Supporting Information

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SI Text

Measuring Language Laterality Based on Task-Based Imaging. To validate the intrinsic laterality index we compared it with a laterality index determined based on actual language task performance. The task-based language laterality index was derived on the group activation map (Fig. S3). The regions showing left-lateralized activation in the group image were used as a mask for each individual subject but excluded the visual cortex. We then summed the number of significant voxels ($z > 1.25$) within the mask of each hemisphere and then computed a laterality index defined as

$$\text{Laterality Index} = \frac{L - R}{L + R} \quad \textbf{[S1]}$$

where L is the sum voxel count in left hemisphere mask and R is the sum voxel count in the right hemisphere mask.

Within the mask, the seed pairs were analyzed, yielding 322 left-lateralized regions that were combined into a single measure of language system iLI (Fig. S4*A*). In the previous analyses described in the main text, we set a threshold of 0.3 to ensure a relatively small number of the most lateralized regions were identified, sufficiently constrained to allow for a well-powered factor analysis. Here we define a language laterality index to be comparable to the task-based estimates. We used the mask derived from the task activation map and selected all left-lateralized regions within the mask. Note that no information about between-subject variability in the task-based or intrinsic laterality estimates is used to define the language mask. The task-based and intrinsic language laterality indices showed significant correlation between subjects, suggesting language iLI successfully captures between-subject variation in language lateralization ($r = 0.48$, $P < 0.005$; Fig. S4*B*). As a further validation check, we also computed the language iLI on 17 patients with epilepsy; 16 patients showed left-lateralized language (iLI > 0) and 1 patient showed right-lateralized language (iLI $= -0.05$). The patient revealing right-lateralized language iLI was recruited to perform the language task in MRI. Results confirmed atypical language lateralization (Fig. S4*C*). The other 16 patients all showed left-lateralized language in the task-based measure. These findings indicate that intrinsic laterality can measure language lateralization and may provide an efficient method for presurgical planning.

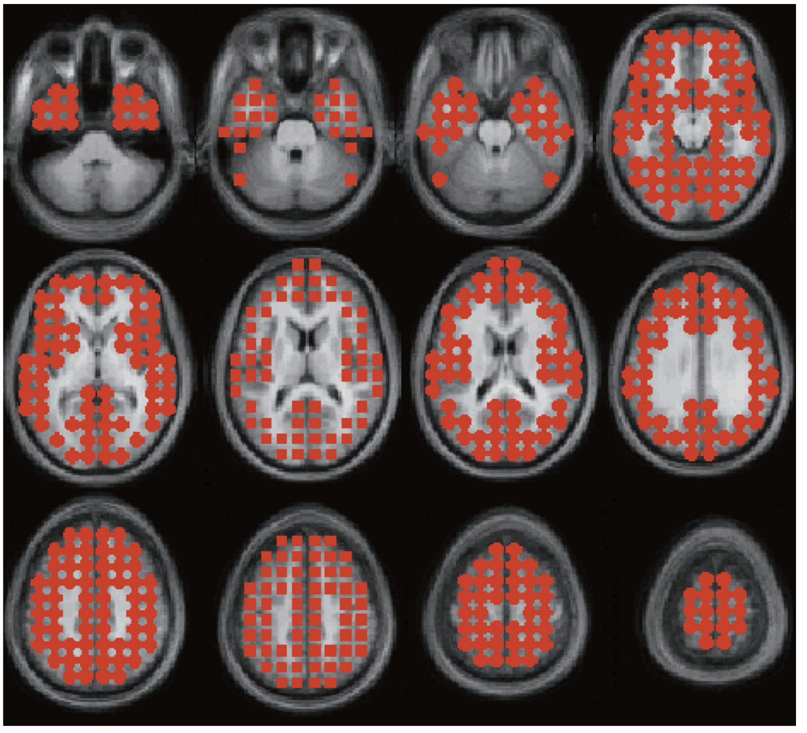

Fig. S1. Seed regions used for laterality analysis cover the cerebral cortex. Four hundred equally spaced spherical regions (7-mm radius) were selected as the seed regions to study intrinsic laterality (200 seed regions per hemisphere). The seed regions were spaced to cover the entire cerebral cortex mantle excluding the cerebellum. The placements of the seed regions are displayed on transverse sections on top of the mean structural image from the 100 included subjects contributing to Fig. 1.

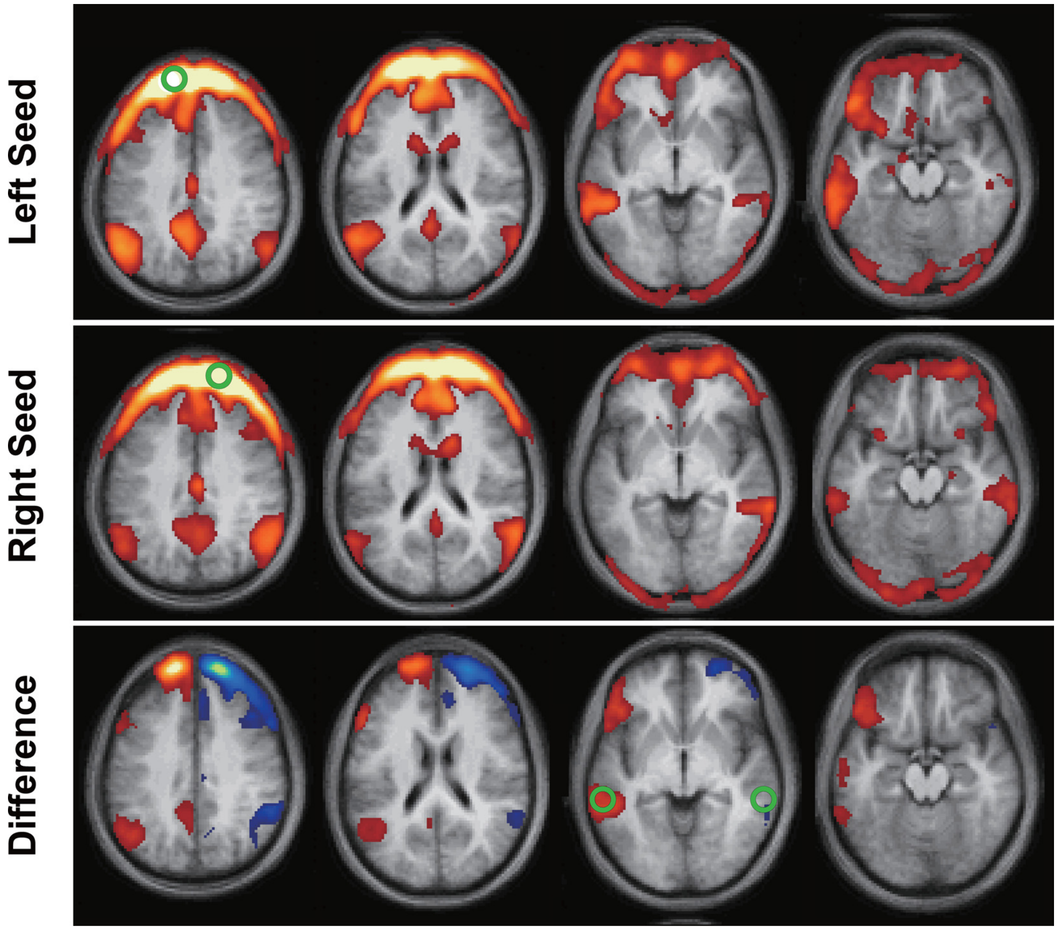

Fig. S2. Procedure to identify lateralized correlations. An example pair of correlation maps for right- and left-lateralized seed regions illustrates how lateralization is determined. The functional correlation maps for a mirrored pair of right and left seed regions in frontal cortex. The first row shows the functional correlation map with a left-hemisphere seed region. The seed region is indicated by a circle. The second row shows the correlation map based on the right-hemisphere seed. The third row is the difference between the first 2 rows; the asymmetric correlations can be easily identified. The temporal regions (indicated by the circles) are strongly correlated to the left hemisphere seed region but have weaker correlations to the right hemisphere seed region. The present approach quantifies this asymmetry and was conducted for all possible seed and target region combinations to determine those seed regions with the most asymmetric functional correlations. Local anatomic asymmetries may contribute to the observed functional correlations.

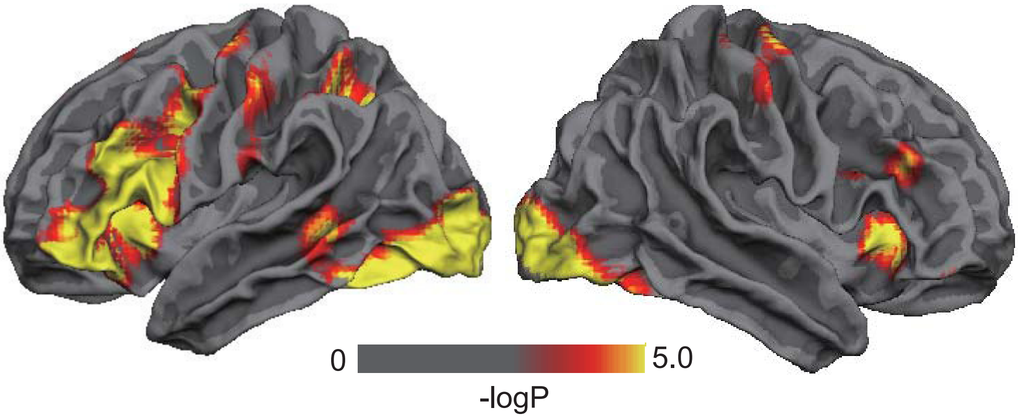

Fig. S3. fMRI activation during actual language tasks. A cortical surface projection shows the group results ($n = 35$) of the semantic classification task on words on the left- and right-lateral surfaces. The language task blocks were contrasted with baseline fixation to identify regions significantly increasing activation during the language task. Note the strong asymmetric response in particular for prefrontal cortex along the inferior frontal gyrus. This activation map was used as a mask for the analysis reported in Fig. S4.

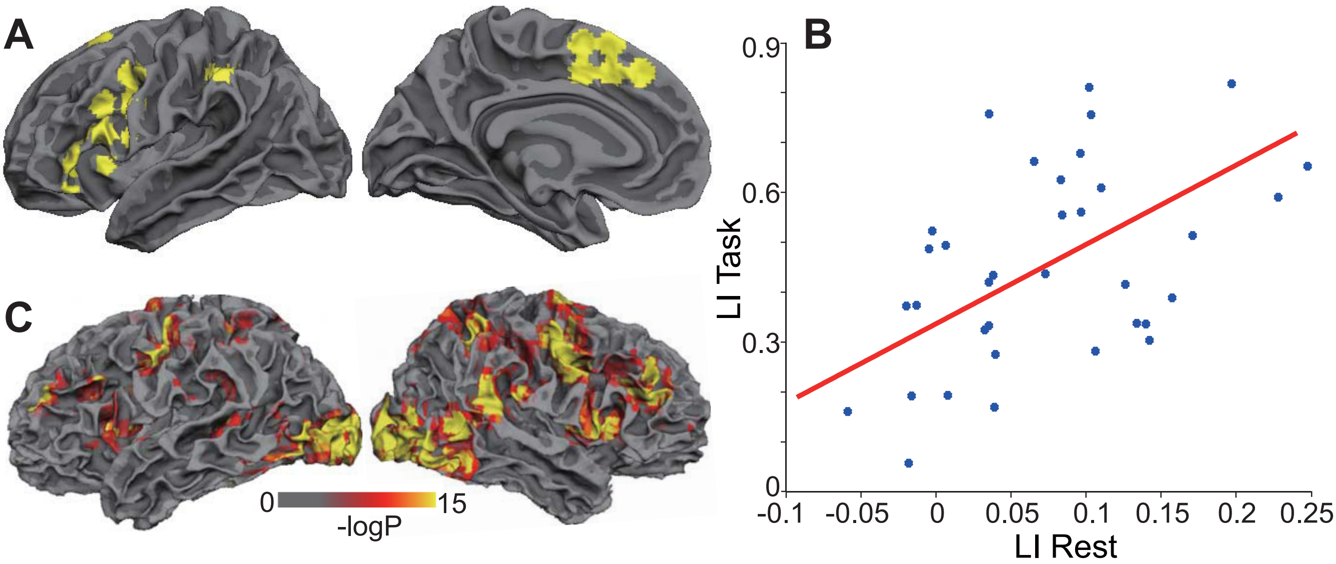

Fig. S4. Intrinsic laterality within the language system correlates with task-based estimates of language laterality. (*A*) Seed pairs falling within the mask defined by the group results ($n = 35$) of task-based fMRI are displayed. Seed regions included those along the lateral surface and midline. (*B*) The intrinsic language laterality index shows a significant correlation with the task-based language laterality index ($r = 0.48$, $P < 0.005$). (*C*) In an independent cohort of patients, an atypical subject was found to have a right-lateralized language laterality index of −0.05. Consistent with atypical dominance, the language task elicited strong activation in right prefrontal and temporal language areas.

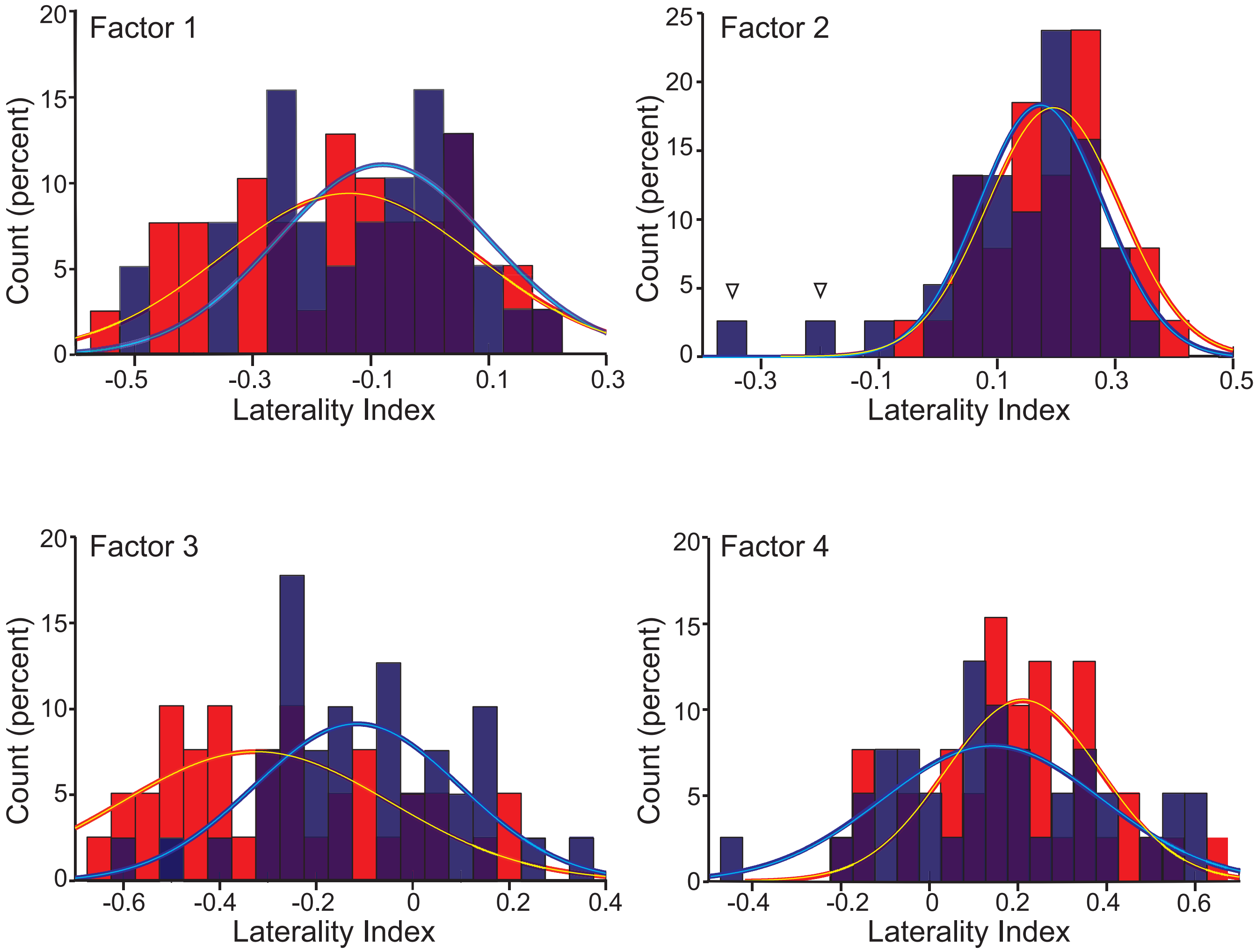

Fig. S5. Four factors are differentially associated with hand dominance. The distributions of the laterality indices for the 4 factors are displayed split by hand dominance (blue = left-handed, red = right-handed). Two left-handed individuals (indicated by arrows) display factor 2 estimates that are greater than any right-handed subjects. Factor 3 showed a significant effect of hand dominance. The factor 3 effect was not carried by a few individuals but rather reflected a shift in the distribution of laterality scores. Control analyses revealed the effect was not due to thresholding the iLI to zero when correlation strength was weak (see text). However, local anatomic asymmetries cannot be ruled out as an explanation.

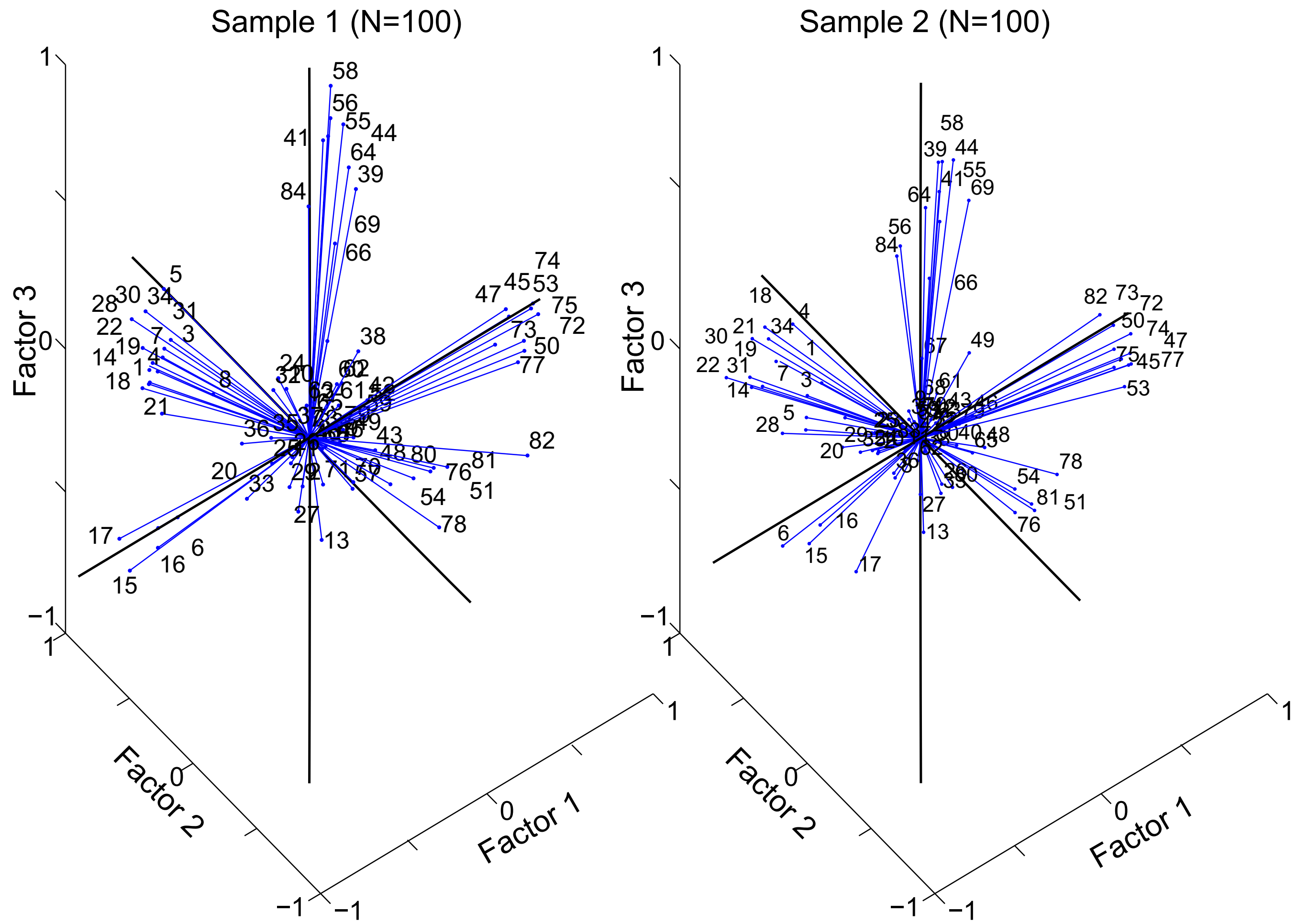

Fig. S6. Loading values for the top 3 factors that resulted from the factor analysis. Loading values for the 84 variables are plotted in the space spanned by the 3 largest factors. The variables are labeled by numbers 1–84 corresponding to the included regions. The results on 2 independent data samples show similar clusters of regions corresponding to each factor, indicating these factors are highly reproducible.