Quantifying the 2D Shape of Frontal Gyri in Bipolar Disorder via the LCPC Transform

Patent Pending

Tissue Spatial Geometrics Laboratory

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Abstract

Background: Bipolar Disorder affects 7 million people in the United States. Previous studies have reported anatomical changes in cortical and ventricular regions of the brain via analyzing MRI scans. A rapid, objective diagnosis of BD based on MRI scans is needed for more efficient and cost-effective predictions.

Method: An objective axial slice was chosen from each patient based on the roof of the corpus callosum. The inner edge of the gray matter along the right precentral gyrus and inferior frontal gyrus was manually segmented using Fiji/ImageJ. The Linearized Compressed Polarized Coordinates (LCPC) Transform was applied to the segmentations using a horizontal grid system. The resulting frequency plots for each sample were analyzed either as multidimensional data or reduced into a scalar value by summing all magnitudes for a sample into one value.

Results: The preliminary data herein suggests that the precentral and frontal gyri exhibit shape changes during physiological aging across ages 20-40, and that this pattern of change as a function of age is distinct in bipolar disorder patients. The LCPC Transform can reveal insights into brain fold patterns as both a scalar output and a multidimensional output.

Conclusion: The LCPC Transform is a promising spatial method for objectively and rigorously quantifying complex shapes in ways that are distinct from area, surface area, and volume. More samples need to be analyzed before solid conclusions can be made.

Background

According to the National Alliance of Mental Health, as of March 2021, roughly 2.8% of American, about 7 million people, are currently diagnosed with Bipolar Disorder (BD). BD is a neurological condition that causes emotional fluctuations ranging from extreme mania to deep depression. There are three different forms of bipolar disorder: BD-I, BD-II, and Cyclothymic. BD-I patients exhibit manic and depressive states that last from one to two weeks, depending on the severity, and can lead to suicidal ideation. Having similar symptoms with BD-I, BD-II is defined by the patterns of hypomania, which is less severe than mania, and depressive episodes. A milder form of BD is Cyclothymic Disorder. Though harder to determine, it resembles the hypomania of BD-II, but to less severe extents.

BD was found to associate with an enlarged putamen (Hallahan, 2011; Gong, 2019), enlarged left temporal lobe (Hallahan, 2011), and enlarged ventricles (McDonald, 2004; Kempton, 2008; Arnone, 2009; Hallahan, 2011). BD also affects the prefrontal cortex (Lyoo, 2004), and anterior cingulate cortex (Drevets, 1997). BD patients exhibit less gray matter in the paralimbic regions of the brain (Ellison-Wright, 2010). Additionally, the cingulate cortex and insula exhibit loss of gray matter (Goodkind, 2015), an effect also observed in the prefrontal cortex (Wise, 2017). Recently, in the largest analysis of BD brain scans to date, Hibar et al. (2018) found reduced cortical thickness in the left pars opercularis, left fusiform gyrus, and left rostral middle frontal cortex.

Our lab has found several regions of the brain that exhibit distinct shape changes in BD patients (unpublished) as measured by the Linearized Compressed Polar Coordinates (LCPC) Transform (arXiv:1801.06752), which was invented by Dr. David H. Nguyen, PhD. This method quantifies complex shapes without measuring area, surface area, or volume. This project measures the shape of the right precentral and inferior frontal gyri in a 2D axial slice in control vs. BD patients. Shape is a related, but distinct spatial feature compared to area, surface area, and volume. For example, a square and a diamond can have the exact same area while being distinct shapes; and thus, area is inadequate for quantitatively stratifying these two shapes.

Hypothesis

Measuring the shape, without volume or area, of brain folds via the LCPC Transform can quantitatively stratify non-affected patients from those affected by bipolar disorder.

Methods

MRI images of brains were obtained from the UCLA LA5c study archived on OpenNeuro. In order to objectively measure the same region across all patients, the roof of the corpus callosum served as an anatomical marker (see Figure 1 for details). The inner edge of the gray matter of the precentral gyrus and the inferior frontal gyrus was manually segmented in Fiji/ImageJ (see Figure 2 for details). This region was chosen because visual inspection suggested subtle differences between controls and BD patients.

The LCPC Transform was applied in the form of a horizontal grid system. The Fast Fourier Transform was done with a "sampling time" of 200 pixels and a sampling frequency of 40, resulting in 19 frequency bins for a single-sided frequency plot. All measurements and calculations were scripted in the R coding language. Data was plotted in R or Excel.

The LCPC Transform translates a shape into a frequency spectrum, and thus represents spatial information as multidimensional data in the form of frequency bins that each have a magnitude. By overlaying a coordinate system, such as a grid of horizontal lines (see Figure 2 for details), over a shape, the distance between each intersection of the shape's edge and the lines has a distance value. By summing all distance values that are on the same line, a 2D shape can be reduced to pairs of coordinates: the summed distance on a line and the order of that line relative to the other lines. This set of coordinate pairs are a discrete sinusoid wave that can undergo the Fast Fourier Transform to create a frequency plot. The frequency plots of many samples can be treated as multidimensional data. Additionally, each frequency plot can be summarized into a scalar value but summing all the magnitudes in it; thus, reducing the multidimensional output into one value for descriptive statistics.

Figure 1. How to pick the same objective axial slice in each sample. The axial slice of interest is the first slice, moving from chin to forehead, immediately above the corpus callosum (orange). The slice should exhibit a clear gray matter region, in at least one hemisphere, in the area above the roof of the corpus callosum, signifying the absence of the corpus callosum.

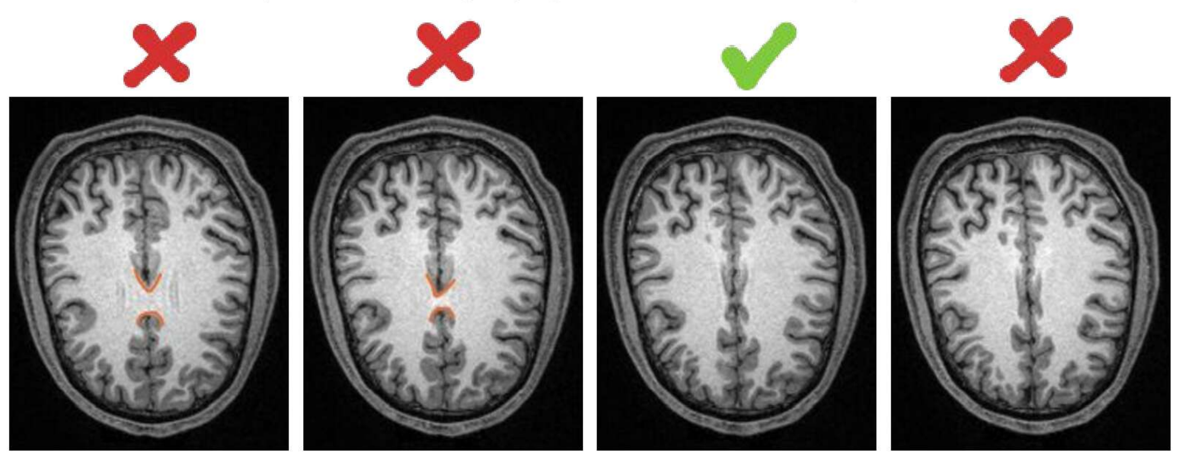
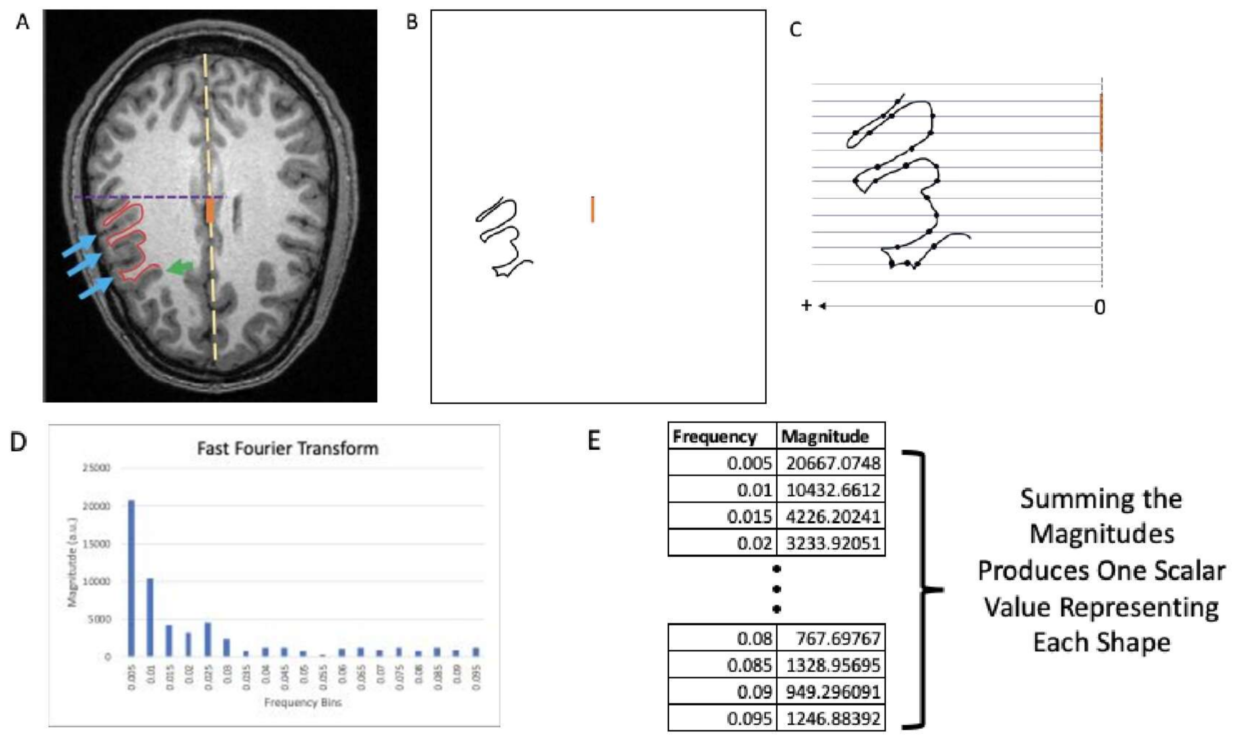


Figure 2. Applying a horizontal grid system to analyze the shape of the inner gray matter. **(A)** The region of interest is the precentral gyrus extending to the inferior frontal gyrus on the right hemisphere (blue arrows), but which ends at the most prominent ramus (green arrow) of the inferior frontal sulcus. Note that the anterior-most gyri of the inferior frontal gyrus in this axial slice may not be present in every patient; it is helpful to also locate this ramus on the left hemisphere. The inner edge of the gray matter (red) is manually segmented. A 1x5-pixel line (orange) is added along the midline (yellow), that starts at the same vertical location of the segmented edge (purple line). This line serves as an anatomical reference. **(B)** The segmentations in A are converted to a mask. **(C)** A horizontal grid system is overlaid on the mask in B and the distance is calculated for every intersection of a grid line and the object; the anatomical reference (orange) serves as the origin of each grid line. The LCPC transform is then applied to the set of distances that characterize each object. **(D)** A frequency plot resulting from the Fast Fourier Transform that represents the shape of the object in B. The data comprising the frequency plot can be analyzed via multidimensional statistical tools, such as Principal Component Analysis (See Figure 3C & Figure 5). **(E)** A scalar representation of the frequency data in D can be derived by summing the magnitudes of all frequency bins in D. This reduces the frequency plot of each sample into one value for each sample, which allows for ease of analysis via descriptive statistics (See Figures 3A-B & Figure 4).



Frequency	Magnitude
0.005	20667.0748
0.01	10432.6612
0.015	4226.20241
0.02	3233.92051
⋮	
0.08	767.69767
0.085	1328.95695
0.09	949.296091
0.095	1246.88392

Results

Figure 3. Scalar and multidimensional representations of the LCPC output. **(A)** A scalar (a.k.a. one value per sample) representation of each patient reveals a periodicity of every half-decade between ages 20-40 in male controls. This periodicity is also observed in other regions analyzed by the LCPC method (data not shown). **(B)** In bipolar disorder, the feature of interest exhibits a parabolic pattern between ages 20-40. This is also observed in other regions of the brain analyzed by the LCPC method (data not shown). **(C)** The first three principal components of Principal Component Analysis (PCA) of the 19 frequency bins of each sample suggest that the LCPC transform can can stratify age groups, but more samples are needed to verify this finding.

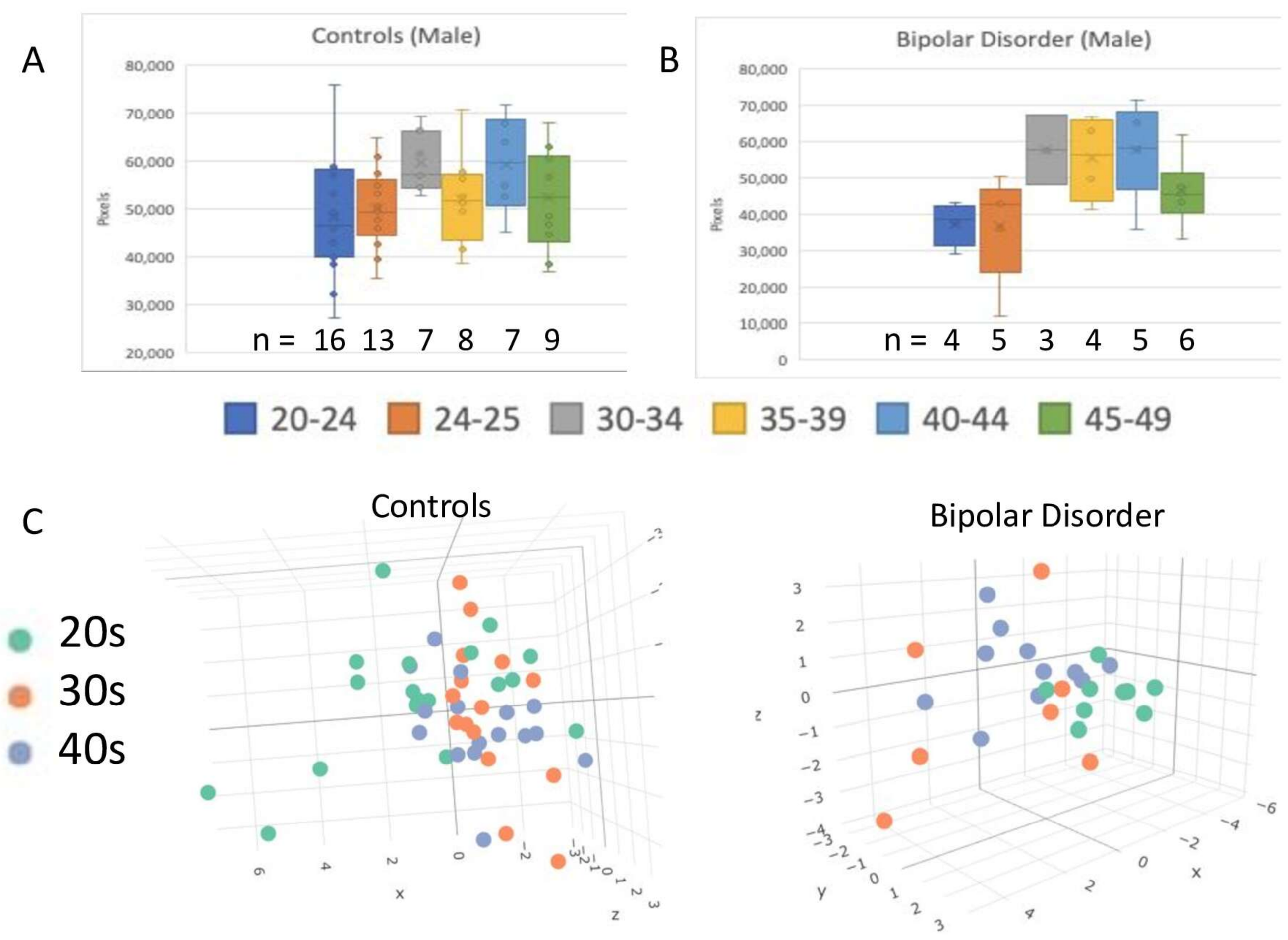


Figure 4. The shape of the precentral and inferior frontal gyri fluctuates with each half-decade in males ranging from ages 20-40. A t-test between control patients aged (n=29) and bipolar disorder patients (n=9) aged 20-29 shows significance; p=0.01 (data not shown).

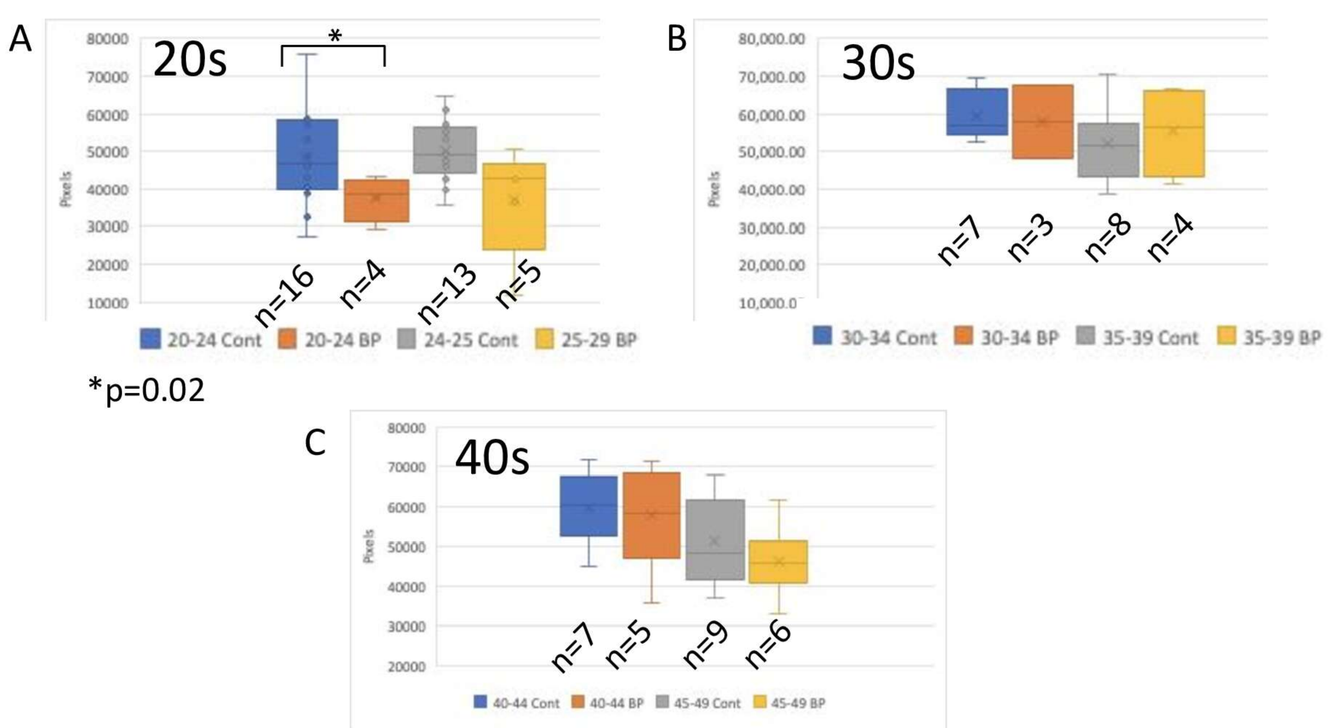
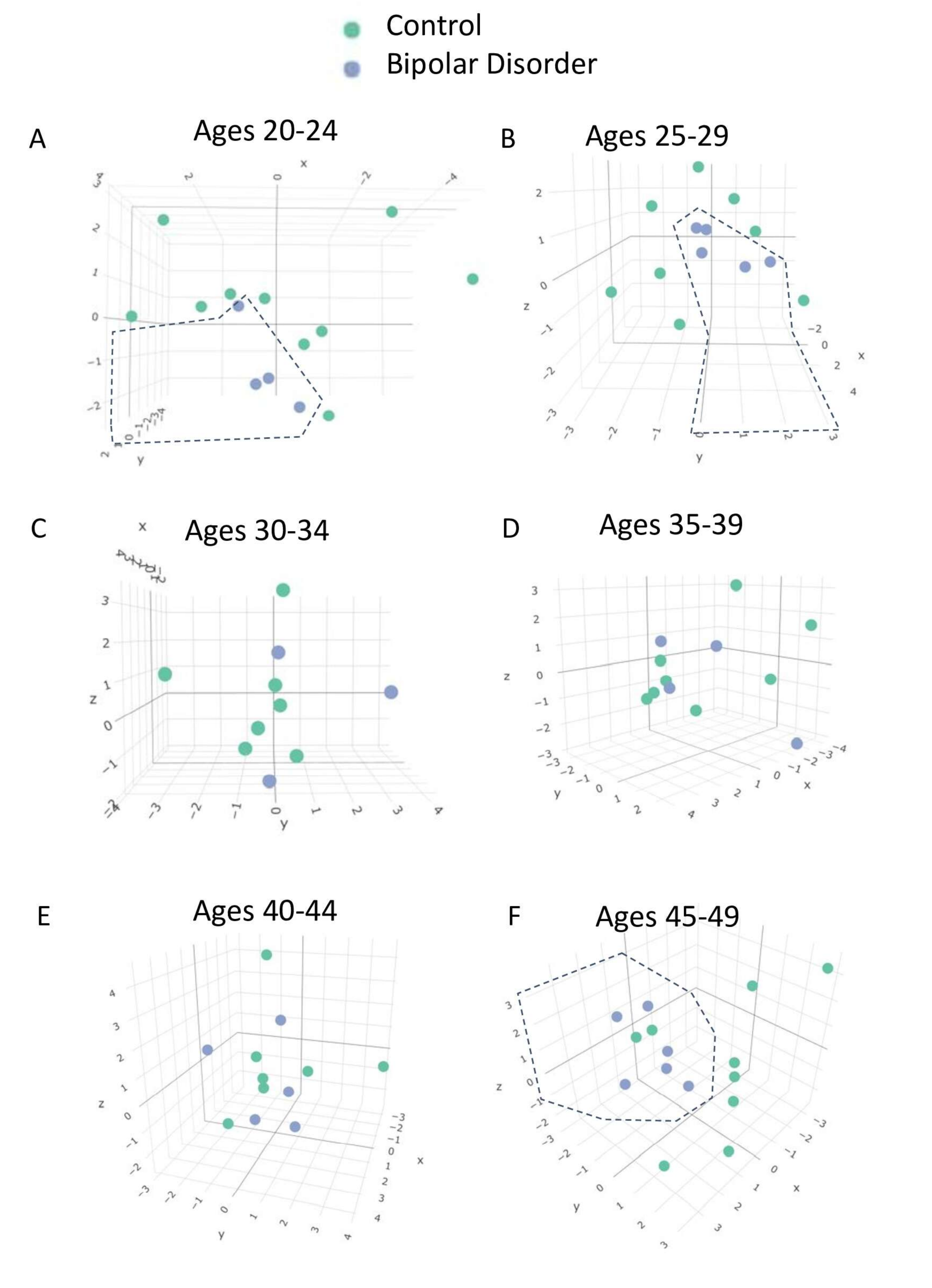


Figure 5. Principal component analysis (PCA) of gyri shape comparing controls to patients affected by bipolar disorder. (A-F) PCA of the 19 frequency bins of each patient was done to gain a multidimensional perspective of the LCPC output. The preliminary data herein suggest distinct 3D regions that stratify control patients vs. those with bipolar disorder (see dotted lines in A, B, and F). The suggestive spatial distinction in age groups shown in A, B, and F match the scalar-value differences observed in Figures 4A and 4C.



Conclusions

- The LCPC Transform is a promising spatial method for objectively and rigorously quantifying complex shapes in ways that are distinct from area, surface area, and volume.
- The preliminary data herein suggests that the precentral and inferior frontal gyri exhibit shape changes during physiological aging across ages 20-40, and that this pattern of change as a function of age is distinct in bipolar disorder patients.
- The LCPC Transform can reveal insights into brain fold patterns as both a scalar output and a multidimensional output.
- More samples need to be analyzed before solid conclusions can be made.

References

Arnone D, Cavanagh J, Gerber D, Lawrie SM, Ebmeier KP, McIntosh AM. Magnetic resonance imaging studies in bipolar disorder and schizophrenia: meta-analysis. *Br. J. Psychiatry*. 2009;195(3):194–201.

Ellison-Wright I, Bullmore E. Anatomy of bipolar disorder and schizophrenia: a meta-analysis. *Schizophr. Res.* 2010;117(1):1–12.

Gong Q, Scarpazza C, Dai J, He M, Xu X, Shi Y, et al. A transdiagnostic neuroanatomical signature of psychiatric illness. *Neuropsychopharmacology*. 2019; 44: 869– 875.

Goodkind M, Eickhoff SB, Oathes DJ, Jiang Y, Chang A, Jones-Hagata LB, et al. Identification of a common neurobiological substrate for mental illness. *JAMA Psychiatry*. 2015;72: 305–15.

Hallahan B, Newell J, Soares JC, Brambilla P, Strakowski SM, et al. Structural magnetic resonance imaging in bipolar disorder: an international collaborative mega-analysis of individual adult patient data. *Biol. Psychiatry.* 2011;69(4):326–35.

Hibar DP, Westlye LT, Doan NT, Jahanshad N, et al. Cortical abnormalities in bipolar disorder: an MRI analysis of 6503 individuals from the ENIGMA Bipolar Disorder Working Group. *Mol Psychiatry.* 2018 Apr;23(4):932-942.

Kempton MJ, Geddes JR, Ettinger U, Williams SC, Grasby PM. Meta-analysis, database, and meta-regression of 98 structural imaging studies in bipolar disorder. *Arch. Gen. Psychiatry.* 2008;65(9):1017–1032.

Lyoo IK, Kim MJ, Stoll AL, et al. Frontal lobe gray matter density decreases in bipolar I disorder. *Biol Psychiatry*. 2004;55:648–651.

McDonald C, Zanelli J, Rabe-Hesketh S, Ellison-Wright I, Sham P, et al.. Meta-analysis of magnetic resonance imaging brain morphometry studies in bipolar disorder. *Biol. Psychiatry.* 2004;56(6):411–417.

Wise T, Radua J, Via E, Cardoner N, Abe O, Adams TM, et al. Common and distinct patterns of grey-matter volume alteration in major depression and bipolar disorder: evidence from voxel-based meta-analysis. *Mol Psychiatry*. 2017;22: 1455–1463.