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The Effects of Prenatal Buprenorphine Exposure on the Neurobehavioral Development of the Child

Zaineb Zubair
Rowan University

Maryam Zubair
Rowan University

Juan Alonso
Rowan University

Abdullah Zubair
Rowan University

ROWAN-VIRTUA School of Osteopathic Medicine

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Zaineb Zubair, BS., Maryam Zubair, MD., Juan Alonso, BS., Abdullah Zubair, MD

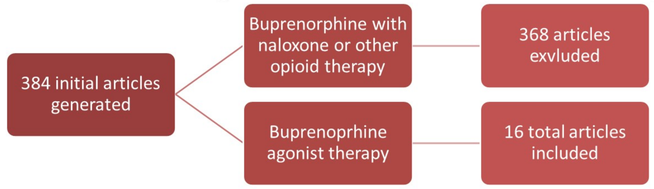
Background

- Neurobehavior encompasses an infant's ability to understand and respond to appropriate stimulation as a product of their central and peripheral nervous system development and coordination.
- Neurobehavior is significantly affected by mu opioid receptor stimulation and therefore by opioid use disorders.
- Current guidelines for pregnant women with substance use disorders advise prenatal maintenance of opioid agonist therapy using buprenorphine.
- Studies have shown that buprenorphine has had better outcomes with neonatal abstinence syndrome within the first month of life compared to other opioid agonist therapies and has therefore been deemed safe and effective.
- Very few studies have been conducted on the child's neurobehavioral development beyond the first month of life.
- Many scales and tools have been developed to assess various aspects of neurobehavioral development. All are listed below:

NICU Network Neurobehavioral Scale	• Neonatal Behavioral Scale • Measures the effects of stimulants on behavioral state, sensory, and interactive responses
Enfant 4010	• Uses stimuli generated from a computer • Measures visual evoked potentials • Visual evoked potentials measures the maturation of central nervous system (CNS)
Infant Toddler Sensory Profile	• Standardized assessment using a caregiver questionnaire • Measures child's sensory processing abilities
Wechsler Preschool and Primary Scale of Intelligence (WPPSI-R)	• IQ test to assess a child's verbal and performance scores and processing speed • Ages 2 and up • Measures comprehension, sentences and other subsets of these two
McCarthy Scale of Children's Abilities (MSCA)	• Psychological test • Children ages 2 and up • 5 scales: verbal, perpetual performance, quantitative, memory, and motor
Brown Attention Deficit Disorder and Strengths and Difficulties Questionnaire	• Children ages 3 and up • Scales used for impairment of executive functions and behavior

Methods

- A literature review was generated using key search terms
- The articles were then sorted based on the inclusion and exclusion criteria. This was sorted multiple times independently by the authors.
- The literature review was performed on PubMed, Dynamed, and Rowan University Library databases.
- All publications from 2002, since buprenorphine was approved by the USA Food and Drug administration, were pulled for analysis.



Results

- The literature review revealed that the available studies broadly covered three stages of life: fetal, neonatal/infant, and toddler.
- Neonatal and infant were combined into one category due to studies overlapping these similar ages or using the terms interchangeably.

Fetal

- More likely to exhibit higher level of fetal heart rate variability that eventually normalized later in gestation
- **Less motor activity** regardless of gestational age

Neonatal/Infant

- More likely to have depressed **initial** ability to self-regulate with poor quality of movement
- Infants eventually showed **no significant residual deficiency** in neurological development

Toddler

- Various results
- Some studies showed no significant deviations from normal development
- Some showed **significant cognitive and motor underdevelopment**, especially around preschool-aged children
- **All** buprenorphine-exposed children met the criteria for ADHD

Conclusion

- There are no current studies with children over the age of 3 years old, despite prenatal buprenorphine use for over 20 years
- Long-term effects seem to vary based on the scales used to measure neurobehavioral development
- Genetic studies done on rodents indicate a long-term effect of buprenorphine on the central nervous system that might result in decreased neurogenesis that has yet to be addressed because of a lack of longitudinal research in children and adolescents
- There are multiple limitations to this literature review:
  - Inconsistent scales to measure neurobehavioral development
  - Various control groups amongst the different studies causing a lack of consistency when comparing the data
  - Factors that influence neurobehavioral development were isolated differently amongst each study, such as tobacco use, other illicit drug use, etc.

Clinical Relevance

- These results reveal an overarching need of further longitudinal studies beyond the preschool age
- Potential long-term effects of opioid agonist therapy could necessitate change of the current guidelines and policies in place
- There are many limitations in this review that the field of addiction medicine could benefit from further exploration
- Further research could benefit from assessing specific neurobehavioral outcomes throughout various ages since there are so many subsets of neurobehavioral development

References