EXPOSURE TO METHAMPHETAMINE PRENATALLY MODIFIES WHITE MATTER INTEGRITY AND NEURO-COGNITIVE FUNCTION IN CHILDREN

Annerine Roos
Stellenbosch University
Cape Town, South Africa
Prevalence and mechanism

- Significant increase in methamphetamine (MA) use in pregnant women:
  - USA: 8% in 1994 to 24% in 2006\(^1\)
  - South Africa: 7% of local Cape population\(^2\)
    - Women (aged 20 years, 64% mixed race):
      - 66% non-pregnant – 238 out of 356;
      - 92% pregnant – 24 out of 26 women

- Dopamine involved in reward, motivation and pleasure
- MA increases release and blocks reuptake of dopamine
  - High levels in the brain create a “rush” that becomes less over time with deeper and longer “lows”.

\(^1\)Terplan et al, 2009; \(^2\)Jones et al, 2011
Mechanism and potential effects

- MA neurotoxic to dopamine and serotonergic receptors³
- Brain imaging studies:
  - altered white matter integrity in dopamine-rich striatal areas, and connecting frontal and parietal areas.⁴,⁵
- MA may also affect motor coordination, executive function, attention and memory in children⁶

However, few studies document the neural effects that prenatal MA-exposure may have on child development.

³McCann & Ricaurte, 2004; ⁴Colby et al, 2012; ⁵Cloak et al, 2009; ⁶Chang et al, 2004
Diffusion tensor imaging (DTI)

- DTI measures white matter integrity in the following ways:
  - Fractional Anisotropy (FA) – principal diffusion along axons. Lower FA indicate damage/disorganization of tracts.
  - Mean Diffusivity (MD) – global average of diffusion directions. Higher MD indicate general diffusion disruption.
  - Radial Diffusivity (RD) – perpendicular diffusion towards membranes. Higher RD indicate myelin degeneration or damage.
  - Axial Diffusivity (AD) – diffusion along axons. Lower AD indicate axonal damage.

Beaulieu et al, 2002
Aims

- To investigate white matter integrity and associations with cognitive performance in children with prenatal MA exposure, compared to healthy controls as measured by DTI.
Methods

- **Participants (6-7 years of age):**
  - 17 MA exposed children (9 males, 8 females)
  - 15 healthy controls (5 males, 10 females).

- **DTI imaging:**
  - Siemens Allegra 3T MRI scanner

- **Cognitive Assessments:**
  - *Executive function and memory*: Kaufman Assessment Battery for Children-II, Boston Naming Test, Grooved Pegboard
Data analyses

- **Tract-Based Spatial Statistics (TBSS):**
  - A tool to create a mean FA white matter “skeleton” to map individual diffusion data, and determine group differences.

- **GLM using FSL and Statistica:**
  - To investigate differences between groups in white matter parameters, and associations with neuropsychological variables.
  - Controlled for gender and smoking status.
  - Corrected p-values at p<0.05.
Results

Changes in white matter integrity:

- ↓ FA
- ↑ MD and ↑ RD ($p<.01)$:
  - Left external capsule [a], and
  - Bilateral fornix stria terminalis [b].
- Tracts traversing striatum, limbic and frontal areas

Associations of FA with poorer cognitive performance ($p<.05)$:
- Motor coordination $\rightarrow$
  - ↑ FA in right external capsule
- Executive function $\rightarrow$
  - ↓ FA in right external capsule
  - ↑ FA in fornix stria terminalis
Discussion

- Dopamine-rich striatum targeted by methamphetamines
- Altered white matter integrity in striatum, and frontal areas\(^8,^9\)
- Main diffusion parameters were affected -
  - general and specific disruptions of white matter tracts
- Poor organization and pruning of brain networks implicated in the developing brain of children due to prenatal substance exposure\(^{11}\)
- Associations of poorer motor coordination and executive function with FA in striatal and frontal areas\(^8,^10\)
- Compensatory organisation of brain circuitry may explain why FA is higher in some tracts and lower in others in relation to executive function; the connectivity of one network may be strengthened at the expense of another network that is inefficient.\(^{12}\)

\(^{8}\text{Colby et al, 2012; }^{9}\text{Cloak et al, 2009; }^{10}\text{Sowell et al, 2010; }^{11}\text{Lebel et al, 2012; }^{12}\text{Roussotte et al, 2012}\)
Discussion

- Limitations:
  - Small sample size
  - Accuracy of reporting on drug use
  - Polysubstance use e.g. of alcohol and nicotine
  - Poverty and other environmental factors may affect brain structure,
    yet participants were from similar SES, ethnicity, and matched for age and gender.

- Future longitudinal studies may clarify how prenatal MA exposure affects white matter structural connectivity at different stages of brain maturation.
Thank you

The Team
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