, i.e. the residualized index scores. Statistical maps are thresholded at 1% False Discovery Rate.

Supplementary Figure 7



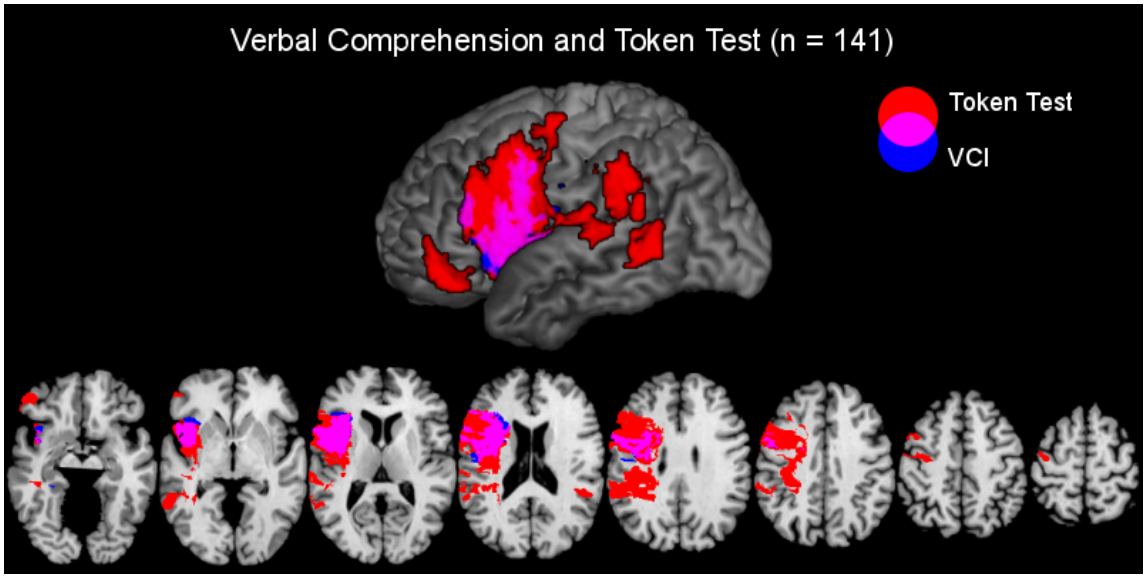
Supplementary Figure 7. Overlap of the results of separate VLSM analyses for each gender on each WAIS index scores. Statistical maps are thresholded at 1% False Discovery Rate.

Supplementary Figure 8



Supplementary Figure 8. Overlap of the results of VLSM analyses for young and old patients (median-split) on each WAIS index scores. Statistical maps are thresholded at 1% False Discovery rate.

Supplementary Figure 9



Supplementary Figure 9. Overlap of 2 VLSM analyses for the Verbal Comprehension Index from the WAIS (blue) and the Token Test (red) in a subset of the patients, who were administered both tests (n = 141). The map was computed using the non-parametric Brunner-Munzel statistic and thresholded at 1% false discovery rate.

Supplementary Methods

1. Scanning Parameters

43 patients underwent computerized axial tomography (CT) scans and for 198 patients high-resolution anatomical T1 weighted images were acquired on a 1.5 T General Electric Signa scanner with a 3D SPGR sequence. A total of 124 coronal slices were acquired (in-plane resolution 1x1 mm, inter-slice distance 1.6 mm, field of view 24 cm).

2. Sources of possible subject selection bias.

Neuroanatomical Data. The group of patients that has been mapped out of those available in the Patient Registry has two potential sources for biased sampling: (1) mapped subjects are those that have lesions clearly demarcated from ventricle changes and from enlarged sulci, and who do not show technical artifacts in the damaged regions; (2) because of the time consuming process of manually mapping lesions, all the lesions mapped have been those of subjects that would be expected to be of interest in research studies, rather than an a priori random sampling among all lesions. Despite these biases, we in fact achieved very good sampling that covered most of the brain and that achieved sufficient statistical power at locations where we report effects.

Neuropsychological Data. Another possible selection bias arises from the capability of the patients to complete a particular neuropsychological test. For instance, the instructions to all WAIS subtests are presented verbally to the patients, thus requiring basic verbal comprehension abilities. Patients without this basic understanding of test instructions were not tested. This might bias the findings of language-related lesion-deficit relationships.

3. Descriptive statistics for both test versions (WAIS-R, WAIS-III)

The majority of our patients were administered one or several subscales of the WAIS-R (ranging from 70 for vocabulary to 194 for block design). Fewer patients were administered one or several subscales of the WAIS-III (ranging from 52 for object assembly to 81 for matrix reasoning). The exact numbers of patients for each subscale in both test versions are provided in the table below which also lists the mean standardized scores for each subscale. In addition, for those patients that were administered one or several subscales from *both* test versions we also compute a product moment correlation coefficient.

	WAIS-R			WAIS-III			Correlation	
Scale	*mean*	*sd*	*n*	*mean*	*sd*	*n*	*r*	*n*
Vocabulary	9.8	2.6	71	10.1	3.0	71	0.84	20
Similarities	10.1	2.5	171	10.1	3.0	74	0.68	34
Arithmetic	9.6	2.9	189	9.8	3.1	81	0.75	43
Digit Span	8.8	2.9	189	9.3	2.7	82	0.69	43
Information	9.4	2.8	187	10.1	3.1	75	0.89	39
Comprehension	9.7	2.3	94	10.3	3.7	73	0.82	27
Picture Completion	9.8	2.7	108	9.9	3.1	78	0.56	32
Digit Symbol/Coding	8.8	2.9	189	9.3	2.9	86	0.69	51
Block Design	9.6	3.0	201	10.4	3.0	87	0.82	49
Picture Arrangement	9.6	2.8	163	10.0	2.7	71	0.51	30
Object assembly	10.5	3.2	86	10.5	2.7	54	0.13	17
Letter-Number Sequence				9.5	3.2	71		
Matrix Reasoning				10.4	3.0	84		
Symbol Search				9.9	3.1	72		

4. Conversion of WAIS-R to WAIS-III scores

As a validation of the latest test version, the WAIS-III along with its predecessor (the WAIS-R) has been administered to a sample of 192 subjects . The test manual provides the mean data for all subscales on both test versions [3]. The data from letter-number sequencing are omitted in the original table. This table is part of the Wechsler Adult Intelligence Scale–Third Edition.

	WAIS-R		WAIS-III			
Scale	*mean*	*sd*	*mean*	*sd*	*r*	*mean difference*
Vocabulary	10.8	2.8	10.2	2.8	.90	-0.6
Similarities	11.3	2.7	10.4	3.0	.79	-0.9
Arithmetic	10.1	2.7	10.4	3.0	.80	+0.3
Digit Span	10.4	3.1	10.3	3.3	.82	-0.1
Information	10.5	2.8	10.5	3.0	.83	0
Comprehension	11.0	2.9	10.5	2.9	.76	-0.5
Picture Completion	11.1	2.6	10.7	3.0	.50	-0.4
Digit Symbol/Coding	11.8	3.0	10.6	3.1	.77	-1.2
Block Design	11.4	2.9	10.7	3.0	.77	-0.7
Picture Arrangement	11.1	2.8	10.5	3.2	.63	-0.6
Object Assembly	11.3	3.1	10.4	3.0	.69	-0.9
Letter-Number Sequencing						
Matrix Reasoning			10.3	2.8		
Symbol Search			10.1	3.0		

Because we wanted to base our analyses on the most recent test version (WAIS-III), we converted the WAIS-R standardized scores to WAIS-III equivalent standardized scores by adding the mean difference to each subscale of the WAIS-R scores from the table above. This conversion was performed only for those patients who were administered the WAIS-R version alone. For all subjects who received WAIS-III scores, those scores were entered into our analyses and any scores from subtests repeated with the WAIS-R were disregarded.

5. Computation of IQ and index scores

The test manual describes in detail how the different subscales of the WAIS-III are combined into IQ and index scores for different cognitive domains. The index scores are the result of an obliquely (promax) rotated factor analysis on the data from the normative sample (The Psychological Corporation, 1997).

The canonical procedure for computing IQ and index scores is to sum the standardized scores of several subscales and then look up the resulting IQ or index score in a conversion table provided in the manual (Tables A1 and A2 of the manual). The WAIS-III IQ and index scores are comprised of the following subscales:

Verbal IQ:	Vocabulary, Similarities, Arithmetic, Digit Span, Information, Comprehension
Performance IQ:	Picture Completion, Digit Symbol/Coding, Block Design, Matrix Reasoning, Picture Arrangement
Verbal Comprehension:	Vocabulary, Similarities, Information
Perceptual Organization:	Picture Completion, Block Design, Matrix Reasoning
Working Memory:	Arithmetic, Digit Span, Letter-Number Sequencing
Processing Speed:	Digit Symbol/Coding, Symbol Search

Calculating an IQ or index score (as prescribed in the WAIS-III test manual) is a non-specific way of combining the data, because it obscures information about subscale variations within a particular IQ or index score. Because our archival dataset did not provide data on all subscales for all patients, calculating the IQ or index scores in the canonical way caused a severe reduction in sample size due to missing data. We therefore chose a different approach that is based on the mean of the contributing subscales, which exhibits identical properties as the sum in the canonical approach.

Using the combination of the subscales from above to compute IQ and index scores, we calculated the mean from all the contributing and available subscales, ignoring any missing data on any of them. This way we were able to compute an IQ or index score, even if a patient did not have a full data set on all relevant subscales. This resulted in a total of 241 patients. The table below provides the number of patients (percentage in parentheses) whose IQ and index scores were based on each possible number of subtests.

Score	No. of subscales	1 subtest	2 subtests	3 subtests	4 subtests	5 subtests	6 subtests
POI	3	82 (34%)	79 (33%)	79 (33%)			
PSI	2	152 (68%)	72 (32%)				
VCI	3	20 (9%)	82 (36%)	125 (55%)			
WMI	3	12 (5%)	152 (65%)	70 (30%)			
VIQ	6	3 (1%)	10 (4%)	14 (6%)	65 (27%)	23 (10%)	119 (50%)
PIQ	5	7 (3%)	24 (10%)	65 (27%)	70 (30%)	75 (31%)	

We then rescaled the range of the conversion table that translates the canonical sum of the subscales to IQ and index scores to our new range which is based on the mean the subscales and linearly interpolated the resulting IQ and index scores. Because our approach is essentially a linear transformation of the conversion table to a new range, we were able to use it to compute identical IQ and index scores based on the mean rather than on the sum of the subscales.

We validated our modified algorithm in those patients that had data on *all* relevant subscales for each index score by computing a Pearson's correlation coefficient between the scores based on the sum of the subscales and our modified algorithm based on the mean and found perfect correlation ($r = 1$) for all IQ and index scores.

Supplementary Analyses

VCI scores of patients with lesion in left temporo-parietal cortex

We tested whether patients with lesions in the left temporo-parietal area (Wernicke's area) had significantly different VCI scores than the rest of the sample. Because these patients had been tested on the WAIS, they must have had basic verbal comprehension abilities to understand test instructions. If the VCI scores in these patients did not differ from the rest of the sample, then this would lend indirect support for our explanation of the absence of a significant lesion-deficit effect for VCI in Wernicke's area.

We defined the location of lesions in Wernicke's area by placing a spherical search volume of 20 mm radius at the location x=-40, y=-17, z=28 in the space of the template brain. Subsequently, we identified patients who had lesions that overlapped at 40% with this search volume as patients with left temporo-parietal lesions. The VCI score of these patients was then compared against the rest of the sample in a 2-sample t-test. The results suggested that

the VCI scores of these selected patients did not differ significantly from the rest of the sample (T_{225}= 0.64, p>0.5) (see Discussion).

REFERENCES

Abdi, H. (2007). RV coefficient and congruence coefficient. In Encyclopedia of Measurement and Statistics, N. Salkind, ed. (Thousand Oak, CA: Sage).

Rorden, C., Karnath, H.O., and Bonilha, L. (2007). Improving lesion-symptom mapping. J Cogn Neurosci *19*, 1081-1088.

The Psychological Corporation (1997). WAIS-III/WMS-III Technical Manual (San Antonio, TX: Author).