

Impaired brain clearance in Schizophrenia

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Introduction

The coupling between the coherent global grey matter activity (gGM-activity) and cerebrospinal fluid movement (gGM-CSF-coupling) is thought to drive glymphatic fluid movement in humans.¹ Since gGM-coherence is severely impaired in patients with schizophrenia,² the glymphatic system might be impaired in the disorder. Therefore, we hypothesized impaired brain clearance function in Schizophrenia.

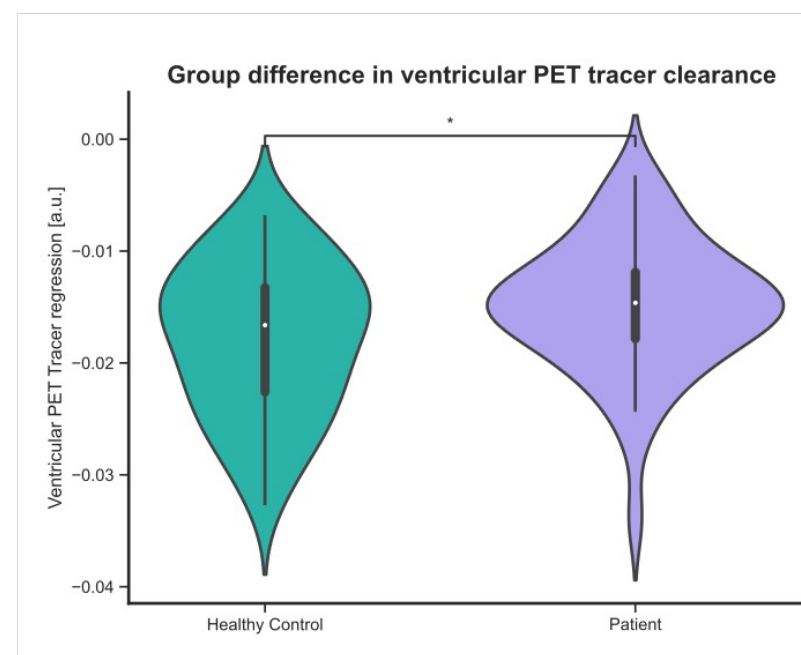
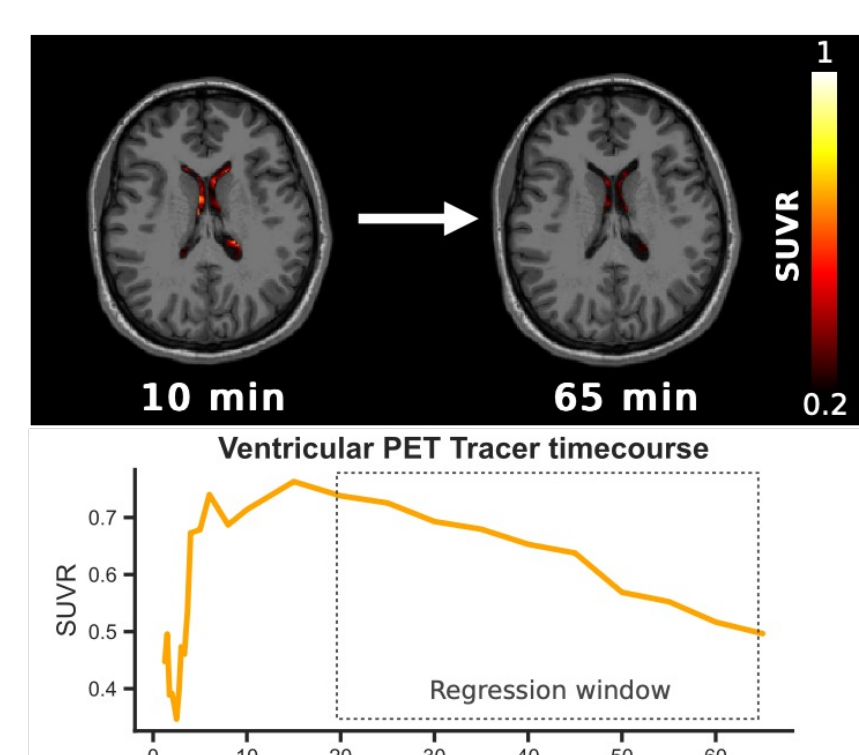
Methods

Forty-seven patients with Schizophrenia and 44 healthy controls were assessed by both cognitive testing and simultaneous PET-MRI, including ¹⁸F-DOPA-PET, resting-state fMRI, and T1-MRI. As proxies for brain clearance function, we used global gGM-CSF-coupling assessed by Pearson's correlation between the fMRI signal time courses from gGM and CSF of the fourth ventricle and clearance rate of the ¹⁸F-DOPA-tracer from the lateral ventricles.

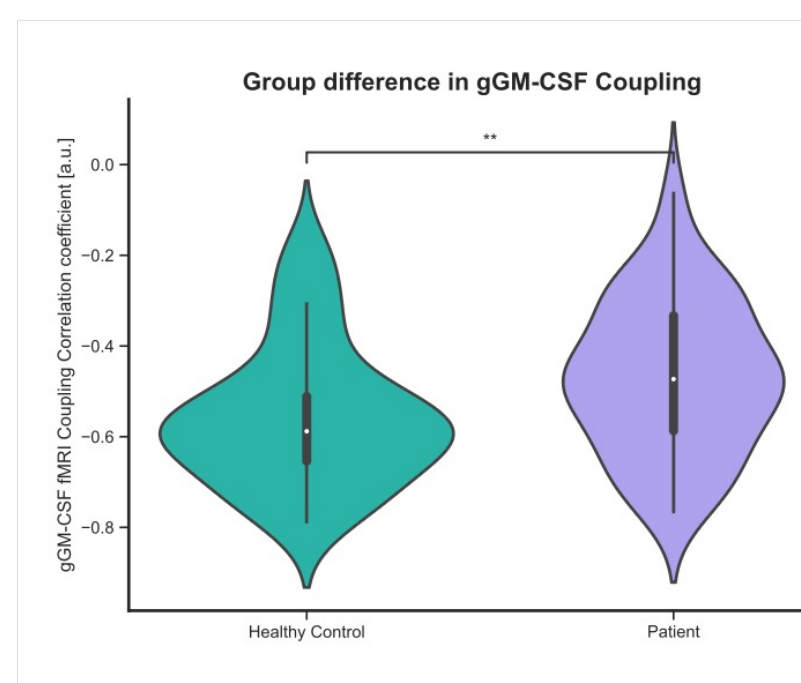
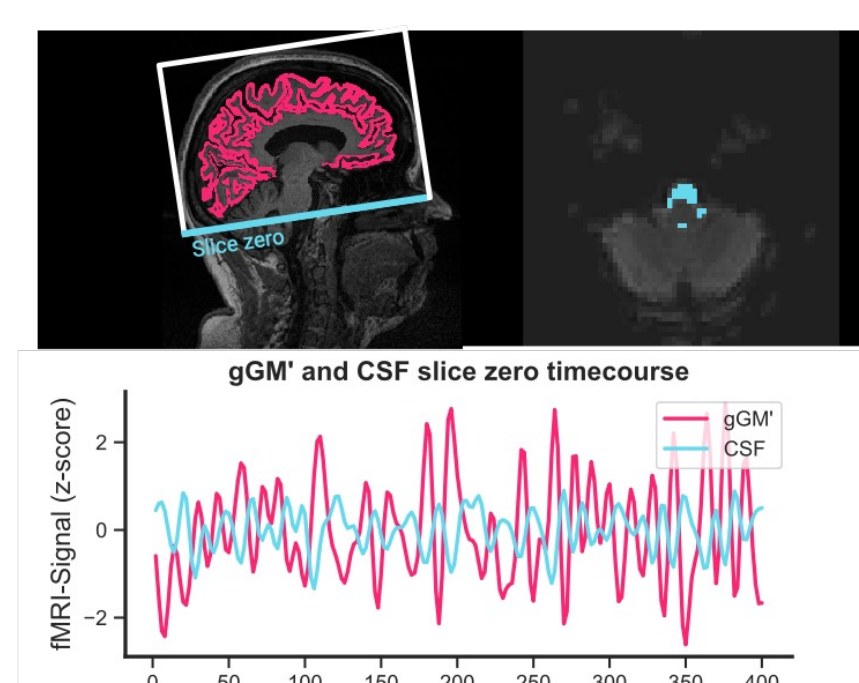
Functional hypothesis: Impaired brain clearance in Schizophrenia, associated with cognitive symptoms

1. Impaired brain clearance in Schizophrenia

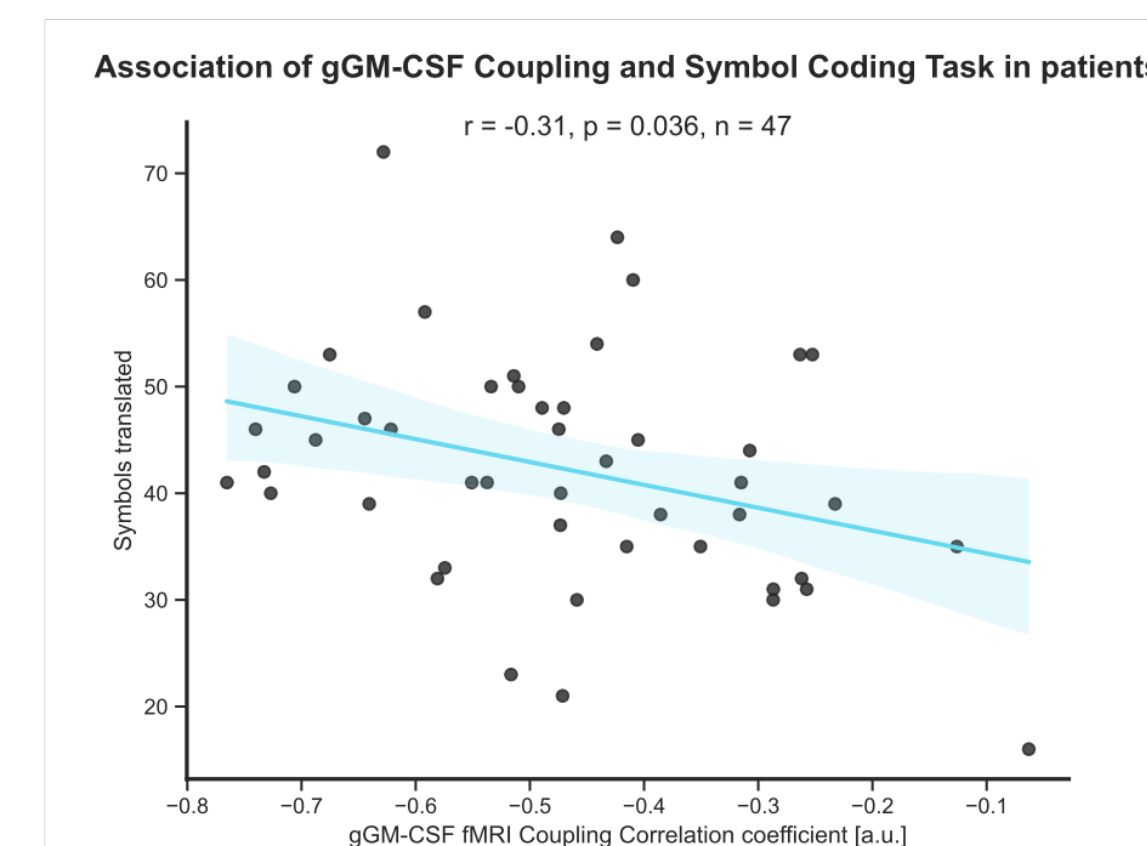
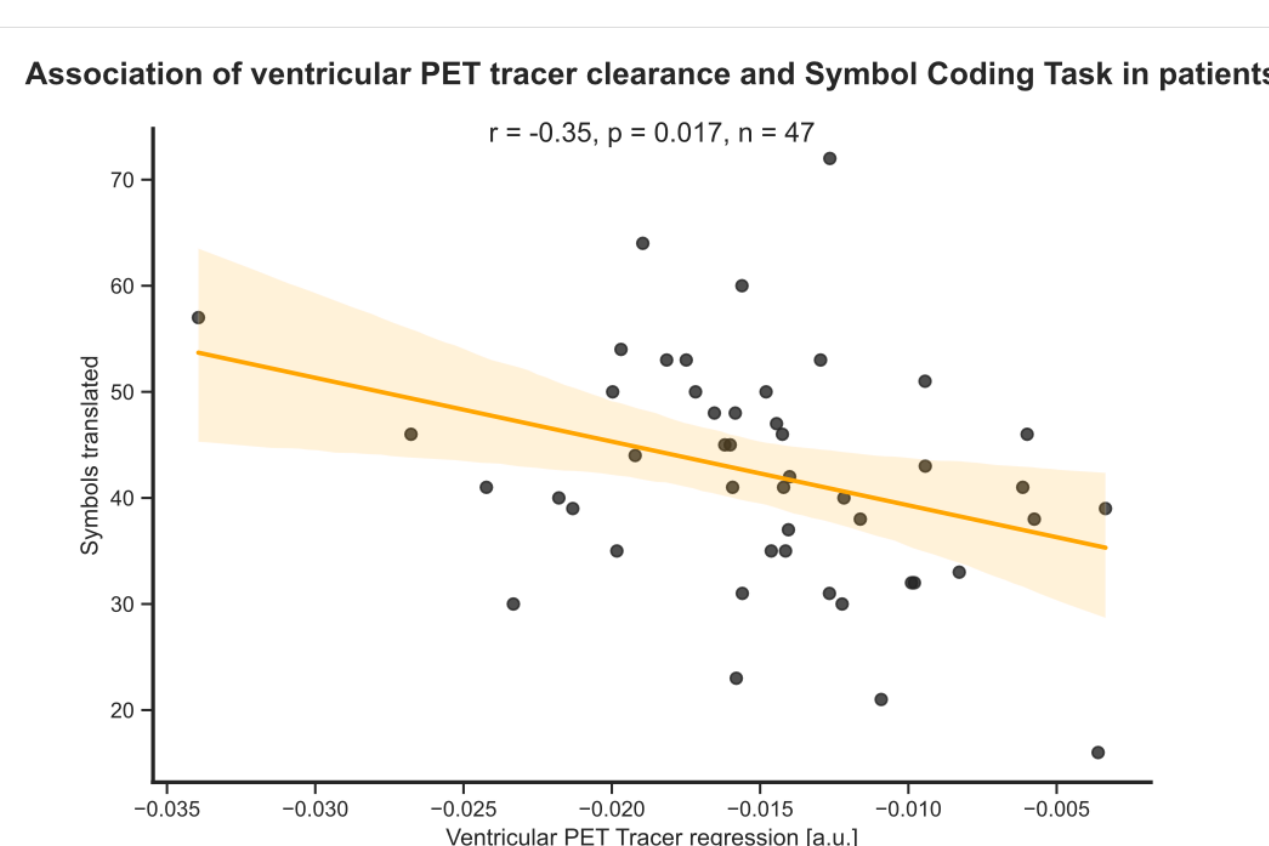
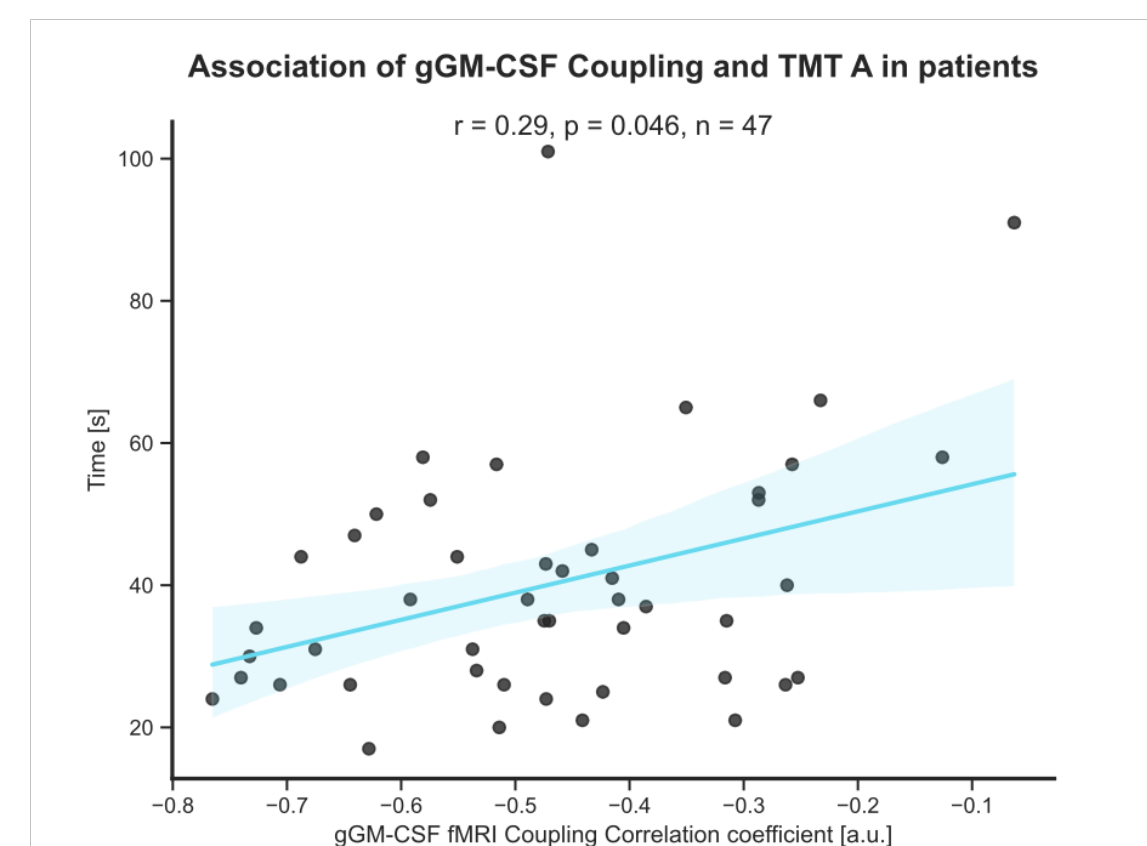
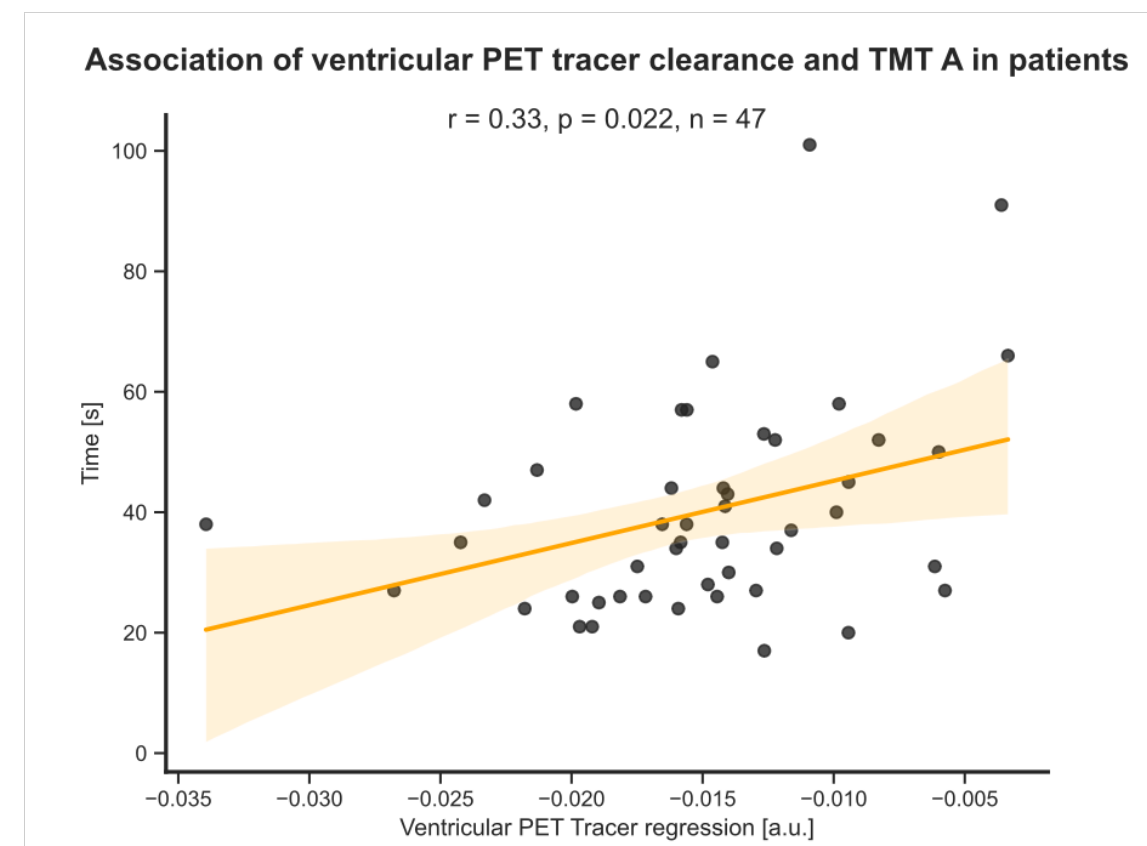
18F-DOPA-PET: CSF clearance



resting-state fMRI: gGM-CSF-fMRI coupling

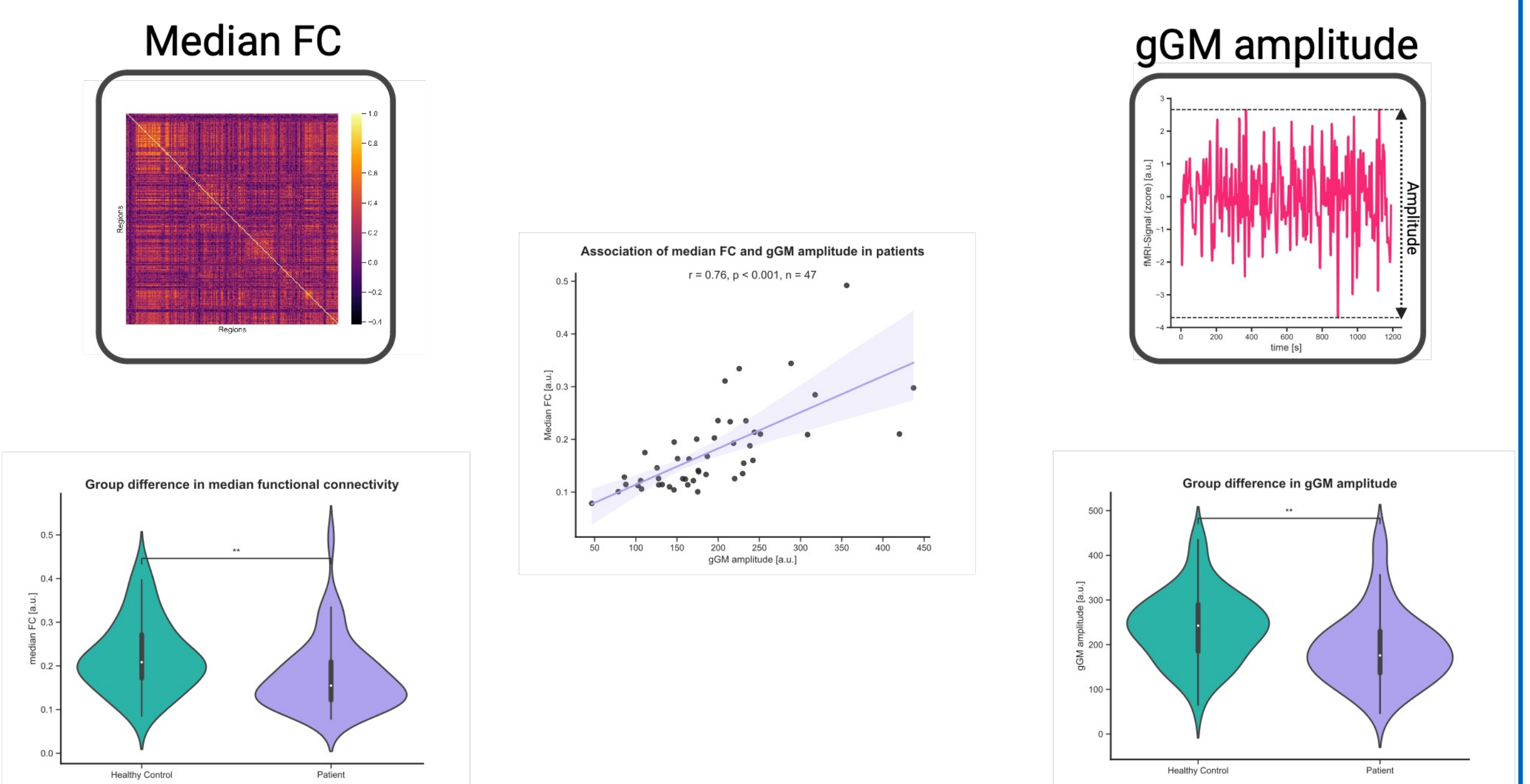


2. Association of brain clearance impairment with cognitive symptoms

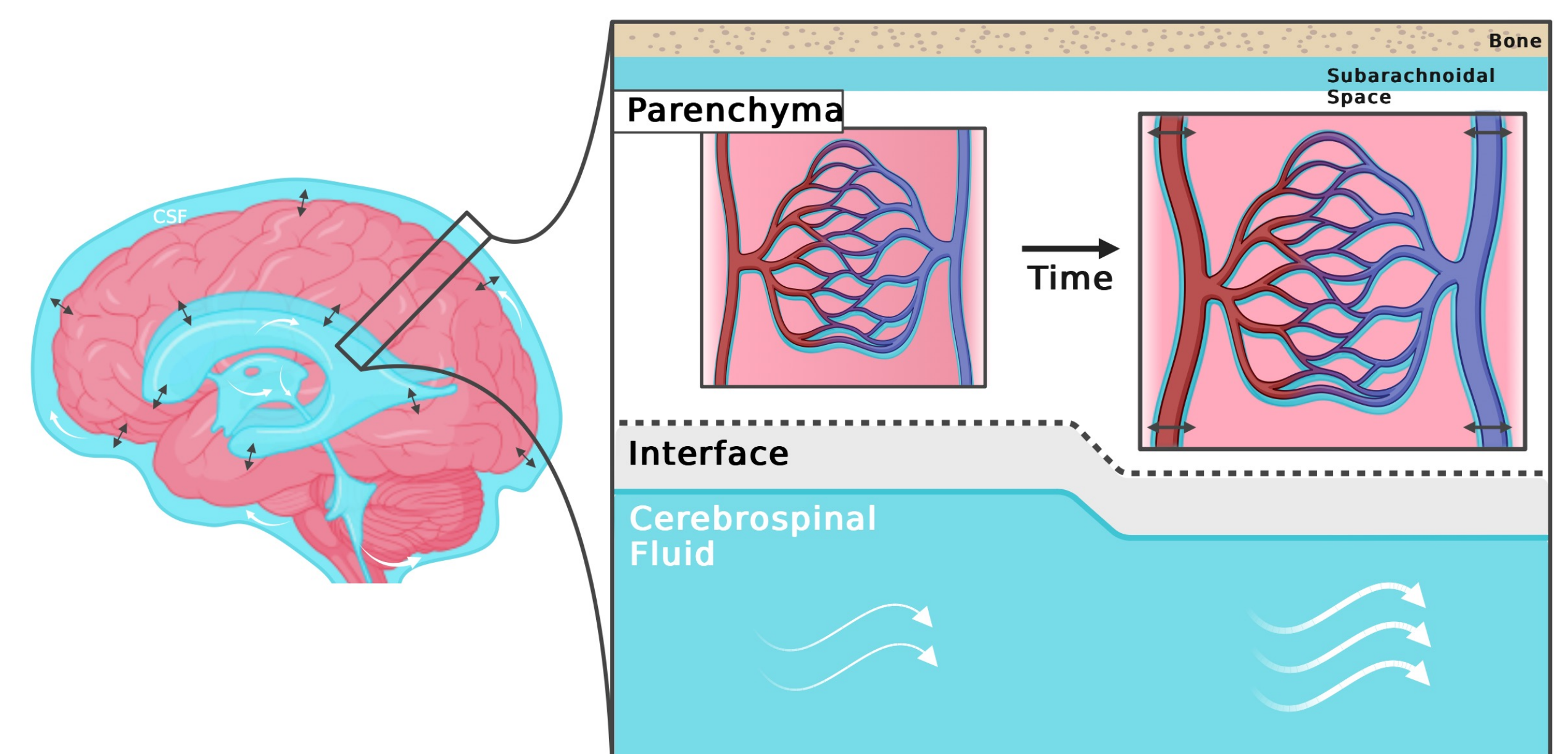


Mechanistic hypothesis: Impaired gGM coherence leads to slower ventricular CSF clearance

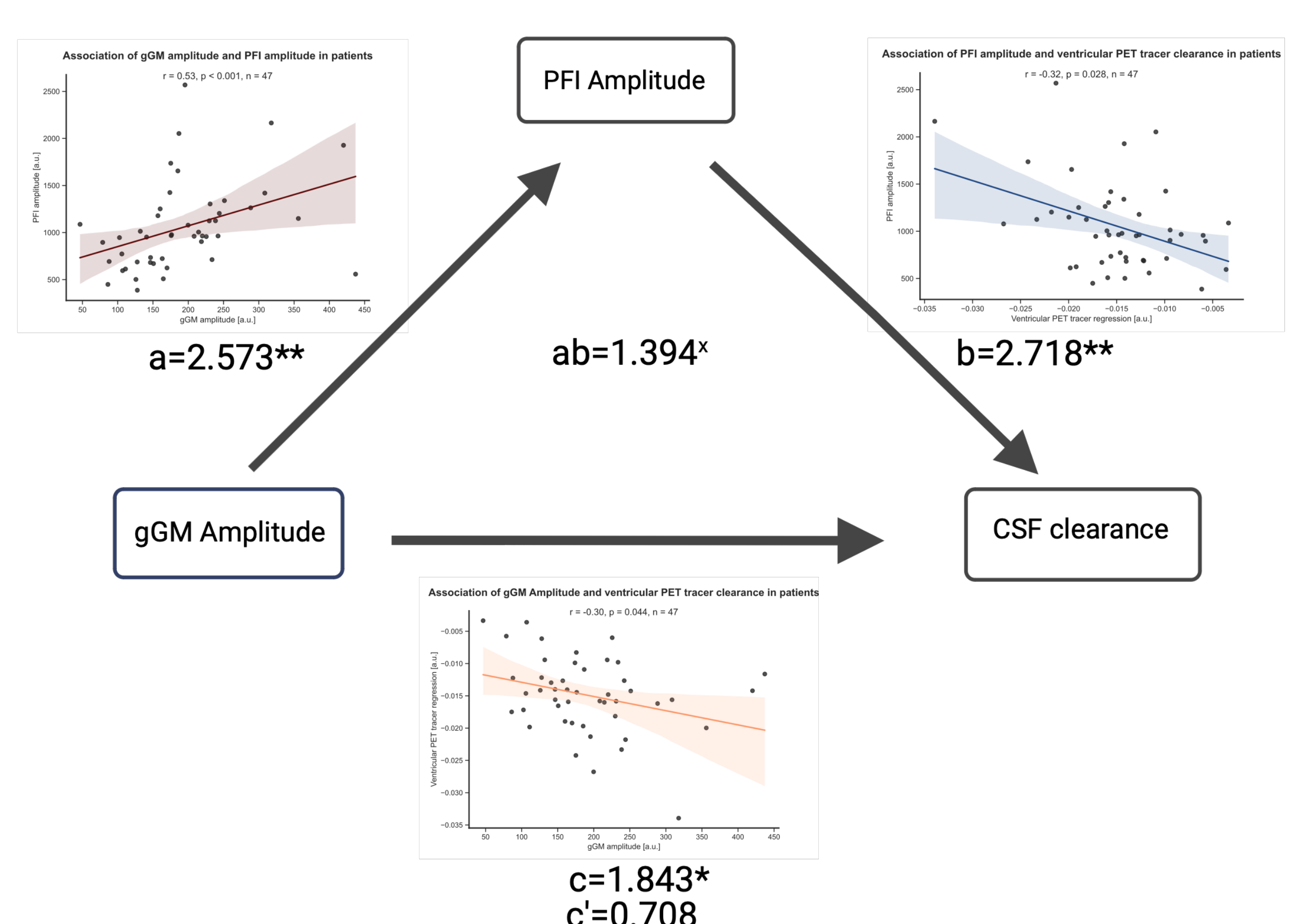
1. gGM coherence correlates with gGM blood volume



2. Ventricular border movement: Parenchymal-Fluid-interface (PFI)



3. Ventricular border movement mediates the relation between gGM blood volume and CSF clearance



Discussion

Results demonstrate an impairment of brain clearance in patients with Schizophrenia, which is associated with cognitive symptoms. Further analyses showed that lower gGM coherence mediated by ventricular deformation might be the underlying cause of this pathomechanism.

