Rationale: Improvements in medicine have led to the increased survival of infants born very prematurely (<32 gestational weeks) as well as term-born infants after an episode of perinatal asphyxia. Both premature birth and an incident of hypoxia/ischemia may succeed in the damage of the constantly developing brain. In prematurely born neonates the most common brain injuries are periventricular white matter injury (PWMI) and intraventricular hemorrhage (IVH). In term-born infants, hypoxic-ischemic encephalopathy (HIE) may be a cause of neurodevelopmental impairment. Neonatal brain injuries remain an important cause of mortality and morbidity, often with life-long consequences. The mechanisms connected with the development, course, and recovery after neonatal brain injury and their impact on the disruption of the further development of the immature brain are unsatisfactorily explained. Urinary proteomics and metabolomics are hi-tech, non-invasive tools to study mechanistic data concerning cellular events and functions that may contribute to the predisposition, development, progression, diagnosis, and treatment of brain disorders. The use of advanced magnetic resonance imaging (MRI) techniques: DWI, ASL, allows for visualization of neuronal density, synaptogenesis, and myelination alterations. Proton magnetic resonance spectroscopy (^{1}H-MRS) enables non-invasive measurement of the in-vivo concentrations of neurometabolites. Moreover, these unconventional MRI techniques enable the quantitative assessment and can deliver numerical data on the concentration of neurometabolites, neuronal density, and the level of myelination and thus provides the basis for building multidimensional models taking into account clinical, radiological and omics data.

Objective: This project aims to understand better mechanisms driving neonatal brain injuries in prematurely- and term-born neonates and their impact on further brain development. The following hypotheses will be studied in detail:

1. There is a difference in urinary proteome and metabolome profile between preterm infants with IVH and/or PWMI and preterm infants without these complications.
2. There is a difference in urinary proteome and metabolome profile between HIE full-term infants and non-HIE full-term infants.
3. There is a difference in urinary proteome and metabolome profile between preterm infants with IVH and/or PWMI and HIE full-term infants.
4. There is a correlation between urinary proteome and metabolome profile and MRI findings (DWI parameters and ^{1}H-MRS metabolite concentrations)

Methods: A prospective cohort study will be performed at the Neonatal Intensive Care Unit, University Children's Hospital, Jagiellonian University Medical College, Krakow. Patients will be recruited simultaneously into two groups (PREMATURITY group and HIE group). Recruitment is planned for two years, and it is envisaged to include at least 100 newborns:

a) At least 60 newborns born <32 weeks of gestation. These children will be further divided into the study and control groups depending on the development of neonatal brain damage.

b) 20 newborns with moderate to severe HIE qualified for therapeutic hypothermia. Besides, it is planned to recruit 20 full-term newborns without any brain pathology that will form a control group.

Every day in the first week of life, and for premature babies also on the 28th day of life and at term-equivalent age, urine samples will be collected in a non-invasive way from all study participants. These samples will then undergo metabolome and proteome analysis. Also, magnetic resonance imaging of the brain with DTI and ^{1}H-MRS will be performed in all premature babies and term-born newborns with HIE. All data will be analyzed using advanced methods integrating metabolomic, proteomic, and neuroimaging results with the cooperation of the VA Center for Personalized Medicine, University of Texas Health San Antonio, US.

Expected results: The project will expand knowledge of pathomechanisms governing neonatal brain damage and related metabolic processes. It may allow the establishment of a set of reliable predictors and biomarkers of neonatal brain damage, as well as the discovery of proteomic or metabolomic surrogates of magnetic resonance spectroscopy. Also, our work can initiate research into possible therapeutic interventions that can improve long-term outcomes in patients with neonatal brain damage.