Maternal adverse childhood experiences (ACEs) and infant visual-limbic white matter development

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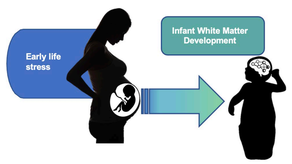
BACKGROUND

- Exposure to adverse childhood experiences (ACEs) has deleterious and intergenerational consequences for mental health.
- Emerging evidence suggests that maternal history of stress exposure **prior to conception** may impact **maternal-placental-fetal endocrine, immune and inflammatory stress biology**.
- Given the extraordinary pace of brain maturation in utero, such alterations within the early intrauterine environment may have cascading effects on the developmental trajectory of the infant brain.
- **Experimental studies** in rodents demonstrate that maternal history of stress exposure prior to conception alters **offspring brain morphology**.
- Goal of current study was to examine the association between **maternal ACEs (high vs. low)** and **infant white matter microstructure** of fronto limbic (e.g. uncinate, cingulum, and fornix) and sensory processing circuits (e.g. inferior fronto occipital and inferior longitudinal fasciculus).
- We additionally conducted exploratory analyses to examine whole brain effects of maternal ACEs beyond *a priori* circuits.

METHODS

- ***n = 101*** pregnant individuals and their infants **(52% female). Maternal adverse childhood experiences** were assessed using the Adverse Childhood Experience Questionnaire (ACE-Q). Participants reported experiencing an average of 2.16 ACEs, with 47 (46.5%) reporting ≥2 ACEs and 54 (53.5%) reporting 0 or 1 ACE(s). **Neonatal white matter microstructure**, as indexed by fractional anisotropy (FA) was assessed via DTI.
- A series of ANCOVA models were used to examine differences between maternal ACEs (high and low) and neonatal FA across white matter tracts, covarying for postconceptional age at scan (PCA) and motion during scan.

A)



B)

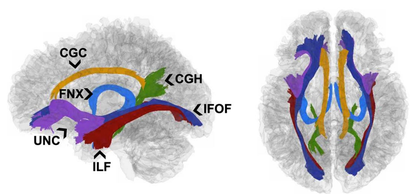


Figure 1) A. Conceptual model. **B).** *A priori* white matter tracts analyzed within the current study (*n*=6). Red = inferior longitudinal fasciculus (ILF); purple = uncinate (UNC); light blue = fornix (FNX); dark blue = inferior frontal occipital fasciculus (IFOF); green = cingulum (hippocampal component; CGH); yellow = cingulum (anterior component; CGC).

RESULTS

High maternal ACES predicts lower neonatal inferior longitudinal fasciculus fractional anisotropy (FA)

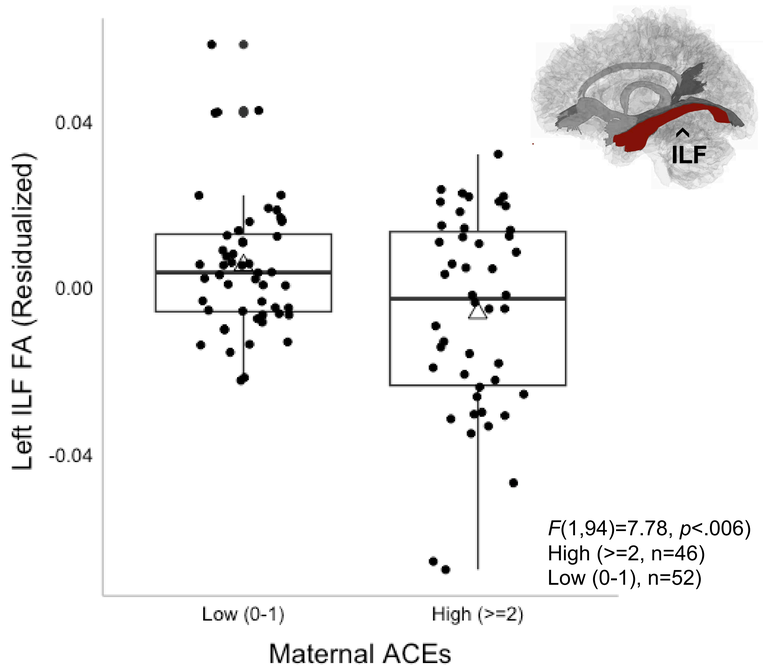


Figure 2. Infants of mothers with high maternal ACEs (n=46) relative to low ACEs (n=52) had lower left inferior longitudinal fasciculus FA. Left ILF residuals plotted after covarying for postconceptional age at scan and motion.

White Matter Tract	FA	
	F-Stat	P value
Cingulum (Anterior) (left)	1.174	0.281
Cingulum (Anterior) (right)	1.317	0.255
Cingulum (Hippocampal) (left)	0.453	0.503
Cingulum (Hippocampal) (right)	0.877	0.351
Fornix (left)	0.001	0.983
Fornix (right)	2.122	0.149
Uncinate Fasciculus (left)	2.954	0.089
Uncinate Fasciculus (right)	2.08	0.152
Inferior Longitudinal Fasciculus (left)	7.782	0.006*
Inferior Longitudinal Fasciculus (right)	4.287	0.04*
Inferior Frontal Occipital Fasciculus (left)	2.988	0.087
Inferior Frontal Occipital Fasciculus (right)	1.622	0.206

Exploratory whole brain analyses: High maternal ACEs predicts WM microstructure in visual processing, as well as additional corticothalamic + corticofugal prefrontal circuits

	FA		RD		AD	
White Matter Tract	F-Stat	P value	F-Stat	P value	F-Stat	P value
Cingulum (Anterior) (left)	1.174	0.281	2.156	0.145	0.225	0.636
Cingulum (Anterior) (right)	1.317	0.255	3.258	0.075	2.351	0.129
Cingulum (Hippocampal) (left)	0.453	0.503	0.806	0.372	2.731	0.102
Cingulum (Hippocampal) (right)	0.877	0.351	1.570	0.213	0.028	0.868
Corpus Callosum Genu	2.32	0.131	5.057	0.027*	6.377	0.013*
Corpus Callosum Motor	0.505	0.479	0.199	0.657	1.069	0.304
Corpus Callosum Parietal	1.794	0.184	1.092	0.299	0.005	0.943
Corpus Callosum PreMotor	0.11	0.741	0.962	0.329	1.703	0.195
Corpus Callosum Tapetum	0.108	0.744	0.499	0.481	1.987	0.162
Corpus Callosum Splenium	2.381	0.126	0.849	0.359	1.058	0.306
Cortico-Fugal-PreFrontal (left)	3.648	0.059	6.897	0.01*	3.483	0.065
Cortico-Fugal-PreFrontal (right)	3.875	0.052	6.933	0.01*	4.161	0.044*
Cortico-Fugal-Motor (left)	1.674	0.199	1.715	0.193	0.206	0.651
Cortico-Fugal-Motor (right)	1.575	0.213	1.079	0.302	0.402	0.527
Cortico-Fugal-Parietal (left)	5.166	0.025*	0.582	0.447	1.076	0.302
Cortico-Fugal-Parietal (right)	1.698	0.196	0.848	0.359	0.404	0.527
Cortico Spinal (left)	1.756	0.188	0.24	0.626	0.774	0.381
Cortico Spinal (left)	1.549	0.216	0.259	0.612	0.779	0.38
Cortico-Thalamic-Prefrontal (left)	1.376	0.244	11.488	0.001*	8.212	0.005*
Cortico-Thalamic-Prefrontal (right)	3.456	0.066	7.605	0.007*	5.668	0.019*
Cortico-Thalamic-Motor (left)	1.97	0.164	0.308	0.58	0.201	0.655
Cortico-Thalamic-Motor (right)	0.011	0.917	0.744	0.391	2.559	0.113
Cortico-Thalamic-Parietal (left)	7.209	0.009*	1.775	0.186	2.14	0.147
Cortico-Thalamic-Parietal (right)	1.153	0.286	0.711	0.401	0.01	0.919
Fornix (left)	0.001	0.983	0.008	0.930	0.017	0.897
Fornix (right)	2.122	0.149	1.382	0.243	0.099	0.753
Inferior Longitudinal Fasciculus (left)	7.782	0.006*	4.600	0.035*	0.153	0.697
Inferior Longitudinal Fasciculus (right)	4.287	0.041*	5.101	0.026*	0.753	0.388
Inferior Frontal Occipital Fasciculus (left)	2.988	0.087	2.286	0.134	0.180	0.673
Inferior Frontal Occipital Fasciculus (right)	1.622	0.206	3.698	0.057	1.574	0.213
Optic (left)	0.643	0.425	6.594	0.012*	5.945	0.017
Optic (right)	0.213	0.646	4.568	0.035*	4.353	0.04*
Uncinate Fasciculus (left)	2.954	0.089	5.662	0.019*	3.383	0.069
Uncinate Fasciculus (right)	2.08	0.152	2.677	0.105	1.413	0.237

CONCLUSION

- Maternal ACEs predicts neural circuit development of the **inferior longitudinal fasciculus**, a white matter fiber tract within the **visual-limbic pathway** that subserves the integration of visual and emotional processing. Variability in sensory circuit development may have implications for the maturation of higher order emotional and cognitive circuits and later mental health.
- WM microstructure was only assessed once in this study. Future studies should utilize **repeated assessments** to examine continued maturational effects across development.
- Identifying the neurobiological mechanisms underlying such intergenerational risk is critical for **optimizing risk identification** and developing early targeted interventions and protective processes, ideally before conception, to limit the transmission of risk for psychopathology.

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