Stratifying Bipolar Disorder, Schizophrenia, and Gender via Cerebellar Peduncle Morphology

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General Summary

Shape, area, and perimeter are related but distinct features of 2D spatial information.

This project measures these three features in the cerebellar peduncles of a 2D axial slice and provides evidence that they can objectively stratify patients affected by bipolar disorder, Schizophrenia, and non-affected controls.

These three features can also quantitively stratify males from females in specific half-decades ranging from ages 20-40.

These findings support other morphological features in the brain that objectively stratify bipolar disorder from controls in males and females (data not shown).

Methods in Brief

Figure 1A shows how to find the slice of interest. The cerebellar peduncles were measured at the same anatomical location in each patient via an axial view (Figure 1A). Moving from chin (ventral) to top of head (dorsal), the slice of interest is the first one in which the "shoulders" of midbrain-pons (orange) are visibly distinct from the cerebellar peduncles (blue).

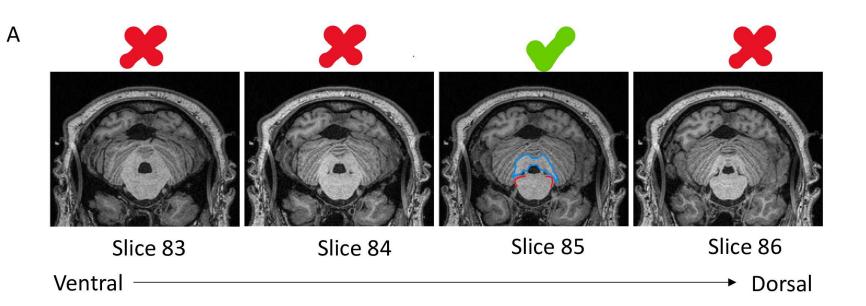
Figure 1B shows examples of the various cerebellar peduncle shapes.

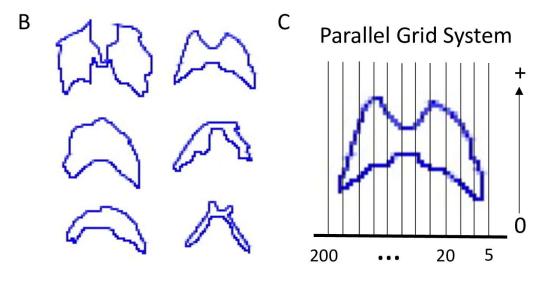
Figure 1C is a schematic of the parallel grid system applied to the cerebellar peduncles for the Linearized Compressed Polar Coordinates (LCPC) Transform (arXiv:1801.06752).

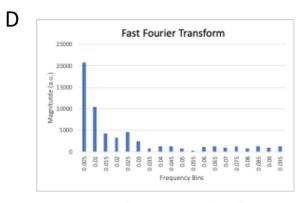
Figure 1D is a hypothetical frequency spectrum resulting from the Fast Fourier Transform applied to the result of 1C. By summing all magnitudes in the spectrum into one value, the shape in C can be represented in scalar form.

Figure 1. Methodology

See Methods section for details about this figure.







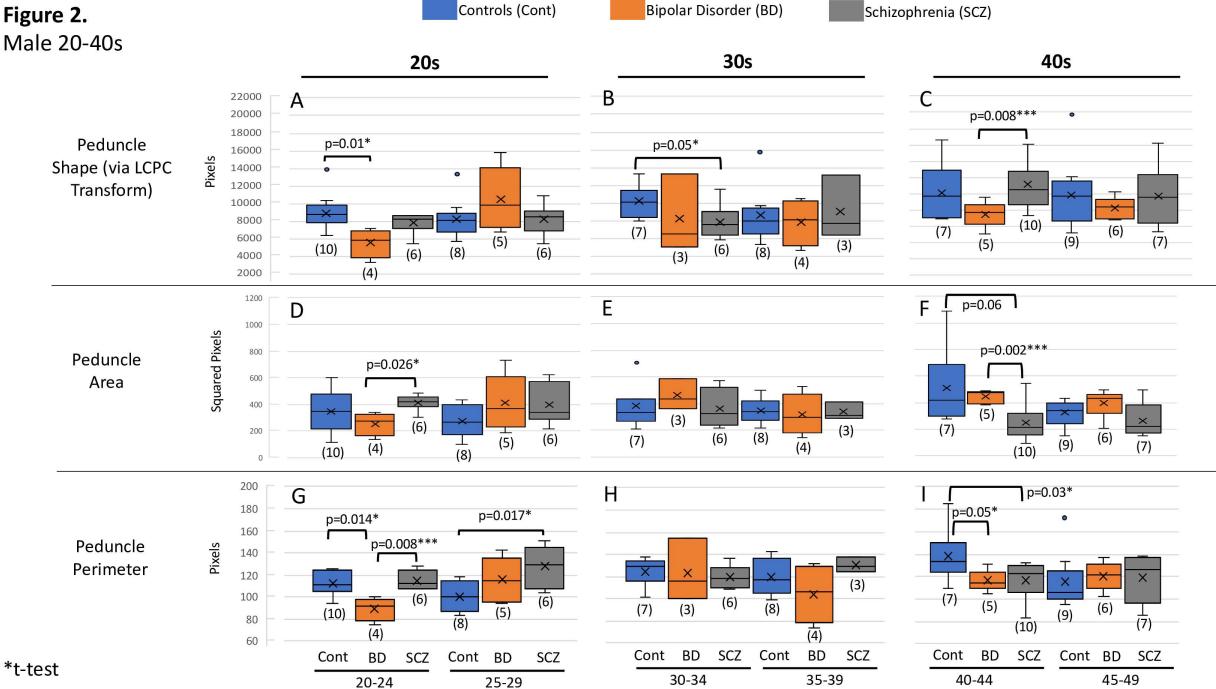
Sum Bin Magnitudes =
A Scalar Value Representing
the "Shape" in C.

Results

Highlights of Results

- The shape, area, and perimeter of the cerebellar peduncle differs in patients with bipolar disorder (BD), Schizophrenia (SCZ), or non-affected controls in specific half-decades ranging from ages 20-40 (Figure 2).
 - These three features do not always correlate in terms of which half-decade they effectively stratify controls vs. BD or controls vs. SCZ.
 - The early 20s (20-24) and early 40s (40-44) half-decades are particularly prone to major changes in cerebellar peduncle shape (Figure 2: A, C, F, G, I).
 - Cerebellar peduncle shape is less effective than area in stratifying female controls vs BD, or controls vs. SCZ (Figure 3).
 - ***The cerebellar peduncle shape changes in opposite ways in BD vs Controls compared to SCZ vs. Controls (Figure 2: C, D, F, G, I). This suggests that the cerebellar peduncles are good features by which to develop machine learning models that separate BD from SCZ in males. This is relevant because BD with hallucinations is often misdiagnosed as SCZ. Previous studies have reported changes in the cerebellar volume, connectivity to the cortex, and white matter volume but not peduncle shape. Volumetric measures are anatomically agnostic, but our approach objectively relies on anatomical location (Figure 1A) in the dynamically changing brain.
- The 30s appear to be a transition period in which these features of the cerebellar peduncle are the similar in affected patients and controls (Figure 2: B, E, H).
- The cerebellar peduncles in males vs. females can serve as morphological marker separating gender in certain half-decades better than others (Figure 4: C & E).
- The cerebellar peduncles are an effective measure of how gender-specific the changes due to BD are in male vs. female brains (Figure 4: B, D, F).

Figure 2. Male 20-40s



20s **30**s Figure 3. **40s** Female 20-40s 30000 C В Α 25000 Peduncle 20000 Shape (via LCPC 15000 Transform) 10000 (3) ___ (12) (3) (4) (5) ___(7) 5000 (4) 工(9) (3) 1400 p=0.03* Ε F D 1200 p=0.04*Squared Pixels p=5.6e-5*** p=0.03* 1000 800 **Peduncle** × 600 Area (3) (5) (3) 上 (9) 400 <u>__</u> (4) <u>|</u> (12) (3) 200 (5) (3) (4)0 300 Н G p=0.03*250 Peduncle 200 Perimeter 150 T (3) (3) × (5) (4) 100 (4) ___ (12) (5) (3) (7) 50 Cont BDCont BDCont BD Cont BDCont BD Cont BD*t-test 35-39 30-34 40-44 45-49 20-24 25-29

