C.3

Exploring reduced incidence of pediatric neuro-autoimmune disorders during COVID-19 restrictions

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Background: Infections are hypothesized to trigger certain autoimmune diseases; however, there is a lack of epidemiologic data surrounding pediatric neuro-autoimmune disorders during the COVID-19 pandemic. Our retrospective study assessed the incidence of pre-defined autoimmune disorders at the Children's Hospital of Eastern Ontario from October 2017-June 2024. Methods: Inpatient/outpatient charts were queried to identify subjects with neuro-autoimmune disorders or type 1 diabetes (T1D) as a non-neurological autoimmune comparison group. Monthly incidences were compared between three COVID-19 pandemic restriction periods: the pre-restrictions (October 2017-March 2020), intra-restrictions (April 2020-June 2022), and post-restrictions periods (July 2022-June 2024). Poisson regression models were fit to the incidence data. To evaluate incidence of specific neuro-autoimmune disorders, crude monthly incidences of six diagnosis categories were compared: 'Guillain-Barré syndrome', 'anti-NMDAR encephalitis', 'juvenile dermatomyositis', 'multiple sclerosis (MS)', 'acute demyelinating disorders', and 'other'. Results: Incidence of neuro-autoimmune disorders, but not T1D, decreased during the intra-restrictions period compared to the pre-restrictions period (IRR=0.57, 95% CI: 0.33-0.95, $P<0.05$). Grouping neuro-autoimmune subjects by diagnosis category showed a trend towards decreased incidence during the intra-restrictions versus pre-restrictions periods for all groups except MS. Conclusions: Incidence of certain neuro-autoimmune disorders, but not MS and T1D, decreased during pandemic restrictions, which may be due to reduced transmission of key infectious triggers.

C.4

Clinical, radiological, and etiological features in a cohort of 94 patients with schizencephaly

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Background: Schizencephaly is a congenital brain malformation involving a cleft in the cerebral hemisphere lined with abnormal gray matter with an estimated incidence of 1.5 per 100,000 live births. Methods: This study aims to characterize the radiological, etiological, and clinical features of schizencephaly, identifying factors predictive of patient outcomes. A retrospective cohort of 94 individuals, both adult and pediatric, was analyzed across four tertiary care centers. A neuroradiologist systematically reviewed imaging, while charts were reviewed for clinical features. Results: Several perinatal risk factors were identified, including young maternal age and prenatal infections. However, genetic testing yielded only one pathogenic COL4A1 mutation. MRI findings showed frequent additional malformations, including those in the pituitary, corpus callosum, and fornix. Clinical characteristics included neurodevelopmental delay (71.6%), seizures (50.0%), and motor impairments (53.3%). Outcomes were heterogeneous, with bilateral and open-lip clefts associated with more severe developmental delays, while seizure rates were comparable across subtypes. Conclusions: The complexity of schizencephaly is highlighted in the largest cohort reported with high rates of seizures, neurodevelopmental delays, and motor impairments, but outcomes varied widely based on imaging features, underscoring the importance of individualized management. The low yield of genetic findings emphasizes prenatal environmental risk factors as etiological contributors.

C.5

The generation of alternative transcripts as a method of regulating phosphorylation in Sonic Hedgehog (Shh) Subtype Medulloblastoma (MB)

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Background: Protein phosphorylation is critical in development and tumor progression, but kinase promiscuity limits selective regulation. Alternative transcription start sites (ATSS) and alternative splicing (AS) may generate isoforms with or without the phosphorylation sites, offering a mechanism of precise control. Sonic Hedgehog (Shh) medulloblastoma (MB), the most common pediatric cerebellar tumor, arises from granule neuron precursors (GNPs) via aberrant Shh signaling. Highly proliferative postnatal day 7 (P7) GNPs and MB share transcriptomic and molecular characteristics, acting as a model for further investigation. Here, we examined the regulation of phosphorylation sites in the mRNA level in P7 GNP and MB. Methods: Integrated phosphoproteomics, proteomics, and RNA-Seq datasets were analyzed to identify candidates producing alternative transcripts with phosphorylation changes in murine P7 GNPs and *Ptch1*$^{+/-}$ MB. Differential isoform expression was validated via RT-qPCR and RNA-FISH. Results: *Rnf220* and *Septin9* were identified as candidates that utilize ATSS to produce differential isoforms with or without the phosphorylation sites. RT-qPCR and RNA-FISH showed significant upregulation of their long isoforms in Shh MB compared to GNPs. Conclusions: Alternative transcript generation may act as a novel mechanism for regulating phosphorylation in Shh MB. Differential expression of *Rnf220* and *Septin9* phosphorylated isoforms suggests their involvement in MB development, warranting further functional investigations.