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Crisis in the NICU and the Medley with Midazolam

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Extremely preterm neonates (<28-week of gestation) are often exposed to repetitive and high doses of sedative medications to minimize pain and agitation from invasive procedures such as surgery and mechanical ventilation. The intensive use of analgesics and sedation in the Neonatal Intensive Care Unit (NICU) has been raising concerns about the potential implications for brain and cognitive development. Midazolam (MDZ), a short-acting benzodiazepine, is widely used as a sedative agent in the NICU. Previous literature has provided evidence that the use of anesthetics or sedative agents during the brain growth spurt, a maturation period that occurs postnatally in mammals, leads to higher synaptic alterations due to accelerated programmed cell death (apoptosis). However, there remains existing gaps on how such early-life exposure to MDZ impacts other key neurodevelopment processes and behavior during adolescence and if these changes persist into adulthood. Using preclinical animal system, we employ a comprehensive characterization on how early life exposure to midazolam impacts neurodevelopment outcomes at different tiers – phenotypic, molecular, behavioral, and high throughput- “omics” levels. Our preliminary data demonstrated that chronic 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. The results from this study will provide better understanding on MDZ effects on neurodevelopment and provide potential therapeutic targets to overcome the neurodevelopmental issues that may arise from frequent use of MDZ in neonates.