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Nghi M. Nguyen

Jordan Hernandez

Adrian Flores

Jina Yi

Reeyan Bhakat

See next page for additional authors

Authors

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Child Health Research Institute

University of Nebraska Medical Center

Children's Hospital & Medical Center

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Nghi M Nguyen[1,2], Jordan Hernandez [2], Adrian Flores [1,3], Jina Yi [1,4], Reeyan Bhakat [5], Neetha N. Vellichiramma [2], Chittibabu Guda [2], Somwya Yelamanchili [1], and Gurudutt N. Pendyala[1,3]*

[1]Department of Anesthesiology, University of Nebraska Medical Center (UNMC), Omaha, NE

[2]Department of Genetics, Cellular Biology, and Anatomy, UNMC, Omaha, NE

[3]Department of Cellular and Integrative Physiology, UNMC, Omaha, NE

[4]Department of Pharmacology & Experimental Neuroscience, UNMC, Omaha, NE

[5]Department of Neuroscience, University of Southern California, Los Angeles, CA

*Correspondence: gpendyala@unmc.edu; Tel.: +1-402-559-8690

Epidemiologic studies of human patients have revealed a correlation between childhood exposure to general anesthetic and sedative agents and subsequent cognitive deficits. This association is supported by data from animal models, which shows that developmental exposure to both anesthetics and sedatives causes lasting impairments in learning. This study focused on midazolam (MDZ), a common benzodiazepine regularly used as a sedative agent on neonates in the Neonatal Intensive Care Unit (NICU). However, a knowledge gap that remains is how long-term exposure to MDZ during very early stages of life impacts synaptic alterations and neurobiological mechanisms. Elucidation of these mechanisms is of high clinical importance and may develop neuroprotective therapeutic strategies for optimizing outcomes for uniquely vulnerable NICU populations. Using a preclinical rodent model system, we mimicked a dose-escalation regimen from postnatal day 3 (P3) pups until P21 to comprehensively characterize how early-life exposure to MDZ impacts neurodevelopment outcomes at different tiers — phenotypic, molecular, behavioral, and high throughput- "omics" levels. Our data demonstrated that repetitive exposure to MDZ at an early age stunts neurodevelopment during the early stages of life disrupts the blood-brain barrier, and alters the synaptic components and neurochemistry, which may be indicative of behavioral deficits at later development. Additionally, our bioinformatics analysis from purified synaptosome identified enrichment of proteins associated with actin-binding and protein depolymerization process. One potential hit identified was alpha adducin (ADD1), belonging to the family of cytoskeleton proteins, upregulated in the MDZ group and whose expression was further validated by western blot. Our study has provided a comprehensive characterization of MDZ effects on development at multiple tiers yielding novel insights on how long-term exposure to MDZ impacts development. Notably, the identification of ADD1 as a potential target and further characterization of its downstream mechanisms can give additional insights into its role as a potential therapeutic for treating neurodevelopmental alterations associated with long-term MDZ use in neonates.