PRENATAL METHAMPHETAMINE EXPOSURE IS ASSOCIATED WITH SMALLER CAUDATE VOLUMES IN NEONATES

Fleur L Warton[1], Ernesta M Meintjes[1,2], Christopher MR Warton[1], Christopher D Molteno[3], Pia Wintermark[4], Andre van der Kouwe[5], Joseph Jacobson[1,3,6], Sandra Jacobson[1,3,6]

[1]Department of Human Biology, Faculty of Health Sciences, University of Cape Town, South Africa; [2]MRC/UCT Medical Imaging Research Unit, Faculty of Health Sciences, University of Cape Town, South Africa; [3]Department of Psychiatry, Faculty of Health Sciences, University of Cape Town, South Africa; [4]Department of Pediatrics, McGill University, Montreal Children's Hospital, Montreal, Canada; [5]Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA; [6]Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI, USA

INTRODUCTION

- Methamphetamine (Meth) use has been linked to dopaminergic neuron damage[1,2].
- Prenatal exposure to Meth (PEM) is associated with neuropsychological, behavioural and cognitive alterations[2,3,4].
- Few neuroimaging studies have examined structural effects in children with PEM:
  - MRS and DTI have shown alteration in neurometabolism and micro-structure[5,6.]
  - MRI has shown volumetric changes in a number of brain regions
- No studies of PEM-associated volumetric changes in the neonatal brain.
- Studies in neonates allow the separation of prenatal drug exposure effects from potential confounding effects of a poor postnatal environment

METHODS

- Cape Coloured mothers were recruited prenatally and interviewed 3x during pregnancy regarding Meth use:
  - Exposed mothers reported using Meth at least twice per month during pregnancy,
  - Control mothers had no exposure to Meth/other drugs, minimal/no exposure to alcohol (no more than 2 drinks no more than 2x during pregnancy).
- 16 infants were scanned without use of sedation on a 3T Siemens Allegra using a circularly-polarised birdcage coil, custom built for use with neonates.
- Two multiecho gradient echo acquisitions were performed with flip angles 5 and 20 degrees respectively
  - Imaging parameters were: FOV 144mm, 128 slices, TR 20ms, TE 1.46/ 3.14/ 4.82/ 6.5/ 8.18/ 9.86/ 11.54/ 13.22ms, 1mm^3 isotropic resolution.
  - Individual echoes from the two acquisitions were split, tissue parameters estimated and image volumes synthesised at an optimal contrast flip angle of 24°.
- The caudate nuclei were manually traced and the volumes calculated using FreeView software (FreeSurfer image analysis suite http://surfer.nmr.mgh.harvard.edu/).

RESULTS

	Controls (n=10)	Meth - exposed (n=6)	*p*
Sex (M/F)	8/2	4/2	
Gestational age (wk)			
Mean	41.7 ± 2.4	41.3 ± 2.4	0.73
Birth Weight (g)			
Mean	3113 ± 258	2950 ± 469	0.46
Cigarettes (/day)			
Mean	3.0 ± 3.2	8.1 ± 7.0	0.06
Meth (days/month)			
Mean	0	7.2 ± 10.7	**0.046**
Range	0	1.4 - 28.6*	
Left caudate (mm^3)			
Mean	1314 ± 139	1192 ± 176	0.15
Right caudate (mm^3)			
Mean	1295 ± 108	1182 ± 159	0.11

Table 1. Neonatal characteristics for methamphetamine-exposed and healthy control infants. *Highest data point (28.6, an extreme outlier) was recoded to 7, which is 1 point higher than the next highest observed value.

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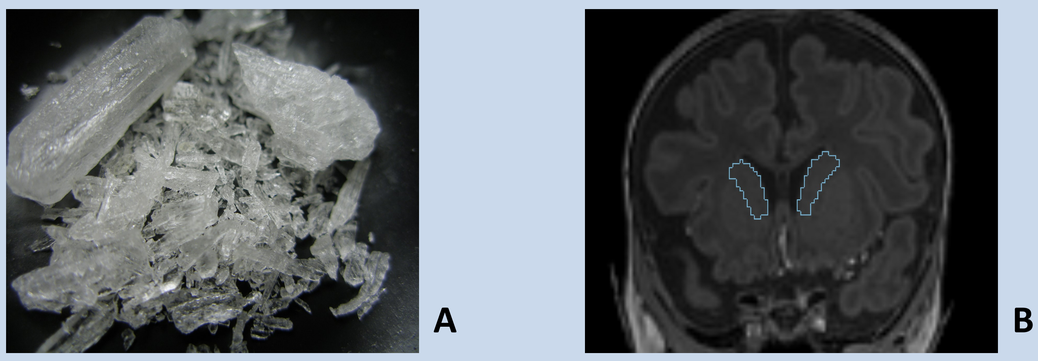

Figure 1. ***A****. Crystal methamphetamine.* ***B****. Left and right caudates traced in coronal view.*

- The caudates of the PEM group were smaller than those of the controls, but the difference fell short of statistical significance
- When PEM was treated as a continuous variable (days/month), there was a strong negative correlation between PEM and bilateral caudate volume
  - Left: r = -.66, p = 0.005
  - Right: r = -.67, p = 0.005
- These associations remained significant after controlling for maternal smoking and infant sex
  - Left: pr = -.56, p = 0.39
  - Right: pr = -.70, p = 0.005

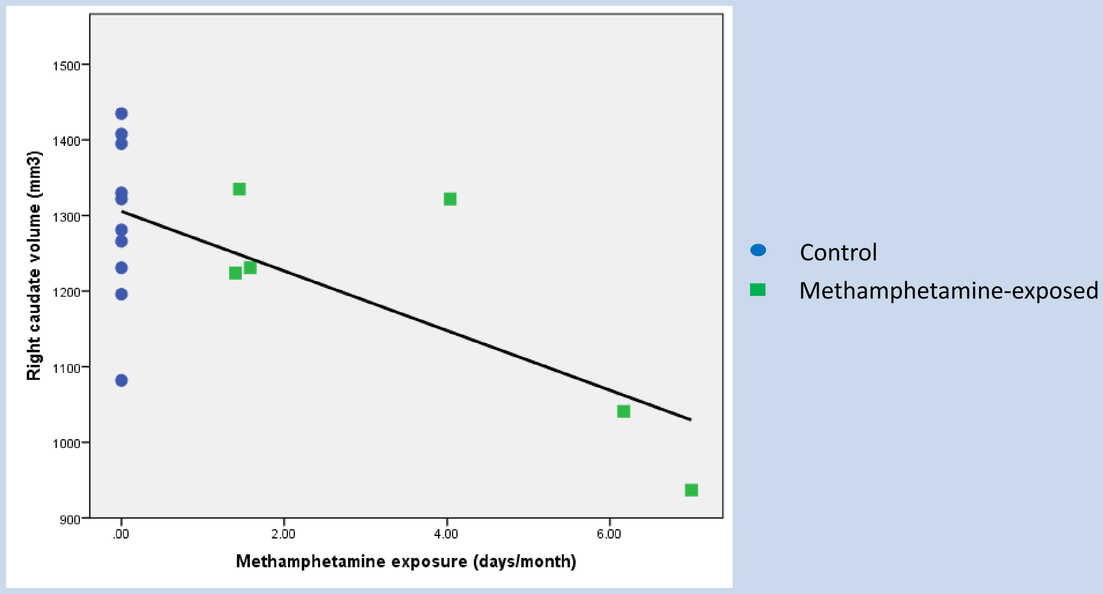

Figure 2. Relation between degree of methamphetamine exposure and right caudate volume. One outlier on methamphetamine exposure was recoded.

CONCLUSION

Increasing meth exposure was strongly associated with bilateral reduction in caudate volume in the brains of newborn infants, providing evidence for a dose-dependent effect. This novel finding corroborates evidence of reduced volume of the striatum in older children with PEM[7], and supports the hypothesis that PEM induces long-lasting changes in dopamine-rich regions of the brain and that these can already be detected in neonates.

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