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The first 1000 days influence life-course brain health: interdisciplinary fetal/neonatal neurology training

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Newborn Brain Society (NBS) leadership presented survey results from participants in neonatal neurocritical care programs (NNCCPs).[1] Responses were tabulated from established NNCCP programs, primarily completed by neonatologists and child neurologists. Improved competency assessments across skillsets were broadly discussed. Training recommendations focused on high-risk neonatal care. Between 50 and 70% of programs are >5 years old, with 1- or 2-year training experiences. Approximately half of the trainees published scholarly contributions. These co-authors acknowledged limited opportunities for training without standardization by existing programs. Novel curricula were generally suggested to complement traditional neonatal neurocritical care training, applying educational goals for physicians from diverse backgrounds. No details were provided to critically consider how programs can be improved to provide training of prenatal, neonatal, and pediatric information.

Worldwide NNCCPs continue to expand, given growing interests in neonatal neurology by professional organizations similar to the NBS. Organizational objectives broadly support the dissemination of information for clinical service, education, and research. The emphasis, however, remains focused on neonatal neurocritical care, often including developmental follow-up. Sophisticated technologies utilizing enhanced informatics suggest novel diagnostic approaches for trainees in educational venues focused on neonatal neurocritical care. Revised secondary source publications provide selective literature reviews, extracted from an ever-expanding body of interdisciplinary peer-reviewed literature. As in an earlier publication,[2] no details were offered regarding interdisciplinary curricula to more accurately assess variability in the therapeutic efficacy of neonatal interventions. Trimester-specific gene-environment interactions influence the maternal/placental/fetal (MPF) triad and impact the postnatal expression of neonatal health or disease.

NNCCP would be more effective as one of three components of a fetal/neonatal neurology program (FNNP), assessing the MPF triad, neonate, and child from conception until 2 years of life. Developmental origins and life-course theories further integrate this training experience. Diagnostic skills regarding trimester-specific gene/environment interactions of the developing MPF triad strengthen childhood and adulthood assessments regarding brain health or disease.[3] Timelier diagnoses could apply state-of-the-art technologies for more effective preventive, rescue and reparative neurotherapeutics into old age.

Developmental neuroscience principles have applied this 1000-day perspective into national public-health programs.[4,5] Developmental neuroplasticity across the lifespan is strongly influenced by experiences during critical/sensitive periods of brain maturation. Interactions among MPF triad, neonatal and pediatric factors result in long-lasting adaptive or maladaptive neuroplasticity during these first 1,000 days. These effects maintain brain health or promote disease expression throughout adulthood and across generations.[6] Worldwide application to public health priorities will help lower the burden of disease across regions and nations.

A FNNP applies knowledge of trimester-specific mechanisms affecting the MPF triad, with resultant brain malformations and/or destructive lesions. Maladaptive MPF triad interactions impair progenitor neuronal/glial populations within transient embryonic/fetal brain structures by processes such as maternal immune activation that start during the first half of pregnancy. Destructive lesions later result during the second half of pregnancy from ischemic placental syndromes expressed as the great obstetrical syndromes.[7] Trimester-specific MPF triad diseases then negatively impact peripartum, neonatal, and pediatric outcomes.

The developmental principle of ontogenetic adaptation[3] helps guide the diagnostic process during the first 1000 days. This approach combines horizontal phenotypic identification of form and function over time with vertical systems-biology analyses at each developmental age. Effective interventions require trimester-specific identification of MPF triad phenotypes, with the application of systems biology principles from genetic through interrelated organ systems during each developmental niche.[8] This vertical perspective re-considers multi-systemic interactions for the fetus, neonate, and child. Embryonic/fetal brain alterations in neuronal connectivity occur within transient brain structures such as the ganglionic eminence and subplate zone with effects on neuronal structure and function into peripartum through delivery and childhood time periods.

The NNCCP component of a FNNP addresses diagnostic and therapeutic approaches regarding four great neonatal neurologic syndromes (GNNS) after birth; encephalopathy, conditions of prematurity associated with encephalopathy, seizures, and stroke. These complex phenotypes represent trimester-specific MPF triad experiences throughout the entire pregnancy.[3] Neurocritical care practices can provide more patient-specific diagnostic and neuroprotective efficacy when considering prenatal effects of the MPF triad for those presenting with GNNS.

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Only a minority of MPF triads present as symptomatic newborns with GNNS requiring neonatal neurointensive care. The majority remain asymptomatic or express less easily detectable diseases until childhood sequelae present. Primary care practitioners and early intervention programs become the first opportunity to consider "the first 1000-day" perspective in the outpatient clinic. Trimester-specific MPF triad and/or neonatal factors must be considered with appropriate and timely pediatric sub-specialty referrals within the pediatric component of the FNNP.

Children may present with communicable and non-communicable disorders requiring hospitalization, either altering the primarily neurologic function or as part of a multi-systemic disorder. Prenatal/neonatal conditions considerations will improve the diagnostic process for the acutely ill child. Earlier diagnoses will promote more effective preventive, rescue, and/or reparative therapeutic interventions. This 1000-day perspective fosters interdisciplinary cooperation, yielding innovative diagnostic/therapeutic pathways, educational curricula, and research agenda.

Trimester-specific curricular development should be prioritized for the FNNP trainee. Uses and limitations regarding levels of maternal care should be assessed when considering fetal brain diseases within the MPF triad. FNN topics can be applied to specific conditions affecting the MPF triad in the outpatient obstetrical setting, beginning during the first trimester. Referrals for high-risk maternal/fetal medical care offer opportunities to integrate obstetrical, genetic, and pediatric subspecialty perspectives into an interdisciplinary diagnostic approach. Antepartum fetal testing offers the FNNP trainee experiences with practical applications, emphasizing sensitivity and specificity limitations regarding positive or negative results. Consideration of trimester-specific disease processes such as maternal immune activation[9] and ischemic placental syndrome[10] introduce the trainee to the systems-biology perspectives that explain disorders affecting the developing MPF triad during specific gestational age ranges. Interdisciplinary MFM conferences and maternal hospitalizations offer opportunities to re-adjust serial assessments of MPF triads to improve peripartum and postnatal care. Cognizance of prenatal care during labor and delivery instructs the trainee on the uses and deficiencies of surveillance testing when adverse events occur closer to delivery.

Neonatal neurocritical care consultations incorporate trimester-specific MPF triad factors when evaluating complex phenotypes represented by the GNNS. Neonatal critical care rounds offer opportunities to refine a multi-systemic diagnostic process from critical care interventions through convalescent neonatal medical management. Integration of neurodiagnostic and system-specific test results includes serial neuroimaging, neurophysiological, placental/cord pathology, and genetic studies. Serial assessments better provide the healthcare team with information for the family regarding diagnosis, prognosis, and anticipatory care. Dissemination of pregnancy and hospital summaries to primary care practitioners better inform providers of the first 1000-day perspective. Pediatric critical care and subspecialty colleagues enhance the trainee's in-hospital and ambulatory evaluations, as the child experiences later medical complications.

The FNNP provides faculty with opportunities to enhance their experiences beyond formal training. Career-long learning from more experienced colleagues will strengthen the mentoring process and is mutually beneficial. These experiences can be applied for promotion, research training, and doctoral dissertations. These opportunities also improve the practitioner's diagnostic acumen by continued participation in educational venues. Research advances benefiting the MPF triad, neonate, and young child require collaborative efforts from all members of the FNNP.

Foundational familiarity with FNN can influence clinical service, educational, and scholarship perspectives beyond neonatology and pediatric neurology training. Training modules for adult neurology, psychiatry, rehabilitative medicine, health-professional therapies, and nursing need to be designed. Developmental origins of brain health and disease should be included in core training competencies for this diverse group of trainees as they embark on their specific clinical practices or academic careers. Epidemiologists, social scientists, ethicist/palliative care experts, engineers, and computer scientists add breadth and depth to this interdisciplinary training experience. Neuroinformatics and multi-modal data-set analytic skills taught by computer scientists, epidemiologists, and statisticians prepare trainees to develop appropriate research skills when reviewing the peer-reviewed literature to develop effective research collaborations. FNNP training encourages the creation of large relational datasets used by multi-center birth cohorts and interventional studies. Large and diverse populations can better analyze complicated causality pathways across disciplines.

Gene–environment interactions beginning before conception, influence short- and long-term effects on the brain development of the MPF triad, neonate, or child. Serial diagnostic assessments regarding loss or gain of genetic expression include inherited and post-mitotic alterations. Complex genetic/epigenetic mechanisms influence phenotypic expressions of diverse sequelae across the lifespan, encompassing developmental disorders, epilepsy, cerebrovascular diseases, and neurodegenerative disorders. Phenotypic heterogeneity of neurologic sequelae confronted by the pediatric and adult neurologist reflects the variable timing and severity of communicable and non-communicable diseases, influenced by factors during the first 1000 days.

Effective diagnostic/therapeutic strategies developed by the FNNP will help reduce disease burden across the lifespan. A life-course approach to the developmental origins of brain health fosters more effective healthcare policy to lower healthcare costs and improve the quality of life. Lower disease burden for women needs to be prioritized during and beyond their reproductive years. This constitutes one of the multiple sustainable goals advocated for resource-poor as well as resource-rich nations regarding women, children, and their families.[11] A socially responsible FNNP applies biopsychosocial factors to outcomes research sensitive to geographic, racial, ethnic, gender, and healthcare disparities.[3]

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COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

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