CANADIAN NEUROLOGICAL SCIENCES FEDERATION
FÉDÉRATION DES SCIENCES NEUROLOGIQUES DU CANADA

The journal

Canadian Journal of Neurological Sciences

Volume 38 Number 3 (Supplement 1) May 2011

46th Annual Congress of the Canadian Neurological Sciences Federation

Vancouver, British Columbia, Canada

46e congrès annuel de la Fédération des sciences neurologiques du Canada

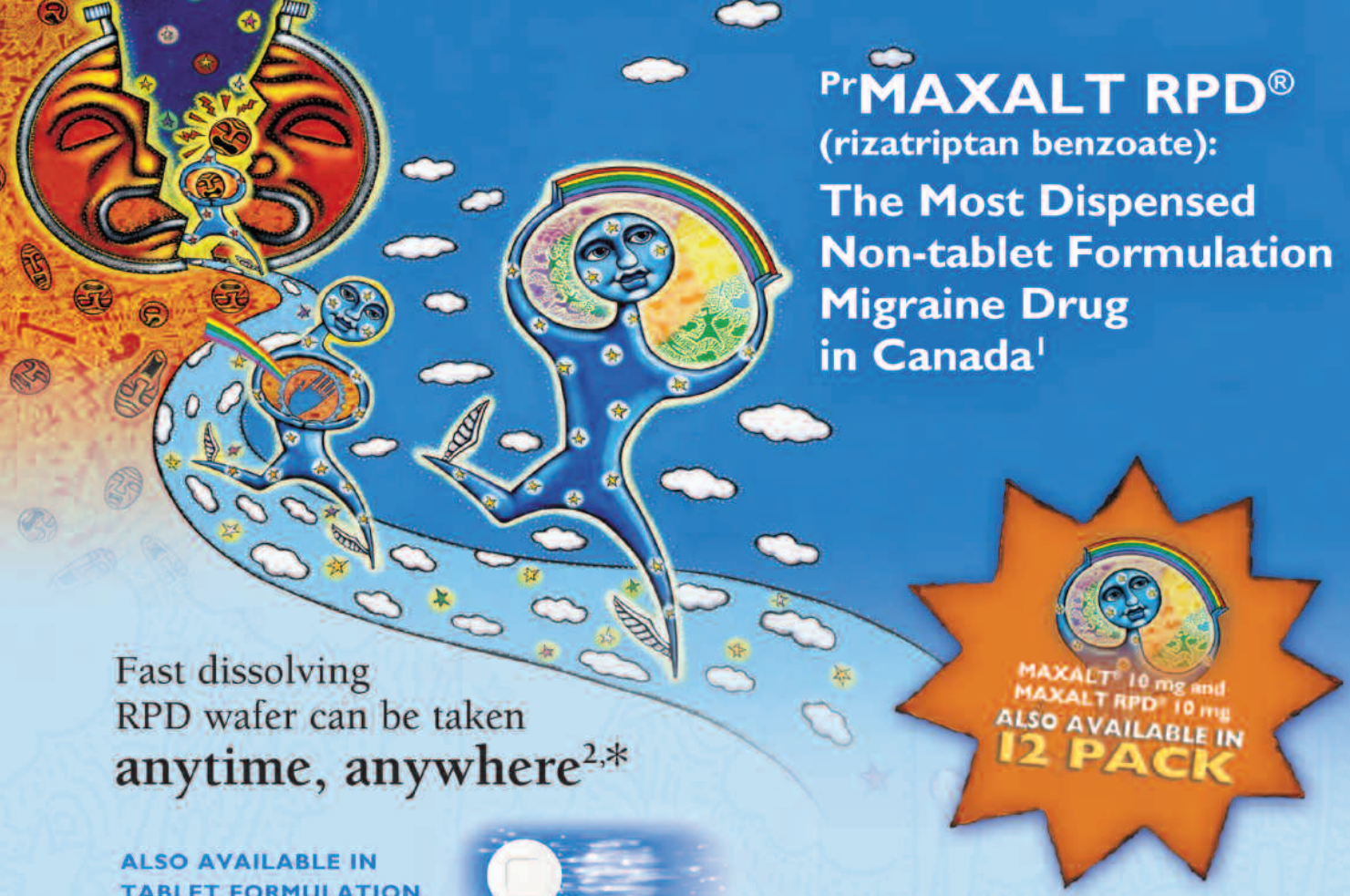
ABSTRACTS / RÉSUMÉS

AN INTERNATIONAL JOURNAL PUBLISHED BY THE CANADIAN NEUROLOGICAL SCIENCES FEDERATION

The official Journal of: The Canadian Neurological Society, The Canadian Neurosurgical Society, The Canadian Society of Clinical Neurophysiologists, The Canadian Association of Child Neurology

PM 40007777
R 9824

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press



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1. Brogan Inc. Geographic Prescription Monitor (GPM®) September 2008 to August 2009.
2. Data on file, Merck Frosst Canada Ltd.: Product Monograph, MAXALT®, 2009.

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https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

See prescribing summary on page S87-S90

Volume 38 Number 3 (Supplement 1) May 2011

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Canadian Neurological Sciences Federation

VANCOUVER, BRITISH COLUMBIA • JUNE 15-17, 2011

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ABSTRACTS AND PROGRAM

SUPPORTED BY AN EDUCATIONAL GRANT FROM MERCK CANADA

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https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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The journal

Canadian Journal of Neurological Sciences

Volume 38 / Number 3 / Supplement 1 / May 2011

The official journal of: / La Revue officielle de:

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La Société Canadienne de Neurologie

The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

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Postage paid at Calgary, Alberta.

Le Journal Canadien des Sciences Neurologiques est publié 6 fois par an. L'abonnement annuel est de 120 $C (non-membres au Canada); 140 $C (Etats Unis et ailleurs); l'abonnement annuel for pour les institutions est de 150 $C (non-membres au Canada); 170 $C (Etats Unis et ailleurs); Voir www.cjns.org pour détails. Copie simple: 30 $C plus affranchissement et manutention. Toutes les communications doivent être adressés à Journal Canadien des Sciences Neurologiques, 709 - 7015 Macleod Trail SW, Calgary, AB Canada T2H 2K6. Téléphone (403) 229-9575; Fax (403) 229-1661. E-mail journal@cjns.org; Web:www.cjns.org.

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ISSN 0317 - 1671

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

46th Annual Congress of the

Canadian Neurological Sciences Federation

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ABSTRACTS

SOCIETY PRIZE PRESENTATIONS

PLATFORM PRESENTATIONS

Thursday, June 16, 2011

Friday, June 17, 2011

POSTER PRESENTATIONS

Friday, June 17, 2011

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Welcome to Vancouver!!!

Surrounded by water on three sides and nestled alongside the Coast Mountain Range, Vancouver is the largest city in the Province of British Columbia with over half a million residents and one of the mildest climates in Canada. Home to spectacular natural scenery and a bustling metropolitan core, Vancouver was Host City to the Olympic and Paralympic Winter Games in 2010. Whether just relaxing in a park or bike riding around the seawall, there is always something to do in Vancouver.

Photos Courtesy of City of Vancouver

Bienvenue à Vancouver!!!

Située sur une péninsule et nichée le long de la chaîne montagneuse côtière, Vancouver est la plus grande ville de la province de Colombie-Britannique avec plus d'un demi-million d'habitants et l'un des climats les plus doux du Canada. Avec des décors naturels spectaculaires et une agglomération métropolitaine animée, Vancouver a accueilli les Jeux olympiques et paralympiques en 2010. Que vous vous détendiez dans un parc ou que vous vous promeniez en vélo le long de la côte, il y a toujours quelque chose à faire à Vancouver.

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2011 Society Prize Papers

The Herbert Jasper Prize

Canadian Society of Clinical Neurophysiologists

Comparison of the costal and crural diaphragm EMG with increments in tidal volume

N Amirjani (Randwick, Sydney) A Hudson (Randwick, Sydney) J Butler (Randwick, Sydney) S Gandevia (Randwick, Sydney)*

Introduction: The inspiratory action of the diaphragm relies on the synchronous activation of its two parts, the costal and the crural diaphragm. An increase in the inspiratory volume or flow augments the costal diaphragmatic motor unit discharge pattern (Butler et al., J Physiol, 1999; 518: 907, Gandevia et al., Am J Respir Crit Care Med. 1999;160:1598). However, the individual contribution of the costal versus crural diaphragm to meet a higher inspiratory demand in humans is unknown. *Methods:* We compared the electromyographic activity (EMG) of the costal and crural diaphragm in 5 healthy persons, with voluntary inspiratory tasks to increase the tidal volume. Subjects were instructed to increment their inspiratory volumes up to 90% greater than quiet breathing, and also occasionally to sigh voluntarily. The EMG of the costal diaphragm was recorded with a standard monopolar needle. An esophageal catheter, mounted with five pairs of electrodes, recorded EMG of the crural diaphragm. *Results:* The amplitude of the root mean square EMG was measured for both costal and crural diaphragm across four breaths at each inspiratory volume, and their correlatation assessed with the Pearson correlation coefficient. The group results revealed a comparable increase in EMG of the two muscular components of the diaphragm ($r = 0.96$, $p<0.05$ for incremental breaths and $r=0.99$, $p=0.000$ for sighs). *Conclusion:* In humans, the costal and crural diaphragm are activated proportionally in concert to accommodate voluntary increases in the inspired volume.

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Andre Barbeau Memorial Prize

Canadian Neurological Society

Regulation of α-synuclein oligomerization and ubiquitinylation by molecular chaperones

LV Kalia (Toronto) SK Kalia (Toronto) H Chau (Toronto) AM Lozano (Toronto) BT Hyman (Boston) PJ McLean (Boston)*

Background: Parkinson's disease (PD) is a common neurodegenerative condition in which α-synuclein (α-syn) accumulates due to abnormalities in protein homeostasis. Recent evidence demonstrates that α-syn can self-associate into soluble oligomeric species and implicates these oligomers in neurodegeneration. Here we test the hypothesis that α-syn oligomers may be modulated by the molecular chaperones CHIP, which possesses intrinsic E3 ubiquitin ligase activity, and BAG5. *Methods:* Luciferase-based protein-fragment complementation assays were used to investigate α-syn oligomerization in living cells. Ubiquitinylation of α-syn by CHIP was examined in vitro and in cell lysates. We tested for protein complexes containing α-syn, CHIP, and BAG5 using pull-down assays, co-immunoprecipitations, and immunohistochemistry. *Results:* We find that α-syn is ubiquitinylated by CHIP and exists within a protein complex with CHIP and BAG5. The interaction of CHIP with BAG5 results in inhibition of CHIP E3 ubiquitin ligase activity and reduces α-syn ubiquitinylation. We demonstrate that non-ubiquitinylated α-syn has an increased propensity for oligomerization. Furthermore, BAG5 mitigates the ability of CHIP to reduce α-syn oligomerization. *Conclusions:* Our results identify CHIP as an E3 ubiquitin ligase of α-syn and suggest a novel function for BAG5 as a modulator of CHIP activity with implications for CHIP-mediated regulation of α-syn oligomerization in PD and other synucleinopathies.

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Francis McNaughton Memorial Prize

Canadian Neurological Society

An Ontario-based cost-utility analysis comparing the standard of care with direct decompressive surgical resection followed by radiotherapy in the palliative care of patients with metastatic spinal cord cancer

JC Furlan (Toronto) KKW Chan (Toronto) G Sandoval (Toronto) KC Lam (Toronto) CA Klinger (Toronto) RA Patchell (Phoenix) MG Fehlings (Toronto) A Laporte (Toronto)*

Background: This cost-utility analysis compares radiotherapy alone (RT) with decompressive surgery and postoperative radiotherapy (S+RT) for palliative care of metastatic spinal cord compression (MSCC). *Methods:* A cost-utility analysis for both treatment options, based on the randomized clinical trial (Patchell et al., Lancet 2005), was performed from the perspective of a public health care insurer. Ontario-based costs were adjusted to 2010 US dollars. *Results:* The S+RT strategy is more costly but more effective than RT-alone strategy, with an incremental cost-effectiveness ratio (ICER) of US$ 240,442.48 per quality-adjusted life year (QALY) gained. The Monte-Carlo simulation revealed that, by adopting the S+RT strategy, there would a reasonable chance (18.11%) of not paying extra for one additional QALY gained at willingness-to-pay of US$ 50,000. The acceptability curve showed that at the level of

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

US$ 1,683,000 per one additional QALY, the proportion of ICERs reached the maximum of 91.11%. *Conclusions:* Given the increasing focus on the provision of cost-effective medical care, our results suggest that a change of the palliative treatment protocols for MSCC patients towards a S+RT approach is more likely to increase the healthcare costs. However, the gain in terms of patients' quality of life is relatively significant and should be considered by health care policy makers.

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K.G. McKenzie Prize in Basic Neuroscience Research

Canadian Neurosurgical Society 1st prize

Extending the therapeutic window for reperfusion after stroke in non-human primates using a PSD-95 inhibitor

DJ Cook (Toronto) LM Teves (Toronto) M Tymianski (Toronto)*

Stroke is the third leading cause of death and carries the greatest socioeconomic burden of disease in North America. Early reperfusion by thrombolysis or mechanical means is the only treatment for acute ischemic stroke that is clinical proven; however, many patients do not qualify for reperfusion therapy due to a limited therapeutic window. As a potential strategy to increase the therapeutic window for reperfusion we tested the hypothesis that Tat-NR2B9c administered 1h into a 4.5h transient middle cerebral artery occlusion(MCAO) in cynomolgus macaques would improve stroke outcomes and reduce stroke volumes 7d following stroke by preserving salvageable tissue in the ischemic period. 12 cynomolgus macaques underwent open MCAO. Six animals received Tat-NR2B9c(2.6mg/kg) and 6 received placebo 1 hour following MCAO. The MCA was reperfused 4.5h after MCAO. Animals underwent perfusion MRI immediately after MCAO and diffusion weighted and T2 weighted MRI at 3h, 48h and 7d following MCAO to define stroke volume and perfusion-diffusion mismatch. Animals underwent serial clinical examination post-MCAO using the Non-Human Primate Stroke Scale(NHPSS). Tat-NR2B9c and placebo treated animals had equivalent volumes of tissue at risk by perfusion imaging at baseline. There was a 25% reduction in stroke volume measured by diffusion and T2 MRI (P=0.011). NHPSS was improved in Tat-NR2B9c treated animals at 7d (P=0.031). Tat-NR2B9c confers a neuroprotective effect as measured by neurological outcome and stroke volume when administered 1h into a 4.5h MCAO in cynomolgus macaques. This result suggests that early administration of a neuroprotectant can preserve ischemic tissue and improve outcomes with delayed reperfusion.

K.G. McKenzie Prize in Basic Neuroscience Research

Canadian Neurosurgical Society 2nd prize

Understanding how a cell transplantation paradigm leads to functional recovery from spinal cord injury: the importance of remyelination

GWJ Hawryluk (North York) MG Fehlings (Toronto)*

Background: The mechanism by which transplanted cells lead to functional recovery following spinal cord injury is unclear. Better understanding is required to augment recovery. *Methods:* Two weeks following clip compression spinal cord injury (SCI) rats underwent cellular or control transplantation. Cellular transplants included wild-type mouse neural precursor cells (NPCs) and NPCs derived from shiverer mice unable to produce myelin. Most transplanted animals also received minocycline, cyclosporin and an infusion of EGF, bFGF and PDGF. Hind-leg motor function was assessed according to the BBB scale. qPCR was performed for candidate trophins on transplanted tissue. H&E/LFB staining was used to assess grey and white matter, cyst and lesional tissue. Mature oligodendrocytes, inflammatory cells and axonal preservation was quantitated. *Results:* NPC transplantation, pharmacotherapy and trophin administration led to a synergistic increase in the expression of numerous trophins. Pharmacotherapy and trophin infusion led to grey and white matter sparing. Trophin infusion was associated with a significant increase in cyst and lesional tissue volume as well as inflammatory cell numbers. No experimental therapy preserved axons. Animals transplanted with wild-type NPCs without trophin infusion showed significantly greater functional recovery than any other group. Animals transplanted with shiverer NPCs performed worst on functional testing. *Conclusions:* These results suggest that remyelination by exogenous cells is their most important contribution to functional recovery following SCI. Trophin infusion via an osmotic mini-pump is harmful and best avoided. These findings may allow the functional recovery associated with NPC transplantation to be augmentated.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

K.G. McKenzie Prize in Clinical Neuroscience Research

Canadian Neurosurgical Society 1st prize

A Phase I trial of deep brain stimulation of memory circuits in Alzheimer disease

AW Laxton (Toronto) DF Tang-Wai (Toronto) MP McAndrews (Toronto) D Zumsteg (Toronto) R Wennberg (Toronto) R Keren (Toronto) J Wherret (Toronto) G Naglie (Toronto) C Hamani (Toronto) GS Smith (Toronto) AM Lozano (Toronto)*

Background: Alzheimer disease (AD) is characterized by functional impairment in the neural elements and circuits underlying cognitive and memory functions. We hypothesized that fornix/hypothalamus deep brain stimulation (DBS) could modulate neurophysiological activity in these pathological circuits and possibly produce clinical benefits. *Methods:* We conducted a phase I trial in 6 patients with mild AD receiving ongoing medication treatment. Patients received continuous stimulation for 12 months. Three main lines of investigation were pursued including: (1) mapping the brain areas whose physiological function was modulated by stimulation using standardized low-resolution electromagnetic tomography, (2) assessing whether DBS could correct the regional alterations in cerebral glucose metabolism in AD using positron emission tomography (PET), and 3) measuring the effects of DBS on cognitive function over time using clinical scales and instruments. *Results:* DBS drove neural activity in the memory circuit, including the entorhinal, and hippocampal areas and activated the brain's default mode network. PET scans showed an early and striking reversal of the impaired glucose utilization in the temporal and parietal lobes that was maintained after 12 months of continuous stimulation. Evaluation of the Alzheimer's Disease Assessment Scale cognitive subscale and the Mini Mental State Examination suggested possible improvements and/or slowing in the rate of cognitive decline at 6 and 12 months in some patients. There were no serious adverse events. *Conclusions:* There is an urgent need for novel therapeutic approaches for AD. Modulating pathological brain activity in this illness with DBS merits further investigation.

K.G. McKenzie Prize in Clinical Neuroscience Research

Canadian Neurosurgical Society 2nd prize

Immediate post-coiling occlusion status of ruptured intracranial aneurysms: effect on long-term clinical and angiographic outcomes

MK Tso (Calgary) P Kochar (Calgary) M Goyal (Calgary) ME Hudon (Calgary) WF Morrish (Calgary) JH Wong (Calgary)*

Background: Subarachnoid hemorrhage secondary to a ruptured intracranial aneurysm is increasingly treated by endovascular coiling. This study analyzed the long-term clinical and angiographic outcomes of coiled ruptured intracranial aneurysms, stratified by the immediate post-coiling occlusion status. *Methods:* Patients initially treated with endovascular coiling (2002-2006) were identified at the Foothills Medical Centre (N=86). Long-term clinical outcomes utilized the modified Rankin Scale (mRS 0-6,0=no symptoms,6=death). Angiograms were graded based on the Raymond-Roy occlusion classification: complete obliteration (class 1), residual neck (class 2), and residual fundus filling (class 3). Associations between initial occlusion status and other variables utilized the Kruskal-Wallis test or Chi-Square test with $P < 0.05$ considered statistically significant. *Results:* Twelve (14.0%) aneurysms were completely occluded, 66 (76.7%) had a residual neck, and 9 (9.3%) had residual fundus filling. There were no significant differences in baseline clinical parameters. There were no significant differences in long-term clinical outcomes in surviving patients (mean mRS 1.1-1.2, P=0.584). Twenty-nine patients had recanalization at a mean of 13.0 months, but this had no significant effect on long-term mRS (P=0.904). Further interventions were performed in 16 patients (18.6%). Initial occlusion status was not associated with further intervention (P=0.576) and reintervention had no significant effect on long-term clinical outcomes (P=0.552). Recurrent rupture occurred in one patient (1.2%) 33.1 months after the initial coiling procedure. *Conclusions:* The majority of the ruptured aneurysms were initially incompletely coiled. Patients had good clinical outcomes in long-term follow-up. Recurrent rupture was rare. Recanalization remains a significant long-term issue but reintervention appears safe.

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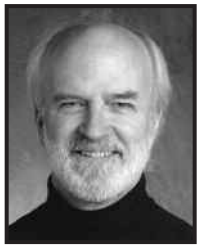

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Platform Presentations

CNS / CSCN Chair's Select Plenary Presentations

A-01

Characteristics and functional outcome in pontine infarcts. On behalf of the SPS3 Investigators

TS Field (Vancouver) J Szychowski (Birmingham) K Peri (Birmingham) L McClure (Birmingham) O Benavente (Vancouver)*

Background: A quarter of pontine infarction cases are due to small vessel disease. Risk factors and functional outcomes distinguishing small-vessel pontine vs. non-pontine infarcts are not well-defined. *Methods:* We compared baseline characteristics, clinical features and functional outcomes of pontine and non-pontine infarcts of patients with MRI-proven lacunes from the Secondary Prevention of Small Subcortical Strokes (SPS3) study. *Results:* Of 2574 patients, 574 (22%) had pontine infarcts. Pontine patients were more often male (68% vs. 61%, $p < 0.01$), hypertensive (75% vs. 54%, $p = 0.04$) and diabetic (46% vs. 34%, $p < 0.01$). More Hispanics (38% vs 29%), Blacks (19% vs. 13%) and fewer Whites (40% vs 54%, $p < 0.01$) had pontine infarcts. White matter disease on MRI was less prevalent (21% vs. 3%; $p < 0.01$). There was no difference in age (64 vs. 63), multiple infarcts (19% vs. 20%; $p < 0.72$), or intra- (14% vs. 14%) and extracranial (2% vs. 1%) stenosis. Clinical syndromes differed (pure motor 41% vs. 33%, sensorimotor 20% vs. 34%, ataxic hemiparesis 18% vs. 7%, pure sensory 20% vs. 34%; $p < 0.01$). Pontine infarcts had worse functional outcomes (mRS ≥2, 29% vs. 23%; $p < 0.01$). In a multivariable logistic regression model, there was a higher odds of pontine infarct for hypertensives (2.3 (1.3-4.2)), diabetics (1.9 (1.3-2.9)), and Blacks vs. Whites (2.0 (1.3-3.3)). *Conclusions:* In our population, pontine more than non-pontine infarcts are more likely to be associated with diabetes, hypertension and Black ethnicity. These differences may define future therapeutic strategies.

A-02

Perfusion imaging predicts outcome in TIA and minor stroke

N Asdaghi (Calgary) KS Butcher (Edmonton) A Qazi (Calgary) JI Coulter (Calgary) M Goyal (Calgary) MD Hill (Calgary) AM Demchuk (Calgary) SB Coutts (Calgary)*

Background: Clinical deterioration occurs in many patients presenting with minor or transient ischemic symptoms. We tested whether baseline perfusion (PWI)-diffusion weighted imaging (DWI) abnormalities predict infarct growth and clinical progression. *Methods:* Patients with minor stroke (NIH Stroke Scale ≤ 3) and transient ischemic attack (TIA) presenting within 12 hours of symptom onset were prospectively enrolled and imaged. DWI and PWI (within 24 hours) and follow-up FLAIR (30 days) infarct volumes were measured with planimetric techniques. PWI-DWI mismatch volumes were calculated as Tmax+4s delay – DWI lesion. Infarct growth volume was measured as day30 FLAIR -DWI lesion. *Results:* 137 patients were included; 54% had DWI and 41.6% had PWI deficits at baseline. Clinical deterioration occurred in 9.5% within 72 hours. 119 patients had follow-up imaging, of whom 17.6% developed infarct growth. Patients with clinical worsening had significantly higher baseline mismatch volumes (median= 45 ml, IQR= 83.3) than those who did not progress (median=0 ml, IQR= 1, $P<0.001$). A mismatch volume of 10ml predicted clinical worsening with 77% sensitivity and 86% specificity (Area Under Curve (AUC)= 0.814, [0.66, 0.9]) and radiographic infarct growth with 81% sensitivity and 91.5% specificity (AUC=0.883, [0.78, 0.98]). Linear regression showed that for every 10ml of mismatch, there would be 2.5ml infarct growth on day 30 FLAIR [$R=0.80$, $p<0.001$]. *Conclusion:* In a population of minor stroke and TIA patients, early MR perfusion-diffusion mismatch strongly predicts clinical deterioration and infarct growth. These findings suggest that there may be a group of patients with minor symptoms in whom reperfusion strategies may be beneficial.

A-03

MRI follow-up of longitudinally extensive spinal cord lesions in NMO and OSMS

T Wang (Vancouver) DKB Li (Vancouver) R Sadjadi (Vancouver) I Al-Thubaiti (Vancouver) A Kuan (Vancouver) A Traboulsee (Vancouver)*

Background: Longitudinally extensive spinal cord lesions (LESCL), extending more than 3 vertebral lengths, on MRI, are common in neuromyelitis optica (NMO) and the opticospinal form of Asian Multiple Sclerosis (OSMS). The study objective was to follow-up pre-existing LESCL in the absence of recent recurrent symptoms. *Methods:* The initial and follow-up MRI scans of 16 NMO and 2 OSMS patients with at least one initial LESCL were retrospectively reviewed for changes in size and longitudinal extent, blinded to the clinical indication for the examination. Results for scans obtained within 3 months of acute transverse myelitis symptoms were excluded and only those obtained for routine follow-up were analyzed. *Results:* Follow-up of 25 pre-existing LESCL in 18 patients showed 6 resolved, 7 unchanged, 10 smaller (3 residual LESCL, 2 non-LESCL [< 3 vertebral lengths] and 5 LESCL splitting into 14 smaller lesions (5 LESCL, 9 non-LESCL), 2 larger and the development of 1 new LESCL. *Conclusions:* In the absence of recurrent clinical symptoms, 64% of pre-existing LESCL on follow-up resolved (24%) or became smaller (40%) either by shrinking in size or being split up into smaller lesions, 57% of which were non-LESCL, lesions more typical for classical MS. This project was funded through a grant from the Foundation of the Consortium of Multiple Sclerosis Centers' MS Workforce of the Future program

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

A-04

Comparison of the costal and crural diaphragm EMG with increments in tidal volume

N Amirjani (Randwick, Sydney) A Hudson (Randwick, Sydney) J Butler (Randwick, Sydney) S Gandevia (Randwick, Sydney)*

Introduction: The inspiratory action of the diaphragm relies on the synchronous activation of its two parts, the costal and the crural diaphragm. An increase in the inspiratory volume or flow augments the costal diaphragmatic motor unit discharge pattern (Butler et al., J Physiol, 1999; 518: 907, Gandevia et al., Am J Respir Crit Care Med. 1999;160:1598). However, the individual contribution of the costal versus crural diaphragm to meet a higher inspiratory demand in humans is unknown. *Methods:* We compared the electromyographic activity (EMG) of the costal and crural diaphragm in 5 healthy persons, with voluntary inspiratory tasks to increase the tidal volume. Subjects were instructed to increment their inspiratory volumes up to 90% greater than quiet breathing, and also occasionally to sigh voluntarily. The EMG of the costal diaphragm was recorded with a standard monopolar needle. An esophageal catheter, mounted with five pairs of electrodes, recorded EMG of the crural diaphragm. *Results:* The amplitude of the root mean square EMG was measured for both costal and crural diaphragm across four breaths at each inspiratory volume, and their correlatation assessed with the Pearson correlation coefficient. The group results revealed a comparable increase in EMG of the two muscular components of the diaphragm ($r= 0.96$, $p<0.05$ for incremental breaths and $r=0.99$, $p=0.000$ for sighs). *Conclusion:* In humans, the costal and crural diaphragm are activated proportionally in concert to accommodate voluntary increases in the inspired volume.

A-05

Regulation of α-synuclein oligomerization and ubiquitinylation by molecular chaperones

LV Kalia (Toronto) SK Kalia (Toronto) H Chau (Toronto) AM Lozano (Toronto) BT Hyman (Boston) PJ McLean (Boston)*

Background: Parkinson's disease (PD) is a common neurodegenerative condition in which α-synuclein (α-syn) accumulates due to abnormalities in protein homeostasis. Recent evidence demonstrates that α-syn can self-associate into soluble oligomeric species and implicates these oligomers in neurodegeneration. Here we test the hypothesis that α-syn oligomers may be modulated by the molecular chaperones CHIP, which possesses intrinsic E3 ubiquitin ligase activity, and BAG5. *Methods:* Luciferase-based protein-fragment complementation assays were used to investigate α-syn oligomerization in living cells. Ubiquitinylation of α-syn by CHIP was examined in vitro and in cell lysates. We tested for protein complexes containing α-syn, CHIP, and BAG5 using pull-down assays, co-immunoprecipitations, and immunohistochemistry. *Results:* We find that α-syn is ubiquitinylated by CHIP and exists within a protein complex with CHIP and BAG5. The interaction of CHIP with BAG5 results in inhibition of CHIP E3 ubiquitin ligase activity and reduces α-syn ubiquitinylation. We demonstrate that non-ubiquitinylated α-syn has an increased propensity for oligomerization. Furthermore, BAG5 mitigates the ability of CHIP to reduce α-syn oligomerization. *Conclusions:* Our results identify CHIP as an E3 ubiquitin ligase of α-syn and suggest a novel function for BAG5 as a modulator of CHIP activity with implications for CHIP-mediated regulation of α-syn oligomerization in PD and other synucleinopathies.

A-06

An Ontario-based cost-utility analysis comparing the standard of care with direct decompressive surgical resection followed by radiotherapy in the palliative care of patients with metastatic spinal cord cancer

JC Furlan (Toronto) KKW Chan (Toronto) G Sandoval (Toronto) KC Lam (Toronto) CA Klinger (Toronto) RA Patchell (Phoenix) MG Fehlings (Toronto) A Laporte (Toronto)*

Background: This cost-utility analysis compares radiotherapy alone (RT) with decompressive surgery and postoperative radiotherapy (S+RT) for palliative care of metastatic spinal cord compression (MSCC). *Methods:* A cost-utility analysis for both treatment options, based on the randomized clinical trial (Patchell et al., Lancet 2005), was performed from the perspective of a public health care insurer. Ontario-based costs were adjusted to 2010 US dollars. *Results:* The S+RT strategy is more costly but more effective than RT-alone strategy, with an incremental cost-effectiveness ratio (ICER) of US$ 240 442.48 per quality-adjusted life year (QALY) gained. The Monte-Carlo simulation revealed that, by adopting the S+RT strategy, there would a reasonable chance (18.11%) of not paying extra for one additional QALY gained at willingness-to-pay of US$ 50,000. The acceptability curve showed that at the level of US$ 1,683,000 per one additional QALY, the proportion of ICERs reached the maximum of 91.11%. *Conclusions:* Given the increasing focus on the provision of cost-effective medical care, our results suggest that a change of the palliative treatment protocols for MSCC patients towards a S+RT approach is more likely to increase the healthcare costs. However, the gain in terms of patients' quality of life is relatively significant and should be considered by health care policy makers.

CACN Chair's Select Plenary Presentations

B-01

A national analysis of pediatric injuries related to child restraint seats: are children at higher risk for injury outside the vehicle than inside?

A Singhal (Vancouver) E Desapriya (Vancouver) I Pike (Vancouver)*

Introduction: The widespread use of Child Restraint Seats (CRS) has been effective in decreasing mortality and morbidity associated with Motor Vehicle Collisions (MVC). However, anecdotes suggest the use of CRS has been accompanied by an increase in infant falls from hand-held carrier/car seats. The current study explores the frequency of CRS-related injures both inside and outside of motor vehicles. *Methods:* The Canadian Hospital Injury Reporting and Prevention Program (CHIRPP) is a Canada-wide prospective emergency department surveillance program. A review was conducted in children under 1 year of age, of the cause and location

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

of injuries related to CRS use from 1995-2007. *Results:* There were 4131 injuries involving CRS, and a remarkable 66.7% of these occurred outside the vehicle. The most common factor in non-MVC related injuries was improper use of restraints while carrying the infant in the carrier/seat. Head injuries comprised the largest proportion of the non-MVC injuries, with almost 1500 injuries. The odds ratio for head injury was 42.7 ($p<0.0001$), a statistically significant finding suggesting that an infant in a CRS is far more likely to sustain a head injury outside the vehicle than in an actual MVC. *Conclusions:* This national study suggests than an unintended by-product of the widespread use of CRS is injury related to falls out of the CRS. This represents a previously unreported public-health issue affecting a substantial number of children. Education of the public regarding this issue, and promoting the proper use of CRS, will likely prevent many of these types of injuries.

B-02

Characteristic of post-traumatic headaches after pediatric mild traumatic brain injury

KM Barlow (Calgary) D Dewey (Calgary) S Crawford (Calgary)*

Background: There are few epidemiological descriptions of post-traumatic headaches in adults or in children. Indeed, perhaps because of this, ICHD-II does not require post-traumatic headaches to have specific headache features, only that the headaches temporally relate to a head injury. *Objectives:* To describe the clinical characteristics of headaches in post-concussion syndrome following a mild traumatic brain injury in children. *Methods:* A prospective cohort study of symptom survival in children (0-18 years) following mTBI in comparison to children with extra-cranial injury reported previously (Barlow et al, 2010). *Results:* 39 (75%) of 52 symptomatic children consenting to examination had significant headaches. The headaches were characterized as migraine-like, 53%, tension type 5%, musculoskeletal 5%, stabbing headache 10%, uncategorized 20% and occipital neuralgia in one case. Headache characteristics are shown in table 1 and table 2. *Conclusion:* Lew et al found a wide variation of migraine-like headache frequency (1.9 - 40.7%) in his systematic review although it only identified 5 studies. Our study is the first based on data from a population study and reveals mixed headache types but the commonest is migraine-like in the child and the family.

Barlow KM, et al, AA prospective epidemiological study of post-concussion syndrome in pediatric mild traumatic brain injury; Pediatrics 2010;126;e374-e381

Lew HL, et al, Headache After Traumatic Brain Injury: A Focused Review
Am J Phys Med Rehabil 2006;85:619–627

Table 1

The characteristic of the post-traumatic headaches

Age	Average 11.1 year (SD 4.3)
Sex	Male: 20 (51%)
Time since injury	Median: 2 months
N=39	Number (%)
Location	
Frontal	21 (53)
Temporal	7 (18)
Holocephalic	5 (13)
Retro-orbital	3 (8)
Occipital	2 (5)
Length of headache	
Minutes	4 (10)
1-2 hours	12 (30)
2-4 hours	13 (33)
>4 hours	7 (18)
Frequency	
Daily	17 (44)
3 or more/week	5 (13)
1-2 per week	7 (18)
1/week or less	8 (20)

Table 1

Associated features	
Nausea	19 (49)
Vomiting	4 (10)
Photophobia	14 (36)
Phonophobia	13 (33)
Pre-existing headache characteristics	
Migraine	18 (46)
Probable migraine	4 (10%)
Non-specific	6 (15%)
Family history of migrain	22 (56%)

B-03

BOLD signal alterations and white matter changes in children post mTBI: An fMRI and DTI study

RS Saluja (Montreal) J Chen (Toronto) R Aleong (Toronto) G Leonard (Montreal) I Gagnon (Montreal) M Keightley (Toronto) A Ptito (Montreal)*

Background: Mild traumatic brain injuries (mTBI) in children are of relatively high incidence (180 per 100 000/year) and account for 75-85% of all pediatric head injuries. While some children with mTBI suffer only temporary fluctuations in the level of consciousness, many have persistent cognitive deficits. Although some work has been done on mTBI in adults using functional magnetic resonance imaging (fMRI), little has been done in children or with diffusion tensor imaging (DTI). *Methods:* Children aged 10-17 who suffered mTBIs were recruited from the Montreal Children's Hospital. These subjects were age and sex matched to healthy controls. To date, 19 mTBI children and 50 controls were recruited. Each underwent fMRI (working memory and navigation tasks), DTI, and neuropsychological testing. DTI was analyzed using tract-based spatial statistics (TBSS) and region of interest (ROI) analyses and compared to fMRI results. *Results:* FMRI demonstrated decreased BOLD signal in the dorsolateral prefrontal cortex (DLPC) bilaterally during working memory tasks and posterior parahippocampal gyri during navigation tasks post mTBI. When compared to DTI findings, TBSS demonstrated that the fractional anisotropy (FA) maps from children with mTBI differed from controls in multiple areas including the regions listed above. This was corroborated by ROI analyses, particularly the right DLPC ($p=0.005$). *Conclusion:* These results demonstrate that fMRI and DTI abnormalities are present in children post mTBI, and that the areas of BOLD signal changes correlate well with areas of diminished FA values, suggesting that DTI and fMRI can be key complementary tools in the evaluation of pediatric mTBI.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

B-04

Correlation of Apgar scores with patterns of brain injury in term newborns with hypoxic-ischemic encephalopathy

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Objectives: Apgar scores primarily evaluate brainstem function and low scores often indicate hypoxic-ischemic(HI) insult. Our hypothesis is that low Apgar scores in term newborns with HI encephalopathy(HIE) are associated with a pattern of central injury involving predominantly basal nuclei and brainstem dysfunction whereas high scores occur with cortical/subcortical injury and relative preservation of brainstem function. *Methods:* Term newborns (≥36 weeks gestation) with HIE had MRI and diffusion-weighted MRI(DWI) performed on the third day of life (n=65). Using a previously validated scoring system, major patterns of HI brain injury were classified as: normal, basal nuclei, total (severe combined basal nuclei and watershed injury), watershed, and focal-multifocal. The 5-minute Apgar scores were stratified as high (≥ 5) (n=36) or low (≤ 4) (n=29) and correlated with patterns of injury. *Results:* When dichotomized, 5-minute Apgar scores differed significantly across patterns of injury (p=0.02). High Apgar scores, observed in 36/65 newborns, occurred differentially across patterns of injury (p=0.002): basal nuclei injury (1/9), total injury (2/9), watershed injury (5/8), focal/multifocal injury (7/11), normal MRI/DWI (21/28). Of 7 infants with low Apgar scores but normal MRI, 4/7 had received systemic cooling therapy. *Conclusions:* Apgar scores at 5 minutes differed across common patterns of HI brain injury in term newborns. Low scores occurred in less than half of infants, which is consistent with a predominance of cortical/subcortical injury associated with relative preservation of brainstem function. These observations may explain in part the unexpected high Apgar scores sometimes reported in association with HIE.

CNSS Chair's Select Plenary Presentations

C-01

Management of chronic subdural hematomas: is there a difference between the surgical options?

SA Almenawer (Hamilton) B Yarascavitch (Hamilton) K Reddy (Hamilton) F Farrokhyar (Hamilton)*

Background: Chronic subdural hematoma is a frequent neurosurgical entity. The gold standard treatment for chronic subdural hematoma is not well established and choosing a surgical technique is still controversial, therefore research to determine the best surgical option continues. *Methods:* We conducted a retrospective analysis of 626 patients with chronic subdural hematomas treated surgically between January 2004 and July 2010. Twist drill craniostomy was compared to burr hole craniostomy with the recurrence rate as a primary outcome and mortality, morbidity and the need for rehabilitation as secondary outcomes. We also examined recurrence rates for redo procedures comparing craniotomy, twist drill craniostomy and burr hole craniostomy. *Results:* Four hundred twenty-one patients underwent burr hole craniostomy with a recurrence rate of 21.8% while 205 patients had twist drill craniostomy with a recurrence rate of 22.9% (p = 0.760). No statistical difference was found comparing recurrence rates for one burr hole, 23.5% to two burr hole craniostomy, 20.1% (p = 0.421) and no difference was also found for drainage versus no drainage of burr hole craniostomy, 20.8% and 22.9%, respectively (p = 0.637). *Conclusion:* We did not find a statistical difference comparing twist drill craniostomy and burr hole craniostomy with regard to recurrence rates, morbidity, mortality or need for rehabilitation. One burr hole is as sufficient as two burr holes and the use of a drain post operatively does not decrease the recurrence rate after burr hole craniostomy. Even for redo surgeries, we did not find a difference in recurrence rates between the various surgical options.

C-02

Predictors of outcome following traumatic spinal cord injury

D Yavin (Calgary) AF Al-Habib (Riyadh) RJ Hurlbert (Calgary)*

Background: Numerous determinants of prognosis following spinal cord injury (SCI) have been proposed. Herein we report clinical and radiologic features predictive of outcomes following traumatic SCI. *Methods:* A secondary analysis was performed of outcomes collected during a randomized-controlled trial evaluating minocycline in consenting adult patients with traumatic SCI. Outcome measures included the American Spinal Cord Injury Association (ASIA) Impairment Scale (AIS) score, Functional Independence Measure (FIM), London Handicap Score (LHS) scale, Short Form 36 (SF36), and Spinal Cord Injury Measure (SCIM). Nine clinical and radiologic features were evaluated as predictors of outcome via a multivariate regression. *Results:* Fifty-two patients were enrolled from June, 2004 to August, 2008 and followed for a mean duration of 13.5 months. Mean patient age was 36.7 years, 73% were male, and 67% of injuries occurred in the cervical spine. At baseline mean AIS was 129.0. Twelve-month mean AIS, FIMS, LHS, SF36, and SCIM were 178.5, 99.4, 75.5, 87.3, and 59.8, respectively. Features independently associated with outcomes at 12 months were age (FIMS P=0.004, LHS P=0.016, and SCIM P=0.014), ASIA classification (AIS P=0.002, SCIM P=0.008, SF36 P=0.05), gender (SF36 P=0.001), length of parenchymal damage of T2-weighted MR imaging (AIS P=0.033, SF36 P=0.03), level of injury (AIS P=0002, SCIM P<0.001, LHS P=0.004, FIMS P<0.001), maximum canal compromise (LHS P=0.045), and the presence of intramedullary hematoma (SF36 P<0.022). *Conclusions:* Predictors varied with domains of outcome with age, ASIA classification, length of parenchymal damage of T2-weighted MR imaging, and level of injury consistently predictive of outcomes.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

C-03

Effect of clazosentan on clinical outcome after aneurysmal subarachnoid hemorrhage and surgical clipping: results of the CONSCIOUS-2 study

R Macdonald (Toronto) R Higashida (Toronto) E Keller (Toronto) S Mayer (Toronto) A Molyneux (Toronto) A Raabe (Toronto) P Vajkoczy (Toronto) I Wanke (Toronto) D Bach (Basel) A Frey (Basel) A Marr (Basel) S Roux (Basel) N Kassell (Charlottesville)*

Introduction: CONSCIOUS-2 assessed whether clazosentan improves VSP-related morbidity/all cause mortality after aSAH. *Methods:* CONSCIOUS-2 was a randomized, double-blind, placebo-controlled trial. Inclusion criteria were: age 18–75 years; ruptured saccular aneurysm secured by surgical clipping; diffuse clot; and WFNS grades I–IV. Patients were randomized 2:1 to intravenous clazosentan (5mg/h) or placebo for up to 2 weeks. The primary endpoint at week 6, assessed centrally, was: all-cause mortality; VSP-related new cerebral infarcts; delayed ischemic neurological deficit due to VSP; rescue therapy in the presence of confirmed angiographic VSP within 6 weeks of aSAH. The main secondary endpoint was extended Glasgow Outcome Scale (GOSE; dichotomized) at week 12. *Results:* There were 1147 patients (clazosentan n = 764, placebo n = 383). The primary endpoint occurred in 21% of clazosentan and 25% of placebo patients (relative risk reduction [RRR] 17%, 95% CI, -4 to 33%; p = 0.10). Poor outcome (GOSE score ≤4) occurred in 29% of clazosentan and 25% of placebo patients (RRR -18%, 95% CI, -45 to 4%, p = 0.10 [logistic regression adjusted for WFNS]). Mortality was 6% with clazosentan and 6% with placebo. Treatment-emergent lung complications, anemia, and hypotension occurred in 34%, 22% and 12% of clazosentan patients, respectively. Equivalent values for placebo were 18%, 15%, and 4%. *Conclusions:* Clazosentan led to a non-significant 17% reduction in mortality/VSP-related morbidity but no effect on functional outcome. Pulmonary complications, anemia, and hypotension were more common in patients treated with clazosentan.

C-04

Immediate post-coiling occlusion status of ruptured intracranial aneurysms: effect on long-term clinical and angiographic outcomes

MK Tso (Calgary) P Kochar (Calgary) M Goyal (Calgary) ME Hudon (Calgary) WF Morrish (Calgary) JH Wong (Calgary)*

Background: Subarachnoid hemorrhage secondary to a ruptured intracranial aneurysm is increasingly treated by endovascular coiling. This study analyzed the long-term clinical and angiographic outcomes of coiled ruptured intracranial aneurysms, stratified by the immediate post-coiling occlusion status. *Methods:* Patients initially treated with endovascular coiling (2002-2006) were identified at the Foothills Medical Centre (N=86). Long-term clinical outcomes utilized the modified Rankin Scale (mRS 0-6,0=no symptoms,6=death). Angiograms were graded based on the Raymond-Roy occlusion classification: complete obliteration (class 1), residual neck (class 2), and residual fundus filling (class 3). Associations between initial occlusion status and other variables utilized the Kruskal-Wallis test or Chi-Square test with $P < 0.05$ considered statistically significant. *Results:* Twelve (14.0%) aneurysms were completely occluded, 66 (76.7%) had a residual neck, and 9 (9.3%) had residual fundus filling. There were no significant differences in baseline clinical parameters. There were no significant differences in long-term clinical outcomes in surviving patients (mean mRS 1.1-1.2, P=0.584). Twenty-nine patients had recanalization at a mean of 13.0 months, but this had no significant effect on long-term mRS (P=0.904). Further interventions were performed in 16 patients (18.6%). Initial occlusion status was not associated with further intervention (P=0.576) and reintervention had no significant effect on long-term clinical outcomes (P=0.552). Recurrent rupture occurred in one patient (1.2%) 33.1 months after the initial coiling procedure. *Conclusions:* The majority of the ruptured aneurysms were initially incompletely coiled. Patients had good clinical outcomes in long-term follow-up. Recurrent rupture was rare. Recanalization remains a significant long-term issue but reintervention appears safe.

C-05

Extending the therapeutic window for reperfusion after stroke in non-human primates using a PSD-95 inhibitor

DJ Cook (Toronto) LM Teves (Toronto) M Tymianski (Toronto)*

Stroke is the third leading cause of death and carries the greatest socioeconomic burden of disease in North America. Early reperfusion by thrombolysis or mechanical means is the only treatment for acute ischemic stroke that is clinical proven; however, many patients do not qualify for reperfusion therapy due to a limited therapeutic window. As a potential strategy to increase the therapeutic window for reperfusion we tested the hypothesis that Tat-NR2B9c administered 1h into a 4.5h transient middle cerebral artery occlusion(MCAO) in cynomolgus macaques would improve stroke outcomes and reduce stroke volumes 7d following stroke by preserving salvageable tissue in the ischemic period. 12 cynomolgus macaques underwent open MCAO. Six animals received Tat-NR2B9c(2.6mg/kg) and 6 received placebo 1 hour following MCAO. The MCA was reperfused 4.5h after MCAO. Animals underwent perfusion MRI immediately after MCAO and diffusion weighted and T2 weighted MRI at 3h, 48h and 7d following MCAO to define stroke volume and perfusion-diffusion mismatch. Animals underwent serial clinical examination post-MCAO using the Non-Human Primate Stroke Scale(NHPSS). Tat-NR2B9c and placebo treated animals had equivalent volumes of tissue at risk by perfusion imaging at baseline. There was a 25% reduction in stroke volume measured by diffusion and T2 MRI (P=0.011). NHPSS was improved in Tat-NR2B9c treated animals at 7d (P=0.031). Tat-NR2B9c confers a neuroprotective effect as measured by neurological outcome and stroke volume when administered 1h into a 4.5h MCAO in cynomolgus macaques. This result suggests that early administration of a neuroprotectant can preserve ischemic tissue and improve outcomes with delayed reperfusion.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

C-06

A Phase I trial of deep brain stimulation of memory circuits in alzheimer disease

AW Laxton (Toronto) DF Tang-Wai (Toronto) MP McAndrews (Toronto) D Zumsteg (Toronto) R Wennberg (Toronto) R Keren (Toronto) J Wherret (Toronto) G Naglie (Toronto) C Hamani (Toronto) GS Smith (Toronto) AM Lozano (Toronto)*

Background: Alzheimer disease (AD) is characterized by functional impairment in the neural elements and circuits underlying cognitive and memory functions. We hypothesized that fornix/hypothalamus deep brain stimulation (DBS) could modulate neurophysiological activity in these pathological circuits and possibly produce clinical benefits. *Methods:* We conducted a phase I trial in 6 patients with mild AD receiving ongoing medication treatment. Patients received continuous stimulation for 12 months. Three main lines of investigation were pursued including: (1) mapping the brain areas whose physiological function was modulated by stimulation using standardized low-resolution electromagnetic tomography, (2) assessing whether DBS could correct the regional alterations in cerebral glucose metabolism in AD using positron emission tomography (PET), and 3) measuring the effects of DBS on cognitive function over time using clinical scales and instruments. *Results:* DBS drove neural activity in the memory circuit, including the entorhinal, and hippocampal areas and activated the brain's default mode network. PET scans showed an early and striking reversal of the impaired glucose utilization in the temporal and parietal lobes that was maintained after 12 months of continuous stimulation. Evaluation of the Alzheimer's Disease Assessment Scale cognitive subscale and the Mini Mental State Examination suggested possible improvements and/or slowing in the rate of cognitive decline at 6 and 12 months in some patients. There were no serious adverse events. *Conclusions:* There is an urgent need for novel therapeutic approaches for AD. Modulating pathological brain activity in this illness with DBS merits further investigation.

Neuro-Oncology (Medical and Radiation Oncology, Imaging, Tumour Surgery, Basic Science)

D-01

Receptor tyrosine kinase inhibition in pediatric high-grade glioma

KH Au (Edmonton) A Guha (Toronto)*

Background: In spite of current maximal therapy, the outcome for pediatric high-grade glioma (PHGG) remains poor. Recent genomic and expression profiling of PHGG specimens have revealed distinct molecular characteristics including amplification of the platelet-derived growth factor receptor A (PDGFRA) locus and increase in PDGFR-α and PDGFR-β expression and activation. We hypothesise that targeting of PDGFR using the small-molecule inhibitor nilotinib will reduce the tumourigenic behaviour of PHGG cell lines. *Methods:* PHGG-derived cell lines SF-188 and SJ-G2 were grown in various nilotinib concentrations (0μM, 3μM, 5μM, 10μM and 20μM). Cell viability was determined using MTS assay. Proliferation was assessed using BrdU assay and apoptosis examined with caspase 3/7 assay. *Results:* Viability of cell line SF-188 was significantly decreased in the presence of 3μM nilotinib. BrdU labelling was unchanged, but caspase 3/7 activity was significantly increased, suggesting that the viability effect is mediated by an increase in apoptosis. Viability of cell line SJ-G2 was also decreased in the presence of 3μM nilotinib, but with a significant decrease in BrdU labelling and no change in caspase 3/7 activity, suggesting a primarily anti-proliferative mechanism. *Conclusions:* The PDGFR inhibitor nilotinib is effective in reducing the viability of PHGG cell lines at clinically-relevant concentrations. Future studies will investigate the alterations in downstream activators, and pursue testing of nilotinib safety and efficacy in a PHGG mouse model.

D-02

Outpatient brain tumor and spinal surgery: a prospective study of 1003 patients

T Purzner (Toronto) J Purzner (Toronto) E Massicotte (Toronto) M Bernstein (Toronto)*

Background: Out-patient craniotomy, biopsy and spinal decompression have been performed in our center for over a decade. Early feasibility studies suggest they are safe, successful, cost-effective and well-tolerated. However, a large-scale study of this magnitude has not yet been performed. The primary objective of this study is to characterize post-operative complications and the rate of successful discharge from the Day Surgery Unit (DSU). We also discuss cost-savings, patient satisfaction and benefits to flow of care. *Methods:* From August 1996 to December 2009, 1003 consecutive patients were prospectively selected as out-patient candidates. Retrospective chart review was done and analysed by intention to treat. *Result:* Of 249 craniotomies, 92.8% were successfully discharged from the DSU, 5.2% were admitted from the DSU and 2.0% were discharged and later readmitted. Of 602 spinal decompressions, 97.3% were successfully discharged, 2.5% were admitted and 0.2% were discharged and later readmitted. Of 152 brain biopsies, 94.1% were successfully discharged, 4.6% were admitted and 1.3% were discharged and later readmitted. No patients experienced a negative outcome as a result of early discharge. Total cost savings over the period of this study is estimated to be $3,437,160.00. *Conclusion:* Out-patient craniotomy, biopsy and spinal decompression are safe, successful and cost-effective.

D-03

Establishing Canadian practice trends for management of brain metastses

P Goetz (Toronto) E Monsalves (Toronto) D Fewer (Winnipge) G Zadeh (Toronto)*

Patients with brain metastases are a rapidly evolving population, in particular as control of systemic cancers are improving. The level of evidence to support our clinical care of patients with brain metastases is limited and in neuro-oncology we are faced with the daily challenge of designing the best management strategy for individual patients. In order to understand better the practice trends across Canada we carried out a questionnaire that surveyed neurosurgeons and radiation oncologist involved in treating brain metastases. We present the results of our survey in order to

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

demonstrate the range of existing clinical practice across Canada, identify specific Canadian health care relevant and applicable practice patterns and reflect areas in need of further development. Furthermore, our hope is that presentation of the survey results will also provide a forum to engage clinicians involved and interested in treating brain metastases to form a national working-group for brain metastases that can focus on identifying clinical needs of medical communities involved in care of patients with brain metastases.

D-04

Prostate adenocarcinoma to the lumbosacral plexus: MRI evidence to support direct perineural spread

M Hébert-Blouin (Montréal) KK Amrami (Rochester) RP Myers (Rochester) AS Hanna (Rochester) RJ Spinner (Rochester)*

Introduction: Prostate adenocarcinoma frequently recurs either at local or distant sites despite aggressive treatment. Not widely known and recognized, the intraneural occurrence of prostate adenocarcinoma at the level of the lumbosacral plexus is thought to be from direct perineural spread. We hypothesized that this mechanism of spread could be supported by high-resolution imaging. *Material and Methods:* The clinical data and imaging studies of 4 patients evaluated at our institution between 2004 and 2009 for lumbosacral plexopathy due to intraneural prostate adenocarcinoma were retrospectively reviewed. Imaging consisted of MRI in all cases (high-resolution n=3) and PET/CT (n=2). *Results:* In all patients presenting with painful lumbosacral plexopathy found to have intraneural lumbosacral prostate adenocarcinoma, high-resolution MRI and PET/CT studies revealed similar findings: abnormal soft tissue signal could be seen from the prostate (n=1) or prostatic bed (n=3) area along the expected course of the neurovascular bundle to the level of the sciatic notch. At the level of the notch, the abnormality involved the sacral nerve roots and sciatic nerve. Consistent with neoplastic infiltration, the imaging findings were confirmed at biopsy in 3 patients. *Conclusion:* The potential for prostate adenocarcinoma to spread to the lumbosacral plexus has not been previously appreciated. Since the imaging findings are often subtle even with high-resolution MRI, we believe that intraneural lumbosacral plexus involvement may be under-recognized. With the use of high-resolution MRI and PET/CT studies, this study supports the direct perineural spread of prostatic adenocarcinoma to the lumbosacral plexus via the neurovascular bundle.

D-05

Dysembryoplastic Neuroepithelial Tumours in pediatric patients: longterm follow up

M Nadi (Toronto) E Bouffet (Toronto) J Drake (Toronto)*

Background: Dysembryoplastic Neuroepithelial Tumour (DNET) is a rare generally benign pediatric brain tumour whose optimal management and long term outcome is uncertain. *Methods:* We retrospectively reviewed all patients identified with a DNET at the Hospital for Sick Children who presented between 1987 to 2010. Patient demographics, clinical presentation, operative procedures, pathology, and outcome were determined. *Results:* Of the 38 patients identified, 23 were males (60 %), 36 (95%) presented with seizures at an average age of 7.3 yrs. The most common seizure presentation was partial complex, 15 cases, or with secondary generalization, 12 cases. The most common tumour location was frontal, 15 cases, or temporal, 11 cases. Average duration of follow was 5.5 yrs. 14 of 17 patients who underwent a gross total excision were seizure free off medication compared to 4 of 17 patients with residual tumour. One patient with early tumor regrowth received radiation therapy. He subsequently received chemotherapy (thioguanine, vincristine, procarbazine and lomustine) as he was showing evidence of dissemination. Repeat resection 4 years after initial diagnosis revealed malignant transformation with BAF47 negative cells, suggestive of rhabdoid tumour. All patients are alive at last follow up. *Conclusion:* Pediatric DNET are rare tumours with an excellent overall prognosis. Gross total excision where possible provides excellent tumour and seizure control. Tumours not amenable to complete excision are more problematic and require ongoing surveillance. The need for adjuvant treatment is exceptional and should raise the issue of some atypcal DNET that may have a different behaviour.

D-06

ECT2 and RASAL2 mediate mesenchymal-amoeboid transition in human astrocytoma cells

A Weeks (Toronto) J Rutka (Toronto)*

Malignant astrocytomas are highly invasive brain tumors. Previously, we have shown that the Rho family of cytoskeletal GTPases are key regulators of astrocytoma migration and invasion. Expression of the guanine nucleotide exchange factor, ECT2, is elevated in primary astrocytomas and predicts both survival and malignancy. Here we show that mice bearing orthotopically implanted human astrocytoma cells with diminished ECT2 following ECT2 knockdown exhibit longer survival and less invasive lesions than controls. While ECT2 is normally expressed in the nucleus, we show that ECT2 is aberrantly localized to the cytoplasm in both astrocytoma cell lines and primary human astrocytomas. ECT2 co-localizes with RAC1 and CDC42 at the leading edge of migrating astrocytoma cells. Inhibition of ECT2 expression by RNAi resulted in a 25% decrease in RAC1 and CDC42 activity but no change in RHO activity, suggesting that ECT2 is capable of activating these pro-migratory Rho family members. Interestingly, ECT2 overexpression in astrocytoma cells resulted in transition to an amoeboid phenotype that was abolished with the ROCK inhibitor, Y-27632. We performed cytoplasmic fractionation of astrocytoma cells followed by ECT2 immunoprecipation and mass spectrometry to identify interactors responsible for modulating ECT2's activity toward RAC1 and RHO/ROCK. We identified RASAL2 as a putative ECT2 interacting RHO-GAP in astrocytoma cells. Loss of RASAL2 by RNAi leads to a conversion to an amoeboid phenotype with increased invasion of astrocytoma cells. Our studies demonstrate that ECT2, in conjunction with RASAL2, play a significant role in mesenchymal-amoeboid transition in human astrocytoma cells.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

D-07

Role of the mTOR inhibitor everolimus in treating patients with neurological manifestations of Tuberous Sclerosis Complex (TSC): rationale and current clinical trials

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Rationale: TSC is a devastating disorder characterized by tumors in multiple organ systems and associated disabling neurological disorders including epilepsy, mental retardation, and autism. TSC lesions occur throughout the body including the kidney (angiomyolipomas), lungs (lymphangiomyomatosis), and brain (cortical tubers and subependymal giant-cell astrocytomas [SEGAs]). TSC is caused by mutations in the *TSC1* or *TSC2* genes, which result in constitutive mTOR activation that drives the pathogenesis of TSC. *Methods:* Recently, an open-label, phase II trial (NCT00411619) of everolimus, an oral, selective mTOR inhibitor, demonstrated a significant reduction in SEGA volume and a decreased seizure frequency. Based on these data, additional phase II studies have been launched or are being planned to explore the benefit of everolimus in patients with neurological manifestations of TSC. In addition, the ongoing EXIST-1 trial (**EX**amining everolimus **I**n a **S**tudy of **T**SC; NCT00789828), a randomized, prospective, double-blind, multicenter study, is the first placebo-controlled phase III study in patients with TSC. *Results:* Based on the phase II trial, the FDA recently approved everolimus for TSC patients with SEGAs who require treatment but are not candidates for surgery. Additional rationale supporting mTOR inhibition as a therapeutic target in patients with TSC and detailed study designs will be presented.

Key studies of everolimus in patients with neurological manifestations of TSC

Key studies of everolimus in patients with neurological manifestations of TSC				
Phase	Design	N	Primary endpoint	Status
II	Nonrandomized, open-label study in TSC-associated SEGAs	25	SEGA response rate	Ongoing (NCT00411619)
I/II	Nonrandomized, open-label study in TSC-associated SEGAs	20	Reduction in seizure frequency	Recruiting (NCT01070316)
III	Randomized, double-blind, placebo-controlled study in TSC-associated SEGAs	99	SEGA response rate	Recruiting (EXIST-1; NCT00789828)
II	Randomized, double-blind, placebo-controlled study in patients with TSC	100	Effect on neurocognitive behaviors	Planned
II	Randomized, double-blind, placebo-controlled study in patients with TSC	55	Efficacy on neurocognition	Planned
II	Nonrandomized, open-label study in patients with TSC-associatedintractable epilepsy (everolimus concomitant with existing anticonvulsant regimen)	40	Reduction in seizure frequency	Planned

D-08

Identification of a genetic signature for bone invasive versus non-invasive meningiomas

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Introduction: Though meningiomas are mainly benign tumors, a subset demonstrate bone tropism, resulting in hyperostosis and invasion into adjacent neural and soft tissue. Consequently surgical resection of bone-invading meningiomas is challenging and repeat surgery is often required, resulting in significant patient morbidity. The molecular pathophysiology of bone invading meningiomas is not known. Our study focuses on indentifying differentially expressed genes involved in bone tropism of meningiomas, with hopes to identify novel therapeutic targets. *Methods:* Two distinct bone invading meningioma subtypes and their control counterparts were identified based on radiological characteristics: 1) spheno-orbital (control: non-invading sphenoid wing meningioma) and 2) transbasal meningioma (control: anterior skull base meningioma with no bone invasion). RNA was extracted from paraffin-embedded tissue, processed on Illumina Whole Genome DASL assay. Data were analyzed using Multi Expression Viewer Software (MEV). Quantitative real-time PCR (RT-qPCR) was used to verify micro-array data. Three different meningioma cell lines were used to verify functional relevance of identified genes in addition to Tissue microarray (TMA) analysis of commercially available antibodies. *Results:* RNA microarray data identified novel genes over-expressed in invasive menigiomas: PDGFRα, MMP16, MMP19, Matrilin4 and ADAMTS4. Upregulation of these genes were verified using quantitative real-time PCR, both in tumor specimens and meningioma cell lines. TMA analysis identified increased expression of both MMP2 and integrin-β1 in tumor cells, and an increase of vascular MMP2 expression in non-invasive compared to invasive meningiomas. *Conclusions:* Our results identify novel differentially expressed genes in bone-invading meningiomas, providing promising therapeutic targets that can be tested in clinical trials.

D-09

The learning curve for endoscopic endonasal transsphenoidal resection of pituitary tumors

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The learning curve for surgical skills has important implications in the incorporation of new procedures, resident training, and surgical innovation. The majority of reports suggest that the curve reaches an asymptote at 20 to 30 cases. In this study, the learning curve for endoscopic endonasal transsphenoidal resection of pituitary tumors was determined by measuring patient outcomes with respect to complication rates. We hypothesized that there would be a difference in complication rate comparing the first 30 cases to subsequent operations.

We conducted a retrospective review of 120 consecutive patients treated over a four year period. Patients were divided into four equal groups based on the order in which they were operated on. Outcome measures included: all complications, incidence of CSF leak,

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

requirement for lumbar drain, postoperative endocrinopathy, need for re-admission, and length of hospital stay (LOS).
In the first group, 10 patients had CSF leaks, 9 required lumbar drains, and the average LOS was 4.1 days. In the second group, 3 patients had CSF leaks (10%), 1 required a lumbar drain, and the average LOS was 3.6 days. Comparing the first group to others there was a significant difference found with respect to CSF leaks, lumbar drains and LOS.
Our results indicate that a surgical learning curve exists for endoscopic transsphenoidal surgery and comprises the first 30 cases. These results are comparable to similar studies of acquisition of new surgical procedures.

D-10

Stereotactic radiosurgery of melanoma and renal cell carcinoma brain metastases

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Objective: Renal cell carcinoma (RCC) and melanoma brain metastases have traditionally been considered to be radioresistant, however, stereotactic radiosurgery (SRS) is becoming more accepted as a treatment option for these subtypes. We aimed to evaluate the role of SRS for local control of RCC and melanoma brain metastases. *Methods:* We retrospectively reviewed our prospectively maintained database of Gamma Knife-SRS treated patients between 2006-2010. We identified 33 RCC and 17 melanoma patients. Demographic features, dosimetry parameters, and radiological features were examined as predictors of response. *Results:* Median follow-up was 5 months (range, 1 to 41 months). 57.6% of the patients had multiple metastases. 56.3% metastases had been treated previously with whole brain radiotherapy (WBRT) with the remaining having received SRS alone upfront. Median prescription dose was 21 Gy (range, 15 to 24 Gy). Mean tumor volume was 1.34 cm^3 (range, 0.005 to 13.36 cm^3). Median RTOG conformality index was 1.96 (range, 1.04 to 9.76). Local control rates were 86.6%, 91.7%, 95.8%, and 84.2% at 3, 6, 12, and 18 months respectively. Smaller metastases demonstrated better local control rates. Three (3.1%) of the treated brain metastases required local salvage therapy in the form of surgical resection. Twenty-four (25.0%) of the metastases were treated with WBRT 2 to 21 months after SRS for distant brain failure. *Conclusions:* SRS is a valuable option for local control of RCC and melanoma brain metastases. RCC and melanoma respond as favourably as other tumor subtypes for local control and delay of WBRT is safe without significant difference in local control rates.

Neuromuscular and Epilepsy (EEG, Basic Science, Imaging, Neurology and Epilepsy Surgery)

E-01

Increased BDNF in the Transgenic Model of Atypical Absence Seizures

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Background: Brain derived neurotrophic factor (BDNF) overexpresion (Croll et al., 1999) or chronic infusion of BDNF (Berzaghi et al., 1995; Scharfman et al., 2002) were implicated in seizure exacerbation. Therefore, we compared the BDNF expression in three subunit mouse lines of GABAB Transgenics (Tg), known to have a subunit dependent degree of seizure severity (Stewart et al. 2009). *Methods:* Genotyping for Wild type (N=5), transgenic R1b (N=2), R2 (N=2) and Double Tg (N=3) subunit mouse lines. We used PCR analysis with primers complimentary to the receptor subunits. Cortex, cerebellum and hippocampus were dissected, homogenized and transferred onto nitrocellulose membrane after electrophoresis. BDNF Expression was measured three times in integrated density [idv] values. *Results:* The BDNF expression in Tg hippocampus was increased: idv R1b [599312.5], R2 [608026.5], and DTg [618514.3], compared to WT [400684.4]; BDNF was lower in Tg cortex: R1b [157276], R2 [157395], and DTg [156674] compared to WT [105372.8]. With a simultaneous decrease in the Tg cerebellum R1b [0.2144899], R2 [0.215981], and DTg [0.2059223] compared to WT [0.22143253]. *Conclusion:* The BDNF level changes appear subunit specific and may contribute to an imbalance between excitation and inhibition in GABAB Tg mice. (Supported by Epilepsy Canada)

E-02

How to measure fatigue in epilepsy? The validation of three scales for clinical use.

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Fatigue is defined as extreme and persistent mental or physical tiredness or exhaustion.
The main objective of this study is to validate three instruments to measure fatigue (Fatigue Symptom Inventory-FSI, Fatigue Assessment Instrument-FAI, Fatigue Severity Scale-FSS) in patients with epilepsy (PWE). We used concurrent validity as a method of validation. Reliability of the fatigue scales was assessed in PWE. We applied the three selected questionnaires plus the Beck Depression Inventory in PWE, healthy volunteers (HV) and patients with other neurological conditions.
We studied 67 PWE, 34 HV and 56 patients with different neurological conditions. The FSI scores were as follows: HV 2.2 + 1.3, PWE 3.9 + 2.3, multiple sclerosis patients (MSP) 4.5 + 0.9, patients with migraine (PWM) 4.6 + 1.5, and patients with radiculopathy (PR) 4.4 + 1.4. For the FAI: HV 3.0 + 1.1, PWE 4.2 + 1.3, MSP 4.5 + 0.9, PWM 4.3 + 1.5, and PR 4.4 + 1.4. For the FSS the corresponding scores were; HV 2.6 + 1.1, PWE 4.2 + 1.5, MSP 4.8 + 1.4, PWM 4.4 + 1.9, and PR 4.5 + 0.9. The correlation between

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

the BDI and the FSS was 0.52 (p<0.001), between the BDI and the FSI was 0.62 (p<0.001), and between the BDI and the FAI was 0.54 (p<0.001).
PWE have consistently higher fatigue scores then healthy controls, and comparable with other neurological conditions. The FSI, FAI and FSS display concurrent validity and high intra-observer reliability in PWE, therefore they useful in assessment of fatigue in epilepsy.

E-03

Seizure control following surgical excision of cerebral vascular malformations

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Background: Approximately 40% of patients with cerebral vascular malformations (CVM), such as arteriovenous malformations (AVM) and cavernous malformations (CM), present with seizures. In addition to eliminating the risk of future hemorrhage, surgical excision of CVM is believed to lead to seizure control. The purpose of our study was to evaluate seizure outcome in patients with CVM who presented with seizures, and to compare our results with the existing literature to evaluate quality of care in Canada. *Methods:* A retrospective chart review of patients with CVM who presented with seizures and underwent microsurgical resection by a single surgeon between 1994 and 2010 at Vancouver General Hospital was performed. 48 patients fit the criteria for the study and their clinical information was documented. *Results:* Of the 135 patients with microsurgical resection of CVM, 48 patients (36%) presented with seizures and average time between presentation and excision was 6.3 months. After a mean follow-up period of 13 months, 60% of patients with AVM and 80% of patients with CM could be evaluated as Engel Class I. 6% of patients experienced post-operative neurological deficits and there were no mortalities. The long-term relief of seizures following microsurgical resection are currently being evaluated. *Conclusions:* In this series, 36% of patients with CVM presented with seizures, and 64% experienced Engel Class I seizure control post-lesionectomy. Results for CM appear to be somewhat better than for AVMs. The results suggest that surgery is a safe and effective treatment for seizures associated with CVM.

E-04

Ambulatory Elelctroencephalography (EEG) in adults: diagnostic yield, tolerability and customer satisfaction

*L Hernandez-Ronquillo (Saskatoon), *F Moien Afshari (Saskatoon), JF Tellez-Zenteno (Saskatoon)*

Background: Ambulatory EEG is a technique that allows recording of continuous EEG activity when patients are at home without the necessity of admission to hospital for prolonged video EEG monitoring. *Methods:* This is a prospective cohort study. We applied two questionnaires to the neurologist, before and after the ambulatory EEG in order to assess the diagnostic yield. *Results:* Forty nine patients, aged 13-73 years, undergoing ambulatory electroencephalography (EEG) were prospectively recruited over 36 months at the Royal University Hospital, Saskatchewan. Our population consisted of fifteen males (30%) and thirty four females (70%). The age at onset of events was 30.2 + 18.98 years with 7.42 + 10.36 years of evolution. Most of the patients had had previous routine EEG (98%) and 74% (37 EEG) of them were normal. The most frequent reason (53% of the time) for ordering an ambulatory was for the characterization of the spells (query non epileptic events), in 31% (15) of the cases the ambulatory was order for the characterization of the spells with potential epileptic diagnosis. In 8% the ambulatory was order for work up in candidates for epilepsy surgery. In another 8% of the patient the indication were characterization of the spells in patients with epilepsy and quantification of spikes. *Discussion:* In this study, we found most of the patients did have previous EEG with no clinical answer, and in the end had a high diagnostic yield (70%) comparable with our V-EEG monitoring (88%) despite a shorter recording (1-2 vs. 4.4+2 days).

E-05

Paediatric myasthenia: first year of active national surveillance.

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Background: This is the first population-based study to systematically evaluate the clinical features and incidence of pediatric myasthenia (PM) in Canada. *Methods:* Paediatric specialists participating monthly to the Canadian Paediatric Surveillance Program anonymously reported confirmed PM cases and completed a standardized clinical questionnaire containing de-identified data. Inclusion criteria: Any child up to 18 years old with at least one of the following clinical features: a) fluctuating ptosis or extraocular weakness; b) history of skeletal muscle weakness or fatigue AND c) a supportive test of either a clinical response to acetylcholinesterase inhibitor, positive acetylcholine receptor or muscle-specific kinase antibodies, a significant electrodecremental response with repetitive stimulation, or an abnormal single fiber EMG. *Results:* To date, 33 confirmed cases were reported from Ontario, Alberta, Manitoba, Quebec, and Newfoundland. There were 20 generalized and 9 ocular reports of PM in children plus 4 congenital myasthenic syndromes. There were 12 incident cases in 2010: 8 generalized and 4 purely ocular. Age of onset ranged from birth to 17 (median = 7) years for the generalized form compared to 22 months to 11 (median=5) years for the ocular subtype. Positive acetylcholine receptor titres were found in 10/20 (50%) of generalized cases and 6/9 (67%) ocular patients. *Conclusions:* This ongoing study, which represents the largest descriptive series of PM in North America, provides valuable information about clinical characteristics and raises awareness regarding the diagnosis. A high index of suspicion is required even in seronegative patients.

E-06

Congenital myotonic dystrophy: Canadian surveillance and cohort study

C Campbell (London)

Background: Congenital Myotonic Dystrophy (CDM) is a rare manifestation of genetic anticipation in DM1 families. A five year Canadian Pediatric Surveillance Program was conducted to determine the incidence of CDM in Canada. This study will help provide a clear definition of CDM, clarify phenotype-genotype relationships and describe the burden of illness and family impact of CDM. *Methods:* The surveillance period was March 2005 to February 2010. An incident case was a new genetically diagnosed case of CDM under the age of three, which required hospital

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

admission for greater than 72 hours due to DM1 neonatal symptoms. All confirmed cases were invited to enrol in a cohort study collecting clinical information and quality of life data. *Results:* A total of 121 cases were reported, with 38 confirmed as CDM. The incidence of CDM in Canada is 2.1/100,000 live births. Of confirmed cases 4 were identified in 2005, 10 in 2006, 8 in 2007, 4 in 2008 and 12 in 2009. The cases were reported from eight provinces and one territory. The highest reported incidence was Ontario with 15, British Columbia- 7, and Quebec- 6. Validation of cases was completed. Twenty two of the children were the index cases for their families. Seventeen children are currently enrolled in the cohort study. *Conclusion:* Surveillance and prospective examination of CDM at a population level is important, as the impact of this rare disease is systemic, chronic and associated with significant morbidity and mortality throughout childhood.

E-07

Safety and Efficacy of low-dose ataluren in boys with nonsense mutation dystrophinopathy

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Background: Ataluren is an investigational new drug for nonsense mutation Duchenne and Becker muscular dystrophy (nmDBMD), which comprises ~12% of all dystrophinopathy cases in Canada. *Methods:* In this Phase 2b, randomized, double-blind, placebo-controlled study, 174 boys ≥5 years old with nmDBMD received daily TID placebo, low-dose ataluren (10, 10, 20 mg/kg), or high-dose ataluren (20, 20, 40 mg/kg) orally for 48 weeks. The primary outcome measure was 6-minute walk distance (6MWD). *Results:* Ataluren was generally well tolerated at both dose levels. The mean change in 6MWD from baseline to Week 48 was 29.7 m better in the low-dose arm compared to placebo; a post-hoc permutation test based on a mixed-model repeated-measures approach showed a nominal p-value of 0.058 for low-dose ataluren versus placebo. There was no difference between high-dose ataluren and placebo in 6MWD. These results are consistent with a bell-shaped dose-response curve. Patients receiving low-dose ataluren had a significantly longer time to persistent 10% worsening in 6MWD relative to placebo (Cox regression, p=0.039). *Conclusions:* This study advances knowledge on the natural history and clinical endpoints for nmDBMD. Although the primary endpoint did not reach statistical significance, the data suggest that low-dose ataluren may provide clinical benefit to nmDBMD patients.

E-08

Low-pressure headaches in adult patients with traumatic brachial plexus injury

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Introduction: Brachial plexus injury (BPI) are generally not thought to be associated with headaches. However, it is well known that CSF leaks can occur in BPI patients from nerve root avulsion and that CSF leaks may be associated with low-pressure headaches. In the literature, only a few cases are reported. It is unknown if the prevalence of headaches in patients with BPI is low, or if they are unrecognized. The aim of this study is to determine the prevalence of low-pressure headache in patients with BPI. *Methods:* All patients presenting at our brachial plexus clinic with adult traumatic BPI were asked to complete a questionnaire on the presence and quality of headaches following their injury. The patients' and injury's characteristics were subsequently reviewed. *Results:* From December 2008 to July 2010, 145 patients filled the questionnaire. Of these patients, 22 reported new onset headaches occurring after their injury, seven of these patients having positional headaches. In patients with positional headaches, consistent with low-pressure headaches, 6 had a clear preganglionic brachial plexus injury. Available imaging studies revealed 2 patients with pseudomeningoceles, 1 with a pseudomeningocele and evidence of CSF tracking in the soft tissue, and 2 with CSF tracking into the pleural space. *Conclusion:* In this retrospective study, 15% (22/145) of patients with traumatic BPI suffered from a new-onset headache after their injury, a third of these (7/22) having characteristics of low-pressure headache. These headaches, likely secondary to a CSF leak associated with the BPI, occur in a significant proportion of patients and have been under-recognized.

E-09

Ulnar Neuropathy at the Elbow (UNE): evaluation of the causative role of elbow leaning and flexion, and of the efficacy of conservative management

JD Stewart (North Vancouver)

Background: Very few trials have assessed the efficacy of conservative management of ulnar neuropathies at the elbow (UNEs). This prospective study evaluates the notion that UNEs are often caused by habitual elbow leaning, prolonged elbow flexion during sleep, or both; and to test the hypothesis that avoiding these will correct the neuropathy. *Methods:* Patients selected were those with moderate UNEs as determined by standard clinical and electrodiagnostic criteria. Exclusions were acute or chronic elbow trauma, perioperative UNEs, known diabetes. Patients were taught to avoid habitual elbow leaning and prolonged elbow flexion and followed 2 monthly. *Results:* Of 37 patients with 38 moderate UNEs, 25 (66%) slept with the elbow tightly flexed and 21 (55%) were habitual elbow leaners.

Following conservative management 23 (61%) patients improved to their satisfaction, and 10 (26%) recovered fully. The time to these end points varied from 2 months to 3 years. Five (13%) patients worsened and were referred for surgery. *Discussion:* This prospective study supports the concept that elbow leaning and prolonged flexion are important causes of otherwise unexplained UNEs, and shows that avoidance of these habits is effective treatment in 87% of patients with moderate UNEs.

E-10

Aetiology of carpal tunnel syndrome in children in British Columbia

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Background: Mucopolysaccharidosis (MPS) and mucolipidosis (ML) are the most common causes of carpal tunnel syndrome (CTS) (35-70%) in children with no history of trauma. *Methods:* All nerve conduction studies in the Electrophysiology-Laboratory (1992-

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

2010) were reviewed. All individuals who had CTS release surgery were included. *Results:* 1979 individuals (age 0-18 years) underwent nerve conduction study. 45/1979 had CTS. 18/45 (40%) individuals had history of trauma. 27/45 (60%) individuals had no history of trauma. In this group 6/27 individuals had diagnosis of MPS (3 with type I; 2 with type II and 1 with type VI). However, in 21/27 of them, there was no specific diagnosis. Eleven of 45 individuals with CTS underwent carpal tunnel release surgery including 5 of the 6 with MPS. Another 6 individuals had carpal tunnel release surgery, but they were not in the nerve conduction study database. *Summary:* CTS may have a role as a screening indicator for diagnosis of MPS and ML. Disease specific enzyme replacement therapy is available for MPS type I, II, and VI to improve patients' quality of life and disease related morbidity. This retrospective study will allow us to investigate individuals with CTS for specific underlying aetiology in a prospective study.

Trauma, Critical Care

F-01

Comparison of hypertension, hypervolemia, and transfusion to augment cerebral oxygen delivery after subarachnoid hemorrhage

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Background: Critical reductions in cerebral blood flow (CBF) and oxygen delivery (DO2) underlie delayed cerebral ischemia (DCI) after subarachnoid hemorrhage. Unless DO2 is promptly restored, irreversible injury (i.e. cerebral infarction) may result. Hemodynamic therapy with induced hypertension and hypervolemia aims to raise CBF and thereby improve DO2. Transfusion is an alternate strategy which may augment DO2 by improving arterial oxygen content. The relative efficacy of these interventions has not been assessed, specifically their ability to restore DO2 to regions where it is impaired. *Methods:* We analyzed data from three prospective studies utilizing 15O-PET to measure the effects of: 1) fluid bolus of 15 ml/kg normal saline (n=9); 2) raising mean arterial pressure 25% (n=12); 3) transfusing one unit of RBCs (n=17), to aneurysmal SAH patients at risk for DCI. PET was performed at baseline and immediately after the intervention. We compared change in DO2 between groups globally and in brain regions with low baseline DO2 (< 4.5 ml/100g/min). *Results:* Global CBF or DO2 did not rise after any of the interventions, except when transfusing patients with hemoglobin < 90 g/l. All interventions improved CBF and DO2 to regions with low baseline DO2, but the improvement was greater after transfusion (+23%) than hypertension (+14%) or hypervolemia (+10%);$p<0.001$. Transfusion also tended to reduce the number of vulnerable regions (by 47% vs. 12% for hypertension, 7% for fluid),$p=0.33$. *Conclusions:* Hypertension, hypervolemia, and transfusion all improve DO2 to vulnerable brain regions at risk for ischemia. Transfusion may provide the greatest benefit, especially amongst patients with anemia.

F-02

Intravenous milrinone in the treatment of cerebral vasospasm and ischemia induced by aneurismal subarachnoid hemorrhage

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Introduction: In subarachnoid hemorrhage, delayed cerebral ischemia (DCI) secondary to cerebral vasospasm leads to significant morbidity and mortality. Current therapies focus on increasing blood flow using hypertension, hypervolemia and angioplasty. Milrinone, a phosphodiesterase inhibitor, combines vasodilating and inotropic properties. We present 102 patients with DCI treated with intravenous milrinone, normovolemia, and maintenance of homeostasis (the MNH protocol). We describe the safety profile of milrinone in this context and the neurological outcomes associated with this approach. *Methods:* Retrospective chart review of all patients with aneurismal subarachnoid hemorrhage (SAH) from April 1999 to January 2006. DCI is defined as deterioration in neurological status unexplained by metabolic, infectious or other neurologic disease, with abnormalities on angiography or transcranial Doppler (99/102). We excluded patients who were moribund on admission and did not improve after initial therapy as well as patients who died less than 48 hours after admission. *Results:* 102 patients with DCI treated with the MNH protocol. Severity divides equally among Hunt and Hess (HH) grades 1-4, with few grade 5. Modified Fisher score was 3-4 in 80.4%. Mean Milrinone use was 9.4 days. Only occasional mild tachycardia was reported. Mean patient follow up was 46.26 months. New CT ischemia attributed to vasospasm was seen in 35%, but did not correlate with outcome. Functional outcome was good (MRS≤2) in 76.47% (78/102). Younger age and lower initial HH grades were predictors of good outcome. *Conclusion:* Treatment of DCI with milrinone, normovolemia, and maintenance of homeostasis was safe and achieved MRS≤2 in 76.4% of patients.

F-03

Understanding how a cell transplantation paradigm leads to functional recovery from spinal cord injury: the importance of remyelination

GWJ Hawryluk (North York) MG Fehlings (Toronto)*

Background: The mechanism by which transplanted cells lead to functional recovery following spinal cord injury is unclear. Better understanding is required to augment recovery. *Methods:* Two weeks following clip compression spinal cord injury (SCI) rats underwent cellular or control transplantation. Cellular transplants included wild-type mouse neural precursor cells (NPCs) and NPCs derived from shiverer mice unable to produce myelin. Most transplanted animals also received minocycline, cyclosporin and an infusion of EGF, bFGF and PDGF. Hind-leg motor function was assessed according to the BBB scale. qPCR was performed for candidate trophins on transplanted tissue. H&E/LFB staining was used to assess grey and white matter, cyst and lesional tissue. Mature oligodendrocytes, inflammatory cells and axonal preservation was quantitated. *Results:* NPC transplantation, pharmacotherapy and trophin administration led to a synergistic increase in the expression of numerous trophins. Pharmacotherapy and trophin infusion led to grey and white matter sparing. Trophin infusion was associated with a significant increase in cyst and lesional tissue volume as well as

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

inflammatory cell numbers. No experimental therapy preserved axons. Animals transplanted with wild-type NPCs without trophin infusion showed significantly greater functional recovery than any other group. Animals transplanted with shiverer NPCs performed worst on functional testing. *Conclusions:* These results suggest that remyelination by exogenous cells is their most important contribution to functional recovery following SCI. Trophin infusion via an osmotic mini-pump is harmful and best avoided. These findings may allow the functional recovery associated with NPC transplantation to be augmentated.

F-04

Brain CT Scan Compared to Somatosensory Evoked Potential (SSEP) grade for predicting outcome in comatose patients with Traumatic Brain Injury (TBI)

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Background: Early SSEP grade is a strong predictor of final GOS in comatose TBI patients. Unfortunately, SSEP testing is either not available or difficult to obtain in many centers. The purpose of this study was to compare the predictive value of early brain CT scan to that of SSEP grade. *Methods:* Eighty-four comatose patients with TBI had brain CT Scans within 24 hours after TBI (Day 1). The CT scans were graded according to the Trauma Coma Data Bank Classification system. In the same patients, Day 1 SSEPs were graded based on the combined results from left-right brain (Grade I = absent-absent, II = absent-abnormal, III = absent-normal, IV = abnormal-abnormal, V = abnormal-normal, VI- normal-normal. GOS was measured 1 year after injury. A receiver operating characteristic (ROC) curve analysis was performed to compare Day 1 CT grade to Day 1 SSEP grade in predicting 1 year GOS. *Results:* The ROC area-under-the-curve was 0.84 for SSEP grade and 0.79 for brain CT grade (P=0.5126) *Conclusion:* Although Day 1 SSEP grade was marginally better than Day 1 brain CT grade in predicting GOS one year after TBI, the two were not significantly different.. Accordingly, Day 1 CT grade is a useful tool for predicting outcome in comatose patients with TBI.

F-05

Determination of the efficacy of phenytoin on prevention of late post-traumatic seizure

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Background: Phenytoin is commonly used for prevention of late post-traumatic seizure worldwide. However, there is a lack of high-quality evidence demonstrating benefit. *Methods:* This study was a prospective, quasi-randomized clinical trial. We randomly assigned 1160 patients with Traumatic Brain Injury (TBI) into two case (n=580) and control (n=580) groups. All patients with significant head injury and GCS<8 or GCS>8 but sustaining a cortical brain lesion, were included. The intervention group (case) was treated with phenytoin for a full year. Serum levels of phenytoin were maintained in the high therapeutic range (4 - 8 µmol/L of free phenytoin). The control group received placebo. Patients were followed for five years. The primary outcome was new or recurrent seizure. *Results:* The two groups were equal in distribution of age, sex and the type of treatments, medical versus surgical. 24/580 patients (4.1%) had a late seizure in the phenytoin group compared to 5/580 (0.86%) in the placebo group. Phenytoin treatment was associated with a greater risk of seizures (p=0.0005; RR=4.8; 95% CI, 1.8-12.5). *Conclusion:* Administration of the Phenytoin, not only did not decrease the risk of late-post traumatic seizure, but also has been associated with greater risk of seizure.

F-06

Epileptiform activity in neurocritical care patients: prevalence & risk factors

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Background: Non-convulsive seizures have been reported to be common in neurocritical care patients. Many jurisdictions do not have resources to enable routine use of continuous electroencephalography (cEEG), instead relying on intermittent EEG, for which the diagnostic yield remains uncertain. Identification of risk factors could help select patients at highest risk of seizures for cEEG monitoring. *Methods:* We performed a cohort study involving consecutive patients admitted to regional adult ICUs with TBI, SAH, ICH, anoxic encephalopathy, ischemic stroke or CNS infections. Patients with GCS scores ≤12, who underwent ≥ 1 EEG, were identified. EEGs were reviewed for the presence of inter-ictal and periodic epileptiform discharges (PEDs), as well as electrographic seizures. Multivariate analysis was used to identify predictors of epileptiform activity. *Results:* Of 1321 patients, 732 met inclusion criteria and 393 had ≥ 1 EEG. The prevalence of epileptiform discharges, PEDs and electrographic seizures was 25%, 9% and 7%, respectively; these were most common with anoxic encephalopathy and CNS infections, and least with TBI. Independent predictors included a history of preceding convulsive seizure(s), increasing age, deeper coma and female sex (Table). *Conclusions:* If confirmed prospectively, the risk factors identified here could be used to help select high risk patients for cEEG.

Value	Epileptiform Discharges Odds Ratio (95% CI)	P Value	PEDs Odds Ratio (95% CI)	P Value	Electrographic Seizures Odds Ratio (95% CI)	P
Age (per decade)	1.32 (1.15-1.52)	< 0.0001	1.39 (1.11-1.76)	0.005	1.19 (0.95-1.48)	0.12
Sex (F vs. M)	2.20 (1.33-3.65)	0.002	2.40 (1.11-5.21)	0.03	2.83 (1.27-6.29)	0.01
Initial GCS Score	0.85 (0.77-0.94)	0.001	0.82 (0.68-0.98)	0.03	0.90 (0.76-1.05)	0.17
Clinical Seizure	2.71 (1.49-4.94)	0.001	2.81 (1.13-7.00)	0.03	2.68 (1.13-6.32)	0.02
Modified APACHE II	0.99 (0.94-1.04)	0.64	1.02 (0.95-1.09)	0.63	1.01 (0.94-1.09)	0.75
Prophylactic AED	1.50 (0.85-2.65)	0.17	1.80 (0.77-4.22)	0.17	1.03 (0.43-2.50)	0.94
Diagnostic Category						
Anoxic Injury	3.00 (1.61-5.59)	0.02	4.50 (1.50-13.46)	0.007	0.75 (0.17-3.31)	0.70
CNS Infection	1.37 (0.56-3.33)	0.49	6.07 (1.63-22.65)	0.007	1.62 (0.34-7.84)	0.55
Stroke (all)	0.71 (0.34-1.49)	0.36	0.86 (0.22-3.38)	0.83	1.23 (0.35-4.36)	0.75
TBI (reference)	1.00	1.00	1.00	1.00	1.00	1.00

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

F-07

HIT: Hemicraniectomy in Trauma. A retrospective cohort pilot study

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Background: Intracranial hypertension secondary to malignant cerebral edema carries a high mortality rate in patients with traumatic brain injury (TBI). Decompressive craniectomy is controversial and appears to be used as a last resort in the attempt to relieve medically refractory intracranial hypertension. At our institution, a significant number of patients with traumatic brain injury and evidence of lateralized increased intracranial pressure undergo emergent decompressive hemicraniectomy within the first few hours after injury in an effort to minimize secondary injury. We report a retrospective cohort study looking at early decompressive hemicraniectomy for severe TBI with evidence of preponderant lateralized injury. *Methods:* Records of TBI patients undergoing emergent decompressive hemicraniectomy were reviewed. Using Chi square statistics, 14 day mortality and 6 month GOS scores were compared to those predicted by the CRASH Head Injury Prognostic Model (http://www.crash.lshtm.ac.uk), observing age, GCS, pupilary response, CT and extracranial injuries. *Results:* 98 patients met the criteria for review. 20 patients died prior to discharge with an average age of 47.25. The surviving 78 had an average age of 37.2 and further analysis is currently underway to examine the association between early hemicraniectomy and 6 month morbidity. Observed retrospective cohort data will be presented and compared to that predicted with best critical care management of TBI by the CRASH Prognostic model. *Conclusions:* Our preliminary results suggest improvement in 14 day mortality and indicate that decompressive hemicraniectomy may be considered as an initial step for treating malignant intracranial hypertension in the setting of severe lateralized traumatic brain injury.

F-08

Intracranial pressure monitors in traumatic brain injury: a systematic review

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Background: Elevated intracranial pressure (ICP) is an important cause of secondary brain injury in patients with traumatic brain injury (TBI). Significant variability exists in using ICP monitors between centers. We conducted a systematic review to examine the relationship between mortality and ICP monitor use in patients with severe TBI. *Methods:* In duplicate and independently, we searched MEDLINE (1966 – May 2010) and EMBASE (1977 –May 2010). We searched selected conference abstracts, and relevant article bibliographies. Selection criteria were: (1) adults, (2) traumatic brain injury, (3) ICP monitor use, (4) point estimate and 95% confidence interval for mortality with ICP monitoring, and (5) described adjustment for confounders. *Results:* The search revealed 255 citations, 83 articles for text review and 6 studies included in the final study. Patients with ICP monitors were younger, had higher injury severity scores, received more ICP reduction therapy and spent more time ventilated. Four studies found no significant relationship between ICP monitoring and survival, one study demonstrated improved survival, and one study demonstrated worse survival. *Conclusions:* There is no convincing evidence as to the isolated benefit of ICP monitors in severe TBI. This may relate to the heterogeneity of studies performed or to the inability to control for confounding variables in TBI. Further research is needed to identify which patients may benefit from ICP monitoring.

F-09

Lumbar drains in patients with severe septic meningitis

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Despite early antibiotics therapy and steroids, severe septic meningitis in adult patients requiring an intensive care unit admission still carries a morbidity and mortality rate, which exceeds fifty percent. We studied the use of a lumbar drains as an adjuvant modality to the treatment of this uncommon patient population.

Retrospective chart review conducted for all adult patients, from January 2000 to December 2010; with severe meningitis with altered level of consciousness, requiring admission to the Neurocritical and intensive care units at McGill University Health Centers. The primary outcome was mortality and severe morbidity in the acute phase. The secondary outcome included Glasgow outcome scale (GOS) at 1 month and 3 months.

Of all NICU admissions, 7 patients received a lumbar drain at the initial phase of their treatment along with broad-spectrum antibiotics and steroids. Time to insertion of lumbar drains ranged from 12 to 30 hours. The opening pressure was high in all patients (above 50 cmH_2O). With the exception of one patient, the target drainage was 80-120 cc per 8-hour shift irrespective of the intracranial pressure. There was no mortality in our group, and so far 85%of patients of the achieved GOS of 5. Only 1 patient had GOS of 3, who was interestingly the patient with the limited drainage strategy.

The use of lumbar drainage as an adjuvant therapy in adult patients with severe septic meningitis without coagulopathy admitted to the intensive care unit is a significant contributor to reduced mortality and severe morbidity.

F-10

Emerging trends in evidence based medicine - knowledge translation in critical care neurosurgery

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Introduction: Classic evidence based medicine is evolving into the "epistemological based medical practice" paradigm, with incorporation of emerging molecular, physiological, biochemical and genetic epidemiological principles into a knowledge translation (KT) framework. *Methods:* This exploratory review illustrates how KT principles can be applied to the subspecialty of critical care neurosurgery in the epistemiological based medical practice approach. *Results:* Evidence based summaries and knowledge translation tools now represent the first step in the knowledge translation framework. Dissemination and utilization of generalizable knowledge then proceeds with the integration of both local quality improvement (plan-do-check-act cycle) initiatives, and organizational knowledge translation (observational-exploratory-explanatory-pragmatic cycle) efforts. Sustainability is ensured with

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

efforts to secure adoption. Careful use of advanced neurological monitoring techniques in the neuro-ICU is such an example, with integration of molecular/biochemical/genetic evidence (susceptible individuals with spectrum of secondary insults after primary closed head), physiological principles (how these individuals react in the face of altered cerebral autoregulation), classic epidemiological principles (prospectively investigating matched cohorts who experience vasospastic phases of TBI), and knowledge translation efforts (adoption of transcranial doppler derived indices indicative of disrupted autoregulation, and treatment variations based on changes in these values). *Discussion:* Epistemological based medical practice with integration of local quality improvement and organizational knowledge translation efforts are crucial to ensure that the impact of specific interventions is maximized for the welfare of patients. The practising clinician should make every attempt to adopt these principles for the benefit of his or her patients.

MS, Neurology, Dementia

G-01

Efficacy of sc IFN beta-1a weekly or three times weekly in patients with CIS

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Background: The Phase III, double-blind, placebo-controlled REbif FLEXible dosing in early Multiple Sclerosis (REFLEX) study assessed the effects of two dosing frequencies of subcutaneous (sc) IFN beta-1a on risk of conversion to multiple sclerosis (MS) in patients with a first demyelinating event. *Methods:* Patients with a first demyelinating event suggestive of MS and ≥2 clinically silent T2 brain MRI lesions were randomized to the serum-free formulation of sc IFN beta-1a 44 mcg, three times weekly (tiw) or once weekly (qw; plus placebo twice-weekly for blinding), or placebo tiw for ≤24 months. Primary endpoint was time to McDonald MS; the main secondary endpoint was time to clinically definite MS (CDMS). *Results:* 517 patients were randomized (171 tiw, 175 qw, 171 placebo); the mean (SD) age was 30.7 (8.2) years; 64.2% were female. Baseline characteristics were similar across groups. Two-year cumulative probabilities of McDonald MS were 62.5%, 75.5% and 85.8% in the tiw, qw and placebo groups, respectively; hazard ratios (HR; 95% confidence intervals [CI]) 0.49 (0.38–0.64) and 0.69 (0.54–0.87), corresponding to risk reductions versus placebo of 51% and 31%; p<0.000001 and p=0.008. Two-year cumulative probabilities of CDMS were 20.6%, 21.6% and 37.5% in the tiw, qw and placebo groups, respectively; HR (95% CI) versus placebo: 0.48 (0.31–0.73; p=0.0004) and 0.53 (0.35–0.79; p=0.0023). *Conclusions:* sc IFN beta-1a 44 mcg, at both frequencies, significantly delayed McDonald MS and CDMS vs placebo. The delay in conversion to McDonald MS was more pronounced with tiw than with qw.

Disclosure: Study supported by Merck Serono S.A. – Geneva, Switzerland.

G-02

CMV seropositivity at first attack in children decreases MS risk independent of other common childhood viruses

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Background: Prior Epstein-Barr virus (EBV) infection likely increases risk of MS diagnosis in children and adults, but the effect of other viruses in determining MS risk has yet to be determined. *Methods:* Serum obtained at first attack of central nervous system demyelination (ADS) from 302 children enrolled in the Canadian prospective demyelinating disease study was analyzed using ELISA for IgG antibodies against EBV, cytomegalovirus (CMV), varicella-zoster virus (VZV), and herpes simplex virus (HSV). Fisher's exact test was used to compare proportions of children displaying seropositivity for each virus. A multivariable Cox proportional hazards model was created to determine adjusted hazard ratios (HR) for MS controlling for age and gender. *Results:* Children diagnosed with MS were more likely than those with monophasic ADS to be seropositive for remote EBV infection (37/49 vs 82/185, p<0.001) and less likely to be seropositive for CMV (10/52 vs 66/179, p=0.02) with no differences in HSV (6/36 vs 26/110, p=0.48) or VZV (30/33 vs 83/97, p=0.55) exposure rates. HR for MS associated with remote EBV exposure was 2.53 (95% CI 1.31 to 4.90) with an independent protective effect of CMV exposure (HR 0.44, 95% CI 0.22 to 0.87) also observed. No statistical interactions were found between EBV and CMV. *Conclusions:* Analysis to date suggests that CMV exposure may be an independent protective factor for childhood-onset MS. The increased risk of MS conferred by remote EBV seropositivity is unaltered by CMV exposure status, a finding to be confirmed through analysis of the entire cohort.

G-03

Systematic review/meta-analysis of an association between traumatic injury and MS

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Background: To date, literature reviews on traumatic injury as a risk factor for MS have been narrative. The purpose of this study was to conduct a systematic review/meta-analysis of available research to evaluate the probability of such an association. *Methods:* Relevant studies in all languages from 1950 to 2010 were sought, using electronic databases that included Medline, Embase, Cochrane DSR, Ovid HealthStar, CINAHL, ISI Web of Science and Scopus. Two independent reviewers screened studies for inclusion in the review, including an assessment of their quality based on the Newcastle-Ottawa Scale. A meta-analysis was performed to quantify the pooled effect of any association from articles which provided the necessary data. *Results:* 5,137 articles were found in the search. 10 case-control and 3 cohort studies were finally included in the systematic review. 8 case-control studies which could be used in a meta-analysis produced an odds ratio of 1.27 (95% CI 0.90, 1.81) for the association between traumatic injury and MS, not statistically significant. Likewise the 3 cohort studies produced a non-significant

incidence ratio of 0.99 (95% CI 0.87, 1.11). *Conclusions:* Consequently this best evidence synthesis suggests that traumatic injury is not a risk factor for the development of MS.

G-04

A Canadian multicenter observational study of natalizumab in multiple sclerosis: comparability of randomized controlled versus observational studies

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Background: Natalizumab is approved for the treatment of relapsing multiple sclerosis. We compared the effectiveness of natalizumab in a multicenter observational study versus efficacy in the pivotal randomized placebo controlled study (RCT). *Methods:* A retrospective observational study of 266 patients treated with natalizumab for at least 13 consecutive infusions between February 2007 and September 2010 was conducted at several Canadian MS Centers. Demographic, clinical (EDSS, annualized relapse rate (ARR)) and patient self-report quality of life (QOL) data were analyzed. *Results:* Two hundred and sixty-six patients had 13 or more infusions (range: 13 to 45; mean 27). Mean age was 42 years, 74% were female, and 89% had used prior disease modifying therapies. Pre and post treatment ARR were 1.0 and 0.18 respectively (82% reduction; p<0.0001). Pre and post treatment mean EDSS scores were 3.5 and 3.3 respectively (6% reduction, p=NS). Of 133 completing QOL questionnaire, 82% reported improvement or no change, 13% had mixed results, and 5% had worsening of physical and/or cognitive symptoms. Thirty-five (13%) patients discontinued treatment (6 (2.3%) due to worsening disease). One hundred ninety-one (72%) had complete adherence, while 32 (12%) missed 1, 19 (7%) missed 2 and 21 (8%) missed 3 or more infusions. There were no cases of PML. *Conclusions:* Patients treated with natalizumab experienced a major reduction in ARR, with stabilization or improvement in EDSS and an improvement in QOL. Findings are very similar to results of RCT.

G-05

Has disability progression in multiple sclerosis patients temporally changed?

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Background: Recent natural history studies suggest that multiple sclerosis (MS) is a more slowly progressing disease than previously thought. We investigated whether MS disease progression has changed over time in British Columbia (BC), Canada. *Methods:* The BC MS database was queried for relapsing-onset MS (R-MS) patients with symptom onset from 1975-1995, first assessed in a BC MS clinic within 15 years from onset. Patients were grouped by 5-year onset intervals (1975-<1980,1980-<1985,1985-<1990,1990-<1995). Outcome was defined as reaching sustained confirmed Expanded Disability Status Scale (EDSS) score 6 within 15 years disease duration. Life tables, linear trend test and multivariate Cox model were used for analysis. *Results:* 2247 R-MS patients (73% women) with adult-onset MS (mean onset:32 years) were included. No significant temporal change was found in the proportion of patients reaching EDSS 6 within 15 years from onset (28%, 26%, 27%, 22% for intervals 1975-<1980,1980-<1985,1985-<1990, 1990-<1995,respectively,p=0.13). Findings were unchanged when adjusting for other factors. *Conclusions:* Rates of disease progression remained stable over two decades of MS onset in BC, Canada. Our findings imply that differences between natural history studies may relate to variability in factors related to geographical location or methodology. The relationship between these factors and MS progression merits further studies.

G-06

Analysis of genetic risks in Alzheimer Disease in 2 Canadian cohorts: CSHA and ACCORD

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Background: Recent genome-wide association studies identified several potential susceptibility loci for late-onset AD (LOAD). Here, we examine the effect of single nucleotide polymorphisms in CR1, CLU, PICALM and TOMM40 on the risk of developing LOAD combining 2 large Canadian cohorts – (i) the Canadian Study of Health and Aging (CSHA) and (ii) the Canadian Collaborative Cohort of Cognitive Impairment and Related Dementia (ACCORD). *Methods:* We compared genotype frequency in controls (n=636) vs. those diagnosed with AD at baseline or at follow-up (n=667) with the combined cohorts. Initial genotypes were compared with chi-square tests, and odds ratios were obtained by multivariate logistic regression using covariates with age, sex, education, and APOE. *Results:* We found significant association with the CR1 (p=0.02) and TOMM40 (p=10-5) gene, but not with CLU (p=0.37) or PICALM (p=0.18). For CR1, odds ratio for developing AD in heterozygote carriers of the A allele the rs6656401SNP is 1.36 (95% C.I. 1.03-1.81), while homozygote carriers is 2.03 (95% C.I. 1.01-4.05). For TOMM40, the O.R. for AD are 1.6 and 2.7 in those carrying one copy and two copies of the A allele respectively. The effect of CR1 is reduced when age was included as a covariate, whereas the effect of TOMM40 remains after adjusting for the effect of APOE. *Conclusions:* CR1 and TOMM40 increase risk of LOAD in these two well-characterized Canadian cohorts. CR1 lowers the age of onset of AD, whereas TOMM40 appears to be an additional risk factor for developing AD independent of it is proximity to APOE.

G-07

Idebenone in Leber's Hereditary Optic Neuropathy (LHON): RHODOS study results

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Background: No medication is approved for LHON, which causes progressive irreversible blindness. Most patients have 1 of 3 mitochondrial DNA point mutations affecting respiratory chain complex-I. The RHODOS study evaluated the effects of idebenone

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

on visual acuity (VA) in LHON patients. *Methods:* LHON patients (N=85; mean age, 33.7 years; 86% male; mutations: 67% m.11778G>A, 20% m.14484T>C, 13% m.3460G>A) were randomized 2:1 to receive idebenone (Catena®) 900 mg/day or placebo for 24 weeks. The primary endpoint was best recovery in VA. The main secondary endpoint was change in best VA. *Results:* Baseline VA was logMAR 1.59±0.62 (n=82); 46% of patients could not read any letter from 1 meter. Estimated treatment effects in favor of idebenone were 3 letters (p=0.291) for best recovery in VA, 6 letters (p=0.078) for best VA, and 5 letters (p=0.026) for the difference in VA for all eyes. In patients with discordant VA between eyes and at highest risk of disease progression (n=30), estimated differences favoring idebenone were 14 letters (p=0.011) for best recovery in VA, 21 letters (p=0.003) for best VA, and 17 letters (p=0.0001) for the difference in VA for all eyes. *Conclusions:* Idebenone may prevent vision loss and promote visual recovery among LHON patients.

G-08

Involuntary multidirectional saccades with myoclonus and ataxia: an opsoclonus-myoclonus-ataxia syndrome variant

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Background: Opsoclonus is involuntary, arrhythmic, chaotic, multidirectional saccades without intersaccadic intervals. Opsoclonus-myoclonus-ataxia syndrome (OMS) consist of opsoclonus, myoclonic jerks of the limbs and trunk, cerebellar ataxia and encephalopathy. The pathophysiology is not clearly understood. The two plausible hypotheses are: 1) a dysfunction of omnipause cells or 2) a malfunction of Purkinje cells and their inhibitory projection to the fastigial nucleus. In studies, inactivation of fastigial nucleus produces saccadic overshoot dysmetria with intervals between saccades. *Case Report:* We present a healthy 25-year-old patient who came to the hospital because of one-week progression of binocular diplopia and gait unsteadiness. At the initial neurological examination, the patient had mild dysarthria, severe ataxia and gazed-evoked nystagmus in all directions. Two weeks later, she developed myoclonus and multidirectional saccades with intersaccadic interval without opsoclonus or flutter despite prolonged ENG monitoring.*
Investigations to exclude the presence of tumor, infection or systemic diseases came back negative.
Final diagnosis was an idiopathic OMS despite the absence of opsoclonus. She was treated with intravenous immunoglobulin for a total of 8 days and improved progressively. *Conclusion:* This is the first case reporting involuntary multidirectional saccades with intersaccadic intervals in a patient with OMS. This saccadic intrusions are similar to macro square- wave jerks but with a multidirectional components. This case supports the second hypotheses that opsoclonus may be caused by disinhibition of the fastigial nucleus. * A video of the patient is available

G-09

fMRI activation during matrix reasoning tasks in presymptomatic FTD

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Background: Functional Magnetic Resonance Imaging (fMRI) has shown differential brain response in several neurodegenerative diseases at asymptomatic stage. We hypothesize that matrix reasoning tasks may identify changes in fMRI in presymptomatic FTD progranulin mutation carriers. *Methods:* An event-related fMRI design study using a matrix reasoning task was performed in 6 first degree relatives of autopsy-confirmed FTD cases with known GRN mutations: 2 were carriers and 4 non-carriers. The task consisted of 0-relational, 1-relational, and 2-relational reasoning modeled after Raven's Progressive Matrices, with increasing task complexity from 0 to 2-relational. A 2-sample t-test (SPM8) was used to compare activation between carriers and non-carriers during each matrix reasoning task. *Results:* In the comparison between 1- and 0-relational tasks, carriers relative to non-carriers produced greater activation in bilateral posterior cingulate cortices, right anterior cingulate cortex, left middle frontal gyrus, right inferior frontal gyrus, and right middle temporal gyrus. By contrast, in the comparison between 2- and 1- relational tasks, non-carriers relative to carriers produced greater brain responses in bilateral medial frontal gyri, left middle frontal gyrus, right inferior frontal gyrus, right posterior cingulate cortex, and bilateral cerebelli. Performance of carriers was worse than non-carriers at all levels of task complexity, with poorest performance at 2-relational. *Conclusions:* We found significant differences in fMRI activation patterns between carriers and non-carriers during matrix reasoning tasks. These differences were dependent on task complexity, and interpretation of differences should occur in relation to behavioral performance. Compensatory mechanisms may be involved to some extent in latent neurodegeneration before symptoms emerge in FTD.

Neurosurgery and Spine

H-01

The medial opticocarotid recesss: an anatomical study of an endoscopic keyhole to the ventral cranial base

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Background: The medial opticocarotid recess (MOCR) has become an important landmark for expanded endonasal endoscopic approaches to the cranial base. The goal of this study was to examine the anatomical features of this structure and outline its role as a keyhole for endoscopic approaches to the sellar and suprasellar regions. *Methods:* Ten cadaveric specimens and 96 skull specimens were examined. Anatomical dissections were done endoscopically. *Results:* The lateral tubercular recess (LTR) is an osseous depression located at the lateral-most edge of the tuberculum sellae when viewed from a ventral perspective through the sphenoid sinus. Intracranially, the LTR corresponds to the lateral tubercular crest

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

(LTC). The MOCR is a teardrop shaped osseous indentation formed at the medial junction of the paraclinoid carotid canal and the optic canal. The middle clinoid process is distinct from the MOCR and dorsally it is situated inferior to the LTC. The distal osseous arch (DOA) of the carotid sulcus connects the lateral opticocarotid recess (LOCR) to the LTR and corresponds dorsally to the optic strut-tubercular bridge. The DOA is lined by the anteromedial segment of the distal dural ring of the internal (ICA) carotid artery; hence, it represents an endoscopic ventral landmark for the paraclinoid segement of the ICA. *Conclusion:* The MOCR and middle clinoid process are two different structures. Because of its strategic location at the confluence of the optic canal, the carotid canal, the upper portion of the sella, and the anterior cranial base, the MOCR functions as a keyhole for endoscopic sellar and suprasellar approaches.

H-02

The nasoseptal flap for skull base defects: an institutional experience

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Background: Endoscopic expanded endonasal approaches have become popularized over the past decade for exposure and resection of skull base and intradural lesions. These resections carry a significant risk of intraoperative CSF leak and post-operative CSF leaks following reconstruction. A vascularized nasal septal pedicled flap, based on a branch of the posterior septal artery was developed for reconstruction of these dural defects. *Methods:* A retrospective review of patients who underwent endonasal skull base surgery between the years 2005 and 2010 at the University of Toronto was performed to identify patients that were reconstructed with the nasoseptal pedicled flap. Risk factors for flap failure were identified. *Results:* Sixty-nine patients had dural defects reconstructed with the nasoseptal flap. Three of these patients (4%) had postoperative CSF leaks one of which was transient and did not require further intervention. Two of the 3 patients who developed leaks had undergone prior radiotherapy. *Conclusion:* Compared to pre-existing strategies, the use of the nasoseptal flap delivers a low CSF leak rate. The rate reported here (4%) is consistent with recently published series as was the association with prior radiotherapy. Given this data, the nasoseptal flap has proven to be a reliable reconstructive approach for skull base defects. Quality of life and patient satisfaction studies are required to further determine its role and are the subject of on-going research.

H-03

Health status of patients with idiopathic normal pressure hydrocephalus: a correlation between utility and SF-36

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Introduction: INPH is a clinical syndrome of progressive mental deterioration. Our object is to determine the predictors of health status of these patients. *Method:* General health status questionnaire SF-36 and utility questionnaire HUI 3 were completed by INPH patients via a web-based online survey tool. Correlation analyses were performed. *Results:* A total of 72 respondents were obtained – 49% male and 51% female. Average age was 68 years. The calculated health scales and the associated Canadian norms are: Physical Functioning 42.4 (85.8), Role limitations Physical Health 36.3 (82.1), Pain 62.4 (75.6), general health 52.9 (77.0), Vitality 36.5 (65.8), social functioning 56.3 (86.2), Role limiting emotion 53.2 (84.0), emotional well-being 66.45 (77.5). Physical health summary measure was 48.4 (80.13) and mental health summary measure was 53.0 (78.4). Each of the health scales and summary measures were significantly lower than the norms for the population ($p<0.001$). The overall health related QoL utlity score was 0.51. Correlation between demographic data and healh status measurements yielded the following significant relationships. (1) The SF-36 physical health and mental health summary measures, and the overall score were directly correlated with utility score ($P<0.001$), (2) Age at first diagnosis was directly correlated with employment status ($P<0.001$) and social status ($P=0.013$), (3) Time between diagnosis and shunting was directly correlated with the overall SF-36 score and the physical health score ($P=0.032$), (4) The presence of shunt revision was negatively correlated with utility score. *Conclusion:* Utility scores and SF-36 scores demonstrate good correlation in INPH patients.

H-04

Blood-brain barrier opening with MRI-guided transcranial focused ultrasound enhances gold nanoparticle uptake into rat brain

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Background: Focused ultrasound (FUS) has been used to reversibly disrupt the blood-brain barrier allowing delivery of large molecules into the brain of animals. The application of FUS to delivery of gold nanoparticles into the brain for potential tumour therapeutics has not been described. Hypothesis: MRI-guided FUS may enable the entry of polyethylene glycol coated 50 nm gold nanoparticles (AuNPs) into brain parenchyma. *Methods:* AuNPs (~ 14 mg AuCl mass/kg) were administered in rats by tail vein followed by microbubbles at sonication with peak rarefaction pressure of ~0.25 MPa (558 kHz transducer). BBB opening was confirmed by contrast-enhanced T1W MRI. Inductively coupled plasma mass spectrometry was used for gold content analysis in brain, liver, spleen, blood, and kidneys. Silver augmentation localized AuNPs on histology. *Results:* BBB opening resulted in higher gold content in the brain (1593 ± 425 ng Au/gm brain S.E.M. Right Hemispheres versus 474 ± 46 ng Au/gm brain S.E.M. Left Hemispheres, $P = 0.007$). AuNPs are observed in the brain only in the region of BBB opening and highly biodistribute to spleen. *Conclusion:* MRI-guided transcranial FUS targets the entry of circulating AuNPs into the brain. This technique holds promise for delivery of targeted AuNPs to human brain tumours.

H-05

Functional MRI of the human spinal cord: from sensory stimulation to spinal networks

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Introduction: To date, we have relied on clinical examination to infer damage to motor and sensory circuits after traumatic spinal cord injury (SCI). Here, we demonstrate fMRI data that assess how these

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

sensory circuits change after SCI. *Methods:* Heat (44°C) was applied to 2 dermatomes above and 2 below the level of SCI. Spinal fMRI data was collected on a 3T system (SSFSE, TE=30msec, TR=1sec, SEEP contrast). Data were spatially normalized and analyzed using the general linear model (P=0.001). A connectivity analysis was performed on both an individual and group basis by selecting a prime cluster (active volume =10 mm^3) in the dorsal horn and outlining the temporal course of subsequently related clusters (active volume=10 mm^3), using a correlation coefficient R=0.5. Spinal fMRI data were correlated with objective clinical outcomes assessments (ASIA sensory score and FIM). *Results:* 30 people were examined: 15 control, 5 ASIA A complete SCI and 10 incomplete SCI. SCI was chronic, >12 months prior to analysis. Connectivity analysis shows consistent changes in the neural activation pattern in persons with incomplete SCI whereby more volume of the spinal cord responds to thermal stimulation. There is a relative paucity of activity in persons with complete injury. Functional activity correlates with clinical measures. *Conclusions:* This represents the first attempt at understanding spinal networks by examining activity in the dorsal horn of the human spinal cord and its subsequent time course through the brainstem. Incomplete injury results in a novel activation pattern, potentially indicating reorganization of neural circuits within the human spinal cord.

H-06

High resolution rapid scanning X-ray fluorescence imaging to track superparamagnetic iron oxide (SPIO) labeled neural stem cells in an experimental stroke model

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Background: We utilized synchrotron-based rapid scanning X-ray fluorescence (RS-XRF) to detect iron in SPIO-labeled stem cells after intravascular transplantation in a stroke model. *Methods:* Stroke was induced in NodScid mice using a hypoxia-ischemia model. $5x10^5$ SPIO-labeled human derived embryonic neural progenitor cells (hNPC) were injected into the ipsilateral carotid artery. Control animals received stereotactic injection of SPIO-labeled hNPC or saline. Animals were sacrificed. MRI, RS-XRF and histology were performed. *Results:* Prussian blue staining and MRI demonstrated significant homing of hNPC to the ischemic hemisphere but not to the contralateral hemisphere ($p<0.01$). RS-XRF depicted distinct areas of Fe signal distributed in the ischemic hemisphere correlating with MRI findings. High-resolution scans depicted single cells in clusters with an average iron content of 7.0632pg. Intraparenchymal cell grafts appeared as focal signal on MRI and RS-XRF. Saline controls produced artifact on MRI, which correlated to Fe signal on RS-XRF very distinct from the cellular morphology of SPIO-labeled hNPC. *Conclusions:* Synchrotron-based RS-XRF allows for high-resolution quantitative Fe specific imaging of single cells. We have demonstrated its application in a multimodality imaging paradigm to track SPIO-labeled hNPC in a stroke model. We found excellent correlation between MRI, RS-XRF and histology.

H-07

Management of complex non-traumatic compressive spinal deformity in pediatric patients

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Introduction: Complex non-traumatic compressive spinal deformity in children is characterized by spinal deformity or instability co-existent with spinal cord or nerve root compression. The condition poses significant challenges in terms of preservation of neurological function and maintenance of stability in a growing spine. *Methods:* We retrospectively retrieved from a prospective operative database all patients meeting this criteria from 2000 to 2010 treated by the primary author. Patient demographics, clinical presentation, operative procedures, outcomes and complications were extracted from the hospital records. *Results:* Of 38 patients, 20 boys (52.6%), age 1.4-16.7 yrs (mean 10.3 yrs), 55.3% presented with a neurological deficit ranging from mild spasticity to ventilator dependent quadriplegia. The most common etiologies were neoplasms (23.7%), Trisomy 21 (18.4%) and Klippel-Feil syndrome (15.8%). The most common locations were C1-C2 (39.5%), Cervico-thoracic (28.9 %) and thoracic (15.8%). Pre-operative traction was used in 36.8%. All patients were operated by a combined neurosurgery and orthopedic team with intraoperative neurophysiological monitoring. Virtually all received spinal instrumentation and autologous bone grafts; 73.7% received halo immobilzation; 13.2% required an unplanned second surgery and 18.4 % experienced a complication usually transient and/or minor. *Conclusions:* Complex non-traumatic compressive spinal deformities represent a varied and generally high risk group best managed in multi-disciplinary teams. Pre-operative traction, selective halo immobilization, universal intra-operative neurophysiological monitoring, may reduce peri-operative complications and are generally well tolerated. Functionally important loss of spine growth, and delayed progressive deformity has not been a significant problem to date.

H-08

Graded Redefined Assessment of Sensibility Strength and Prehension (GRASSP): psychometric development of an upper limb impairment measure for individuals with traumatic tetraplegia

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Upper limb function is important to individuals with tetraplegia and represents overall function, leading to a concentrated emphasis on restorative neuro-rehabilitation and research. There are no specific measures to establish the efficacy of new interventions for the upper limb after tetraplegia. The GRASSP was developed to fill this void. *Objectives:* 1) To develop a scoring system for the GRASSP; 2) To establish interrater and test retest reliability, construct/concurrent validity; and 3) To determine relationships of domains within GRASSP and GRASSP to upper limb function. *Methods:* The International Standards of Neurological Classification for Spinal Cord Injury, Spinal Cord Independence Measure III (SCIM), Capabilities of Upper Extremity Function (CUE) and repeated GRASSP (x3) were administered (sample n=72). Analysis: Guttman scaling to develop the scoring system; intraclass correlation

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

coefficients to establish reliability, Pearson correlation coefficients to establish validity with SCIM and CUE were used. Structure equation modeling was used to establish relationships between GRASSP domains and function. *Results:* GRASSP subtests defined individuals impairment and demonstrated cumulative predictive pattern 80% of the time. Interrater and test retest reliability ranged from 0.83-0.99. Construct validity was confirmed by level of agreement (kappa statistic 0.412-0.511). GRASSP subtests demonstrated concurrence with the SCIM and CUE. Impairment showed the strongest concurrence with self-perception of function (0.57-0.83, $p<0.0001$). Quantifying impairment showed that sensation and strength have different direct and indirect influences on upper limb function. *Conclusion:* The GRASSP is reliable, valid and is sensitive in defining upper limb function. GRASSP should be used to track neurological functional changes longitudinally.

H-09

Levels of evidence in neurosurgical literature: are we improving?

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Background: Recognition of evidence based medicine (EBM) has been well documented and supported across surgical subspecialties for over a decade. We aimed to quantify the levels of evidence (LOE) of publications in the neurosurgical literature and compare this to a previously published baseline. *Methods:* Clinical neurosurgical literature published in *Neurosurgery* from October 2009 - September 2010 was reviewed. Articles were evaluated by two independent reviewers to determine their LOE based on the criteria published by the Centre for Evidence Based Medicine. This was compared to a LOE benchmark for the year 2000 (Rothoerl, 2005) as well as to other surgical specialties. *Results:* Four hundred forty-three articles were reviewed and 368 met eligibility criteria. Five studies (1%) were Level I, 26 (7%) were Level II, 29 (8%) were Level III, 115 (31%) were Level IV, and 94 (26%) were Level V. There was no significant difference in the distribution of levels of evidence between the year 2000 and 2010. Publications of larger sample sizes were associated with higher levels of evidence (Levels I/II) ($p<0.01$). No other variables, including number of authors, neurosurgical field, or number of collaborating centres, were significantly associated with higher LOE. In comparison to other surgical specialties, the ratio of higher levels of evidence to lower levels in neurosurgery was below the mean. *Conclusions:* Over the past decade, the neurosurgical literature has remained unchanged in terms of the mean level of evidence published annually, with Level I evidence still being least represented, and on average, falls below the mean across other surgical specialties.

H-10

Financial, medical and social benefits of day-case craniotomy

P Goetz (Toronto) M Bernstein (Toronto)*

Background: Outpatient craniotomy for supratentorial tumours (OC) is a safe alternative to routine admission; advantages include reduced cost and morbidity (e.g. nosocomial infection, thromboembolism, medical error) and improvement in patient flow. We aimed to compare costs associated with inpatient and OC at our institution (TWH) and determine bed-shortage related cancellation rates. *Methods:* Costing data from five in-patient overnight admissions and five OC's operated by the senior author between March 2009-2010 were obtained. Selected in-patients could have been managed as out-patients (i.e. comorbidity confounders eliminated). Operating theatre logs between June and November 2010 were analysed to establish cancellations rates and their causes. *Results:* A 39% cost-saving was achieved at TWH in OC vs in-patient, based on nursing, food, laboratory and pharmacy costs. Over the six months analysed, 34 of 698 (5%) elective procedures were cancelled on the day of surgery - the vast majority due to bed shortages. 50% of all elective cases were craniotomies. Thus, greater use of OC could have diminished cancellation rates. Further benefits include reduction of: bed-related emergency refusals, waiting lists and admission-related morbidity. *Conclusions:* OC is a proven, resource-efficient option. Introducing it into mainstream practice, with appropriate training, would provide significant advantages in socialized medical systems with ever-increasing financial constraints.

Stroke and Neurovascular

SUPPORTED BY AN EDUCATIONAL GRANT FROM HOFFMAN LA ROCHE

I-01

Characteristics of Posterior Communicating (Pcom) Artery Aneurysms causing Third Nerve Palsies (TNP).

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Approximately 10-20% of posterior communicating (Pcom) artery aneurysms are associated with third nerve palsies (TNP). Recent reports suggest endovascular coiling of Pcom aneurysms allows for high levels of TNP recovery (60-100%). Pcom aneurysms are believed to cause TNP via mechanical compression and/or a pulsatile affect on the nerve, but recovery after coiling suggests it may be more than a mass effect that causes this problem. We performed a chart and imaging review of Pcom aneurysms in order to delineate the characteristics of Pcom aneurysms that are associated with TNP. We found 47 patients (48 aneurysms), with available charts and imaging, diagnosed with Pcom aneurysms from January 1998 to October 2010. We performed a detailed analysis of the morphology and flow of contrast through the aneurysms. We found 10 aneurysms associated with an ipsilateral TNP. The aneurysms causing third nerve palsies had a significantly greater height (8.09 ± 0.74 vs 6.26 ± 0.31, $p<0.05$) and neck-aspect ratio (3.58 ± 0.94 vs 2.01 ± 012, $p<0.05$) than aneurysms that did not. There was no difference between the two groups in terms of the aneurysm width, neck size, and lateral angle. The aneurysms associated with TNP were much more frequently associated with pooling of contrast within the aneurysm than those that were not associated with TNP (80% vs 2.6%, $p<0.001$), suggesting that pooled blood within an aneurysm may contribute to TNP. These previously unreported findings might explain why aneurysm coiling and preventing pooling of contrast in the dome allows for very good outcomes of TNP after coiling.

I-02

Prevalence of Fabry disease in young adults with cryptogenic ischemic stroke

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Background: Identification of ischemic stroke (IS) etiology is central for secondary prevention. Despite investigation, etiology remains idiopathic in 30% of young adults with IS, of which up to 4% may be accounted for by Fabry disease (FD). Potential markers of FD include vertebrobasilar IS and proteinuria. We sought to determine the prevalence of FD in our population of young patients with idiopathic IS. *Methods:* Since 2001-02, consecutive individuals hospitalised for IS have been prospectively registered in a single-center neurovascular database and followed-up clinically. Idiopathic IS patients aged 18-55 were identified and screened for FD by questionnaire, examination and genetic sequencing of α-GAL gene. *Results:* We identified 143 young individuals with idiopathic IS. We excluded 48 individuals lost to follow-up or deceased, while two declined study participation. We screened 93 patients, including 89 (96%) Caucasians, 4(4%) Blacks, 70 (75%) French-Canadians, 33 (35%) with vertebrobasilar IS. None had clinical evidence of FD. One patient had idiopathic hypertrophic cardiomyopathy, another had proteinuria. No significant mutation in the α-GAL gene was found in 54 cases (prevalence=0%; 95%CI=0.0-7.9%); results of 39 cases are pending. *Conclusions:* Even though these are preliminary data, our findings may suggest low prevalence of Fabry disease in our idiopathic IS population.

I-03

Carotid Artery angioplasty and stenting in patients < 70 years of age

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Background: Recent studies have suggested that CAS is equivalent to, or safer than, CEA in average risk patients <70 years of age. We examined a consecutive series of patients who underwent CAS in order to determine the influence of patient age on outcome. *Methods:* A retrospective, longitudinal cohort study of patients who underwent CAS at St. Michael's Hospital, Canada between January 2001 and November 2010 was performed. The primary outcome measures were 30-day stroke and 30-day composite death, stroke and myocardial infarction (MI). Patients were stratified based on age <70 and ≥70 years. *Results:* One hundred and sixty consecutive patients underwent 168 CAS procedures. The 30-day risk of stroke was 3.7% while the composite outcome of death/stroke/MI was 8.1%. Death/stroke/MI affected 6.8% of patients. When stratified by age <70 and ≥70 years, the 30-day stroke rate was 0 versus 7.3% (p=0.03), and the composite outcome of death/stroke/MI was 2.5 versus 13.4% (p=0.02), respectively. *Conclusions:* Patients <70 years of age undergoing CAS have a low rate of major complications, comparing favourably to published CEA adverse event rates, and supporting the recent carotid stenosis literature that in the younger population CAS has a similar or lower complication rate than CEA.

I-04

Canadian experience with the Pipeline embolization device for repair of unruptured intracranial aneurysms

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Introduction: Flow diverting stents, such as the Pipeline Embolization Device (PED), have emerged as a novel means of treating complex intracranial aneurysms. We have retrospectively analyzed the initial Canadian experience with this technology, providing insight into technical challenges, clinical and radiographic outcomes, and complication rates. *Methods:* Cases were compiled from seven Canadian centers. Each centre prospectively tracked their initial experience; this data was retrospectively pooled and updated for analysis. *Results:* A total of 110 PED cases were performed at the participating centers between June 2008 and December 2010. This study was limited to unruptured aneurysms with a minimum of 3 months follow-up (96 cases). The aneurysms were relatively large (mean diameter 18 mm) and complex (neck width 7.5 mm; partially thrombosed 26 %). Most were located in the anterior circulation (76%), of which the majority arose from the cavernous (34%) and supraclinoid (58%) segments of the internal carotid. The overall occlusion rate was 69% with an entry remnant observed in 16% (follow-up range 3-30 months). Progressive aneurysm occlusion was observed over time. The overall mortality rate was 4.2%. Typical endovascular complications occurred, however atypical complications such as delayed aneurysm rupture (1 case) and distal territory hemorrhage (3 cases) were also observed. *Conclusions:* Flow diverting stents represent an important tool in the treatment of intracranial aneurysms. The relative efficacy and morbidity of this treatment must be considered in the context of available alternative interventions.

I-05

Coiling of small aneurysms is not associated with increased morbidity

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Purpose: Coiling of small aneurysms can be challenging. Our study investigates the procedural rupture rates and long-term durability of endovascular coiling for small (< 4mm) aneurysms compared to an age and location-matched control group of non-small (>4) aneurysms. *Methods:* We performed a retrospective review of aneurysms coiled between 2003-2008. Small aneurysms were defined as measuring ≤ 4 mm. To account for factors such as vessel tortuosity and location, we chose a control group matched by age and aneurysm location based on a power analysis. *Results:* Between January 2003-Dec 2008, 34 small aneurysms were coiled. For the control group, 68 aneurysms matched to sex, age and location were reviewed. There was no significant difference between the two groups for sex, age initial degree of obliteration and mean follow-up period. The mean size of small vs non-small aneurysms was 3.25 mm (1.5-4) and 8.47 mm (4-25). The frequency of intraprocedural perforations was 4/34 (0.11) and 3/68 (0.04), for the small and non-small cohort, respectively (p=0.22). In comparison, during a similar time period, a total of 360 saccular aneurysms were coiled, overall perforation rate was 3.6%. All patients who had a perforation in the

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

small aneurysm group had a good clinical outcome vs 1/3 in the non-small group (2 deaths). There was no retreatments in the small aneurysm group and 5 (0.07) in the non-small group (p=0.116). *Conclusion:* Coiling of small, < 4 mm aneurysms is feasible and durable. There is an increase in frequency of intraprocedural rupture with coiling of small aneurysms which is not associated with increased morbidity.

I-06

Testing flow diverters in experimental aneurysms: identification of factors responsible for treatment failures

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Background: Flow diverters (FD) are the latest most promising tool to treat intracranial aneurysms. Nonetheless, treatment failures, including hemorrhage of unruptured aneurysms, have been reported to occur following FD stenting. *Methods:* Twenty-nine aneurysms of various types (fusiform, bifurcation, and lateral wall) were surgically created in canines and treated with FDs. FDs were deployed in a linear configuration for lateral wall or fusiform aneurysms, or curving 90º for bifurcation aneurysms. Angiography was carried out prior to and immediately following implantation, at 2 weeks and immediately before sacrifice at 12 weeks. Macroscopic photography of specimens was performed, followed by biopsies of selected regions of the tissue formed on the surface of FDs. *Results:* FDs occlude lateral wall aneurysms, but fail to do so when they cover stented branches. FD also fail in bifurcation aneurysms, when they are curved 90º, or when they are too porous (insufficient metal strut coverage per surface area). In all cases of failure, devices were covered with neointima except for small holes, causing leaks responsible for continued aneurysm patency. Branch occlusion was not observed angiographically in spite of near-occlusion demonstrated at pathology. *Conclusion:* Experimental canine aneurysms are useful pre-clinically to investigate the causes of failure of flow-diverting stents. Factors such as FD porosity, degree of stent curvature, and coverage of arterial branches affect the efficacy of FD stenting.

I-07

Different strokes for different folks: the Toronto Chinese-Canadian Stroke Study- 1990 to 2010

JY Chu (Toronto) JK Chu (Atlanta) DK Chu (Hamilton) JV Tu (Toronto)*

Introduction: It has been recognized in the past few decades that different ethnic groups living in Canada may have different stroke patterns and epidemiology. *Method:* Two retrospective case-controlled studies were carried out between 1990 and 2000 to study the stroke characteristics and epidemiology of Chinese-Canadians living in Toronto. Statistical analysis was carried out by the Institute of Clinical Evaluative Sciences. A further smaller scale study was also carried out in the late 2000s to look at the relationship between stroke and diabetes mellitus amongst this population. *Results:* Chinese-Canadians were found to have 1/6 the prevalence of extracranial vascular stenosis. They have a higher frequency of intracranial vascular disease which may be due to the higher frequency of hypertension and diabetes mellitus. Higher incidence of intracranial hemorrhage was found compared to Caucasian controls which may be due to the lack of awareness and optimal treatment of their hypertension.
Details of the results of these studies including statistical and clinical data will be presented. *Conclusions:* This is the first long term retrospective study of the stroke patterns and epidemiology for Chinese-Canadians residing in Toronto. Further prospective population-based study will be essential to study the important interactions between genetics and environment in the pathogenesis of different strokes for different folks.

I-08

The 3C score: deriving optimal CT based imaging characteristics for predicting clinical outcome in acute ischemic strokes with proximal occlusions

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Purpose: To derive a computed tomogram angiography (CTA) based imaging score based on extent of ischemic core, leptomeningeal collaterals and clot burden and determine ability to discriminate clinical outcomes with or without therapy. *Methods:* This was a single center study of patients with acute ischemic stroke and M1 MCA±intracranial ICA occlusions. Good clinical outcome was modified Rankin Score ≤2 at 90 days. Based on prior studies we have identified three characteristics on CTA that are predictive of good outcome independent of age and inital NIHSS: CTASI, clot burden score and regional leptomeningeal collateral score. The 3C score (range 0-6) comprises 3 imaging measurements at baseline: 1. CTA-SI ASPECTS categorized as 0-4=0 points, 5-7=1, 8-10=2. 2. Collaterals (rLMC score 0-10=0, 11-16=1, 17-20=2) and 3.Clot burden (CBS 0-5=0, 6-7=1, 8-10=2). Primary measure of discrimination of clinical outcome was the c statistic. *Results:* There were 133 patients (mean age 66, median NIHSS 16). The c statistic for the 3C score was 0.75, indicating moderate to good discrimination of good outcomes. By comparison, the c statistic for NCCT ASPECTS was 0.62 and for CTA-SI ASPECTS was 0.66, and for a multivariable model containing age and NIHSS was 0.67. The relationship between 3C score and the probability of good outcome was similar across all treatment categories. *Conclusion:* The 3C score is better at discriminating chance of good clinical outcome than NCCT, CTA-SI ASPECTS or the combination of age and NIHSS in patients with acute ischemic strokes. Based on these preliminary analyses, the score warrants further validation studies in independent patient cohorts.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

I-09

Does etiology help predict long-term stroke recurrence and mortality in young adults with ischemic stroke?

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Background: There is limited data concerning recurrence of ischemic stroke (IS) and mortality in young adults. Furthermore, it remains unclear whether the outcome differs between etiological subgroups, including IS of undetermined etiology. *Methods:* Since 2001-02, consecutive individuals hospitalised for IS have been prospectively registered in a single-center database and followed-up clinically. Cases of IS aged 18-50 were included and recurrent IS and all-cause mortality outcomes were compared between etiological subgroups. The TOAST classification was used but we considered arterial dissection and isolated patent foramen ovale (iPFO) as separate subgroups. *Results:* We identified 450 young adults with IS. Etiology was determined in 360/450 (80%) and remained undetermined in 90/450 (20%) despite extensive investigation. Median follow-up duration was 41 months. Recurrence rate by subgroup was: large-artery atherosclerosis (10/38, 26%), cardioembolism (13/83, 16%), small-vessel occlusion (5/35, 14%), arterial dissection (8/61, 13%), iPFO (7/53, 13%), other determined causes (26/90, 29%), undetermined etiology (15/90, 17%). IS recurrence rate did not differ between etiological categories (p=0.08). Mortality rate was 9/360 (2.5%) for determined etiologies and 3/90 (3.3%) for undetermined etiology (p=0.71). *Conclusions:* Recurrent IS and death affect a substantial proportion of young adults with IS, but are not predicted by the main IS etiological categories.

I-10

Predictors of outcome for anticoagulated patients with intracranial hemorrhage and a survey of practice: present management may be sub-optimal

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Background: Little information is available to guide management decisions involving anticoagulated patients with intracranial hemorrhage (ICH). These patients are challenging to manage because of high risk for both further bleeding as well as thromboembolism (TE). *Methods:* A systematic review of the literature was performed to identify reported cases of ICH while on anticoagulant therapy. Variables describing patient characteristics, their management and outcome were extracted. Additionally, a survey of neurosurgical management was performed at the 2010 AANS meeting. *Results:* Tissue plane of the hemorrhage (p<0.0001), indication for anticoagulation (p=0.0103), and type of anticoagulant (p=0.0029) were significantly associated with outcome. Older age (p<0.0001), supratentorial index hemorrhages (p<0.0001), failure to restart anticoagulation (p<0.0001), and prior history of hypertension (p<0.0475) were significantly associated with worse outcome. A hemorrhagic or TE complication following the index hemorrhage was also associated with worse outcome (p=0.0704). Patients presenting with supratherapeutic anticoagulant levels did worse (p=0.0552) than patients with subtherapeutic or therapeutic anticoagulation levels. Gender, sidedness of the index hemorrhage and surgical management were not significantly associated with outcome. Most neurosurgeons wait at least one week to re-start anticoagulation. *Conclusions:* This study provides prognosticators and suggests a number of means by which outcome may be improved for these patients. These findings strengthen the notion that 72h post-hemorrhage may be an optimal time to resume anticoagulation, however most neurosurgeons delay resumption for at least one week subjecting their patients to high TE risk. Efforts to educate physicians about the data from this and related studies are indicated.

PEDIATRICS

J-01

Prediction of brain volume of preterm infants by clinical history and MRI imaging after birth

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Introduction: Brain volume in infants as assessed by MRI at term is an established predictor of normal development. This study examined perinatal clinical parameters and imaging findings such as lesions, myelination, and brain volume in preterm infants as predictors of brain volume at term. *Methods:* Twenty-eight preterm infants (<33 weeks gestational age (GA)) underwent MRI after birth and at term. These data were used to identify pathology, measure brain volume, and compute magnetization transfer ratios (MTR), the latter a measure of tissue structure and myelination. MTR was computed for white mater, the pons and subcortical nuclei. Clinical data included: medical history and body measurements at the time of the first scan. *Results:* The best predictor of brain volume at term was brain volume at first scan, even after correcting for differences in the age at scan. Higher birth weight and normal pregnancy history also predicted greater brain volume at term. First scan MTRs were negatively correlated with brain volumes in both scans and with normal pregnancy history. *Conclusions:* Complications of pregnancy and low birth weights were associated with small brain volume and increased myelination after birth and at term. These findings suggest a role for neonatal imaging in predicting neurodevelopment.

J-02

Comparison of quantitative diffusion and MR spectroscopy parameters at 24 and 72 hours of life in term newborns with hypoxic-ischemic encephalopathy

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Background: Hypoxic-ischemic encephalopathy (HIE) is characterized by decreased diffusivity (DAV), fractional anisotropy (FA), NAA/choline, and increased lactate/choline at 72 hours in injured brain. Early quantitative measures would be ideal since qualitative MRI is inadequate on the first day. We hypothesized that early quantitative diffusion tensor imaging (DTI) and proton MR spectroscopic imaging (MRSI) parameters are predictive of changes at 72 hours. *Methods:* 18 newborns (median 39.6 weeks) with HIE

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

were prospectively studied with MRI, DTI, and MRSI at 24 and 72 hours. DAV and FA (microstructure), and NAA/choline and lactate/choline (metabolism) were determined in predefined regions of interest. Linear regression for repeated measures was used. The effects of therapeutic hypothermia (n=4) were explored. *Results:* Qualitative MRI showed complex variations of findings between 24 and 72 hours. In white matter, DAV, FA, and NAA/choline at 24 hours were strongly associated with values at 72 hours (all P<0.001). In gray matter, DAV and NAA/choline values at 24 and 72 hours were associated (both P<0.04). Therapeutic hypothermia attenuated the relationship of values from 24 to 72 hours: DAV in white (interaction P=0.04) and gray matter (interaction P=0.08), and gray matter lactate/choline (interaction P=0.01). Cooling was associated with higher NAA/choline in gray and white matter (both P<0.007) and white matter FA (P=0.008). *Conclusions:* In term newborns with HIE, quantitative MR values at 24 and 72 hours of life are strongly associated, providing objective measures of injury before qualitative images. Cooling attenuated the progression and severity of brain injury.

J-03

Uncovering the clinical, electroencephalographic and imaging features of Filaminopathy – Defining the clinical aspects of a pathological diagnosis.

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Background: Filaminopathy has recently emerged as a pathological diagnosis from patients who have undergone cortical resections for refractory epilepsy. It describes the abnormal finding of filamin inclusions in astrocytes. We have observed this diagnosis in children who had epilepsy surgery for refractory epileptic spasms. Typically patients with epileptic spasms are difficult to treat and often not considered as suitable epilepsy surgery candidates. Recent advances in imaging and EEG techniques have led to a greater number of these children achieving good seizure outcomes following epilepsy surgery. Little is known about clinical features of filaminopathy or its natural history in terms of outcome following epilepsy surgery. *Objectives:* To evaluate the features of patients with filaminopathy and assess their outcome following epilepsy surgery. *Methods:* A single center retrospective review of all children with epileptic spasms who underwent intracranial EEG monitoring using subdural grid electrodes and were assessed for resective surgery over an 8 year period. Clinical features, imaging and EEG findings were compared with outcome for those with and without filaminopathy. *Results:* Twenty children who underwent invasive EEG monitoring with refractory epileptic spasms were identified. Clinical, EEG and imaging features of filaminopathy were described. In the 4 patients with filaminopathy, ictal EEG showed prominent voltage attenuation after the combination of high frequency oscillations and slow waves. *Conclusions:* This is the first study which examines clinical, EEG and imaging features to establish this pathological diagnosis as a clinical condition. We are planning a multi-center prospective study to further evaluate this entity.

J-04

Spectrum of neurological dysfunction in neurocutaneous melanocytosis

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Background: Neurocutaneous melanocytosis is a rare neurocutaneous syndrome defined by the presence of multiple congenital nevi and melanocytic deposits in the central nervous system. We sought to define the spectrum of central nervous system abnormalities in children with neurocutaneous melanocytosis. *Methods:* Retrospective review of cases of neurocutaneous melanocytosis referred to the paediatric neurology service at our centre between 2003-2010. *Results:* Fourteen cases were identified, of which 8 are currently living. Median age at death was 54 months (19-125 months), median age of survivors was 31 months (12-82 months) with one patient age 31 years lost to followup. Six patients had diffuse leptomeningeal deposits of whom five died, including three who developed intracranial melanoma. Four patients presented to our centre with leptomeningeal melanoma, of which three died and one lost to followup. Six patients had epilepsy. Six cases had diffuse leptomeningeal deposit, 6 multifocal and 1 unifocal melanocytic deposit. One case had normal neuroimaging however had focal seizures with focal epileptic discharges. One patient had a Dandy Walker malformation. In addition, three patients had dorsal spinal arachnoid cysts and one had a benign cervical spindle cell tumour. Three patients had profound developmental delay; the other 11 patients were normal or had only mild delay. *Conclusions:* Children with neurocutaneous melanocytosis exhibit a wide range of intracranial and intraspinal abnormalities as well as a wide range of outcomes.

J-05

Childhood opsoclonus myoclonus syndrome: a new era

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Background: The long-term outcome of childhood opsoclonus myoclonus syndrome (OMS) patients has historically been poor, with 70-80% having serious neurological sequelae. We hypothesized that in the last decade the outcome has improved with the introduction of multimodality therapy at diagnosis. *Methods:* We performed a retrospective review of children diagnosed with OMS in British Columbia from 2000-2010. We reviewed the charts in regards to demographics, presence of malignancy, therapy and outcome. *Results:* 4/12 patients had associated stage 1 neuroblastoma at diagnosis which was resected. Treatment: 1 none; 1 neuroblastoma resection alone; 10 steroids; 9 IVIg and steroids; 8 had a third agent : imuran, rituximab and/or cyclophosphamide. Five have long-term neurological dysfunction, four are still on treatment, seven are neurologically normal. *Conclusions:* The present approach of multimodality immunotherapy appears to raise the possibility of a more optimistic outcome in regards to long-term neurological function in children with OMS. Further prospective studies are required to evaluate this further.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

J-06

Late ependymoma recurrence: A Canadian pediatric multicentre study

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Background: Most ependymoma recurrences occur within the first three years. We hypothesized that late relapses (LR) may have an indolent course, and that the incidence is low. *Methods:* We performed a retrospective review of children diagnosed with ependymoma in Canada from 1986-2005. We identified those with a first relapse, early relapse was defined as ≤5 years; LR >5 years. *Results:* 12/16 centers participated in this multicentre study. There were 121/233 (52%) relapses; 7 (3%) (PF 1; ST 2; SP 4) LR. 4/7 (57%) are alive at a median OS of 4.2 yrs (1-10.5). Cases 1 and 2, SP ependymomas were salvaged with involved field radiation. Case 3, a ST ependymoma grade III had three relapses salvaged with repeated resection plus conformal radiation. The incidence of LR in relapse free survivors at 5 years from diagnosis is 6%. 114 patients relapsed early: at median of 1.4 yrs (0.1-4.7); OS 34% (39/114): 25% of PF ependymomas; 41% of ST ependymomas, and all SP. *Conclusions:* The risk of late relapses in childhood ependymoma is 3%, the risk among long-term survivors is 6%. LR is most common in SP ependymoma. Durable survival is more likely in both early and LR SP and ST childhood ependymomas.

J-07

Mitochondrial enzymes at epileptic foci in paediatric brain resections

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Background: In seeking tissue markers for identifying epileptic foci in brain resections we previously described α-B-crystallin. Mitochondrial respiratory chain enzymes might provide another marker of epileptogenic neocortex and hippocampus. *Methods:* Frozen unfixed sections of brain resections at electrophysiologically localised epileptic foci from 10 epileptic infants and children were studied. Two had hemimegalencephaly, one had tuberous sclerosis and the remainder had focal cortical dysplasias. None had primary mitochondrial disease. Tissues included sections of hippocampus, temporal or frontal neocortex. Oxidative enzyme histochemistry was applied using a protocol applied to muscle biopsies. Immunoreactivities for neuronal and glial cell markers, α-B-crystallin and transmission EM also were performed for correlation. *Results:* Oxidative activities in adjacent neurons were variable and only scattered neurons were strong. Neuronal somata often were difficult to distinguish from surrounding neuropil because of similar intensity of mitochondrial activity. No differences were detected between neurons within and outside epileptic foci. In cortical tubers and hemimegalencephaly, many dysmorphic neurons were intense; balloon cells exhibited low activity. *Conclusions:* Mitochondrial respiratory chain enzymes demonstrated histochemically are not reliable markers of epileptic foci in the same manner as α-B-crystallin. Scattered cells with intense oxidative activity might be actively discharging "epileptogenic" neurons.

J-08

Central nervous system blastomycosis in children: the Manitoba experience

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Background: Blastomycosis dermatiditis is a granulomatous fungal infection that frequently affects the lungs, bone, and skin. Although central nervous system (CNS) involvement occurs in 15% of patients, the clinical features, diagnostic challenges, and management of this condition in children remain poorly understood. *Objective:* To retrospectively review the clinical presentations, imaging, pathology, management, and outcomes of all children with CNS blastomycosis treated at Winnipeg Children's Hospital. *Results:* Since 2001, 7 children were treated for CNS blastomycosis at our institution. Three children presented with skull/scalp masses, 2 with brain abscess, 1 with spinal cord abscess, and 1 with intracerebral hemorrhage/cerebritis. 3/7 children had primary pulmonary involvement. 3/7 had negative CSF cultures despite active infections. All required tissue biopsy to confirm diagnosis. All children had travel history to endemic areas of northern Ontario. Once diagnosed, all children underwent intravenous antifungal therapy. All children remain alive with no episodes of relapse at a mean follow-up of 2.5 years. *Conclusions:* CNS blastomycosis is a potentially life-threatening condition with a highly variable clinical presentation. Prompt diagnosis requires a high index of suspicion especially when evaluating children with travel history to endemic areas. Early consideration should be given to tissue biopsy to confirm CNS involvement.

J-09

Utilization of pediatric palliative care services in children with a progressive neuromuscular condition at the end of life

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Introduction: Recent studies and consensus statements have expressed the need to involve palliative care services in the end of life care for children with progressive neuromuscular diseases, yet there have been no reviews of the utilization of palliative care services by children with these diseases. *Methods:* We conducted a retrospective chart review of all children who had a neuromuscular disease who received end of life care at a local children's hospice. *Results:* Twenty cases were identified in which the child died of a progressive neuromuscular disease. Most of the cases were spinal muscular atrophy type 1 or Duchenne's muscular dystrophy. Services utilized by these patients included respite care, transition services, pain and symptom management care, and end of life care. A review of all symptoms experienced at the end of life demonstrated patients often experienced respiratory distress, pain, nausea/vomiting, and anxiety. However, most symptoms were well controlled during the last 24 hours of life. *Conclusion:* This study found that the utilization of services differed depending on the disease trajectory and that respite played a critical role in the care of children with neuromuscular diseases. This study highlights how different disease populations have different needs in regards to palliative care.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

J-10

Withdrawal of ventilation in a non-ICU setting for patients with neurological disease: more than a procedure, it's a philosophy of care

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Introduction: The emergence of pediatric hospice and home-based programs over the last 10 years have made the withdrawal of life-sustaining therapies in a non-ICU setting possible. Many of the children have a primary or secondary neurologic condition. *Methods:* A retrospective chart review from 2004 to 2009 of all cases of withdrawal of ventilation at one Canadian hospice was conducted. Data collected included patient and family demographics, referral characteristics, drug and withdrawal protocols, psychosocial supports and memory making. *Results:* Over a five-year period 18 withdrawals of ventilation occurred in the hospice. There was a significant increase in the number of cases per year over that period. The patients ranged in age from 2 days to 16 years. Neurologic diagnoses included: hypoxic encephalopathy, metabolic, mitochondrial and genetic syndromes and neuromuscular disease. Time from withdrawal of ventilation to death ranged from 1 minute to 43 days. *Conclusion:* Withdrawal of ventilation is possible in a hospice setting. Multiple medical and emotional interventions can be achieved in a more family centered home like environment at the end of life. Further study as to the benefits of the setting with respect to patient comfort at the end of life and bereavement needs to be conducted.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Poster Presentations

Epilepsy (EEG, Basic Science, Imaging, Neurology and Epilepsy Surgery)

P-001

Temporal lobe epilepsy surgery outcome in patients in sixth decade and beyond

N Pillay (Calgary) RF Avendano (Calgary) W Hader (Calgary) L Partlo (Calgary) S Wiebe (Calgary)*

Background: Many studies on epilepsy surgery exclude patients older than 50 years, citing higher risks to cognitive function, poorer seizure and psychosocial outcomes, and postsurgical complications. We examined the seizure, neuropsychological, and psychosocial outcomes after temporal lobe epilepsy surgery in patients >50 years old. *Methods:* We studied 23 patients with refractory, localization-related temporal lobe epilepsy who were age >50 years old at time of surgery, had standard presurgical workup, and were followed for >1 year. *Results:* Mean age at onset and at surgery was 27 years (range 3-59) and 56.8 years (range 50-71), respectively. Intractable epilepsy duration was 31 years (range 3-62). Selective amygdalohippocampectomy was done in 17 patients and 6 had standard anterior temporal lobectomy. Hippocampal sclerosis was the etiology in 12 patients. Mean follow up was 4.4 years (range 1-10 years). Fourteen (60%) patients became seizure free. Four patients started driving, and none started work if previously unemployed. The measures remained stable in the few subjects who had complete pre-post neuropsychological assessments *Conclusion:* Complete seizure freedom rate was no different than those published for younger patients. Some patients were able to obtain a driver license, but there was no change in employment status.

P-002

Epileptic spasms beyond infancy: Electroclinical, neuroimaging and the role of epilepsy surgery

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Purpose: Epileptic spasms beyond infancy are rare and the etiology and prognosis poorly understood. The objective of this report is to describe the electroclinical, neuroimaging,response to treatment and the role of epilepsy surgery in a series of children with epileptic spasms. *Methods:* Retrospective review of patients with epileptic spasms documented during video-Electroencephalography (EEG) recordings in a tertiary pediatric centre between January 1, 1999 and June 30, 2010. *Results:* 14 patients were identified, eight males.The mean age at onset of epileptic spasms was 2-14 years ; The etiology was malformations of brain development (n=6), tumors (n= 2), infarction (n=1), chromosomal abnormality (n= 1) and in 4, a cause was not identified. The interictal EEG showed normal background or paroxysmal delta and theta slowing. The most common ictal EEG finding was suppression with beta activity. Seizures were refractory to a median of 6 antiepileptic drugs (1-13). Nine patients had focal or multifocal cortical resection, one patient had callosotomy and vagal nerve stimulation, 5 were seizure free. *Conclusion:* Epileptic spasms beyond infancy are rare. The ictal EEG commonly demonstrates diffuse attenution and beta. Malformatons of brain development are the most common cause. Seizures are commonly refractory to antiepileptic drugs. Epilepsy surgery may be effective in a subset of patients.

No	Age of onset (years)	Etiology	Spasm description	Number of Antiepileptic Drugs tried/failed	Other seizure type
1	6	focal cortical dysplasia	jogling in torque, stiffening of trunk, extension of arms/legs - often followed by a cluster	12	Cp, Sp, 2° Gen
2	12.5	focal cortical dysplasia	clusters of spasms with grimacing, head deviation to the L, stiffening and/or vocalization	8	Cp,2° Gen
3	5	perinatal left frontotemporal infarct	aura, stiffening of L arm, forward head and trunk flexion, may fall, confused, duration ~20s, occur in clusters	8	Cp, Sp
4	1	cryptogenic	onic bilateral arm flexion with pupil dilation and nystagmus, loss of balance, duration <20s, occur in clusters	13	Gen
5	2	subcortical band heterotopia	aura of anxiety, tonic flexion of arms, tonic extension of legs, head drops, will fall if standing, duration 2-3s, occur in clusters	8	Cp, Sp, 2° Gen
6	4.6	left cingulate DNET	dizzy sensation, extension of both arms, may fall, duration 10-12s, olivo has sudden jerks with stiffening in clusters	1	Cp, Sp
7	7.5	cryptogenic	often nocturnal, aura of pain R arm, L eyelid twitching, posturing of R arm, difficulty speaking±aware, duration 5-15s, ±occur in clusters	9	Cp, Sp
8	3	cryptogenic	onic spasms - very brief with stiffening of the shoulders, trunk (lolds), and upper limbs. Duration a couple of seconds, occur in clusters.	9	Cp, Gen
9	8.75	focal cortical dysplasia	posturing of L arm/leg, ±jerking, speech arrest, ±decreased conscious-ness, often followed by clusters of spasms of L leg	8	Cp, Sp
10	7.5	focal cortical dysplasia	lexion of head, stiffening of limbs and trunk, ±decreased conscious-ness, thrashing/grunting, duration 15-20s, often followed by clusters of spasms	14	Cp, Sp, 2° Gen
11	5	cryptogenic	spasm-like events, adduction and stiffening of arms, elevation of head, occur in clusters X 10s-1min, ±altered awareness	7	Gen, Cp, 2° Gen
12	0.88	chromosome 8 duplication	decreased responsiveness, slight upward eye rolling ±shoulder shrugging, ±head drop or falling, duration 2-5s, occur in clusters of up to 30 min	1	Cp
13	2.8	focal cortical dysplasia	aura, head flexion, +/-tonic posturing of the upper extremities, ±vomiting before or after the seizure	3	Cp
14	2.8	Right cingulate lesion	aura, stiffening of the shoulder, grimacing, head and eyes deviation to the L, unresponsiveness	2	Cp, Sp

P-003

A Case of 'seasonal' epilepsy correlated with temperature and atmospheric pressure

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Background: Epilepsy is a disorder of complex etiologies, with seizure exacerbation often triggered by multiple factors. Circadian seizure patterns have been confirmed in the literature but circannual or seasonal patterns of epilepsy have not been investigated to the same extent. *Methods:* The medical history of a now-12-year old female with medically-refractory epilepsy and autism spectrum disorder was reviewed. The detailed home seizure records for a 5 ½ year period (May, 1999 to September, 2005) were compared with meteorological data (temperature, humidity, atmospheric pressure, geomagnetic fields, solar radiation and sunspots). *Results:* Epilepsy was diagnosed at 6 months of age. On EEG, her seizures have focal onset from either the left or right hemisphere with secondary generalization. Over the period studied, seizures occurred predominantly between September and May, occurring in clusters over days. Significant correlation was found between seizure occurrence and lower temperatures (Pearson $r = -0.348$, $p < 0.05$) and atmospheric pressures ($r = -0.617$, $p < 0.01$). *Conclusions:* This case is a novel example of epilepsy with increased seizure frequency

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

correlated with lower temperatures and atmospheric pressures. Environmental factors may modulate neuronal excitability likely via neurovascular or other molecular signaling for seizure clustering. Further circannual investigation of epilepsies is warranted.

P-004

Impact of AVM associated bleeding events on seizure occurrence and outcome

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Background: Brain AVM (bAVM) patients have seizures in 20-30%. The risk of hemorrhage associated with an unruptured bAVM is 2-4% per year with increase in rupture rate of 6-9% following a rupture event. We analyzed seizure outcome in bAVM patients with focus on bAVM rupture..
Methods and Patients: 30.1% of 1106 consecutive patients of the Toronto Brain AVM Study Group (1982-2007) presented with seizures during their care (sz-group). 155 patients with complete clinical and neuroradiological data were analyzed (follow up 7.35±5.43 years) and compared to 50 control patients (follow-up of 5.04±4.8 years) with no seizures (non-sz-group).Treatment consisted of surgical resection, radiosurgery, embolization, either alone or in combination. 49 variables underwent univariate analysis. Engel seizure outcome scale was used as outcome measure. *Results:* Initial presentation of ICH was found significantly more (P<0.01) in the non-sz-group than in the sz-group (52% versus 14.8%). bAVMs in the non-sz-group were smaller than AVMs leading to seizures (68.1% ≤3cm). Patients with seizures associated with hemorrhage had worse seizure outcomes, independent of treatment modality (P=0.02). Engel Class I seizure outcome was found in 73.6% of patients who had no ICH at presentation versus 26.4% with ICH. *Conclusion:* Patients presenting with seizures experienced fewer ICH events during or before therapy, suggesting that their seizure presentation led to earlier treatment; circumventing a haemorrhage. Evidence of ICH at presentation or later was associated with worse seizure outcome. We propose that rigorous initial treatment of AVMs to achieve obliteration following a first seizure will prevent epileptogenicity and lead to best seizure outcome.

P-005

The clinical characteristics of sustained refractory status epilepticus in children

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Introduction: Status epilepticus (SE) is the most common neurological emergency of childhood. In 30-50% of cases, SE is refractory to conventional anticonvulsant therapy, necessitating high-dose suppressive therapy. Some cases of refractory SE remain sustained for more than 24 hours. *Objective:* To describe the clinical features of sustained refractory SE in children. *Methods:* Case series of children diagnosed with SE who were admitted to the Paediatric Intensive Care Unit at The Hospital for Sick Children and received high-dose suppressive therapy for >24 hours. *Results:* 54 patients (34 males; 20 females) were identified. Age ranged from 4 days to 17 years. The most common etiological classification of SE was acute symptomatic (40.7%). Almost half of the patients (48.1%) had a prior history of epilepsy. The median duration of high-dose suppressive therapy was 5 days (Range: 1-58 days). The overall mortality was 13.0%. Younger children (<4 years) were more likely to be seizure free at hospital discharge (OR = 3.48; p-value <0.05). Patients with a shorter duration of treatment (≤5 days) were also more likely to be seizure free at discharge (OR = 3.01; p-value <0.05). *Conclusions:* This large single-center case series confirms prior reports that acute symptomatic etiologies were the most common cause of sustained refractory SE in children. However, nearly half of the children also had a prior history of epilepsy. Younger age and shorter duration of treatment were associated with better outcomes. Prospective, long-term follow-up studies are required to better characterize long-term outcomes and their relationship to etiology and therapy.

P-006

Remote memory impairment and accelerated long-term forgetting in a case of cryptogenic temporal lobe epilepsy

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Background: Autobiographical amnesia has recently been described in patients with transient epileptic amnesia, although can occasionally occur in other forms of epilepsy. The deficits are often undetected by standard memory tests, yet can have a profound impact on a patient's life. *Methods:* We report a case of selective memory loss in the context of cryptogenic adult-onset dominant temporal lobe epilepsy. We provide a review of the current literature, highlighting theoretic mechanisms for this targeted amnesia. *Results:* A previously healthy right-handed middle aged businessman with no seizure risk factors presented with a two year history of memory dysfunction and spells suspicious for seizures. While his neuropsychology testing revealed preservation of most cognitive domains, there was a unique pattern of autobiographical amnesia, reflecting both temporally-graded retrograde memory loss, and anterograde accelerated long-term forgetting (failure to retain initially learned new information beyond a few days). A careful neuropsychiatric assessment, and neurologic and systemic exam were otherwise normal. Continuous video/EEG monitoring captured several episodes of déjà vu and stereotypic complex partial seizures originating from the left anterior mid-temporal region. 3T MRI and MRS showed no pathology. Infectious, metabolic, autoimmune, and paraneoplastic studies were normal. His disabling memory impairment has persisted despite clinical control of his seizures for over one year. *Conclusions:* This unique form of epilepsy-associated amnesia may relate to seizures disrupting consolidation and degrading the neural representations of remote memories. Alternatively, epilepsy and memory loss may be independent results of an unidentified common etiology or subtle structural pathology.

P-007

Depth electrodes use in pediatric epilepsy surgery

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The surgical removal of the epileptogenic zone in medically intractable seizures depends on accurate localization to minimize the neurological sequale and ensure against future seizures. To date, few

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

studies have demonstrated the use of depth electrodes in a pediatric population. Here, we report our study of pediatric patients at our epilepsy center who were successfully operated for medically intractable seizures by the use of intracranial depth electrodes. In addition, we detail three individuals with distinct clinical scenarios and describe our technical approach to surgery. *Methods:* We retrospectively reviewed 16 pediatric epilepsy patients who presented at the University of Alberta Comprehensive Epilepsy Program between 1999 and 2010 with medically intractable epilepsy. Patients underwent cortical resection following depth electrode placement according to the Comprehensive Epilepsy Program surgical protocals after failure of surface electroencephalogram and magnetic resonance imaging to localize ictal onset zone. *Results:* The ictal onset zone was successfully identified in all 16 patients. Treatment of all surgical patients resulted in successful seizure freedom (Engel class I) without causing new neurological complications. *Conclusion:* Intracranial depth electrode use is safe and able to provide sufficient information for the identification of epileptogenic zone in pediatric patients previously not considered for epilepsy surgery.

P-008

Systematic review and metaanalysis of randomized trials on first line and adjunctive levetiracetam

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Context: New evidence suggests that levetiracetam may be as effective as traditional agents, with better safety profile. *Objective:* To synthesize evidence regarding efficacy and tolerability of levetiracetam as first line, adjunctive or prophylactic antiepileptic agent. *Study Selection & Data Extraction:* Eligible studies were randomized controlled trials of levetiracetam used in adults with epilepsy. MEDLINE, EMBASE, CENTRAL, CINHAL, PAPERSFIRST, PROCEEDINGSFIRST, PROQUEST and conference proceedings identified studies (to September 30, 2010). Two investigators independently selected, appraised studies, collected and analyzed data. *Results:* Of 10 eligible randomized trials, 8 investigated adjunctive levetiracetam for refractory seizures, 1 as monotherapy for newly diagnosed seizures, 1 as monotherapy for prophylaxis. 8 RCTs of adjunctive levetiracetam were of moderate quality (GRADE criteria), with 2 showing lack of allocation concealment. Meta-analyses showed adjunctive levetiracetam was more effective than placebo in achieving at least 50% reduction of seizure frequency, when added to baseline antiepileptic regimen (pooled RR 2.15 [1.65,2.82], I-squared = 45%, p value (heterogeneity) = 0.08, p value (overall effect) < 0.01). Likelihood of serious adverse events necessitating withdrawal from study was not significantly different between levetiracetam and control (pooled RR 1.37 [0.88,2.13], I-squared = 0%, p value (heterogeneity) = 0.84, p value (overall effect) = 0.17). Subgroup analyses suggested similar effects across different dosages. Sensitivity analysis of studies with adequate concealment showed similar effects. *Conclusions:* Levetiracetam is an effective adjunctive agent for refractory epilepsy. More studies are needed to establish whether it is effective as monotherapy for newly diagnosed seizures, and for prophylaxis in traumatic brain injury.

P-009

Autistic Spectrum Disorder (ASD) and temporal lobe epilepsy:

VL Muro (Vancouver) K Mc Millan (Vancouver) MB Connolly (Vancouver)*

Introduction: One third of individuals with autism develop epilepsy. The neuropathological basis is poorly understood. *Purpose:* To describe the clinicopathological findings in 3 children with ASD and refractory temporal lobe epilepsy (TLE) treated surgically. *Methods:* Retrospective review of medical records. *Results:* Three of 67 patients who had temporal lobe surgery for refractory epilepsy, identified from the epilepsy data base were also diagnosed with ASD. All were male and seizures were refractory to 4-10 antiepileptic drugs. MR imaging demonstrated findings consistent with mesial temporal lobe sclerois (MTS), bilateral in two and unilateral in one. One patient had febrile status epilepticus due to bacterial meningitis at the age of 6 months. 2 children had recurrent febrile and afebrile status epilepticus. Following unilateral anterior temporal resection, 2 patients are seizure free for 4.5 and 10 years respectively. The 3rd patient developed seizures from the contralateral temporal lobe and died during a seizure. Neuropathological examination demonstrated hippocampal sclerosis, abnormal lamination of neurons, large neurons and ectopic neurons in the white matter (microdygenesis). *Conclusions:* Microdysgenesis and mesial temporal sclerosis may be the pathological basis of epilepsy in children with ASD. Malformations of brain development and early status epilepticus may predispose to the development of ASD

P-010

Status epilepticus amauroticus and posterior reversible encephalopathy syndrome (PRES).

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Introduction: Transient visual loss is a common aura of occipital lobe seizures but visual loss for hours has rarely been described as a manifestation of occipital lobe status epilepticus. *Purpose:* To describe profound visual loss due to focal status epilepticus of occipital lobe origin in 2 patients with MRI findings consistent with PRES. *Methods:* Retrospective review of clinical records. *Results:* Case 1: A 15 year old male with Wegener's granulomatosis and chronic renal failure on hemodialysis developed acute headache, hypertension, vomiting, blurred vision followed by blindness (no light perception), and a secondarily generalized clonic seizure. EEG demonstrated independent right and left occipital seizures. Following phenytoin, visual acuity was 20/20 within 48 hours. Case 2: A 10 year old girl with Beta-thalassemia treated with allogenic bone marrow transplantation, had sudden onset of headache, hypertension, bilateral visual loss, encephalopathy and nystagmus. EEG showed status epilepticus of biposterior quadrant origin. Following phenytoin, vision was normal within 72 hours. *Conclusions:* Reversible status amauroticus due to occipital lobe status epilepticus may be the presenting symptom of PRES and EEG examination should be performed

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-011

High-dose diazepam therapy in children with continuous spike-waves during slow-wave sleep (CSWS)

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Background: EEG findings of continuous spike-waves during slow-wave sleep (CSWS) can cause neuropsychological regression and behavior disorders. Our objective is to elucidate the efficacy of high-dose diazepam (DZP) therapy in children with CSWS. *Methods:* We retrospectively studied 10 children (3 girls; 7 boys; age range of 4-15 years) who had CSWS during overnight EEG and underwent high-dose DZP therapy. EEG findings were assessed during and after the high-dose DZP therapy. *Results:* Four patients were diagnosed as epilepsy with CSWS, 5 with Landau-Kleffner syndrome (LKS), one with atypical benign partial epilepsy. Eight patients had a history of seizures and 6 had normal MRI. Regarding the initial EEG effect, a complete remission of CSWS was obtained in two patients, partial resolution of CSWS in 6 and no change in 2. Follow-up EEG showed recurrence of CSWS in one patient. Three patients with LKS who had initial partial response showed remission of CSWS at follow-up EEG. Eight patients showed moderate to significant cognitive/behavioral improvement although 5 had partial resolution of CSWS. *Conclusions:* High-dose DZP therapy was effective in patients with LKS. Cognitive/behavioral improvement can be expected in patients even with partial response on EEG.

P-012

Variability in the diagnosis and management of Electrical Status Epilepticus of Sleep (ESES): A survey by the Canadian Pediatric Epilepsy Network

R Ramachandrannair (Hamilton) C Go (Toronto)*

Aim: To understand the variability of the criteria for definition of ESES and the treatment methods used by pediatric neurologists for this condition. *Method:* A survey consisting of 27 questions were mailed to 82 pediatric neurologists working at pediatric academic health centers across Canada. There were questions on experience with ESES, diagnostic criteria, diagnostic modality, and principles of treatment, methods, duration and monitoring of treatment. *Results:* 61 (74%) surveys were returned. Experience with ESES over the previous 5 years in terms of number of patients was; none: 12, 1-5: 39, 6-10:5 & >10: 5. 44% opined routine sleep EEG (with or without sleep deprivation) or prolonged daytime sleep EEG with one sleep cycle is sufficient to make the diagnosis of ESES as opposed to 44% who voted for overnight EEG. 45/61 (74%) indicated ability to provide comments on the diagnostic criteria or treatment options of ESES. 80% based the diagnosis of ESES on clinical and EEG findings. Visual impression of near continuous SW activity during sleep was the method used by 50% of neurologists to diagnose EEG pattern of EEG. Only 22% recommended manual calculation of SW index. Minimum SWI recommended was 85% by 24(53%) and 50% by 13 (29%). First line management options were, Valproic acid 22(49%), high dose diazepam 13 (29%) and, steroid 4 (9%). *Conclusion:* There is high variability among Canadian pediatric neurologists regarding the experience, diagnostic criteria, type of EEG and mangement options used in the managemnt of ESES.

P-013

Electrical status epilepticus of sleep: diazepam challenge test

R Ramachandrannair (Hamilton) GM Ronen (Hamilton)*

Different treatment modalities are associated with variable success in ESES.High dose diazepam challenge test is used to identify suitable patients for nocturnal high dose diazepam maintenance therapy. Our objective is to quantify the effect of high dose diazepam on the sleep EEG of children with ESES and to identify the variables that correlate with the EEG response. *Methods:* Inclusion criteria: 1.Children aged 3-12 years diagnosed with ESES 2.ESES defined as spike-wave index (SWI) of >85% during sleep or >50% if the awake EEG showed a SWI of <20%.
1mg/kg of Diazepam (maximum 40mg) was given in 2 equal half doses 2 hours apart in the evening PO or PR. Sleep SWI was calculated after the second dose of diazepam. Good response: decrease in sleep SWI by >50%. *Results:* Of the 15 children with ESES, 11 had diazepam challenge test. Six (55%) had a good response. Sex or age of onset of ESES was not associated with EEG response. Delay in administering diazepam after onset of ESES was significantly greater in the non-responder group (Responders: Mean 0.42 yrs with SD 0.24; Non-responders: Mean 4.5 years with SD 3.3; unpaired t-test p=0.01). Duration of ESES significantly correlated with EEG improvement, greater improvement with shorter duration of ESES (duration of ESES Vs pre-post DZP SWI; Pearson correlation: r2 = 0.297, one sided p= 0.04) *Conclusions:* In children with ESES, good EEG response following high dose diazepam challenge test is associated with shorter duration of ESES. This finding needs to be validated by a large prospective cohort.

P-014

Development and validation of an epilepsy case definition for use with administrative data

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Background: There are currently no ongoing surveillance activities for epilepsy in Canada. We conducted this study to: (1) develop and validate coding algorithms for epilepsy using inpatient and physician claims data; and (2) assess whether adding an emergency room database enhances the epilepsy case validity. *Methods:* Epilepsy status was determined by two trained physicians in a random selection of charts from 13 neurologists' practices from 2003 and 2006. The optimal algorithm to identify epilepsy cases was developed by linking the reviewed charts with the following administrative databases: provincial health care insurance plan registry, hospital discharge abstract database, ER visits database, and physician claims database in Calgary. We calculated sensitivity, specificity, positive predictive value and negative predictive value for each ICD-9 and ICD-10 administrative data algorithm. *Results:* Of 2253 charts reviewed, 44% represented epilepsy cases, 1% convulsion and 55% other diagnoses. Of 18 algorithms assessed, the best coding algorithm to identify epilepsy cases was 2 physician claims in 2 years or 1 hospitalization coded with an ICD-9 or 10 epilepsy code: Sn 88.9%, Sp 92.4%, PPV 89.2%, NPV 92.2% (2003) and Sn 93.1%, Sp 93.0%, PPV 91.9%, NPV 94.0% (2006). Adding the ER database improved Sn and NPV but lowered Sp and PPV. *Conclusions:* A majority of epilepsy cases can be accurately

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

identified in administrative data using the following case definition: "2 physician claims within 2 years or 1 hospitalization" coded with an ICD-9 or 10 epilepsy code. Validity of administrative data in recording epilepsy improved over time.

P-015

Increased neurogenesis in developing succinic semialdehyde dehydrogenase deficient mice

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Background: The succinic semialdehyde dehydrogenase (SSADH) deficiency is a rare disorder of GABA degradation. The clinical phenotype includes epilepsy, developmental delay, psychomotor retardation, ataxia, and shortened lifespan. Currently there is no effective treatment for SSADH deficiency. During development, a murine analog of SSADH deficiency exhibits failure to thrive, ataxia and a seizure disorder that transitions from absence seizures to fatal status epilepticus, within four weeks. Therefore, we set out to study the brain volume and neurogenesis in the dentate gyrus of SSADH deficient mice. *Methods:* In postnatal SSADH deficient mice (n=7) and the wild type (WT) litter-mate controls (n=7), we examined neurogenesis using Bromodeoxyuridine to label dividing cells. We also examined the volume of the granule cell layer and the hilus of the dentate gyrus. Differences between groups were compared using Student's t-test. *Results:* Mutant mice had significantly lower granule cell layer ($p<0.05$) and hilar ($p<0.001$) volumes compared to the control group. Mutant mice were also found to have significantly higher numbers of BrdU-positive nuclei in both regions than controls (gcl, $p<0.001$; hilus, $p<0.01$), indicating higher levels of neurogenesis. *Conclusion:* Data showed increased neurogenesis with diminished volume of dentate gyrus in SSADH deficient mice compared to the WT mice.

P-016

Vagal nerve stimulation in continuous spike and wave in slow wave sleep

WA Stewart (Rothesay)

Background: Continuous spike and wave in slow wave sleep (CSWS) is a challenge to treat. In addition to conventional therapies, steroids and IVIg are often utilized to try and improve the clinical picture and EEG. *Methods:* This 11 year old girl presented at 5 years of age with cognitive regression and loss of speech. An EEG demonstrated CSWS. Despite treatment with many anticonvulsants, steroids and IVIg she showed no improvement and had side effects from almost every treatment. Her seizures were relatively infrequent, but her behaviour, language and social regression have posed a significant challenge for her family. *Results:* Following discussions with this family and colleagues, a VNS was inserted in this child to try and improve her quality of life. The current was titrated to 1mA with significant improvement. She started talking and was much more compliant and happier. Her behaviour has significantly improved. There has also been significant improvement in her EEG. *Discussion:* The seizures in CSWS usually resolve and the continuous discharges last until an average of 11 years of age. Despite this, there can be ongoing cognitive problems and behaviour challenges. In this child the VNS has resulted in a significant improvement in her quality of life. It suggests this may be an option for younger children who are unresponsive to other therapies.

Movement Disorders (Basic Science, Neurology, Imaging and Functional Neurosurgery)

P-017

Idebenone effects in Friedreich's Ataxia patients: design of the PROTI study

WT Andrews (Charlestown) N Coppard (Charlestown) P Giunti (London)*

Background: Clinical trials assessing effects of idebenone on neurological function in Friedreich's Ataxia (FRDA) patients provided mixed results. However, patients receiving idebenone have reported improved quality of life and activities of daily living, raising questions about the assessment tools used in clinical trials. A double-blind, randomized study will evaluate Patient Reported Outcomes in FRDA patients after withdrawal from Treatment with Idebenone (PROTI) in participants of the 2-year MICONOS extension study (MES). *Methods:* Approximately 80 patients who completed ≥1 year of MES will be randomized to receive placebo or continue idebenone 1350 or 2250 mg/day for 2 months. Patients may enter multiple study cycles after 12, 18, and/or 24 months of MES treatment. The primary endpoint is the proportion of patients accurately identifying if they were randomized to idebenone. Secondary endpoints include the proportion withdrawing because of recurring or worsening FRDA symptoms; changes in Modified Fatigue Impact Scale, 9-Hole Peg test, speech capability, International Cooperative Ataxia Rating Scale score; and clinical global impression of change. *Results:* The sensitivity of assessment tools in the evaluation of idebenone efficacy in FRDA patients is explored. *Conclusions:* The results will provide valuable information regarding the potential therapeutic use of idebenone in the treatment of FRDA.

P-018

Demographics of Canadian FRDA patients on idebenone and review of a patient ADL survey

WT Andrews (Charlestown)

Background: Idebenone was approved with conditions (NOC/c) for the treatment of symptoms of Friedreich's Ataxia (FRDA) in Canada. The Canadian FRDA (Idebenone) Patient Support Program maintains a database of all patients on idebenone. *Methods:* Demographic characteristics were collected with regard for patient confidentiality. Changes in activities of daily living (ADLs) among program participants on idebenone for at least 3 months were assessed by questionnaire during recorded phone interviews. *Results:* Of the program participants, 155 had confirmed FRDA (62 male, 91 female [gender not recorded for 2 patients]). Mean age was 27.5 years (range, 2–73 years). Of 17 patients who completed the ADL questionnaire, most reported improvement or no change in speech (15/16), swallowing (12/15), cutting food and handling

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

utensils (11/14), dressing (15/16), personal hygiene (16/16), falling (12/16), walking (8/12), quality of sitting position (14/16), bladder function (15/17), fatigue (14/17), vision (16/17), ability to exercise (13/16), ability to sit straight (15/16), and ease of mobility in a wheelchair (11/12). *Conclusions:* The FRDA (Idebenone) Patient Support Program provides insight into the demographics of the Canadian FRDA population. In a survey of program participants with this chronic, progressive disease, most reported ADLs were unchanged or improved since starting idebenone therapy.

P-019

Frame based vs. frameless stereotaxy in essential tremor: A retrospective review comparing clinical and radiographic efficacy, operating time and cost effectiveness

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Object: Deep brain stimulation (DBS) of the Ventral Intermediate Thalamus (VIM) for medically refractory essential tremor (ET) is an established treatment modality, however traditionally presents several inconveniences that come with frame-based neurosurgery. The recent introduction of the Nexframe® image-guided system, a skull mounted aiming device, has allowed DBS electrode implantation to be done in a completely frameless setting. In this study, comparison is made between the clinical efficacy, operating time and cost effectiveness of frame based vs. frameless stereotactic DBS. *Methods:* 16 patients (8 frame-based and 8 frameless) have undergone unilateral DBS electrode implantation in the VIM by the senior author (I.M.). All patients suffer from ET. Magnetic resonance images were obtained pre and post-operatively for each patient and were fused together in order to compare the location of the electrode tip and that of the desired target. Improvement in tremor control was measured by comparing pre and post operative scores in the Clinical Rating Scale for Tremor (CRST). Operating time, hospitalization time and the resultant cost per patient were also measured and compared between cohorts. *Results:* There was no significant difference between the two groups with respect to clinical or radiographic efficacy, hospitalization time or cost per patient. There was a significant difference in surgical time between groups, representing a 42% reduction in total operative time in patients treated with frameless DBS. *Conclusions:* The Nexframe® system reduces OR time significantly without compromising clinical efficacy or adding cost. This may potentially translate into nearly twice as many patients being treated per operative day.

P-020

Craniofacial-lingual movements in acute ICU-acquired quadriplegia, a new syndrome

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Background: The syndrome of involuntary craniofacial lingual movements (ICFLM) in the setting of acute ICU-acquired quadriplegia (critical illness neuromyopathy - CINM) following sepsis-associated encephalopathy (SAE) has not been previously described. We suggest a localization and treatment for this disabling condition. *Methods:* Four patients (2 female) from our neurocritical care centre were quadriplegic from CINM when they developed the abnormal movements following severe sepsis, multi-organ failure and SAE. *Results:* Extensive serologic studies, review of medications and repeat magnetic resonance (MR) imaging failed to identify an etiology for the abnormal movements. CSF protein was elevated in 3 cases. Movements were of large amplitude, of moderate speed and semi-rhythmic in the jaw, tongue and palate, persistent and extremely bothersome to all patients. Injection with Botulinum toxin type A (BoNT A) was very beneficial. *Conclusions:* ICFLM, in the setting of flaccid quadriplegia from CIMN and following SAE, is consistent with focal craniofacial brain stem myoclonus and constitutes a new syndrome. BoNT A treatment may be helpful in treatment.

P-021

Lingual dyskinesia and tics: a novel presentation of copper metabolism disorder

HR Goez (Edmonton) FD Jacob (Edmonton) J Yager (Edmonton)*

Background: Abnormalities of copper metabolism were linked with neurological disorders affecting movement; however, their diagnosis is elusive, especially in cases with atypical characteristics. *Methods:* Case report. *Results:* A previously-healthy 16 year old male presented with acute onset of abnormal hemilingual wave-form movements, with his tongue deviating to the left in a twisted fashion. Movements were suppressed when patient was asked to extrude his tongue; they did not interfere with swallowing or speech, and did not persist during sleep. Upon examination sudden ballismic and tic-like movements of all limbs were noted, which could be suppressed voluntarily. Otherwise normal neurological evaluation. Extensive metabolic, hematologic and serologic investigations were normal. Serum ceruloplasmin and copper levels were low; 24-hour urine collection revealed normal copper excretion, but penicillamine challenge showed increased urinary copper. These increased values were higher than the norm, but still significantly lower than the diagnostic value for Wilson's disease. Brain MRI was normal. Screening for Wilson's and Huntington's disease was negative. Patient was started on zinc gluconate supplement. After 8 weeks the movements disappeared, although copper and ceruloplasmin levels were not normalized. *Conclusions:* This is the first case presenting association between copper metabolism disorders, tics and hemilingual dyskinesia in humans.

P-022

Effects of Compound Celecoxib and Diclofenac vs placebo on movement disorders in a rat model of Parkinson's disease

V Hooghoghi (Tehran)

To examine the effect of Celecoxib and Diclofenac compound on movement disorder of parkinsonism. In the study the substantia nigra pars compacta in rat has been destroyed by using electrical lesion (10Sec;1mA DC) to create PD Model. Then Diclofenac (1, 3 mg/kg) and Celecoxib (2, 4, 8 mg/kg) have been administered to parkinsonian rats. It is remarkable that the locomotor activity and rigidity were changed dramatically. The compound of Celecoxib and Diclofenac lessened the rigidity and improved the locomotor activity of parkinsonian rats as compared to the Placebo groups. Based on the results of the locomotor activity and rigidity tests using in parkinsonian rats, we found that compound Celecoxib and Diclofenac had a significant rigidity-improving effect.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-023

The influence of administration of NSAIDs (COX-I inhibitors) and Steroidal anti inflammatory compound can alter the striatal Dopamine level

V Hooghoghi (Tehran)

In the present study, effects of intra-striatal injections of the compound of Diclofenac and Dexamethasone in Normal and Parkinsonian rats have been investigated. It was found that the Cox-I inhibitor, Diclofenac (1.3 mg/kg) and steroidal anti inflammatory, Dexamethasone (0.5, 1 mg/kg) simultaneously on dopaminergic neurotransmission in normal and substantia nigra pars compacta (SNc)-lesioned rats has an enormous effect. According to the results of the study the release of Dopamine in Parkinsonian rats that received the compound was much more than those receiving Diclofenac or Dexamethasone only. This demonstrated that NSAIDs and steroidal anti inflammatory agents significantly attenuate decreases in dopamine concentration.

P-024

Cerebellar GABA-B subunit 2 (GBR2) receptor in Essential Tremor

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Background: The pathophysiology of essential tremor (ET) is unknown. Studies of ET have shown dysfunction of the GABAergic system. The GABA-B receptor is a metabotropic receptor composed of two different subunits; subunit 1 (GBR1) which binds to GABA, and subunit 2 (GBR2) which binds to G proteins. It is unknown which subtype of GABA function may be altered in ET. *Methods:* ET cases seen at our clinic were autopsied within 24 hours of death. Frozen cerebellar cortex of 9 ET (M-3, F-6) and 5 normal controls was studied by Western blot. *Results:* Mean onset age was 41 years (range 5 to 65 years) and mean age at death was 80 years. Seven of 9 had positive family history of tremor, 7/9 had head tremor, and 6/9 had resting tremor. Three patients improved with propranolol (one did not tolerate and 5 did not try it); one benefited from primidone (unknown status in one, and the other 7 did not try it). Mean GBR2 protein levels (as measured by Western blot gray level) were higher in the ET group ($p<0.05$). There was no association between GBR2 levels and onset age, tremor severity, family history of tremor or response to drug therapy. *Conclusion:* GBR2 protein expression is increased in ET. Further studies are needed to determine the significance of these receptor changes in ET.

P-025

Role of Arvid Carlsson in the development of L-Dopa for Parkinson's disease

A Rana (Toronto) S Gangat (Toronto)*

Objective: To discuss role of Arvid Carlsson in the development of L-Dopa for Parkinson's disease. *Background:* Levodopa which is a precursor of dopamine is found in leguminous plants. Plants with the highest concentration have been used to treat symptoms of Parkinson's disease in Indian medical doctrine of Ayurvidic medicine since 5000 B.C. Levodopa in pharmacological form was introduced in 1960s. Many scientists have played an important role in the development of levodopa in its present form. We wanted to discuss the role of Arvid Carlson in this regard. *Methods:* We reviewed all available resources including internet, webpages and books to study the work of Arvid Carlsson. *Results:* In 1957 Arvid Carlsson (born in 1923), a Swedish scientist demonstrated in his experiments on animals that dopamine was a neurotransmitter in the brain and that dopamine levels in the basal ganglia were particularly high. He then showed that decreases in dopamine levels resulted in decreased control of movements similar to bradykinesia seen in Parkinson's disease. In 1959 at the international pharmacology meeting, he speculated that dopamine was responsible for causing Parkinson's disease. He won the 2000 Nobel Prize for his work on dopamine. In 1960 Oleg Hornykiewicz, in Vienna found dopamine deficiency in striatum of Parkinson's disease patients in post mortum analysis and in 1966 he published a major review article stating that dopamine deficiency was the cause of Parkinson's disease. *Conclusion:* Arvid Carlson played a remarkable role in the discovery of L-Dopa, which is still gold standard treatment for Parkinson's disease.

P-026

Paroxysmal non-kinesigenic dyskinesia OR partial seizures

A Rana (Toronto) S Gangat (Toronto)*

Objective: To discuss the differentiation of Paroxysmal non-kinesigenic dyskinesia from Partial seizures. *Introduction:* Paroxysmal non-kinesigenic dyskinesia is a rare hyperkinetic movement disorder, characterized by episodes of involuntary movement which may include dystonia, chorea, athetosis, or ballism without any changes in consciousness. These episodes may be confused with partial seizures. *Methods:* A 66 year old right handed female developed intermittent involuntary posturing of her left hand about six to seven years ago. They were currently occurring twice a week and were lasting from one to several minutes. She had no control over these episodes and there was no change in her consciousness during these attacks. She reported that there was no warning prior to these episodes. She denied any specific triggers that may precede the attack such as sudden movement, or stress. *Results:* An MRI of the brain was normal and during a 48 hour ambulatory EEG she had one episode of posturing without any electrocardiographic changes. She was started on Clonazepam with a significant improvement of her symptoms. *Conclusion:* Paroxysmal non-kinesigenic dyskinesia, which may be confused with partial seizures, may be responsive to benzodiazepines.

P-027

Head trauma and the risk ot Parkison disease: a meta-analysis of observational studies

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Head trauma has been implicated in the etiopathogenesis of Parkinson disease (PD). We performed a meta-analysis to investigate the association between head trauma and the risk of developing PD. We included observational studies if they 1) clearly defined PD; 2) defined head trauma leading to concussion; 3) presented odds ratios (ORs) and 95% confidence intervals (95% CI) or provided data to compute these parameters. Random effect model

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

was used to estimate the pooled adjusted OR. Heterogeneity between studies was evaluated with the Q test and the I2 statistics. We did sensitivity analysis to assess the influence of each study and repeated the analysis by excluding the studies with the largest weights. We used funnel plot and Egger's test to assess the presence of publication bias. After reviewing more than 2600 article titles, 28 articles were selected for full review. A total of 19 studies (17 case control, one nested case control, and one cohort study) with 17898 cases and 77945 controls were included in the meta-analysis. The pooled OR for the association of PD and head trauma was 1.53 (95% CI: 1.28-1.83). Five studies were found to be the source of heterogeneity in this study. After removing these five studies, the pooled OR 95% CI was 1.44 (1.32- 1.58; I2= 0%), and the association of trauma and risk of development of PD remained statistically significant. The results of our meta-analysis indicate that a history of head trauma that results in concussion is associated with a higher risk of developing PD.

P-028

Friedreich's ataxia (FRDA) complicated by Leber's Hereditary Optic Neuropathy (LHON): an unfortunate coincidence?

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A recent study of 26 patients with FRDA showed loss of retinal nerve fibre layer in all, but only five patients had visual symptoms. Two had sudden devastating vision loss mimicking LHON (Fortuna et al, 2009). We present a similar patient with FRDA who was found also to possess the LHON mtDNA 11778 mutation. *Case Report:* A 30-year-old woman was diagnosed at age 9 with Friedreich's ataxia, based on the presence of limb and truncal ataxia, areflexia, upgoing toes, decreased position sense and scoliosis. By age 18, she required a wheelchair. Genetic testing showed an expanded GAA trinucleotide repeat in one allele of the FRDA gene and a heterozygous mutation in exon 4 (c.467T>C; previously reported to be associated with FRDA). At age 30, she had painless bilateral vision loss starting in the right eye and deteriorating over 3 months to perception of hand movement in both eyes. Ophthalmoscopy initially showed disc hyperemia, vascular engorgement and peripapillary telangiectasia and later regression of the fundus findings with development of marked optic disc pallor. Genetic testing revealed homoplasmy for the LHON 11778 mutation. We conclude that LHON should be considered in the diagnosis of FRDA patients who have rapid loss of vision. Whether LHON and FRDA are linked remains to be determined.

P-029

Psychogenic movement disorders in children: characteristics and predictors of outcome

T Soman (Toronto) J Faust (Toronto)*

Objectives: 1) Identify characteristics of children presenting with psychogenic movement disorders 2) Identify strategies effective in management. *Background:* Psychogenic Movement Disorders (PMD) are movement disorders associated with underlying psychological or psychiatric disorders. Symptoms can mimic organic movement disorders affecting gait, speech or several parts of the body. There are no tests to reliably diagnose PMDs making it a challenging condition to diagnose and treat. *Methods:* A retrospective review of patients in pediatric movement disorder clinic was undertaken using clinic database, chart review and review of videos. Diagnosis was made by movement disorder specialists. The disorder was classified according to the organic disorder most closely resembled i.e dystonia, myoclonus, tremor etc. All patients were investigated for organic disorders. *Results:* 300 patients were seen in the movement disorder clinic between 2005-2009. Thirteen patients (4.3%) were identified with PMD. Ten female patients affected. Age range was 6-17 years (mean age=13.1y). Common presentations were dystonia (5), tremor (3) and myoclonus(2). Psychological stressors and /or psychiatric co-morbidities were identified in 10 patients. Five patients were involved in competitive sports. Ten patients improved or recovered completely (77%), one was lost to follow-up. Two main factors were identified for effective treatment of children and adolescents presenting with PMD: 1) A multi-disciplinary approach 2) Family involvement. *Conclusion:* Children have a better prognosis than adults. PMD is more prevalent in teenage girls. Involvement in competitive sports or other competitive activities might be a risk factor. A multi-disciplinary approach and involvement of the child's family is essential for effective treatment.

P-030

Dopamine replacement therapy does not influence affective state in Parkinson disease

C Xia (Montreal) AC Simioni (Montreal) LK Fellows (Montreal)*

Background: Previous studies of the effect of dopamine replacement therapy (DRT) on Parkinson disease (PD) patients' emotional state have yielded mixed results. Some work argues that DRT enhances positive affect, with DRT withdrawal having the opposite effect. Other studies have failed to find any significant relationship between DRT and affect. Details of design and the validity of affect measures have varied across studies. *Methods:* We examined the effect of DRT on current affective states of twenty patients with mild-moderate Parkinson's disease without depression, using a well-validated self-report questionnaire, the Positive and Negative Affect Schedule. Motor symptoms were also evaluated using the unified Parkinson's disease rating scale (UPDRS). The subjects were tested twice, once while taking their usual DRT, and once after an 18-hour DRT washout. Control data were obtained from 15 demographically-matched healthy subjects. *Results:* DRT improved motor symptoms, with a significant decrease in UPDRS scores from the off- to the on-DRT state (PD-off 18, PD-on 13; $p < 0.001$). However, DRT had no significant effect on current positive affect (PD-off 32.5, PD-on 33.8; $p = 0.37$) or negative affect (PD-off 13.9, PD-on 13.1; $p = 0.25$). PD patients, regardless of DRT status, consistently reported less positive affect and more negative affect than control subjects ($p < 0.05$). *Conclusion:* Compared to healthy controls, PD patients reported less positive and more negative affect. However, DRT had no detectable effect on either positive or negative affect. These findings argue that while PD influences emotional state, this is not through a dopamine-sensitive mechanism.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Neuro-Oncology (Medical and Radiation Oncology, Imaging, Tumour Surgery, Basic Science)

P-031

Frameless stereotactic radiosurgery for brain metastases - the BC Cancer Agency experience

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The traditional management of brain metastases has included surgery, whole brain radiotherapy, chemotherapy, and stereotactic radiosurgery (SRS). Frame-based radiosurgery techniques are well established. However the advent of frameless systems offers advantages including improved patient comfort and convenience for patients. Few papers describe clinical outcomes for frameless SRS; we therefore evaluated survival and local tumor control of patients with brain metastases treated with a frameless LINAC based system. We conducted a retrospective, population-based review of 53 patients with 97 lesions. Patients had 4 or fewer metastases with a Karnofsky score > 70 and ECOG score > 2. A localizing MRI was co-registered, using the BrainLAB system to a CT taken with the patient wearing a thermoplastic mask. The lesion(s) were then contoured and a physics plan developed. A Linac stereotactic unit equipped with ExacTrac was then used to deliver the prescribed treatment dose.

Median follow-up from SRS was 9 months with 22/53 patients alive at last follow-up. Median actuarial survival was 11 months. Median dose (80% isodose line) was 2400 cGy. Follow-up imaging was available in 83/97 lesions of which 13 demonstrated progression. Cumulative 6 month local control was 89% with inferior control for melanoma metastases (68%) versus other tumor types (96%). There was a trend toward improved control for tumors < 1 cm^3 (94%) versus those > 1 cm^3 (84%).

Frameless SRS using LINAC equipped with ExacTrac appears equivalent to frame-based techniques in the treatment of brain metastases.

P-032

Posterior interhemispheric transprecuneus approach to choroid plexus tumors in children: Technical note and case illustration

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Background: The posterior interhemispheric transprecuneus(PIT) approach is an effective microsurgical approach that avoids damage to the optic radiations. Despite the prevalence of choroid plexus tumors among children, we are unaware of any prior descriptions of this approach among the pediatric population. *Objective:* To describe the technical aspects of the PIT approach in children, illustrated by a case of a two-year old girl with a choroid plexus papilloma. *Discussion:* Pre-operative imaging demonstrated a large, enhancing mass arising from the atrium of the left lateral ventricle with associated hydrocephalus. Given the vascular supply of the tumor as well as concerns regarding visual pathway preservation, we selected the PIT approach. In the prone position, through a left parasagittal occipito-parietal craniotomy, the left occipital lobe was gently retracted and a small corticotomy made in the precuneus just posterior to the splenium of the corpus callosum. Through this corridor, early devascularization and gross total resection of the tumor was achieved. The patient is disease free at 17 months follow-up with no evidence of visual field deficit. *Conclusions:* The PIT approach is an effective microsurgical approach in children allowing wide access to the atrium, early visualization of the choroidal arteries, and avoids injury to the optic radiations.

P-033

Gamma Knife Radiosurgery for the treatment of non-surgical cystic cerebral metastases

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Background: Treatment options for cystic cerebral metastases include surgery, whole-brain radiation therapy (WBRT), and stereotactic radiosurgery (SRS). Larger cystic lesions are regarded as unsuitable for SRS: higher radiation doses required carry an associated risk of radiation toxicity and the non-cellular component may not respond to radiation. Such lesions often require surgery. We aimed to assess the role of Gamma Knife Radiosurgery (GKRS) in the treatment of non-surgical cystic brain metastases. *Methods:* 223 consecutive patients with brain metastases underwent GKS between February 2006 and July 2009. Lesions with a greater and less than 50% cystic component were identified. Clinical, radiological and dosimetry parameters were reviewed to establish the response to SRS and identify potential predictive factors of response. *Results:* 57 lesions in 40 patients were analyzed. The primary cancer was lung, breast and other in 47%, 16% and 37% respectively. Mean tumour volume was 4.4 ml (range 0.11–23.18 ml). Mean prescription dose was 20.1 Gy (range 15-24 Gy). Mean follow-up was 12.5 months (range 1.8-56). Mean conformality index was 1.6 (range 0.83-3.2). Local control rates were 94, 87, 72 and 51% at 3, 6, 12, and 18 months respectively; they were superior in lung compared to non-lung subtypes and unaffected by percentage of cystic component. *Conclusions:* These results support the use of GKRS in the management of non-surgical cystic metastases despite a perceived poorer response in the reported literature. Our local control rates are comparable to a matched cohort of non-cystic brain metastases. Tumour subtype was as predictor of response.

P-034

Tumour control rate using LINAC radiosurgery in the treatment of growing vestibular schwannomas

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Introduction: Radiosurgery is a recognized treatment for vestibular schwannoma, with a published tumour control rate of 86-100% in unselected series. Recent natural history studies have demonstrated that up to 70% of vestibular schwannomas remain quiescent and that growing tumours tend to continue to grow. Our objective was to look at tumour control rate following radiosurgery in a series including only vestibular schwannomas demonstrated to be growing on serial imaging. *Methods:* A retrospective chart review was performed that yielded 46 patients with vestibular schwannomas that had grown on pretreatment serial imaging and that were treated with LINAC

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

radiosurgery at our institution (1999 to 2006). Patients were followed clinically and with MRI at 6-12 month intervals. Minimum follow-up was 2 years, mean follow-up was 5 years. *Results:* 8 of 46 patients had progressive increase in tumour size during the follow-up period. 4 patients required re-referral to a neurosurgeon for further treatment (i.e. treatment failures). This yielded a tumour control rate of 83% and a treatment failure rate of 9%. The mean time to treatment failure was 43 months. *Conclusions:* While radiosurgery is a relatively effective treatment for vestibular schwannoma, it appears to be less effective in the treatment of growing tumours than previously reported for unselected series. Long-term prospective data needs to be collected and published to clarify this issue. The effect of radiosurgery on subsequent surgical treatment of these tumours is also important to clarify given the significant rate of treatment failure.

P-035

Malignant scalp lesions following brain tumour radiation: report of 3 cases

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Background: Complications of radiation for brain tumours can include all layers exposed in the field of radiation. Malignant scalp lesions are not very common. We report 3 cases of malignant skin lesions following radiation for supratentorial gliomas. *Methods:* 20 year old male was operated upon for cystic glioma in the left posterior sylvian region followed by radiation. Approximately a year later he developed a basal cell carcinoma of the scalp over the radiated area. This was excised without any sign of recurrence. Pathology indicated basal cell carcinoma. Years later he developed a left sided schwannoma of the 9th cranial nerve which was excised. A year or so before he died, 40 years after the initial operation, he developed a glioblastoma multiforme opposite to the original tumour, which was removed. 12 year old female had removal of a right temporal astrocytoma, Grade III, followed by radiation. She developed skin necrosis and infection and years later the area overlying the radiated scalp showed evidence of basal cell carcinoma.

42 year old man was operated upon at the age of 16 for a pineal germinoma followed by radiation. He did well until 2010 when he developed a number of skin lesions which were proven to be basal cell carcinoma. *Result:* Besides the known complications of radiation for intracranial lesions (necrosis, swelling, myelin and neuromal loss, vasculitis etc.) malignant scalp lesions should also be considered.

P-036

Natural history of intracanalicular schwannoma

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Background: Since the advent and accessibility of MRI, detection of smaller vestibular schwannomas (VS) has become more frequent. There are several strategies for treatment of VS, including conservative management with serial scans, surgery, or stereotactic surgery. All of these are reasonable options when faced with a small VS. There are few studies in the current literature describing the natural history of intracanalicular VS. We present a study examining patterns of growth and hearing loss in purely intracanalicular VS. This may help physicians in making treatment decisions regarding VS. *Methods:* Retrospective review of 60 conservatively managed patients with intracanalicular schwannomas. Patients with a diagnosis of neurofibromatosis-2. Main study parameters were growth of tumor and audiology results. Tumor growth was measured along the axis of the internal auditory canal. *Results:* Mean age was 56 years. The mean follow-up period was 3.1 years. Mean size of tumor on presentation was 7.8 mm and 8.3 mm at last follow-up. The median growth rate was 0mm/year (mean = 0.25/year). Mean PTA at first presentation was 50.1, and at last follow-up, 54.5. Mean word recognition score at first presentation was 76.1%, and at last follow-up, 74.8%. *Conclusion:* Intracanalicular VS have a minimal yearly growth rate. Despite a small decrease in hearing, patients continue to maintain serviceable/aidable hearing over time. Conservative management is the best strategy for management of these tumors.

P-037

Colloid cyst- a case study

EAJ Sehmer (Preston)

Background: Colloid cysts are congenital benign tumours that most commonly arise from the third ventricle. They are a rare cause of headache and of sudden death with an incidence of three per million people per year. *Case Presentation:* A healthy 20 year old female presented with a seven day history of headache which worsened at night. She also complained of a two day history of double vision, and 'flashers and floaters' in both eyes. An MRI scan showed a colloid cyst in the roof of the third ventricle with lateral ventricular dilatation. *Conclusion:* This report reviews a common presentation of a colloid cyst that needs to be considered in the differential diagnosis of headaches in young people. With an early diagnosis, they are less likely to cause hydrocephalus, increased intracranial pressure, intracystic haemorrhage and sudden death.

P-038

Sensory symptoms of vestibular schwannomas

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Objective: To determine the anatomic cause of non hearing symptoms *Background:* Vestibular schwannomas are common lesions with diverse presentations. Although typically afflicting hearing, sensory deficits in trigeminal and facial nerves may be seen. Prior studies have shown sensory dysfunction to be significant determinants of quality of life; however, the etiology of these symptoms is unclear. *Hypothesis:* Tumor contact with cranial nerves (CN) cause dysfunction. *Method:* retrospective chart review *Results:* 66 consecutive patients were identified. 42% had trigeminal nerve dysfunction and 52% had radiographic evidence of contact between tumor and CN V. All patients with trigeminal symptoms had contact between the nerve and tumor on imaging. In asymptomatic patients with evidence of tumor contact, there was a trend towards longer symptom histories. In comparison, 39% of patients had CN VII dysfunction. Radiographic evidence of contact between CN VII and tumor was not consistently identifiable; however, patients were more likely to have a lesion arising from the internal auditory canal (IAC) and/or obstructing the opening of the porus acousticus with absence of a normal CSF space. *Conclusion:* This study is the first to look at radiographic findings related to vestibular schwannoma

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

sensory symptoms. We show that contact between the trigeminal nerve and tumor are likely responsible for CN V symptoms. In comparison, facial nerve dysfunction appears to originate from compression at the level of the opening of the IAC. Given the detrimental effects of sensory malfunction, a better anatomic understanding of the cause may help guide therapies appropriate for this lesion.

P-039

Spatio-temporal response of normal brain to ionizing radiation

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Radiation therapy (RTx) plays a critical role in treatment of malignant gliomas. However the biological response to ionizing radiation (IR) in normal brain is poorly understood. We postulate that Bone Marrow Derived Progenitor Cells (BMDC) are involved in modulating radiation response in normal brain. Using real-time in-vivo imaging of intracranial vasculature through a cranial window chamber coupled with high-precision stereotactic radiation delivery, we examined the spatio-temporal response of normal brain to IR, with particular focus on neo-vascularization. In normal brain there is a dose dependent recruitment of BMDC to site of IR, in addition to a temporal response, where BMDC is seen as early as 12hrs post IR and persists beyond 21 days. This is in contrast to needle injection alone where BMDC dissipate 7 days post injury and furthermore different from when tumor cells are present in the brain. The BMDC do not migrate outside of the radiation field and do not differentiate into other cell types, which is in striking contrast to glioma intracranial models, where tumor cells trigger a distinct differentiation of BMDC into macrophages, GFAP+astrocytes and monocytes. Our results are the first to demonstrate an early dose dependent recruitment of BMDC to site of radiation in normal brain. BMDC that is recruited to site of IR requires a second signal, such as seen in response to glioma models, in order to differentiate to form other cell types. Increased integration of BMDC into the vasculature as perictyes following IR is suggestive of a protective role of BMDC.

P-040

Gamma knife stereotactic radiosurgery: an institutional review in the treatment of cavernous sinus meningiomas

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Introduction: Cavernous sinus meningiomas are complex surgical lesions. Stereotactic Radiosurgery poses a unique and effective means of controlling tumor progression. *Methods:* We retrospectively reviewed all cavernous meninigiomas treated with Gamma Knife (GK) radiosurgery between November 2003 and Oct 2010. Clinical data, and treatment parameters evaluated. *Results:* We treated 30 patients, 4 were lost to follow up. Presentations included: headache (9), 5th nerve dysesthesia/paresthesia (13), 6th nerve palsie (11), 3rd nerve palsy (8), Horner's (2), blurred vision (9), relative afferent papillary defect (1), incidental (1). Treatment planning consisted of MRI and CT in 17 of 30 patients (56.7%), the remainder with MRI (44.3%).

Average follow up time was 36.1 months, with mean age of 55.1 years. There were 8 males (26.7%) and 22 females (74.3%). Lesion locations: right cavernous sinus 17/30, Meckel's cave (5), prepontine cistern (4), sellar/suprasellar (7), and temporal lobe (3). Internal carotid artery encasement was entire in 10 patients, partial in 12. Twelve patients had previous surgical debulking prior to radiosurgery. Average diameter and volume was 3.4cm and 7.9 cm^3 respectively. Average dose at the 50% isodose line was 13.5 Gy. Tumor size decreased in 9 patients (30.0%), remained stable in 19 patients, and increased in 2. Overall 28 out of 30 (93.3%) patients achieve tumor regression or stasis.

Transient complications occurred in 17 patients. Permanent complications occurred in 4 patients: new trigeminal neuralgia (1), occipital neuralgia (1), atypical facial pain (1), and panhypopituitarism (1). *Conclusion:* GK is effective in treatment of cavernous sinus meningiomas, with low serious permanent complication rate.

P-041

Plaque-type blue nevus with multiple ipsilateral meningeal melanocytomas: a case report

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Introduction: Meningeal melanocytomas (MM) are among the rarest primary intracranial tumors described in the literature. The presence of a nevus of Ota and association with ipsilateral MM is scarcely described in the literature, with only 7 cases known. Similarly, even rarer is the association of an ipsilateral plaque-type blue nevus and a MM. We describe a new case report of 25 year old female with a suspected right temporal nevus of Ota, who presented with her first seizure, and radiological evidence of two meningeal based lesions: one in the right cavernous sinus, and the other right temporal region. Pathological diagnosis of intermediate grade meningeal melanocytoma was made. MIB-1 was 5-10%. Dermatopathology of the cutaneous lesion indicated a final diagnosis of plaque-type blue nevus. As a result, this is an almost unique case of plaque-type blue nevus associated with ipsilateral intermediate grade meningeal melanocytoma, with little described in the literature to date. The patient currently remains asymptomatic with absence of recurrence or progression, now 4 years after initial surgery. *Conclusion:* Meningeal melanocytomas remain a rare entity with poorly defined natural history and prognosis. Further long term follow up studies need to be conducted on a larger cohort of patients in order to fully understand their nature.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Neuromuscular (Basic Science, EMG/NCS and Peripheral Nerve Surgery)

P-042

Peripheral nerve stimulation for chronic neurogenic pain

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Peripheral nerve stimulation (PNS) has been used for treatment of neuropathic pain for more than 40 years. Recent interest in the utilization of this technique stems from the many modification of the original procedure and the refinement of the available hardware. This rendered the procedure less traumatic and more effective, and thus more widely accepted as a neuromodulation technique for the treatment of various chronic pain syndromes including post-traumatic and postsurgical neuropathy, occipital neuralgia, and complex regional pain syndromes, and in relatively new indications for neuromodulation, such as migraines and daily headaches, cluster headaches.

We present a review of the principle and indications for the use of PNS, and review our single institution experience, that comprises 24 peripheral nerve stimulators as well as 8 occipital nerve stimulators over 13 years. We will review the protocol of our approach including the surgical nuances for our implantation technique.

Collaborative efforts in future research will lead to a growth in our clinical experience with the utilization of PNS and will help in identifying the best candidates for it. This, along with the development and refinement of the available hardware would lead to a more specific patient selection for each modality of treatment, increasing the efficacy and success of the intended treatment.

P-043

Lupus neuropathy mimicking chronic inflammatory demyelinating peripheral neuropathy: A challenging case with literature review

JY Chu (Toronto)

Introduction: There are many forms of neuropathy affected by systemic lupus erythematosis (SLE). Based on clinical presentation, sometimes it can be very difficult to distinguish the demyelinating form of lupus related symmetrical neuropathy from chronic inflammatory demyelinating neuropathy (CIDP). The following is a case report with interesting clinical, electrophysiological and diagnostic imaging findings. *Methods:* A 26 year-old woman presented with symptoms and findings of a subacute onset of symmetric lower limb weakness. Provisional diagnosis was acute Guillain-Barre syndrome after initial lumbar puncture and electromyography. She was treated successfully with intravenous immunoglobulins(IVIG) and recovered. She presented with a relapsing type of neuropathy about 2 years later and initially was thought to have CIDP but failed to respond to repeated courses of IVIG. Subsequent immunological blood work and nephrology consultation confirmed that she has SLE with Class III and V lupus nephritis. She was then started on high dose of oral Prednisone, Cellcept but failed to respond. She was then treated with biweekly IV Cyclophosphamide in the hope of stabilizing her lupus nephropathy and neuropathy. Her neuropathic pain was controlled with oral pregabalin (Lyrica) 75 mg BID. Detailed clinical, electrophysiological and diagnostic imaging results will be presented with an extensive literature review. *Conclusions:* Lupus neuropathy is a challenging clinical neuromuscular disorder to recognize and to diagnose correctly. It can mimic CIDP and requires astute and careful investigations in order to manage such condition successfully.

P-044

Understanding knowledge and attitudes towards NIV in patients with DM1

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Background: Chronic respiratory failure (CRF) contributes to morbidity and mortality in myotonic dystrophy type 1 (DM1). Each year there are admissions to the ICU with acute or chronic respiratory failure. Our goal was to explore patients' understanding of risk of breathing difficulties and awareness of non-invasive ventilation (NIV). *Methods:* A literature review and random review of 25 charts of patients with muscular dystrophy were used to develop a draft. The 25 item questionnaire was finalized after review by 3 neuromuscular clinicians, a respiratory therapist and physiotherapist familiar with neuromuscular CRF. The questionnaire was piloted in the clinic (n=10) before being mailed to patients with muscular dystrophy. *Results:* 96/161 surveys were returned (60%) from the group naïve to NIV; 33/96 had DM1 (34%). DM1 affected ability to breath normally (47% agree/ strongly agree), quality of sleep (57%) and quality of life (QOL) (77%). 8 reported that breathing affected their sleep. Symptoms of ineffective nighttime ventilation were endorsed by >50% with 30% aware of NIV. All agreed that they would adopt treatments designed to increase QOL; 89% would consider life-extending treatments. *Conclusions:* Individuals with DM1 endorse symptoms of ineffective ventilation and are willing to be educated about the potential benefits of NIV.

P-045

Intracerebral malignant peripheral nerve sheath tumor in a child with neurofibromatosis type 1 and middle cerebral artery aneurysm treated with endovascular coil embolization

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Background: Among the neoplastic conditions that affect patients with neurofibromatosis type 1(NF-1) are malignant peripheral nerve sheath tumors(MPNSTs), which typically arise from peripheral nerves of the limbs, trunk, lumbar and brachial plexuses. Ionizing radiation is an established risk factor for MPNSTs, especially in those with NF-1. Patients with NF-1 are also at increased risk of intracranial aneurysms. *Methods:* A 9-year old girl suffered an intracerebral hemorrhage secondary to a right middle cerebral artery(MCA) bifurcation aneurysm. Following decompressive craniectomy and stabilization, she underwent endovascular coil embolization without complication. Given a family history of NF-1, the child underwent genetic testing which was positive for NF-1. *Results:* Despite good clinical recovery, follow-up imaging at 14 months demonstrated a large frontotemporal mass encasing the right MCA bifurcation. She underwent craniotomy and subtotal resection of the mass which was found to be an intracranial MPNST. She

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

recieved chemotherapy and focal radiation and remains alive at 6 months post-resection. *Conclusions:* To our knowledge, this represents the only case of intracranial neoplasm arising in the region of an endovascularly repaired intracranial aneurysm. While patients with NF-1 represent a population with genetic susceptibility to radiation-induced tumors, the contributions of these factors to the pathogenesis of intracerebral MPNSTs remains poorly understood.

P-046

Inclusion body myositis presenting as fascioscapulohumeral muscular dystrophy

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Background: We report a case of inclusion body myositis (IBM) that presented with findings more clinically consistent with fascioscapulohumeral muscular dystrophy (FSHD). *Methods:* Case report *Results:* A 42 year old male presented with a three year history of progressing, symmetric, proximal upper extremity weakness, with no symptoms of lower extremity weakness. Examination revealed periscapular and pectorialis wasting with reversal of the axillary creases bilaterally. There was bilateral facial and neck extensor weakness and severe weakness of biceps brachii and triceps bilaterally. The long finger extensors were minimally weak. There was no demonstrable weakness of the volar forearm muscles or the quadriceps femoris. Myotatic reflexes were hypoactive; the patellar reflexes were present bilaterally. Electromyography demonstrated denervation potentials and small amplitude units with early recruitment predominantly restricted to proximal upper extremity muscles. Serum creatine kinase was 558 U/L. Genetic testing for FSHD was negative. Right deltoid biopsy confirmed findings consistent with inclusion body myositis. *Conclusions:* We present a case of biopsy confirmed IBM with fascioscapulohumeral distribution weakness. There are currently no authoritative guidelines published for the clinical diagnosis of either fascioscapulohumeral muscular dystrophy or inclusion body myositis. This case highlights the usefulness of muscle biopsy in the diagnosis of muscular diseases where the clinical presentations may not always conform to the typical phenotype.

P-047

Acute Sensory Neuronopathy Syndrome: A report of two cases

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Background: Acquired sensory neuronopathy is a rare syndrome with limited identifiable etiologies. The most common presentation involves a subacute, progressive sensory ataxia. The most frequent identifiable causes are Sjogren's syndrome and paraneoplastic disease. An idiopathic, rapidly progressive variant, acute sensory neuronopathy syndrome (ASNS), was first described in 1980. This entity typically follows a febrile illness, is likely immune mediated, and clinically may be indistinguishable from sensory autoimmune inflammatory demyelinating polyneuropathy (sAIDP). The presence of diffusely diminished or absent sensory nerve action potentials (SNAPs) in the absence of other demyelinating features generally differentiates ASNS from sAIDP electrophysiologically. *Methods:* We describe the clinical course, investigations, and use of IVIg in two cases of ASNS. *Results:* Case 1 – A 50-year-old female developed rapidly progressive pain, asymmetric sensory paresthesiae, and urinary retention following a respiratory tract infection. Case 2 – A 30-year-old male presented with ascending paresthesiae, allodynia, and urinary frequency in the absence of an antecedent illness or vaccination. Objectively, both had sensory impairment with resultant ataxia, pseudo-athetosis, and diffuse areflexia. Electrodiagnostic studies confirmed diffusely absent SNAPs. Cerebrospinal fluid (CSF) demonstrated albuminocytological dissociation. No associated autoimmune disease, infection or malignancy was identified. Both patients were treated with IVIg. At one year, despite some residual sensory impairment, both patients had recovered function close to their premorbid baseline. *Conclusions:* The presence of an acute sensory ataxic syndrome associated with CSF albuminocytological dissociation and absent SNAPs on electrophysiological studies, should raise the possibility of ASNS. An empirical trial of IVIg may be warranted, given that this is likely an immune-mediated condition.

P-048

RGNEF, a novel NFL mRNA binding protein, is upregulated after sciatic injury in C57BL/6 but not NFL -/- mice

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Background: RGNEF is the human homologue to p190RhoGEF, a NFL mRNA binding protein that regulates murine NFL mRNA stability. RGNEF forms pathological aggregates in ALS motor neurons and is a regulator of human NFL mRNA stability. Because NFL mRNA steady state levels are reduced in degenerating spinal motor neurons in ALS, we sought to determine the role of RGNEF in the physiologic response to injury and whether this response was altered in the NFL -/- model of motor neuron degeneration. *Methods:* C57BL/6 and NFL -/- mice underwent a sciatic crush injury. Lumbosacral spinal cord sections were immunostained for TDP-43, RGNEF, GFAP and IBA-1 at days 1, 3, 7, 14, and 28 post-injury. RGNEF expression was quantified by immunoreactivity scoring as previously validated by Moisse et al. ANOVAs were performed with Student-Newman-Kuels post-hoc analysis for all scores. *Results:* GFAP and IBA-1 staining confirmed a transient glial response to sciatic crush injury in both strains. As previously described, cytosolic TDP-43 expression was upregulated in response to injury in C57BL/6 mice. This response was delayed in NFL -/- mice. Cytosolic RGNEF expression following injury exhibited a sustained upregulation from day 3 until day 28 that was significantly greater in C57BL/6 mice as compared to NFL -/- mice who did not show RGNEF upregulation ($p=0.002$). *Conclusions:* These results support the role of RGNEF as a neuronal injury response factor and further implicate its role in NFL mRNA metabolism.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-049

Patient perspectives and intervention for ptosis in oculopharyngeal muscular dystrophy

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Background: Oculopharyngeal muscular dystrophy (OPMD) is characterized by ptosis, dysphagia and positive family history. No qualitative studies address the severity of ptosis, its burden of disease or patient perspective on surgical intervention. *Methods:* A literature survey and a retrospective chart review of 31 patients with OPMD was used to develop a 27 item questionnaire, which was reviewed by clinicians (3) and an OPMD patient. *Results:* Mean age of ptosis onset was 52 years. Thirty-six operations (15 levator palpebrae advancement, 26 frontalis sling) were performed on 14 patients. 8 levator advancements and 2 frontalis slings required re-operation.
14/31 returned surveys: 71% felt ptosis affected vision, 57% had to extend their neck in order to see. On a 7-point Likert scale, responders rated items including ptosis affecting image (5.5) and mood (3.8). 9/14 had surgery: 78% noted gradual return of ptosis, 89% had dry eyes requiring eye drops and 1/9 developed an infection. All patients reported they would recommend surgery to future patients. *Conclusions:* Ptosis in OPMD represents an important clinical burden to patients. Frontalis sling surgery resulted in a lower re-operation rate than levator palpebrae advancement. Patients should be educated about the progressive nature of ptosis and its successful surgical intervention.

P-050

Measuring quality of life in muscular dystrophy (MD): A pilot using INQoL

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Background: Patients with MD rate quality of life (QOL) highly, however, there are few available instruments specific to muscle disease. Fifteen subjects with MD participated in a study exploring the relationship between muscle mass, quantitative EMG and functional performance. The Individualized Neuromuscular Quality of Life questionnaire (INQoL) was designed to measure the impact of six symptoms and the effect of muscle disease on five domains. Treatment effect is captured, and an overall QoL score is calculated. *Method:* Subjects completed the INQoL as part of the study, and underwent a neuromuscular examination. Questionnaires were reviewed for completeness and scored. *Results:* Fourteen completed the INQoL: 10 males; mean age 40.4±17.8 (3 FSHD, 6 LGMD, and 5 BMD). Mean QoL for FSHD 19.2±6.44, LGMD 25.0±2.7 and BMD 21.4±9.23. Maximal isometric quadriceps strength assessed by a dynamometer was 157.9 ± 58.2 N•m (mild weakness) and 34.6 ± 20.88 N•m (moderate to severe weakness). Mean QoL was 20.6 ± 7.9 (mild weakness) and 25.0±2.4 (moderate to severe weakness). *Conclusion:* In this small sample, QOL was rated highly and did not differ based on severity or diagnosis. The INQoL was easy to administer and could be incorporated into clinic visits to follow perceived QoL over time.

General Neuroradiology

P-051

Crossed cerebellar diaschisis and bright pulvinar in non-convulsive status

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Background: In confused patients, neuroimaging is helpful to diagnose acute neurological insult.Crossed cerebellar diaschisis (CCD) and bright pulvinar in brain MRI are rare in patients with non-convulsive status epilepticus. CCD has been described initially in stroke patients. However these changes didn't respect vascular territories. *Methods:* Two case report. *Results:* A 53-year-old man was found confused, incontinent and nonverbal. Electroencephalograpy (EEG) findings are consistent with non-convulsive status epilepticus. Brain MR images showed restricted diffusion on DWI, and increased signal on FLAIR and T2 weighted images in the left frontal, peri-insular and temporal regions, left medial pulvinar nucleus, as well as involvement of the right cerebellar hemisphere indicating CCD. The second case: A 77-year-old women, presented with generalized tonic clonic seizure and prolonged confusion.EEG findings are consistent with non-convulsive status epilepticus. Brain MR images revealed increased signals on FLAIR and T2 weighted images involving the left tempro-occipital, peri-insular regions and left pulvinar. These MR abnormalities had been resolved gradually on follow up MRI at 2 and 7 weeks. *Conclusion:* We report these two cases with two different brain MRI variables (CCD and bright pulvinar). It is crucial to exclude non-convulsive status epilepticus in acutely obtunded patient with these MRI findings.

P-052

Kinnier Wilson and movement disorders

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Objective: To discuss work of Kinnier Wilson in Movement disorders. *Background:* Wilson disease is an inherited and chronic disease of brain and liver with progressive neurological deterioration. It occurs due to a disturbance of copper metabolism and was first described in detail by Kinnier Wilson in 1913. *Methods:* We reviewed all available resources including web and books to study the work of Dr. Kinnier Wilson. *Results:* Kinnier Wilson was a British neurologist who was born December 6, 1878 in Cedarville, New Jersey, U.S.A. His father died when he was only one year of age. His mother moved back to Edinburgh, where he received his medical education at the University of Edinburgh. In 1902 Wilson became house physician at the Royal Edinburgh Infirmary. In 1904 he joined the National Hospital for Nervous Diseases, Queen Square London, where he worked with other well known neurologists including William Richard Gowers, John Hughlings Jackson, and Victor Alexander Haden Horsley. In 1912, he presented his thesis entitled "Progressive lenticular degeneration: A familial nervous disease associated with cirrhosis of the liver" at the University of Edinburgh and won a gold medal. Although a similar condition called Westphal-Strümpell's pseudosclerosis had already been described, but the lenticular or hepatic aspects of this condition were not described before. Since then this condition has

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

been know as Wilson's disease. He died of cancer in London in May 1937. He was 59 years of age when he died. *Conclusion:* The role of Kinnier Wilson will always be remembered in neurology and movement disorders in Particular.

P-053

Acute Intermittent Porphyria (AIP): Neuroimaging Features

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Background: AIP, an inherited disorder of heme biosynthesis, is characterized by episodes of pain, systemic and neurologic symptoms (including seizures). There are few reports of the neuroimaging findings in patients with AIP. Recognition of these abnormalities can help to diagnose this disorder. *Patients:* A 46 year-old woman presented with fever, respiratory failure and hypotension secondary to pneumonia, then had generalized seizures. Non-contrast head CT and MR imaging showed diffuse, cerebral swelling. Urine porphyrins were elevated. Treatment with carbohydrate loading and intravenous hematin was successful. CT three days later was normal. A 21 year-old woman with recurrent abdominal pain attributed to endometriosis developed a generalized seizure. CT and MRI showed low density changes in the subcortical white matter in frontal, parietal and occipital lobes, features characteristic of the posterior reversible leukoencephalopathy syndrome (PRES). Urine porphrins were elevated. Three weeks after treatment the MR imaging was normal *Discussion:* The diagnosis of AIP is often delayed because of the protean clinical manifestations. Patients often have seizures so imaging studies are performed. When these show features of PRES or diffuse brain swelling the diagnosis of AIP should be considered. These imaging abnormalities reverse with treatment.

Dementia

P-054

Vitamin D insufficiency in northern BC and effects on cognition: D-COG 1st phase results

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Introduction: Vitamin D3 (cholecalciferol) may be important for cognition and insufficiency has been associated with Alzheimer's disease. Supplementation (in animals) increases acetlylcholine levels, hippocampal neuronal densities and enhances neuroprotection. Few human studies have assessed its importance in cognition. We hypothesized that a significant proportion of northern British Columbians would have insufficient levels (<75 nmol/L) that would impact cognitive functioning. *Methods:* D-COG is a 3-phase pilot study examining the effects of cholecalciferol on cognition. The 1st Phase was conducted between July and October 2010. Blood cholecalciferol levels were analyzed via mass spectrometry and cognitive functioning was assessed with the Symbol Digit Modalities Test, phonemic fluency test, Digit Span and CANTAB computerized testing battery. *Results:* 32 participants were recruited of which 72% were female, aged 52±16 yrs, with 14±3 yrs of education. Nearly half (46%) were cholecalciferol insufficient and these participants performed significantly worse on Backward Digit Span, which assesses working memory: mean 5.8±2 versus 7.9±2, t(30)=-2.5, p=0.018. *Conclusions:* A significant proportion of northern British Columbians are cholecalciferol insufficient, even during the summer months, and this is associated with inferior working memory functioning. To what extent cholecalciferol levels drop during the winter and whether supplementation significantly elevates levels and cognitive performance is not known but will be assessed in the 2nd and 3rd Phases of D-COG.

P-055

Seizure threshold in Alzheimer's Disease: what can we learn? a systematic evaluation of neuroepidemiology and neurobiology

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Background: Current insights in the pathophysiology of brain diseases suggest that studying co-morbidities both in humans and the animal model are a promising innovative approach to arrive at new concepts. The following research project focused on the neuroepidemiological and neurobiological evidence of the overlap between seizures and Alzheimer's Dementia (AD). *Method:* A systematic literature search was performed (1989 to 2010) using the keywords "seizure", "epilepsy", "dementia", and "Alzheimer's disease". Pubmed revealed 565, EMBASE data bank 1,120 hits. Reviews,case reports, and original papers without sufficient information were excluded. 145 papers were analyzed. The clinical analysis included phenomenology, dynamics and outcome of seizure presentation in AD, the experimental analyis seizure threshold and hyperexcitability in AD models. *Results:* Clinical studies revealed that seizures in AD only occur sporadically, commonly present as generalized tonic-clonic seizures, and usually have an excellent treatment prognosis. Seizures occurred more frequently in a) advanced stages of late-onset AD, b) in sporadic forms of AD (ApoE), c) in selected genetic mutations of Early-onset AD (EOAD), and d) in patients with Down's Syndrome with dementia and neuropathological findings of AD. Amyloid-beta induced destabilization of neuronal hippocampal networks and triggered aberrant patterns of neuronal circuitry and epileptiform discharges. Vice versa, recurrent epileptic discharges lead to cognitive decline and accumulation of amyloid-beta (Palop and Mucke 2009). *Conclusion:* Clinical and experimental data confirm that AD and seizure activity possibly share causal mechanisms. This may have implications for future treatment strategies including the use of antiepileptic drugs in AD to prevent seizure-associated accumulation of amyloid-beta.

P-056

Linkage analysis in familial Late Onset Alzheimer Disease

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Background: We sought to identify gene(s) that contribute to the etiology of late-onset Alzheimer's disease (LOAD). By combining new molecular genetic techniques with clinical data and longitudinal family history data we are poised to find both susceptibility and causative genes for Alzheimer's disease (AD) and related dementias.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Current efforts are focused on LOAD because it is the most prevalent dementia. *Methods:* Since 1984 it has been routine for patients and family members of the UBC Hospital Clinic for Alzheimer's disease and Related Disorders (UBCH-CARD) to meet with a genetic counsellor. Several hundred biological samples have been collected over the same period. *Results:* From the 4379 family histories available it is possible to select a small number of candidate families for affected-only Linkage Analysis (LA). Selection criteria for LA include: clinic patients who have given informed consent for research use of their biological sample; patients with probable or definite AD; onset at age 65 and older; family history with multi-generation AD reports; records indicating clinically probable or neuropathologically confirmed AD available for a minimum of 2 additional affected family members. We will present the results of the affected-only LA. *Conclusions:* AD has typical onset during or after the seventh decade of life. Autosomal dominant inheritance of LOAD has escaped detection as carriers of these mutations often do not survive to an age where clinical symptoms are observable. Following LA, we will be sequencing the implicated regions of the genome to identify novel causative gene(s) for LOAD.

P-057

Differential fMRI brain activation in Alzheimer Disease during passive music listening

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Background: Musical Memory may be preserved in patients with Alzheimer Disease (AD). The neural substrates involved in musical memory have not been systematically studied. We investigated the brain regions involved in music processing and recognition by comparing the pattern of activation in fMRI during passive music listening. *Methods:* Five patients with mild to moderate AD and 5 age-matched controls were studied. We used a block design paradigm with 45s of familiar music excerpts followed by 30s of silence vs. the same excerpts randomly scrambled 300-500ms segments concatenate back to 45s. A mixed-model 2X2 ANOVA was used to compare group (AD vs. controls) and stimulus (familiar vs. scrambled melodies) differences using a p-value of 0.01 and minimum cluster size of 200 μL. *Results:* We found significant interaction effects in fMRI activation patterns in AD subjects vs. controls in a number of areas during passive listening, with the largest differences in the right middle and superior temporal gyrus, left cerebellar declive, and left superior and middle temporal gyrus. AD subjects showed significantly decreased activation in these areas in response to familiar intact vs. scrambled melodies, whereas controls showed a significantly increased activation in the same areas in response to these listening conditions. *Conclusions:* AD subjects and normal controls showed different brain activation while listening to familiar melodies. This may suggest recruitment of novel brain areas for music processing in AD. Further exploration and understanding of this change may allow us to utilize music as a diagnostic and therapeutic tool in management of AD.

P-058

Voxel-based morphometric study of brain volume changes in patients with Alzheimer's disease assessed according to the Clinical Dementia Rating score

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We evaluated the volume reduction of gray matter (GM) and white matter (WM) in patients with an Alzheimer's disease (AD) assessment based on the Clinical Dementia Rating (CDR) score. Patients with AD (n = 61), with no subcortical WM ischemia, and healthy control patients (n = 33) underwent T1-weighted spoiled gradient echo sequences, which were analyzed using voxel-based morphometry. Global GM atrophies were observed in patients with CDR score of 1 or a CDR score of 2, and WM atrophies were observed in patients with CDR score of 2. Regional GM atrophies were found in the right inferior frontal gyrus, bilateral dorso-lateral and medial temporal lobes; WM atrophies were found in the bilateral temporal subcortex (familywise error, $p < 0.01$). A CDR score of 0.5 was associated with atrophy in the left olfactory gyrus. The peak z-score and spatial extent of volume reduction increased with increasing CDR score and were higher on the left side. GM atrophies increased with increasing CDR scores and suggest a possible pathomechanism of AD.

P-059

Gray and white matter volume reductions with age in healthy Korean adults with exclusion of white matter hyperintensity; voxel-based morphometric study

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Understanding the changes of brain volume due to normal aging in healthy adults may help us better appreciate the age-related changes in the brain related to neurodegenerative diseases. The objectives of our current study are: 1) to evaluate the volumes of gray matter, white matter and cerebrospinal fluid in healthy adult with exclusion of white matter hyperintensity and 2) to identify their regional changes which have been controversial. We cross-sectionally analyzed magnetic resonance images from 108 normal Korean subjects (42-80 years of age) using voxel-based morphometry. Global volumes of each tissue revealed no change up to age of 50-59 group and decline afterward. There were negative correlations between gray matter (3.04 cm^3/year) and white matter (2.31 cm^3/year) and age, and a positive correlation between CSF (5.56 cm^3/year) and age. Gray matter, white matter and CSF volume normalized with total intracranial volume were changed at 0.21%/year, 0.16%/year and 0.36%/year. Gray matter volume reduces in the frontal, parietal and temporal lobes with age. These were not observed in the medial temporal lobes or posterior cingulate. White matter losses occurred in the anterior corpus callosum, frontal and other periventricular areas. These findings provide essential information about the rates and regional patterns of age-related changes in brain volume for an Asian population and serves as a baseline for comparison with other pathologic conditions.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

General Neurology

P-060

Inter-temporal seizure propagation

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Background: While human hippocampal (HPC) electrical stimulation indicate potential inter-HPC propagation times of 90-180 ms, inter-HPC ictal propagation times reportedly vary from 0.5 to > 100 sec suggesting several alternate propagation routes and delays. Ictal spread by mesial temporal seizures to contralateral temporal lobe may pass directly by the dorsal HPC commissure or first to temporal neocortex, then the corpus callosum. However studies with bilateral frontal and temporal implanted electrodes found that ipsilateral then contralateral frontal spread usually precedes contralateral temporal ictal involvement. We studied propagation routes and patterns by bitemporal and bifrontal subdural electrodes. *Method:* Among adult candidates for temporal lobectomy whose non-invasive data failed to localize epileptogenesis, bilateral temporal and frontal subdural electrodes were placed. Requisite placements on each side were: mesial temporal (7-12 electrodes), 2 temporal neocortical lines (14-24 electrodes), 2 frontal lobe lines over orbital, mesial and convexity surfaces (24-36 electrodes). *Results:* Of 6 seizures (4 patients) with contralateral temporal spread, one propagated through the frontal lobes; of 5 seizures without evident frontal involvement, 4 propagated directly while one first involved ipsilateral temporal lobe convexity. *Conclusion:* Frontal lobe involvement is not requisite for contralateral temporal seizure propagation.

P-061

The study of frequency of different types of headache

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Introduction: Headache is the 7th reason to visit the doctor and it is divided in two main groups; 1. Primary 2. Secondary. According to the time it divided in acute, subacute and chronic headaches, primary headaches include; migraine tension and cluster. In secondary headaches there is a background problem such as hematoma, tumor, meningitis, or encephalitis. Regarding the effect of headache on patient's life, we wanted to study the frequency of different type of headache. *Methods and Materials:* this study was performed on 1000 patient who suffered from headache. They were asked to fill out a standard questioner form. According to HIS criteria type of headache was diagnosed. *Results:* Headache among women with 3 to 1 ratio is more common then men. Most frequent was 79.7% for primary, 20.3% for secondary. Migraine with 41.6% is the most common type of headache and tension 34.1% after it. The prevalence of cluster was 3%. Among secondary headaches; Vascular, trauma, infections and tumors were the most frequent. There is statistically meaningful relationship between age, gender, consumption OCP (in women). *Discussion:* This study have shown that headache is a common problem among young and adult people; and some factors such as age, gender activity and life style, OCP and NSAID effect it. Therefore the correct diagnosis and appropriate treatment, awareness of side effects of drugs and improvement in life style seem to be necessary.

P-062

Relationship of clinical functioning based on pegboard measurements versus PET data in Parkinson's disease: a longitudinal analysis

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Background: Assessing the relationship between the clinical characteristics of Parkinson's Disease (PD) and Positron Emission Tomography (PET) imaging has previously been carried out only with cross-sectional data, using correlation coefficients. *Methods:* We have studied 78 PD patients over a period of 8 years, obtaining longitudinal PET data averaged over the anterior, mid, and posterior regions of the putamen, using 3 different radiotracers: [^{11}C](±)dihydrotetrabenazine (DTBZ); 6-[^{18}F]-fluoro-L-dopa (FD); and [^{11}C]d-threo-methylphenidate (MP), as well as simultaneous longitudinal Purdue Pegboard (PPB) and United Parkinson's Disease Rating Scale (UPDRS) measurements. *Results:* We found that exponential models provided a good fit to both longitudinal PPB and PET measurements. Using normal control values, we standardized the PPB and PET data to render them commensurate. DTBZ gave the earliest prediction among the ligands (some 12.5 years) of PPB decline of the same degree, while MP and FD gave somewhat later prediction intervals. Comparing the rates of decline between DTBZ and PPB, PPB was seen to decline at a fixed higher rate throughout the duration of symptoms. The rates of decline of MP and PPB were equal at symptom onset, but PPB proceeded to decline at an increasingly more rapid rate. For the first seven years following symptom onset, FD declined more rapidly than PPB, following which PPB overtook FD, and continued to decline at an increasingly more rapid rate. *Conclusion:* The PPB therefore showed interesting clinical reflections of corresponding PET measurements throughout symptom duration, and may suggest compensation of clinical symptoms at earlier stages of PD.

P-063

Attention deficit in a French Canadian patient with chorea-acanthocytosis

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Introduction: Chorea-acanthocytosis is a rare autosomal recessive disease characterized by chorea, oro-lingual involuntary movements and frontal subcortical dysfunction. *Case Report:* We present a patient of French Canadian origin with a diagnosis of chorea-acanthocytosis. Well-described neuropsychiatric manifestations of chorea-acanthocytosis usually correspond to frontal subcortical dysfunction. In our patient, hyperactivity, impulsivity and attention deficit were evident on initial examination and later detailed by neuropsychological evaluation. These features manifested together with the initial movement disorder and rapidly became a major issue in management, making transfer from her home necessary at age 33, less than 18 months after initial diagnosis. *Discussion:* Caudate atrophy is one of the major pathological findings in chorea-acanthocytosis. Preferential depletion of dopaminergic neurons has been described previously in this disorder. Disturbances of frontal cortical-striatal loops are the basis of current models for understanding the cognitive and behavioral anomalies in chorea-acanthocytosis. Mutations in dopamine receptors and transporters,

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

as well as reduced size of caudate have been described in attention deficit with hyperactivity disorder (ADHD). *Conclusion:* We believe that dysfunction in both diseases of the same cortical-subcortical loop involving the caudate nucleus and orbitofrontal cortex might explain why our patient with chorea-acanthocytosis presented with manifestations of ADHD.

P-064

A rare case of acute severe combined demyelination

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Background: We report a case of combined Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM). There are few reported cases of combined central nervous system (CNS) and peripheral nervous system (PNS) post-infectious demyelination. *Methods:* Case report *Results:* A 19 year old male presented with sore throat, lymphadenopathy and fever followed by progressive areflexic weakness, respiratory failure and monocular visual loss. Brain MRI revealed five supratentorial demyelinating lesions, two of which were enhancing. Orbital MRI demonstrated enhancement of the right optic nerve, and examination findings were consistent with posterior optic neuritis. MRI spine showed enhancement of the cauda equina. Cerebrospinal fluid findings and nerve conduction studies were consistent with GBS. Treatment consisted of intravenous gammaglobulin, followed by high dose intravenous glucocorticoids prescribed to accelerate recovery of the optic neuritis. *Conclusions:* We believe this case is consistent with a diagnosis of acute severe combined demyelination (ASCD), described in the literature by Amit et al in 1986. Few reports of encephalo-myelo-radiculo-neuropathy exist, and it remains uncertain whether these cases represent a variant of ADEM, or a separate clinical entity involving unique mechanisms of cross-antigenicity to a component of myelin shared between the CNS and PNS.

P-065

The neurobiology of sexual orientation - total medical evidence presentation

J Goldstein (San Francisco)

Homosexuality is a constantly debated issue as to whether it is determined at birth or a choice (nature vs. nurture). The works of the Kinsey Reports and Dr. Evelyn Hooker published in the 1950s resulted in the removal of homosexuality from the DSM4 in 1973. Since then, it has been mentioned as an illness only in the context of being a putative exacerbating factor in anxiety states. Recent studies reveal a clear cut neurobiology to sexual orientation.

Neurobiologist Simon LeVay conducted a study of brain tissue samples from 41 human autopsies performed at several hospitals in New York and California. He found a significant size difference of the interstitial nuclei of the anterior hypothalamus between homosexual and heterosexual men. In addition, Dr. Ivanka Savic-Berglund and Dr. Per Lindström of the Karolinska Institute, Stockholm, performed fMRI and PET measurements of cerebral blood flow. Using volumetric studies, they found significant cerebral size differences between homosexual and heterosexual subjects; the brains of homosexual men resembled heterosexual women and homosexual women resembled heterosexual men. Pheromonal studies also have added to the scientific knowledge of sexuality. Sex-atypical connections were found among homosexual participants. Amygdala connectivity differences were found to be statistically significant and provided evidence towards sexual dimorphism between heterosexual and homosexual subjects. Extensive controls were performed during testing to exclude analytical variability. A totally evidence-based medicine presentation will provide current data regarding homosexuality showing differences, or similarities, between the brains of homosexuals and heterosexuals.

P-066

Transdermal sumatriptan for acute treatment of migraine

J Goldstein (San Francisco)

Migraine is a widespread neurologic disorder characterized by episodes of headache accompanied by photophobia, phonophobia, gastrointestinal symptoms and, often, cutaneous allodynia. Presenting symptoms can vary considerably, but gastrointestinal disturbances are common. Current pharmacotherapy for migraine includes analgesics, nonsteroidal anti-inflammatory drugs, and several 5HT-agonists in various oral, nasal spray, and subcutaneous formulations. Among the 5HT-agonists, sumatriptan is the most frequently prescribed, but its therapeutic limitations (ie, poor absorption, low bioavailability, adverse events) cause some migraineurs to delay or avoid treatment and may lead to suboptimal outcomes. Transdermal sumatriptan (Zelrix®) is a new, single-use, disposable patch that delivers sumatriptan via iontophoresis, a less invasive method for systemic delivery. Pharmacokinetic data indicate that transdermal sumatriptan delivery is fast, consistent, and predictable. Results from well-controlled clinical studies demonstrate significant superiority versus placebo within 1 hour post-activation for pain relief (P=0.0135) and nausea-free (P=0.0251); at 2 hours post-activation, transdermal sumatriptan significantly outperformed placebo for pain-free (P=0.009), pain relief (P=0.0135), photophobia-free (P=0.0028), phonophobia-free (P=0.0002), and migraine-free (P=0.0135). Transdermal sumatriptan is well tolerated, and reported adverse events are mostly mild, transient application site reactions. This article reviews the evidence in support of the efficacy and safety of transdermal sumatriptan for acute treatment of migraine.

P-067

Isolated unilateral hypoglossal nerve palsy due to infectious mononucleosis

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Hypoglossal nerve palsy is a rare clinical entity among the cranial neuropathies with a broad differential diagnosis. The most common etiologies, including tumours, trauma, stroke, and vascular insufficiency all typically present with other neurological or systemic symptoms or physical findings. Thus, isolated hypoglossal nerve palsy presents a diagnostic challenge that requires a systematic investigative approach. Here we report an interesting case of a 57 year-old male with a six-month history of isolated unilateral hypoglossal nerve palsy following a recurrent mononucleosis infection. The only relevant history was of a remote episode of mononucleosis ten years earlier. All investigations, including serial MRI scans of the brain were normal. The patient

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

was diagnosed with post-infectious hypoglossal nerve palsy. This case demonstrates an uncommon etiology of isolated hypoglossal nerve palsy and underscores the importance of a systematic approach to the history, physical exam, differential diagnosis and investigative workup.

Differential Diagnosis	History, Physical Exam and Investigations
Malignant Tumours	History
•Metastasis	•Onset and precipitating events
•Chordoma	•Associated neurologic deficits; vision, hearing loss, dysphasia, paresis, ataxia, dysmetria
•Nasopharyngeal Carcinoma	•Previous cancer, weight-loss, night sweats
•Lymphoma	•Recent trauma, surgery
Benign Tumours	•Cardiovascular risk factors
•Schwannomas	•Arthralgia, autoimmune disease
•Meningiomas	•Fever, malaise, recent infection
•Ependymomas	Physical Examination
•Craniopharyngiomas	•Confirm hypoglossal nerve palsy, unilateral vs bilateral, dysarthria, fasciculations
•Vagal paragangliomas	•Examine for other cranial nerve deficits
•Neurinomas	•Paresis, paraesthesia, dysmetria, ataxia
•Intraneural ganglion cysts	•Papilledema
•Chondromyxoid fibromas	•Evidence of head trauma, C-spine stability
•Bony dysplasia	•Evidence of primary cancer
•Atlanto-occipital synovial cysts	•Stigmata of autoimmune disease
Trauma	•Neck stiffness, lymphadenopathy, splenomegaly, nidus of infection
•Penetrating wounds	Investigations:
•Blunt injury	Routine
•Occipital condyle fractures	•CBC
•Odontoid fractures	•ESR, CRP
Vascular	•Coaulation studies (INR,PTT)
•Carotid artery dissection and ectasia	•Serum glucose
•Vertebral artery dissection and ectasia	•MRI/MRA of the head and neck
•Cerebrovascular insufficiency	As indicated
•Dural arteriovenous fistulas	•Autoimmune disease studies
Iatrogenic	•CSF analysis and culture
•Anesthesia related airway complications	•HSV, CMV, EBV serology
•Bronchoscopy	•Imaging for primary cancer
•Epidural anesthesia	
•Neck irradiation	
Systemic	
•Guillain Barre Syndrome	
•Multiple Sclerosis	
•Rheumatoid Arthritis	
•Ankylosing Spondylitis	
•Diabetes Mellitus	
Infectious	
•Meningitis	
•Osteomyelitis	
•Poliomyelitis	
•Syphilis	
•Herpes Simplex virus	
•Cytomegalovirus	
•Epstein-Barr virus	
Other	
•Chiari Malformation	
Idiopathic	

P-068

Assessment of HIV positive patients with neurocognitive impairment and CSF HIV-RNA viral load

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Background: Prevalence of HIV associated neurocognitive disorders (HAND) is high even in patients receiving antiretroviral therapy (ART). An HIV Neurocognitive Disorder Clinic (NDC) was established at St Paul's Hospital in the Immunodeficiency Clinic (IDC) to assess HIV patients with HAND. *Methods:* HIV+ adult patients (>18 years) with cognitive impairment not readily explained by another diagnosis are referred to the IDC NDC clinic. HIV-related treatment and laboratory results were obtained through the BC Centre for Excellence in HIV/AIDS Drug Treatment Program (DTP) database. Montreal Cognitive Assessment and HIV dementia scale were performed. Viral load in CSF was measured by a RT-PCR Taqman assay. *Results:* 7 patients were assessed for CSF viral load. All were male, 6/7 Caucasian, with a median age 48 years (IQR 46.5-56). Median number of years since HIV diagnosis was 11 (IQR 5.5-21.5), and 4 had a history of opportunistic infections. Median nadir CD4 was 100 cells/mm^3 (IQR 40-185) and median most recent CD4 600 (IQR 435-675). All were on ART, median duration 8 years (IQR 3-12 years). Plasma viral load was <50 copies/ml in all patients. Only 4/7 patients had low score on neurocognitive testing (median of 26 on MOCA and 10 on HIV dementia scale). Viral load in CSF was undetectable in 6/7 patients; in 1 the CSF viral load was 328 copies/ml with no resistance to ARVs. *Conclusion:* Our pilot data on a group of stable patients on effective ART with symptoms of HAND did not demonstrate any correlation with CSF HIV RNA viral load.

P-069

Can web-based software improve residents' ability to localize neurologic lesions?

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Background: Accurate neuroanatomical lesion localization has implications in diagnosis, selection of appropriate investigations, treatment decisions and patient outcomes. Based on our successes with a localization prototype, we created a comprehensive, interactive, web-based application - ALVIN (Anatomical Lesion Verifier In Neurology), which assists its users in localizing neurologic lesions. We propose to undertake a randomized study to validate the effectiveness of ALVIN as a neuroanatomical lesion localization tool. *Methods:* One hundred non-neurology residents will complete a computer-based module composed of 25 vignettes describing real patient encounters. Each vignette will comprise a history and physical exam component, after which the resident will be required to localize the lesion to one of twelve broad regions of the neurologic system. The intervention group will use ALVIN while the control group will have unrestricted internet access. Overall performance between the groups will be compared using an unpaired t-test. Pre and post-questionnaires will collect demographic and qualitative data. *Results:* We hypothesize that residents using ALVIN will localize neurologic lesions with greater accuracy compared to residents with unrestricted internet access. *Conclusions:* By examining the diagnostic utility of ALVIN, the proposed study will determine the validity of its use as a clinical tool and will serve as a guide for future investigations.

P-070

From dollars to sense: understanding the cost of neurological hospital admissions in Canada

T Rajapakse (Calgary) N Jette (Calgary)*

Background: Understanding the economic impact of neurological conditions is important in planning Canadian health services. Our objective was to assess the cost of hospitalization, average acute inpatient length-of-stay (LOS) and volume of neurological patients

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

seen between 2008-2009 in Canada. *Methods:* The Canadian Institute for Health Information Patient Cost Estimator tool was used to generate estimates of cost for neurological case mix groups in Canada. Estimated average cost per patient (CPP) with average LOS and volume of such admissions nationally (total and stratified by age) in 2008-2009 were obtained. *Results:* The total number of patients admitted with the conditions of interest was 35, 433.
The CPP and LOS per condition were:
Dementia: $19,110, 15-18d;
Parkinson's disease: $11,720, 11-13d;
CNS hemorrhage: $12,059, 3-11d;
Ischemic stroke: $9,866, 7-11d;
Neuromuscular conditions: $9,622, 6.7d;
Demyelination: $7,062, 5-11d;
CNS Neoplasms: $7,844, 7.4d;
Epilepsy (excluding status epilepticus): $3,458, 3.2d;
Migraine/other headache: $2,713, 2-3d.
Conclusions: Dementia is resource intensive compared to other neurological conditions. However, even ambulatory care sensitive conditions such as migraine and epilepsy add considerable demands on inpatient resources. Neurological health services research, including cost analyses, is essential to guide decisions regarding future funding and policy development for those with neurological conditions.

P-071

RLS, Polyneuropathy or Both

A Rana (Toronto) S Yousef (Toronto)*

To discuss coexistence of restless legs syndrome and polyneuropathy. *Introduction:* Symptom of RLS may have some similarity to polyneuropathy. NCS may help to differentiate these two conditions however in many cases of small fibre polyneuropathy or early polyneuropathy NCS are normal. In these cases it may be difficult to differentiate these two conditions. However in some patients two conditions may co exist. We present several of our patients who had co-existenting restless RLS and polyneuropathy. *Methods:* We present several patients who had polyneuropathy confirmed by NCS and in addition had clinical features of RLS requiring treatment of each condition individually. *Results:* NCS showed distal symmetric axonal sensory polyneuropathy. These patients continued to suffer with symptoms of RLS in spite of treatment for polyneuropathy and required dopamine agonists resulting in resolution of their symptoms. *Conclusion:* RLS may coexist with polyneuropathy and should be carefully differentiated with the help of detailed history and NCS.

P-072

Dilemma of Restless legs syndrome and Benign Cramps

A Rana (Toronto) S Yousef (Toronto)*

Objective: To discuss the overlapping features and differential of restless legs syndrome and benign muscle cramps. *Background:* Benign cramps and symptoms of RLS are commonly reported by many healthy individuals as well as in Parkinson's disease wearing off periods. There are no diagnostic investigations which causes a diagnostic dilemma in many patients as the treatment differs for each condition. We report several cases with overlapping features of these conditions. *Methods:* A chart review of several of our patients revealed many overlapping features of RLS and benign cramps.
Mr. J.G. was a 56 year old male with discomfort in legs and no improvement upon walking but massaging helped.
Mrs. S.A. who was a 45 year old female with pulling sensation in both calves, thighs and occasionally her arms, worse in the evenings, interfering with her sleep and not relieved by walking. Massaging did not help her symptoms.
Mr. K.K. was a 63 year old male with DM-II who had cramping of his left leg involving the mid calf and mid thigh area at night time from1:30 a.m. and would continue until 7:00 a.m. and would go away if he would get up and walk around. He had difficulty sitting still due to restlessness of his legs. *Results:* Restless legs syndrome and benign cramps have overlapping features. *Conclusion:* Careful history taking is the most important tool to differentiate these conditions and further research is needed in this area.

P-073

Incidence of amantadine induced livedo reticularis

A Rana (Toronto) S Muneeb (Toronto)*

Objective: To study the incidence of amantadine induced livedo reticularis in Parkinson's disease patients. *Background:* Amantadine is used both in early stage of Parkinson's disease mainly for tremor as well as in late stages for dyskinesia. One of side effect of amantadine is livedo reticularis. It is reddish blue reticular discoloration of the skin and most often localized on lower extremities. We did a chart review of our Parkinson's disease patients on Amantadine and found 12% of incidence of livedo reticularis due to amantadine. Upon discontinuation of the drug patient's rash improved. *Methods:* A chart review of our Parkinson's disease patients on amantadine was done. *Results:* In these patients amantadine caused livedo reticularis. Although there was no itching or any other medical complications but still all of these patients found the rash bothersome and required discontinuation of amantadine. *Conclusion:* In our study we found 12 % incidence of livedo reticuaris with amantadine. The patients should be warned of livedo reticularis due to amantadine as this may be cosmetically bothersome to many patients.

P-074

Interesting presentation of central pontine myelinolysis (CPM)

A Rana (Toronto) S Muneeb (Toronto) A Rana (Toronto)*

Objective: To discuss an interesting presentation of central pontine myelinolysis (CPM) *Background:* Central pontine myelinolysis (CPM) is a rare neurological disorder characterized by a symmetric, demyelinating lesion of the central pons. The disorder is frequently associated with the rapid correction of serum sodium in hyponatremic patients. However, other conditions such as chronic alcoholism, malnutrition and liver disease have also been found to predispose patients to CPM. *Methods:* A 55 year old man with a history of alcohol abuse presented with decreased level of consciousness. Upon arrival to the hospital, he was found to be hyponatremic with serum sodium of 109mEq/L. He was admitted to hospital and sodium correction was initiated. Serum sodium levels following his admission to the hospital were as follows, Day of admission was 109mEq/L
Day # 2 was 112mEq/L Day #3 was 126mEq/L
Day # 4 was 132mEq/L Day # 14 138 mEq/L

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

On third day he was found to be lethargic, with diffuse weakness and with quardreparesis. *Results:* Magnetic resonance imaging (MRI) of the brain revealed an abnormal signal within the central pons, consistent with central pontine myelinolysis *Conclusion:* In alcoholic and chronically debilitated patients, the hyponatremia should be reversed slowly and the administration of fluids for it should be kept to a minimal rate.

P-075

Don't just see them alone if they are on Dopamine agonists

A Rana (Toronto) S Gangat (Toronto)*

Objective: To discuss the importance of parallel history in Parkinson's disease patients on dopamine agonists, as patients themselves may not report the history of ICDs.
Introduction: Dopamine agonists used in the treatment of Parkinson's disease may cause abnormal behavioral side effects such as pathological gambling, eating, hypersexuality, shopping and punding. There have been reports that patients with PD have trouble telling lies but patients may decline pleasurable side effects of Dopamine agonists. *Methods:* We report two patients who denied ICD when asked directly but their caregivers provided the parallel history which was later affirmed by the patients.
First patient Mr. J.W. a 68-year old left handed male with Parkinson's disease was on pramipexole and developed an intense increase in sex drive. He had difficulty controlling his inner urge to have sexual intercourse. His frequency of sexual intercourse increased to several time a week. He never reported this in spite of being asked on follow up visits. This was very bothersome for his wife who decided to bring this to the attention of the patient's neurologist.
Our second patient Mr.K.K. was a 39 year old male with PD who was on Pramipexole and denied ICD but his sister provided a parallel history and reported that patient had developed gambling which was affirmed by the patient. *Results:* Upon decreasing the dose of Pramipexole, both patient's ICDs behaviors resolved. *Conclusion:* Parallel history from the family members, caregiver or spouse on each follow up visit is important because patients may not report some of these behaviors

P-076

One dopamine agonist can cause multiple impulse control disorders

A Rana (Toronto) K Mian (Toronto)*

Objective: To report a variety of impulse control disorders (ICD) and Punding with Pergolide in a patient of PD. *Introduction:* Many recent reports have suggested dopamine agonists can cause impulse control disorders. ICDs are defined as 'the failure to resist an impulse, drive, or temptation to perform an act that is harmful to the person or to others. ICD behaviors may be very diverse and include gambling, hypersexuality, hobbyism, compulsive shopping, and complex stereotyped behaviors such as punding. Recognition of these disorders is important because they can cause considerable distress to patients and caregivers, and may go unrecognized if patients are not screened with a parallel history for these disorders. *Methods:* We present a 45 year old male with idiopathic Parkinson's disease. He was on pergolide for Parkinson's disease when he developed compulsive gambling, hypersexual behavior, compulsive shopping and punding. He started buying different types of screwdrivers unnecessarily by shopping at the Home Depot at least few times a week resulting in a huge collection of screwdrivers in his garage. *Results:* A single dopamine agonist can cause a variety of impulse control disorders in one patient. *Conclusion:* It is essential to screen every patient with a parallel history for a variety of impulse control disorders.

P-077

Prevalence of cryptoccocal meningitis in non-immuno-compromised patients.

A Rana (Toronto) A Rana (Toronto) S Khan (Toronto)*

Objective: To discuss the importance of considering cryptoccocal meningitis in non-immunocompromised patients. *Background:* Cryptococcal Meningitis (CM) is most commonly known as an opportunistic infection in immuno-compromised hosts, especially those suffering from HIV/AIDS. However, recent reports have indicated the rising prevalence of CM within apparently immuno-competent hosts. Hence this condition should be considered even in immuno-competent patients. *Methods:* A 45-year old man presented with severe headaches, dizziness, and progressive decline in loss of consciousness. Acyclovir and a triple coverage of ceftriaxone, vancomycin and ampicillin, were started for herpes encephalitis and bacterial meningitis, respectively. He was generally healthy, however he started a new job about a month prior to admission to hospital where he worked in a fairly confined space with a propane powered forklift. *Results:* Initial CSF results indicated a white blood cell count of 121, of which 70% were neutrophils and 20% lymphocytes. Blood glucose and protein levels were 3.4 and 1.89, respectively. Bacterial gram stain was negative. India ink staining was not performed initially as he was otherwise healthy. Later the results of India ink staining and further CSF studies indicated the presence of the cryptoccocal antigen, suggesting the patient had CM. Subsequently, the patient was treated with Amphotericin B. but he passed away approximately a week after. MRI and CT scan indicated progressive cerebral edema. HIV, VDRL and active TB tests were negative. *Conclusion:* CM should be included in differential diagnosis of meningitis even in immuno-competent patients.

P-078

Comorbidity of migraine in a local major headache clinic

L Ren (Hamilton) R Giammarco (Hamilton)*

Background: Migraine is one of the top diseases world-wide causing disability. Many studies have shown that comorbidity with a number of medical conditions and poor social economic status are common in migraineurs. Therefore, analyzing the local data about migraineurs will help us to raise awareness of their comorbidities, identify them earlier, and finally treat patients as a whole to improve their overall quality of life. *Methods:* This is a retrospective study. We reviewed the medical records of patient visits in a major headache clinic run by a neurologist in Hamilton, Ontario, in 2010 and evaluated the comorbidities of migraineurs. *Results:* There were a total of 320 visits with 217 patients. Among these patients, 147 patients are diagnosed with migraine according to the 2nd edition of The International Headache Classification (ICHD-II) criteria, with a female to male ratio of 4.25. Positive family history is 45% in female

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

migraineurs and 39% in male migraineurs. Top three comorbidities are depression (16%), asthma (9%), and hypertension (8%) in female migraineurs, hypertension (18%), depression (4%) and gastroesophageal reflux disease (4%) in male migraineurs. *Conclusion:* In this retrospective chart review study, we have identified the more common comorbidities in our local area, which are depression, hypertension and asthma.

P-079

Sensitivity and bias in decision-making under risk: A new clinical test of the perception of reward and its value

ME Sharp (Vancouver) LJ Lanyon (Vancouver) J Viswanathan (Vancouver) JJS Barton (Vancouver)*

Background: There are few clinical tests of decision-making under risk. The most well-known, the Iowa Gambling task, assesses the ability to learn cumulative probabilities of gain or loss and to forego large rewards for smaller ones. However, tests that characterize sensitivity and bias in decisions between prospects varying in magnitude and probability of gain may provide insights in conditions with anomalous reward-related behaviour. *Objective:* We designed a simple test of how subjects integrate information about the magnitude and the probability of reward, and tested healthy subjects to determine their discriminative thresholds and choice bias in decisions under risk. *Design/ Methods:* Twenty subjects were required to choose between two explicitly described prospects, one with higher probability but lower magnitude of reward than the other, with the difference in expected value between the two prospects varying from 3 to 23%. *Results:* Subjects showed a threshold sensitivity of 9.0% difference in expected value. Regarding choice bias, there was a 'risk premium' of 9.4%, indicating a tendency to choose higher probability over higher reward. An analysis using *prospect theory* showed that this risk premium is the predicted outcome of hypothesized non-linearities in the subjective perception of reward value and probability. *Conclusions:* This simple test provides a robust measure of discriminative value thresholds and biases in decisions under risk. *Prospect theory* can also make predictions about decisions when subjective perception of reward or probability is anomalous, as may occur in populations with dopaminergic or striatal dysfunction, such as Parkinson's disease and schizophrenia.

P-080

The use of technology to enhance clinical care and teaching

WA Stewart (Rothesay)

Background: In this digital age, there are limitless opportunities to utilize technology to enhance learning and clinical practice. Students entering medical programs are extremely familiar with many of these technologies. For physicians who have been in practice for a period of time, their use is daunting and may pose a significant challenge. *Methods:* The presentation will review how different technologies can be used to enhance clinical practice and stimulate learning. This will include electronic medical records, podcasting/vodcasting, on-line conferencing, e-learning, iPad/iPod Touch Applications, Wikis, and others. *Results:* Some examples of the use of these technologies are as follows: electronic medical records allow self-scheduling and prompted recalls; e-learning can fill knowledge gaps due to limited in-patient access; podcasting permits access anytime/anywhere to allow review of information; iPad/iPod Apps provide a variety of sophisticated tools for use in clinical practice and teaching and are familiar to the new generation; on-line conferencing and Wikis allow on-line interaction with multiple participants. A brief overview of how each can be used will be presented. *Conclusions:* Many of these technologies are unfamiliar to physicians, but with some limited training can be of significant benefit in a teaching clinical practice.

P-081

Canadian post-stroke spasticity patients: the BOTOX® Economic spasticity trial

T Wein (Montreal) L Satkunam (Edmonton) S Sharma (Toronto) J Wissel (Beelitz-Heilstaetten,) N Wright (Marlow)*

Background: There are few detailed descriptions of patients with post-stroke spasticity (PSS), a serious and painful consequence of stroke. *Methods:* In the BOTOX® Economic Spasticity Trial, adults with focal PSS were randomised to botulinum toxin A (BoNT-A)+standard care (SC) or placebo+SC as part of their rehabilitation regimen, for ≤2 treatment cycles, followed by an open-label phase of ≤52 weeks. Eligible patients were BoNT-A-naïve, had preserved function and were considered likely to benefit from intervention, in the limb to be treated. Baseline characteristics of the Canadian cohort are presented here. *Results:* When compared with the total study population (n=274), the Canadian cohort (n=22) comprised a lower percentage of men, but higher percentages of patients aged <65 years and >1 year since stroke. In both populations, patients were mostly unemployed at study entry. Physiotherapy was received by 73% and occupational therapy (OT) was received by 37% of all patients during the 12 weeks prior to baseline; in the Canadian cohort these proportions were 27% for both physiotherapy and OT. The majority of other baseline characteristics were similar for both groups, including quality of life scores. *Conclusions:* In both Canada and the wider population, spasticity remains a problem >1 year after stroke

Multiple Sclerosis

P-082

The Toronto EDSS calculator: an application for MS health care providers

JE Alfonsi (Toronto) L Lee (Toronto)*

Introduction: The Kurtzke Expanded Disability Severity Score (EDSS) is an important metric used to assess the disability and the progression of Multiple Sclerosis (MS). However, the EDSS algorithm can be time consuming to calculate, and individual interpretations can lead to inter-observer variability. *Objective:* To develop an application to reliably and quickly calculate the EDSS using a handheld device. *Method:* An application was designed and coded for all Apple handheld devices using Apple's iOS 4.0 at the Sunnybrook Health Sciences Centre in Toronto, Canada. The assigned functional impairments were scored according to the papers published by Kurtzke. To improve reliability of scoring, written instructions and video examples of disabilities were included to demonstrate physical findings corresponding to various levels of functional impairment. Consensus of the video impairments was

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

reached amongst the MS Neurologists at the University of Toronto MS program. *Results:* The application, entitled EDSS Calculator, is currently available for download from the Apple store. A patient's EDSS can be rapidly computed using handheld devices (Apple iPhone, iPod Touch, iPad). A summary of the patient's score in each functional system as well as their total EDSS can be readily saved electronically and easily printed. *Conclusion:* This is the first application that has been developed to enable a rapid and accurate calculation of the EDSS using Kurtzke's algorithm on a handheld device. Reliability of the scoring is facilitated by the accompanying written instructions and videos. This allows MS health care workers to document patient disability scores electronically and facilitate the long-term monitoring of MS patients' disabilities.

P-083

Multiple Sclerosis like events associated with anti-TNFα treatment: four new case reports

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Objective: to report four new cases of MS-like events associated with anti-TNFα treatment.
Background: Anti-TNFα treatments for rheumatological disorders may trigger demyelination in three forms: clinically isolated syndromes, manifesting a previously silent multiple sclerosis (MS) or exacerbating previously known MS. *Methods:* We describe four patients with neurological symptoms and white matter lesions on MRI seen in the last year (MS Clinic, London, Ontario) for evaluation of possible MS. Thorough investigations included laboratory, neuroimaging (sequential MRI) and cerebrospinal fluid (CSF) studies. *Results:* All four patients were Caucasian women within the same decade (ages between 42 and 51 years). Neurogenic bladder was the most common clinical onset, followed by sensory impairment. Only one patient met McDonald's modified criteria for MS. This same patient was the only one with positive oligoclonal banding in CSF. Three of them had underlying rheumatoid arthritis; the fourth had ankylosing spondylitis, and was the only one with family history of MS (a brother). Regarding the precise anti-TNFα treatment, etanercept and adalimumab were each associated with two cases, but we did not see any with infliximab. *Conclusions:* White matter lesions associated with anti-TNFα treatment and demyelinative neurological disorders are exceptional findings, with few reports of MS. In our four patients, only one met criteria for definite MS.
Given the precarious knowledge about this association, the question of whether pre-treatment spinal and cerebral MRI should be done in asymptomatic patients before anti-TNFα remains unsettled. On the other hand, precautionary anti-TNFα discontinuation is recommended in patients with demyelinating lesions and neurological findings.

P-084

Neuromyelitis optica diagnostic criteria: UBC experience

O Kwon (Vancouver) R Sadjadi (Vancouver) AJ Kuan (Vancouver) I Al-Thubaiti (Vancouver) Frykman (Vancouver) D Li (Vancouver) A Traboulsee (Vancouver)*

Background: Current NMO criteria, 2006 Mayo criteria, may be too restricted to identify NMO spectrum disease (NMOSD). Furthermore, the disease marker, NMO-IgG/AQP4 Ab, has been reported to have less than ideal sensitivity in those that fulfill 2006 criteria. The NMO Database at UBC was designed to include demographical, clinical, serological, and radiological data of patients with a clinical suspicion of NMO and to evaluate the utility of current criteria in clinical practice and hopefully to improve criteria to include those patients with NMOSD or at high risk for NMO/NMOSD. *Methods:* All NMO referrals were evaluated according to 1999 and 2006 Mayo criteria. The UBC criteria included: possible (severe ON, severe TM, NMO-like MRI lesion, or high-risk ethnicity), probable (severe ON and severe TM), and definite NMO (NMO-IgG/AQP4 Ab seropositivity). *Results:* Of Ninety-five patients whose data were available, eighteen had confirmed diagnoses other than NMO and were excluded. Seventy-seven patients had 37.3±13.9 years of onset ages. Fifty-seven (74%) were women. Sixteen patients were seropositive for NMO-IgG/AQP4 Ab. Thirteen patients fulfilled the 1999 or 2006 Mayo Criteria. Sixty-two patients met one of the UBC criteria: 39 possible, 23 probable or definite. *Conclusions:* The main reason of low sensitivity of the Mayo criteria stemmed from its prerequisite of both ON and TM and undervalued role of NMO-IgG/AQP4 Ab. The UBC criteria identified twice as many cases as the Mayo criteria and included a new category for possible NMO. The value of identifying the at-risk group as possible NMO, should allow for closer monitoring without overdiagnosing NMO.

P-085

Perinatal outcomes of women with multiple sclerosis using disease-modifying drug

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Background: The incidence of disease-modifying drug (DMD) exposure during pregnancy in multiple sclerosis (MS) is unknown and limited data exists regarding the potential harm of DMD exposure during pregnancy. We investigated the incidence and effect of *in utero* DMD exposure on perinatal outcomes. *Methods:* We conducted a retrospective analysis by linking the British Columbia (BC) MS database with the BC Perinatal Database Registry. We compared delivery (labor duration, assisted vaginal delivery and Cesarean section) and neonatal (birth weight, gestational age, 5-minute Apgar score and congenital anomalies) outcomes in women exposed and unexposed to a DMD within one month prior to conception and/or during pregnancy. Findings were reported as odds ratios (OR) with 95% confidence intervals (CI). *Results:* 311 women with relapsing-remitting MS delivered 418 babies between April 1998 and March 2009. Of these, 21/418 (5%) were DMD exposed. We found a trend towards a greater risk of assisted vaginal delivery in the DMD exposed versus DMD naïve group (OR = 3.0; 95% CI: 1.0 - 9.2). All other comparisons of perinatal outcomes were

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

unremarkable. *Conclusions:* The incidence of DMD exposure was reassuringly low. Further studies are needed to ascertain the safety of DMD exposure during pregnancy in MS.

P-086

A platform for effective communication with multiple sclerosis patients

RAC Siemieniuk (St Catharines)

Background: Many MS patients seek intravascular management of chronic cerebrospinal venous insufficiency (CCSVI) against medical advice; relationships between some patient groups and the medical community have thus been strained. MS patients often rely on internet chat forums for support and information regarding MS and CCSVI; we evaluated this information in hopes of improving physician-patient communication. *Methods:* Nine popular chat forums were evaluated between January 1st-10th, 2011. The most recent forum posts, up to a maximum of 50 per site, were rated on the strength of recommendation for hasty CCSVI treatment and on the presence of misleading or incorrect information. *Results:* Of 116 forum posts evaluated, 50% recommended immediate CCSVI treatment, 25% recommended it with caution, 19% argued that information was needed before pursuing treatment, and 6% argued against CCSVI treatment indefinitely. 28% of posts contained misleading/incorrect information, occurring most often in posts strongly advocating treatment ($p<0.05$). Desperation, in addition to distrust of pharmaceutical companies, physicians, and government were common themes. *Conclusions:* Quality of CCSVI information on internet forums varied, however posts making strong arguments for treatment had greater unreliability. With a deeper understanding of information contained on chat forums, physicians may be able to communicate more effectively with MS patients.

P-087

Patient-reported outcome measures in neuromyelitis optica: UBC experience

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Background: Neuromyelitis optica (NMO) is an uncommon, severe demyelinating central nervous system disease affecting the optic nerve and spinal cord. Unique clinical course and recent identification of a specific antibody biomarker differentiates NMO from other similar demyelinating diseases such as multiple sclerosis (MS). Limited population studies describing clinical presentation and epidemiology of NMO have shown increased prevalence in non-Caucasian groups, particularly in Asian populations. An NMO clinic and research centre has been established at the University of British Columbia (UBC) to develop a patient registry, to provide patient support, and to investigate the emerging cases of NMO, which may be a reflection of the changing ethnic profile of the province. In this ongoing descriptive study, NMO patients self-characterize their illness perception, associations, and impact on well-being. *Methods:* All new consecutive consenting NMO referrals aged 19 years or older prospectively assessed their symptom presentation and level of impairment via self-rated questionnaires, adapted from those used for MS. Psychometric properties of the questionnaires were described in NMO patients. *Results:* Level of impairment, quality of life, and mental well-being in those affected by NMO can be measured systematically by adapted self-rated questionnaires. *Conclusions:* Subjective assessments may help to confirm clinical severity of NMO and may assist in treatment management, but rating scales specific to NMO need to be developed in order to accurately track disease course and guide particular recommendations.

General Neurosurgery

P-088

Duration of intra-operative stimulation on trial as a predictor of success of spinal cord stimulation for chronic pain syndromes

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Electrical stimulation of the dorsal column of the spinal cord stands out as a major method of neuromodulation. Its popularity stems from the long lasting support to the "gate theory" in which electrical stimulation of the gate prevents passage of nociceptive impulses and reduces pain sensation. Current applications of spinal cord stimulation are numerous and include a myriad of painful conditions, vascular ischemia, and cognitive recovery in vegetative states. The mechanism by which spinal cord stimulation achieves its effects is not well defined. There is little known about the effect of the duration of intraoperative stimulation (IOS) trial on the success of the spinal cord stimulation trial. We are going to present the results of 59 patients reviewed over 24 months. The major finding of this study is that the longer the IOS trial, the higher the chances for failure of SCS. We will also review the effect of the polarity of the SCS lead as well as the effect of different diagnoses on the success of SCS.

P-089

Silent Corticotroph Adenomas, Clinical Behavior and Comparison to Non-Functional Adenomas

HI Alahmadi (Toronto) SL Asa (Toronto) J Wilson (Toronto) G Zadeh (Toronto)*

Background: silent corticotroph adenomas represent a distinct pathological entity of non-functional pituitary adenomas with some literature suggesting an aggressive clinical behavior. *Methods:* we conducted a retrospective review of all silent corticotroph adenomas at our institution over the last 10 years. We reviewed clinical, radiological and pathological features. Recurrence rate was reported and compared to a matched cohort of non-functional adenomas. Statistical analysis was carried out to detect statistically significant trends. *Results: T*wenty-one patients had silent corticotroph adenomas. Follow up was available for 17 patients who were included in the final analysis. Nine patients (53%) were female. Mean age was 52 years (range 24-78 years). Eight patients (47%) had vision-related presentation. Two patients (12%) presented with acromegaly secondary to double adenoma (had silent corticotroph and somatotroph adenoma). One patient presented with apoplexy. All the tumors were macroadenoma and five of them (29%) had frank cavernous sinus invasion. Gross total resection was achieved in 9 cases (53%). Three tumors (18%) recurred over a mean follow up period of 31 months. Compared to non-functional adenomas,

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

silent corticotroph adenomas were more likely to be invasive adenomas but the difference in recurrence rate was not statistically significant. *Conclusion:* silent corticotroph adenomas are more likely to be invasive adenomas with a trend towards earlier recurrence.

P-090

Inappropriately low-pressure (negative-pressure) hydrocephalus: experience with 20 patients examining the role for endoscopic third ventriculostomy

MG Hamilton (Calgary) A Price (Dallas)*

Background: Most patients with acute hydrocephalus have ventriculomegaly and high intracranial pressure (ICP). However, there is a subset of patients who are symptomatic with acute ventriculomegaly and inappropriately low ICP. *Methods:* Two patient groups are presented. Each patient experienced clinical deterioration that included a significant decrease in level of consciousness with new and significant ventriculomegaly. Group 1 patients (n=10) were managed without endoscopic third ventriculostomy (ETV). Group 2 is a series of patients (n=10) managed with ETV. *Results:* Treatment for both groups involved insertion of an EVD with ICP < 5 cm H_2O. Further treatment consisted of either neck wrapping with a tensor bandage, and/or lowering the EVD to negative levels to facilitate drainage of CSF, which resulted in clinical improvement, and resolution of ventriculomegaly. All 20 patients had obstruction to CSF flow into the subarachnoid space (SAS). Group 1 patients were treated until shunt revision/insertion was possible (n=7), ICP normalized and the EVD could be removed (n=2), or death (n=1). Patients in Group 2 all underwent ETV and ICP patterns normalized in all. Group 2 patients were managed with an EVD until shunt revision/insertion was required (n=2), ICP normalized and the EVD could be removed (n=7), or death (n=1). *Conclusions:* Inappropriately low-pressure acute hydrocephalus is an important entity in both children and adults. A possible hypothesis invokes loss of an effective subarachnoid space (SAS). ETV reestablishes communication between the SAS and ventricles producing a rapid return of normal ICP patterns and a significant decrease in the number of shunt-dependant patients.

P-091

Meningioma with Intracranial Haemorrhage secondary to Ruptured Aneurysm

PY Ho (Edmonton) I Alnaami (Edmonton) M Wheatley (Edmonton)*

A 34-year-old male first presented with headache. A CT scan revealed an acute intracerebral hemorrhage surrounding an ill defined mass lesion. An MRI revealed a presumptive bifrontal parafalcine meningioma with associated intracerebral haemorrhage. Because of the intracerebral hemorrhage, he had two cerebral angiograms and both were reported as negative. It was presumed that the meningioma had bled peritumorally. Elective surgery was then planned after resolution of the intracerebral hemorrhage. Prior to the planned surgical resection he had another cerebral angiogram with preoperative embolization. The preoperative cerebral angiogram, however, disclosed a posterior pericallosal aneurysm adjacent to the presumptive meningioma. Meningiomas are rarely associated with aneuryms. This is the first report of a meningioma with associated aneurysm presenting with intracranial haemorrhage after a negative cerebral angiogram. The etiology of aneurysms associated with meningiomas will be discussed. Peritumoral or intracerebral hemorrhage associated with meningiomas is not a rare phenomena. Should cerebral angiography be obtained in all patients with peritumoral hemorrhage? We should remain suspicious of an associated aneurysm when patients with brain tumors present with peritumoral hemorrhage.

P-092

Mechanical properties of in-vivo rabbit brain

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Background: Many physiological and pathological states of the brain are systems of mechanics, and therefore understanding the mechanical properties of brain is important for understanding injury mechanisms, subsequent pathological states, and diagnostic and therapeutic interventions. Brain, assumed to exhibit viscoelastic material behavior, requires consideration of all mechanical and physiological variables that may affect its response to pressure or deformation in the context of direct mechanical testing. The objective of this work was to obtain quantitative data from in-vivo rabbit brain deformations, appropriate to viscoelastic theories and for mathematical modeling, in different physiological states relevant to mechanical ventilation and blood pressure manipulation. *Methods:* Step-loaded stress-relaxation indentations of brain were performed on seven living rabbits. Each animal was anesthetized and mechanically ventilated, with euvolemia and normthermia maintained, and arterial blood pressure and pCO_2 monitored. Indentations were performed through a left craniectomy window, directly on the brain surface. Stress-relaxation tests were performed at defined ranges of blood pressure and pCO_2, which were manipulated by intravenous phenyleprhine and ventilatory flow rate respectively. *Results:* Differences exist in times of relaxation, elasticity, and viscosity between different ranges and combinations of blood pressure and pCO_2, in the in-vivo rabbit brain undergoing step-loaded stress-relaxation indentation. *Conclusions:* In-vivo indentation testing of rabbit brain can be conducted successfully to quantify viscoelastic properties of brain and correlate mechanical properties with physiological variables. Changes in viscoelastic properties of in-vivo rabbit brain are associated with different ranges of mean arterial pressure and pCO_2.

P-093

Acute subdural hematoma from an oligodendroglioma: case report and review of literature

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Background: Acute subdural hematoma secondary to hemorrhage within a brain tumour is a rare occurrence.
Methods / Case Report: After presenting with seizures, a 43 year-old man had a biopsy proven oligodendroglioma diagnosed eleven years ago. He received focal cranial radiation. Neuroimaging had shown stability until one year ago. The left frontal-parietal tumour was showing gradual enlargement with a new area of enhancement. His seizures had become harder to control. Resection was not deemed to be safely feasable and he had started his first cycle of temozolomide

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

chemotherapy. At the start of his second week of chemotherapy, while at work, he developed a severe left-sided headache with progressive impairment of speech and right-sided hemiplegia. He became unconscious and required intubation. Computerized tomography of the head revealed a large left-sided acute subdural hematoma with shift of midline structures. There was evidence of intra-tumoural hemorrhage. He was taken urgently to the operating room and underwent evacuation of the acute subdural hematoma, evacuation of the intra-tumoral blood, and biopsy of the tumour wall in the vicinity of the hemorrhage. The biopsy showed oligodendroglioma with anaplastic features. He made neurological recovery to his baseline. The literature was reviewed for cases of brain tumour causing acute subdural hematoma. *Results/ Conclusions:* Review of the literature revealed a paucity of cases where a brain tumour had caused an acute subdural hematoma. The literature review will be shown Clinicians should consider acute subdural hematoma in patients with a brain tumour that present with acute neurologic deterioration.

P-094

Current practice in idiopathic normal pressure hydrocephalus

S Mohammed (Toronto) R Kurlan (Rochester) MD Cusimano (Toronto)*

Introduction: Idiopathic Normal Pressure Hydrocephalus (INPH) is a clinical syndrome of progressive mental deterioration, including gait unsteadiness, dementia and urinary incontinence associated with hydrocephalus in the setting of normal cerebrospinal fluid (CSF) pressure. After nearly four decades, there is still no gold standard for its diagnosis and management. *Method:* A survey of 60 questions, divided into sections: demographics, present practice (diagnosis, treatment and outcome) was sent to 1300 neurosurgeons, neurologists and geriatricians of North America via an online survey tool. *Results:* 238 neurosurgeons, 121 neurologists and 6 geriatricians responded to date. This represented 6793 years of clinical practice, yearly evaluation of 5175 possible INPH patients and yearly shunting of 2470 probable INPH patients. 47.5% of the respondents stated that gait disturbance is the minimal clinical requirement for shunting, while 21.9% preferred the full clinical triad. Patient age, length of history and opening pressures were not regarded as exclusion criteria for shunting by 85% of respondents. CT (51%), MRI (83%) and neuropsychological testing (37.5%) were the most common pre-shunt investigations. 63% agreed that improvement with one time CSF tap-test is sufficient for shunting. 92% preferred VP shunts while 3% preferred LP shunts. Programmable valves (67%) were the most commonly used. Under drainage and subdural effusions were the most widely reported complication of shunting. 78 % of respondents had a CT brain as the preferred post–op image. *Conclusions:* The management of INPH is controversial and varies dependent upon the several factors.

P-095

Opinions on the need for a Randomized Control Trial on Idiopathic Normal Pressure Hydrocephalus

S Mohammed (Toronto) MD Cusimano (Toronto)*

Introduction: Idiopathic Normal Pressure Hydrocephalus (INPH) is a clinical syndrome of progressive mental deterioration, including gait unsteadiness, dementia and urinary incontinence associated with hydrocephalus in the setting of normal cerebrospinal fluid pressure. After nearly four decades, there is still no gold standard for its diagnosis and management. *Methods:* A survey on the opinions of an RCT for INPH was sent to 1300 neurosurgeons, neurologists and geriatricians of North America via an online survey tool. *Results:* 314 respondents were obtained. 63% were neurosurgeons and 29% were neurologists. 84% of respondents agreed that there is considerable uncertainty in how best to diagnose INPH or what investigations to use to make a diagnosis. 90% indicated that they felt that there is significant variation in clinicians approach to INPH. 66% said that there was uncertainty if shunting is the best option. Programmable shunt was believed to be the standard of care in 51% of respondents. 51% indicated that they were not sure if shunting was beneficial in the short term (<1 year) while 67% were not sure for the long term (> 1 year). The majority (77%) agreed that there is a need for a RCT. 68% said that they will refer patients for randomisation while 72% will enroll their own patients. With regards to a control for the RCT, 44% indicated no shunt while, 31% indicated a programmable valve with the system shut off. *Conclusions:* There is a need for a RCT to determine how best to diagnose and manage INPH

P-096

Case report: Endoscopic associated iatrogenic Terson's syndrome

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A 46-year-old male patient was found to have a colloid cyst located in the anterior roof of the third ventricle. Endoscopic surgical resection was planned on an elective basis. The patient developed a Cushing response secondary to a disparity in irrigation inflow and outflow volume through the endoscopy equipment. Postoperatively, he developed reduced visual acuity secondary to bilateral intra-ocular hemorrhages. We report a rare case of iatrogenic Terson's syndrome that was caused by inadvertent raised intracranial pressure during an attempt at endoscopic resection of a colloid cyst located in the third ventricle. The mechanisms that contributed to the precipitous increase in intracranial pressure are discussed in detail. We also outline the chronology of monitoring parameters and emergency management. Neuro-endoscopy remains an attractive option for the surgical management of intra-ventricular tumors and hydrocephalus, though one needs to be cognisant of the attendant risks. The major factor that contributed to this adverse event was related to equipment.

P-097

Anatomical Labeling that Can Allow Both Serial Magnetic Resonance Imaging and Histological Evaluation with Nanoparticles in Brain and Spinal Cord

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Serial imaging of a specific location in the neural axis is important in research studies involving electrophysiology, traumatic brain injury, regeneration, and neuroanatomy. The use of a superparamagnetic iron oxide (SPIO) nanoparticle contrast agent for magnetic resonance imaging (MRI) conjugated with a fluorescent

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

dye enables concurrent serial MRI and eventual histological assessment of the same animal. SPIO nanoparticles were functionalized with a silica shell to incoporate a fluorescent dye, and biotinylated dextran amine (BDA) for bioactivity. Studies were done in vitro with adult Sprague Dawley rat neural progenitor cells to assess cellular uptake of the nanoparticles and in vivo in the Sprague Dawley rat sensory-motor cortex and spinal cord (n=4). Nanoparticle concentrations to a level of 10 mM had a limited effect on cell death and apoptosis of neural progenitor cells and a labelling efficiency of 88±5% of cells at 10 mM (n=3). Nanoparticles were assessed for MRI labelling of the brain for a period of 3 weeks, and the contrast persisted in location over this time period and could be distinguished with MRI from iron associated with hemorrhage. While staining for iron with Prussian blue could be coincided with iron staining from hemorrhage, the fluorescent signal from the nanoparticle could be distinguished from hemorrhage at three weeks post injection. Thus, these iron nanoparticles can allow location specific labelling of the neural axis which can be visualied by MRI over time and confirmed with fluorescence microscopy.

P-098

Diabetes insipidus after endoscopic pituitary surgery

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Background: The endoscopic transnasal resection (minimally invasive pituitary surgery) of pituitary adenomas is currently the procedure of choice. There has been concern about the incidence of diabetes insipidus (DI) post this approach. We report the incidence and predictors of DI after this procedure. *Methods:* a retrospective chart reviews of patients who had diabetes insipidus after endoscopic surgery of pituitary adenomas at Hamilton General Hospital in 2009 *Results:* (29.7 %) of patients had DI after the endoscopic resection of pituitary adenomas. (81.8%) were transient D.I. (81.8 %) of patients with DI were females, (54.5%) of their tumors had negative stain, (54.5%) of them had intraoperative CSF leak, (45.4%) of them had hypernatremia and (90.9%) of them received DDAVP, *Conclusions:* The incidence of diabetes insipidus after endoscopic resection of pituitary adenoma is similar to nonendoscopic transsphenoidal resection. It is usually transient DI. Risk factors are intraoperative CSF leak and hypernatremia and possibly female gender, macroadenoma and negatively stained adenoma.

P-099

Prevalence and importance of brain stem injury in early post traumatic mortality

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Trauma and especially motor vehicle accident is a major cause of death. Some victims died at the scene or very early after accident. Brain stem (BS) injury should be consider as an important cause of instantaneous mortality.

In this study, all cadavers who referred to Legal Medicine Organization of Mashhad evaluated during March 2009 to September 2009. 67 cases of early traumatic death, without any other reasonable cause of death, have been selected for possible brain stem injury.

During autopsy BS had been removed and fixed. All specimen were reviewed in 6 sections (mid sagittal, mid midbrain, midpons, mid medulla, midbrain –pons, and pontomedullary junctions; macroscopically, and mid brain, pons, and medulla microscopically) looking for possible, hematoma, contusion, edema and necrosis.

Macroscopic evaluations (in 3 sections) revealed 37 (55.2%) hematoma, and 9 (13.2) contusion in all sections. In microscopic studies, hematoma, contusion, edema and necrosis was noticed in 30, 11, 18 and 5 cases respectively.

Brain stem injury should be considered as a major cause of instantaneous death in trauma.

SPINE

P-100

Degenerative vertebral disc disease in children: a case series

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Background: Back pain, while infrequent in children, can be associated with disc disease related to different pathophysiologic processes and the unique anatomical features of the growing skeleton. With increasing childhood obesity and more intense athletic activities at younger ages, degenerative disc disease may be under-recognized and more problematic than previously thought. *Method:* A single centre review of all patients presenting to tertiary care pediatric neurology, neuromuscular or orthopedic clinics identified as having degenerative disc disease by imaging of spine. *Results:* Ten patients were identified. The mean age at presentation was 14.3 years, Presenting symptoms included back pain n=6, weakness n=2, sensory disturbance n=1 and radicular headache n=1. Mean BMI was 24 with 3/10 patients having a BMI >30. The mechanism of disc disease was presumed to be chronic trauma n=4, acute trauma n=2, spondylolithesis n=1 and unknown n=3. MRI was performed in all patients with 3 patients also having EMG/NCS. The most common disc level involved was L4-L5 (n=3) with multiple levels in 2 patients. Management was surgical in 2 patients with the remainder receiving pain management, rest and physiotherapy. One patient had recurrent new radicular symptoms with a new disc herniation in the follow up period. *Conclusion:* This case series demonstrates the variability of mechanisms and clinical characteristics of disc disease in children. Larger case series will need to be completed to understand the role of potential risk factors for disc disease, such as obesity and athletic activity.

P-101

Winged-cage construct in spine stabilization following cervical corpectomy

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Background Context: To investigate the safety and efficacy of a distractible titanium cage with wings after cervical corpectomy in obtaining mechanical stability without arthrodesis of the cervical spine. *Methods:* Two year retrospective study of 24 patients with

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

cervical myelopathy who underwent single- or multi-level corpectomies. A titanium anterior distractible device with wings (ADDPLUS, Ulrich, Germany) was used as an adjunct to spondylodesis. The average follow-up was from 6 to 24 months and 2 patients were lost to follow-up. *Results:* Absence of hardware failure and technique related complications without subsidence. Non-ambulatory patients recovered the ability to ambulate. Clinical symptoms improved in all (which was validated on the Odom's criteria and the JOA cervical myelopathy questionnaire), except one for radicular symptoms. Revision surgery had to be performed in one patient for screw pull out with cage dislocation. In 2 patients, the procedure was technically challenging due to loss of cervical lordosis as the wings on the cage are preset for cervical lordosis. *Conclusions:* This procedure decreases operative complexity, avoids posterior implant extrusion, and autograft site morbidity. This construct is mechanically stable without boney fusion.

P-102

Accuracy of intraoperative CT with neuronavigation for pedicle screws in a community setting

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Background: Spinal fusion is commonly performed at hospitals across North America. Imaging used to aid pedicle screw placement has advanced from anatomical knowledge to x-ray films to live fluoroscopy and recently neuronavigation. Our community hospital recently introduced intraoperative CT with neuronavigation for pedicle screw placement. This study examines accuracy of screw placement using this technique. *Methods:* 14 consecutive cases (87 screws) of instrumented thoracic and lumbar spinal fusion performed at Bay Medical Center by a single surgeon with neuronavigation from December 2009 to June 2010 were reviewed. Patient demographic and clinical data was collected. Screw placement was graded using a published scale. *Results:* Patients included 10 males and 4 females, age 22 to 77 years (average 54.3). Clinical presentations included neurogenic claudication (6), discogenic pain (1), myelopathy (1), spondylolisthesis (2), radiculopathy (1) and fracture (3). Of 87 screws, 85 (97.7%) were fully contained in bone. Both violating screws perforated laterally and were deemed clinically insignificant. *Conclusions:* This review shows that intraoperative CT with neuronavigation is a safe and accurate technique for pedicle screw placement in a community hospital setting. Our accuracy rate was superior to most published conventional fluoroscopy methods and comparable to the rates of other computer-based studies.

P-103

Factors associated with outcomes of patients who develop a spinal hemorrhage during a thromboprophylaxis regimen

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Background: Using pooled data from a systematic review, this study examines the potential factors associated with spinal hematoma among patients who develop central nervous system (CNS) hemorrhage while on thromboprophylaxis. *Methods:* Three reviewers screened publications and extracted data on all cases of a CNS hemorrhage. First, all cases were grouped into brain, posterior fossa and spinal hemorrhage. Second, the spinal-hemorrhage group was subdivided into complete recovery, incomplete recovery, no recovery and death. *Results:* Data were extracted from 63 publications detailing 497 patients. The CNS groups were comparable regarding age, sex, prior trauma, hypertension and indication for thromboprophylaxis. Spinal-hemorrhage group had greater antiplatelet use ($p=0.014$), lower frequency of supratherapeutic thromboprophylaxis ($p=0.03$), later restarting time of thromboprophylaxis ($p=0.035$) and more frequent indication for surgery ($p=0.001$) than the other CNS groups. However, all three groups were comparable regarding complications and functional outcomes. Outcomes among the spinal-hemorrhage subgroups were unaffected by sex; prior trauma; indication, type and status of thromboprophylaxis; management and its complications. Younger individuals had a lower survival after spinal hemorrhage ($p=0.015$). *Conclusions:* Our results suggest that individuals with spinal hemorrhage were treated differently from patients with other CNS hemorrhage. However, site of CNS hemorrhage did not affect the frequency of post-treatment complications and functional outcome.

P-104

Routine open versus minimally invasive decompression and instrumented lumbar interbody fusion: a retrospective analysis

IUl Haq (Thunder Bay)

Study Design and Objective: A quantitative meta-analysis was conducted to evaluate the approach related morbidity, clinical outcome and fusion rates after open or minimally invasive lumbar decompression and instrumented interbody fusion for degenerative disease. The main aim of the study was to determine the fusion rate and clinical outcome for both techniques based on published series and author's own experience. *Summary of Background Data:* Traditional open technique for decompression and instrumented fusion is the standard procedure for lumbar degenerative disease. Despite good clinical results, problem may arise due to unnecessary trauma to the musculoligamentous complex. The postero-lateral approaches have advanced to incorporate minimally invasive decompression and instrumented spinal fusion techniques. The results are retrospectively reviewed in the literature as there exists no controlled comparison between open and minimally invasive techniques. *Methods and Results:* Computerized searches of MEDLINE, EMBASE, Pub Med, and Evidence, Based Medicine Reviews Multifile (EBMZ) databases for the last 20 years were undertaken. Studies published in foreign language journals were not included. Text words, key words and subject headings in the searches included: spinal decompression instrumented fusion, lumbar degenerative disease, interbody fusion, minimally invasive techniques and outcome. From the search results, the full texts of 25 articles, considered to be most appropriate, were selected and examined. *Conclusion:* Fusion rate and clinical outcome for both open and minimally invasive techniques are comparable and in some series higher in minimally invasive techniques. However, prospective studies investigating long-term functional results are needed to determine the superiority of one technique over the other.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-105

Natural history of syringomyelia in pediatric patients

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Introduction: The natural history of syringomyelia in pediatric patients remains uncertain. The purpose of this research is to analyze the natural history of syringomyelia in pediatric patients, in whom no surgerical treatment was undertaken. *Methods:* A review of the neurosurgery database at British Columbia's Children's Hospital identified all patients with syringes. Patients were included in this study if they had at least two magnetic resonance images (MRI) of the spine, at least 1 year apart, while being managed non-operatively. MRI scans and patient files were analyzed to determine radiographic and clinical features, and to assess for changes over time. *Results:* 17 patients were included in the study. 6 had Chiari I malformation and none had tethered cord. Symptoms at presentation were mild, and included numbness in limbs (n=4), headaches (n=3), mild sensory deficits (n=2), mild motor deficits (n=2), or intermittent incontinence (n=8). Syringes were cervical in 4, thoracic in 12. and lumbar in 1, and the mean maximum diameter was 6.1 mm (range 3.1-13.3). The syrinx either remained unchanged (n=7) or diminished in size (n=8) in 15/17 patients (88%). Two patients (both with cervical syrinx, both with Chiari) showed an increase in syrinx size, one of whom also worsened clinically. These 2 patients who exhibited syrinx growth had the largest syringes (over 10mm diameter) in the series. *Conclusions:* Syringomyelia often remains stable or decreases in patients managed non-operatively. It may be that cervical syringes, particularly ones associated with Chiari, and greater than 10mm in diameter, have an increased risk of growth over time.

P-106

Ring Apophyseal Fracture in Pediatric Lumbar Disc Herniation – A Common Entity

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Background: Lumbar disc herniation (LDH) can be associated with ring apophysis fracture (RAF), which is found in 6% of adult cases. However, the incidence and management of RAF in pediatric disc herniation is not well documented. The purpose of this study is to determine the prevalence of RAF in pediatric disc herniation, look for associated factors and to analyze how the fracture affects prognosis. *Methods:* We retrospectively studied patients who underwent CT scan for lumbar disc herniation. Patient charts and imaging were reviewed, and we compared patients with RAF and patients without RAF for clinical and outcome features. *Results:* RAF was present in 20 of 42 pediatric patients with LDH. There was a significant correlation with gender (p=0.02, 55% of males having RAF and 20% of females) and association with central herniations (p=0.003). Age, LDH level, and history of trauma were not associated with RAF. Review of operative notes in RAF patients suggested that herniated lumbar discs frequently had solid components, were difficult to remove, and required mechanical reduction of the fracture segment. At 1 year or greater follow-up, 37% of patients with RAF were symptom free, compared with 50% of patients with no RAF. *Conclusion:* RAF is more frequently associated with LDH in children than in adults. Gender and central disc hernation are associated with RAF. There is a trend to worse overall outcomes when RAF is present.

P-107

Intra-operative localization of the spine using custom metal ruler and fluoroscopy: technical note

BA Yarascavitch (Hamilton) K Reddy (Hamilton)*

Background: Intraoperative localization of the correct spinal level remains an ongoing challenge for spine surgeons and pre-operative or intra-operative fluoroscopy remains the mainstay in the majority of centres. Upper lumber and thoracic spine localization can be especially error prone as one must count up or down from known levels. *Methods:* To reduce counting errors, we use a patterned marked radio-opaque metal ruler secured to the side or back of the patient to 'label' vertebral levels during counting. This ruler has unique cut-outs at regular intervals that provide a backdrop during fluoroscopy that are correlated to vertebral bodies. *Results:* This versatile technique has been used in both anterior-posterior and lateral fluoroscopy for localization in the cervical, thoracic, and lumbar spine. Perhaps the most useful application is in localization of the upper thoracic spine in obese patients where soft-tissue density limits the visualization of the vertebral bodies. The marking ruler provides a stable reference point to reliably count levels and non-invasively mark the operative level for re-checking. *Conclusions:* We present a simple and inexpensive method for increasing accuracy in the intra-operative localization of spinal segments. We believe this method increases surgeon confidence in the correct spinal level and reduces errors in localization during fluoroscopic counting.

P-108

Minimally invasive treatment of spinal cord cysts using a tubular retractor system: case series

BA Yarascavitch (Hamilton) K Reddy (Hamilton)*

Background: Traditional open shunting of syringomyelia and cysts of the spinal cord can be problematic when the morbidity of an open operation is amplified by baseline neurological deficit secondary to the abnormality. *Methods:* We present a series of four cases treated with cyst-fenestration and/or shunting of spinal cysts by means of a tubular retraction system. In all cases, the METRx tubular retraction system (Medtronic Sofamor Danek, Memphis, TN) was utilised to provide access to perform a hemi-laminectomy and access to the spinal canal. Entry of the cyst was then carried out based on configuration and the catheter secured in place followed by tunnelling. *Results:* Using this technique, two patients underwent syringopleural shunting, one patient underwent cystoperitoneal shunting of an epidural cyst, and a fourth patient underwent syrinx fenestration with concurrent terminal ventriculostomy using the same tubular retractor system. All four patients had radiographic and clinical improvement post-operatively. *Conclusions:* We believe that, although technically challenging, insertion of syringopleural and spinal cystoperitoneal shunts using minimally invasive techniques can decrease procedure-related morbidity and patient discomfort, allowing for shorter hospital stays and increased patient satisfaction while providing a durable solution to various types of spinal cysts.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

PEDIATRICS (NEUROLOGY, NEUROSURGERY)

P-109

Reliability and validity of the agitated behavior scale in children with traumatic brain injury

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Background: Agitation is observed in children with traumatic brain injury (TBI) and can negatively impact recovery. Currently there is no validated tool to measure agitation following TBI in children. We prospectively examined reliability and validity of the Agitated Behaviour Scale (ABS) in children with TBI at multiple Canadian children's hospitals. *Methods:* The ABS is a 14-item scale ranging from 14 (no agitation) to 52 (severe). We included children older than 5 years admitted to the pediatric intensive care unit with TBI. The ABS was completed by nurses 3 times daily for up to 4 days following extubation. Daily video recordings were taken and an ABS score was applied by a blinded assessor. Agitation was also rated once a day by a physician using a visual analogue scale (VAS). *Results:* To date, 19 subjects from 3 sites have completed at least two consecutive days of the ABS. The mean nurses ABS rating for days 1 through 4 was 22.3, 19.3, 20.0 and 18.8. Inter-rater reliability between the nurse and blinded assessor was strong ($r=0.64$, $p<0.001$). There was a high agreement between the blinded assessor ABS score and the physician VAS rating both on total mean scores ($r=0.907$, $p\leq0.01$) and on individual day scores ($r=0.392$, $p=0.032$). There was correlation between physician VAS and nurses daily ABS scores, but this was not statistically significant ($p=0.052$). *Conclusions:* At the half way point of enrollment, there is a strong inter-rater reliability for the ABS scale; and a significant correlation between ABS score and physician rating of agitation.

P-110

A Study of familial infantile seizures in BC's First Nations families

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Background: Benign Familial Infantile Seizures (BFIS) is an autosomal dominant epilepsy syndrome characterized by normal development, no remote neurological insult and onset in infancy of seizures typically localized to the occipital-parietal region. Past genetic studies have mapped this condition to chromosomes 16p12-q12, 19q or 2q24. *Method:* We report the electro-clinical features and linkage results on a form of BFIS affecting 25 patients from 10 First Nations families in BC. *Results:* The mean age of seizure onset and offset was 4 months and 7 months respectively. Seizure duration was less than 2 minutes and involved bilateral motor activity. Seizures tended to cluster and occur during sleep. Response to medication was good. Twelve out of 25 had later speech/language delay and/or school difficulties compared to one out of 37 related controls. The inheritance pattern appears to be autosomal dominant with incomplete penetrance. Sixteen interictal and 5 ictal video-EEGs were available on 16 patients. The interictal EEG demonstrated frontal epileptiform activity and/or frontal slowing in 11 and was normal in five. Ictal video-EEGs revealed bilateral tonic posturing followed by fine jerking movements associated with diffuse attenuation and postictal frontal slowing. Sequencing of candidate genes *KCNQ2/3*, and *SCN2A* were negative. Linkage analysis demonstrated linkage to chromosome 16p12-q12 in all families with maximum LOD score of 3.3 on 16p12.1, which includes voltage-gated calcium channel gene *CACNG3*. *Conclusions:* The electro-clinical features in this form of BFIS are suggestive of frontal lobe seizures. Genetic studies support linkage to 16p12-q12 with *CACNG3* as a candidate gene.

P-111

The role of awake craniotomy in children: technical aspects and review of 3 cases

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The role of awake craniotomy is well established in adults undergoing surgical resection of epileptic foci or intracranial tumors. This technique facilitates intra-operative mapping of functionally eloquent cortex, allowing maximal lesion resection while limiting post-operative morbidity. Studies evaluating the use of awake craniotomy in children are limited. We retrospectively review the indications, intra-operative findings, and outcomes of all children who underwent awake craniotomy at Hospital for Sick Children, Toronto. Three children (mean age=16.3 years) underwent awake craniotomy at our institution. Indications for awake craniotomy in this group included left frontal tumors adjacent to the patients' speech area in all cases. Intra-operative mapping techniques included direct cortical stimulation, electroencephalography, motor evoked potential monitoring, and free running electromyography. In one case, positive speech arrest was encountered during direct cortical stimulation guiding surgical resection of a recurrent glioblastoma. In one case, inconsistent speech arrest was obtained which allowed surgical resection of a low-grade glioma. In the final case, no speech arrest was detected. All procedures were well tolerated with no complications. Awake craniotomy is a safe and useful adjunct in selected children undergoing surgical management for intracranial tumors. Close collaboration between neurosurgeons, anesthetists, neuropsychologists, and neurophysiologists is important to achieve excellent outcomes.

P-112

Agitation following pediatric traumatic brain injury

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Background: Agitation is commonly observed in children who have experienced a traumatic brain injury (TBI). Agitated behaviour can be distressing and can negatively impact rehabilitation in the acute phase of recovery. *Methods:* As part of the multicentre Attention and Traumatic Brain Injury (ATBI) study acute agitation is being prospectively evaluated with clinical parameters and a 14-item scale, the Agitated Behaviour Scale. This scale (ranging from 14-57) is completed by a health care giver and its reliability and validity in paediatrics are being examined in the ATBI study. To date a single

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

centre has complete agitation information. The agitation characteristics and the ABS scores are documented here to describe the profile of acute agitation following TBI. *Results:* To date, 12 subjects have completed all agitation components. The subjects' mean age was 13 years and 7 were male. All were alive at the time of discharge. The mean initial GCS, Pediatric Trauma Scores and PRISM were 7.1, 6.3, and 14.3 respectively. The average total ABS score was 20.8, with greater agitation seen in DAI (mean = 20.7, n=6) than multiple contusions (18.8,n=4). The mean length in PCCU and hospital were 10.4 and 26.5 days, respectively. There was a positive correlation between mean ABS and length of hospital stay (r=0.83 p=0.01). *Conclusions:* This ongoing prospective study is providing valuable information about the clinical profile of acute agitation and its impact on injury recovery in the pediatric TBI population.

P-113

Unusual presentation of copper metabolism disorder with Niemann-Pick C mutation

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Background: Abnormal copper metabolism was linked with Wilson's and Menkes' disease. Another disorder causing symptoms similar to copper metabolism disorder is Niemann-Pick type C. A definite connection between the above two has never been established. *Methods:* Case report. *Results:* A previously healthy 17 year old male presented with slowly-progressing dysarthria and gait abnormality. Patient exhibited moderate supranuclear gaze palsy. Fundoscopy was normal. Mild dystonia and axial ataxia were evident. Deep tendon reflexes in lower limbs were brisk with negative Babinski. Extensive metabolic screening was normal; however, serum copper and ceruloplasmin were low, as well as 24-hours urine copper. Acid sphingomyelinase was normal. MRI was normal. Muscle and gastrointestinal biopsies revealed severe copper depletion. Screening for Wilson's and Menkes disease was negative. Patient was found to carry two mutations in cis in the NPC1 gene, establishing him as a Niemann-Pick C carrier. We began oral supplementation of copper gluconate, which normalized copper, ceruloplasmin, and stabilized the patient clinically; however, no reversal was apparent. *Conclusions:* We suggest a possible mechanism whereby copper deficiency may enhance expression of Niemann-Pick phenotype in carriers: since copper deficiency increases cholesterol synthesis, this might increase intracellular storage of cholesterol in NPC carriers, thus enhancing the NPC phenotype.

P-114

Fetal exposure to alcohol, developmental brain anomaly and vitamin A deficiency

HR Goez (Edmonton) O Scott (Edmonton) S Hasal (Edmonton)*

Background: Prenatal alcohol exposure can cause hydrocephalus, through an unknown mechanism. Ethanol also disrupts the homeostasis of vitamin A, an important morphogen in the developing neural tube, particularly in the floor plate which dictates midline formation. *Methods:* Case report. *Results:* A two week old baby presented with irritability, episodic vomiting and high intracranial pressure. Ultrasound revealed triventricular hydrocephalus, and a shunt was inserted. Family history and delivery were unremarkable; his mother reported heavy alcohol consumption throughout pregnancy. Head circumference was >95%. Axial and upper limb tone was normal, and lower limb tone was increased. Deep tendon reflexes were brisk, with bilateral positive babinski and clonus in lower limbs. Fundoscopy demonstrated blurring of discs. MRI revealed a non-communicating hydrocephalus secondary to aqueductal stenosis. Extensive metabolic screening was normal, including vitamins E and D; however, vitamin A was extremely low. Maternal vitamin A was normal. Patient did not have any other systemic features of vitamin A deficiency. *Conclusions:* This is the first case presenting a possible association between prenatal alcohol exposure, vitamin A deficiency and congenital hydrocephalus in humans, which might be mediated through disruption of retinoic acid homeostasis at the floor plate of the developing neural tube.

P-115

Pontocerebellar Hypoplasia type 3 with severe vitamin A deficiency

*FD Jacob (Edmonton) S Hasal (Edmonton) HR Goez (Edmonton)**

Background: Pontocerebellar hypoplasia is a heterogenous group of congenital neurodevelopmental disorders characterized by hypoplasia and atrophy of cerebellar cortex, dentate nuclei, pontine nuclei and inferior olives. *Methods:* Case report. *Results:* A 14-month-old male presented with significant motor and linguistic delay. He had no history of developmental regression or seizures, and was a social child. Family history, pregnancy and delivery were unremarkable. His head circumference was below 2nd percentile, whereas weight and height were both below 5th percentile. He had no dysmorphic features. Neurological examination revealed symmetrical pupils with minimal reaction to light, but no nystagmus. Fundoscopic examination demonstrated optic atrophy. Deep tendon reflexes were brisk, and plantar response was extensor bilaterally. MRI revealed pontocerebellar hypoplasia with optic chiasm atrophy. Extensive metabolic workup and karyotyping were normal, as well as screening for vitamins D and E; however, vitamin A was severely low. No extra-CNS malformations were found. Dietary assessment determined his vitamin A intake to be appropriate. *Conclusions:* Our case helps further define the phenotype of this rare abnormality. We also suggest a possible connection between vitamin A deficiency and formation of pontocerebellar hypoplasia, as studies have shown that development of cerebellum and hindbrain patterning is significantly influenced by vitamin A.

P-116

Preservation of language in the ataxic infant in a case of cerebellar agenesis

*FD Jacob (Edmonton) HR Goez (Edmonton)**

Background: Primary cerebellar agenesis is a rare disorder of unknown etiology, with most cases being sporadic. Complete cerebellar agenesis has been associated with other central nervous system abnormalities such as microcephaly and holoprosencephaly. In most cases, language is delayed and speech is often dysarthric. *Methods:* Case report. *Results:* An 8-month-old male presented with

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

ataxia and head titubation, noticed since birth. Ultrasound at 36 weeks gestation revealed enlarged posterior fossa, no cerebellar tissue, a normal corpus callosum and no evidence of hydrocephalus. Family history, pregnancy and delivery were unremarkable. Significant motor delay was noted at both 8 and19 months; however, receptive and expressive language skills were deemed age-appropriate, and his words were clear with no dysarthria. Extraocular movements were full, with bilateral intermittent esotropia. Upon fixing of the head, horizontal nystagmus and saccadic intrusions on smooth pursuit exam were noted. He had mild truncal hypotonia. Truncal ataxia as and dysmetria were present bilaterally and symmetrically. MRI revealed complete cerebellar agenesis with an otherwise normal structural brain. Extensive metabolic screening and karyotyping were normal. *Conclusions:* This case highlights the clinical variability of cerebellar agenesis, as receptive and expressive language skills were intact, and adds to the clinical phenotype of this rare condition.

P-117

Ponto-cerebellar hypoplasia – A misonomer. Fetal MRI facilitates the diagnosis of a degenerative disease

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The pontocerebellar hypoplasias (PCH) are autosomal recessive disorders of pontocerebellar dysgenesis with fetal onset of neurodegeneration and symptoms at birth. We report a case where fetal MR and early neonatal MR aided in the diagnosis of a rapidly degenerative genetic condition and discuss new genetics insights into these diseases. *Case:* A male was born at term to 31 year old mother G5 P3 A1. The parents are consanguineous. Abnormal fetal USS at 22 weeks suggested pontocerebellar hypoplasia. Fetal MRI 29 weeks: small cerebellum, marked hypoplasia of the pons and brainstem. The gyral pattern was immature at 22-23 gestational-equivalent.

At birth he was microcephalic, dysmorphic, and required ventilatory support. Ther was optic nerve atrophy, absent corneal responses and abnormal bulbar function. Motor examination revealed contractures, hypertonicity and increased deep tendon responses. MR day 2: Pontocerebellar atrophy, decrease brain parenchyma and volume loss when compared to in utero MR. This was in keeping with a degenerative process. He died at 25 days. *Discussion:* This case demonstrates the utility of careful in-utero and early neonatal MR comparison which can aide the diagnosis of a degenerative disease. The PCH I and II are the commonest types of this rare disorder and TSEN54 is the commonest mutation. We believe this baby's clinical phenotype however is remarkably similar to 3 siblings reported by Leroy et al.

Leroy et al, Congenital pontocerebellar atropy and telecephalic defects in three siblings: a new subtype. Acta Neuropathol, 2007
Namavar et al, Clinical, neuroradiological and genetic findings in pontocerebellar hypoplasia Brain (2011) 134(1): 143-156.

P-118

Language lateralization in children with congenital and acquired brain lesions

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Children with epilepsy have a higher incidence of atypical, right or bilateral hemisphere language dominance than typical children. The objective of this study was to identify the effects of acquired and congenital brain lesions on language dominance in children.

A retrospective cohort of 64 children (36 male, aged 5-18) with MRI documented brain lesions were examined. All children underwent presurgical fMRI from January 2005 - December 2008 at the Hospital for Sick Children. Routine 1.5 or 3 tesla MRI scanning was performed to investigate for structural abnormalities, and was reported by a pediatric neuroradiologist. Lesion type was classified as congenital or acquired. A minimum of 2 standard language paradigms were used for fMRI language lateralization. fMRI was analyzed using AFNI and rated for lateralization and localization of frontal and temporal language areas. Atypical language lateralization was defined as right or bilateral hemisphere dominance for frontal and/or temporal language areas. Children with acquired lesions were more likely to demonstrate atypical language, 16/32 (50%), than children with congenital lesions, 9/32 (28%). Atypical language was exhibited in 9/22 (41%) children with LT lesions in contrast to 3/16 (19%) with RT lesions ($p<0.05$). For LT lesions, 8/14 (57%) children with acquired lesions demonstrated atypical language compared to 1/8 (13%) with congenital lesions ($p<0.05$). For LF lesions, 3/4 (75%) children with acquired lesions demonstrated atypical language in contrast to 3/8 (38%) with congenital lesions.

Children with acquired brain lesions are more likely than children with congenital lesions to demonstrate right hemisphere or bilateral language dominance.

P-119

COL4A1 mutation in a pediatric patient presenting with a Todd's paresis

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Background: We present a unique case of complete right hemisphere stroke in the context of partial status epilepticus in a pediatric patient subsequently diagnosed with COL4A1 gene mutation. This association has not been previously reported. *Methods:* A retrospective chart and imaging review of paper and electronic records was conducted. *Results:* This patient had a history of neonatal seizures and porencephaly identified on MRI associated with mild hemiparesis. She presented at age six with a secondarily generalized seizure followed by postictal left hemiparesis significantly worse than her baseline. Potential etiologies for anterior and posterior circulation ischemia, triggering factors or associated findings such as encephalitis, lactic acidosis, and right common carotid artery dissection were ruled out. The patient's mother and maternal aunt had congenital porencephaly and hemiparesis, but not seizures. All three individuals were found to have a COL4A1 gene (c.4031G>C) missense mutation. *Conclusions:* This case demonstrates that COL4A1 mutations should be considered in patients with a history of porencephaly who

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

present with seizures of unknown etiology and have accompanying clinical and/or radiological evidence of postictal manifestations that are out of keeping with their initial presentations. The potential pathophysiologic events leading to such an extensive ischemic injury in our patient are discussed.

P-120

Neonatal morbidity and mortality in congenital DM1

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Congenital Myotonic Dystrophy (CDM) is a systemic disease with prominent neuromuscular manifestations caused by a CTG trinucleotide repeat expansion mutation in the DMPK gene. Hypotonia, feeding and respiratory difficulties are evident during the neonatal period. Prolonged ventilation (>30 days) has been implicated as a prognostic indicator of certain mortality. *Methods:* Incident cases of CDM were collected over a five-year period (2005-2010) via the Canadian Pediatric Surveillance Program. Reporting physicians completed forms examining neonatal medical characteristics and complications. *Results:* Thirty-seven cases of genetically confirmed CDM were reported. CTG repeat length ranged from 550-3100 (n=29). 29 and 27 children required feeding assistance and respiratory interventions, respectively. Neonatal morbidities included respiratory (n=13), GI (n=13), orthopedic, CNS, cardiac and infections. 20 children required assisted ventilation between 1 and 186 days. Four were ventilated for ≥ 30 days, with one death at 186 days due to septic shock. Repeat length was correlated with days hospitalized (p=0.015) and in the ICU (p=0.002). Seven children died during infancy (7/38; mortality 19%), four as the result of withdrawal of life support at approximately 1 month. *Conclusion:* Neonatal morbidity and mortality is high among children with CDM1. Increasing CTG repeat size is correlated with increasing time in hospital. Withdrawal of life support is still occurring at 30 days, however, prolonged ventilation (≥ 30 days) was not associated with complete mortality in this sample.

P-121

Is low creatine kinase a nonspecific screening marker for creatine deficiency syndromes?

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Background: The creatine deficiency syndromes (CDS), guanidinoacetate methyltransferase (GAMT), L-arginine:glycine amidinotransferase (AGAT), and creatine transporter (CRTR) deficiencies are inborn errors of the creatine metabolism. *Methods:* Urine guanidinoacetate and creatine-to-creatinine-ratio were measured. The GAMT and SLC6A8 genes were sequenced. *Results:* Case 1: A 4-year-old boy with global developmental delay had markedly elevated urinary creatine-to-creatinine-ratio at age 3 years. Cerebral creatine deficiency in a cranial MR-spectroscopy and a known disease causing (c.1216delTTC; p.F107del) mutation in the SLC6A8 gene confirmed the diagnosis of CRTR. His creatine kinase (CK) was low (45 U/L; reference range 60-305) at the time of diagnosis. Case 2: A 37-month-old girl with developmental regression had markedly reduced creatine in a cranial MR-spectroscopy at age 21 months. Elevated urinary GAA (611 μmol/mmol creatinine; reference range 16-228) and homozygous known disease causing mutation (c. 327G>A) in the GAMT gene confirmed the diagnosis of GAMT deficiency. CK was low (31 U/L; reference range 60-305) at the time of diagnosis. *Summary:* Biomarkers of CDS are not readily and widely available in many centers. We present two patients with CDS who have low CK at the time of diagnosis. This might be a potential screening biomarker with low specificity and sensitivity in CDS.

P-122

Two new patients with GAMT deficiency in British Columbia: a treatable cause of intellectual disability

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Background: Guanidinoacetate-methyltransferase deficiency (GAMTD) is an inborn error of creatine metabolism characterized by intractable epilepsy, global developmental delay (GDD), and movement disorder. Creatine and ornithine supplementation and arginine restricted diet are effective in treating epilepsy and movement disorder. *Methods:* Guanidinoacetate was measured in urine. Creatine was measured by cranial-MR-spectroscopy. GAMT enzyme activity was measured in cultured skin fibroblasts. *Results:* Patient-1 presented with GDD and regression at age 9-month. She was identified by absent creatine peak in a cranial-MR-spectroscopy. Patient-2 presented with GDD and afebrile generalized tonic-clonic seizure at age 13 months. She was identified by elevated urine guanidinoacetate level. Patient-1 was 2-year-9-month and Patient-2 was 2-year-3-month at the time of diagnosis. Both had elevated guanidinoacetate levels in urine, plasma and CSF. Both had none-detectable GAMT activity in cultured skin fibroblasts. Both were treated with creatine (400 mg/kg/d), ornithine (400 mg/kg/d) and arginine restricted-diet (275 mg/d). *Conclusion:* GAMTD is one of the treatable causes of intellectual disability and epilepsy. Successful treatment of GAMTD in an asymptomatic neonate highlights the importance of early diagnosis and treatment to prevent intellectual disability. Patients with GDD and epilepsy should be investigated for this disorder to identify treatable causes.

P-123

Stridor at birth predicts grave outcome in neonates with myelomeningocele

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Background: Stridor, associated with vocal cord paralysis, in neonates with myelomeningocele (MMC) usually appears after birth. Control of hydrocephalus and Chiari malformation (CM) decompression often improve symptoms. Occasionally, stridor presents at birth and may be secondary to maldevelopment or prenatal ischemia of the brainstem, which is less likely to improve with decompression.

In this study we tested the hypothesis that unlike stridor which develops after birth, stridor at birth predicts a dismal outcome, despite aggressive surgical treatment. *Methods:* Retrospective review of newborns with MMC, CM and stridor from 1975 to 2010

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

in our institution was performed. Outcomes of patients with stridor at birth were compared with those who developed stridor later in infancy. Autopsy findings were reviewed when available. *Results:* 6 patients who presented with stridor at birth were identified. Five of six also had other symptoms of brain stem dysfunction. Five had CM decompression and treatment of hydrocephalus, if present, within two weeks after birth. All patients died: three within 1 month, the oldest at 62 months. In 3 patients with autopsies, vernix caseosa meningitis was present. 8 patients presented with stridor later in infancy. CM decompression was done in 7. The mortality rate after CM decompression was worse in patients with stridor at birth than those presenting later with stridor (Chi-square p-=0.015). *Conclusions:* In newborns with MMC, stridor at birth may predict dismal outcome despite CM decompression. Non-operative management may be an option in this population. The severe irreversible brainstem dysfunction may be related to vernix caseosa meningitis.

P-124

Audacious hope for youth with a progressive neuromuscular condition? The need to provide support for the transition to adult care.

SA Poitras (Vancouver) L Straatman (Vancouver)*

The term transition implies an act of change or transformation from one stage to another. For youth 16-20 and their families who live and cope with a progressive neuromuscular condition it becomes a time of apprehension. With increasingly effective health care interventions, these youth are living into adulthood. There is now a greater need to develop strategies to help provide a smooth transition to adult services. The affected youth are developmentally ready to make plans for their futures, but must do so with a more present reality that life "time" is limited. Furthermore they must develop new professional relationships moving from child health programs to adult programs.

The objective is to present a transition planning framework for youth with progressive neuromuscular conditions as they and their family contemplates the process of adjustment to adult care services. Information and research will provide context for the challenges and issues experienced by this population. The adult services system can pose barriers and impede acquisition of developmental norms and their ability to realize their hopes. Provision of guidance, psychological support, resources, funding and advocacy are required to facilitate adjustment and bridge relationships for this population. Pediatric professionals utilizing a transition framework in the community is an instrumental part of supporting youth and their families with decision making and facilitating this process. Paying attention to the "transition" for youth as they mature into young adults will enhance their quality of life and promote adjustment to this stage of development.

P-125

Choroid Plexus Papilloma: A rare presentation with a novel surgical approach

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A 6-week-old boy, born prematurely at 35 weeks' gestational age, presented with hydrocephalus secondary to a choroid plexus papilloma in the third ventricle, extending to the aqueduct of Sylvius and into the fourth ventricle. On admission, he was found to have clinical signs of raised intracranial pressure. MRI revealed a homogeneously enhancing mass primarily in the third ventricle. The initial surgical procedure was insertion of a ventriculo-peritoneal shunt, followed by an endoscopic biopsy, which allowed the surgeons to mobilize the tumour into the right lateral ventricle. This facilitated a subsequent transcortical approach to completely remove the tumor. The authors present a case of choroid plexus papilloma in an uncommon location with a unique surgical approach and a successful outcome with no neurological deficits. We detail our surgical approach and the complexity of approaching a tumor located in the third ventricle of an infant.

P-126

A standardized approach to idiopathic pain in children with neurological conditions

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Background: Children with neurological conditions often experience pain of unknown origin. Some pain sources can be identified through physical examination, laboratory and imaging. Many times no source is found. At that stage, empiric therapies are undertaken to reduce pain/irritability. Unfortunately, there is no standardized approach for treatment. *Methods:* 6 physicians specializing in pediatric pain and/or palliative medicine were recruited to pilot a targeted approach to pain management. To initiate the study, these physicians were presented with a case study of a child with a neurological condition displaying pain-like behaviors. Physicians were asked to list their top 5 medications and the order in which they would trial them. *Results:* 6 expert physicians partly agreed on the drugs to be trialed. There was no consensus on the sequence in which the drugs should be used. *Conclusions:* Because we do not fully understand the disruptions resulting in pain in children with rare neurological conditions, medication choices and sequences are highly empiric, as demonstrated in the study. The lack of consensus leads to ineffectiveness and frustration for families and professionals alike. There is evidence that standardized approaches revised in a continuous quality improvement process can result in better care, and further study is warranted.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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Clinical trajectory and symptoms in progressive conditions.

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Background: Children with progressive neurological or genetic/metabolic conditions and their families experience a complex clinical trajectory and symptoms. Unfortunately, there is a paucity of literature on symptom trajectory describing onset, severity, frequency, assessment, treatment or resolution. *Methods:* A comprehensive, systematic literature search identified research on symptoms for this vulnerable population. The search was carried out using neurological or genetic/metabolic conditions, considered to be both progressive and life-threatening plus one of the following criteria: symptom resolution, assessment, late effects and/or diagnostic methods. Symptoms included pain, psychiatric disorders, fatigue, lethargy, sleep disorders, digestive, respiratory, oral symptoms and body temperature changes. Articles were published in medical journals, and indexed in at least one of the major online databases: MEDLINE, EMBASE, PsycINFO, and Cochrane Library. *Results:* The search yielded 1399 abstracts. Two physicians reviewed each abstract and of these, 161 articles were retrieved for full review. Of these only a few studies met criteria and are included in the final articles selection, and will be presented as relevant and topical for future research. *Conclusions:* There is little guidance regarding symptoms experienced by children with these conditions. Further research is necessary to assist clinicians in assessing and treating symptoms to improve the quality of care for these children.

P-128

CNS Evolutionary Developmental Clues

D Sinclair (Montreal)

The goal in the study of nervous system developmental abnormalities is to, primarily, understand them to a point where we can deduce a remedy and then, secondarily, prevent its recurrence and, perhaps eventually rid these entities entirely from humans.

However, it is my contention that we should also look to these abnormalities for clues as to reasons for their existence in our species. These developmental and genetically acquired dysfunctions are, in fact, signals of selection pressures that have been in play for millions of years and which have shaped the present day development of our nervous system.

So how do we deduce clues to human evolution from anomalies in development, so as to better understand the evolutionary constraints placed upon the hominid species?

Many of the answers lie in the rapidly expanding field of molecular phylogenetics and its power to uncover the temporal changes in genes and proteins between species.

I will briefly review some genetic theory and laboratory analyses that permit genomic comparisons, with attention directed to a few recently studied genes that appear to have had profound affects on determining THE defining feature separating apes and hominids from other simians over the past 2.5 million years – brain size.

The genes that control brain development are good candidates for exploring the genetic basis of brain evolution because evolutionary changes in these genes have the potential to alter the developmental outcome of brain morphology and function.

P-129

Mercedes Benz pattern craniosynostosis: diagnosis, management and outcome

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Background: "Mercedes Benz" pattern craniosynostosis caused by bilateral lambdoid and sagittal synostosis (BLSS) is a rare disorder, characterized by step-like deformity of the occiput, anterior turricephaly and mild brachycephaly. Associated anomalies include Chiari I malformation (CM), hydrocephalus and cranial venous anomalies. Surgical management typically comprises synostectomy and foramen magnum decompression (FMD). Outcomes after surgery are poorly described. The purpose of this study was to review the results of early FMD and synostectomy on hydrocephalus, CM and skull shape in BLSS. *Methods:* We retrospectively reviewed one centre's experience with BLSS with respect to presentation, associated developmental delay, hydrocephalus, CM, anomalous venous drainage of the brain, management strategy and the outcome. *Results:* 5 children with BLSS were managed over 25 years. 4 underwent single stage synostectomy and bony FMD between 3 to 6 months. 4 had CM at presentation. At follow-up (1-9 years) all had asymptomatic tonsillar herniation below the foramen magnum. One developed asymptomatic syringomyelia. Two of four with venograms had cranial venous anomalies, which did not create problems during surgery. None of three patients with ventriculomegaly required ventriculo-peritoneal shunting. Head shape in three of the four operated patients appears normal, although two had prominent frontal bossing in early childhood, which progressively became less obvious. One child, who is a year old, still has prominent frontal bossing. *Conclusions:* Early synostectomy and bony FMD is a safe surgical option for BLSS, and may stabilize CM and hydrocephalus and normalize head shape. MRI follow-up for development of syrinx is advisable.

P-130

Modern multimodality management of aneurysmal bone cysts of the spine in children

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Introduction: Aneurysmal bone cysts (ABCs) are non-neoplastic lesions often found in the pediatric spine. Management is challenging, and may require pre-operative embolization and surgical resection and spinal instrumentation. We summarize our institutional experience and address ABC management challenges in children. *Methods:* We reviewed the clinical, neuroimaging, and pathological features, and treatment outcomes for spinal ABCs treated at the Hospital for Sick Children over the past 10 years. *Results:* We have treated 10 patients (4 male, mean age 9.6 years at presentation) for spinal ABC since 2000. Seven patients presented with axial pain alone while 3 presented with added radiculopathy. There were 3 cervical, 4 thoracic, 2 lumbar, and 1 sacral ABC. Spinal angiography was performed in 5/10 patients. Nine patients underwent surgical resection, and 8/10 were surgically fused. Average intraoperative blood loss was 2200mL. No associated malignancies were found. One patient died from a complication of

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

percutaneous sclerosis. All remaining patients were neurologically intact at mean follow-up of 30.2 months. *Conclusions:* Management of pediatric spinal ABCs remains challenging due to their vascular nature, associated bony destruction, and ongoing spinal growth. Complete resection with instrumentation is often necessary to provide cure and prevent spinal deformity.

P-131

The utility of joint pediatric neurology education retreats

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Background: Canadian pediatric neurology training programs generally accept 1-2 trainees per year. There are no Canadian educational events solely focused on pediatric neurology. *Methods:* All nine pediatric neurology residents from the Children's Hospital of Eastern Ontario and Montreal Children's Hospital were invited to a two-day educational retreat. The first day consisted of expert didactic and interactive lectures from faculty under the umbrella theme of neurogenetics. An observed standardized clinical evaluation (OSCE) reflecting various pediatric neurology topics occurred on day two. Each resident was given a standardized grade. Trainees filled out evaluation forms with respect to the utility of the event. *Results:* 7 residents attended the retreat. Six participants strongly agreed that the teaching sessions were valuable, and agreed that the OSCE stations were a fair way to judge their knowledge level. The mean score for the OSCE was 74.5% (range 55.5 – 92%). The OSCE was able to differentiate senior trainees (PGY 4-5, mean score 85%) from junior trainees (PGY 2-3, mean 66.2%) (p= 0.02). All agreed (2) or strongly agreed (5) that they would attend a similar future event and it would help prepare them for the Royal College Examination. *Conclusion:* This successful retreat encourages future focused pediatric neurology multi-centre educational retreats with the eventual goal of a Canada-wide annual program.

IMAGING

P-132

CTA source images are more reliable than non-contrast CT for detection of early cerebral ischemia

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Background: Very little is known regarding how the reliability of NCCT and CTASI changes over time from stroke onset. To address this, we compared the relationships between CTA- SI and NCCT at different time points after stroke. *Methods:* Acute ischemic stroke patients with identified proximal anterior circulation occlusions (ICA, MCA M1, proximal M2) from the Calgary CT angiography database were studied. The cohort was categorized based on time from stroke onset to scan: 0-90 min n=16); 91-180 min (n=16); 181-360 min (n=16); and >360 min (n=16). NCCT Brain and CTASI were interpreted at separate sessions weeks apart by 2 neuroradiologists and 2 stroke neurologists in random order. ASPECTS was scored to determine extent of early ischemic changes. Reliability was assessed using intraclass correlation coefficients. *Results:* Among 64 subjects included in the study the median NCCT ASPECTS was 7.3 (IQR6-9) and the median CTASI ASPECTS was 5.5 (IQR4-6). The least agreement among readers was in detection of early ischemic changes on NCCT Brain in the ultraearly phase (<90 minutes) (0.48,0.80,0.81,0.89). By contrast the inter-rater reliability of determination of the CTA SI abnormality was similarly high irrespective of the time period.(0.96, 0.94, 0.87, 0.89) *Conclusion:* Using ASPECTS methodology, NCCT brain is not reliable to identify the extent of ischemia in the ultraearly (<90 minutes from stroke onset) phase of stroke. Acute ischemic stroke trials should consider use of CTASI to estimate the extent of early ischemia in the very early phase after stroke when using imaging selection criteria for eligibility.

P-133

Eloquence of region and extent of brain ischemia detected by DWI predicts degree of 24h NIHSS score improvement after arterial recanalization in ischemic stroke.

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Introduction: We hypothesized that improvement of NIHSS score at 24 hrs or delta NIHSS(ΔNIHSS) achieved with recanalization may be influenced by eloquence of region and the extent of brain ischemia within a vascular territory on baseline imaging. *Methods:* From the prospectively collected Keimyung University stroke database, patients with proximal anterior circulation occlusions who recanalized (TIMI 2/3) after IV/IV+IA therapy were analyzed. Two readers evaluated baseline DWI and graded ischemic infarcts to16 anatomical regions as 7 cortical MCA (M1-M6, insula), 5 subcortical MCA (3 corona radiata, basal ganglia; posterior limb of internal capsule (IC)), 2 ACA and 2 PCA. Based on the number of infarct regions involved, patients were categorized into four groups: minimal (0-3 infarct regions), moderate (4-6),large(7-9) and extensive (>9). *Results:* Among 265 patients, subset of 101 patients who recanalized were studied. ΔNIHSS >10 was seen in 25 (25%) of subjects. Median ΔNIHSS was: 12 for minimal involvement, 10 for moderate, 0 for large and -1 for extensive (p=0.007).There was significant improvement in ΔNIHSS in patients with < 6 areas of involvement (p<0.001). The most eloquent regions where involvement predicted less ΔNIHSS were: basal ganglia (4/25, 16%) (OR 0.23 95%CI 0.07-0.75, p=0.01) and posterior limb of IC (1/25, 4%) (OR 0.09, 95%CI 0.01-0.7,p=0.006).The least eloquent region involved showing significant ΔNIHSS was M4 (14/25, 56%) (p=0.01, OR- 3.1 95% CI-1.22-7.93). *Conclusions:* Patients with more than six infarcted regions had marginal improvement in ΔNIHSS. Patients with involvement of basal ganglia and IC have least chance for a significant improvement in NIHSS score.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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Anterior choroidal artery involvement is predictor of poor neurological outcomes in distal ICA occlusions

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Introduction: Distal internal carotid occlusions with ischemic stroke is shown to have poor outcomes despite recanalization therapy. We hypothesized that anterior choroidal artery involvement despite endovascular therapy is one of the factors responsible for poor neurological outcomes. *Methods:* The CT angiogram database of the Calgary stroke program was reviewed for patients with acute ischemic stroke with distal ICA occlusions (Tor L) who received IV+IA/IA therapy were analyzed.CTor MRI done from day 1–7 after the procedure was evaluated for involvement of areas presumed to be supplied by anterior choroidal artery.Internal capsule with or without extension into paraventricular corona radiata interpreted as area supplied by anterior choroidal artery. MRS ≤2 at 3 months was used as good outcome. Recanalization was defined as TIMI 2-3. *Results:*Among 1454 patients in CTA database, 90 patients were identified to have distal ICA occlusions (T/L).41 (45.5%) patients underwent endovascular therapy with or without IV thrombolysis. Post-procedure, internal capsular involvement was seen in 29 (70%) patients. Of these,14 patients (48.27%) achieved recanalization (TIMI2/3) and good neurological outcome was seen in 5 (17%) patients. Among 12 (30%) patients with sparing of anterior choroidal artery territory, 8 (66.6%) patients had good neurological outcomes, with recanalization in all patients. Sparing of the anterior choroidal artery with recanalization post endovascular was strong predictor of good neurological outcomes (RR 3.9, 95% CI 1.5-9.3, p=0.004). *Conclusion:*Anterior choroidal artery territory involvement is common among patients with carotid terminus occlusions. Ischemia to anterior choroidal artery territory is an important predictor of clinical outcome despite recanalization of the ICA.

P-135

Enhancing ASPECTS interpretation on CT through use of an online interactive training tool (aspectsinstroke.com)

M Goyal (Calgary) J Modi (Calgary) BK Menon (Calgary)*

Purpose: The Alberta Stroke Program Early CT Score (ASPECTS) is a 10-point scale that grades the extent of ischemic change within the territory of middle cerebral artery. ASPECTS is a well-validated, reliable scoring system. It has been used as a prognostic and treatment stratifying tool in acute ischemic stroke. We have developed an online teaching tool (ASPECTSINSTROKE.COM), which helps in understanding ASPECTS by providing interactive training. *Methods:* We did a survey to determine the barriers to ASPECTS use by residents, nursing staff and physicians involved in acute stoke patient care. We found that providing interactive training through a website would improve understanding of the scoring system. The website training section consists of interactive examples with brief clinical history, early and follow-up NCCT scans. Expert interpretation is provided at the end of scoring. A feedback system through email is included within the website to further facilitate learning. *Results:* The website was launched in the month of September 2010. A total of 657 visits from September 15, 2010 to January 14, 2011 was recorded with average website usage time per user of 5 minutes ('Google analytics'). The highest visits were recorded from North America followed by Europe and Asia. A trend towards increasing usage over time was noted. *Conclusion:* An interactive web approach is an efficient and effective alternative method for teaching interpretation of early ischemic changes on non-contrast CT using ASPECTS. We plan to validate the usefulness of this approach through an ongoing study.

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Role of biological markers in predicting findings of multimodal thrombus imaging: implications for aetiology and recanalization

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Background: Thrombi exhibit different characteristics on CT (hyperdense MCA "HDMCA" sign), CT angiogram (clot burden score) and gradient echo MR (susceptibility vessel sign "SVS"). These features may predict recanalization and stroke aetiology. Their association with biomarkers like cell count, serum glucose, and d-dimer is unknown. *Methods:* This is a cohort of patients with acute ischemic strokes from the Keimyung Stroke Registry, Korea (2005-2009). Clinical and biochemical data were collected prospectively. Imaging analysis was done at the University of Calgary. *Results:* 264 patients with anterior circulation strokes (46% females, median age 68 years) underwent intraarterial "IA" therapy (combined IV/IA in 115). HDMCA was seen in 44.4% and SVS in 60%. Median clot burden score was 6. Compared to CTA, sensitivity and specificity of HDMCA was 47.2 and 81% and SVS 65.5 and 75% in detecting thrombus. Presence of the SVS was associated with cardio-embolic source (OR 2, p 0.03) and its absence with underlying large artery disease (OR 0.34, p 0.011). HDMCA did not correlate with source of thrombus. Platelet count > 250,000/uL (OR 0.6, p=0.049) and WBC count>10,000/uL (OR 0.4, p=0.014) were associated with lower odds of identifying HDMCA. Hemoglobin levels> 12.5 (OR 2.4, p=0.02) predicted SVS, while each minute delay in the time of onset to MR lowers the odds of SVS by 0.1, p=0.04. Only small clot burden (score>5) predicted recanalization post IA (OR 3.3, p 0.026). *Conclusion:* Thrombi show diverse characteristics on different imaging modalities. HDMCA sign suggests hypocellular thrombi. SVS sign suggests RBC-rich thrombi. Only thrombus burden predicts recanalization.

P-137

Predictors of poor leptomeningeal collateral status in acute ischemic strokes: Analysis of data from the Keimyung Stroke Registry

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Introduction: We plan to comprehensively evaluate factors responsible for reduced leptomeningeal collateral status in patients presenting with acute ischemic strokes. *Methods:* This is a cohort of acute ischemic strokes patients from the Keimyung Stroke Registry, Korea (2005-2009). Clinical and biochemical data were collected prospectively. Imaging analysis was done at the University of Calgary. Outcome was the 90-day modified Rankin Scale. *Results:* 168 patients (mean age 66.8 years, 51.8% male, median NIHSS 14) with M1 MCA± intracranial ICA occlusions were included. Median onset to CT time was 117 minutes (IQR 78-190). Significant

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

leukoaraiosis, measured by the van Swieten scale, was noted in 33/168 (22.3%) patients. The distribution of leptomeningeal collateral status was: poor 33.3%, moderate 48.2%; and good 18.5%. On univariate analysis, increased waist diameter, blood glucose at baseline, HbA1c, INR, serum uric acid and CRP along with low HDL levels were associated with poor collateral status ($p < 0.05$). In a multivariable model, the only predictors of poor collateral status were raised blood glucose at baseline (OR 1.007 95% CI 1.001-1.013, p=0.02) and low serum HDL level (OR 0.96 95% CI 0.94-0.98, p=0.01). Good leptomeningeal collateral status, absence of significant leukoaraiosis and recanalization (TIMI 2-3) were independent predictors of good clinical outcome (mRS 0-2) ($p<0.05$). *Conclusion:* Poor leptomeningeal collateral status is associated with raised blood sugar and low serum HDL level at baseline, suggesting the possibility of endothelial dysfunction in collaterals. Interventions aimed at modulating endothelial dysfunction may alter collateral flow and be an area of future acute stroke intervention.

NEUROVASCULAR/ENDOVASCULAR SURGERY

SUPPORTED BY AN EDUCATIONAL GRANT FROM HOFFMAN LA ROCHE

P-138

Endovascular treatment of giant and large cerebral aneurysms associated with optic pathway compression, case series

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Objective: To evaluate the role of endovascular techniques to improve or arrest visual deterioration caused by large or giant aneurysm. Description of the course of treatment includes various interventional methods, subsequent complications. *Design and Method:* Retrospective, observational case series. Authors reviewed data obtained in 7 patients in whom compression of the intracranial optic nerve / chiasm caused by a Large or giant ICA aneurysm was the only identifiable cause for visual loss. Multiple endovascular treatments were applied according to the patient's clinical needs.The main outcome of this study,measures the patient's visual function, extent of aneurysm closure, and the requirement for additional intervention *Results:* In all 7 patients the endovascular treatment was the preliminary approach.In the initial procedures 3 patients were treated directly with endovascular parent vessel occlusion. 4 patients underwent endovascular coiling with preservation of ICA. After initial coiling 2 patients had good clinical outcome with no need for further procedure. 2 patients required additional intervention including repeat coiling and open surgery.Complete occlusion of the aneurysm using coils was achieved in one patient. Near complete occlusion was the outcome in 3 patients. Follow up mean was 24 months. *Conclusion:* Endovascular coiling with sparing parent vessels is a safe and valid option in the treatment of un-ruptured large and giant cerebral aneurysms with optic pathway compression. The optimal therapy for this particular group of aneurysms is undetermined yet. Growth mechanism of giant cerebral aneurysm is a vital element that could establish a new approach or help in directing the current treatments.

P-139

Spot sign in aneurysmal subarachnoid hemorrhage

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Background: The computed tomogram angiography (CTA) "spot sign" helps identify patients with intracerebral hemorrhage most at risk for continuing bleeding. We sought its presence in patients with aneurysmal subarachnoid hemorrhage (SAH). *Methods:* We examined the non-contrast CT scans and CTAs of all patients with aneurysmal SAH admitted to our institution in 2010. We searched for the spot sign in the subarachnoid, intraventricular, and intracerebral blood. Imaging was reviewed by two experienced neuroradiologists. A parallel and independent chart review was conducted to extract demographic and baseline data. *Results:* Of the 72 patients with SAH, 41 had CT angiograms during their admission. 10 (24%)patients had an associated intraventricular hemorrhage (IVH) and 10(24%) had ICH.

CTA spot sign was negative in all hemorrhages confined to the subarachnoid space and in those with an associated intraventricular extension (0/31 patients). In contrast, in patients with an associated ICH, 9/10 (90%) had positive CTA spot sign within the intra-cerebral hematoma. *Conclusion:* Spot sign was documented in 90% of intra-cerebral hematomas occurring in the context of a subarachnoid hemorrhage. It is negative in patients with SAH or SAH with associated IVH without ICH. Further studies are warranted to validate this finding and explore its clinical significance.

P-140

An unusual case of spinal artery aneurysm presenting as paraplegia: clinical, neuroimaging diagnosis and management

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Introduction: Spinal artery aneurysm is a very rare cause of subarachnoid hemorrhage and is even more rarer in causing myelopathy with paraplegia. *Method:* A 77 years old woman presents with acute onset of paraplegia and has clinical findings of a thoracic myelopathy. An MRI suggests possible vascular malformation at lower thoracic levels with subarachnoid hemorrhage (SAH). A selective spinal artery angiography demonstrates a posterior spinal artery aneurysm ay lower thoracic area. *Result:* The patient was successfully treated with interventional neuroradiology modalities including embolization and coiling. She recovered remarkably and was able to regain a lot of her lower limb motor strength after spending a period of time at Neuro-rehabilitation. *Conclusion:* Spinal artery aneurysms are rare cause of Subarachnoid Hemorrhage (SAH). Dissection is the most common etiology of posterior spinal aneurysms. Workup with spinal MRI/angiography are necessary in highly suspcious cases such as those with repeated SAH and negative cerebral angiograms. Interventional neuroradiology treatment modalities and possible surgery are treatment options for such rare condition.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-141

Endovascular coiling of middle cerebral artery aneurysms: results from a single-center experience

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WITHDRAWN

P-142

Canadian UnRuptured aneurysm Endovascular vs. Surgery: the first 8 months of the CURES trial

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Background: The best treatment for patients with unruptured intracranial aneurysms (UIA) remains uncertain. Surgical clipping is widely considered to provide more consistent and permanent aneurysm exclusion and better long-term protection from hemorrhage but may result in greater morbidity than endovascular treatment. A randomized comparison of the two treatments has not been done. *Purpose:* To compare anatomical results, treatment morbidity and mortality, and long-term clinical outcome of surgical clipping versus endovascular coiling of intracranial aneurysms in a randomized controlled trial. *Methods:* To date, 16 patients with UIAs between 3 and 25 mm have been randomized amongst the five active Canadian centers. So far, all patients enrolled have aneurysms located in the anterior circulation. There has been only one treatment-related complication following coiling of a left middle cerebral artery aneurysm. *Conclusion:* CURES is a two-phase RCT comparing angiographic and clinical outcomes. The lead-in phase aims to verify superior anatomical results of clipping and determine its risks. Phase II will compare clinical outcomes including overall re-treatment rates and bleeding at 5 years.

P-143

Cardiac MRI for the detection of proximal sources of embolism in stroke and TIA patients

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Background: We examined the use of cardiac MRI for detecting proximal sources of embolism in stroke and TIA patients. *Methods:* 22 non-consecutive patients with ischemic stroke (n= 20) or TIA (n = 2) without evidence of large artery atherosclerosis on CT angiography were included. All patients underwent transthoracic echocardiography (TTE), 24 hr Holter monitoring and cardiac MRI (axial HASTE, cine TruFISP, early and delayed contrast enhanced inversion recovery, and 3D MR angiogram of the thoracic aorta and great vessels). Medium and high risk cardioembolic sources were noted according to TOAST classification. *Results:* Cardiac MRI detected 3 medium risk sources (hypokinetic left ventricular segment n=3), 5 high risk sources (left ventricular thrombus n=1; dilated cardiomyopathy n=1; akinetic left ventricular segment n=2; transmural myocardial infarction n=1), one cardioembolic source not included in the TOAST classification (non-compaction cardiomyopathy), and one non-cardiac proximal source of embolism (left subclavian artery stenosis) in 5 patients. TTE detected 4 medium risk cardioembolic sources (mitral annulus calcification n=2; hypokinetic left ventricular segment n=1; atrial septal aneurysm n=1), 3 high risk sources (akinetic left ventricular segment n=2; dilated cardiomyopathy n=1), and one non-cardiac proximal source of embolism (aortic arch atherosclerosis) in 7 patients. *Conclusion:* Cardiac MRI detected 10 potential sources of athero- or cardioembolism in 5 patients; four of these sources were not detected by TTE or CT angiography. Cardiac MRI may be a useful noninvasive test to detect potential proximal sources of embolism.

P-144

Long-term Angiographic recurrence of cerebral aneurysms treated with microsurgical clipping

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Introduction: The recurrence rate of clipped aneurysms is 1-3% and the proportion of these that are symptomatic or require re-treatment is low. The durability of this procedure has become increasingly relevant with advancing endovascular techniques. In this study, we reviewed clipped aneurysms with long-term angiograms to assess aneurysmal re-growth, the natural history of residual aneurysms and formation of denovo aneurysms. *Methods:* From a cohort of patients with ruptured and/or unruptured aneurysms treated with microsurgical clipping between 2004-2007, we included those with 3 year angiograms. In those with residual on post-operative angiography, we determined if there was progression by comparing the post-operative and 3 year angiograms. *Results:* There were 100 aneurysms in 85 patients that showed no evidence of re-growth or re-bleeding. A stable residual neck was demonstrated in 12 patients and 67% of these had complex aneurysms of the middle cerebral artery bifurcation or posterior communicating artery. 83% had residual less than 3mm. All were asymptomatic and did not require re-treatment. There was one patient (1%) with a small recurrence (2mm) that did not require intervention and one patient (1%) with a denovo aneurysm. *Conclusions:* Microsurgical clipping of aneurysms is a durable treatment with a low rate of recurrence and re-bleeding. In our study, we had one patient with recurrence who was asymptomatic and did not require intervention. Those with residual necks did not show angiographic progression or require treatment. The rate of denovo aneurysms was small. We plan to compare this with a similar cohort of endovascularly treated patients.

P-145

The roadmap for the Internal carotid artery in expanded endoscopic endonasal approaches

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WITHDRAWN

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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Bayesian analysis for clinical outcome prediction in aneurysmal subarachnoid hemorrhage

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Introduction: Bayesian techniques allow researchers to incorporate existing state of knowledge regarding population parameters being studied before any new data is integrated. Prior distributions can be vague or highly informative. Non-informative priors represent the lowest level of pre-determined opinion about the parameters being studied. Prior probability distributions are then linked with likelihood functions to generate posterior probability distributions. *Methods:* The Tirilazad Database was analyzed, with inclusion of all 3552 patients and 50 predictor variables. The outcome variable was the patient's Glasgow Outcome Score at 3 months follow-up. Traditional multiple logistic and linear regression techniques were performed. Results from these techniques were compared with those generated from Bayesian statistical analysis. *Results:* Statistically significant predictor variables from regression techniques were entered into the WinBUGS Bayesian program, using non-informative prior normal distributions. Model stability was confirmed, and 95% credible intervals were generated. Consensus was achieved in the statistically significant variables between traditional regression techniques and Bayesian analysis. They include: presence of intraventricular blood, age, admission neurological status, admission angiographic vasospasm, prior history of subarachnoid hemorrhage, history of hypertension, history of myocardial infarction, fever, vasospasm (angiographic, clinical), vasospasm requiring treatment, ruptured aneurysmal size, presence of cerebral edema and development of delayed ischemic neurologic deficits. *Discussion:* Bayesian analysis is a useful technique that, when combined with traditional regression approaches, can increase the robustness of a clinical prediction model for aneurysmal subarachnoid hemorrhage.

P-147

Crossing the Circle of Willis to deploy stents in aneurysm coiling and embolizations

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Background: The PCOM and ACOM may be used as routes of endovascular access across the midline and from anterior to posterior circulation to coil aneurysms or perform embolization. The purpose of our study was to describe our rationale, technique and outcomes in patients who had aneurysms coiled with stent-assistance or embolizations in which the PCOM or ACOM was traversed to provide optimal access. *Methods:* We retrospectivley reviewed our endovascular database to retrieve patients in which stent-assisted aneurysm coiling or embolization was performed via a PCOM or ACOM route. *Results:* Between 2003-2011, there were six patients treated, 5 by stent-assisted coiling and one hemangioblastoma embolization. Three wide-neck basilar tip aneurysms were treated, 2 by placing a stent horizontally from P1-P1 after approaching from the ICA via PCOM and one using a retrograde placement of a stent from basilar artery to PCOM. Two patients had anterior cerebral aneurysms treated, one by telescopic horizontal stent placement form A1 to M1 via ACOM and one by double "Y" stent across the ACOM. One patient had a microcatheter placed form ICA-PCOM-retrograde basilar-AICA for pre-operative embolization of a hemangioblastoma. Five of 6 patients had no complications, one patient had mRS=1 after developing diplopia and a small amount of SAH. *Conclusion:* Stent-assisted coiling via a PCOM or ACOM route is feasible and useful in managing complex aneurysms. These alternate routes are helpful for difficult embolization access issues.

P-148

Combined open and endovascular approach for deployment of flow diversion stent

CM McDougall (Edmonton) C O'Kelly (Edmonton) M Chow (Edmonton)*

Background: We describe an unconventional approach for endovascular therapy and the first use of the Pipeline embolization device (PED ev3 Irvine CA) deployed from direct open carotid puncture access. *Methods/Results:* A 60 year old male presenting with a sixth nerve palsy was found to have a giant cavernous segment internal carotid artery aneurysm. The standard methods of intracranial endovascular access failed secondary to vascular tortuosity. A new approach was required for PED deployment. Conventional surgical exposure of the carotid artery was undertaken for puncture and successful delivery of PED in order to treat the aneurysm. *Conclusion:* This technique has significant disadvantages but allows endovascular access which might not otherwise be possible. The PED can be feasibly deployed using this method.

P-149

Treatment decisions in Canadian post-stroke spasticity patients

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Background: Treatment of post-stroke spasticity (PSS) is dependent on multiple factors. *Methods:* In the BOTOX® Economic Spasticity Trial, adults with PSS were randomised to botulinum toxin A (BoNT-A)+standard care (SC) or placebo+SC as part of their rehabilitation regimen, for up to 2 treatment cycles, followed by an open-label phase of up to 52 weeks. Eligible patients were BoNT-A-naïve, had preserved function and were considered likely to benefit from intervention in the limb to be treated. The treatment patterns for the Canadian cohort are presented here. *Results:* The median (range) time since stroke was 20.4 months (8.4192.9) and 77% of patients demonstrated multifocal (involving both upper and lower extremities) spasticity. Study medication was injected in the lower limb (22.7%), upper limb (13.6%) or both upper and lower limbs (63.6%); right (36.4%) and left sides of the body (63.6%). The median (range) number of physiotherapy sessions/week prior to baseline was 2 (13) and occupational therapy was 1 (13). Mean±standard deviation Resistance to Passive Movement Scale scores were: 17.6±7.53 (overall), 10.7±5.97 (upper limb only), and 7.0±2.36 (lower limb only). *Conclusions:* In this population, overall muscle tone was impaired, and the majority of patients required treatment in both upper and lower limbs.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

P-150

Embolization prior to stereotactic radiosurgery for cerebral arteriovenous malformations: effect on obliteration rates

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Background: Cerebral arteriovenous malformation (AVM) rupture can cause significant morbidity and mortality. Therapeutic modalities include microsurgical resection, endovascular embolization, and stereotactic radiosurgery (SRS). Recent studies have suggested that prior embolization is a risk factor for failure of radiosurgical therapy. This study investigates whether embolization before SRS decreases AVM obliteration rates after radiosurgery. *Methods:* Patients with AVMs undergoing SRS at the Alberta Radiosurgery Centre (2002-2007) were identified. Clinical status pre-SRS and at latest follow-up were evaluated using the modified Rankin Scale (mRS 0-6,0=no symptoms,6=death). The pre-SRS and latest follow-up angiograms were analyzed. Association between pre-SRS embolization and AVM obliteration rates were calculated using the Fisher exact test with $P<0.05$ considered significant. *Results:* Twenty-nine patients were identified: 10 (34.5%) were unruptured and 19 (65.5%) had ruptured. Mean age at time of SRS was 44.2 years with 23.2 months between initial diagnosis and SRS. The majority of AVMs had Spetzler-Martin grade ≤ 3 (93.1%). The clinical outcomes pre-SRS and at latest follow-up were similar (mean mRS = 0.9-1.2, 42.0 months). Pre-SRS embolization was observed in 10 patients (34.5%). Cerebral angiographic follow-up at least 3 years post-SRS was available for 23 patients at a mean of 40.0 months with a 87.0% obliteration rate. Pre-SRS embolization was not associated with AVM obliteration ($P=0.73$). One patient (2.4%) died secondary to recurrent AVM rupture 4 months post-SRS. *Conclusions:* Embolization was not associated with decreased AVM obliteration rate after SRS in this study. SRS, with or without prior embolization, appears to be a safe and effective therapeutic modality for cerebral AVMs.

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Analysis of the neurogenic potential of human umbilical cord matrix stem cells

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We previously characterised a population of stem cells from the human umbilical cord matrix (Wharton's jelly, WJ) obtained at full-term birth. In the present study, the neurogenic differentiation potential of WJ cells was evaluated, using five different physiological protocols, which did not involve the use of toxic reagents or gene transfection. Differentiation was carefully examined using positive controls (human neural stem cells) and negative controls (human newborn fibroblasts), and a combination of immunocytochemistry, Western blotting and PCR to identify a series of indicative markers of the neural lineage. Wharton's jelly mesenchymal stem cells did not differentiate into neural cells using the protocols described. This study also highlights the importance of using the appropriate control cell types in such investigations. Lastly, this study points out that antigenic markers used routinely for neural lineage identification, such as nestin and βIII-tubulin, can also be upregulated under cell stress. It is likely that the transduction of selected genes is necessary for the differentiation of mesenchymal cells into neural ones.

P-152

Gamma Knife Radiosurgery for Cerebral Arteriovenous malformations: results of treatment of 69 consecutive patients at a single centre.

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Background: Treatment for cerebral arteriovenous malformations(AVM) includes stereotactic radiosurgery. This study reports the results of a consecutive series of patients treated with Gamma Knife (GK) for cerebral AVMs at a single Canadian center. *Methods:* We retrospectively reviewed 69 patients treated with GK for cerebral AVM between November 2003 and August 2010. Clinical data, treatment parameters were evaluated. *Results:* 69 patients underwent treatment. Ten were lost to follow-up. Presentations included: seizure (24), hemorrhage (18), persistent headache (12), progressing neurological signs (10), and asymptomatic (9). In 24 patients (34.8%) treatment planning consisted of digital subtraction angiography (DSA), MRI, and CT angiography. We relied on CT angiography and/or MRI scanning only, in 45 patients (65.2%). Forty-one patients had a minimum of 3 years follow up, with an average age of 40.9 years and 58.5% being male. Average dose at the 50% isodose line was 20.3 Gy. Obliteration was observed in 87.8% of this group by MRI, CT, or DSA. Not all obliteration was confirmed by DSA. Of 37 patients with 3 years of follow up and single stage therapy, 35 of 37 (94.6%) demonstrated AVM obliteration. Complications occurred in 12 of 59 (20.3%) patients, and in 11 of 41 (26.8%) with 3 year follow-up. Temporary complications for the 59 included symptomatic cerebral edema (7), seizure (2), and hemorrhage (1). Permanent complications occurred in one patient suffering a cranial nerve V deafferentation, and in 2 patients suffering a hemorrhage. *Conclusion:* GK of cerebral AVM's offers an effective and safe method of treatment, with low permanent complication rate.

VASCULAR NEUROLOGY

SUPPORTED BY AN EDUCATIONAL GRANT FROM HOFFMAN LA ROCHE

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Perinatal arterial stroke: predictors of outcome at 4.5 years of age

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Objective: To assess neurological outcome at 4.5 years in children with arterial stroke diagnosed in the newborn period and to identify predictors of adverse outcome. *Methods:* Twenty-two children diagnosed with perinatal stroke between 1997 and 2002 had serial multidisciplinary standardized follow–up assessments: 5 children to 3 years (mean age: 3.2, range: 2.8-3.6); 17 children to age 4.5 years (mean age: 4.7; range: 4.3-5.6). *Results:* Neurological outcome was as follows: normal (11 children), single disability (3); multiple disabilities (8). Abnormalities included: hemiparesis (6), cognitive impairment (4), language deficit (7), epilepsy (7), visual field defect (4) and hearing impairment (1).

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Adverse outcome occurred in 11/16 children with moderate/large lesions on neuroimaging vs. 0/6 with small lesions and in 4/6 with thalamic/basal ganglia involvement vs. 7/16 without thalamic/basal ganglia involvement.
Although 18/22 newborns had seizures/apnea, adverse outcome occurred in 9/13 children with abnormal background or epileptic activity on neonatal EEG vs. 4/8 with normal EEG. *Conclusions:* Adverse neurological outcome occurs in approximately half of children with arterial stroke diagnosed in the newborn period and includes abnormalities in both motor and cognitive domains. Early neuroimaging and EEG are useful predictors of outcome.

P-154

Long-term outcomes of pediatric ischemic stroke in adulthood

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Background: Childhood stroke is a significant cause of long-term disability. Long-term outcomes are understudied, with follow-up times between 36-48 months. Our aim was to assess the impact of childhood ischemic stroke on young adult's function and independence. *Methods:* Patients diagnosed with arterial ischemic stroke (AIS) and cerebrosinovenous thrombosis (CSVT) from birth to 17 years age were enrolled between 1994-2010 in the Toronto Children's Stroke Registry. We studied outcomes in patients >18 years in a cross-sectional study during 2010. Outcomes included medical, activities of daily living, quality of life, depression, physical and overall function. *Results:* We studied 26 patients; 21 AIS, 5 CSVT. Mean age at stroke was 12.1 years. Mean follow-up time was 11.4 years (3-18 years). Stroke recurred in 4/26 (15%). By modified Rankin Scale, final outcomes were 37% normal, 42% mild, 8% moderate, and 15% severe deficits. Risk factors for poor long-term outcome included: AIS, arteriopathy, and 1-year post-stroke Pediatric Stroke Outcome Measure (PSOM) score ($p<0.05$ univariate). One-year PSOM remained independently predictive ($p<0.0001$ multivariate). Most (77-84%) were independent in driving, relationships, education and employment. *Conclusions:* In adults surviving childhood stroke, outcomes are good in 80%. Most recovery occurs within one-year post-stroke. Focused rehabilitation is critical during this time.

P-155

Large vascular malformation in a child presenting with vascular steal phenomena managed with pial synangiosis

M Ellis (Toronto) D Armstrong (Toronto) P Dirks (Toronto)*

Background: Management of large vascular malformations(VMs) presenting with neurological deficits secondary to vascular steal is challenging and controversial. In many cases, large VMs cannot be cured leaving patients with partially treated VMs, the natural history of which is unknown. Management of Moyamoya disease involves consideration of surgical revascularization in order to enhance blood flow to the hemodynamically compromised hemisphere. *Methods:* A two-year old female presenting with left sided weakness underwent neuro-imaging which demonstrated a 4.5cm VM with complex arterial supply involving vessels of the anterior, posterior, and extracranial circulations. Angiographic evidence of vascular steal involving the right cerebral hemisphere was also noted. *Results:* After two years of conservative management she suffered a large right MCA infarct. After significant clinical recovery, and working on the assumption that the right cerebral hemisphere was hemodynamically compromised as a consequence of VM-related steal, we performed a right-sided pial synangiosis. At 9 months, the post-operative angiogram demonstrated robust neovascularization and the child has not sustained any further ischemic events. *Conclusion:* Given the challenges of treating large VMs presenting with vascular steal and neurological deficits, this report offers an alternative mode of treatment that may augment flow to the hypoperfused cortex and protect against future ischemic events.

P-156

Pilot study of a prospective database for pediatric cerebrovascular malformations at Hospital for Sick Children, Toronto, Canada: Study rationale, methodology and preliminary results

M Ellis (Toronto) G DeVeber (Toronto) P Dirks (Toronto)*

Background: Hemorrhagic stroke is a major cause of mortality and morbidity among Canadian children. Although it accounts for 50% of all pediatric strokes, our understanding of patient risk factors, the natural history of predisposing conditions and the management of these conditions remains poorly understood. Presently, there are no provincial or national registries devoted to the study of hemorrhagic stroke in children. *Objective:* To report preliminary findings from a two-year pilot study of a prospective database for all children with cerebrovascular malformations referred to the Hospital for Sick Children(HSC), Toronto. *Results:* Clinical, radiological, treatment, and outcome data were collected for all patients referred to HSC with a diagnosis of arteriovenous fistula, arteriovenous malfomation, vein of Galen malformation, intracranial aneurysm, cavernous malformation, and Moyamoya syndrome. Consent was obtained for all patients. Case ascertainment analysis will be carried out to compare the enrolled validated cohort to patients identified by ICD codes (non-validated) at our institution with vascular malformations/hemorrhagic stroke. *Conclusion:* This study represents an important step toward improving our understanding of cerebrovascular malformations that predispose children to hemorrhagic stroke. The results of this pilot study may help form the basis for establishing a national registry for children with hemorrhagic stroke.

P-157

The role of computerized tomography angiography contrast extravasation and "Spot Sign" in pediatric acute intracerebral hemorrhage: case illustrations and review of adult literature

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Background: Hematoma expansion is an independent predictor of neurological deterioration, clinical outcome and mortality in adults with primary intracerebral hemorrhage (ICH). Recent efforts have been made to identify specific neuro-imaging features predictive of its occurrence. We discuss the value of computerized tomography angiography (CTA) contrast extravasation and "spot sign" for predicting clinical deterioration in children with ICH. *Methods:* Case #1: 3-year old boy with thrombocytopenia presents with a large left frontal hemorrhage. Post-contrast CT shows diffuse layering of

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

contrast within the hematoma consistent with "contrast extravasation". Following clinical deterioration, the child underwent surgical decompression. Case #2: 6-year old girl with aplastic anemia developed a large right basal ganglia ICH. Post-contrast CT demonstrates a hyperattenuated focus within the hematoma consistent with CTA "spot sign". Six hours later following clinical deterioration, a repeat CT demonstrated hematoma expansion prompting surgical intervention. *Discussion:* The predictive value of CTA contrast extravasation and "spot sign" in the setting of pediatric ICH remains unknown. Here we present two pediatric cases where CTA contrast extravasation and "spot sign" were associated with clinical deterioration requiring urgent surgical intervention. *Conclusion:* CTA contrast extravasation and "spot sign" are potentially valuable neuro-imaging features which may help predict hematoma expansion and clinical deterioration in children with ICH.

P-158

Intracranial and extracranial hemorrhage after IV-tPA at 3-4.5 hours: The VGH Experience

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Background: Evidence from the ECASS III trial has led to an expanded timeframe for administration of intravenous tissue plasminogen activator (IV-tPA) for acute ischemic stroke (AIS). We examined incidence of intracranial (ICH) and major extracranial hemorrhage amongst those at our institution treated with IV-tPA between 3-4.5 hours after symptom onset. *Methods:* Patients receiving IV-tPA for AIS between October 2008-February 2010 were identified retrospectively though our center's case log. Charts were reviewed for those receiving IV-tPA between 3-4.5 hours. We recorded ICH and major bleeding events up to 90 days post-tPA. *Results:* 128 patients received IV-tPA; 26 (20%) were treated within the extended window. Mean time to treatment was 3.4 hours. Five patients were excluded from the analysis (two had aborted infusions; three had intra-arterial intervention). Eight of 21 patients (38%) developed ICH; 2 (9.5%) had symptomatic hemorrhage, 4 (19%) were asymptomatic and 2 had petechial hemorrhage. Four patients had major extracranial bleeding. There was no fatal bleeding. *Conclusions:* One-fifth of patients with AIS treated with IV-tPA at our centre were in the 3-4.5 hour extended window. The incidence of any ICH and symptomatic ICH in this small cohort exceeds that of ECASS III (38% vs. 27% and 9.5% vs. 2.7%, respectively). Patients with ECASS III exclusion criteria were more likely to experience ICH.

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Remodelling of acutely symptomatic unstable carotid atherosclerotic plaques with medical therapy: a single center experience

S Aaron (Calgary) B Menon (Calgary) J Modi (Calgary) S Bal (Calgary) A Demchuk (Calgary) M Goyal (Calgary)

Introduction: We studied the safety profile and efficacy of triple antithrombotic therapy (ASA, clopidogrel and IV heparin) in patients with acutely symptomatic carotid plaques having pedunculated intraluminal thrombi (pILT). *Methods:* A retrospective review of clinical and imaging features of a cohort of patients with strokes/TIAs due to carotid plaques with pILT. All patients received triple therapy within 24 hours of presentation. Two readers blinded to clinical data read baseline and follow-up CTA. Adverse events and imaging changes in plaque characteristics were the outcome measures. *Results:* 17 patients (male 12/17, mean age 65±11 yrs) with anterior circulation strokes 12/17 or hemispheric TIAs 5/17 were studied. Repeat CTA was performed mean 15.3+13.1 days after treatment initiation. Follow up CTAs showed complete resolution of the pedunculated component of the ILTs in all subjects. The mean % stenosis decreased from 62.5% + 18.8% to 44.1% +24.0%. Mean plaque diameter decreased from 0.48±0.11 cm to 0.39 ± 0.15 cm, mean plaque length decreased from 2.12±0.72 cm to 1.73±0.87 cm. During therapy one patient had minor GI bleeding. None had TIAs or strokes. Over a follow-up of 3 months, 1 patient had a hemispheric TIA. Subsequently 11/17 underwent carotid revascularization and 6/17 continued on dual antiplatelets *Conclusion:* In this small series of acutely symptomatic carotid atherosclerotic plaques with pILT, triple therapy appeared to be safe. Triple therapy completely resolved the pedunculated component of ILT and also reduced the degree of stenosis, and plaque diameter. Prospective larger studies are needed to further validate these results.

P-160

Blister-like traumatic carotid-opthalmic pseudoaneurysm in a 15 year old male

FA Haji (London) M Boulton (London) S DeRibaupierre (London)*

Pediatric aneurysms are an uncommon clinical entity, representing less than 5% of all aneurysmal subarachnoid hemorrhage and an incidence of less than 1-3 per million. Of these, aneurysms located at non-branching sites, such as the supraclinoid region of the distal internal carotid artery (ICA), are rare. Both traumatic pseudoaneurysms and blood-blister aneurysms (BBAs) have been described in the intracranial portion of the ICA between the distal dural ring and the ophthalmic artery, although the latter has not been reported in the pediatric population. We report the case of a 15-year-old male who presented following severe cranial trauma with a diffuse basal subarachnoid hemorrhage and limited additional intracranial pathology. CT angiogram demonstrated a small, 2 millimeter blister-like aneurysm of the supraclinoid ICA at a non-branching site that showed rapid enlargement over subsequent studies, despite early endovascular treatment with guglielmi detachable coils, necessitating an open surgical clipping. At the time of surgery, gross pathology of the native internal carotid artery was observed, raising the possibility of a pre-existing blood-blister aneurysm. We review the epidemiology, pathophysiology and diagnostic considerations of these lesions. The endovascular and surgical management of these complex non-branching supraclinoid ICA aneurysms is also discussed.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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Childhood stroke associated with fibromuscular dysplasia

A Kirton (Calgary) M Holland (Calgary) S Benseler (Toronto) A Mineyko (Calgary) C Hawkins (Toronto) D Armstrong (Toronto) A Wade (Calgary) G Sebire (Quebec) A Crous-Tsanaclis (Quebec) G deVeber (Quebec)*

Background: Arteriopathies cause childhood stroke. Fibromuscular dysplasias (FMD) include cerebral-renal arteriopathy with distinct "string-of-beads" angiography. We hypothesized that FMD-associated childhood stroke differs from adult FMD. *Methods:* Children in the Canadian Pediatric Ischemic Stroke Registry and Calgary Pediatric Stroke Programs were screened for FMD or renal arteriopathy (RA). Systematic literature review evaluated the same. Variables included pathological classification, presentations, stroke types, imaging, treatments, and outcomes. The primary aim was a descriptive analysis of pathologically-proven FMD cases followed by comparisons to related conditions. *Results:* We report 81 cases (15 new, 66 literature). For pathologically-proven FMD (n=27), intimal fibroplasia predominated (89%), none had medial fibroplasia. Children presented early (33% <12 months). Angiography demonstrated focal, stenotic arteriopathy (78%) rather than "string–of-beads". RA was present in 63% (92% with hypertension), systemic arteriopathy in 72%, and moyamoya in 35%. Immunosuppression (29%) exceeded antithrombotic (27%) therapies. Outcomes (mean 43 months) were poor in 63% with recurrence in 36%. Clinically-diagnosed FMD (n=31) were more likely older and normotensive with string-of-beads angiography and good outcome. *Conclusion:* FMD causes childhood AIS and is associated with HTN, RA, and systemic arteriopathy. Intimal fibroplasia predominates while "string of beads" angiography is uncommon, suggesting clinical diagnosis is not currently feasible.

P-162

Moya-moya disease with migraine-like presentation in a 37 year old Caucasian female

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Background: We report a case of moya-moya disease (MMD) in a Caucasian patient with a long-standing diagnosis of migraine. *Methods:* Case report *Results:* A 37 year old female presented with a two day history of sensory loss and weakness. She had previously presented with episodic headaches associated with sensory symptoms. Past MRI had shown non-specific white matter changes compatible with migraine. On examination she had weakness and sensory loss in the left upper and bilateral lower limbs. CT and MR angiograms showed termination of the internal carotids distal to the ophthalmic artery bilaterally with prominent collateral circulation. Conventional digital subtraction angiography confirmed the diagnosis of MMD. Investigations ruled out secondary causes of MMD. Diffusion weighted MRI showed restriction in the right hemisphere, and CT perfusion scan showed hypoperfusion of the right frontal lobe. A successful revascularization procedure by direct superficial temporal artery to middle cerebral artery anastomosis was performed. *Conclusion:* MMD is a rare cause of stroke particularly in Caucasians. The presentation is often diverse which can result in misdiagnosis. This case demonstrates the importance of including vascular imaging in younger patients presenting with complicated migraine or symptoms suggestive of stroke. A direct bypass procedure is preferred in symptomatic patients.

P-163

Insular ischemic stroke: clinical presentation and outcome

F Lemieux (Montreal) DK Nguyen (Montreal) M Chevrier (Montréal) L Gioia (Montreal) S Lanthier (Montreal)*

Background: Ischemic stroke limited to the insula is rare and have not been well studied. Our objective is to characterize the clinical presentation and outcome of insular ischemic strokes (IIS). *Methods:* Using the keywords insula(r), infarction, and stroke, we searched the Medline database to identify published IIS cases confirmed by MRI. Minimal extension to an adjacent operculum or subinsular area was accepted. We also reviewed our institutional prospective, consecutive, stroke database to identify additional cases with IIS in 2008-2010. We distinguished the anterior (AIC) and posterior insular cortex (PIC). We collected clinical, demographic, and radiological data. Outcome was determined with the mRS. *Results:* We found 16 published cases of IIS and 3 from our institution. Infarct was limited to the AIC (n=3) or the PIC (n= 10) or affected both (n=6). The five most frequent symptoms were aphasia (n=9), sensory deficit (n=8), dysarthria (n=7), unsteadiness (n=6) and motor deficit (n=4). IIS presentation simulated a lacunar infarct in 4/19 (21%) and a larger middle cerebral artery (MCA) stroke in 11/19 (58%). 11/19 (58%) cases presented findings not commonly associated with lacunar or MCA stroke. The uncommon symptoms included unsteadiness, gustatory or auditory deficits, sensory deficits restricted to specific modalities and somatoparaphrenia without neglect. At 6 months follow-up, mRS was 0 in 4/19 (21%), 1-2 in 7/19 (37%) and unknown in 8/19 (42%). *Conclusion:* IIS presentation is variable. It can mimic lacunar infarct or a larger MCA stroke. Manifestations uncommonly associated with these syndromes can suggest IIS. The outcome is often favorable.

P-164

Stroke associated with HSV meningitis.

*CE Finch (Hamilton) M Fulford (Hamilton) R Ramachandrannair (Hamilton)**

Aim: To report the association between pediatric stroke and HSV meningitis. *Case Report:* 16 month old girl presented with prolonged right focal seizure during a febrile illness of 2 days duration. Examination revealed mild right hemiparesis. MRI Brain showed an arterial ischemic stroke in the left occipital and posterior thalamic region. There was gadolinium enhancement within the ischemic parenchyma and of the meninges adjacent to these areas. CSF showed normal glucose and protein with a cell count of 42 (52% lymphocytes). CSF PCR for HSV-1 was positive. 4 vessel angiography did not reveal any abnormality. Cardiac and thrombophilic work up was normal. She received acyclovir and aspirin. Weakness cleared in 72 hours. There is no residual clinical deficit other than possible right visual field defect at 1 year follow up. *Discussion:* Fever and the gadolinium enhancement on the MRI prompted the lumbar puncture. HSV meningitis is an uncommon etiology for stroke. Vessel wall inflammation is a potential

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

pathology, but angiogram failed to show any vessel abnormality. CNS infection needs to be considered in the work up for pediatric stroke especially in the presence of fever.

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Necrotizing cerebral vasculitis: a rare complication of ulcerative colitis

N Rasool (Halifax) M Schmidt (Halifax) CE Maxner (Halifax) AS Easton (Halifax)*

Background: Neurologic manifestations of ulcerative colitis are rare and include cerebral venous thrombosis, peripheral nerve inflammation and central nervous system vasculitis. Necrotizing cerebral vasculitis is a very rare and fatal complication of ulcerative colitis affecting the cerebral grey and white matter and little is known about the entity and its imaging findings. *Methods:* We report a fatal case of necrotizing cerebral vasculitis in a 50 year old woman with ulcerative colitis. Fourteen days after an exacerbation of her ulcerative colitis, the patient presented with a 24 hour course of progressive neurologic deterioration beginning with a low grade headache and progressing to dysarthria and right sided paralysis,and then to unconsciousness. MRI imaging showed confluent edema and multifocal hemorrhages involving the white matter of the frontal and temporal lobes, the basal ganglia and brainstem. There was prominent swelling and hemorrhage of both hippocampi and the left basal ganglia, with intraventricular extension of hemorrhage from the left basal ganglia. Gadolinium enhancement was seen around the parenchymal hemorrhages and along pial surfaces. *Results:* Autopsy revealed extensive hemorrhagic infarction in the cortex with surrounding edema. Vessels in the cortex and underlying white matter showed mural necrosis and inflammation with edema and fibrin deposition. Some chronic inflammation of the vessels was identified. *Conclusion:* Ulcerative colitis associated cerebral vasculitis is a rapidly progressive, fatal disease. Therefore, individuals with a history of ulcerative colitis and new neurologic deficits should be investigated immediately for the possibility of cerebral angiitis. Current treatments are experimental, although early detection and treatment may result in neurologic recovery.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

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Distinguished Guest Lecture / Conférencier émérite invité
Thursday June 16 / Jeudi 16 juin 08:30-09:15

Andre Picard is one of Canada's top health and public policy observers and commentators.

Currently the public health reporter at The Globe and Mail, he has been a staff writer since 1987. He is also the author of three books and has received much acclaim for his writing and for his dedication to improving healthcare. In 2010, he was awarded a National Newspaper Award as Canada's top newspaper columnist.

He is the public health reporter at The Globe and Mail and author of the best-selling books CRITICAL CARE: Canadian Nurses Speak For Change and THE GIFT OF DEATH: Confronting Canada's Tainted Blood Tragedy. He is also the author of A CALL TO ALMS: The New Face of Charity in Canada.

In 2002, he received the Centennial Prize of the Pan-American Health Organization as the top public health reporter in the Americas. In 2005, he was named Canada's first Public Health Hero by the Canadian Public Health Association.

In 2007, André was awarded a National Newspaper Award for his contribution to a series about cancer care in Canada.

Andre Picard

André Picard est l'un des plus importants observateurs et commentateurs en matière de santé et de politique publique.

Occupant actuellement le poste de journaliste en matière de santé publique pour The Globe and Mail, il est rédacteur attitré depuis 1987. Il est également l'auteur de trois livres et il a été très largement salué pour ses écrits et pour son engagement à améliorer les soins de santé. En 2010, il a reçu une récompense du Concours canadien de journalisme comme meilleur chroniqueur de journal.

Il est le journaliste spécialiste en matière de santé publique pour The Globe and Mail et l'auteur des livres à succès CRITICAL CARE: Canadian Nurses Speak For Change et THE GIFT OF DEATH: Confronting Canada's Tainted Blood Tragedy. Il est également l'auteur de A CALL TO ALMS: The New Face of Charity in Canada.

En 2002, il a reçu le Prix du centenaire de l'Organisation panaméricaine de la santé en tant que meilleur journaliste en matière de santé publique dans les Amériques. En 2005, il a reçu le Prix national de héros de l'Association canadienne de santé publique.

En 2007, André a reçu un prix du Concours canadien de journalisme pour sa participation à une série sur les soins aux personnes atteintes de cancer au Canada.

08:30 **Welcome & Introduction / Accueil et introduction**
Derek Fewer

Please bring this Abstract book with you to the Congress in Vancouver for reference during poster and platform sessions; there will not be another distribution of the Abstract Book at the Congress. This is in response to numerous negative comments about receiving two copies, saves us approximately $10,000 in printing costs and has a positive environmental impact.

In addition, all Congress materials, i.e. Course notes, will be provided to registrants on a CD, mailed to delegates one to two weeks prior to the Congress. Everyone, therefore, will receive all Congress materials - not just for the courses/sessions they attend. We are asking delegates to either bring the CD and their laptop to the Congress and/or to print their required materials ahead of time. No Course materials will be distributed at the Congress. This will save close to $15,000 in printing costs and also has obvious environmental benefits.

Veuillez apporter le présent livret de résumés au congrès à Vancouver aux fins de référence dans le cadre des séances de visionnement des affiches et des séances plateformes. Aucune distribution du livret de résumés n'aura lieu lors du congrès. Nous avons pris cette décision en raison des nombreux commentaires négatifs reçus concernant la réception de deux exemplaires. Nous économisons ainsi environ 10 000 $ en frais d'impression, sans compter l'effet positif sur l'environnement.

Qui plus est, tous les documents relatifs au congrès, comme les notes de cours, seront fournis aux inscrits sur un CD qui sera envoyé par la poste aux délégués entre une et deux semaines avant le début du congrès. Ainsi, tous recevront l'ensemble des documents relatifs au congrès, et non pas seulement ceux concernant les séances et cours auxquels ils participeront. Nous demandons aux délégués d'apporter le CD et leur ordinateur portatif au congrès, ou d'imprimer les documents requis à l'avance. Aucun matériel de cours ne sera distribué lors du congrès. Cela entraînera des économies d'impression de presque 15 000 $, sans parler des bienfaits pour l'environnement.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Maxalt®

rizatriptan benzoate tablets

Maxalt RPD®

rizatriptan benzoate wafers

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: 5-HT_1 Receptor Agonist

INDICATIONS AND CLINICAL USE

Adults

MAXALT® is indicated for acute treatment of migraine attacks with or without aura in adults. MAXALT® is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic, ophthalmoplegic or basilar migraine (see CONTRAINDICATIONS in the Supplemental Product Information section). Safety and effectiveness of MAXALT® have not been established for cluster headache, which is present in an older, predominantly male population.

Pediatrics (<18 years of age)

The safety and efficacy of MAXALT® has not been established in patients under 18 years of age and its use in this age group is not recommended (see WARNINGS AND PRECAUTIONS).

Geriatrics (>65 years of age)

The safety and effectiveness of MAXALT® has not been adequately studied in individuals over 65 years of age. Its use in this age group is, therefore, not recommended (see WARNINGS AND PRECAUTIONS).

Special Populations and Conditions

For use in special populations (see Supplemental Product Information, WARNINGS AND PRECAUTIONS, Special Populations and Conditions).

CONTRAINDICATIONS

MAXALT® is contraindicated in patients with history, symptoms, or signs of ischemic cardiac, cerebrovascular or peripheral vascular syndromes, valvular heart disease or cardiac arrhythmias (especially tachycardias). In addition, patients with other significant underlying cardiovascular diseases (e.g., atherosclerotic disease, congenital heart disease) should not receive MAXALT®. Ischemic cardiac syndromes include, but are not restricted to, angina pectoris of any type (e.g., stable angina of effort and vasospastic forms of angina such as the Prinzmetal's variant), all forms of myocardial infarction, and silent myocardial ischemia. Cerebrovascular syndromes include, but are not limited to, strokes of any type as well as transient ischemic attacks (TIAs).

Peripheral vascular disease includes, but is not limited to, ischemic bowel disease, or Raynaud's syndrome (see WARNINGS AND PRECAUTIONS).

Because MAXALT® may increase blood pressure, it is contraindicated in patients with uncontrolled or severe hypertension (see WARNINGS AND PRECAUTIONS).

MAXALT® is contraindicated within 24 hours of treatment with another 5-HT_1 agonist, or an ergotamine-containing or ergot-type medication like dihydroergotamine or methysergide.

MAXALT® is contraindicated in patients with hemiplegic, ophthalmoplegic or basilar migraine.

Concurrent administration of MAO inhibitors or use of rizatriptan within 2 weeks of discontinuation of MAO inhibitor therapy is contraindicated (see Drug Interactions).

Because there are no data available, MAXALT® is contraindicated in patients with severe hepatic impairment.

MAXALT® is contraindicated in patients who are hypersensitive to rizatriptan or any component of the formulation.

Safety Information

WARNINGS AND PRECAUTIONS

General

MAXALT® should only be used where a clear diagnosis of migraine has been established.

For a given attack, if a patient has no response to the first dose of rizatriptan, the diagnosis of migraine should be reconsidered before administration of a second dose.

Psychomotor Effect

Dizziness, somnolence and asthenia/fatigue were experienced by some patients in clinical trials with MAXALT® (see ADVERSE EVENTS). Patients should be advised to avoid driving a car or operating hazardous machinery until they are reasonably certain that MAXALT® does not adversely affect them.

Cardiovascular

Risk of Myocardial Ischemia and/or Infarction and Other Adverse Cardiac Events

MAXALT® has been associated with transient chest and/or neck pain and tightness which may resemble angina pectoris. Following the use of other 5-HT_1 agonists, in rare cases these symptoms have been identified as being the likely result of coronary vasospasm or myocardial ischemia. Rare cases of serious coronary events or arrhythmia have occurred following use of other 5-HT_1 agonists, and may therefore also occur with MAXALT®. Because of the potential of this class of compounds (5-$HT_{1B/1D}$ agonists) to cause coronary vasospasm, MAXALT® should not be given to patients with documented ischemic or vasospastic coronary artery disease (see CONTRAINDICATIONS). It is strongly recommended that MAXALT® not be given to patients in whom unrecognized coronary artery disease (CAD) is predicted by the presence of risk factors (e.g., hypertension, hypercholesterolemia, smoker, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, or male over 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease. The sensitivity of cardiac diagnostic procedures to detect cardiovascular disease or predisposition to coronary artery vasospasm is unknown. If, during the cardiovascular evaluation, the patient's medical history, electrocardiographic or other investigations reveal findings indicative of, or consistent with, coronary artery vasospasm or myocardial ischemia, MAXALT® should not be administered (see CONTRAINDICATIONS).

For patients with risk factors predictive of CAD, who are considered to have a satisfactory cardiovascular evaluation, the first dose of rizatriptan should be administered in the setting of a physician's office or similar medically staffed and equipped facility. Because cardiac ischemia can occur in the absence of clinical symptoms, consideration should be given to obtaining on the first occasion of use an electrocardiogram (ECG) during the interval immediately following MAXALT®, in these patients with risk factors. However, an absence of drug-induced cardiovascular effects on the occasion of the initial dose does not preclude the possibility of such effects occurring with subsequent administrations.

Intermittent long-term users of MAXALT® who have or acquire risk factors predictive of CAD, as described above, should receive periodic interval cardiovascular evaluation as they continue to use MAXALT®.

If symptoms consistent with angina occur after the use of MAXALT®, ECG evaluation should be carried out to look for ischemic changes.

The systematic approach described above is intended to reduce the likelihood that patients with unrecognized cardiovascular disease will be inadvertently exposed to MAXALT®.

Discomfort in the chest, neck, throat and jaw (including pain, pressure, heaviness and tightness) has been reported after administration of rizatriptan. Because drugs in this class may cause coronary artery vasospasm, patients who experience signs or symptoms suggestive of angina following dosing should be evaluated for the presence of CAD or a predisposition to Prinzmetal's variant angina before receiving additional doses of medication, and should be monitored electrocardiographically if dosing is resumed and similar symptoms recur. Similarly, patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud's syndrome following MAXALT® administration should be evaluated for atherosclerosis or predisposition to vasospasm (see CONTRAINDICATIONS).

Cardiac Events and Fatalities Associated with 5-HT_1 Agonists

MAXALT® may cause coronary artery vasospasm. Serious adverse cardiac events, including acute myocardial infarction, life-threatening disturbances of cardiac rhythm, and death have been reported within a few hours following the administration of 5-HT_1 agonists. Considering the extent of use of 5-HT_1 agonists in patients with migraine, the incidence of these events is extremely low.

Premarketing Experience with MAXALT®

Among the approximately 4200 patients who were treated with at least a single oral dose of either 5 or 10 mg rizatriptan in premarketing clinical trials of MAXALT®, electrocardiac adverse experiences were observed in 33 patients. One patient was reported to have chest pain with possible ischemic ECG changes following a single dose of 10 mg.

Postmarketing Experience with MAXALT®

Serious cardiovascular events have been reported in association with the use of MAXALT®. The uncontrolled nature of postmarketing surveillance, however, makes it impossible to determine definitively the proportion of reported cases that were actually caused by MAXALT® or to reliably assess causation in individual cases.

Cerebrovascular Events and Fatalities Associated with 5-HT_1 Agonists

Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported in patients treated with 5-HT_1 agonists; and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. Before treating migraine headaches with MAXALT® in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms, care should be taken to exclude other potentially serious neurological conditions. If a patient does not respond to the first dose, the opportunity should be taken to review the diagnosis before a second dose is given. It should be noted that patients with migraine may be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, transient ischemic attack).

Special Cardiovascular Pharmacology Studies with Another 5-HT_1 Agonist

In subjects (n=10) with suspected coronary artery disease undergoing angiography, a 5-HT_1 agonist at a subcutaneous dose of 1.5 mg produced an 8% increase in aortic blood pressure, an 18% increase in pulmonary artery blood pressure, and an 8% increase in systemic vascular resistance. In addition, mild chest pain or tightness was reported by four subjects. Clinically significant increases in blood pressure were experienced by three of the subjects (two of whom also had chest pain/discomfort). Diagnostic angiogram results revealed that 9 subjects had normal coronary arteries and one had insignificant coronary artery disease.

In an additional study with this same drug, migraine patients (n=35) free of cardiovascular disease were subjected to assessments of myocardial perfusion by positron emission tomography while receiving a subcutaneous 1.5 mg dose in the absence of a migraine attack. Reduced coronary vasodilatory reserve (~10%), increased coronary resistance (~20%), and decreased hyperemic myocardial blood flow

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

(~10%) were noted. The relevance of these findings to the use of the recommended oral dose of this 5-HT_1 agonist is not known.

Similar studies have not been done with MAXALT®. However, owing to the common pharmacodynamic actions of 5-HT_1 agonists, the possibility of cardiovascular effects of the nature described above should be considered for any agent of this pharmacological class.

Other Vasospasm-Related Events

5-HT_1 agonists may cause vasospastic reactions other than coronary artery vasospasm. Extensive postmarket experience has shown the use of another 5-HT_1 agonist to be associated with rare occurrences of peripheral vascular ischemia and colonic ischemia with abdominal pain and bloody diarrhea.

Increase in Blood Pressure

Significant elevation in blood pressure, including hypertensive crisis, has been reported on rare occasions in patients receiving 5-HT_1 agonists with and without a history of hypertension. In healthy young male and female subjects who received maximal doses of MAXALT® (10 mg every 2 hours for 3 doses), slight increases in blood pressure (approximately 2-3 mmHg) were observed. Rizatriptan is contraindicated in patients with uncontrolled or severe hypertension (see CONTRAINDICATIONS). In patients with controlled hypertension, MAXALT® should be administered with caution, as transient increases in blood pressure and peripheral vascular resistance have been observed in a small portion of patients.

Endocrine and Metabolism

Phenylketonurics

Phenylketonuric patients should be informed that MAXALT RPD® Wafers contain phenylalanine (a component of aspartame). Each 5 mg wafer contains 1.05 mg phenylalanine, and each 10 mg wafer contains 2.10 mg phenylalanine.

Hepatic/Biliary/Pancreatic

Rizatriptan should be used with caution in patients with moderate hepatic insufficiency due to an increase in plasma concentrations of approximately 30% (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the Product Monograph and DOSAGE AND ADMINISTRATION). Since there are no data in patients with severe hepatic impairment, rizatriptan is contraindicated in this population (see CONTRAINDICATIONS and DOSAGE AND ADMINISTRATION).

Immune

Rare hypersensitivity (anaphylaxis/anaphylactoid) reactions may occur in patients receiving 5-HT_1 agonists such as MAXALT®. Such reactions can be life threatening or fatal. In general, hypersensitivity reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens. Owing to the possibility of cross-reactive hypersensitivity reactions, MAXALT® should not be used in patients having a history of hypersensitivity to chemically-related 5-HT_1 receptor agonists.

Neurologic

Care should be taken to exclude other potentially serious neurologic conditions before treating headache in patients not previously diagnosed with migraine or who experience a headache that is atypical for them. There have been rare reports where patients received 5-HT_1 agonists for severe headache that were subsequently shown to have been secondary to an evolving neurological lesion. For newly diagnosed patients or patients presenting with atypical symptoms, the diagnosis of migraine should be reconsidered if no response is seen after the first dose of MAXALT®.

Seizures

Caution should be observed if MAXALT® is to be used in patients with a history of epilepsy or structural brain lesions which lower the convulsion threshold. There have been very rare reports of seizures following administration of MAXALT® in patients with or without risk factors or previous history of seizures (see ADVERSE REACTIONS, Post-Marketing Adverse Reactions, Nervous System in the Supplemental Product Information).

Ophthalmologic

Binding to Melanin-Containing Tissues

The propensity for rizatriptan to bind melanin has not been investigated. Based on its chemical properties, rizatriptan may bind to melanin and accumulate in melanin-rich tissue (e.g., eye) over time. This raises the possibility that rizatriptan could cause toxicity in these tissues after extended use. There were, however, no adverse ophthalmologic changes related to treatment with rizatriptan in the one-year dog toxicity study. Although no systematic monitoring of ophthalmologic function was undertaken in clinical trials, and no specific recommendations for ophthalmologic monitoring are offered, prescribers should be aware of the possibility of long-term ophthalmologic effects.

Renal

Rizatriptan should be used with caution in dialysis patients due to a decrease in the clearance of rizatriptan, resulting in approximately 44% increase in plasma concentrations (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the Product Monograph, and DOSAGE AND ADMINISTRATION).

Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome

Cases of life-threatening serotonin syndrome have been reported during combined use of selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) and triptans. If concomitant treatment with MAXALT® and SSRIs (e.g., sertraline, escitalopram oxalate, and fluoxetine) or SNRIs (e.g., venlafaxine, duloxetine) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea) (see DRUG INTERACTIONS).

Special Populations and Conditions

For use in special populations (see Supplemental Product Information, WARNINGS AND PRECAUTIONS, Special Populations and Conditions).

ADVERSE REACTIONS

(see Supplemental Product Information for full listing)

Adverse Drug Reaction Overview

Serious cardiac events, including some that have been fatal, have occurred following use of 5-HT_1 agonists. These events are extremely rare and most have been reported in patients with risk factors predictive of CAD. Events reported have included coronary artery vasospasm, transient myocardial ischemia, myocardial infarction, ventricular tachycardia, and ventricular fibrillation (see CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS).

Long-Term Safety

In long-term extension studies, a total of 1854 patients treated 16,150 migraine attacks with MAXALT® 5 mg Tablets and 24,043 attacks with MAXALT® 10 mg Tablets over a period of up to 1 year. In general, the types of clinical adverse experiences observed in the extension studies were similar to those observed in the acute studies. However, the incidences of most clinical adverse events were approximately 3-fold higher in extension, as expected, based on increased observation time. The most common adverse events per attack (defined as occurring at an incidence of at least 1%) for MAXALT® 5 mg and 10 mg, respectively, were as follows: nausea (3%, 4%), dizziness (2%, 2%), somnolence 2%, 4%), asthenia/fatigue (2%, 2%), headache (1%, 2%), vomiting (1%, <1%), chest pain (<1%, 1%) and paresthesia (<1%, 2%). Due to the lack of placebo controls in the extension studies, the role of MAXALT® in causation cannot be reliably determined.

To report a suspected adverse reaction, please contact Merck Frosst Canada Ltd. by:

Toll-free telephone: 1-800-567-2594
Toll-free fax: 1-877-428-8675
By regular mail: Merck Frosst Canada Ltd., P.O. Box 1005, Pointe-Claire – Dorval, QC H9R 4P8

DRUG INTERACTIONS

Ergot-Containing Drugs

Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because there is a theoretical basis that these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine or methysergide) and rizatriptan within 24 hours is contraindicated (see CONTRAINDICATIONS).

Monoamine Oxidase Inhibitors

Rizatriptan is principally metabolized via monoamine oxidase, 'A' subtype (MAO-A). In a drug interaction study, when MAXALT® 10 mg was administered to subjects (n=12) receiving concomitant therapy with the selective, reversible MAO-A inhibitor, moclobemide 150 mg t.i.d., there were mean increases in rizatriptan AUC and C_{max} of 119% and 41%, respectively; and the AUC of the active N-monodesmethyl metabolite of rizatriptan was increased more than 400%. The interaction would be expected to be greater with irreversible MAO inhibitors. Drug interaction studies were not conducted with selective MAO-B inhibitors.

The specificity of MAO-B inhibitors diminishes with higher doses and varies among patients. Therefore, co-administration of rizatriptan in patients taking MAO-A or MAO-B inhibitors is contraindicated (see CONTRAINDICATIONS).

Nadolol/Metoprolol

In a drug interactions study, effects of multiple doses of nadolol 80 mg or metoprolol 100 mg every 12 hours on the pharmacokinetics of a single dose of 10 mg rizatriptan were evaluated in healthy subjects (n=12). No pharmacokinetic interactions were observed.

Oral Contraceptives

In a study of concurrent administration of an oral contraceptive during 6 days of administration of MAXALT® (10-30 mg/day) in healthy female volunteers (n=18), rizatriptan did not affect plasma concentrations of ethinyl estradiol or norethindrone.

Other 5-HT_1 Agonists

The administration of rizatriptan with other 5-HT_1 agonists has not been evaluated in migraine patients.

Because their vasospastic effects may be additive, co-administration of rizatriptan and other 5-HT_1 agonists within 24 hours of each other is contraindicated (see CONTRAINDICATIONS).

Propranolol

MAXALT® should be used with caution in patients receiving propranolol, since the pharmacokinetic behavior of rizatriptan during co-administration with propranolol may be unpredictable. In a study of concurrent administration of propranolol 240 mg/day and a single dose of rizatriptan 10 mg in healthy subjects (n=11), mean plasma AUC and C_{max} for rizatriptan were increased by 70% and 75%, respectively, during propranolol administration. In one subject, a 4-fold increase in AUC and 5-fold increase in C_{max} was observed. This subject was not distinguishable from the others based on demographic characteristics. The AUC of the active N-monodesmethyl metabolite of rizatriptan was not affected by propranolol (see DOSAGE AND ADMINISTRATION).

Selective Serotonin Reuptake Inhibitors / Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome

Cases of life-threatening serotonin syndrome have been reported in post-marketing experience during combined use of selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs) and triptans (see WARNINGS AND PRECAUTIONS).

In a pharmacokinetic study with paroxetine and rizatriptan, paroxetine had no influence on the plasma levels of rizatriptan.

Food

Interactions with food have not been studied. Food has no significant effect on the bioavailability of rizatriptan but delays the time to reach peak concentration by an hour. In clinical trials, MAXALT® was administered without regard to food.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

Administration

DOSAGE AND ADMINISTRATION

(see Product Monograph for complete information)

Dosing Considerations

MAXALT® is recommended only for the acute treatment of migraine attacks. MAXALT® should not be used prophylactically. Controlled trials have not established the effectiveness of a second dose if the initial dose is ineffective.

The safety of treating, on average, more than four headaches in a 30-day period has not been established.

Recommended Dose and Dosage Adjustment

ADULTS

MAXALT® Tablets and MAXALT RPD® Wafers

The recommended single adult dose is 5 mg. The maximum recommended single dose is 10 mg. There is evidence that the 10 mg dose may provide a greater effect than the 5 mg dose (see CLINICAL TRIALS in the Product Monograph). The choice of dose should therefore be made on an individual basis, weighing the possible benefit of the 10 mg dose with the potential risk for increased adverse events.

For MAXALT RPD® Wafers, administration with liquid is not necessary. The wafer is packaged in a blister within an outer aluminum pouch. Patients should be instructed not to remove the blister from the outer pouch until just prior to dosing. The blister pack should then be peeled open with dry hands and the wafer placed on the tongue, where it will dissolve and be swallowed with the saliva.

Redosing

Doses should be separated by at least 2 hours; no more than a total of 20 mg (Tablets or Wafers) should be taken in any 24-hour period.

Patients receiving propranolol

A single 5 mg dose of MAXALT® should be used. In no instances should the total daily dose exceed 10 mg per day, given in two doses, separated by at least two hours (see DRUG INTERACTIONS).

Renal Impairment

In hemodialysis patients with severe renal impairment (creatinine clearance <2 mL/min/1.73 m^2), the AUC of rizatriptan was approximately 44% greater than in patients with normal renal function (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the Product Monograph). Consequently, if treatment is deemed advisable in these patients, the 5 mg MAXALT® Tablet or Wafer should be administered. No more than a total of 10 mg should be taken in any 24-hour period. Repeated dosing in renally impaired patients has not been evaluated.

Hepatic Impairment

MAXALT® is contraindicated in patients with severe hepatic impairment (Child-Pugh grade C) due to the absence of safety data. Plasma concentrations of rizatriptan were approximately 30% greater in patients with moderate hepatic insufficiency (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the Product Monograph). Consequently, if treatment is deemed advisable in the presence of moderate hepatic impairment, the 5 mg MAXALT® Tablet or Wafer should be administered. No more than a total of 10 mg should be taken in any 24-hour period. Repeated dosing in hepatically impaired patients has not been evaluated.

Patients with Hypertension

MAXALT® should not be used in patients with uncontrolled or severe hypertension. In patients with mild to moderate controlled hypertension, patients should be treated cautiously at the lowest effective dose.

OVERDOSAGE

No overdoses of MAXALT® were reported during clinical trials.

Rizatriptan 40 mg (administered as either a single dose or as two doses with a 2-hour interdose interval) was generally well tolerated in over 300 patients; dizziness and somnolence were the most common drug-related adverse effects.

In a clinical pharmacology study in which 12 subjects received rizatriptan, at total cumulative doses of 80 mg (given within four hours), two subjects experienced syncope and/or bradycardia. One subject, a female aged 29 years, developed vomiting, bradycardia, and dizziness beginning three hours after receiving a total of 80 mg rizatriptan (administered over two hours); a third degree AV block, responsive to atropine, was observed an hour after the onset of the other symptoms. The second subject, a 25-year-old male, experienced transient dizziness, syncope, incontinence, and a 5-second systolic pause (on ECG monitor) immediately after a painful venipuncture. The venipuncture occurred two hours after the subject had received a total of 80 mg rizatriptan (administered over four hours).

In addition, based on the pharmacology of rizatriptan, hypertension or other more serious cardiovascular symptoms could occur after overdosage. Gastrointestinal decontamination (i.e., gastric lavage followed by activated charcoal) should be considered in patients suspected of an overdose with MAXALT®. The elimination half-life of rizatriptan is 2 to 3 hours (see ACTION AND CLINICAL PHARMACOLOGY in the Product Monograph). Clinical and electrocardiographic monitoring should be continued for at least 12 hours, even if clinical symptoms are not observed.

There is no specific antidote to rizatriptan. In cases of severe intoxication, intensive care procedures are recommended, including establishing and maintaining a patent airway, ensuring adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system.

The effects of hemo- or peritoneal dialysis on serum concentrations of rizatriptan are unknown.

Supplemental Product Information

WARNINGS AND PRECAUTIONS

Special Populations and Conditions

Pregnant Women: In a reproduction study in rats, birth weights and pre- and post-weaning weight gain were reduced in the offspring of females treated prior to and during mating and throughout gestation and lactation. These effects occurred in the absence of any apparent maternal toxicity (maternal plasma drug exposures were 22 and 337 times, respectively, the exposure in humans receiving the maximum recommended daily dose (MRDD) of 20 mg). The developmental no-effect dose was equivalent to 2.25 times human exposure at the MRDD.

In embryofetal development studies, no teratogenic effects were observed when pregnant rats and rabbits were administered doses at the equivalent of 337 times and 168 times, respectively, the human MRDD, during organogenesis. However, fetal weights were decreased in conjunction with decreased maternal weight gain at these same doses. The developmental no-effect dose in both rats and rabbits was 22 times the human MRDD. Toxicokinetic studies demonstrated placental transfer of drug in both species.

There are no adequate and well-controlled studies in pregnant women; therefore, rizatriptan should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Impairment of Fertility

In a fertility study in rats, altered estrus cyclicity and delays in time to mating were observed in females treated orally with an equivalent of 337 times the maximum recommended daily dose (MRDD) of 20 mg in humans. The no-effect dose was 22 times the MRDD. There was no impairment of fertility or reproductive performance in male rats treated with up to 825 times the MRDD.

Nursing Women: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when MAXALT® is administered to women who are breast-feeding. Rizatriptan is extensively excreted in rat milk, at a level of 5-fold or greater than maternal plasma levels.

Pediatrics (< 18 years of age): MAXALT® is not recommended for use in patients under 18 years of age. In a randomized placebo-controlled trial of 291 adolescent migraineurs, aged 12-17 years, the efficacy of MAXALT® Tablets (5 mg) was not different from that of placebo (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the product monograph).

Geriatrics (> 65 years of age): The safety and effectiveness of MAXALT® has not been adequately studied in individuals over 65 years of age. The risk of adverse reactions to this drug may be greater in elderly patients, as they are more likely to have decreased hepatic function, be at higher risk for CAD, and experience blood pressure increases that may be more pronounced. Clinical studies with MAXALT® did not include a substantial number of patients over 65 years of age (n=17). Its use in this age group is, therefore, not recommended.

Special Disease Conditions:
MAXALT® should be administered with caution to patients with diseases that may alter the absorption, metabolism, or excretion of drugs (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions in the product monograph).

Monitoring and Laboratory Tests
No specific laboratory tests are recommended for monitoring patients prior to and/or after treatment with MAXALT®.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Experience in Controlled Clinical Trials with MAXALT®

Typical 5-HT_1 Agonist Adverse Reactions
As with other 5-HT_1 agonists, MAXALT® has been associated with sensations of heaviness, pressure, tightness or pain which may be intense. These may occur in any part of the body including the chest, throat, neck, jaw and upper limb.

Acute Safety
Adverse experiences to rizatriptan were assessed in controlled clinical trials that included over 3700 patients who received single or multiple doses of MAXALT® Tablets. The most common adverse events during treatment with MAXALT® were asthenia/fatigue, somnolence, pain/pressure sensation and dizziness. These events appeared to be dose-related. In long-term extension studies where patients were allowed to treat multiple attacks for up to 1 year, 4% (59 out of 1525 patients) withdrew because of adverse experiences.

Tables 1 and 2 list the adverse events regardless of drug relationship (incidence ≥ 1% and greater than placebo) after a single dose of MAXALT® Tablets and MAXALT RPD® Wafers, respectively. Most of the adverse events appear to be dose-related. The events cited reflect experience gained under closely monitored conditions of clinical trials in a highly selected patient population. In actual clinical practice or in other clinical trials, these frequency estimates may not apply, as the conditions of use, reporting behavior, and the kinds of patients treated may differ.

Table 1
Incidence (≥ 1% and Greater than Placebo) of Adverse Experiences After a Single Dose of MAXALT® Tablets or Placebo (Prior to Subsequent Dose) in Phase III Controlled Clinical Trials†

	% of Patients		
	Placebo	MAXALT® 5 mg	MAXALT® 10 mg
Number of Patients	627	977	1167
Symptoms of Potentially Cardiac Origin			
Upper Limb Sensations*	1.3	1.7	1.8
Chest Sensations*	1.0	1.6	3.1
Neck/Throat/Jaw Sensations*	0.6	1.4	2.5
Palpitations	0.2	0.9	1.0
Body as a Whole			
Asthenia/Fatigue	2.1	4.2	6.9
Abdominal Pain	1.0	1.7	2.2
Digestive System			
Nausea	3.5	4.1	5.7
Dry Mouth	1.3	2.6	3.0
Vomiting	2.1	1.6	2.3
Nervous System			
Dizziness	4.5	4.2	8.9
Somnolence	3.5	4.2	8.4
Headache	0.8	1.8	2.1
Paresthesia	1.0	1.5	2.9
Tremor	1.0	1.3	0.3
Insomnia	0.3	1.0	0.3
Skin and Skin Appendage			
Flushing	1.0	0.6	1.1

*The term "sensations" encompasses adverse events described as pain, discomfort, pressure, heaviness, constriction, tightness, heat/burning sensation, paresthesia, numbness, tingling, weakness and strange sensations.

†Data from Studies 022, 025, 029 and 030.

Table 2
Incidence (≥ 1% and Greater than Placebo) of Adverse Experiences After a Single Dose of MAXALT RPD® Wafers or Placebo (Prior to Subsequent Dose) in Phase III Controlled Clinical Trials†

	% of Patients		
	Placebo	MAXALT RPD® 5 mg	MAXALT RPD® 10 mg
Number of Patients	283	282	302
Symptoms of Potentially Cardiac Origin			
Chest Sensations*	0.4	1.4	1.7
Neck/throat/Jaw Sensations*	0.4	1.4	2.0
Tachycardia	1.1	1.4	0.3
Upper Limb Sensations*	0.4	0.7	2.0
Palpitations	0.4	0.4	1.0
Body as a Whole			
Asthenia/Fatigue	0.4	2.1	3.6
Digestive System			
Dry Mouth	2.1	6.4	6.0
Nausea	5.7	6.4	7.0
Dyspepsia	0.7	1.1	2.0
Acid Regurgitation	0	1.1	0.7
Salivation Increase	0	0	1.3
Musculoskeletal System			
Regional Heaviness	0	0	1.0
Nervous System			
Dizziness	3.9	6.4	8.6
Somnolence	2.8	4.3	5.3
Headache	0.7	1.8	2.0
Insomnia	0	1.4	0.7
Paresthesia	0.4	1.4	3.0
Hypesthesia	0	1.4	0.7
Mental Acuity Decreased	0	1.1	0.3
Tremor	0.7	1.1	0
Nervousness	0.4	1.1	0.7
Respiratory System			
Pharyngeal Discomfort	0	1.1	0.7
Skin and Skin Appendage			
Sweating	0.7	1.1	1.0
Special Senses			
Taste Perversion	1.1	1.4	2.3
Blurred Vision	0	0.4	1.3

*The term "sensations" encompasses adverse events described as pain, discomfort, pressure, heaviness, constriction, tightness, heat/burning sensation, paresthesia, numbness, tingling, weakness and strange sensations.

†Data from Studies 039 and 049.

MAXALT® was generally well-tolerated. Adverse experiences were typically mild in intensity and were transient. The frequencies of adverse experiences in clinical trials did not increase when up to three doses were taken within 24 hours. The incidences of adverse experiences were not affected by age, gender or use of prophylactic medications. There were insufficient data to assess the impact of race on the incidence of adverse events.

Other Events Observed in Association with the Administration of MAXALT®

In the section that follows, the frequencies of less commonly reported adverse clinical events are presented. Because the reports include events observed in open studies, the role of MAXALT® in their causation cannot be reliably determined. Furthermore, variability associated with adverse event reporting, the terminology used to describe adverse events, etc. limit the value of the quantitative frequency estimates provided. Event frequencies are calculated as the number of patients who used MAXALT® 5 mg and 10 mg tablets in Phase II and III studies (n=3716) and reported an event divided by the total number of patients exposed to MAXALT®. All reported events are included, except those

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

already listed in the previous table, those too general to be informative, and those not reasonably associated with the use of the drug. Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are those defined as those occurring in at least 1/100 patients; infrequent adverse experiences are those occurring in 1/100 to 1/1000 patients; and rare adverse experiences are those occurring in fewer than 1/1000 patients.

Body as a Whole

Frequent were warm sensations, chest pain and chills/cold sensations. Infrequent were heat sensitivity, facial edema, hangover effect, abdominal distention, edema/swelling and malaise. Rare were fever, orthostatic effects, and syncope.

Cardiovascular

Frequent was palpitation. Infrequent were tachycardia, cold extremities, hypertension, arrhythmia, and bradycardia. Rare were angina pectoris and blood pressure increased.

Digestive

Frequent was diarrhea. Infrequent were dyspepsia, thirst, acid regurgitation, dysphagia, constipation, flatulence, and tongue edema. Rare were anorexia, appetite increase, gastritis, paralysis (tongue), eructation and glosodynia.

Metabolic

Infrequent was dehydration.

Musculoskeletal

Infrequent were muscle weakness, stiffness, myalgia, muscle cramp, musculoskeletal pain, and arthralgia.

Neurological/Psychiatric

Frequent were hypesthesia and mental acuity decreased. Infrequent were nervousness, vertigo, insomnia, anxiety, depression, euphoria, disorientation, ataxia, dysarthria, confusion, dream abnormality, gait abnormality, irritability, memory impairment, agitation, hyperesthesia, sleep disorder, speech disorder, migraine and spasm. Rare were dysesthesia, depersonalization, akinesia/bradykinesia, apprehension, hyperkinesia, hypersomnia, and hyporeflexia.

Respiratory

Frequent were dyspnea and pharyngeal discomfort. Infrequent were pharyngitis, irritation (nasal), congestion (nasal), dry throat, upper respiratory infection, yawning, respiratory congestion, dry nose, epistaxis, and sinus disorder. Rare were cough, hiccups, hoarseness, rhinorrhea, sneezing, tachypnea, and pharyngeal edema.

Special Senses

Frequent was taste perversion. Infrequent were blurred vision, tinnitus, dry eyes, burning eye, eye pain, eye irritation, ear pain, and tearing. Rare were hyperacusis, smell perversion, photophobia, photopsia, itching eye, and eye swelling.

Skin and Skin Appendage

Infrequent were sweating, pruritus, rash, and urticaria. Rare were erythema, acne, and photosensitivity.

Urogenital System

Frequent was hot flashes. Infrequent were urinary frequency, polyuria, and menstruation disorder. Rare was dysuria.

The adverse experience profile seen with MAXALT RPD® Wafers was similar to that seen with MAXALT® Tablets.

Post-Market Adverse Drug Reactions

The following additional adverse reactions have been reported very rarely and most have been reported in patients with risk factors predictive of CAD: Myocardial ischemia or infarction, cerebrovascular accident.

The following adverse reactions have also been reported:

Hypersensitivity: Hypersensitivity reaction, anaphylaxis/anaphylactoid reaction, angioedema (e.g., facial edema, tongue swelling, pharyngeal edema), wheezing, urticaria, rash, toxic epidermal necrolysis.

Nervous System: serotonin syndrome.

Seizures: There have been very rare reports of seizures following administration of MAXALT® in patients with or without risk factors or previous history of seizures (see WARNINGS AND PRECAUTIONS).

Musculoskeletal: facial pain.

Special Senses: Dysgeusia.

Vascular disorders: Peripheral vascular ischemia

Drug Abuse and Dependence

Although the abuse potential of MAXALT® has not been specifically assessed, no abuse of, tolerance to, withdrawal from, or drug-seeking behavior was observed in patients who received MAXALT® in clinical trials or their extensions. The $5\text{-HT}_{1B/1D}$ agonists, as a class, have not been associated with drug abuse.

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Product Monograph available at
www.merckfrosst.com
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CANADIAN NEUROLOGICAL SCIENCES FEDERATION
FÉDÉRATION DES SCIENCES NEUROLOGIQUES DU CANADA

2011 Congress-at-a-Glance

VANCOUVER

wednesday june 15	07:00 - 08:45	Continental Breakfast
	08:00 - 17:15	Neurosurgery Resident Review – Peripheral Nerve Surgery ***Rajiv Midha, Shobhan Vachhrajani & Ryojo Akagami***
	09:00 - 17:15	Neurology Resident Review – Multiple Sclerosis ***Anthony Traboulsee***
	09:00 - 17:15	ALS ***Charles Krieger***
	09:00 - 12:15	Stroke ***Jeffrey Minuk, Michael Hill & Philip Teal***
	09:00 - 12:15	Update on Frontotemporal Dementia ***Ging-Yuek Robin Hsiung***
	12:30 - 13:45	Lunch & Poster Viewing
	12:30 - 13:45	Co-developed Industry Symposium (Stroke)
	12:30 - 13:45	Co-developed Industry Symposium (Headache)
	14:00 - 17:15	Headache ***Gordon Mackie***
	14:00 - 17:15	Neurocritical Care ***Draga Jichici & Jeanne Teitelbaum***
	14:00 - 17:15	Functional Neurosurgery ***Christopher Honey***
	17:15 – 19:30	Exhibitors Reception
thursday june 16	07:00 - 08:15	Continental Breakfast
	08:30 - 09:15	Distinguished Guest Lecture ***Andre Picard***
	09:30 - 17:00	Child Neurology Day – Tibbles Lecture: ***Ingrid Scheffer***
	09:30 - 12:30	CNS / CSCN Plenary & Chair's Select Abstracts Gloor Lecture: ***Angela Vincent,*** Richardson Lecture: ***Judy Illes***
	09:30 - 12:30	CNSS Plenary & Chair's Select Abstracts Penfield Lecture: ***William Couldwell,*** CNSS Society Lecture: ***Allan Taylor***
	12:45 - 14:00	Lunch, Exhibit & Poster Viewing
	12:45 - 14:00	Co-developed Industry Symposium (Epilepsy)
	12:45 - 14:00	Co-developed Industry Symposium (Neuropathic Pain)
	14:15 - 17:30	Multiple Sclerosis ***Anthony Traboulsee***
	14:15 - 17:30	Neurovascular & Interventional Neuroradiology ***Gary Redekop***
	14:15 - 17:30	EEG ***Seyed Mirsattari***
	14:15 - 17:30	Spine ***Eric Massicotte***
	18:00 - 20:00	Movement Disorders SIG ***Silke Cresswell***
	18:00 - 20:00	Headache SIG ***Gordon Robinson***
	18:00 - 20:00	Neuromuscular Diseases SIG ***Kristine Chapman***
	18:00 - 20:00	Epilepsy Video SIG ***Richard McLachlan***
friday june 17	07:00 - 08:15	Continental Breakfast
	08:30 - 11:15	Platform Sessions
	11:30 - 13:15	Grand Rounds
	13:15 - 15:00	Lunch, Exhibit & Poster Author Stand-by Tours
	13:15 - 15:00	Digital Poster and Exhibit Viewing
	13:15 - 14:45	Scotiabank Private Client Group-Wills & Estate Planning
	15:00 - 18:15	Epilepsy ***Nizam Ahmed***
	15:00 - 18:15	Advances in Neuro-Oncology ***David Eisenstat***
	15:00 - 18:15	Neuro-ophthalmology ***William Fletcher***
	15:00 - 18:15	Advances in Neurobiology ***Zelma Kiss & Peter Smith***
	15:00 - 18:15	Neuromuscular Diseases ***Mike Nicolle & Kristine Chapman***
	15:00 - 18:15	Evidence-Based Neurosurgery in Modern Day Practice ***Brian Toyota, Ramesh Sahjpaul***
	19:00 - 24:00	Presidents' Social Event - A Night at the Commodore

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CANADIAN NEUROLOGICAL SCIENCES FEDERATION
FÉDÉRATION DES SCIENCES NEUROLOGIQUES DU CANADA

Programme du congrès 2011

VANCOUVER

mercredi 15 juin	De 7 h à 8 h 45	Déjeuner continental
	De 8 h à 17 h 15	Revue pour les résidents en neurologie : chirurgie sur les nerfs périphériques ***Rajiv Midha, Shobhan Vachhrajani et Ryojo Akagami***
	De 9 h à 17 h 15	Revue pour les résidents en neurologie : sclérose en plaques ***Anthony Traboulsee***
	De 9 h à 17 h 15	SLA ***Charles Krieger***
	De 9 h à 12 h 15	Accidents vasculaires cérébraux ***Jeffrey Minuk, Michael Hill et Philip Teal***
	De 9 h à 12 h 15	Démence ***Ging-Yuek Robin Hsiung***
	De 12 h 30 à 13 h 45	Dîner et visionnement des affiches
	De 12 h 30 à 13 h 45	Symposium du secteur élaboré conjointement (accidents vasculaires cérébraux)
	De 12 h 30 à 13 h 45	Symposium du secteur élaboré conjointement (Céphalées)
	De 14 h à 17 h 15	Céphalées ***Gordon Mackie***
	De 14 h à 17 h 15	Soins neurologiques intensifs ***Draga Jichici et Jeanne Teitelbaum***
	De 14 h à 17 h 15	Neurochirurgie fonctionnelle ***Christopher Honey***
	De 17 h 15 à 19 h 30	Réception des conférenciers
jeudi 16 juin	De 7 h à 8 h 15	Déjeuner continental
	De 8 h 30 à 9 h 15	Exposé du conférencier invité ***André Picard***
	De 9 h 30 à 17 h	Journée de la neurologie pédiatrique - Conférence Tibbles : ***Ingrid Scheffer***
	De 9 h 30 à 12 h 30	Séance plénière et résumés choisis du président de la SCN/SCNC - Conférence Gloor : ***Angela Vincent,*** Conférence Richardson : ***Judy Illes***
	De 9 h 30 à 12 h 30	Séance plénière et résumés choisis du président de la SCNC - Conférence Penfield : ***William Couldwell*** Conférence de la société SCNC : ***Allan Taylor***
	De 12 h 45 à 14 h	Dîner, visite de l'exposition et visionnement des affiches
	De 12 h 45 à 14 h	Symposium du secteur élaboré conjointement (Épilepsie)
	De 12 h 45 à 14 h	Symposium du secteur élaboré conjointement (Douleur névropathique)
	De 14 h 15 à 17 h 30	Sclérose en plaques ***Anthony Traboulsee***
	De 14 h 15 à 17 h 30	Neuroradiologie d'intervention et neurovasculaire ***Gary Redekop***
	De 14 h 15 à 17 h 30	EEG ***Seyed Mirsattari***
	De 14 h 15 à 17 h 30	Colonne vertébrale ***Eric Massicotte***
	De 18 h à 20 h	Groupe d'intérêt sur les troubles du mouvement ***Silke Cresswell***
	De 18 h à 20 h	Groupe d'intérêt sur les céphalées ***Gordon Robinson***
	De 18 h à 20 h	Groupe d'intérêt sur les maladies neuromusculaires ***Kristine Chapman***
	De 18 h à 20 h	Groupe d'intérêt sur l'épilepsie – vidéo ***Richard McLachlan***
vendredi 17 juin	De 7 h à 8 h 15	Déjeuner continental
	De 8 h 30 à 11 h 15	Séances-plateformes
	De 11 h 30 à 13 h 15	Séances scientifiques
	De 13 h 15 à 15 h	Dîner, visite de l'exposition et présentation des auteurs d'affiches
	De 13 h 15 à 15 h	Visionnement des affiches numériques et visite de l'exposition
	De 13 h 15 à 14 h 45	Séminaire sur les testaments et la planification successorale de la Banque Scotia
	De 15 h à 18 h 15	Épilepsie ***Nizam Ahmed***
	De 15 h à 18 h 15	Neuro-oncologie ***David Eisenstat***
	De 15 h à 18 h 15	Neuro-ophtalmologie ***William Fletcher***
	De 15 h à 18 h 15	Avancées en neurobiologie ***Zelma Kiss et Peter Smith***
	De 15 h à 18 h 15	Maladies neuromusculaires ***Mike Nicolle et Kristine Chapman***
	De 15 h à 18 h 15	Avancées en neurochirurgie ***Brian Toyota, Ramesh Sahjpaul***
	De 19 h à 0 h	Soirée des présidents

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Canadian Neurological Sciences Federation

46th Annual Congress

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If you and your organization would like more information, or would like to discuss how you can partner with CNSF and meaningfully connect with our Congress delegates, please call or email Brett Windle, Corporate Development Coordinator at (403) 229-9544 or brett-windle@cnsfederation.org.

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https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press

INSIGHTS INTO THE MANAGEMENT OF MIGRAINE

ENOUGH WITH MIGRAINE

C'EST ASSEZ

LE POINT SUR LA PRISE EN CHARGE DE LA MIGRAINE

CO-DEVELOPED SYMPOSIUM

WEDNESDAY, JUNE 15TH, 2011 – 12:30 – 1:45 PM

PROGRAM CHAIR

WERNER BECKER, MD, FRCPC
Professor for the Departments of Clinical Neurosciences and Medicine
Director Champ Program, Faculty of Medicine, University of Calgary

PROGRAM SPEAKERS

FARNAZ AMOOZEGAR, MD, FRCPC
Assistant Professor, Department of Clinical Neurosciences
University of Calgary

ELIZABETH LEROUX, MD, FRCPC
Assistant Professor of Neurology
Centre Hospitalier de l'Université de Montréal

LEARNING OBJECTIVES

1. Discuss the optimal therapeutic approach for the treatment of acute migraine;
2. Discuss the optimal prophylactic management of migraine;
3. Review the rationale behind medication choice for prophylaxis of migraine and acute migraine.

Migraine is a common and chronic condition that may be frustrating and debilitating for patients. Selection of an optimal acute treatment approach involves multiple considerations, including the course and severity of the headache and associated migraine symptoms. If a patient experiences frequent or severe attacks that limit functioning and quality of life, prophylactic pharmacologic management may be appropriate.
At this symposium, Canadian experts will provide the latest evidence on the wide range of acute and preventive strategies; and offer clinical insights on individualized treatment selection.

SYMPOSIUM CONJOINT

LE MERCREDI 15 JUIN 2011 – 12 H 30 À 13 H 45

PRÉSIDENT DU PROGRAMME

WERNER BECKER, M.D., FRCPC
Professeur départements de neurosciences cliniques et de médecine
Directeur, Programme Champ, Faculté de médecine, Université de Calgary

CONFÉRENCIÈRES

FARNAZ AMOOZEGAR, M.D., FRCPC
Professeure adjointe du département de neurosciences cliniques
Université de Calgary

ELIZABETH LEROUX, M.D., FRCPC
Professeure adjointe de neurologie
Centre hospitalier de l'Université de Montréal

OBJECTIFS D'APPRENTISSAGE

1. Discuter de la meilleure approche thérapeutique contre la migraine aiguë;
2. Discuter de la meilleure approche prophylactique contre la migraine;
3. Revoir les raisons justifiant le choix des médicaments utilisés pour la prévention de la migraine et le traitement de la migraine aiguë.

La migraine est une affection chronique courante et invalidante. Dans la migraine aiguë, le choix d'un traitement optimal repose sur plusieurs facteurs, dont le cours et la gravité de la céphalée et les symptômes associés à la migraine. En présence de crises répétées ou graves qui limitent la capacité fonctionnelle et la qualité de vie, une pharmacothérapie prophylactique peut être souhaitée.
Lors de ce symposium, des experts canadiens exposeront les données probantes les plus récentes sur les stratégies thérapeutiques de la migraine aiguë et les approches préventives. Ils fourniront les renseignements cliniques nécessaires au choix d'un traitement qui convient à chacun.

This event is co-developed by The Canadian Neurological Society and Merck.

Canadian Neurological Society / Société canadienne de neurologie

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Cette activité a été élaborée conjointement par la Société canadienne de neurologie et Merck.

https://doi.org/10.1017/S0317167100017078 Published online by Cambridge University Press