D.08

Diffusion imaging of cerebral diaschisis in neonatal arterial ischemic stroke

R Srivastava (Calgary) T Rajapakse (Calgary) J Roe (Calgary) X Wei (Calgary) A Kirton (Calgary)*

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Background: Neonatal arterial ischemic stroke (NAIS) is a leading cause of brain injury and cerebral palsy. Diffusion-weighted imaging (DWI) has revolutionized NAIS diagnosis and outcome prognostication. Diaschisis refers to changes in brain areas functionally connected but structurally remote from primary injury. We hypothesized that acute DWI can demonstrate cerebral diaschisis and evaluated associations with outcome. *Methods:* Subjects were identified from a prospective, population-based research cohort (Calgary Pediatric Stroke Program). Inclusion criteria were unilateral middle cerebral artery NAIS, DWI MRI within 10 days of birth, and >12-month follow-up (Pediatric Stroke Outcome Measure, PSOM). Diaschisis was quantified using a validated software method. Diaschisis-scores were corrected for infarct size and compared to outcomes (Mann-Whitney). *Results:* From 20 eligible NAIS, 2 were excluded for image quality. Of 18 remaining, 16 (89%) demonstrated diaschisis. Thalamus (88%) was most often involved. Age at imaging was not associated with diaschisis. Long-term outcomes available on 13 (81%) demonstrated no association between diaschisis score and PSOM categories. *Conclusion:* Cerebral diaschisis occurs in NAIS and can be quantified with DWI. Occurrence is common and should not be mistaken for additional infarction. Determining additional clinical significance will depend on larger samples with long-term outcomes.

D.09

Hereditary neuropathy with liability to pressure palsies in childhood: case series and update from the literature

N Chrestian (Toronto) C Campbell (London) C Poulin (Montreal) H McMillan (Ottawa) J Vajsar (Toronto)*

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Introduction: HNPP presentation in childhood is rare and diverse and most of the published literature is based on case reports. *Materials and Methods:* we analyzed the data of 11 children with deletion in PMP22 gene, reviewed the published reports of HNPP in children and compared our data with the reports from the literature review. *Results:* Peroneal palsy was the most common presentation (50%) followed by the brachial plexus palsy in 30% of cases. The trigger of the demyelinating event was identified only in 27%. 72% of our cohort developed only one acute episode of nerve palsy. Nerve conduction studies were always suggestive of the diagnosis demonstrating 60% of cases a polyneuropathy, 50% of cases conduction block but 100% of bilateral or unilateral electrophysiologic entrapment of the median nerve at the carpal tunnel. *Conclusion:* The clinical presentation of HNPP in childhood is heterogeneous and EMG findings are abnormal. Any unexplained mononeuropathy or multifocal neuropathy should lead to PMP22 gene testing to look for the deletion. Early diagnosis is important for the genetic counselling but also for the appropriate care of these patients.

D.10

Pediatric anti-myelin oligodendrocyte glycoprotein syndrome: case series of a newly recognized central nervous system inflammatory disease

S Venkateswaran (Ottawa) S Thulasirajah (Ottawa) D Pohl (Ottawa) K Rostasy (Innsbruck)*

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Pediatric acquired demyelinating syndromes have overlapping clinical and imaging features, but management and prognosis vary. We describe four children between the ages of 3 and 10 presenting with inflammatory brain disease - one with polyfocal neurological symptoms, one with severe bilateral optic neuritis and two with transverse myelitis, all without encephalopathy. All brain MRIs had extensive involvement of both deep grey and subcortical white matter. Three patients had longitudinally extensive spinal cord lesions. Clinical and radiological findings did not meet criteria for multiple sclerosis, acute disseminated encephalomyelitis, or neuromyelitis optica (NMO). NMO IgG testing was negative. All patients had resolution of clinical and imaging findings after treatment with steroids and IVIg. We found, elevated levels of anti-myelin oligodendrocyte glycoprotein antibodies in all four patients. Three of the children receive monthly IVIg infusions. Two of the patients relapsed once within 18 months of their initial attack and have since remained relapse free for 32 months and 43 months, respectively. The third patient (transverse myelitis) has not had any relapses since her initial attack 15 months ago. It appears that children with this syndrome may have more favourable outcomes when compared to other CNS relapsing inflammatory conditions.

CNS / CSCN
Platform Presentations

E.01

The potential influence of abnormal blood platelet count on mortality, impairment and disability after acute ischemic stroke

JC Furlan (Toronto) J Fang (Toronto) FL Silver (Toronto)*

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Background: We hypothesized that abnormal blood platelet count (BPC) is associated with poorer outcomes after acute ischemic stroke. *Methods:* We included data from the Registry of the Canadian Stroke Network on consecutive patients with acute ischemic stroke admitted between July/2003 and March/2008. Patients were divided into groups as follows: low BPC (<150,000/mm3), normal BPC (150,000 to 450,000/mm3) and high BPC (>450,000/mm3). Primary outcome measures were the frequency of moderate/severe strokes on admission (Canadian Neurological Scale: <8), greater degree of disability at discharge (modified Rankin score: 3-6), and 30-day and 90-day mortality. *Results:* We included 9,230 patients. Both low and high BPC were associated with higher 30-day mortality (p=0.0103) and 90-day mortality (p=0.0189) following acute ischemic stroke. The Kaplan-Meier curves indicate that abnormal BPC is associated

with greater mortality after acute ischemic stroke (p=0.0002). Nonetheless, abnormal BPC was not associated with degree of impairment (p=0.3734), degree of disability (p=0.684), or length of stay (LOS) in the acute stroke care center (p=0.9541) after adjustment for major potential confounders. *Conclusions:* In patients with acute ischemic stroke, thrombocytopenia and thrombocytosis on the initial admission is associated with higher mortality after stroke. Abnormal BPC does not adversely affect the degree of impairment and disability, or LOS in the acute care center after acute ischemic stroke.

E.02

Arterial tortuosity: an imaging biomarker of childhood stroke pathogenesis?

F Wei (Calgary) K Diedrich (Cambridge) H Fullerton (San Francisco) G DeVeber (Toronto) M Wintermark (Stanford) J Hodge (Calgary) A Kirton (Calgary)*

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Background: Arteriopathy causes most childhood arterial ischemic stroke (AIS). Mechanisms are poorly understood but may include abnormalities of arterial structure. Extracranial dissection is common while intracranial dissection may explain idiopathic focal cerebral arteriopathy (FCA). We aimed to quantify cerebral arterial tortuosity and hypothesized increased tortuosity in extracranial dissection. *Methods:* Children with AIS were recruited within the Vascular-Effects-of-Infection-in-Pediatric-Stroke (VIPS) study (controls from the Calgary Pediatric Stroke Program). A validated software method calculated mean tortuosity of major cerebral arteries using 3D time-of-flight MR angiography (MRA). Blinded, multi-investigator reviews defined diagnostic categories. Tortuosity was compared between dissection (spontaneous and traumatic), FCA, moyamoya, meningitis, and cardioembolic, and controls (ANOVA, post-hoc Tukey). *Results:* A total of 116 children were studied. Age and gender were comparable across groups. Tortuosity scores and variances were consistent with validation studies. Tortuosity in controls (1.333±0.039, n=15) was comparable to moyamoya (1.324±0.038, p=0.99, n=15), meningitis (1.348±0.052, p=0.98, n=12) and cardioembolic (1.379±0.056, p=0.19, n=27) cases. Tortuosity was higher in dissection (1.398±0.072, p=0.02, n=22) and FCA (1.421±0.076, p=0.001, n=25). Traumatic (1.391±0.036, n=9) and non-traumatic (1.403±0.090, p=0.671, n=13) scores were not different. *Conclusion:* Children with dissection have more tortuous arteries. Quantified tortuosity may represent a clinically relevant biomarker of vascular biology in pediatric stroke.

E.03

Dorsal striatum mediates cognitive control, not cognitive effort per se, in decision-making: an event-related fMRI study

BD Robertson (London) NM Hiebert (London) KN Seergobin (London) AM Owen (London) PA MacDonald (London)*

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Background: Whether the dorsal striatum (DS) mediates cognitive control or cognitive effort per se in decision-making is unclear because as cognitive control requirements of a task intensify, cognitive effort requirements increase proportionately. We implemented a task that disentangled cognitive control and cognitive effort to specify the function DS mediates in decision-making. *Methods:* Sixteen healthy young adults completed a number Stroop task with simultaneous blood-oxygenation-level-dependent response (BOLD) measurement. Participants selected the physically larger number of a pair. Discriminating smaller physical size differences increases cognitive effort, but does not demand greater cognitive control. We also investigated the effect of interdimensional conflict between physical size and numerical magnitude. Selections in this incongruent case are more cognitively effortful and require greater cognitive control to suppress responding to the irrelevant dimension. Enhancing cognitive effort or cognitive control requirements increases response times and error rates. *Results:* Behavioural interference occurred for both conditions; however, DS BOLD signal only correlated with interference due to increased cognitive control requirements. DS was not preferentially activated for discriminations of smaller relative to larger physical size differences between number pairs, even when using liberal statistical criteria. *Conclusions:* Our findings support the increasingly accepted notion that DS mediates cognitive control specifically and does not index cognitive effort per se.

E.04

Design and development of drugs for Alzheimer's dementia as a protein misfolding disorder

*C Barden (Toronto) F Meier-Stephenson (Halifax) MD Carter (Halifax) S Banfield (Halifax) EC Diez (Toronto) B Kelly (Toronto) E Lu (Toronto) A Meek (Toronto) V Meier-Stephenson (Halifax) L Pan (Toronto) GA Simms (Halifax) B Sweeting (Toronto) Y Wang (Toronto) F Wu (Toronto) A Yadav (Toronto) S Yang (Toronto) M Taylor (Toronto) M Reed (Toronto) DF Weaver (Toronto)**

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Background: There are no disease modifying agents for the treatment of Alzheimer's disease (AD). Pathologically, AD is associated with the misfolding of two peptides: beta-amyloid (plaques) and tau (tangles). *Methods:* Using large-scale computer simulations, we modelled the misfolding of both beta-amyloid and tau, identifying a common conformational motif (CCM; i.e. an abnormal peptide shape), present in both beta-amyloid and tau, that promotes their misfolding. We screened a library of 11.8 million compounds against this in silico model of protein misfolding, identifying three novel molecular classes of putative therapeutics as anti-protein misfolding agents. We synthesized approximately 400 new chemical entity drug-like molecules in each of these three classes (i.e. 1200 potential drug candidates). These were comprehensively screened in a battery of five in vitro protein oligomerization assays. Selected compounds were next evaluated in the APP/PS1 doubly transgenic mouse model of AD. *Results:* Two new classes of molecules were identified with the ability to block the oligomerization of both beta-amyloid and tau. These compounds are drug-like with good pharmacokinetic properties and are brain-penetrant. They exhibit excellent efficacy in transgenic mouse models. *Conclusion:* Computer aided drug design has enabled the discovery of novel drug-like molecules able to inhibit both tau and beta-amyloid misfolding.