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 severity[1].
- 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].
- The vmPFC is crucial in regulating the limbic network, specifically the amygdala[8].
- 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 CM[5].
- This study examined the resting-state functional connectivity (rsFC) patterns specific to CM in the DMN, SN and limbic networks in adults to identify the neural correlates of CM.

Methods

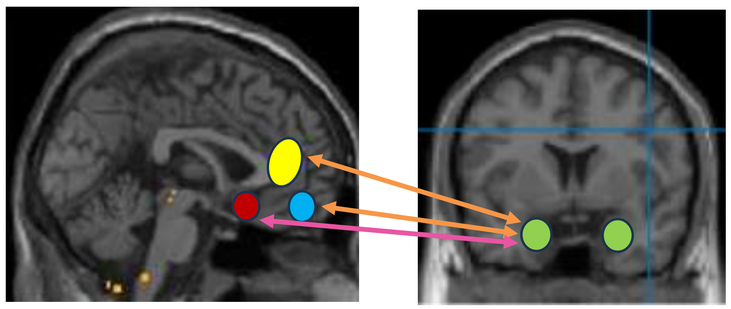
- 56 adults with trauma exposure and clinically significant symptoms of PTSD were studied. Twenty of these adults reported history of CM as determined by the Childhood Trauma Questionnaire (CTQ).
- 3T fMRI scans were collected during resting state. Participants focused on a fixation "plus sign" and let 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.
- Regions of interest (sgACC and vmPFC, rACC and amygdala) were used to examine whether individuals reporting CM differed from individuals reporting no CM in rsFC.
- Z-score images from the effects analyses (two-sample t-tests) implemented in SPM12.
- Small volume correction used for amygdala rsFC.
- Correlational analysis was completed using SPSS.

Discussion

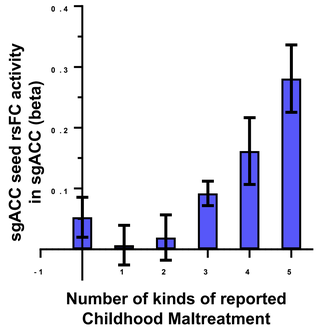
- Adults with current and CM history had increased resting state FC within sgACC and between the sgACC and vmPFC than adults with current PTSD and no history of CM.
- sgACC is a node in the limbic network associated with negative affect, and vmPFC a node of the anterior DMN associated with self-referential procession and rumination, suggesting a possible neural mechanism of vulnerability in CM involving increased negativity in self referential processing.
- CM history also showed decreased amygdala rsFC with rostral ACC, circuitry associated with emotional regulation, suggesting a possible mechanism of deficits in emotional regulation.
- Rumination - Reflection was associated with increased connectivity within the DMN while Brooding was not.
- Brooding correlated with depression but Reflection did not.
- Correlation of sgACC rsFC with Reflection (rather than Brooding) was not hypothesized, but suggests presence of increased negative bias even in "neutral" repetitive thinking.
- This study is relatively small and future studies should investigate the relationship of CM, sgACC-DMN rsFC, rACC-amygdala and rumination / Brooding.

Results

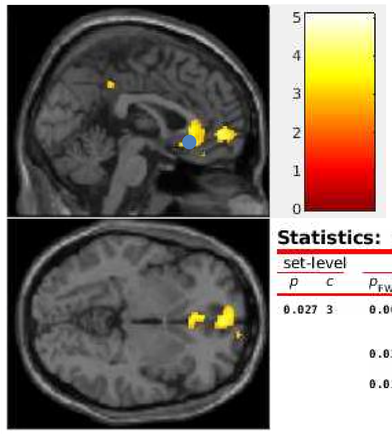
Visualization of expected rsFC with Amygdala



sgACC FC was greater with more forms of CM reported by participants



Increased rsFC between sgACC seed, vmPFC, sgACC in adults with CM history



Statistics: *p-values adjusted for search volume*

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	(Z_E)	p_{uncorr}	
0.027	3	0.005	0.005	129	0.000	0.682	0.315	4.73	4.28	0.000	-4 28 -8
						0.767	0.315	4.65	4.22	0.000	-4 30 0
						1.000	0.744	3.71	3.47	0.000	6 28 0
		0.037	0.013	87	0.001	0.842	0.342	4.56	4.15	0.000	2 52 -2
						1.000	0.643	3.97	3.69	0.000	-6 60 -8
		0.012	0.006	109	0.000	0.960	0.476	4.35	3.99	0.000	8 30 -20
						1.000	0.643	4.01	3.72	0.000	10 42 -16
						1.000	0.754	3.67	3.43	0.000	14 30 -26

	Without CM N=36		With CM N=20		
Gender - Female	N=33	91.6%	N=18	90.0%	ns
Race - White	N=32	88.9%	N=17	85.0%	ns
	Mean	SEM	Mean	SEM	
Age	34.5	3.5	42.3	5.0	ns
CAPS-5 (PTSD)	29.4	1.1	32.7	1.7	ns
PCL-5 (PTSD)	43.5	2.4	47.5	2.6	ns
BDI (Depression)	27.3	1.7	26.9	2.6	ns
RRS - Reflection	12.0	0.7	11.0	0.9	ns
RRS2 - Brooding	13.8	0.7	14.3	0.9	ns
Self Compassion	28.6	1.4	29.0	1.7	ns
AAQ9 - Inflexibility	41.1	1.1	40.9	1.6	ns
ERQ - Reappraisal	24.6	1.3	24.6	1.6	ns
ERQ - Emotional Suppression	15.2	0.9	15.0	1.3	ns
CTQ: Emotional Abuse	8.3	0.7	19.2	0.5	<.001
Physical Abuse	7.1	0.3	13.2	0.9	<.001
Sexual Abuse	8.8	1.0	15.7	1.7	<.001
Emotional Neglect	9.6	0.7	18.7	1.1	<.001
Physical Neglect	7.8	0.5	12.7	0.9	<.001

Pearson correlation between FC and reflective rumination, and self-report measures and brooding rumination (* <.05, ** <.01, *** <.001)

	RRS1_t1 Reflection	RRS2_t1 Brooding
sgACC and vmPFC	0.049	-0.022
sgACC and sgACC	0.297*	0.010
Phq9 total	0.054	0.622***
BDI 21	0.147	0.555***
FFMQ total	-0.015	-0.389**

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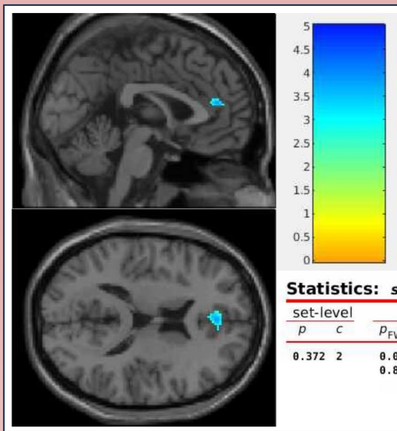
Decreased rsFC between Amygdala and rACC in adults with CM history



Statistics: *search volume: 20.0mm sphere at [0,44,16]*

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	(Z_E)	p_{uncorr}	
0.372	2	0.028	0.033	86	0.011	0.157	0.201	3.97	3.69	0.000	0 44 16
		0.868	0.794	1	0.794	0.870	0.943	2.81	2.70	0.003	12 38 30

Sphere: functional anatomical region associated with rACC