Determinants of cortical gray matter volume: Hypotheses on Developmental Cohorts with Normal and Abnormal Cerebral Morphology

Marie Schaer 1,2,3, Meritxell Bach Cuadra 2, Lucas Tamatis 1, Jean-Philippe Thiran 4, Stephan Eliez 1,4

1 Service Médico-Philosophique, Département de Psychiatrie, University of Geneva School of Medicine; 2 Signal Processing Institute, Swiss Federal Institute of Technology, Lausanne; 3Image & Signal Processing Laboratory, School of Engineering, Geneva; 4 Department of Genetics and Development, University of Geneva School of Medicine

BACKGROUND: CORTICAL GRAY MATTER DEVELOPMENT

Cortical volume represents the amount and size of neurons, dendritic processes, and glial cells. During early brain development, the increase in cortical gray matter volume is allowed by thickening of the cortical mantle, and by expansion of the cortical surface through brain size, and folding of the cortex (gyrification). Later, during childhood and adolescence, maturational processes such as pruning and neuronal loss are reflected by changes in gray matter volume, and thickness (Giedd, 1999; Sowell, 2004).

Cortical gray matter volume was shown to be positively correlated to cognitive abilities (Reiss, 1996), and has frequently been reported altered in psychiatric or neurogenetic conditions. New methods aims at quantifying cortical thickness and gyrification, thus assessing the relationship between cortical thickness, folding, and brain perimeter will certainly help to better understanding of normal and abnormal cortical development.

IMPAIRED CORTICAL DEVELOPMENT: 22q11 Deletion Syndrome (22q11DS)

A genetic disorder caused by a 3Mb deletion affecting 1 in 5'000 live births. Typically characterized by:

- physical anomalies,
- cognitive and learning impairments
- increased risk for psychopathologies.

Gray matter alterations in children / adolescent affected with 22q11DS:

- Decreased gray matter volume, parietal lobe particularly affected
- Numerous cortical dysgeneses (most frequently frontal and parietal)
- Decreased Gyrification Index in the frontal and parietal lobes

In light of previous literature emphasizing an abnormal cortical development particularly in the parietal lobe, this study aims to further characterize the structural changes in parietal cortex of affected individuals.

METHOD: THREE-DIMENSIONAL CHARACTERIZATION OF CORTICAL STRUCTURE

Subjects 34 typically developing individuals with no history of psychiatric or neurological disorders (20 females - 14 males), mean age 16.44 ± 9.29 y.o. (range: 6.9-39.7), mean IQ 110.6 ± 12.7
34 patients with 22q11DS (22 females - 12 males), mean age 17.15 ± 8.82 y.o. (range: 6.1 - 37.4), mean IQ 69.8 ± 10.6

Raw imaging T1-weighted 1.5T MRI, voxel size: 0.94 x 0.94 x 1.5 mm

Image processing Lobar gray matter volume were calculated according to (Eliez, 2000) including: intensity normalization; skull stripping; gray-white matter segmentation; and lobar subdivision according to Talairach grid (Kates, 1999).

RESULTS

1. Cortical Parietal Volume

We observe a linear decrease in parietal gray matter volume with age, with control subjects having higher values than patients.

Gray matter alterations in children / adolescent affected with 22q11DS:

- Decreased gray matter volume, parietal lobe particularly affected
- Numerous cortical dysgeneses (most frequently frontal and parietal)
- Decreased Gyrification Index in the frontal and parietal lobes

In light of previous literature emphasizing an abnormal cortical development particularly in the parietal lobe, this study aims to further characterize the structural changes in parietal cortex of affected individuals.

IMPLICATIONS FOR OUR COMPREHENSION OF NORMAL & ABNORMAL BRAIN DEVELOPMENT

Our results suggest that the more important structural factor contributing to the variance in cortical gray matter volume in normal individuals is gyration process. When the gyration process is disrupted in its early brain development, as in 22q11DS, cortical volume is primarily accounted for by brain perimeter, and normal gray matter volume are not reached.

We also observed decreased gyration with age, which reflects continuous shape remodeling of the maturing cortex. Thus, the processes contributing to the well-known developmental course of gray matter volume may not only rely on cortical thickness changes, but also on maturational morphological changes that are important enough to affect cortical area.