The Neuroendocrinology of Psychopathy

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Dalhousie University
1. Introduction to Psychopathy
2. Somatic Findings in Psychopathy
3. Neural Bases of Psychopathy
4. A Focus on OXT/AVP
5. Future Directions
What is a psychopath?

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The Neuroendocrinology of Psychopathy
The Dual-Deficit Model

<table>
<thead>
<tr>
<th>Affective-Interpersonal</th>
<th>Impulsive-Antisocial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predatory disposition</td>
<td>Disinhibition/impulsivity</td>
</tr>
<tr>
<td>Lack of empathy</td>
<td>Pervasive antisocial behaviour</td>
</tr>
<tr>
<td>Shallow affect</td>
<td>Lack of concern about performance</td>
</tr>
</tbody>
</table>

Table: Broad overview of the dual-deficit (a.k.a two-factor) model of psychopathy.
They were all once children...

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The Neuroendocrinology of Psychopathy
Children with conduct disorder are a heterogeneous population:

1. Those with callous-unemotional traits
2. Those with high mood lability and increased risk for mood and anxiety disorders
Predominant impairments in the following neuropsychological domains:

1. *Emotional* empathy
2. Emotional learning and decision making
Psychopaths Re-offend More...

Salekin et al. J Personality Assessment 2003;80:154-63

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...and Sooner after Release

Olver & Wong. Personality Disorders 2014; Advance Online Pub.
Hypoarousal: Resting HR

**FIGURE 1.** 15-year-olds who become violent criminal offenders by age 24 years have significantly lower resting heart rates than noncriminals, with nonviolent criminal offenders lying in the middle. Values above bars indicate effect size. ■, violent; ●, criminal nonviolent; □, controls.

Hypoarousal: HR Reactivity

<table>
<thead>
<tr>
<th>Study</th>
<th>$d$</th>
<th>$p$</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>El-Sheikh et al., 1994</td>
<td>-1.2290</td>
<td>.0006</td>
<td>-1.92, -0.54</td>
</tr>
<tr>
<td>Garralda et al., 1991</td>
<td>-0.9020</td>
<td>.0027</td>
<td>-1.48, -0.32</td>
</tr>
<tr>
<td>Maliphant et al., 1990a</td>
<td>-1.6715</td>
<td>.0001</td>
<td>-2.50, -0.85</td>
</tr>
<tr>
<td>Maliphant et al., 1990b</td>
<td>-1.4291</td>
<td>.0003</td>
<td>-2.23, -0.63</td>
</tr>
<tr>
<td>Williams et al., 2002</td>
<td>-0.5873</td>
<td>.0430</td>
<td>-1.15, -0.02</td>
</tr>
<tr>
<td>Zahn &amp; Kruesi, 1993</td>
<td>-0.5156</td>
<td>.0401</td>
<td>-1.00, -0.03</td>
</tr>
<tr>
<td>Davies &amp; Maliphant, 1971</td>
<td>-0.4695</td>
<td>.2198</td>
<td>-1.22, +0.28</td>
</tr>
<tr>
<td>Davies &amp; Maliphant, 1971</td>
<td>-1.2674</td>
<td>.0299</td>
<td>-2.42, -0.12</td>
</tr>
<tr>
<td>Pitts, 1997</td>
<td>-0.6232</td>
<td>.0032</td>
<td>-1.01, -0.20</td>
</tr>
<tr>
<td>Raine, 2002</td>
<td>-0.5935</td>
<td>.0001</td>
<td>-0.95, -0.24</td>
</tr>
<tr>
<td>Total sample size</td>
<td>578</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite effect size</td>
<td>-0.7599</td>
<td>.0000</td>
<td>-0.94, -0.58</td>
</tr>
<tr>
<td>File drawer statistic</td>
<td>180</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: CI = confidence interval.*
Hypoarousal: HR Reactivity

Casey et al. Biol Psychol 2013;92:541-48

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Hypoarousal: SCR & Startle

Rothemund et al. Biol Psychol 2012;90:50-9
Hypoarousal: Cortisol

Hypoarousal: Cortisol

Holi et al. Psychopathol 2006;39:102-4

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Hypoarousal: Anti-ACTH Antibody

Anti-ACTH & Cortisol Response


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Role for Testosterone?

![Graph showing predicted cortisol in HLM model for low ICU and high ICU groups with increasing testosterone levels.]

Johnson et al. Dev Psychobiol JT 2014;56:448-58

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## Heritability

<table>
<thead>
<tr>
<th></th>
<th>Proband standardised mean (SD)</th>
<th>Co-twin standardised mean (SD)</th>
<th>Transformed co-twin mean</th>
<th>h²g</th>
<th>c²g</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a) Extreme callous-unemotional MZ twins (N = 612)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MZ twins</td>
<td>1.79 (.56)</td>
<td>1.30 (.96)</td>
<td>.73</td>
<td>.67 (.47-.87)</td>
<td>.06 (-.23-.35)</td>
</tr>
<tr>
<td>DZ twins</td>
<td>1.80 (.57)</td>
<td>.71 (1.05)</td>
<td>.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>b) Extreme antisocial behaviour in children with psychopathic tendencies (N = 234)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MZ twins</td>
<td>2.82 (1.13)</td>
<td>2.15 (1.52)</td>
<td>.76</td>
<td>.81 (.50-1.12)</td>
<td>-.05 (.00-.72)</td>
</tr>
<tr>
<td>DZ twins</td>
<td>2.81 (1.26)</td>
<td>1.00 (1.72)</td>
<td>.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>c) Extreme antisocial behaviour in children without psychopathic tendencies (N = 210)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MZ twins</td>
<td>2.02 (.62)</td>
<td>1.29 (1.24)</td>
<td>.64</td>
<td>.30 (-.10-.70)</td>
<td>.34 (-.40-1.08)</td>
</tr>
<tr>
<td>DZ twins</td>
<td>2.15 (.88)</td>
<td>1.05 (1.66)</td>
<td>.49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Persistence

Predicting Possible Psychopathy at Age 24 with Age 13 Psychopathy

<table>
<thead>
<tr>
<th>Age 13 Psychopathy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPP</th>
<th>NPP</th>
<th>LR+</th>
<th>phi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Top 30%</td>
<td>0.62</td>
<td>0.73</td>
<td>0.16</td>
<td>0.96</td>
<td>2.30</td>
<td>0.20**</td>
</tr>
<tr>
<td>Top 25%</td>
<td>0.48</td>
<td>0.77</td>
<td>0.15</td>
<td>0.95</td>
<td>2.09</td>
<td>0.15*</td>
</tr>
<tr>
<td>Top 20%</td>
<td>0.43</td>
<td>0.82</td>
<td>0.16</td>
<td>0.94</td>
<td>2.39</td>
<td>0.16**</td>
</tr>
<tr>
<td>Top 15%</td>
<td>0.38</td>
<td>0.88</td>
<td>0.22</td>
<td>0.94</td>
<td>3.17</td>
<td>0.21**</td>
</tr>
<tr>
<td>Top 10%</td>
<td>0.29</td>
<td>0.91</td>
<td>0.21</td>
<td>0.94</td>
<td>3.22</td>
<td>0.17**</td>
</tr>
<tr>
<td>Top 5%</td>
<td>0.14</td>
<td>0.96</td>
<td>0.29</td>
<td>0.93</td>
<td>3.50</td>
<td>0.12*</td>
</tr>
</tbody>
</table>

Neural Basis of Moral Deficits

Moral and antisocial

Medial PFC

Posterior cingulate

Ventromedial PFC

Amygdala

Superior temporal gyrus

Angular gyrus

Medial PFC
Neural Basis of Social Behaviour


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Neural Basis of Social Behaviour


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Cognitive Model of Psychopathy

- Genetic and environmental factors:
  - Perinatal factors
  - Genetic factors
  - Trauma, violence and neglect

- Neural:
  - Decreased amygdala responsiveness
  - Decreased striatal and vmPFC responsiveness

- Cognitive:
  - Reduced emotional empathy
  - Impaired decision making
  - Increased threat sensitivity

- Behavioural:
  - Callous-unemotional traits
  - Antisocial behaviour and instrumental aggression
  - Frustration-based reactive aggression
  - Under-regulated responses to social provocation
  - Threat-based reactive aggression
  - Anxiety

Blair. Nat Rev Neurosci 2013;14:786-99

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Neural Basis of Deficits

Blair. Nat Rev Neurosci 2013;14:786-99
Neural Basis of Deficits

Blair. Nat Rev Neurosci 2013;14:786-99

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Amygdalal Connectivity


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Amygdalal Connectivity

OXTR and AVPR Genes


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OXTR & Social Neurosignalling

### OXT/AVP: Behavioural Effects

<table>
<thead>
<tr>
<th>Neuropeptide</th>
<th>Effects</th>
</tr>
</thead>
</table>
| OXT          | ↓ cortisol during social stress  
              | ↓ amygdala during social stress  
              | ↑ empathic accuracy  
              | ↑ eye gaze |
| AVP          | ↑ cortisol during social stress  
              | ↓ trustingness in males  
              | ↑ trustingness in females  
              | ↓ social motivation |
Integrative Model


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Studies of OXTR and Psychopathy

Children with ↑ CU traits have:
- OXTR polymorphisms
- Greater OXTR methylation

...but we don't know much more!
Research Questions

1. (How) would exogenous OXT/AVP alter psychopathic cognition?

2. Do HPA/HPG axis function play moderating or mediating roles?

3. Are changes in OXT/AVP system a state or trait phenomenon in psychopathy?

4. Is OXT integral to theory of mind, or vice versa?
Summary

- Significant public health issue
- Hereditary and persistent
- Deficits in social-emotional processing
- Generalized autonomic hypoarousal
- Significant endocrine correlates
- Impaired amygdalal fx & connectivity