PERINATAL NEUROTRAUMA: A FRESH CONCEPT IN PEDIATRIC BRAIN INJURY RESEARCH

Pediatric brain injury research has yet to fully recognize intrapartum environmental incompatibilities as potentially contributory. Epidemiological studies link exposures introduced during childbirth with neuropsychiatric outcomes, justifying the emerging conceptualization of *perinatal neurotrauma.* Plausibly, a constellation of interacting complexities involving early exposure mechanisms, impacted by elevated maternal body mass index (BMI), could confer a disruptive cascade of neural events which risk future functional and behavioral childhood impairments.

Rising child neuropsychiatric conditions have established association with childbirth complications. Concomitant symptoms of emotional dysregulation, social/academic deficits and neurocognitive deficits persist into adulthood. Precise etiology is unclear, yet complex genetics, epigenetics, pregnancy/childbirth complications appear involved; genetics alone unlikely trigger these outcomes. Logically, perinatal dynamics experienced during highly sensitive developmental periods may adversely impact the malleable fetal brain with risky downstream effects, influencing neurodevelopment.

One specific exposure, synthetic oxytocin (sOT), a synthetic uterine stimulant, usefully expedites >50% of all U.S. childbirths, despite its poorly understood fetal impact. Established repercussions include fetal distress, low Apgar scores, uterine hyperactivity, FHR abnormalities, NICU admissions and ischemia/asphyxia/hypoxia. Putative neuropathophysiological models include fetal intolerance to dose-dependent thresholds; prolonged labor impact; epigenetic triggering, oxytocin receptor hyperstimulation and/or oversaturation; neuroinflammation; hypertonic uterine contraction pressure imposing neuropathogenic alterations/diffuse axonal injury; disharmonious epidural anesthesia, GABA downregulation; blood-brain barrier/placental permeability compromising fetal neuroprotection; and pharmacokinetics of sOT synthesis, involving reagent properties which may threaten placental integrity.

Neuropathogenic alterations linked to perinatal sOT lack confirmation, yet research directly associates this exposure to neuropsychiatric phenotypic presentations with mixed evidence. Exponential increases in sOT intervention, including elective inductions, and dosage inconsistencies amplify concerns regarding potential consequences to child neurodevelopmental trajectory. Labor duration and sOT exposure duration are important algorithms to disentangle, since sOT use is a modifiable exposure.

Interestingly, maternal BMI/adiposity increases odds for newborn LGA/macrosomia and sOT-assisted childbirth due to poor uterine contractility in obese mothers. The shared impact of maternal BMI with perinatal sOT exposure, and its two-fold effect on offspring brain development, is uninvestigated. A temporal relationship could exist between these two factors and disrupted pediatric neurodevelopment.

Common sense biology informs us that the fetal brain, burdened by early overlapping complexities, could shape its neurodevelopmental trajectory, collectively fostering pediatric neuropathophysiological sequelae. The novel concept of perinatal neurotrauma, including early vulnerabilities which may destabilize and/or disrupt fetal

brain development, warrants attention, and begs further investigation as an important child public health issue.

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