

Free-water imaging in cocaine use disorder

Rasgado-Toledo, J.¹, Apurva Shah², Madhura Ingalhalikar², Eduardo A. Garza-Villarreal¹

¹ Instituto de Neurobiología, Universidad Nacional Autónoma de México (UNAM) campus Juriquilla, Queretaro, México.

² Symbiosis Center for Medical Image Analysis, Symbiosis International University, Pune, Maharashtra, India.



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Introduction

Cocaine use disorder (CUD) is a worldwide substance use disorder (SUD) with serious consequences for the individual's health and society, as it produces cognitive deficit, including lack of inhibition and compulsive search for cocaine, that may be secondary to brain pathology (Dackis & O'Brien, 10/2001; Volkow et al., 2019).

Free-water imaging (FWI) is a novel extension of the diffusion tensor imaging (DTI) model method that measures free water molecules in gray and white matter using multi-tensor information (Bergmann et al., 2020). Compared with standard DTI measures, FWI analysis has been shown to be more sensitive to detect disease specific effects such as white matter (WM) deterioration, neuroinflammation, dynamics and conditions of cell formation processes (Andica et al., 2019; Pasternak et al., 2009). Hence, the measurement of free-water seems to be a sensible marker of brain pathology and may provide insight on CUD, which has not been yet explored.

In this study, we used the neurite orientation dispersion and density imaging (NODDI) values that employ a three-compartment model in WM and GM to determine CUD structural pathology in the human brain, as well as its correlation with clinical measures.

Methods

Scanner: Phillips Ingenia 3T system (Philips Healthcare, Best, Netherlands & Boston, MA, USA) with a 32-channel dS Head coil.

T1-weighted images were acquired using a 3D FFE SENSE sequence, TR/TE = 7/3.5 ms, FOV = 240, matrix = 240 x 240 mm, 180 slices, gap = 0, plane = Sagittal, voxel = 1 x 1 x 1 mm.

DWI HARDI used a SE sequence, TR/TE = 8600/127 ms, FOV = 224 mm, Matrix = 112 x 112, 50 slices, gap = 0, plane = axial, voxel = 2 x 2 x 2 mm, scan ~20 min, directions 8 = b₀, 36 = b-value 1,000 s/mm² and 92 = b-value 3,000 s/mm², total = 136 directions.

Participants: 60 CUD participants (3 female) and 43 non-CUD controls (HC; 2 female; matched by age (± 2y), sex, and handedness) from our Mexican substance use disorder neuroimaging dataset (SUDMEX).

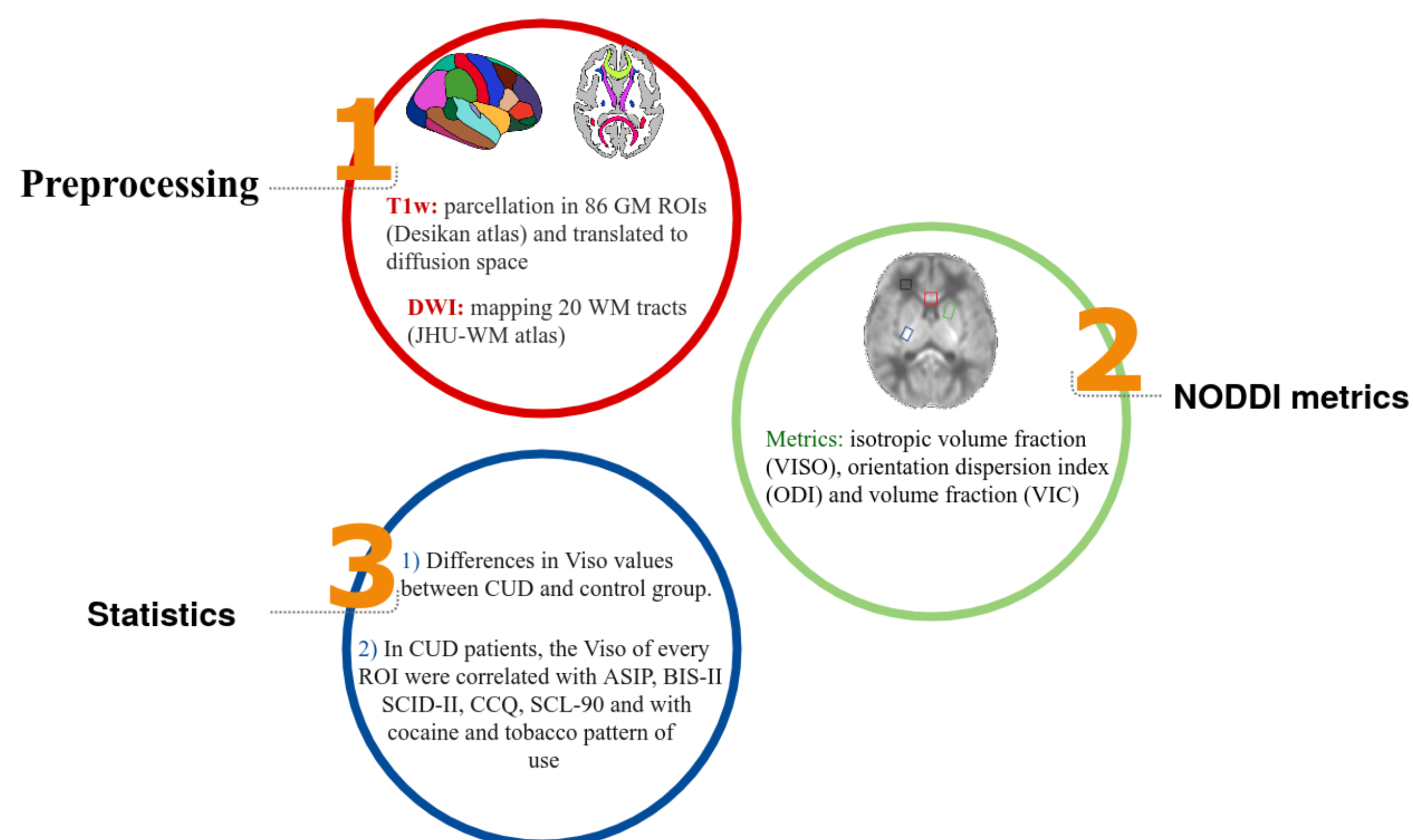


Figure 1: Analysis steps to process data. Abbr: addiction severity index (ASIP) scores, Barratt Impulsiveness Scale (BIS-11), Cocaine Craving Questionnaire (CCQ), psychopathology test scores of Structured Clinical Interview for DSM (SCID-II) and Symptom Checklist-90-R (SCL-90-R)

Results

Free-water analysis

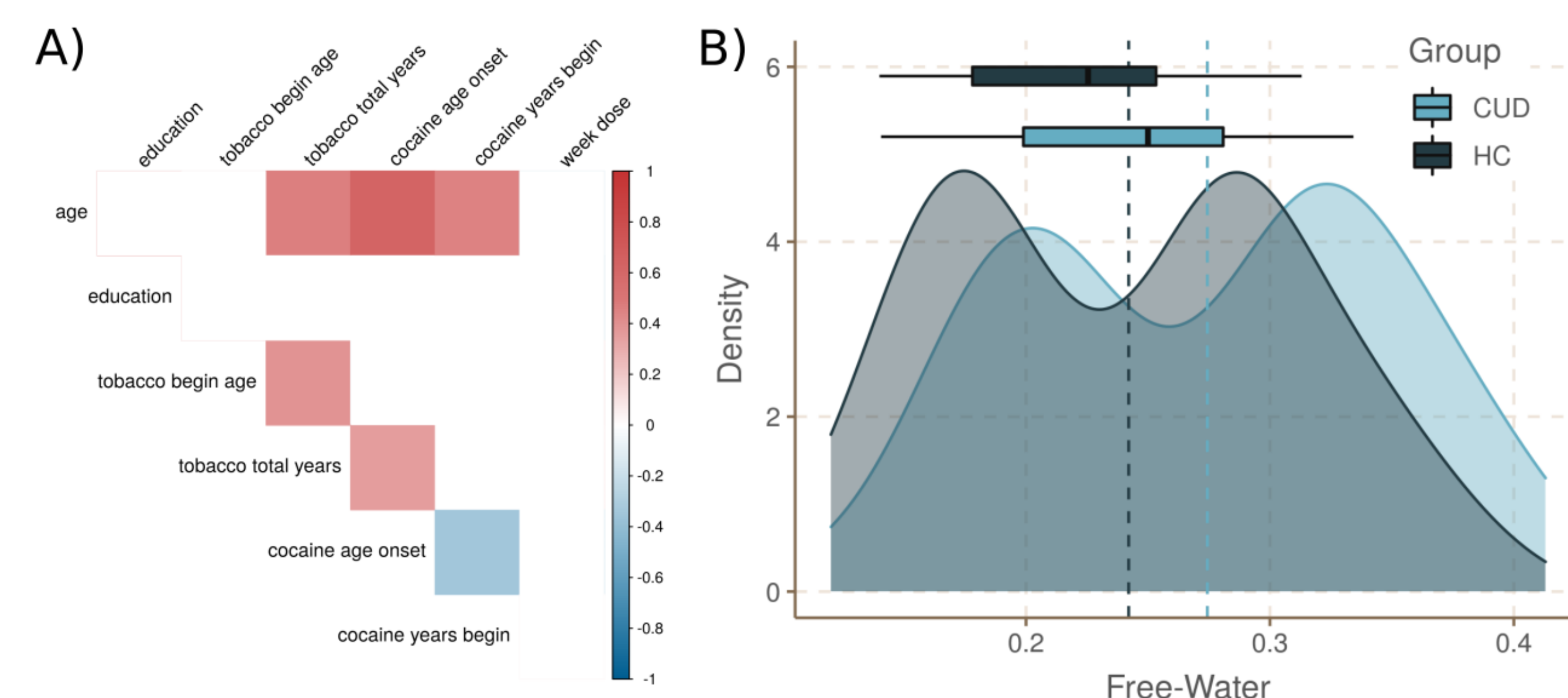


Figure 2: A) Correlation plot among demographic data and drug pattern use, corrected by FDR ($p < 0.05$); B) Distribution of free-water values in each region of interest (WM-Track and GM) for CUD and HC. Lines represent the mean of each group.

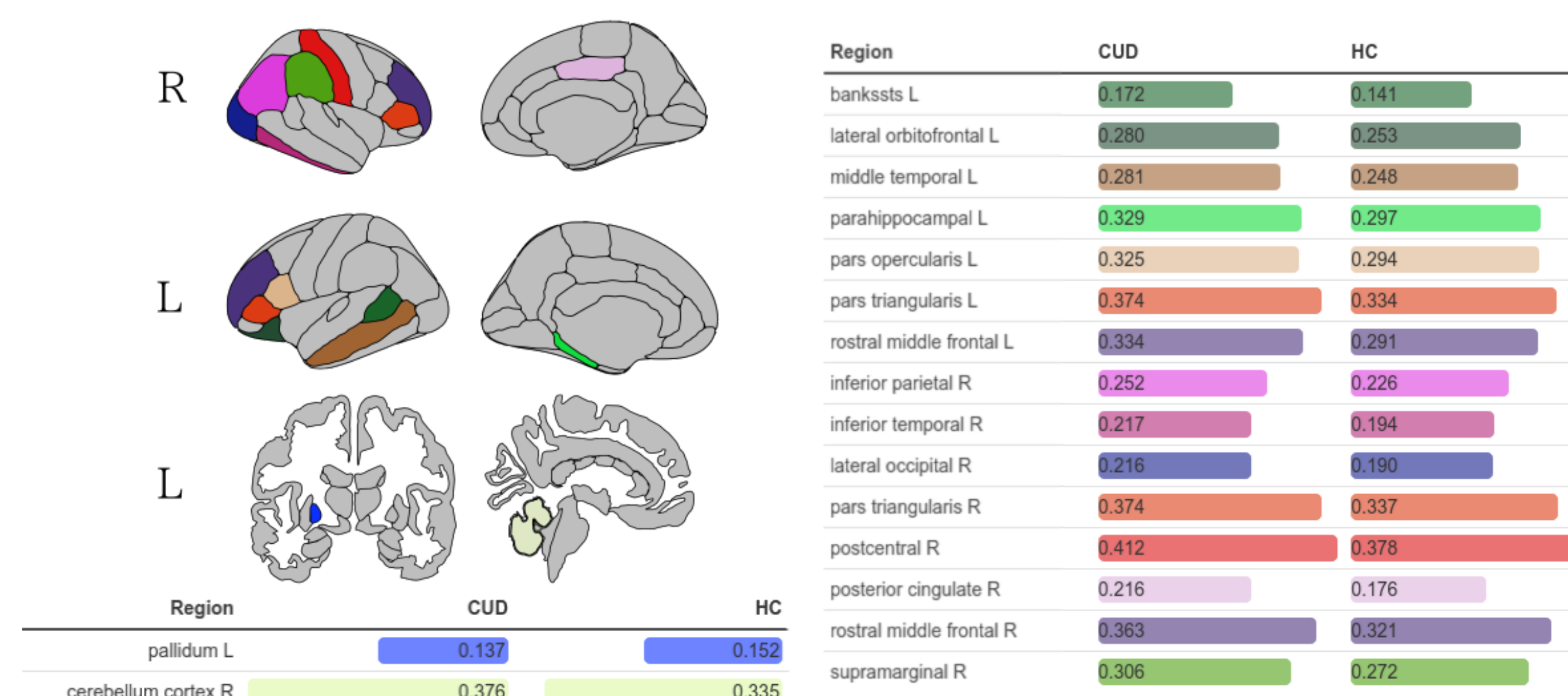


Figure 3: Regions (Desikan-Killiany atlas) with statistical significant difference (FDR correction; $p < 0.05$) of FWI values between CUD and HC. Representational FWI mean values are plotted in left side.

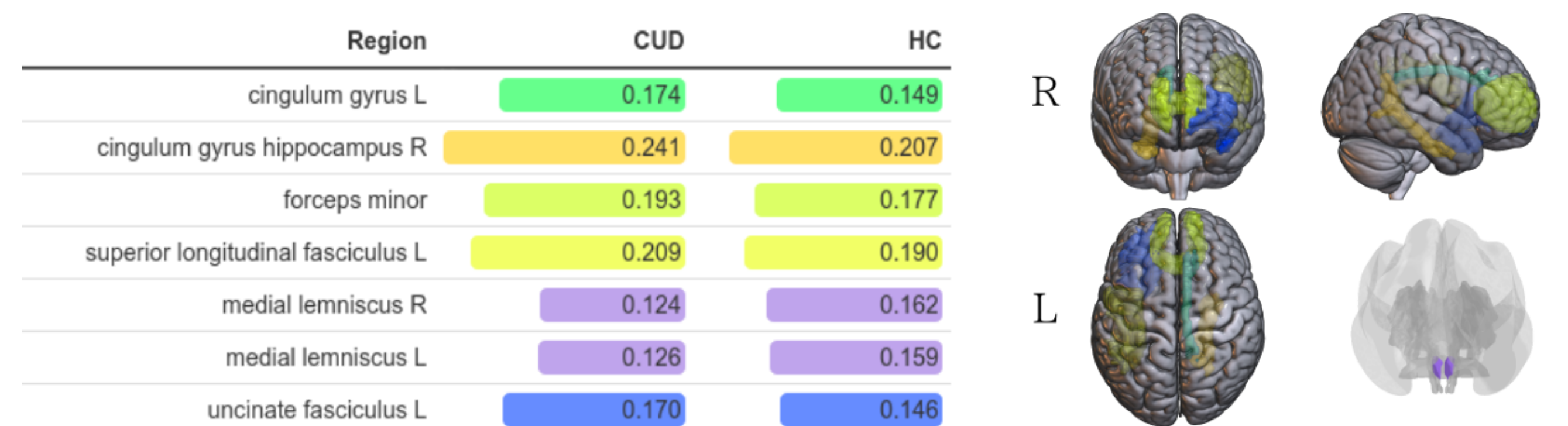


Figure 4: Regions (JHU WM tractography atlas) with statistical significant difference (FDR correction; $p < 0.05$) of FWI values between CUD and HC. Representational FWI mean values are plotted in right side.

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Correlation of free-water and clinical measures

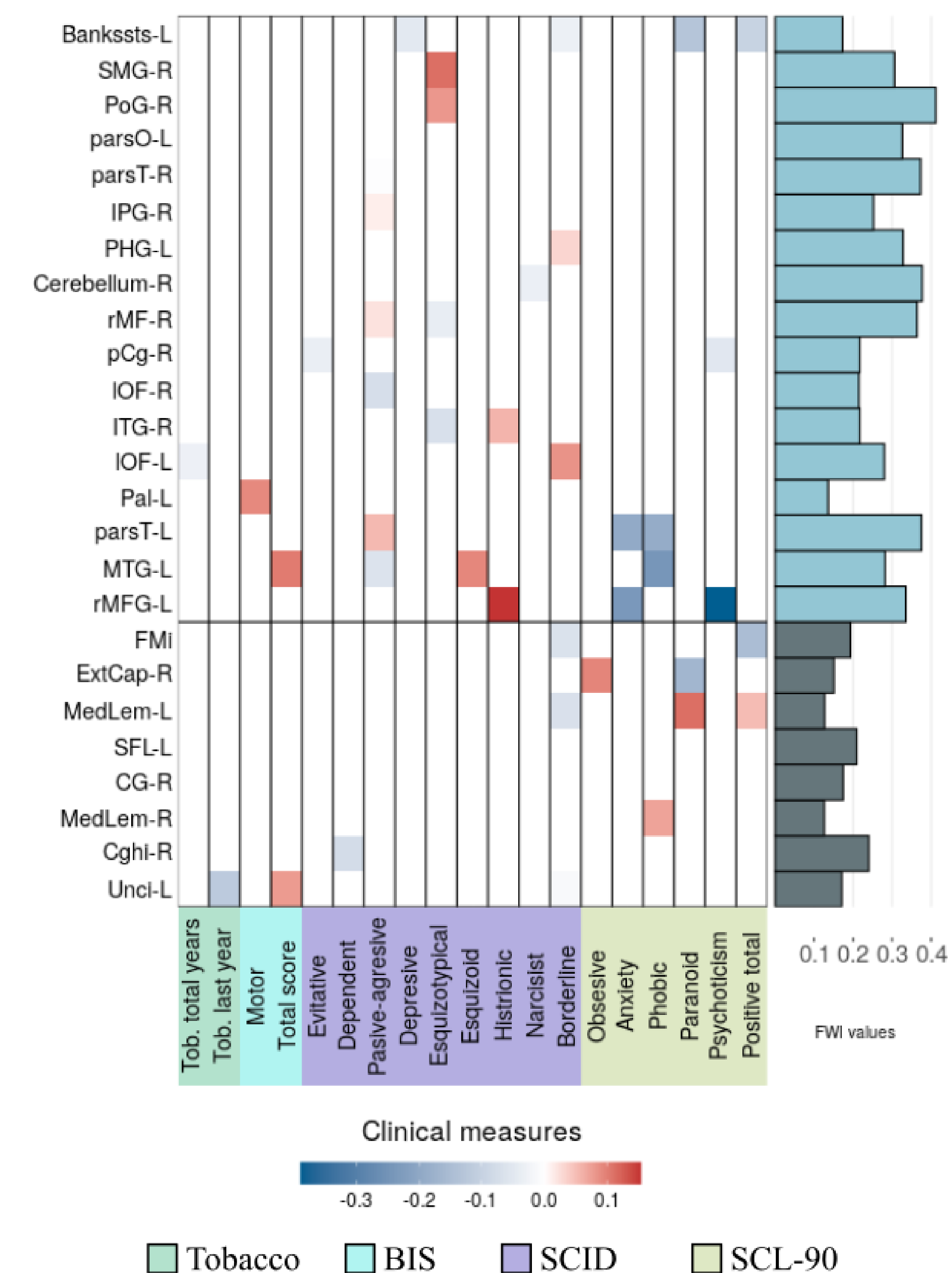


Figure 5: Correlation map between significant structures and clinical measures. Blank space means no significance corrected after FDR ($p < 0.05$). FWI values of each structure are plotted on the right side. Abbr: Barratt Impulsiveness Scale (BIS); Structured Clinical Interview for DSM (SCID-II); Symptom Checklist-90-R (SCL-90-R)

Conclusion

We mainly found a general and widespread increase of FWI that could suggest microstructural tissue degeneration with extracellular fluids that compound the interconnections of cortical regions between frontal hemispheres and with parietal and temporal lobes which is observed by impairments in impulsivity, motivation, reward and decision-making processes commonly observed in consumers (Lane et al., 2010; Lim et al., 2008). These changes may be contributing to cognitive deficits and the strengthening of cocaine use.

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