Subject-based Maturational Coupling as Indicator of Brain Development: A Longitudinal MRI Study

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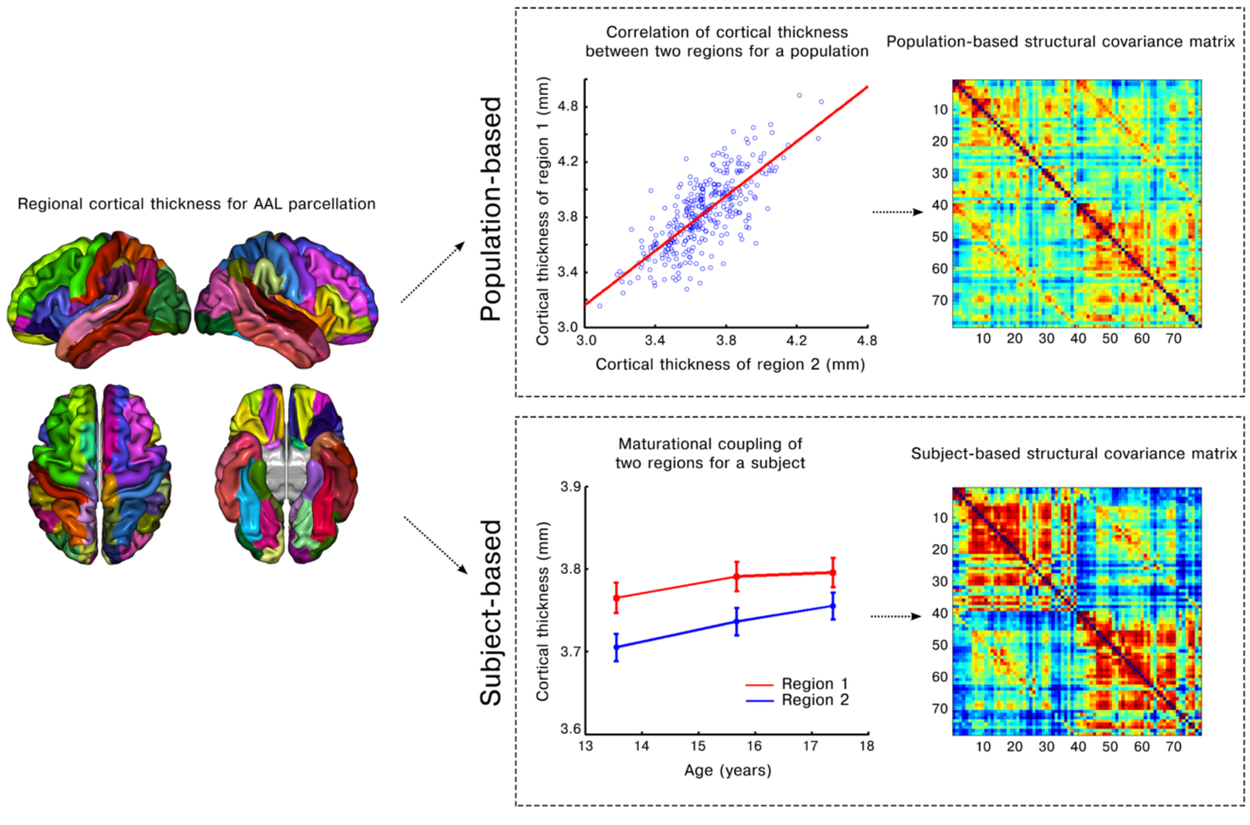
Introduction

- Several neuroimaging studies have shown large-scale structural covariance networks (SCNs) based on correlation of cortical thickness among widely distributed cortical regions in population of healthy and diseased brains[1,2,3]. The mechanism of this population covariance has been hypothetically related to coordinated maturational changes in anatomically connected neuronal populations, possibly reflecting shared mutual trophic factors[2,4]. SCNs have also been observed to be highly heritable[1,5] and, have anatomical and functional correspondence[6,7]. Thus, ideally SCNs can provide insights into the genetic and developmental processes that mould early neuronal wiring patterns to allow normal development of higher-order social and cognitive functions. However, SCNs, being population-based, are limited in studying individual brain development.
- Recent studies have shown population-based maturational coupling of cortical anatomy based on covariance of the rate of change of cortical thickness which are convergent with the population-based structural covariance, and also have functional correspondence[8,9]. Although the studies are useful in our understanding towards the mechanistic basis of SCNs, they are still population-based. Here, we propose a novel methodology that aims to address these limitations. Using longitudinal scans (subjects scanned at 3 time points), we compute the degree of similarity in the trajectory of cortical thickness between two cortical regions, defined as *maturational coupling index* (MCI). We hypothesize that our MCI approach will provide a detailed mechanistic model for SCNs. Additionally, unlike population-based SCNs, MCI approach will allow investigation of brain development at individual subject level, potentially revealing crucial developmental changes.

Materials and Methods

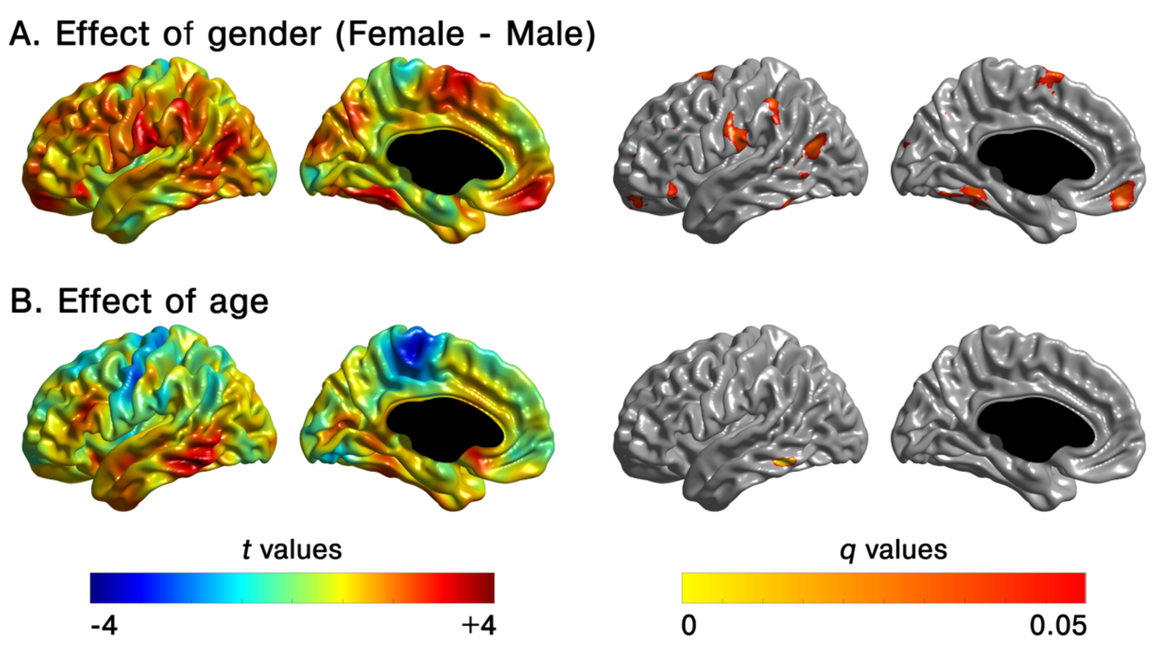
- Data from the NIH MRI study of normal brain development database[11] were used: 423 MRI scans of 141 subjects (males/females = 84/57) aged 6-18 years scanned up to 3 times ~ 2 year intervals.
- Using the MRI scans, cortical thickness was computed at 81,924 cortical regions using a well-validated pipeline (CIVET)[12]. Then, for each subject, we define maturational coupling index (MCI) between any cortical regions as the similarity in the trajectories of cortical thickness of the cortical regions based on the three time points. We thus obtain a maturational coupling matrix for each subject.
- MCIs of bilateral homologous cortical regions were put in a general linear model (GLM), and the effects of gender (controlling age) and age (controlling gender) were calculated. Correction for multiple comparisons was done using false discovery rate (FDR) at $q = 0.05$.
- Seed-based MCIs were calculated for the well known default mode network (DMN). The seed was selected at MNI coordinates (X, Y, Z = 4, -57, 44) based on earlier imaging studies[8,13,14]. The effect of age (controlling gender) on the seed-based MCIs was computed.

Population-based Structural Covariance vs Subject-based Maturational Coupling approach

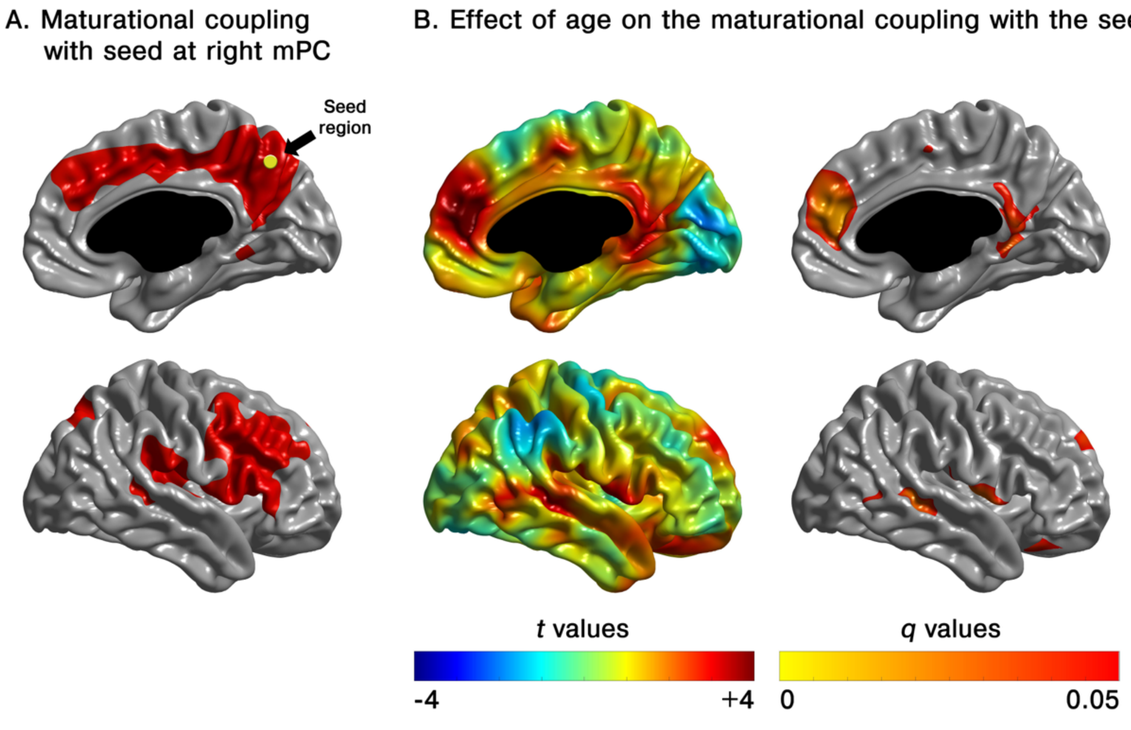


Results (contd.)

Effect of Gender and Age on Maturational Coupling of Homologous Cortical Regions

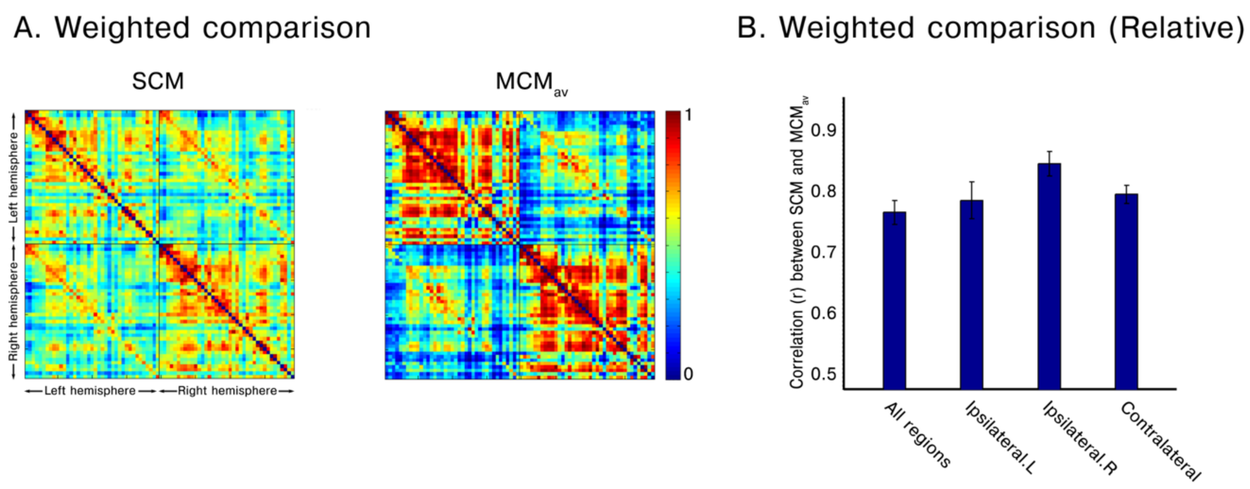


Developmental Changes in Maturational Coupling within the Default-Mode Network



Results

Convergence of Structural Covariance and Maturational Coupling matrix



Conclusion

- We proposed a novel method of quantifying maturational coupling of anatomical changes in individual subjects based on cortical thickness measured at 3 longitudinal time points. Subject-based MCI approach converged well with the population-based SCN approach, potentially providing a mechanistic basis for the existence of structural covariance of cortical regions.
- Gender-effect on maturational coupling of homologous cortical regions revealed significantly greater maturational coupling in several cortical regions including medial and superior frontal, lateral parietal and temporal cortex for females compared to males. The results are consistent with earlier literature that have shown greater bilateral connectivity in females as compared to males[10].
- MCIs generated based on seed placed in DMN captured the relevant networks, and developmental changes in MCIs were observed in medial frontal cortex for DMN, possibly indicating strengthening of DMN with age.

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