Pediatric Neurology 52 (2015) 326–332

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Child Neuroanatomical, Neurocognitive, and Visual Acuity Outcomes With Maternal Opioid and Polysubstance Detoxification

Kristine B. Walhovd PhD [a,b,*], Astrid Bjørnebekk PhD [a,b], Kristin Haabrekke Cand Psychol [c,d], Torill Siqveland PhD [d], Kari Slinning PhD [c,d], Egil Nygaard PhD [a], Anders M. Fjell PhD [a,b], Paulina Due-Tønnessen MD [a,e], Atle Bjørnerud PhD [a,f], Vibeke Moe PhD [c,d]

[a] *Research Group for Lifespan Changes in Brain and Cognition, Department of Psychology, University of Oslo, Norway*
[b] *Department of Physical Medicine and Rehabilitation, Unit of Neuropsychology, Oslo University Hospital, Oslo, Norway*
[c] *The Center for Child and Adolescent Mental Health, Eastern and Southern Norway, Oslo, Norway*
[d] *Department of Psychology, University of Oslo, Oslo, Norway*
[e] *Department of Radiology, Section of Neuroradiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway*
[f] *Intervention Center, Oslo University Hospital, Rikshospitalet, Oslo, Norway*

ABSTRACT

BACKGROUND: Maternal opioid and polysubstance use during pregnancy is associated with an increased risk of child neurocognitive and visual problems and neuroanatomical differences. We hypothesized that, in contrast to findings from a previous study of children born to mothers not detoxified, children born to detoxified mothers would not show gross neuroanatomical and neurocognitive differences. **METHODS:** Mothers with opioid and polysusbstance abuse problems and their infants (n = 11 + 12) were recruited from residential treatment institutions. Comparison mothers and infants (n = 12 + 12) were recruited from child health centers. The studies were approved by the Regional Committee of Medical Research Ethics. Children had magnetic resonance imaging scanning, neurocognitive, and visual acuity testing at 4.5 years. Neuroanatomical, cognitive, and visual acuity characteristics were compared across groups by analysis of variance and general linear models. **RESULTS:** There were no significant differences across groups in neuroanatomical volumes, or cortical thickness, area, or volume. There were no differences in general neurocognitive functioning, but significantly lower left eye visual acuity, and a trend toward lower binocular visual acuity, in the drug-exposed relative to the comparison group. **CONCLUSIONS:** The present study does not demonstrate gross differences relative to a comparison group in neuroanatomical and general neurocognitive characteristics of children born to mothers with opioid and polysubstance abuse who were detoxified during pregnancy. However, visual acuity was significantly lower in the drug-exposed group, requiring attention. There is a pressing need for additional and larger studies of long-term and specific child outcomes in this at-risk group.

Keywords: opioid, detoxification, brain, MRI, neurocognitive, vision, development, outcome

Pediatr Neurol 2015; 52: 326-332

Introduction

Children born to women using opioids and illicit drugs during pregnancy are at increased risk for neuropsychological and mental health difficulties.[1-6] Although some of these difficulties may be associated with increased postnatal risk,[7] maternal opioid and polysubstance abuse may also directly affect the developing central nervous system prenatally.[8-12] A few years ago, we published the first articles showing that children born to mothers with opioid and polysubstance abuse during pregnancy who were raised by adoptive parents in optimized environments nonetheless showed significantly lower neuroanatomical volumes, white matter

Article History:
Received September 4, 2014; Accepted in final form November 18, 2014
* Communications should be addressed to: Walhovd; Department of Psychology; University of Oslo; PO Box 1094 Blindern; 0317 Oslo.
E-mail address: k.b.walhovd@psykologi.uio.no

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http://dx.doi.org/10.1016/j.pediatrneurol.2014.11.008

microstructural maturation, and neurocognitive function than a comparison group.[13,14] We have also recently documented altered neural tract development in methadone-exposed children.[15]

It is not clear to what extent the observed group's differences and difficulties are due to the direct teratogenic effects of opioid and polysubstance exposure during pregnancy, the indirect effects of psychosocial risk associated with the lifestyle of maternal substance use, or genetic vulnerabilities. In all likelihood, no human clinical study can fully disentangle these effects. Opioid maintenance therapy (OMT) has been the preferred treatment for opioid dependence during pregnancy since the early 1970s, and recent numbers suggest that maternal opioid use is rising.[16] Thus it is paradoxical that we know little of the long-term development of children born to opioid-dependent women.[17] In addition to OMT, one option for opioid- and substance-dependent pregnant women may be detoxification. The safety of detoxification has been debated, but few studies exist to document outcomes. Recent exceptions report significant increases in birth weight and gestational age relative to children born to mothers with illicit drug use at delivery.[18,19] However, long-term outcomes are unknown.

In the present article, we examine brain and neurocognitive outcomes of children born to mothers who were hospitalized and detoxified during their pregnancies, hence reducing prenatal opioid and drug exposure. The parents retained custody after birth (see the following section). Although lessening prenatal exposure, postnatal environments are assumed to retain risk factors. We describe the brain and neurocognitive outcomes of these children at age 4.5 years. Furthermore, we discuss these data relative to brain and neurocognitive outcomes of the children in our previous study cohort, who had drug exposure throughout much of their fetal life, but whose postnatal environments were optimized. Gross neuroanatomical differences and neurocognitive correlates were found in children with opioid and polysubstance exposure throughout pregnancy,[13] and there are known central nervous system pathways that may cause these directly prenatally.[8-10] Hence, our hypothesis was that the present children, whom had considerably less prenatal exposure, would evince less neuroanatomical and neurocognitive differences despite less optimized postnatal environments.

Participants and methods

The sample consists of mothers and their infants born in between 2004 and 2008. A more detailed description of the sample and birth outcomes is given elsewhere.[19] The focus of this article is neuroanatomical and neurocognitive outcomes of children whose mothers were detoxified during pregnancy relative to a nonrisk comparison group. The mothers in the substance-associated risk group were recruited from five different residential treatment institutions in Norway. The mothers in the comparison group were recruited from child health centers in Oslo. Originally, 33 mothers of 34 children were recruited for the study group and 30 for the comparison group. In the present sample, we included only children who had neurocognitive testing at 4.5 years (risk group n = 22, comparison group n = 26), who consented to magnetic resonance imaging (MRI) scanning (risk n = 18, comparison n = 18). For some of these, usable MRI data were not obtained (risk n = 1, comparison n = 6) because they did not complete the scanning (e.g. expressed fear of lying down in the scanner, scanning noises, excess movement). Hence, useable MRI data were obtained for 29 children (risk n = 17, comparison n = 12). Furthermore, in the risk group, we included only children whose mothers themselves had reported using illicit drugs during pregnancy and underwent detoxification. For one of the mothers of these 17 children, data on drug use were missing, and three mothers stated that they had not used any illicit drugs during their pregnancies (e.g., one used prescription methadone on a daily basis throughout pregnancy, two said the used because of their residential treatment partner's drug use or fear of relapse). One child in the risk group had a venous malformation in the left orbita, also affecting soft tissue of the left eyeball. There was a left temporal lobe meningoencephalocele and dysplastic changes in the same area, previously documented and likely present at birth. Neural tube defects may in and of themselves be associated with prenatal drug exposure, including opioids,[20] and one case of spina bifida was included in an independent sample of children prenatally exposed to maternal opioid and polysubstance abuse previously published.[13] However, because the present case involved anomalies in the cerebrum, we chose to exclude this child from the present analyses. Hence, data for 12 children were included in the risk group. There was one fraternal twin pregnancy in the risk group; all others were singleton pregnancies. A subset of analyses on birth parameters was rerun with and without the twins included. At the time of the 4.5-year follow-up, three of the children included in the risk group were in foster care, whereas the others lived with their biological parents. A flow chart depicting the study and participant exclusion/inclusion is given in Supplementary Figure 1. The study was approved by the Regional Committee of Research Ethics, and parents and caregivers gave informed consent.

Residential treatment and detoxification

In Norway, there are currently multiple treatment opportunities for pregnant women with substance dependence. For pregnant women who are already enrolled in the OMT program, it is recommended that they continue the medication during pregnancy,[21,22] although the women also have the option of tapering off if they wish. Multiple inpatient clinics specialize in medically supervised detoxification in a residential setting where pregnant women with untreated substance dependence get medical and psychological support to become drug-free during their pregnancies. Pregnant women in OMT who wish to taper off as well as women with opioid and polysubstance dependence who are not in OMT can voluntarily receive help in these residential clinics. In addition, Norwegian legislation since 1996 (cf. Social Service Law § 6-2a, replaced by the Act for Municipal Health and Care Services, Section 10-3 in January 2012) authorizes detention of pregnant substance-using women in residential treatment to protect the fetus. In general, the institutions in the study provide medical supervision of the mothers where possible abstinence is monitored closely. To prevent severe abstinence, opioid agonists and pain relief medication are prescribed in a transitional phase and tapered off. When treating a pregnant woman with substance dependence, her individual state and situation is taken into careful consideration. Hence, a detailed common detoxification protocol unfortunately cannot be provided, except in the situations described here. Close monitoring as well as a supporting environment are provided. While staying in residential care, the mothers and in some cases their partners live together with other families. They receive help and guidance from professional therapists with regard to nutrition, housekeeping, and economy as well as social interaction and psychological treatment. The parents have the possibility of staying in the residences with their children up to 1 year after birth.

Maternal, drug exposure, and birth characteristics

Of the 11 women included in the risk group, seven were in residential treatment on a voluntarily basis, whereas four were admitted to treatment based on the Social Service Law §6-2a. All mothers gave written consent to participate in the study. The mean number of days of pregnancy at the time of admission was 149 (standard deviation [SD] = 69, range 64-255). Three of the mothers were admitted into treatment in their first trimester (≤84 days), four in their second trimester (85-182 days), and four in their third trimester (≥183) days. All were detoxified as part of the institutional treatment.