**Preeclampsia Impact on Adult Brain in a Vasopressin-Induced Model**

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### Introduction

**A Case Study**
- August 18, 2015, 3:47 am. 22-year-old woman goes into labor.
- Blood pressure: 150/100 mmHg
- Urinalysis: proteinaceous (Santillan et al., 2009)

She was seemingly healthy, but doctors were forced to perform emergency cesarean surgery because of her severe preeclampsia.

- Symptoms: convulsions, loss of consciousness, seizure activity, and sleeplessness (Goodlin et al., 2001)

- Years later, her son exhibited difficulty maintaining attention, delays in communication, and lack of reciprocal speech.
- Problems sharing and communicating with his sibling, especially when frustrated.

### Hypothesis

- Vasoactive intestinal peptide (VIP) serves to increase blood volume and pressure (vasopressin (AVP) throughout pregnancy. AVP, also known as proteinacious vasopressin or oxytocin (Salti and Klabunde, 2009). AVP, also known as antidiuretic hormone, is a hypothalamic polypeptide which serves to increase blood volume and pressure (Zulfiqaroglu et al., 2011).

Here, we used an animal model of preeclampsia, where pregnant female mice were prenatally exposed to arginine vasopressin (AVP) throughout pregnancy. AVP, also known as antidiuretic hormone, is a hypothalamic polypeptide which serves to increase blood volume and pressure (Zulfiqaroglu et al., 2011).

### Background Data

#### Embryonic (E18) Cortical Plate Volume

- **The Cerebral Cortex**
  - Cortex plays a role in almost all neural processes including memory and attention.

- **Increased Adult Anxiety-like Behavior**

- **Damage to the cortex can lead to problems with emotional regulation (e.g., anxiety)** (Fuster, 2008)

#### Prefrontal Cortical Area

- **Volume (µm²)**
- **Density (µm²)**

### Methods

- **Mouse Model**
  - AVP- and saline-filled pumps were implanted subcutaneously into mice 3 days prior to breeding for fusion throughout pregnancy.

- **Polymerase Chain Reaction**
  - Used to verify embryonic animal sex

- **Cyrosectioning and Tissue processing**
  - Used cryostat to section adult brain at 50µm
  - Slide mounted tissues

- **Histochemistry**
  - Stained nuclei with DAPI and cover slipped slides

- **Contour tracing**
  - Using Allen Mouse Brain Atlas reference

- **Density estimation (Part II of Microscopy)**
  - Used Stereo Investigator software
  - Random site selection and 50µm x 50µm counting frame

### Results

#### Cortical Measurements

<table>
<thead>
<tr>
<th></th>
<th>Volume (µm³)</th>
<th>Density (µm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saline</strong></td>
<td>1.2E+11</td>
<td>3.5E-04</td>
</tr>
<tr>
<td><strong>AVP</strong></td>
<td>1.0E+11</td>
<td>2.5E-04</td>
</tr>
</tbody>
</table>

**Figure 1A.**

#### Prefrontal Cortex Measurements

<table>
<thead>
<tr>
<th></th>
<th>Volume (µm³)</th>
<th>Density (µm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saline</strong></td>
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</tr>
<tr>
<td><strong>AVP</strong></td>
<td>7.0E+09</td>
<td>3.0E-04</td>
</tr>
</tbody>
</table>

**Figure 3A.**

#### Adult Males, Prefrontal Cortex

<table>
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<th>Volume (µm³)</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Saline</strong></td>
<td>3.0E+10</td>
<td>2.0E-04</td>
</tr>
<tr>
<td><strong>AVP</strong></td>
<td>1.2E+10</td>
<td>1.5E-04</td>
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**Figure 3B.**

### Conclusions

- The mice have recovered or compensated by adulthood in some ways, but some deficits remain at E18.
- With significant cortical volume differences between E18 mice that were exposed to AVP in utero but not in adulthood, it can be inferred that cortical morphogenesis occurs differently after AVP exposure.
- Despite normal cortical volume and cellular density at the time of behavioral testing, cortical function may be affected by this altered trajectory of growth.
- Unlike the whole adult cortex, the prefrontal cortex in AVP-exposed animals exhibits an increased cell density.

### Future Directions

- It is vital to analyze other areas of the brain in order to determine why there are behavioral differences between prenatally exposed AVP mice and controls.
- It is also critical to determine if the composition of the cortex is altered with AVP exposure (e.g., neurons vs glia). This will provide deeper insight into the mechanisms underlying elevated anxiety-like behaviors despite unchanged cortical volume in AVP-exposed offspring.

### Acknowledgements

Special thanks to Dr. Stevens, Serena Gumusoglu, Akanksha Chilkur, and the rest of the Psychiatry and Early Neurodevelopmental Laboratory (PENDL). Also, owe this one in a lifetime opportunity to the Secondary Student Training Program and the Belin Blank Center. This project was supported by the University of Iowa Hypertension Pilot Grant program.

### References


