Stress, vulnerability, and the maternal experience: Electrical network and behavioral assessments of the maternal mouse brain

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Background

Early life stress, vulnerability, and the maternal brain

- Adverse early life experiences can impact the developing brain.
- These early impacts lead to increased vulnerability later in life.
- Alterations to neural networks following female ELS also affect brain components relevant to maternal care and behaviors.
- The maternal brain arises from a cascade of alterations.
- Maternal brain changes may not be entirely adaptive, resulting in increased neuropsychiatric risk over the perinatal period.
- Stress-relevant brain regions largely overlap with those important for maternal engagement behaviors.

Objective: Assess brain-wide electrical dynamics of the maternal brain alongside network signatures of stress and maternal behavior.

Methods and Approach

- Mouse Model: Outbred CD1 strain, commonly used in maternal studies.
- ELS: Combination paradigm of maternal separation, early weaning, and limited nesting
- Behavioral Assessments: Adolescent phenotype panel and adult maternal behavior
- Neurophysiologic Recordings: collected before, during, and fixed times after pregnancy
- Maternal/Vulnerability multi-site depth electrodes include implantation of the following regions: infralimbic and prelimbic cortices (IL and PPI), nucleus accumbens (NAc), basolateral, medial, and lateral amygdala (BLA, MeA, CoA), ventral hippocampus (Vh), and ventral tegmental area (VTA).

Brain-wide network dynamics: A validated and innovative approach

Electome Factors (EFs): electrical functional connectome factors
- Spatiotemporal local field potential (LFP) patterns/signatures with brain state relevance
- Machine learning is used to build models: Discriminative cross spectral factor analysis (dCSFA) previously identified six EFs as latent stress-sensitive networks

Experimental Timeline: ELS through maternal electrophysiology

Brain-wide electrical dynamics

Response and reactivity: A circuit assessment

Females with prior ELS exposure display altered behavioral response and prefrontal reactivity to negative affect stimuli.

Cue-dependent fear conditioning

The PFC-AMY circuit and trait vulnerability

ELS increases freezing with conditioned cue in a tone-shock paired paradigm in adolescence (p<0.001 at 5 min, passing FDR). In adulthood, PFC activation, or reactivity, in response to an aggressor shows a significant effect based on parity (p=0.0091) and stress condition (p=0.0078) at 8-11 Hz.

Brain-wide networks: Negative affect response and motherhood

There is an ELS-specific increase in EF2, but not EF1 network activity during a negative affect task for postpartum females.

Future Directions

- Continue detailed assessment of maternal care focused on early PPDs.
- Further investigate the relationships amongst network characteristics, negative affect responses, and maternal care.
- Evaluate maternal network dynamics while on the nest and building to identify networks of maternal care/engagement.
- Record while manipulating maternal-targeted variables: pup-retrieval task, ultrasonic vocalization playback, oxytocin administration...
- Could an EF relevant to maternal care and engagement really exist?
- How might the activity of this network be altered in ELS-exposed dams?

References and Acknowledgements

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