

Aberrant Functional Connectivity (rsFC) Between Subgenual ACC and Default Mode Network in Adults with History of Childhood Maltreatment

Arushi Badola¹, Jagan Jimmy¹, Subhashini Madhavan¹, Wenfei Yu¹, Anthony P. King¹

¹Department of Psychiatry and Behavioral Health, The Ohio State University

Background

- Childhood maltreatment (CM) involves exposure to physical, sexual, and emotional abuse or neglect^{2,3}.
- CM doubles one's risk of developing MDD in adulthood and is associated with greater MDD symptom severity¹.
- Previous studies have linked CM in Major Depressive Disorder (MDD) patients to increased default mode network (DMN) functional connectivity (FC) – a network involved in self-referential thinking and rumination^{4,7}.
- Depressive rumination is thought to contribute to increased FC between the ventromedial prefrontal cortex (vmPFC) and subgenual anterior cingulate cortex (sgACC)⁶.
- Alterations in FC between the DMN and the salience network (SN) or fronto-parietal network (FPN) have been found in MDD patients with a history of CM⁵.
- This study examined the resting-state functional connectivity (rsFC) patterns specific to CM in the DMN and limbic networks (sgACC seed) in adults to identify neural correlates of CM.

Methods

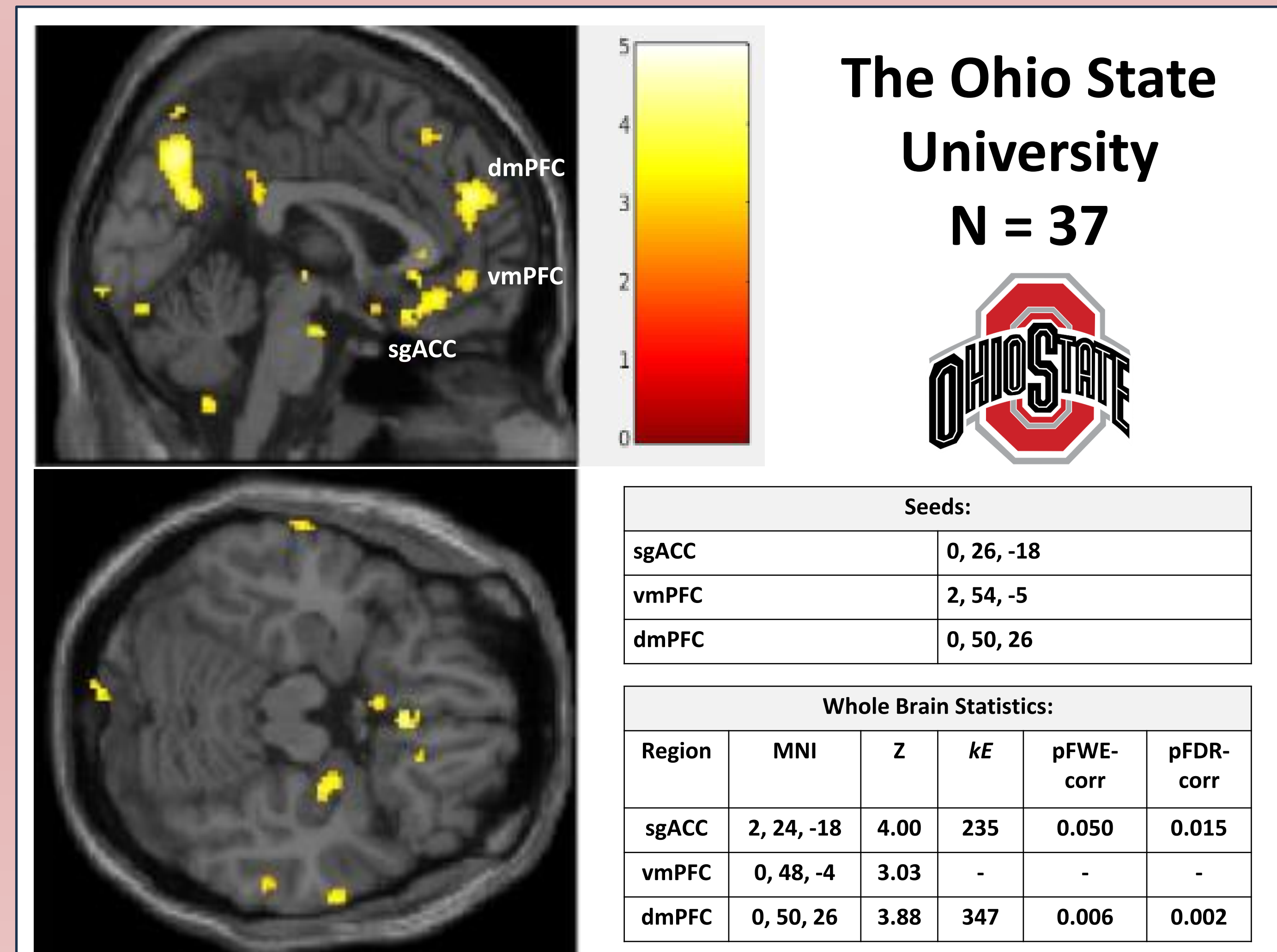
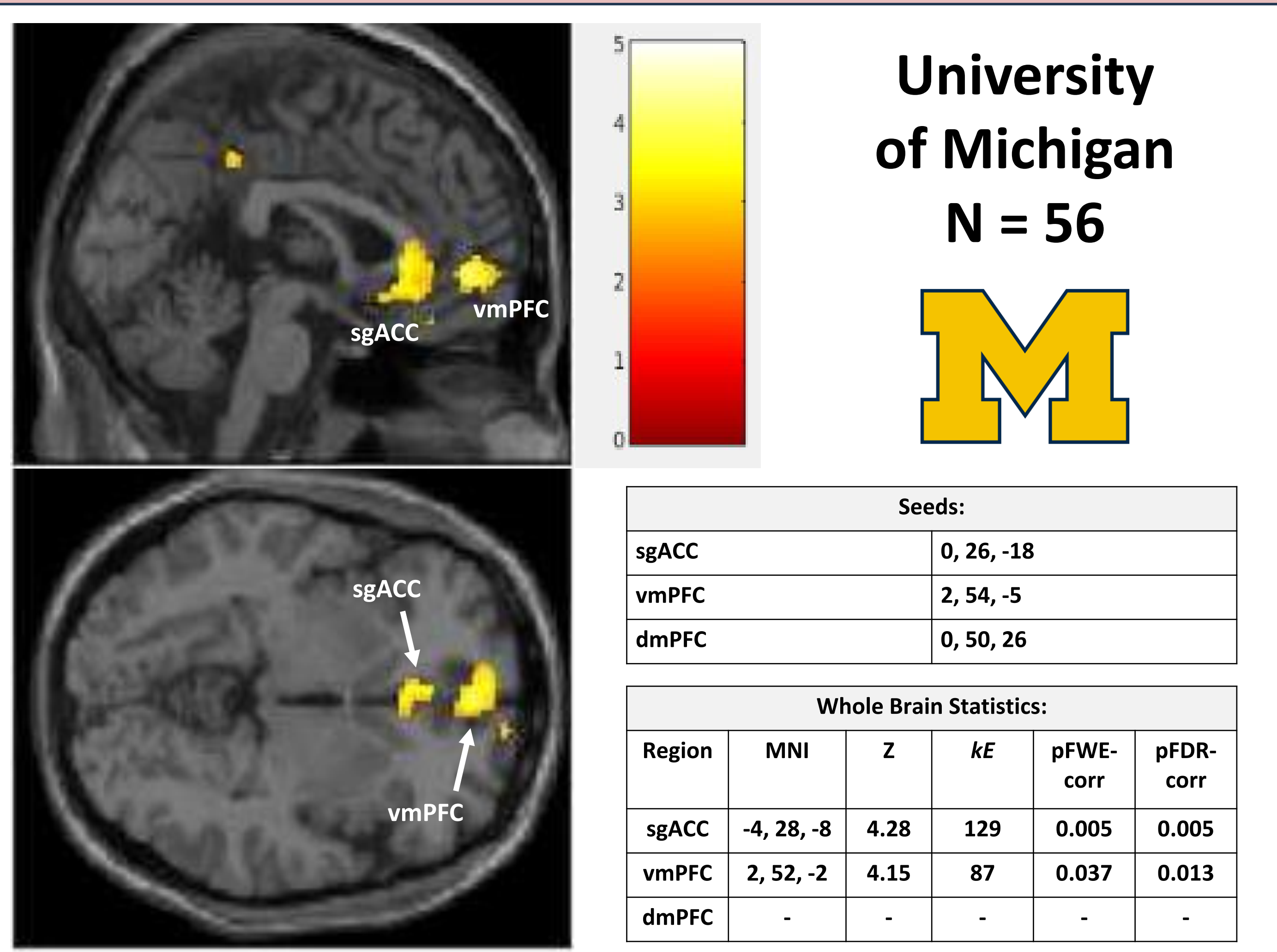
- A total of 93 adults with trauma exposure and clinically significant symptoms of PTSD were studied. 42 of these adults reported history of CM as determined by the Childhood Trauma Questionnaire (CTQ).
- 3T fMRI scans were collected during resting state. Participants focused on a fixation “plus sign” and let their minds wander freely for 8 minutes.
- Seed-based subject level rsFC T-maps were generated using CONN toolbox and entered into second-level random effects model in SPM12 to test the main effects of CM.
- Second-level maps were thresholded at $p < .005$ unc. and whole-brain correction for multiple comparisons (pFWE and pFDR) at cluster level.
- Regions of interest (sgACC and vmPFC) were used to examine whether individuals reporting CM differed from individuals reporting no CM in rsFC.

Discussion

- Adults with CM history and PTSD had increased resting state FC (sgACC seed) within sgACC and between the sgACC and vmPFC than adults with current PTSD and no history of CM.
- This finding was independently replicated in a separate sample, which also found increased rsFC btw sgACC seed and dmPFC.
- sgACC is a node in the limbic network associated with negative affect, vmPFC is a node of anterior DMN associated with self-referential processing and rumination, and dmPFC is DMN node associated with mentalizing, meta-cognition, and rumination.
- Increased connectivity of these regions with the sgACC may suggest a possible neural mechanism of vulnerability in CM involving increased negativity in self referential processing.
- Future work will further investigate other CM-related aberration in connectivity between the DMN, Limbic network, and Salience Network using seed-based analyses as well as whole-brain network analyses. We are also combining data from these two studies and two additional studies for “mega-analyses”.

Results

Independent Replication Across Two Sites (total N=93): Childhood Maltreatment Increases Subgenual ACC Resting State Functional Connectivity with the Default Mode Network



	University of Michigan			The Ohio State University		
	Without CM N=36	With CM N=20		Without CM N=15	With CM N=22	
Gender – Female	N=33 91.6%	N=18 90.0% ns		N=10 66.7 %	N=14 63.6% ns	
Race – White	N=32 88.9%	N=17 85.0% ns		N=11 73.3%	N=21 95.5% ns	
	Mean SEM	Mean SEM		Mean SEM	Mean SEM	
Age	34.5 3.5	42.3 5.0 ns		37.2 3.1	38.2 2.3 ns	
CAPS-5 (PTSD)	29.4 1.1	32.7 1.7 ns		23.9 2.5	28.3 2.1 ns	
PCL-5 (PTSD)	43.5 2.4	47.5 2.6 ns		37.9 3.3	50.3 3.0 <.01	
BDI (Depression)	27.3 1.7	26.9 2.6 ns		23.8 2.8	29.3 2.6 ns	
RRS – Reflection	12.0 0.7	11.0 0.9 ns		13.7 1.1	14.3 0.9 ns	
RRS2 – Brooding	13.8 0.7	14.3 0.9 ns		12.5 1.1	12.4 0.7 ns	
Self Compassion	28.6 1.4	29.0 1.7 ns		29.3 1.2	28.4 1.9 ns	
AAQ9 – Inflexibility	41.1 1.1	40.9 1.6 ns		38.6 1.2	39.9 1.0 ns	
ERQ – Reappraisal	24.6 1.3	24.6 1.6 ns		22.9 1.4	21.5 1.8 ns	
ERQ - Emotional Suppression	15.2 0.9	15.0 1.3 ns		14.1 1.5	17.2 1.2 ns	
CTQ: Emotional Abuse	8.3 0.7	19.2 0.5 <.001		9.5 0.9	20.3 0.7 <.001	
Physical Abuse	7.1 0.3	13.2 0.9 <.001		7.1 0.7	12.6 0.9 <.001	
Sexual Abuse	8.8 1.0	15.7 1.7 <.001		8.1 1.4	14.7 1.7 <.01	
Emotional Neglect	9.6 0.7	18.7 1.1 <.001		10.4 0.9	18.5 0.7 <.001	
Physical Neglect	7.8 0.5	12.7 0.9 <.001		5.9 0.2	11.7 0.7 <.001	

1. Klumparendt, A., Nelson, J., Barenbrügge, J., & Ehling, T. (2019). Associations between childhood maltreatment and adult depression: a mediation analysis. *BMC psychiatry*, 19(1), 1-11.
2. Teicher, M. H., Samson, J. A., Anderson, C. M., & Quesada, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature reviews neuroscience*, 17(10), 652-666.
3. Hoffmann, F., Viding, E., Paus, T., B. G. G. (2018). Evidence for depressive spontaneous thoughts and altered resting-state connectivity in adolescents with a maltreatment history. *Journal of the American Academy of Child & Adolescent Psychiatry*, 57(9), 697-698.
4. Teicher, M. H., & Samson, J. A. (2016). Annual research review: enduring neurobiological effects of childhood abuse and neglect. *Journal of child psychology and psychiatry*, 57(3), 241-266.
5. Denning, M., Tamarit, C., Falón, C., López-Solís, M., Hernández-Ribas, R., Puig, J., & Dees, G. (2016). Dynamic functional connectivity reveals altered variability in functional connectivity among patients with major depressive disorder. *Human brain mapping*, 37(8), 2918-2930.
6. Hamilton, J. P., Farmer, M., Fogelman, P., & Gotlib, I. H. (2015). Depressive rumination, the default-mode network, and the dark matter of clinical neuroscience. *Biological Psychiatry*, 78(4), 224-230.
7. Chou, T., Dickerson, T., Dougherty, D. D., & Hooley, J. M. (2023). The default mode network and rumination in individuals at risk for depression. *Social Cognitive and Affective Neuroscience*, 18(1), msad032.

