

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

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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

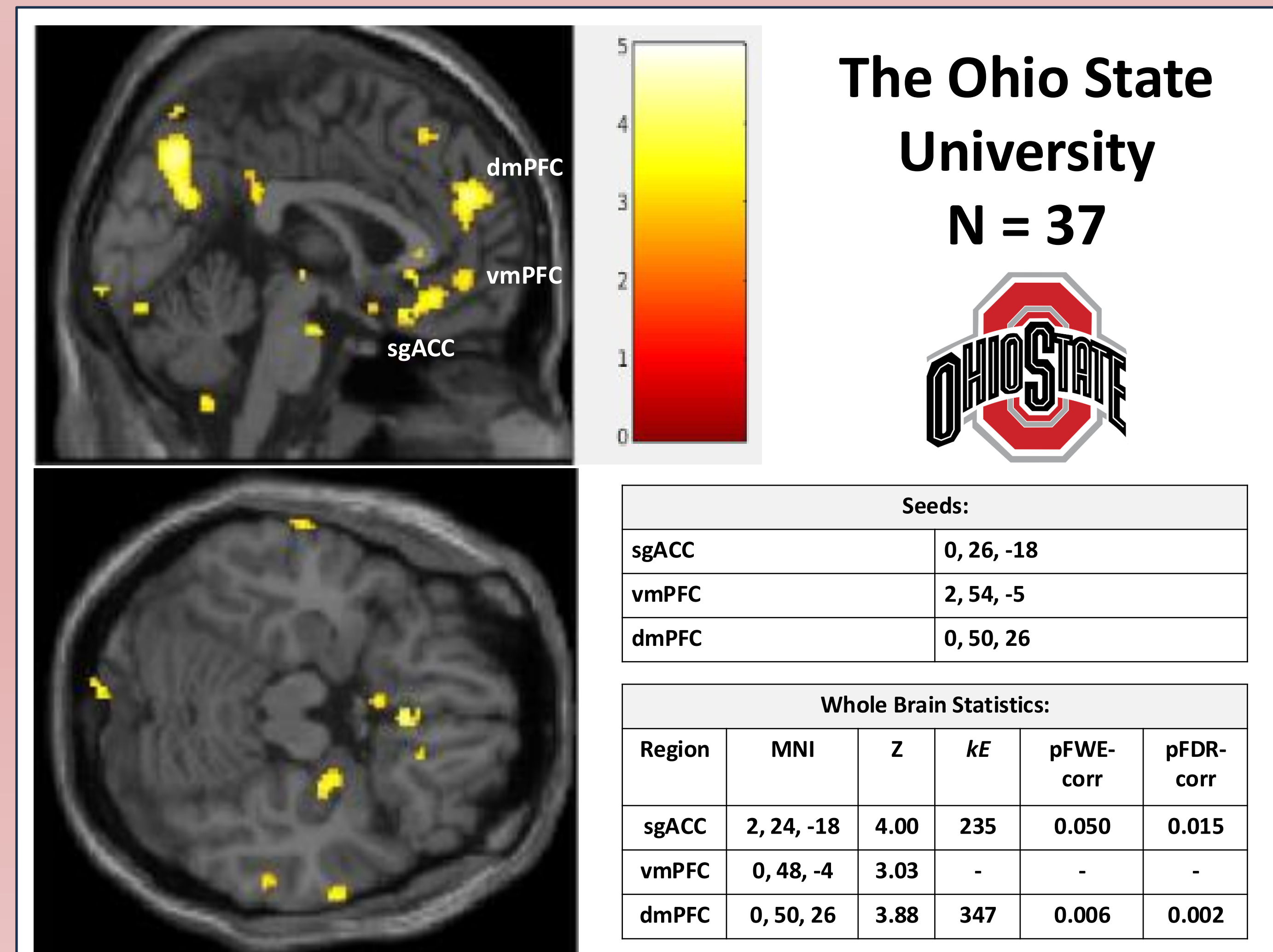
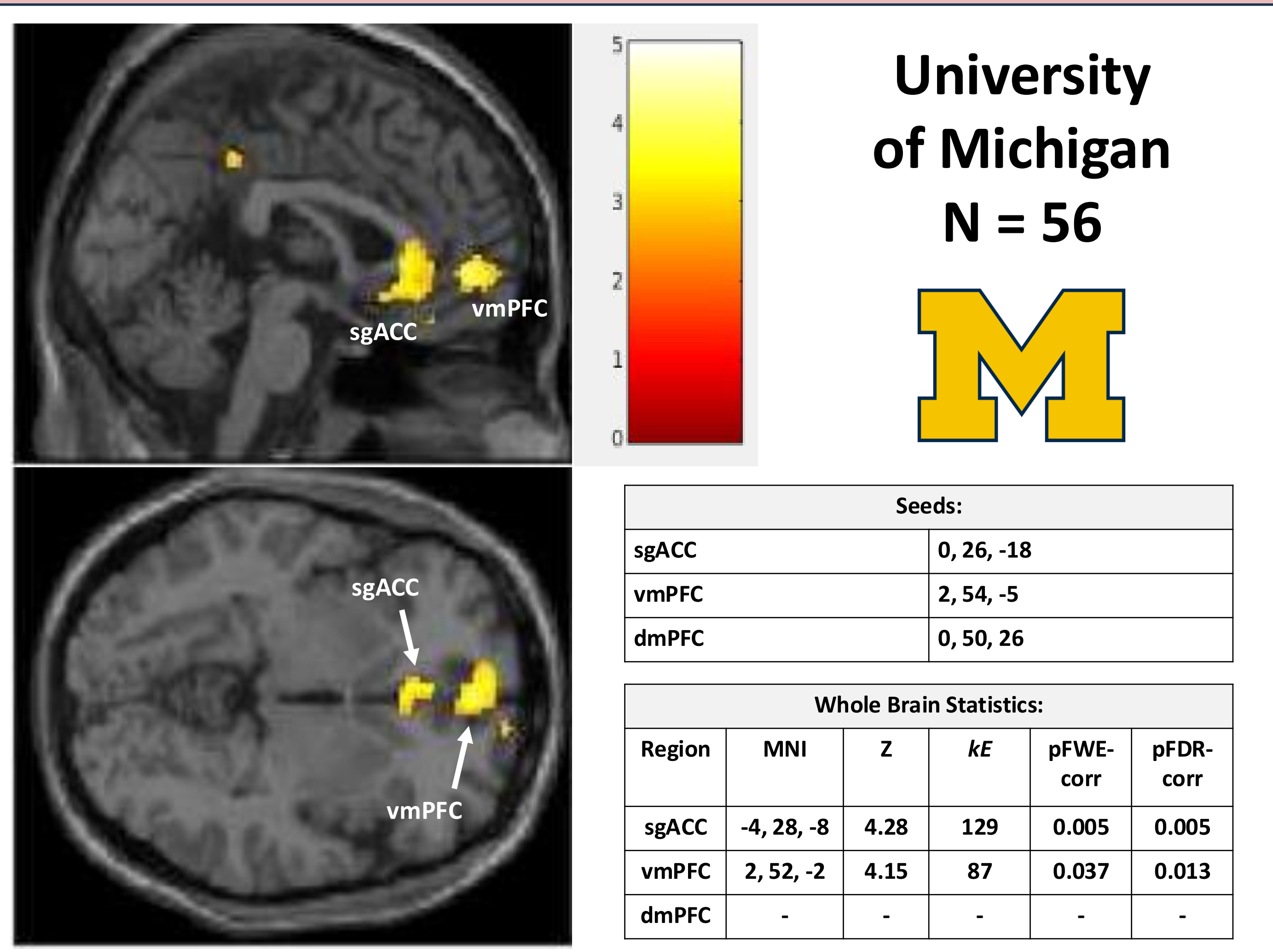
- A total of 93 adults with trauma exposure and clinically significant symptoms of PTSD were studied. 42 of these adults reported history of CM as determined by the Childhood Trauma Questionnaire (CTQ).
- 3T fMRI scans were collected during resting state. Participants focused on a fixation “plus sign” 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

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