

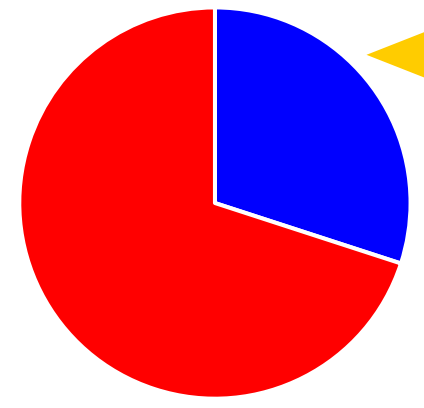
Dynamic functional network connectivity estimated from resting-state fMRI predicts symptom severity in PTSD

Mohammad SE. Sendi¹, Sanne van Rooij², Nathaniel G. Harnett¹, Lauren A. M. Lebois¹, Vishnu P. Murty³, Tanja Jovanovic⁴, Stacey House⁵, Negar Fani², Zening Fu⁶, Victor Vergara⁶, Vince D. Calhoun⁶, Diego A. Pizzagalli¹, Samuel A. McLean⁷, Kerry J. Ressler¹, Jennifer Stevens², Nikolaos P. Daskalakis¹

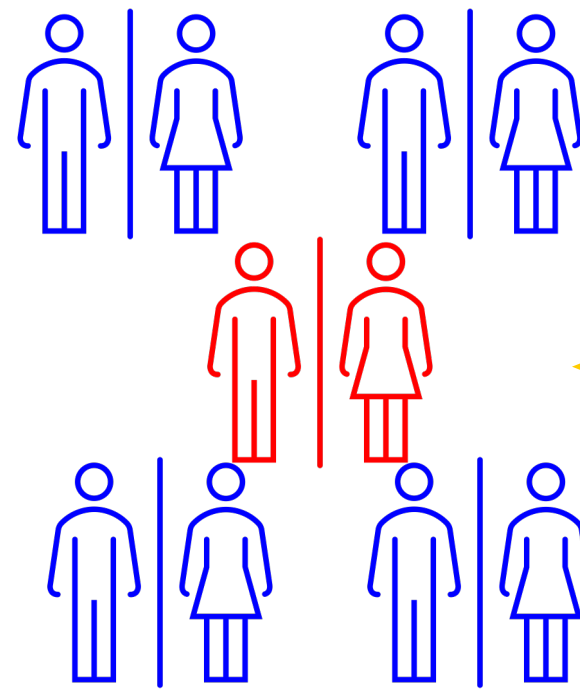
¹ Mclean Hospital and Harvard Medical School, Boston, MA, USA; ²Emory University, Atlanta, GA, USA; ³ Temple University, Philadelphia, PA, USA; ⁴ Wayne State University, Detroit, MI, USA; ⁵ Washington University School of Medicine, St. Louis, MO, USA; ⁶Tri-Institutional Center for Translational Research in Neuroimaging and Data Science (TReNDS), Atlanta, GA, USA; ⁷ University of North Carolina, Chapel Hill, NC, USA.

Introduction

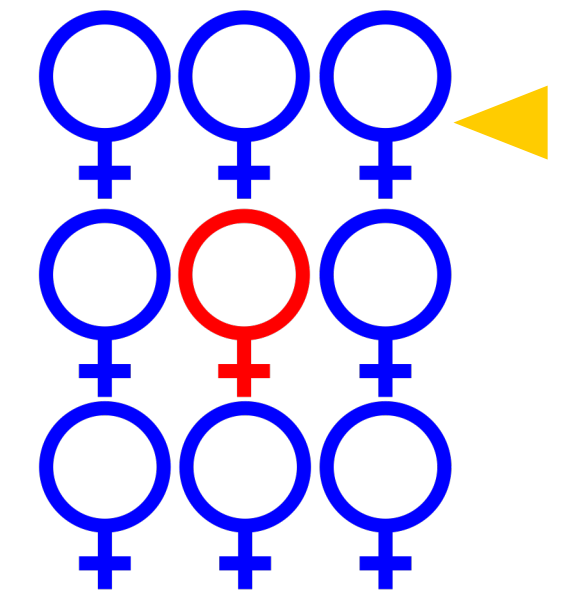
- Finding neuroimaging biomarkers for PTSD is important for improving therapy
- Previous studies have focused on static FNC and ignored its dynamics
- The assumption that brain functional network connectivity is static may be incorrect
- The study aims to identify dynamic FNC features associated with PTSD symptom severity



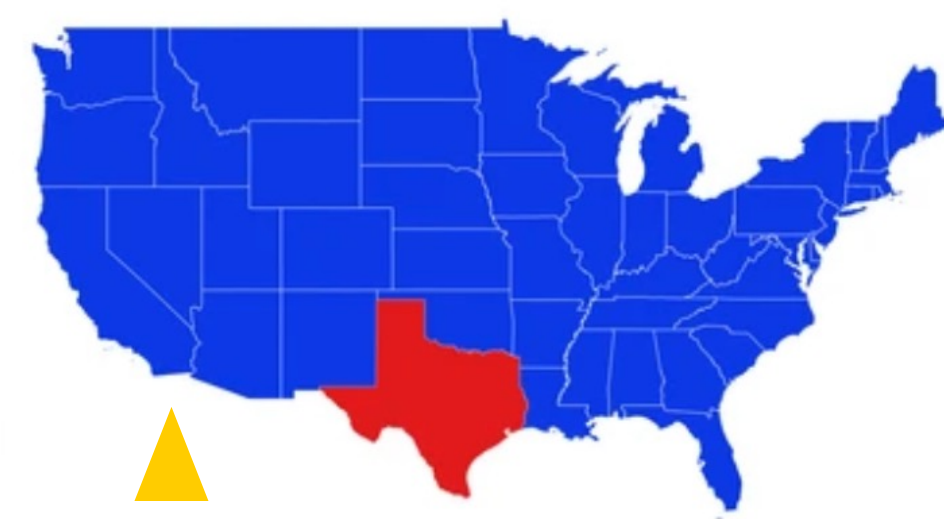
70% of US adults have experienced some type of traumatic event at least once in their lives (N~223 million people)



Up to 20% of these people developed PTSD (N~44 million people)



An estimated one out of every nine women developed PTSD, making them about twice as likely as men.



An estimated of 8% of US adults had PTSD at any given time (N~24.4 million). That is equal to the Texas population.

The goal is to gain a better understanding of the brain dynamic functional network connectivity in patients with PTSD

Conclusion and Future work

Current findings

- Our study identified dynamic functional network connectivity features that predict PTSD symptom severity.
- Dynamic functional network connectivity can be used to predict PCL-5 scores at different time points.
- The visual and sensory motor network connectivity show potential as a biomarker for PTSD.

Future directions

- We are currently investigating whether a polygenic risk score for PTSD can be used to predict clinical and neuroimaging phenotypes.
- Additionally, we are exploring the interaction between genetics, demographic and environmental factors, and neuroimaging features in predicting the trajectory of PTSD.

Grant Support

- T32MH125786 (to W. Carlezon/K. Ressler, MPIs)
- NIMH U01MH110925

Results

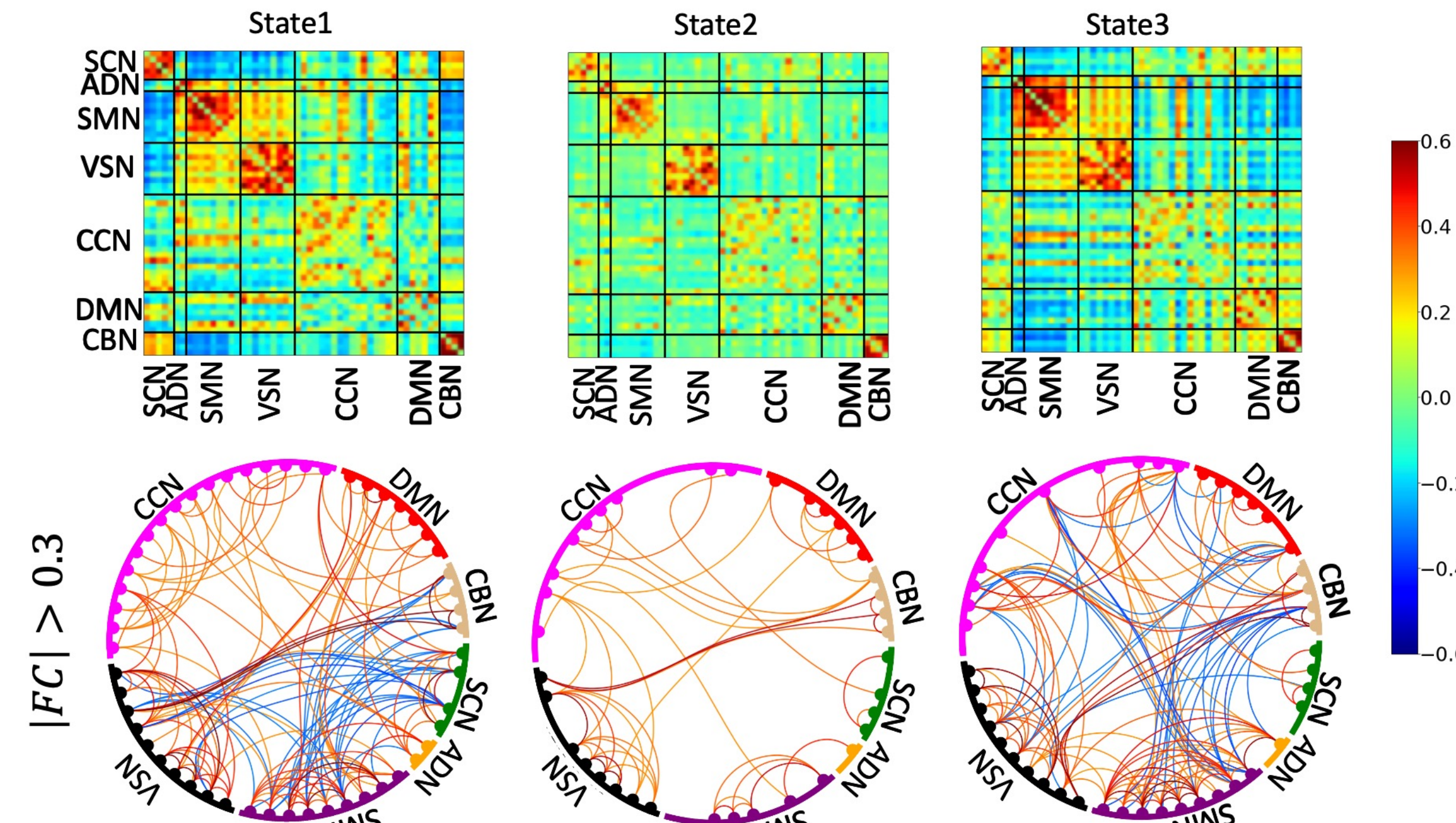
Clinical and demographic measures

	PRE	WK2	WK8	M3	M6	M12
N *	1744	2346	2293	2139	1824	1447
Age at ED (year: mean±sd)	35.07±12.83	39.99±13.23	36.58±13.41	37.08±13.55	37.53±13.62	38.08±13.52
Sex (F/M)	1084/660	1466/880	1454/839	1357/782	1163/661	922/525
Education at ED (year: mean±sd)	14.72±2.49	15.02±2.50	15.08±2.40	14.95±2.42	14.98±2.52	15.15±2.54
BMI at ED (mean±sd)	29.91±7.81	30.24±8.48	30.30±8.53	30.40±8.52	30.47±8.60	30.73±8.71
PCL5 (mean±sd)	31.57±15.76	30.73±18.89	28.01±19.40	24.99±19.19	23.34±18.81	22.07±18.96
PCL5 correlation with age r(p)	-0.0095 (0.6932)	-0.0196 (0.3438)	-0.0059 (0.7762)	0.0215 (0.3204)	0.0558 (0.0172)	0.0414 (0.1154)
PCL5 correlation with education r(p)	-0.1642 (5.61e-12)	-0.0475 (0.0216)	-0.0749 (3.40e-4)	-0.0869 (5.88e-5)	-0.0973 (3.27e-5)	-0.0796 (0.0025)
PCL5 correlation with BMI r(p)	-0.0373 (0.1530)	0.0424 (0.0494)	0.0288 (0.1772)	0.0145 (0.5304)	0.0440 (0.0759)	-0.0452 (0.1047)
Sex related PCL5 difference tstat(p)	1.6814 (0.0929)	8.6502 (9.36e-18)	6.0657 (1.53e-9)	5.3442 (1.00e-07)	5.4980 (4.38e-8)	4.4422 (9.58e-6)

F: female, M: male, ED: Enrolment date, BMI: Body mass index, PC: Principle component, PRE: Pre-trauma, WK2: Week 2, WK8: Week8, M3: Month 3, M6: Month 6, M12: Month 12. *Number of participants used in the analysis after removing the missing data.

- Years of education and sex were identified as the main predictors of PCL-5.
- Sex differences were less significant immediately after trauma.
- Education emerged as a particularly important factor immediately after trauma.

Three dFNC states are identified



- Using k-means clustering, we identified three distinct states.
- State 1 exhibited higher connectivity within the cognitive control network (CCN) and among sensory networks.
- State 2 demonstrated the lowest connectivity when compared to State 1 and State 3.

dFNC predicts PCL-5

PCL5 and dFNC features association accounted for age, sex, education, bmi, and ancestry PC1 &2

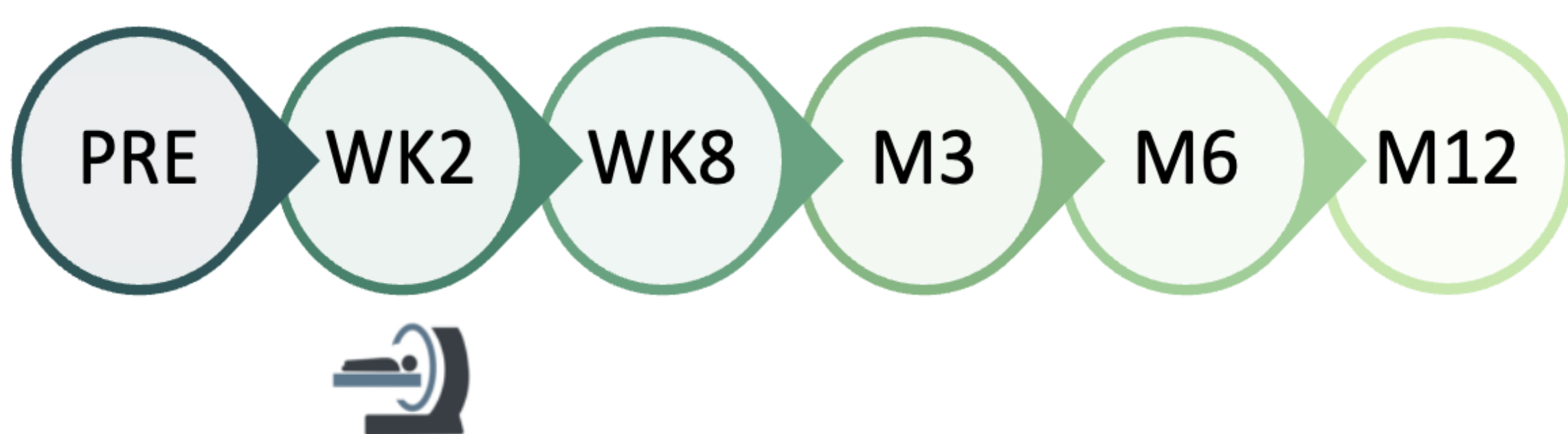
	PRE	WK2	WK8	M3	M6	M12
OCR State1	r=-0.076	r=-0.148	r=-0.070	r=-0.159	r=-0.105	r=-0.130
OCR State2	r=0.143	r=0.090	r=0.085	r=0.1932	r=0.105	r=0.130
OCR State3	r=-0.117	r=0.064	r=-0.034	r=-0.075	r=-0.005	r=-0.006
No of Trans	r=-0.128	r=0.003	r=0.026	r=-0.116	r=-0.052	r=-0.182

Significance: None, $p < 0.05$ & $p > FDR$, $p < FDR$

- State1 OCR had a negative correlation with PCL-5 in WK2 and M3.
- State2 OCR had a positive correlation PCL-5 of M3.
- Number of transition correlated with PCL-5 of M12.

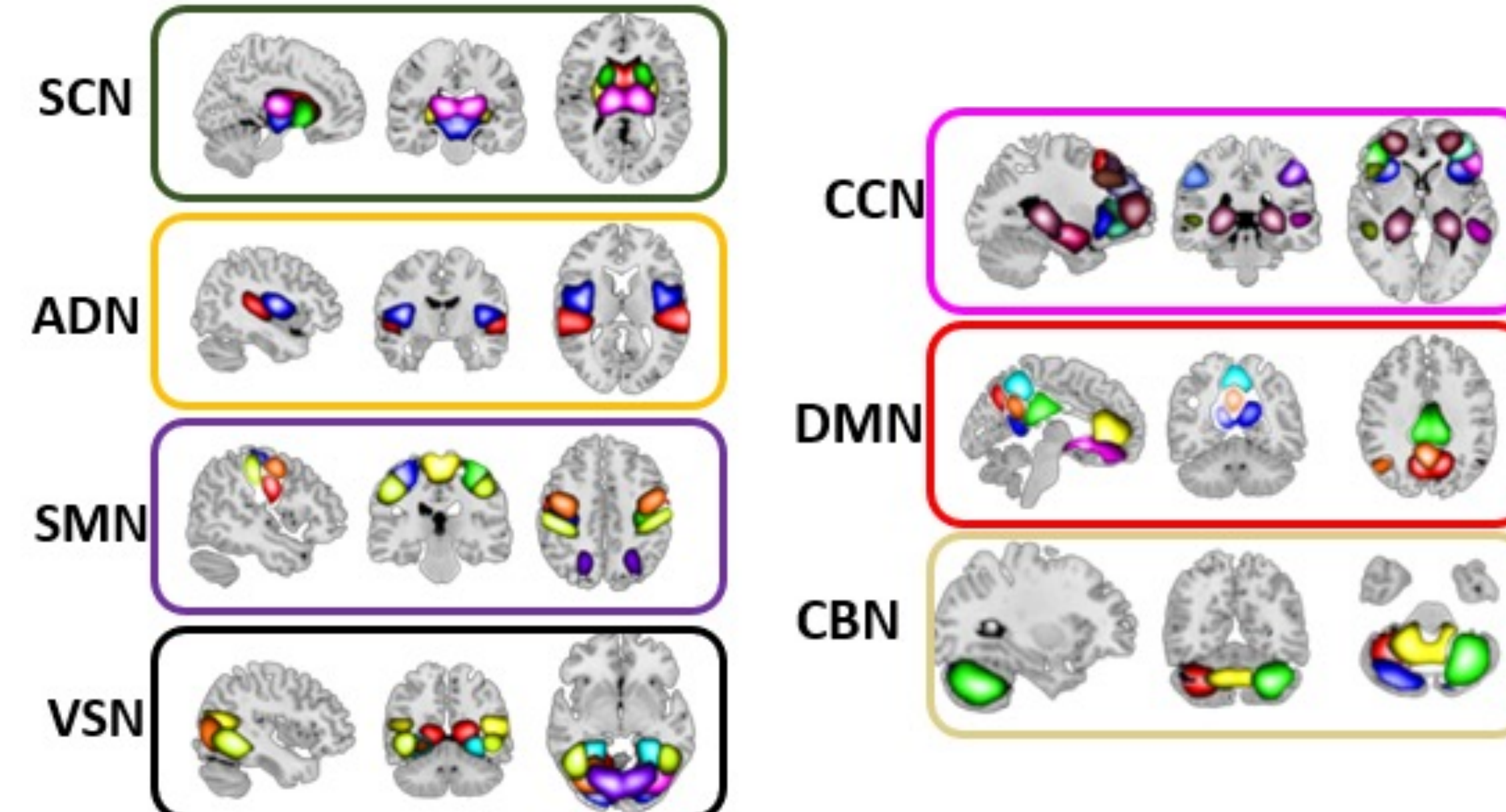
Methods

Clinical Assessment



- Participants were enrolled within 72 hours of trauma exposure from AURORA (Freeze 4.0) study.
- AURORA is a multisite longitudinal study that investigates recovery after trauma
- Trauma incidents included car accidents, falls >10 feet, physical assault, sexual violence, or mass casualty incidents
- PCL5 (measure of PTSD) assessed at different time points: pre-trauma (PRE), week 2 (WK2), week 8 (WK8), month 3 (M3), month 6 (M6), and month 12 (M12) after trauma.

Preprocessing



- Preprocessing:** 53 independent components were extracted from subcortical network (SCN), Auditory network (ADN), sensorimotor network (SMN), visual sensory network (VSN), cognitive control network (CCN), and default mode network (DMN), by Group-ICA.

dFNC pipeline

