Significance of Prenatal Nicotine Exposure on Electrophysiological Markers of Sensory Processing and Attention in Infants

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Senior Honors Thesis Oral Defense
Background

- Nicotine and brain development

Methods

- EEG
- Novel auditory stimuli

Results

- Nicotine inhibits:
  - Auditory stimuli discrimination
  - Overall modulation of auditory stimuli

Discussion

- Prenatal nicotine brain phenotype resembles ADHD
- Theta EEG waves as a biomarker
Everyone knows smoking is unhealthy, especially during pregnancy, yet 12–20% of mothers smoke while pregnant. But why do we care about studying nicotine and the brain?
Background

Known effects of Prenatal Nicotine Exposure:

- Low birth weight
- Premature birth
- Impaired lung function
- Growth restriction
- Sudden Infant Death Syndrome
- Obesity, type II diabetes, and hypertension

Correlative effects of Prenatal Nicotine Exposure:

- Sensory processing difficulty
- Lower language scores
- Cognitive dysfunction
- Attention deficits
- Hyperactivity
- Impulsivity
EEG records ongoing brain activity (Example of 128 channel recording)
EEG Records ongoing brain activity

Frontal Electrodes

19 16 10
12 11 4

MMN Event-Related Potential (ERP) amplitude and latency:
- Attention, memory, & sensory processing

N200 & P300 complex amplitude associated with:
- Cognition, novelty, & information processing

Differences in theta (3-6 Hz) amplitude:
- Predicts cognitive functioning & learning
Event-Related Potentials (ERPs)

- Amplitude of brain wave when a stimulus occurs
- Differences in wave amplitude indicates altered brain activity

Using EEG to study auditory stimuli
Studying brain activity with EEG

Mismatch Negativity (MMN)

- A negative amplitude in response to a “mismatch of stimuli” ie, prediction error
- Brain activity diminishes when stimuli type remains constant (prediction)
- MMN = measure of brain activity when we encounter unexpected stimuli (error)
- To find MMN, we subtract the ERP of the standard stimulus from the ERP of the novel stimulus

Deviant tone ERP - Standard tone ERP = MMN
Hypotheses

1. **Electrophysiology**
   a. Infants with prenatal nicotine exposure (PNE) will have elevated or diminished ERP amplitudes in response to deviant tones compared to controls.
   b. PNE group will have a smaller difference in MMN between standard and deviant tones.

2. **Correlation with behavior**
   a. Diminished MMN will predict poorer behavioral development scores.
Methods

1. N = 30
   20 PNE, 10 control

2. At 3-5 months postpartum:
   Bayley Scales of Infant development
   and EEG

3. 3rd trimester mothers were screened for:
   Cigarettes smoked per day
   CO and carboxyhemoglobin levels

4. Infants exposed to standard tones with occasional deviant tones
Oddball Paradigm

- elicits MMN ERP
- 1:20 ratio Deviant:Standard

standard stimulus

novel stimulus
Results

- Processed EEG data
- Average response to deviants, standards and calculated MMN
- Time-frequency transformation to extract theta (3-6Hz) power
ERSP Results

Changes to frequency composition

E) In response to the deviant tones, **nicotine group showed greater brain activity**

F) In response to standard tones, **nicotine group showed greater brain activity**

J) **Main effect - group:** prenatal nicotine exposure resulted in increased brain activity in response to **ALL tones**

G) **Controls - more brain activity** in response to the deviant tone compared to standard

H) **Nicotine group** - even greater brain activity in response to deviant compared to controls
E) Main effect of tone
  - Theta band $P < 0.001$
  - Controls and nicotine exposure group both show greater ITC in response to deviant tone
  - Confirms research paradigm

G) Interaction Theta $P > .01$
  - The degree to which brain activity changes in response to tones depends on the group
Mean ERP of all participants

E Controls

F PNE

Green – standard tone ERP
Blue – deviant tone ERP
Results - MMN Controls
Results - MMN nicotine exposure
**Correlations**

**Non-significant**

**PNE versus Control group**
MMN, N2, & P3 were not significantly different between controls and PNE group

**Behavior and brain markers**
MMN, N2, P3 amplitude did not correlate with Bayley Scores

**Approached significance**

**Control group**

- MMN and Receptive Communication Score
  \[ r = -0.329 \]
- N2 and Cognition Score
  \[ r = 0.401 \]
- N2 and Receptive Communication Score
  \[ r = 0.379 \]
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Summary

1. **Prenatal nicotine exposure affected responses to auditory stimuli**:
   - Infants exposed to nicotine:
     a. Showed increased response to all auditory stimuli, both novel and expected
     b. Failed to differentiate between novel and standard tones

2. **Diminished MMN did not predict poorer behavioral development scores**
   - However, N200 and MMN correlations with Bayley Scores approached significance in control group
Significance

1) **Current study adds to evidence that nicotine directly alters infant brain function**
   - Previous evidence was simply correlative with behavior but the current study found **direct effects of nicotine on brain activity**

2) **Infants exposed to nicotine may have more difficulty discriminating between sounds as well as filtering out unnecessary auditory stimuli**
   - Recent study found **PNE affects language development** in infants and 3-year-olds, specifically in areas of auditory functioning (e.g., sounds discrimination, imitation, and comprehension) *(Hernandez-Martinez, 2016)*

   - Increases understanding of nicotine’s **teratogenic effects on brain development**
3) **Prenatal nicotine exposure may lead to ADHD**

- We found elevated Theta power which is a brain marker also found in ADHD.
- This, coupled with the similar phenotypic presentation of PNE and ADHD, indicates they act on the same neurocircuitry and research on one may inform the other.

4) **Therapy**

- Practice auditory discrimination.
- Psychoeducation on auditory processing difficulty after nicotine exposure.
Thank you!
Supplemental background: *Biological mechanisms of nicotine in the brain*

- Nicotine binds to acetylcholine receptors (nAChRs)
- nAChRs are essential to **growth**, **connectivity**, and **function** of neural circuitry and neurotransmitter systems
- Rapid brain growth during fetal development makes the brain particularly susceptible to toxins

In rodent models PNE caused:
- Premature cell signaling events that led to AChR structural changes
- Altered expression of nAChRs
- DNA hypomethylation
- Hypersensitivity to nicotine
- Abnormal dopamine function
Slide 15 supplemental: *Individual Participant ERPs*

**Controls**

- Deviant tone
- Standard tone

**Exposed to nicotine**

- Deviant tone
- Standard tone