Language lateralization is correlated with resting-state connectivity within the inferior frontal gyri

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INTRODUCTION

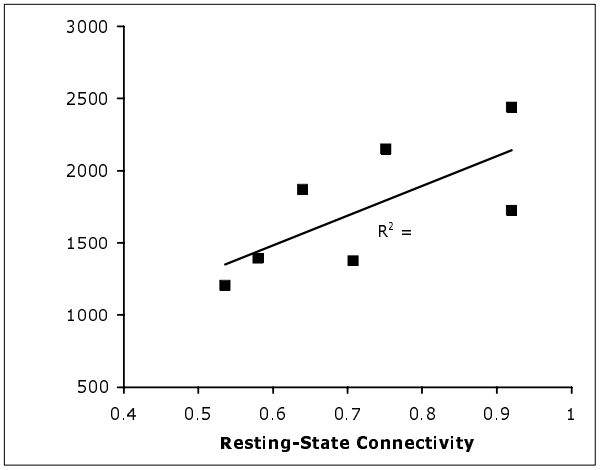
A number of studies have demonstrated that language is lateralized to the left hemisphere in right-handed individuals [1]; however, there are individual differences in the degree of lateralization, depending on handedness [2], gender [3], and pathology [2]. Hence, the neural mechanisms underlying language have not been completely elucidated. One study found that greater connectivity between Broca's area and other language-related areas within the same hemisphere was associated with greater lateralization of language function [4]; inter-hemispheric connectivity was not investigated. Clinical studies have demonstrated that patients recruit additional areas to perform the same tasks as healthy controls [5]. Hence, the fact that pathology results in a disruption of functional connections [6] suggests there may be a significant relationship between resting-state connectivity and language lateralization. Therefore, the aim of the current study was to investigate the relationship between resting-state connectivity and language lateralization, using functional magnetic resonance imaging (fMRI).

METHODS

Seven healthy volunteers (5 females and 2 males) underwent two scans each of resting-state and language fMRI, both of which used a GRE-EPI sequence (TR/TE = 1500/30ms; flip angle = 65°; 64x64 matrix; 24-cm field of view; twenty-four 5-mm thick slices). All images were acquired using a 3 Tesla MR scanner (Signa Excite HD; GE Healthcare, Waukesha, WI), equipped with an eight-channel phased-array radiofrequency head coil. Resting-state scans consisted of five minutes of scanning while the subject relaxed and fixated on a cross. Language fMRI then followed, consisting of a verb generation task in a 27-second alternating task/rest block design. During task periods, three nouns were presented on a projection screen for 9 seconds each, during which time the subject was asked to covertly generate as many verbs as possible associated with the noun. During baseline periods, subjects were asked to fixate on a cross. All data analysis was performed using *FSL* (www.fmrib.ox.ac.uk/fsl) and the General Linear Model. Anatomical images were also collected for registration of fMRI data. For each participant's verb generation activation map, the cluster of activity (Z> 2.3) within the inferior frontal gyrus (IFG) of the left hemisphere corresponding to Broca's area was selected as the seed region for analysis of the resting-state data. For each participant's resting-state data, the average time series of signal intensity was recorded for this seed, and a voxel-based temporal cross-correlation was performed to determine the correlation of each voxel's time series with the seed. Connectivity was calculated as the ratio of the average of the correlation coefficients within the right hemisphere IFG and the correlation coefficients within the left hemisphere IFG. That is, connectivity in the hemisphere contralateral to the seed was normalized to the connectivity within the seed. Based on this connectivity map, the IFG was determined for the right hemisphere. The number of pixels times their average Z-score during the verb generation task (i.e., the total activity) was computed for each of the left and right IFG, and the difference was calculated as the degree of language lateralization.

RESULTS

Language related activation was consistent with previous findings with significant activation within the inferior frontal gyrus (i.e., Broca's area). Resting-connectivity maps exhibited inter-hemispheric connections between homologous language related areas of both hemispheres. As the figure shows, greater differences in activation of the left and right IFG during verb generation was associated with greater connectivity. In fact, there was a linear relationship between resting-state connectivity and language lateralization (r = .71).



DISCUSSION

Because active language tasks tend to generate maps that are left lateralized, it is likely that our resting-state connectivity maps are not the result of participants actively engaging language areas during rest. Our results suggest that subjects exhibiting greater inter-hemispheric communication during the resting state recruit language areas of the right hemisphere to a lesser degree. One possible explanation for this observed relationship is that those brain regions strongly connected to Broca's area in the left hemisphere act silently during performance of a language task. In contrast, when the language areas are not strongly connected between the hemispheres, language-related areas in the right hemisphere are recruited during the performance of language tasks. The relationship between resting-state connectivity and language lateralization provides important information about the neural mechanisms underlying language and could have important implications for understanding language dysfunction in patient populations where task performance is problematic.

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