Statistical Analysis of Gender, Laterality and Diagnosis Effect on Planum Temporale

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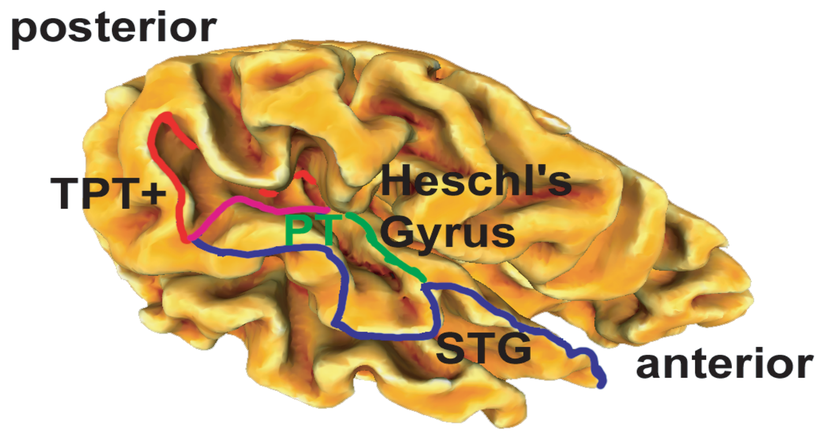
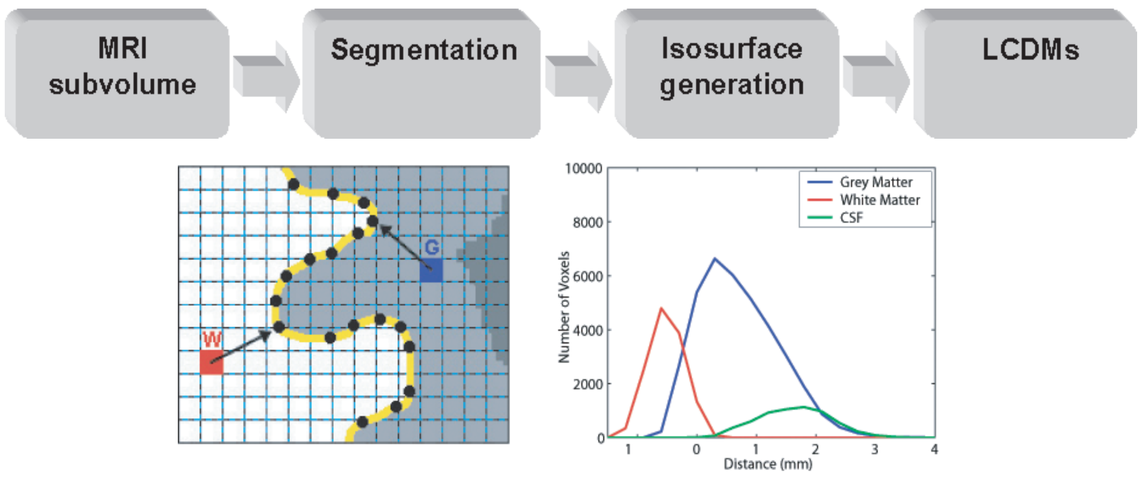
Introduction



Neuroimaging and post-mortem studies have demonstrated conflicting differences in morphometric measures of planum temporale (PT) due to gender, laterality, and neuropsychiatric disorders such as schizophrenia and bipolar disorder [e.g., 1]. These differences may be due to volume being considered as an entity. The highly folded cortical structure of the PT as well as anatomical definitions of its boundaries may confound quantification of morphometric measures. Viewing the neocortex as a thin laminar structure rather than a volume can provide advantages in understanding its shape [2]. To this end, Labeled Cortical Distance Maps (LCDMs) are generated to provide a complete analysis of anatomical variation in the PT. In this study, LCDMs are used to test differences in the PT due to gender, laterality, and diagnosis of neuropsychiatric disorders.

Methods



MPRAGE scans of 1mm^3 resolution from 60 subjects were included in our study, of which 20 were healthy controls (10 males and 10 females, age: 36.5?11.2, mean?SD), 20 were schizophrenia patients (10 males and 10 females, age: 36.5?7.82), and 20 were bipolar disorder patients (10 males and 10 females, age: 40?9.43) were selected.

The above flow chart describes the pipeline for generating LCDMs [1,3]. Bayesian segmentation of ROI masks of the superior temporal gyrus classified image voxels as Gray Matter (GM), White Matter (WM), and cerebrospinal fluid (CSF). Isosurfaces representing the 2-D cortical sub-manifold were generated at the GM/WM interface. Anatomical boundaries of the PT were delineated by dynamic programming generation of principal curves such as gyri, sulci, and fundi. The PT surface provides the natural local coordinates of the 2D manifold associated with the GM/WM surface with the third dimension described by the normal coordinates measuring distance of the GM voxel to the manifold. Distance maps profile the GM cortical mantle index by its distance along the normal axis to the GM/WM surface. LCDMs form a histogram consisting of labeled GM voxels as a function of distance from the GM/WM interface.

Surface area (A) was determined from the triangulated manifold while volume (V) and cortical thickness (T) were respectively derived from the total number of voxels and the 95th percentile distance from the LCDM. The kernel density estimates (normalized histograms) of LCDMs by subject were investigated for left and right PT to determine the outliers in each group. After removing outliers, the LCDMs were pooled by each group for left and right PTs.

A linear model with $V^{1/3}$ as response; diagnosis, gender, and hemisphere as predictor variables was run; likewise for $A^{1/2}$ and T as response variables. There was no significant interaction between gender, diagnosis, and hemisphere, which were then eliminated from the model. LCDM distances were pooled for gender, diagnosis, and hemisphere category combinations. Non-parametric statistical tests were performed to detect differences between pooled LCDM distances for each group with α=0.05 level of significance.

References:

[1] Beasley, C.L., Chana, C., Honavar, M., Landau, S., Everall, I.P., Cotter, D. Evidence for altered neuronal organization within the planum temporale in major psychiatric disorders. Schiz. Res. 73, 69-78, 2005.

[2] Miller, M.I., Hosakere, M., Barker, A.R., Priebe, C.E., Lee, N., Ratnanather, J.T., Wang, L., Gado, M., Morris, J.C., Csernansky, J.G. Labelled Cortical Mantle Distance Maps in the Cingulate Quantify Differences Between Dementia of the Alzheimer Type and Healthy Aging. Proc. Nat. Acad. Sci. 100:15172-7, 2003.

[3] Ratnanather, J.T., Honeycutt, N.A., Lee, N.G., Morris, H.M., Dziorny, A.C., Hurdal, M.K., Barta, P.E., Pearlson, G.D., Miller, M.I. Dynamic Programming generation of boundaries of local coordinatize submanifolds in the neocortex: application to the Planum Temporale. NeuroImage, 20, 359-377, 2003.

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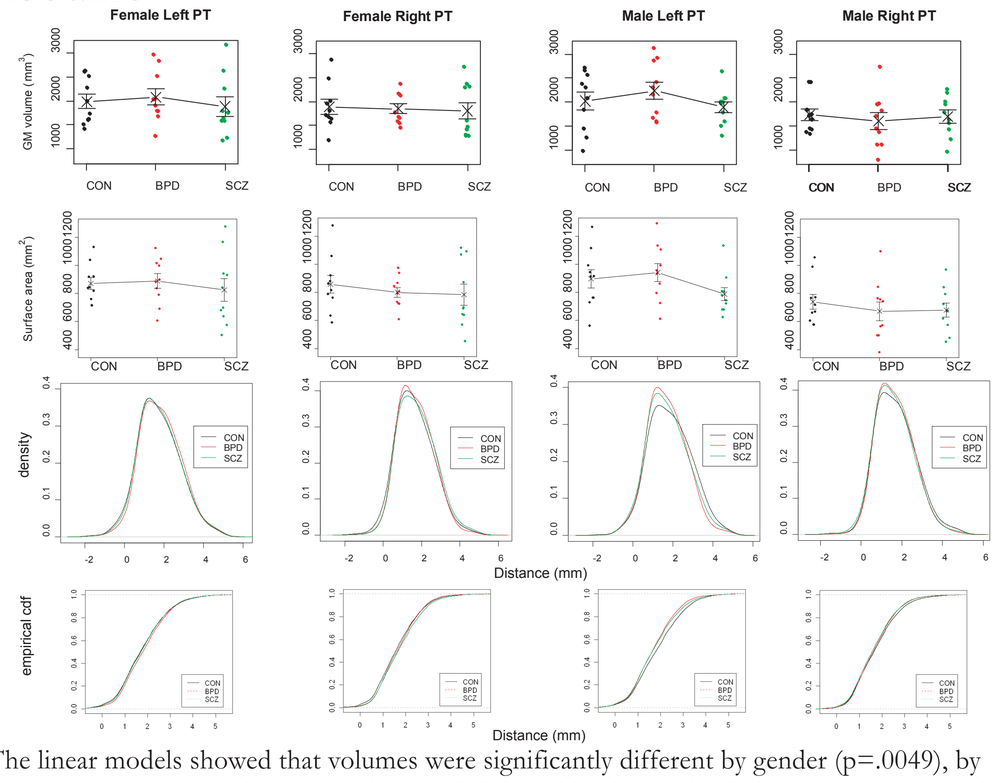
Results



- The linear models showed that volumes were significantly different by gender (p=.0049), by hemisphere after accounting for gender (p=.0021), and by diagnosis after accounting for gender and hemisphere (p=.0047).
- After adjusting for gender and hemisphere influences, control volumes were not significantly different from bipolar volumes but schizophrenia volumes were significantly smaller than both (p=.0072).
- Similar results were obtained for surface areas.
- Thickness values differed significantly for gender (p=.0011) and for hemisphere when gender was accounted for (p=.0065). But, when adjusted for gender and hemisphere, thickness values did not significantly differ for diagnosis (p=.1712).
- From pooled LCDMs, distances for males were significantly larger than females for both left and right control PTs, but smaller for schizophrenia and bipolar PTs (see table).
- Left PT distances were significantly larger than right for all diagnostic groups for both males and females (see table).
- For left and right PT of males, distances for controls were significantly larger than both bipolar and schizophrenia subjects which were not different from each other for left PTs but distances for bipolars were larger than schizophrenia subjects for right PTs (see table).
- For left PTs of females, bipolar distances were larger than both control and schizophrenia subjects which were not different from each other (see table).
- For right PTs of females, schizophrenia distances were larger than bipolar which were larger than control subjects (see table).

Male vs Female					
Left			Right		
MCON>FCON	MBPD<FBPD	MSCZ<FSCZ	MCON>FCON	MBPD<FBPD	MSCZ<FSCZ
<.0001	<.0001	<.0001	<.0001	.0086	<.0001
Left vs Right					
Male			Female		
LCON>RCON	LBPD>RBPD	LSCZ>RSCZ	LCON>RCON	LBPD>RBPD	LSCZ>RSCZ
<.0001	.0001	<.0001	<.0001	<.0001	.0108
Diagnostic Comparison					
Left Male			Right Male		
CON>BPD	CON>SCZ	SCZ>BPD	CON>BPD	CON>SCZ	SCZ<BPD
<.0001	<.0001	.0738	.0009	<.0001	.0001
so BPD <= SCZ < CON			so SCZ < BPD <CON		
Left Female			Right Female		
CON<BPD	CON<SCZ	SCZ<BPD	CON<BPD	CON<SCZ	SCZ>BPD
.0003	.0612	<.0001	<.0001	<.0001	.0288
so CON <= SCZ < BPD			so CON < BPD < SCZ		

Discussion

- A combination of analysis of linear models of morphometric measures (volume, surface area, and cortical thickness) and statistical tests on pooled (by group) LCDMs can be used to quantify differences in the PT due to gender, hemisphere and diagnosis.
- Specifically the former suggest changes in size and shape of the PT while pooled distances indicate structural changes in the PT.
- These results suggest that the size and shape of the PT in schizophrenia and bipolar disorders exhibit different effects with respect to gender and hemisphere.
- Differences in pooled LCDMs between 1 and 2 mm from the gray/white surfaces may be associated with reduced neuronal clustering in bipolar disorders and schizophrenia observed in post-mortem studies of the PT [1].

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