**Methamphetamine effects on adolescent brain development in both sexes**

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**Introduction**
- Females in both humans and rats models often exhibit faster rates of addiction than males.
- Vulnerability to drug addiction in adolescents (ADOLs) may lead to higher relapse rates and faster rates of addiction.
- The brain is developing in adolescence, including the prefrontal cortex (PFC) and the nucleus accumbens (NAc), which are regions involved in self-control and reward systems, respectively.
- Our lab previously found that adult rats of both sexes exposed to amphetamine during ADOL had reduced expression of dopamine D1 receptors (D1R) in the medial PFC but no change in the NAc

**Hypothesis**
- Females will take more methamphetamine than males.
- No significant difference in NAc D1R expression, but reduced PFC D1R levels in both males and females.

**Methods**
- Rats’ activity is measured by an operant cage where a computer records nose poke responses.
- Habituation period rats in cage for 1 day to allow them to become familiarized with surroundings with no reinforcer given.

**Subjects: Male and female Sprague Dawley rats**

**Table 1: Rat's self-administered 0.1 mg/kg METH attached through a metal tether in a nose-poke operant chamber**

<table>
<thead>
<tr>
<th>Reinforcer</th>
<th>Short access (ShA) 2hrs/day</th>
<th>Long access (LgA) 5hrs/day</th>
<th>Tissue collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADOL male</td>
<td>METH P40-47</td>
<td>P48-61</td>
<td>P82</td>
</tr>
<tr>
<td>Adult male</td>
<td>P90-97</td>
<td>P98-111</td>
<td>P132</td>
</tr>
<tr>
<td>ADOL female</td>
<td>METH P40-47</td>
<td>P48-61</td>
<td>P82</td>
</tr>
<tr>
<td>Adult female</td>
<td>P90-97</td>
<td>P98-111</td>
<td>P132</td>
</tr>
</tbody>
</table>

**Behavioral Analysis**

- *n’s=13-18/group
- *p<.05 vs. first ShA session for males
- *p<.01 vs. first LgA session for males
- *p<.05 vs. first LgA session for adolescent-onset
- *p<.05 vs. first LgA session for adult-onset
- **p<.001 vs. each ShA session
- ***p<.001 vs. each LgA session

**Results:**
- Adolescents display increased METH intake compared to adult counterparts.
- Females show increased METH intake compared to males.
- Adolescent females escalated their METH intake the quickest compared to all other groups.

**Protein Analyses**

<table>
<thead>
<tr>
<th>Nucleus Accumbens</th>
<th>ADOL Adult</th>
<th>ADOL Male</th>
<th>Female</th>
<th>Adult Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1R Expression (%)</td>
<td>Control</td>
<td>48kD</td>
<td>39kD</td>
<td>48kD</td>
</tr>
<tr>
<td>n’s=1/2/group</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Results:**
- Males may exhibit lower levels of D1R expression in the PFC.
- Adult-onset male METH rats may be different from the other groups (i.e. brain is less resistant to drug-induced plasticity).

**Discussion**
- Changes in the amount of expression of D1R in the:
  - PFC suggests there are more sex related changes than age.
  - NAC suggests there are more age related changes than sex.

**Question:** Are ADOLs compared to adults more sensitive to drug-induced changes in neural function and behavior? Males to females?
- Based on our current results, it appears that both age and sex influence D1R expression following METH, but their effects may depend on brain region.

**Future Work**
- Study was limited to only expression of protein receptors rather than testing for function of the receptors.
- Future work will include testing for function by use of electrophysiology with similar methods.

**References**
1. Lynch, W.J., 2006
2. Poudel & Gaudam, 2017
3. Chen et al., 2009
4. Casey et al., 2008
5. Kang et al., 2016
6. Image source: Fluofarma

**Acknowledgments**
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