

# Changes in Resting Cerebral Blood Flow in People With Chronic Schizophrenia: Striatal Hyperperfusion Accompanying Widespread Cortical Hypoperfusion

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## INTRODUCTION

- Non-invasive imaging with MRI has led to some initial characterization of brain (dys)function in people with schizophrenia (PSz), supporting a brain dysconnectivity hypothesis of Sz.
- MRI tools/sequences like pseudo-continuous arterial spin labeling imaging (ASL) have been employed less often in studies of Sz.
- ASL can measure tissue perfusion e.g. resting cerebral blood flow (CBF).
- A recent meta-analysis of 13 studies showed that PSz had widespread elevations in CBF across cortical brain regions (frontal, temporal, occipital) relative to controls, but decreased CBF in the putamen (a critical region of the dorsal striatum that receives heavy dopaminergic input) (du Sert et al. 2023).

*This leaves open the questions of (1) whether blood oxygen level dependent MRI signal(s) are predominately increased or decreased in PSz and (2) whether consistent, replicable patterns of activity in PSz can be mapped to specific circuits. In this data-driven analysis, we identify significant differences in resting CBF in PSz vs. healthy control (HC) participants using ASL imaging.*

## METHODS

**Population:** 37 participants that met DSM-IV-TR/DSM 5 criteria for either schizophrenia, schizoaffective, or schizophreniform disorder and 32 HC.

**Quality Control (QC):** Eight participants' ASL data was did not pass QC assessment (Final N = 31 HC and 30 PSz).

**ASL Data Preprocessing:** normalization, smoothing (5 mm FWHM), motion and partial volume corrections. The average CBF signals (in ml/100 g/min) for 246 brain regions of interest were extracted using the Brainnetome atlas.

**Data Harmonization:** During the study, the MR scanner was upgraded from a Siemens Trio 3T MR system to a Siemens PRISMA 3T MR system. The upgrade resulted in different scales of measured CBF intensity for values obtained from the Trio vs. PRISMA scanner. To harmonize these values, we applied the NeuroCombat harmonization procedure.

**Stats:** To account for the patterns of co-dependence of CBF in nearby regions, we applied the innovative FASE autoregressive model to examine PSz vs. HC differences in rCBF; P-values were FDR-corrected for multiple tests.

## RESULTS: PSz vs. HC

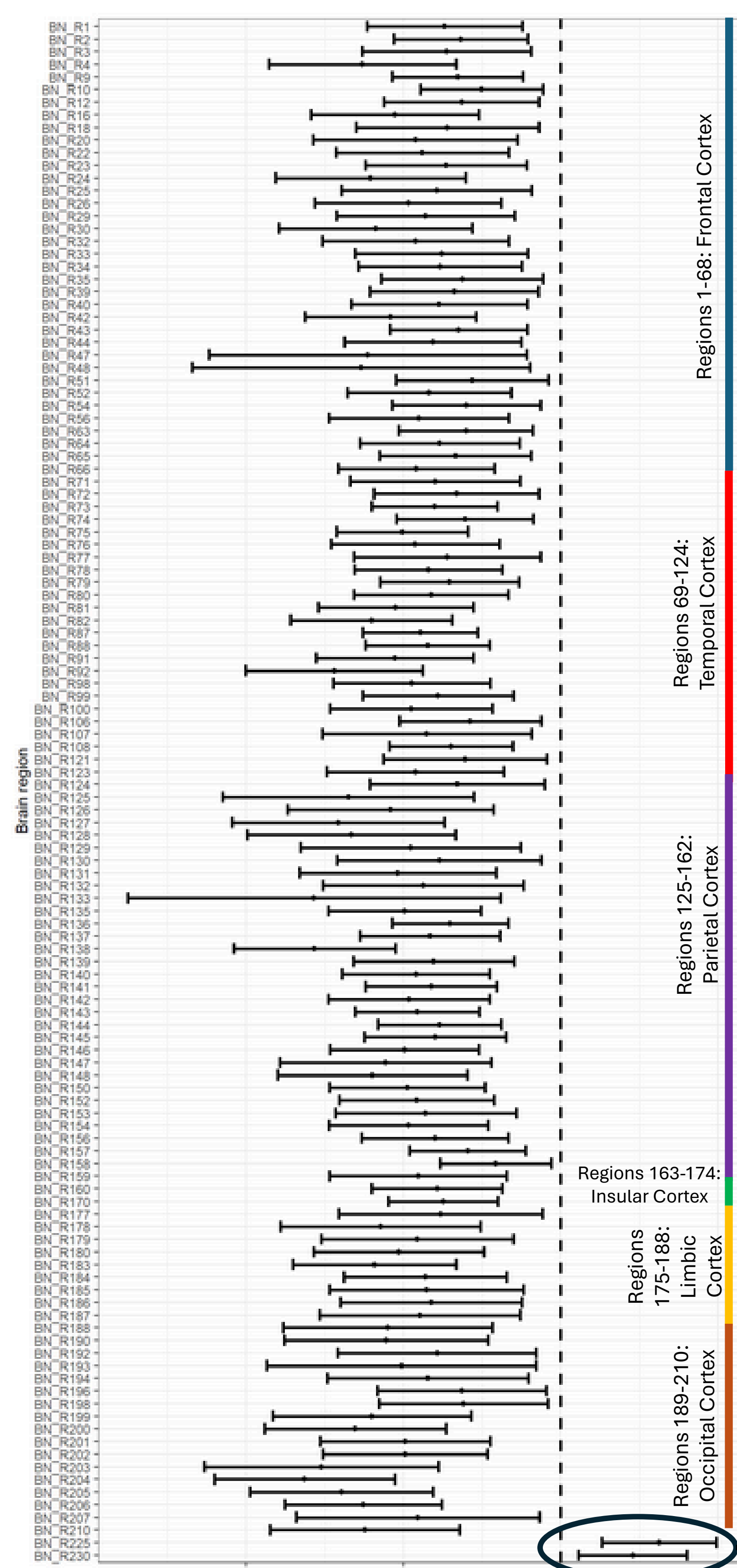
After applying the FASE Autoregressive Model (FARM) to the analysis of CBF in 246 brain regions, we found:

- In PSz (relative to HC), CBF was significantly decreased across 115 cortical brain areas and significantly increased in 2 subcortical striatal regions in PSz: left ventromedial putamen and right dorsolateral putamen.

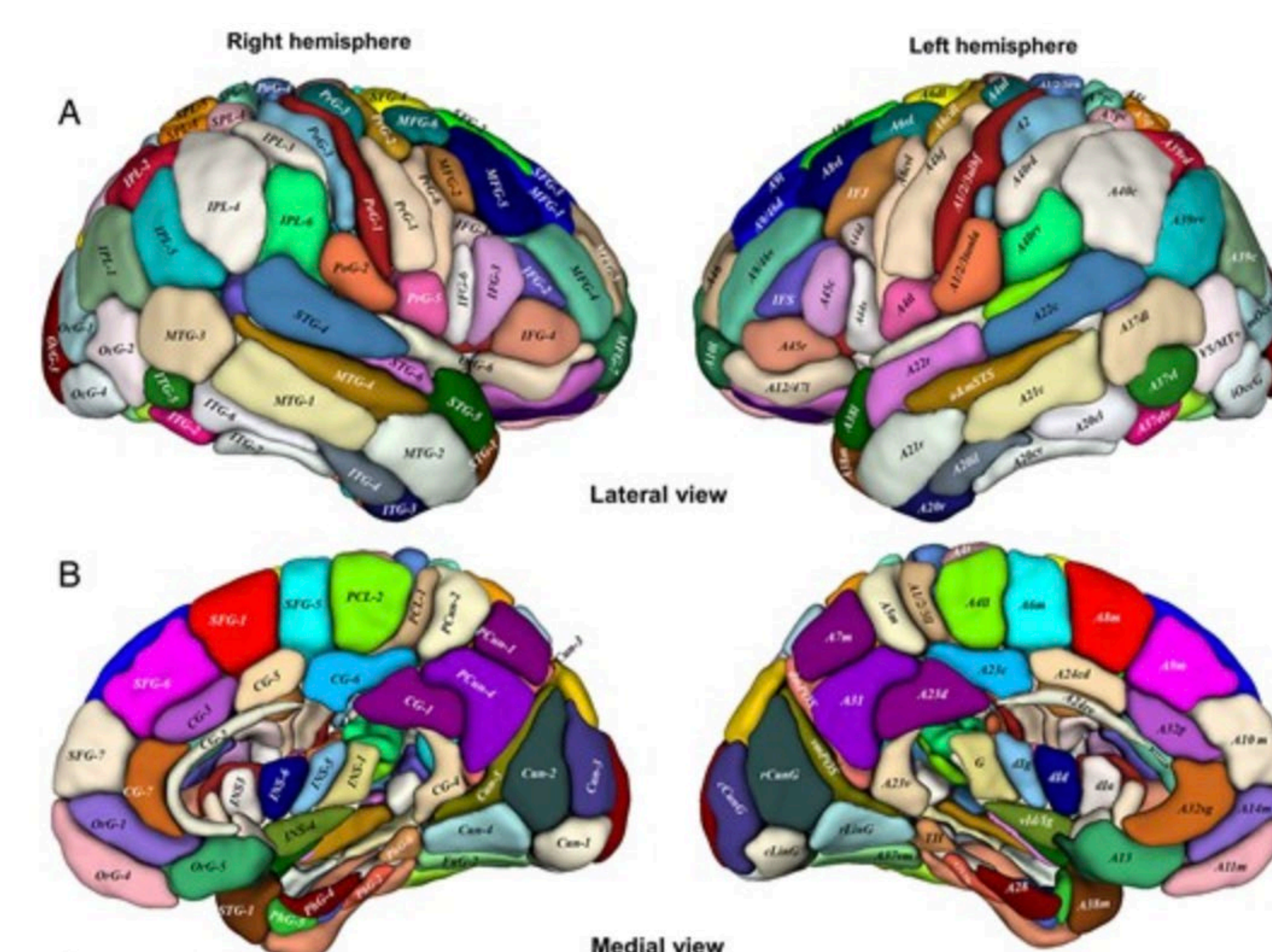
## RESULTS: Exploratory

Exploratory linear regression were performed in the PSz to explore factors that may be related to CBF in these two striatal regions: symptoms, medication.

- CBF in these striatal regions was not significantly associated with overall symptom severity (total BPRS score) nor an estimate of current antipsychotic medication dose (chlorpromazine equivalent dose).



Forest plot displaying the confidence intervals of the regression coefficient for the significant brain regions



The fine-grained parcellation of the Brainnetome Atlas includes 210 cortical regions and 36 subcortical regions. Source: Fan et al. 2016, Cerebral Cortex

## CONCLUSIONS & FUTURE DIRECTIONS

Our findings fall in line with the recent meta-analysis (du Sert et al.), which reported that the strongest effects in PSz were decreased CBF in frontal and other cortical areas, and increased CBF in the putamen. Future research is needed to learn how the observed patterns of resting CBF in PSz are influenced by chronic administration of antipsychotic medications and how changes in CBF may relate to severity of different symptoms.

These two regions (225: left ventromedial putamen; 230: right dorsolateral putamen) were the only regions to show increased blood flow in the PSz.



If you're interested in this research and want to connect, please use this QR code to connect with Dr. Hare on LinkedIn or email: stephanie.hare@som.umaryland.edu

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