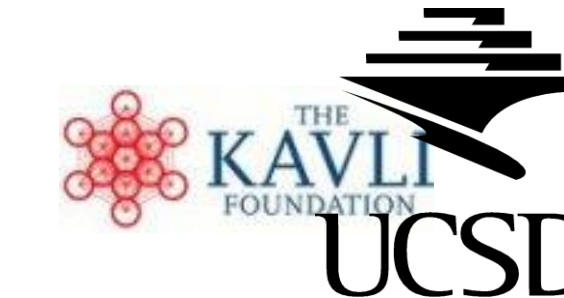




Brain size and the development of interhemispheric connectivity

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Introduction

The length of long-distance cortico-cortical fibers determines, in part, their metabolic cost and the conduction delay associated with them, and so their efficacy for tasks with rapid processing demands (Ringo, Doty, Demeter, & Simard, 1994). Differences in fiber length during development should thus impact the retention of connections between areas involved in temporally demanding tasks, e.g., language (Lewis & Elman, 2008). Children with longer long-distance connections during development should retain fewer of them. We tested this hypothesis using longitudinal data from typically developing children.

Methods

T1-weighted and diffusion data were collected from 19 typically developing males aged 6 to 10 years (mean 8.2; stdev 1.58), with a second scan 12 months after the first.

The corpus callosum (CC) was defined on the Talairach-like MNI-152 nonlinear symmetric T1-weighted template using the automated method described in Lewis et al (2009) and illustrated on the left side of Figure 1.

The template T1 was then registered to the visit 1 T1 volume of each subject, and the visit 1 T1 was registered to the visit 2 T1. The resultant transforms were then used to overlay the template CC on the T1s for both visits for each subject. The fractional anisotropy (FA) volume for each visit was then registered to the T1, and the transform used to overlay the radial diffusivity (RD) volume. The RD measures for each subregion were then extracted. The method is illustrated on the right side of Figure 1.

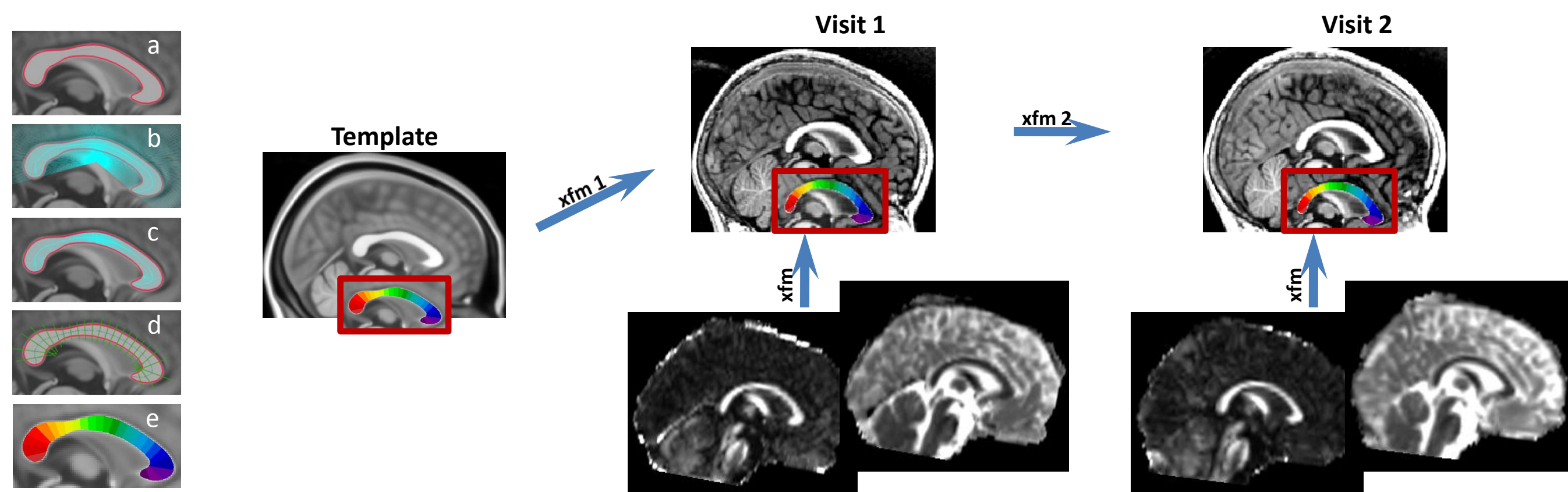


Figure 1: (left) CC template construction: (a) the boundary is determined via an active contour; (b) lines are radiated from the centroid, and the midpoints of those that intersect the CC are calculated; (c) the shortest lines that cross the CC passing through the midpoints in b are found, and their midpoints are calculated; (d) the curve passing through the midpoints in c and extending to the CC boundary is divided into 25 equal length segments; the shortest lines crossing the CC at the ends of a segment define the subregion boundaries; (e) shows the 25 subregions colored from purple at the anterior tip to red at the posterior tip. **(right)** The CC template was fit to individual subjects to derive measures of RD. The template T1 was registered to the visit 1 T1 for each subject, and the visit 1 T1 was registered to the visit 2 T1. The two transforms were then concatenated to overlay the template CC on the subject's visit 2 T1. The FA for each visit was then registered to the corresponding T1, and the transform used to warp the RD volume onto T1.

CIVET was used to extract a white-matter surface; this surface was then walked inward 3mm and used to seed probabilistic tractography using FSL. Each surface vertex was seeded 50000 times, with the 25 subregions of the CC as classification targets. The mean length tract to each CC subregion was calculated, as well as a count of the number of connections to each. The counts for all subjects were used to create a cortical parcellation in which each vertex was assigned to the CC subregion which it connected to most often across subjects (Figure 3-left). The across-subject mean of the mean length of connections from each vertex to the CC subregion of that cortical parcel was then computed (Figure 3-right), and used to interpolate the missing length measures in the individual subject data. The relation between the length of callosal fiber tracts and changes in RD in each segment of the CC was then assessed with a linear model, using random field theory to correct for multiple comparisons.

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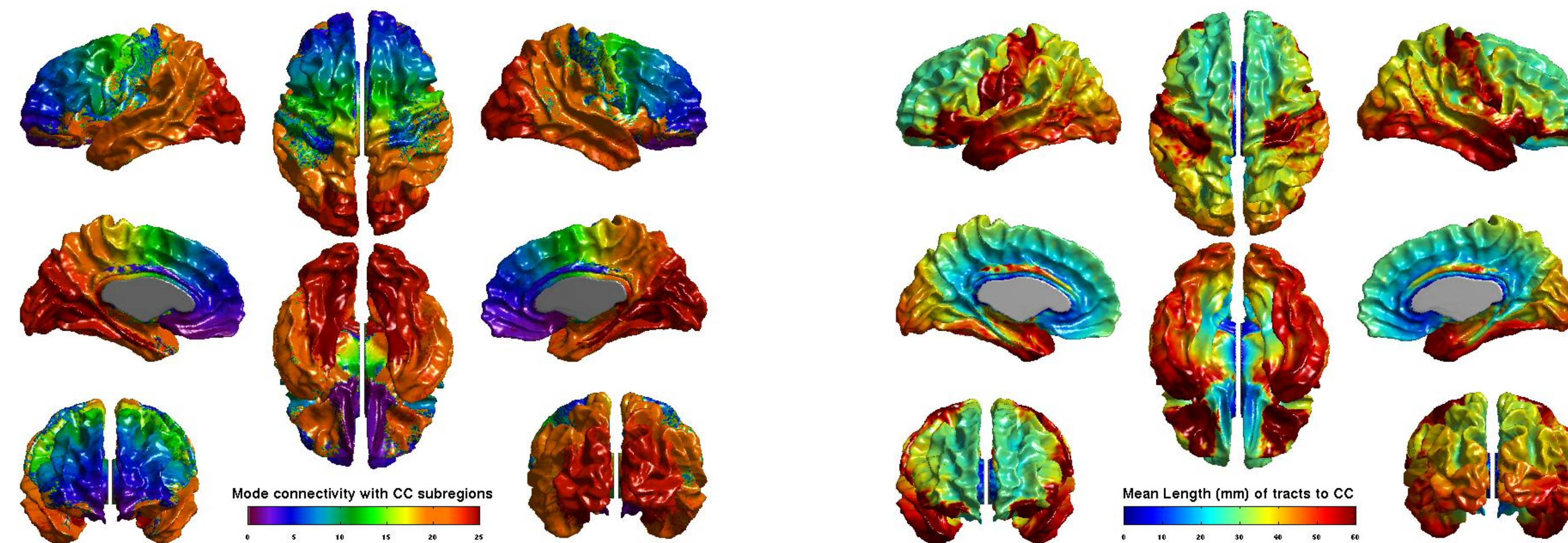


Figure 2: (left) The mode connectivity map with the 25 subregions of the CC. The colors correspond to those in Figure 1. **(right)** The mean length across subjects of tracts from each surface vertex to the CC subregion with which that vertex is associated in the mode connectivity map.

Results

The length of callosal fibers is correlated with change in radial diffusivity in the CC for tracts emanating from broad regions of cortex in both hemispheres. This is illustrated in Figure 3.

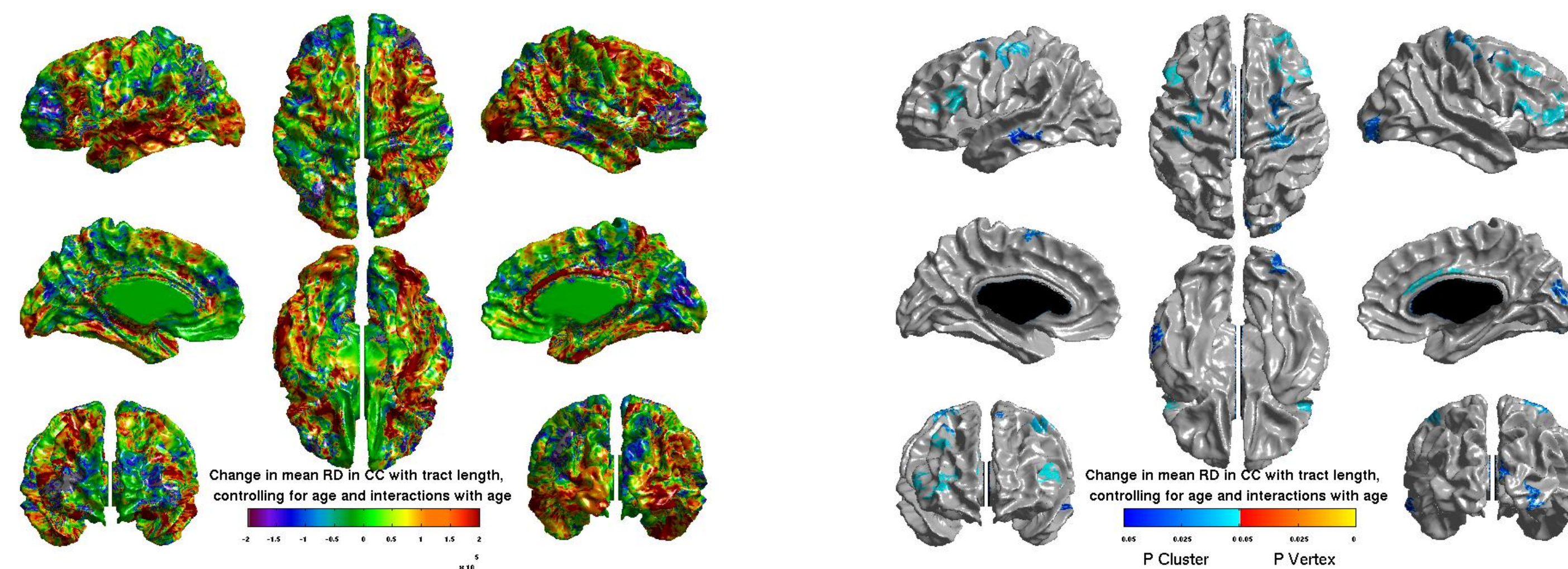


Figure 3: (left) The effects for all points on cortex. The value at each vertex is the value taken from the linear model for the CC subregion with which that vertex is associated in the mode connectivity map (Figure 2 - left). The linear model controls for age and interactions with age. **(right)** The P values adjusted for multiple comparisons using random field theory.

Conclusions

The results support the hypothesis that the length of long-distance fibers impacts their survival during development. This suggests an explanation for different lateralization patterns in the two genders, and for individual variation, as well as for abnormalities in connectivity in developmental disorders in which brain size during development is abnormal, e.g., autism.

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