

# Density, Morphology and Distribution of Interlaminar Astrocytes in Prefrontal Cortex in Bipolar Disorder, Schizophrenia and Controls

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## BACKGROUND

Schizophrenia and bipolar disorder are severe mental illnesses; schizophrenia (SCZ) is characterized by psychotic, negative, and cognitive symptoms, whereas bipolar disorder (BD) is associated with mania and depression, leading to dramatic changes to one's mood that can greatly impact a person's ability to carry out simple everyday tasks.<sup>[1]</sup>

Both illnesses present with heterogenous symptoms among individuals, making diagnosis and treatment difficult. Research looking to elucidate pathophysiological traits among patients could lead to improved treatments.

## GOALS

Research has shown disruption of astrocytes in SCZ and BD<sup>[2]</sup>, including previous studies by our group reporting lower GFAP area fraction and altered astrocyte distribution in white matter in SCZ and BD<sup>[3]</sup>, as well as increased GFAP protein levels in psychosis<sup>[4]</sup>. Interlaminar astrocytes are a subset of GFAP-positive astrocytes located in cortical layer I, which are thought to modulate cortical column development and function.<sup>[5]</sup> The role of this astrocyte subpopulation in SCZ and BD is so far unknown.

Given prior studies have focused mainly on alterations in astrocyte-secreted factors and gene and protein expression, the goal of this project was to determine whether the density, morphology and distribution of GFAP-positive astrocytes present in cortical layer I, predominantly comprised of the interlaminar subtype, differs in BD or SCZ groups.

## METHODS

Sample: Prefrontal cortex from control (n=20), SCZ (n=20) and BD (n=20) subjects. Demographics are listed in Table 1.

Paraffin sections were stained for astrocytes using an antibody against GFAP and imaged via brightfield microscopy. Images were input into FIJI ImageJ to quantify astrocyte cell density and area fraction. Presence or absence of astrocytes with abnormal morphology was documented.

Statistics: Normality tests were performed in Excel, followed by a one-way ANOVA and two-sample t-tests. Chi-squared test was used to compare frequencies for nominal variables. Associations between continuous variables were evaluated with Spearman's Rank correlations.

TABLE 1. DEMOGRAPHICS

Group	N	Sex <sup>#</sup>	Mean Age (years)	Mean PMI (hours)	Antipsychotics (mean lifetime dose)	Smoker
BD	20	12F 8M	47.4	37.4	13960	8
CON	20	6F 14M	45.3	29.9	0	7
SCZ	20	7F 13M	44.7	30.65	90383	15

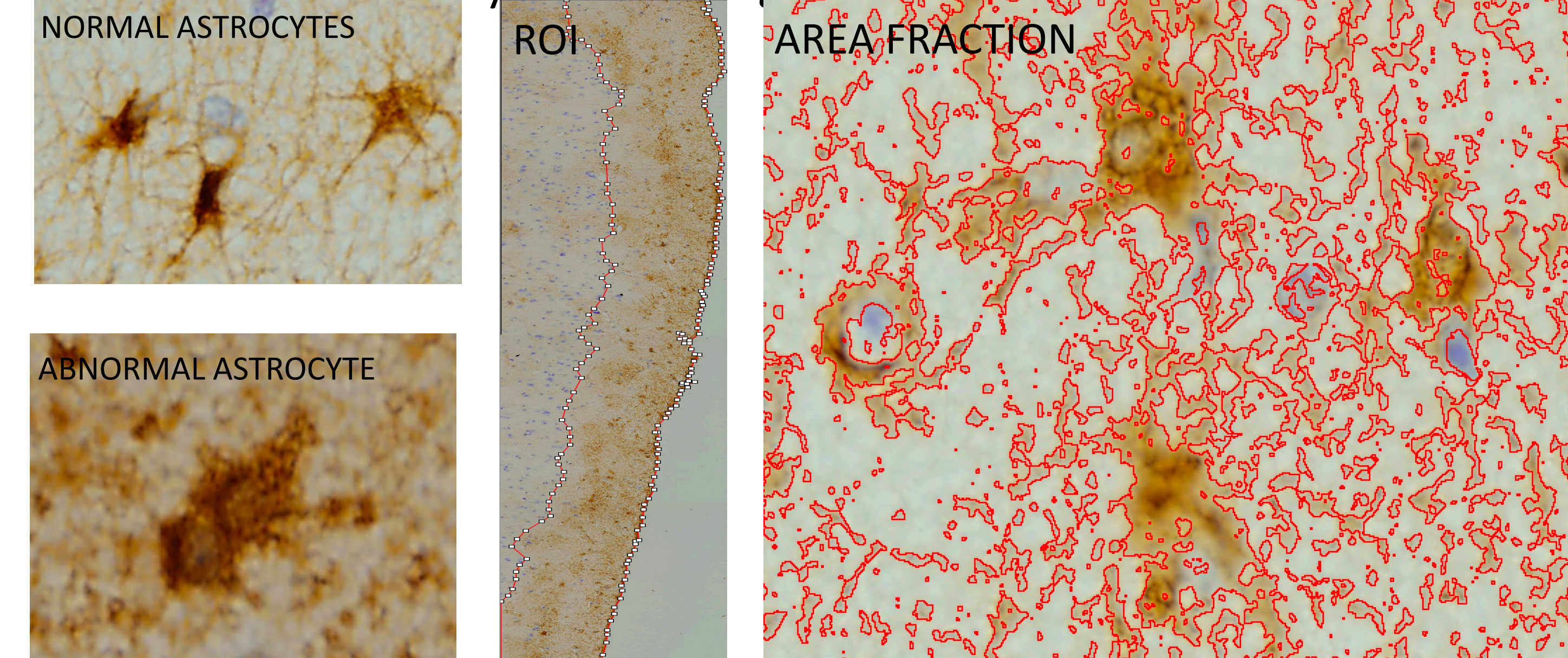
#Female (F), Male (M)

## RESULTS

Astrocytes were considered to be abnormal if they had one or more of the following:

- i) abnormally shaped somas, ii) processes that appeared disconnected/fragmented and iii) processes that appeared swollen or beaded.

Furthermore, a subject was considered to have abnormal astrocytes if the majority of their astrocytes were categorized as abnormal.



## RESULTS

TABLE 2. RESULTS

Group	Cell Density (per mm <sup>2</sup> , mean +/- SE)	Area Fraction (percentage, mean +/- SE)	Number of Subjects with Abnormal Astrocytes
BD	94.94 +/- 8.02*	37.01 +/- 2.51	10
CON	114.80 +/- 8.29	37.81 +/- 1.96	15
SCZ	99.83 +/- 8.13	35.20 +/- 2.18	7

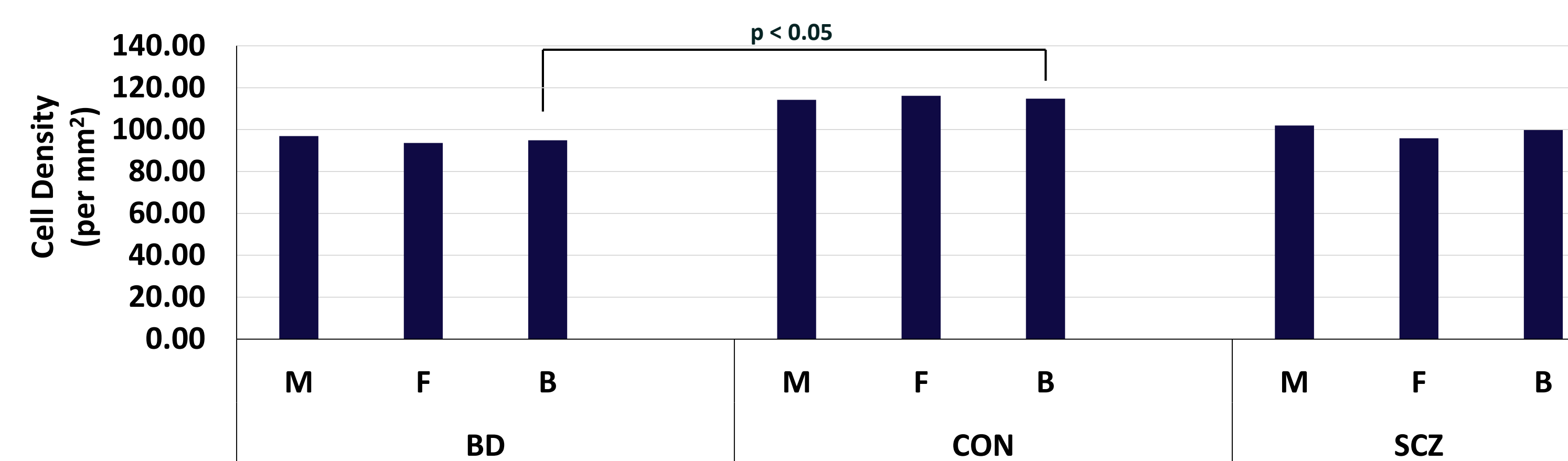
\* p<0.05

Cell Density: In comparing the SCZ and control groups, cell density values were not significantly different between groups (p>0.05). However, cell density was significantly lower in BD in comparison to controls (p= 0.047).

Area Fraction: Area fraction was not significantly different between SCZ or BD and control groups (p>0.05).

Cell morphology: Presence of abnormal-appearing cells differed between groups (chi squared p=0.038), being greater in the control group.

FIGURE 2. SEX DIFFERENCES IN CELL DENSITY



## RESULTS

Cell density and area fraction were not significantly correlated with age, PMI, or antipsychotic dose (p>0.05). Cell density or area fraction did not differ between subjects who smoked and those who did not (p>0.05).

## CONCLUSIONS

Though cell density values were not significantly different between SCZ and controls, they were significantly lower in the BD group compared to the control group. Area fraction values were not significantly different between groups. Abnormal astrocyte morphology was more common in the control group compared to BD and SCZ groups, contrary to our prior findings of abnormal microglial morphology in SCZ.

Future research could focus on elucidating the mechanisms underlying lower astrocyte cell density values in BD patients, which may include effects of medications.

## REFERENCES

- [1] APA. (2013). Diagnostic and statistical manual of mental disorders (5th ed.).
- [2] Blanco-Suárez, Elena et al. J Physiology vol. 595,6 (2017): 1903-1916.
- [3] Hercher, Christa et al. J Psychiatry Neurosci. vol. 39,6 (2014): 376-385.
- [4] Feresten, Abigail H. et al. Schizophr Res. vol. 150, 1 (2013); 252-257.
- [5] Colombo, J A. et al. Int J Dev Neurosci. vol. 15,7 (1997); 823-833.

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