XXIIIrd Canadian Congress of Neurological Sciences
Québec City, Québec, June 14-18, 1988

PRELIMINARY PROGRAM AND ABSTRACTS

Tuesday, June 14
Canadian Association of Child Neurology
Annual Meeting

The Pediatric Neurology Problems of Eastern Quebec

Agenesis of Corpus Callosum and Polyneuropathy	Jean Mathieu Pierre Langevin Eva Andermann Sterling Carpenter
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS)	Jean-Pierre Bouchard
Craniospinal Dysraphism	Gilles Fortin
Quebec Genetic Network: 20 years of Prevention	Claude Laberge

Topics in Pediatric Neurology

The Major Mitochondrial Disorders MERRF and MELAS	Fred Andermann Eva Andermann Eric Showbridge Sterling Carpenter Douglas L. Arnold
Cerebral Circulation in Childhood Epilepsy	Olivier Dulac
Hot Water Epilepsy	Yukio Fukutama

Wednesday, June 15
Pre-Congress Courses

COURSE 1: Mononeuropathies: selected syndromes
Chairmen: John Stewart and Monique D'Amour

Mononeuropathies - overview	J. Stewart
Pathophysiological mechanisms	R. Gilliatt

Ulnar Nerve

Anatomy and causes of damage	J. Stewart
Electrophysiological diagnosis	W. Brown
When not to do surgery	A. Eisen
When to do surgery	R. Moulton

Peroneal Nerve

Anatomy and causes of damage	A. Wilbourn
Electrophysiological diagnosis	A. Wilbourn
Mini panel discussion on management	R. Jones R. Moulton

Thoracic Outlet Syndromes

Anatomy and clinical presentation	R. Gilliatt
Electrophysiological diagnosis	A. Wilbourn
Mini panel discussion on management	R. Gilliatt A. Wilbourn R. Moulton

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Ischemic Mononeuropathies	
Introduction	M. D'Amour
Small arteries disease	S. Metral
Large arteries disease	A. Wilbourn

COURSE 2: Progress in Epilepsy

Chairmen: Pierre Langevin and Frederick Andermann

Current Clinical Concepts	
Epilepsy Syndromes	Fritz Dreyfuss
Generalized Epilepsy in Infancy and Childhood	Olivier Dulac
Benign Myoclonic Epilepsy (Herpin-Janz Syndrome)	Dieter Janz Gertrud Beck-Managetta
Benign Partial Epilepsies of Childhood	Benjamin Zifkin Henri Gastaut
Photosensitivity	Arnold Wilkins
Recent Advances in the Investigation of Patients	
C.T. and M.R.I. Imaging	Denis Melanson
Positron Emission Tomography	Jerome Engel, Jr.
Neuropathological Basis of Epilepsy	Joachim Meencke
Medical Treatment	
Update on Treatment of Generalized Epilepsy	Frederick Andermann
Update on Treatment of Partial Epilepsy	Jean-Marc St-Hilaire
Update on Drug Interactions	Allan Sherwin
New Drugs: Current Developments and Prospects	Joseph Bruni
Epilepsy and Pregnancy	
Malformations in Offspring of Epileptic Patients	Dirk Lindhout
Growth and Development in Children of Epileptic Mothers	Marja Liisa Granstrom
Pharmacogenetics of Anticonvulsant Drugs	Kevin Farrell
Management of Pregnancy in Epileptic Women	Eva Andermann
Surgical Treatment of Epilepsy	
Classical Surgery Revisited	George Ojemann Linda Ojemann
Identification of Candidates for Surgical Treatment	Warren Blume
Indications for Depth Electrode Studies	Guy Bouvier
Modified hemispherectomy	Jean-Guy Villemure
Callosotomy	André Olivier
Summation	Frederick Andermann

Sponsored by the Canadian League Against Epilepsy and the Canadian Association of Child Neurology

COURSE 3: Functional Neuroanatomy

Chairmen: André Parent and Paul Bédard

Anatomy of Epilepsy	André Olivier
Functional Anatomy of Brain Monoamine Systems	Laurent Descarries
Anatomy of Dementia	Marsel Mesulam
Anatomy of Cognitive Function	Sandra Witelson
Anatomy of Pain	Allan Basbaum
Anatomy of the Motor Pathways	Donald G. Lawrence

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Thursday, June 16

MORNING

WELCOME

Denis Gagnon
Vice-Rector (Research)
Laval University

PRESIDENTAL ADDRESS

Ian Turnbull
President
Canadian Neurosurgical Society

Peter Seland
President
Canadian Neurological Society

Plenary session #1 - Guests of the Congress

Chairman: Gérard LeBlanc

Guest of the Canadian Neurological Society
Claude Bélanger
Laval University, Quebec

Penfield Lecturer
Gilles Bertrand
Montreal Neurological Institute

Guest of the Canadian Society of Clinical Neurophysiologists
Pierre Gloor
Montreal Neurological Institute

Royal College Lecture
George Ojemann
University of Washington, Seattle

Canadian Stroke Society Lecturers
Michael Gent
New York

William Haas
London, Ontario

Kenneth G. MacKenzie Memorial Award 1988
Max Findlay, Toronto

Francis McNaughton Memorial Prize for clinical research in neuroscience
Matthew Hogan, Kingston

André Barbeau Memorial Prize for basic research in neuroscience
Mark Guttman, Vancouver

AFTERNOON

FREE COMMUNICATIONS

Neurosurgery
Cerebrovascular Diseases
General Neurology
Movement Disorders
Child Neurology
Neurophysiology

POSTER PRESENTATIONS

Neurobiology
Neuro-oncology
Neuropsychology
Epilepsy
Neuroradiology
Neuromuscular Diseases

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Friday, June 17

MORNING

Symposium - Recent Advances in Cerebrovascular Disease

Presented by the Canadian Stroke Society
Chairmen: Denis Simard and Vladimir Hachinski

Case for Surgery in Asymptomatic Carotid Lesions	John Norris
North American Symptomatic Carotid Endarterectomy Trial	Henry Barnett
Carotid Doppler - An Increasingly Useful Diagnostic Tool	Joseph D'Alton
Treatment of Subarachnoid Hemorrhage	Bryce Weir

Plenary Session #2

Symposium - Interventional Neuroradiology

Chairmen: Mario Hébert and Reginald Langelier

Diagnostic and Therapeutic Puncture of the Spinal Cord Lesions	Denis Melançon
Spine and Spinal Cord Lesions: Endovascular Treatment	Alex Berenstein
Endovascular Treatment of Meningeal and Cerebral Lesions	Jacques Moret

AFTERNOON

FREE COMMUNICATIONS	POSTER PRESENTATIONS
Neurobiology	Neurosurgery
Neuro-oncology	Cerebrovascular Disease
Neuropsychology	General Neurology
Epilepsy	Movement Disorders
Neuroradiology	Child Neurology
	Neurophysiology

Saturday, June 18

MORNING

Plenary Session #3

Symposium - Transplantation in Parkinson's Disease

Chairmen: Harry Robinson and Donald Calne

Foetal Transplants in Monkeys	A. Fine
Transplantation of Cultured Neurons	Seung Kim
Nerve Growth Factors and Neuron Transplantation	Richard Riopelle
Imaging of Transplanted Dopaminergic Neurons	Wayne Martin
Human Dopaminergic Transplantation: Measurement of Clinical and Biological Effects	Stanley Burns
Scandinavian Experience with Dopaminergic Transplantation and Results	Lars Olson
Technique and Results of Human Dopaminergic Transplants	George Allen
Canadian Experience with Human Dopaminergic Transplantation	Ken Petruk
Panel Discussion	George Allen Ken Petruk E. Flores

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XXIIIrd Canadian Congress of Neurological Sciences Abstracts of the Scientific Program

Neurosurgery (Platform)

THURSDAY, JUNE 16TH - P.M.

1.

Results of Early Versus Delayed Surgery for Ruptured Supratentorial Aneurysms

R.O. HOLNESS, A. PARRENT and K. MACEWEN (Halifax, Nova Scotia)

We analyzed our experience with 100 consecutive patients with subarachnoid hemorrhage from supratentorial aneurysms. Early surgery (i.e., within 72 hours of the bleed) was done in 42 patients, 25 of whom were clinical grade 1 or 2. One patient had a fatal rebleed while awaiting early surgery. Utilizing Glasgow outcome scale for post-operative assessment, 23 patients (92%) and excellent or good outcome, two patients died (8%), and one was poor (4%). Delayed surgery (surgery after 72 hours) regardless of reason for delay was performed on 32 patients, 29 of whom (90.6%) had good or excellent outcome, and 3 of whom (9.4%) had poor outcome or died. There was no appreciable difference in outcome with grade 1 and grade 2 patients, whether operated on early or delayed, despite the higher rate of complications in the delayed group. This included 4 rebleeds (12.5%) and 5 patients with severe spasm.

Early surgery was done on 17 patients with grade 3 and 4 SAH including 6 patients with acute ICH from ruptured MC aneurysms. Ten patients had good or excellent outcomes (59%) versus 4 deaths and 3 poor outcomes (41%). This contrasts with the results of delayed surgery in grade 3 and 4 patients. Surgery was possible in 22 of 26 cases (the other 4 expiring from rebleeds or ischaemia before surgery). Of the 22 patients on whom delayed surgery was done, 12 (46%) had a good or excellent outcome versus 6 poor outcomes and 4 deaths (54%). The most significant factor in this latter group was the high rebleed rate (7 out of 26, i.e., 27%).

Our analysis of this experience shows that early surgery in our hands provides at least as good results in good grade patients and superior survival figures in poor grade patients largely by prevention of rebleeds. There was no significant difference in the distribution of aneurysms in various sites of the anterior circulation in the two groups being compared. Further analysis of our data will be presented including long-term results and discussion of acute hydrocephalus treatment of which correlated with the good outcome seen in the early surgery group.

2.

Intraoperative Monitoring of Sensory Evoked Potentials During Aneurysm Surgery

F. GENTILI, H. GHATE and F. SHICHIJO (Toronto, Ontario)

The purpose of the present study was to determine the value of intraoperative recording of sensory evoked potentials (SEP), as a technique for monitoring brain function and for predicting postoperative neurological deficit. Intraoperative monitoring of SEP (somatosensory), brainstem auditory has been carried out using a standard protocol in 75 patients. The data was analysed with respect to waveform morphology, amplitude, latency and their derived variables. Based on retrospective data in over 50 patients, tolerence limits and a grading for SEP changes has been established (Grade I-IV). SEP changes have been closely correlated with postoperative neurological deficit following aneurysm surgery, (sensitivity 87.5%, specificity 83%). Minor changes (Grade I and II) in SEP parameters were seen in the majority of patients monitored and were not associated with postoperative neurological deficit. Grade III and IV changes in SEP parameters were associated with postoperative neurological deficit. Grade III and IV changes in SEP parameters were associated with immediate postoperative deficit or delayed ischemic events in 97% of patients. Persistent Grade III and IV changes were associated with permanent deficits in 75% of patients. Grade III and IV changes that were reversible were associated with good recovery of immediate postoperative deficit in all patients when assessed at 3 months. The cortical wave was lost for periods ranging from 3-35 minutes. Loss of major cortical wave for a greater 20 minutes was invariably associated with immediate postoperative deficit. Our results suggest that continuous monitoring of evoked potentials provide a reliable and objective intraoperative assessment of brain function and so help in reducing the incidence of neurological morbidity during aneurysm surgery. The pattern and reversibility of SEP changes are highly prognostic with regard to long-term outcome in patients with immediate postoperative deficit.

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3.

Basilar Fenestration Aneurysms

G.G. FERGUSON, C.G. DRAKE and S.J. PEERLESS (London, Ontario)

Basilar fenestration aneurysms arise at the proximal carina of a partial duplication of the basilar artery, and were first reported as a curiosity in 1979. These aneurysms provide a major surgical challenge because of their location and frequently awkward projections, and are of particular interest in that a detailed examination of their anatomy supports the theory that intracranial aneurysms arise at points of hemodynamic stress. Re-examination of our case material indicates that most (possibly all) aneurysms in the region of the vertebral-basilar junction arise in relationship to a fenestration.

Our experience extends to 27 cases. The mean age at presentation was 43 years. Twenty-four patients presented with SAH, 2 with brain stem compression, and in 1 the aneurysm was incidental. The majority of the aneurysms were small and 25/27 occurred in the proximal basilar artery immediately beyond the vertebral junction. Twenty-six patients were treated surgically by a variety of approaches (19 suboccipital, 3 transtentorial, 4 transmastoidal). In every instance the aneurysm arose at the proximal crotch of the bifurcation formed by the fenestration. Satisfactory results were obtained in 21/27 cases, which is similar to the results for 38 cases previously classified as V-B junction aneurysms. The first fenestration aneurysm in our series was recognized in 1975, and since 1985, 14 of 16 aneurysms at the region of the V-B junction have been noted to arise at a fenestration.

Recognition of the frequency of fenestration aneurysms in the region of the V-B junction should help the surgeon to avoid confusion regarding the anatomy of the aneurysm during its dissection, and further contributes to our understanding of the pathogenesis of intracranial aneurysms.

4.

Subarachnoid Hemorrhage of Unknown Etiology

L. LALIBERTE, J.-M. BOUCHARD and F. BEDARD (Québec City, Québec)

A group of 68 patients with spontaneous subarachnoid hemorrhage (SAH) of unknown etiology was studied retrospectively. They represent 11.2% of a larger group of 499 patients with SAH caused by a ruptured aneurysm and treated at l'hôpital de l'Enfant-Jésus from January 1980 to January 1988. Men and women were equally affected and the mean age was 46.

The headache was occipital in location (56%) with moderate meningeal signs (82%). A positive CT scan was found in 41% and two-third of these scans showed predominantly medial bleeding in the interpedoncular and parasellar cisterns. The initial angiogram was normal in 60% without any vascular abnormality or spasm. Of these patients, 26 were submitted to a second routine angiogram and 10 of them had spasm either on the basilar artery or the anterior part of circle of Willis. This spasm had disappeared on a third angiogram. None of these patients had clinical signs of vasospasm.

Of the remaining 40% of patients that had an initial abnormal angiogram, seven patients had an infundibulum or a mild to moderate vasospasm. No aneurysm was found on repeated angiogram in any of these 68 patients.

In conclusion, this study confirms a typical pattern of presentation and evolution for a sub-group of patients with SAH of unknown etiology. For these patients, we suggest that a single complete angiogram is sufficient. If doubt persists, a second angiogram has to be done on a 10 day basis and may show moderate spasm on or near the basilar artery. Further studies are needed to determine the causes of this type of SAH and confirms these observations.

5.

Selective Suboccipital Transmeatal Vestibular Nerve Section for Meniere's Disease

G. MOHR, J.J. DUFOUR and L. GIRARD (Montreal, Quebec)

The total vestibular neurectomy remains the procedure of choice for non-responding Meniere's disease. Considering the bilateral involvement and the progressive partial hearing impairment, it seems justified to preserve the cochlear function. Numerous definitive approaches to destroy peripheral organ innervation have been described, although the efficacity of the vestibular neurectomy proves superior. The surgical techniques resume to either the superior temporal (transtemporal) or posterior fossa approach (retrolabyrinthine or sub-occipital) depending on whether the via is ante or retrosigmoid.

The authors propose the sub-occipital retrosigmoid technique with opening of the internal auditory canal. Twenty patients operated between 1980-1987 in neurotological collaboration are discussed.

The main advantages of this procedure are:

— precise identification of the vestibular nerves with the internal auditory canal.
— complete section proximal to Scarpa ganglion
— cessation of vertigo
— excellent compensation
— cochlear function preserved in most cases
— low incidence of complications

6.

Surgical Management of Giant Pituitary Adenomas

G. MOHR, J. HARDY, R. COMTOIS and H. BEAUREGARD (Montreal, Quebec)

From 1962 through Oct. 1987, 77 patients with "Giant" pituitary adenomas (SSE types C and large D) were treated surgically, representing 9.6% of 800 cases: 53 cases of NON SECRETING adenomas and 24 cases of SECRETING adenomas including 13 Prolactinomas, 7 Somatotropic, 1 Corticotropic, 2 Gonadotropic and 1 thyreotropic adenomas.

A total of 99 surgical procedures was carried out in 77 patients: a single transsphenoidal (T.S.) operation was performed in 57 patients (74%), 6 of which had already undergone previous surgery elsewhere. Early T.S. re-operations within 2 months were done in 8 patients including 2 two-staged procedures, 4 post-op hematomas, 1 CSF-leak and 1 chiasmapexy; 9 patients underwent a late re-operation for residual of recurrent tumor and 3 further patients were submitted to a craniotomy after one or more T.S.

From 48 patients with adequate follow-up, 19 (39%) showed residual or recurrent tumor after first T.S. operation, either based on biological data or on CT-Scan, and 12 of these underwent repeat surgery. Radiotherapy was given to 23 of these 48 patients. Bromocriptine was administered post-operatively to 6 of 14 secreting adenomas with adequate follow-up.

Visual function was assessed in 63 patients after surgery: 31.7% showed total recuperation, 57% partial recuperation and 8% no change, whereas 1 patient became worse. Post-operatively, major hypopituitarism (ACTH or more) occurred in 42.6% patients, minor hypopituitarism (TSH, HGH, LH-FSH) in 24% and 32.7% had no hormonal deficit.

7.

Petrous Meningiomas: A Review of Seventeen Cases

L. MACDONALD, P. MULLER, W. TUCKER and A. HUDSON (Toronto, Ontario)

Seventeen patients with petrous meningiomas were retrospectively reviewed; the average follow up was 5 years. There were 15 females and two males; their ages ranged from 42 to 68 years. The most common clinical presentation was headaches and 8th nerve dysfunction and the average duration of symptoms was 6 years. Computed tomography was performed in 15 cases. The mean tumor size was 2.5 cm (range 0.5-4 cm). Intratumoral calcification was visible on the CT of 4 patients. Also, 4 cases had abnormalities of the petrous bone present on CT bone window settings, 2 with bony erosion of the petrous apex and 2 with flaring of the porous acousticus. Meningioma was suspected preoperatively in 10 of 15 patients. The most common site of tumor origin was at or medial to the porous acousticus.

There was no operative mortality after initial resection. Complete excision was obtained in 12 cases. Postoperative morbidity included increased hearing loss in 6 patients, permanent facial nerve palsies in 4, corneal hypethesia in 3 and cerebrospinal fluid fistulae 2.

There have been 4 tumor recurrences, 2 in those patients where a complete resection was anticipated. Two of the 4 died after re-operation. There was one late death from a brain abscess secondary to cecal perforation by a ventriculoperitoneal shunt.

Of these 17 patients, 14 are alive at an average follow up of 5 years. It seems justified to recommend initial radical surgical excision of these benign tumors where possible in order to minimize tumor recurrence.

8.

Stereotactic Biopsy of Brain Lesions: Indications and Complications

M. BERNSTEIN (Toronto, Ontario)

Stereotactic surgery is an important tool in the management of patients with mass lesions of the brain. Between January 1986 and December 1987 the author performed 75 stereotactic procedures - 20 for Iodine-125 interstitial brachytherapy, 5 for aspiration of cystic structures of known histology (4 recurrent tumor cysts, 1 abscess), and 50 for biopsy of a new intracranial mass lesion. Regarding indications for stereotactic biopsy, 35 patients had lesions which were considered too deep or in too eloquent brain for safe open surgery. Eight had multiple lesions and 7 had lesions which were too diffuse or indistinct for open surgery.

A definitive diagnosis was established in 46 cases (92%). In the other 4 abnormal tissue was obtained and certain important differential diagnoses were excluded but a definitive pathological diagnosis could not be made. The pathological diagnoses were as follows: astrocytoma grade IV - 16, astrocytoma grade III - 9, astrocytoma grade II - 11, metastatic tumor - 5, lymphoma - 3, epidermoid tumor - 1, pineocytoma - 1, and inflammatory tissue - 4 (probable toxoplasmosis in 3 and non-infectious in 1). The 3 patients with inflammatory lesions suggestive of toxoplasmosis all were HIV-I-positive.

Neurological complications were defined as any increase in neurological deficit which was attributable to the biopsy: there were 5 such cases for an overall complication rate of 10%. Three patients sustained intratumoral hemorrhages, and 2 patients sustained increased neurological deficit unrelated to hemorrhage which resolved in time.

It is concluded based on this small series that stereotactic surgery is a powerful tool for the neurosurgeon and specifically neuro-oncologist; however, it does carry significant risks which may be underestimated in the literature.

9.

La Causalgie Mineure et les Membres Fantômes Douloureux à Caractère Névralgique: Leur Traitement par Stimulation Epidurale

S.N. MARTINEZ, P. MOLINA-NEGRO and N.T. TRAN (Montréal, Québec)

Depuis 1979, 197 patients référés au Centre de la Douleur de l'Hôpital Notre-Dame ont été traités par implantation d'électrodes épidurales ou cérébrales profondes.

L'étude concernée porte sur 33 de ces patients:

a) 25 patients ayant une causalgie mineure dont 13 cas au niveau des membres supérieurs et 12 cas au niveau des membres inférieurs;
b) 8 patients ayant un membre fantôme douloureux avec sensation algique dans le même territoire nerveux depuis le début de la pathologie.

La technique d'implantation et les résultats de la stimulation seront présentés.

10.

Neurotization Procedures for Brachial Plexus Root Avulsion

T.P. DOORLY and A.R. HUDSON (Toronto, Ontario)

More than 70% of patients with supraclavicular plexus lesions have one, several or all roots avulsed. Such lesions preclude spontaneous functional recovery and are not amenable to conventional techniques of nerve repair, but may be helped by nerve transfer procedures. Neurotization procedures involve the transfer of the proximal stump of an intentionally transected healthy nerve (motor or sensory) into the distal stump of an avulsed nerve, usually with an interfasicular nerve graft between donor and recipient stumps.

We have reviewed 38 patients with brachial plexus injury who have been followed for more than 18 months after neurotization procedures. There were 34 males and 4 females. Ages ranged from 14 to 34 years. 27 patients (71%) sustained their injury following a motorcycle accident. Patients were selected for neurotization procedures after clinical, electrophysiological and radiological tests, combined with surgical exploration in the majority, demonstrated lesions otherwise unrepairable. Age and motivation of the patient, time since injury and condition of the limb were important considerations.

To restore motor function, the 2nd to 5th intercostal nerves were isolated and anastomosed to the musculocutaneous, axillary, median, ulnar or radial nerves, depending on the patient's deficit. Best results were obtained with intercostal to musculocutaneous transfers with 48% of patients achieving voluntary contraction against gravity and resistance. In 14 patients with anaesthetic hands, the cervical plexus was anastomosed to either the median or ulnar nerves. Protective sensation was restored in 44%. Technical details of this surgery will be discussed.

In carefully selected patients neurotization procedures can avoid amputation and convert a devastating disability into a functionally useful limb.

11.

Spinal Cord Concussion

T.J. ZWIMPFER and M. BERNSTEIN (Toronto, Ontario)

Concussion is a clinical syndrome, usually traumatic in origin, characterized by immediate neurological dysfunction which is fully reversible. Cerebral concussion has been well studied clinically and has been reproduced experimentally. In comparison, spinal cord concussion (SCC) remains a confusing and difficult area due to the lack of clinical and experimental data. We undertook a retrospective chart review of SCC injuries in an attempt to characterize the clinical and radiological features, to identify any predisposing factors, to obtain follow-up and to form a management plan.

A spinal cord injury was classified as a SCC if the following four criteria were met: (i) trauma immediately preceded the onset of deficits, (ii) neurological deficits were documented and consistent with spinal

cord involvement, (iii) complete recovery by 48 hours post-injury and (iv) the absence of functional or hysterical features.

Nineteen cases were identified, the majority in young males. Athletic injuries and falls were the most common mechanisms of injury. The cervical cord was involved in 16 cases and 3 at the thoracolumbar junction. The majority (14/19) presented with a combined sensorimotor deficit. All patients were treated with bedrest and spinal immobilization until fully recovered. All had complete recovery, 14 within 24 hours of injury.

One patient suffered an unstable spinal fracture requiring halo immobilization. There was no evidence of ligamentous instability, spinal stenosis or canal encroachment in the other cases. Myelography was not performed due to their complete and rapid recovery.

In follow-up of 11 of 19 patients, two, both children, suffered recurrent SCC of the cervical cord. No permanent cord injuries occurred, with a maximum follow-up of three years.

The absence of ligamentous instability, spinal stenosis or canal encroachment in all but one case, was an unexpected finding. This suggests to us that SCC may be an indirect cord injury involving absorption of transmitted kinetic energy rather than a transient cord compression. Possible mechanisms are reviewed.

12.

Treatment of Spinal Cord Injury with Direct Electric Current, Laminin and Arac

M.J. POLITIS and M. ZENAKIS (Vancouver, B.C.)

The reactive-glial millieu distal to the site of axon injury in the mammalian CNS does not support appreciable axonal regeneration. Previous studies in this laboratory indicate that AraC administration can inhibit reactive gliosis, and exogenous laminin or direct electrical current can promote axonal elongation in damaged rat optic nerve. In the present studies, these interventions were used after rat spinal cord injury.

Weight-drop lesions were used. Laminin was introduced into spinal cord by intraspinal injection or subdural implantation of Elvax pellets containing the substrate. AraC was administered by daily i.p. injection. Electric fields were applied to spinal cord by placing one of two lead wires supradurally on either side of the lesion. Wires were connected to Traxon galvanic stimulators (American Biointerface Corp., N.Y.) which delivered 1.5 uamp DC. Leads were placed so that the rostral one was anodal, cathodal (CR) or inactive in three different experimental groups.

Blinded behavioral studies were done 1 to 3 weeks postoperatively. Inclined plane tests were used and supplemented by assessment of gait, toe spread, and strength of withdraw reflexes. In morphological studies, the number of axonal profiles in dorsal columns 4 mm rostral to the lesion site was counted. In some rats, HRP tracer studies were done.

Results showed significant functional improvement (over lesioned controls) in rats where laminin-containing Elvax pellets were implanted in combination with systemic AraC injection. Dorsal columns in this group displayed elongation of axons rostral to the lesion site. Preliminary tracer studies indicate growth of rubrospinal and vestibulospinal fibers caudal to the lesion site. Galvanotropic studies indicated significant functional recovery in CR animals, with axonal growth in dorsal columns.

Electrophysiological studies and further tracer studies are in progress.

Neurosurgery (Poster)

FRIDAY, JUNE 17TH - P.M.

13.

Von Hippel-Lindau Disease: Regular Follow-Up and Neurosurgical Implications

F.B. MAROUN, J. GREEN, I. BOWMER, N. LUSH, J.C. JACOB, M. MANGAN and A.M. HOUSE (St. John's, Newfoundland)

Twenty-nine members of a family affected by one or more aspects of Von Hippel-Lindau disease are presented. Organs involved were distributed as follows:

Retina 17 (58%)	Adrenal Glands 14 (48%)
Cerebellum 6 (20%)	Spinal Cord 2 (7%)
Kidney 1 (3%)	

Eleven patients died (average age of death 37 years) with 4 related to their CNS lesions. Team approach in dealing with the disease is important and management of neurosurgical lesions is greatly dependent on it.

14.

Spinal Dysraphism: Concepts in Clinical Recognition and Management

J.C. JACOB, F.G. MAROUN and W.D. HENEGHAN (St. John's, Newfoundland)

The clinical feature in recognition of occult spinal dysraphic lesions in a child with previously identified and treated overt myelomeningocele and hydrocephalus, is the fact of progression of clinical disability (progressive motor deficit, spasticity or spinal deformity and change in bladder and bowel function). An important prerequisite therefore is documentation of the details of the clinical state, or function, in follow-up so that a change from documented status can be appreciated so appropriate radiologic imaging procedures are utilised to define the nature and extent of the morphologic anomalies. "New" clinical features in the follow-up of the dysraphic child should raise suspicion of occult spinal lesions which in turn leads to corrective therapeutic procedures. Several cases will be presented to illustrate these concepts.

15.

Surgical Management of Iatrogenic Accessory Nerve Lesions

T.P. DOORLY and A.R. HUDSON (Toronto, Ontario)

Injury to the spinal accessory nerve with resultant loss of trapezius muscle function causes pain and significant disability. The vast majority of accessory nerve injuries are iatrogenic and result from a surgical procedure in the posterior triangle of the neck. Despite previous reports on this subject, accessory nerve injury is still common and is often associated with diagnostic delay and uncertainty as to the best mode of therapy.

We have reviewed 20 patients who have been followed for more than 18 months after microsurgical exploration and repair of iatrogenic accessory nerve injury. Detailed clinical and electrophysiological assessment determined the degree of impairment, the extent of regeneration and the need for surgical exploration. Operative findings ranged from a neuroma in continuity to complete excision of a segment of nerve. Sequential microsurgical dissection and nerve action potential recording were employed to preserve functioning portions of nerve and to isolate portions requiring repair.

The results of surgery have been analyzed with regard to the age of the patient, the type of injury, the length of time from injury to repair, the operative findings and type of repair required. Clear guidelines now exist for the investigation and microsurgical repair of iatrogenic accessory nerve injury. These will be presented.

16.

New Adjustable Anti-Siphon Valve For Pressure-Controlled Cerebrospinal Fluid Shunting

J.H. SAMPSON and E.R. CARDOSO (Winnipeg, Manitoba)

The numerous available valves for cerebrospinal fluid (CSF) shunting do not operate satisfactorily and frequently require multiple revisions. The described anti-siphon valve (ASV) is based on a unique conceptual approach and design that combines the properties of anti-siphoning and intraventricular pressure regulation in a single and simple device.

The ASV has a tubular configuration with the same diameter as the shunt tubing. A mobile membrane seals an oval defect in the tube wall and rests on a thin semi-circular partition within the tube. The mobile membrane is driven by the pressure gradient between the intraluminal and external compartments. In the erect position the intraluminal pressure at the level of the ASV will depend upon its height along the shunt tubing, as the hydrostatic pressure from the fluid column above the ASV creates positive pressure, while the one from below generates negative pressure. Negative intraluminal pressure pulls the membrane against the partition, shutting off the ASV and halting the flow of CSF. This prevents CSF overdrainage caused by siphoning. If pressure adjustments are required, the ASV could be pulled up or down along the shunt tubing, thus precluding the need for conventional valve replacements. In the horizontal position the ASV stays patent.

Results of bench testing showed reliable pressure control and prevention of siphoning within wide range of proximal pressures, varying from -10 to 35 cm H_2O.

17.

Cruciate Paralysis Secondary to Luxation of C1 on C2 Vertebra

D. LADOUCEUR and M. VEILLEUX (Sherbrooke, Québec)

Cruciate paralysis is typically characterized by involvement of the lower cranial nerves and bilateral upper extremity paralysis.

Following a craniocervical trauma, an 88 year old woman presented a transient bilateral flaccid upper extremity paralysis associated with an alteration of consciousness, absent gag reflex, dysphonia and a paucity of tongue movement.

Cervical spine films showed a luxation of the C1 on C2 vertebra and a type III odontoid process fracture. Craniocervical Computed Tomography scanning confirmed standard film findings.

Electrophysiological studies confirmed involvement of the lower cranial nerves on needle electromyography and somatosensory evoqued potentiels of the upper and lower extremities showed a prolonged central conduction time.

The involvement of the lower cranial nerves allowed us to rule out a central cord syndrome in a patient with a bilateral upper extremity paralysis.

18.

Trandural Thoracic Disc Rupture: A Case Report and Review of the Literature

M.G. HAMILTON and H.G. THOMAS (Calgary, Alberta)

Herniated thoracic discs are uncommon, accounting for only 0.25-0.75 percent of all symptomatic protruded discs. Transdural thoracic disc rupture has only very infrequently been reported.

We present a 71 year old male who was hospitalized for investigation of increasing back pain and a one week long history of bilateral leg pain. His past history was remarkable for colonic carcinoma (Duke's B1) resected two years previously. While in hospital, he developed lower limb weakness and paresthesias progressing to almost complete paraplegia. Twelve hours before referral to our Neurosurgery service, he lost voluntary bladder control. Emergency myelography demonstrated an intradural, extramedullary lesion at the T12 level. The patient was brought urgently to the operating room.

We approached the operative procedure anticipating discovery of an intradural tumor deposit. A T12/L1 laminectomy was performed and widened laterally with partial removal of the left facet. Upon opening the dura, we discovered an extruded disc fragment displacing and compressing the cord posteriorly. This was removed with microscopic technique.

Post operatively, this patient did well. He had a rapid (although not complete) return of both the motor and sensory function and complete return of voluntary bladder control. Two months post operatively, he was able to walk with the aid of two canes and was otherwise well.

In summary, we present a patient with rapidly progressive paraparesis with myelography demonstrating an intradural, extramedullary defect caused by an transdural T12 disc rupture. This diagnosis, although uncommon, should not be forgotten when dealing with this clinical presentation. The literature will be reviewed.

19.

Cerebral Elasticity and Ventricular Size Part I: Normalization of Ventricles Following Shunting

E.R. CARDOSO and M.R. DEL BIGIO (Winnipeg, Manitoba)

The size of cerebral ventricles on computerized tomograms of 27 hydrocephalic patients was measured prospectively prior to and one week after cerebrospinal fluid (CSF) shunting. Planimetric measurements of the ventricular size in relation to the size of the cerebrum were compared before and after standard shunting with the same type of low pressure valve in series with an anti-siphon device. The mean size of cerebral ventricles in neonates with posthemorrhagic hydrocephalus was 0.31 ± 0.2% of the cerebral size. The mean size at 1 week post-shunting was 0.25 ± .24%, representing an average 14.4 ± 9.3% reduction of ventricular size. The mean size of ventricles in elderly patients changed from 0.22 ± 0.05% of the cerebral size initially to 0.19 ± 0.05 post-shunting, representing an average 9.7 ± 3.5% reduction. On the other hand, older children and young adults showed a much greater average reduction of ventricular size of 56.7 ± 5.2%, going from 0.3 ± 0.1% of the cerebral size pre-operative to 0.15 ± 0.1% after shunting. The amount of reduction of ventricular size nor with length of symptomatic disease.

These findings suggest that reduction of ventricular size following CSF shunting is related to age. Possible factors involved are discussed. We postulate that the size of cerebral ventricles in hydrocephalic patients may depend upon the intrinsic elastic properties of the cerebral parenchyma as much as upon the dynamic balance between formation and absorption of CSF.

20.

Cerebral Elasticity and Ventricular Size Part II: Age-Relate Development of Extracerebral Fluid Collections

E.R. CARDOSO, M.R. DEL BIGIO and G. SCHROEDER (Winnipeg, Manitoba)

The authors postulate that the size of cerebral ventricles in communicating hydrocephalus (CH) and other cerebro-spinal fluid (CSF) disorders may be related to the volume and elastic properties of the brain, besides the decrease in CSF absorption. Furthermore, cerebral volume and elastic properties may also contribute to the age distribution of chronic subdural hematomas (CSH).

The medical literature was reviewed for the age distribution of 349 cases of CH, 569 cases of CSH, 289 cases of pseudotumor cerebri (PC), and 77 cases of slit-ventricle syndrome (SVS).

An age-related incidence was found: CH and CSH predominated in neonates less than 18 months old and adults older than 55 years, while PC and SVS occurred mainly in older children and young adults. The latter patient groups seem to show a greater resistance to ventricular dilatation in the presence of decreased CSF absorption. This may be related to larger volume and state of maturity of the cerebrum in this age group. On the other hand, neonates and the elderly more readily develop subdural collections or, in association with impairment of CSF absorption, enlarged ventricles.

Cerebral and extracerebral developmental factors, such as open cranial sutures, cerebral atrophy, cerebral water and myelin contents, may contribute to the age-related incidence of the four diseases investigated. Similarly, the development of ventriculomegaly may depend upon cerebral elastic properties besides the primary disturbance of CSF dynamics.

21.

Intrasellar Meningioma

T.P. DOORLY, R.R. TASKER and J.H. DECK (Toronto, Ontario)

Although meningioma is the third most common parasellar tumor of adults, an intrasellar meningioma is a very rare finding with less than ten reported cases. Radiologically it may not be possible to distinguish an intrasellar meningioma from a pituitary adenoma. Basal serum prolactin levels greater than 200 ng/mL are virtually diagnostic of prolactinoma but exceptions have been reported. An intrasellar meningioma may therefore be an unexpected finding at transsphenoidal surgery.

We report the case of a 42 year old female who first presented with lethargy, amenorrhea and galactorrhea eighteen months after an uncomplicated labour and delivery. Skull X-ray was normal. Serum prolactin levels were elevated. Bromocriptine therapy was commenced with an initial good response. However one year later endocrine assessment revealed a deficit of anterior pituitary lobe hormones and a serum prolactin level greater than 240 ng/mL. CT brain scan revealed an intrasellar tumor with modest suprasellar extension. At transsphenoidal surgery a relatively fibrous and vascular tumor was encountered and the majority resected. Histological examination established the diagnosis of meningioma.

Two years after surgery the patient remains well on endocrine replacement therapy. Repeat CT scans show a small amount of residual tumor. The limited reported experience with this tumor suggests adequate treatment by the transsphenoidal route.

22.

Carotid Artery Dissection in Ehlers Danlos Syndrome

E.A. SCHNEIDER, N.A. RUSSELL and B.G. BENOIT (Ottawa, Ontario)

Ehlers Danlos Syndrome includes a group of inherited disorders of connective tissue with abnormalities of collagen composition. Blood vessel fragility, with rupture or dissection of arteries is a frequent complication. Of particular note to neurologists and neurosurgeons is its association with intracranial aneurysms and carotid cavernous fistula.

We present the case of a 25-year-old male with biopsy proven Ehlers Danlos Syndrome who developed dissection of an extracranial internal carotid artery following minor head trauma. To our knowledge, this is the first documented case of extracranial carotid dissection occurring in association with Ehlers Danlos Syndrome.

23.

Brain Abscess Secondary to Gingival and Nasal Bleeding

H.M. JABER, F.E. LeBLANC, F.W. RAMSAY and M.E. MacRAE (Calgary, Alberta)

Brain abscess is infrequently caused by transient bacteraemia.[1]

Gingival and nasal bleeding, especially during dental work and cleaning, drew little attention as a source of brain abscess in healthy individuals with no history of heart disease.

We present three adult patients with brain abscess, all with no evidence of heart disease. The only source of infection identified in these patients was gingival bleeding during dental cleaning in the first patient, during periodontal work in the second patient, and following nasal bleeding in the third patient suffering from Osler-Weber-Rendu disease. These patients had no history of dental abscess.

The offending organisms were consistant with the normal flora of the oral cavity in the first and second patients and consistent with the nasal flora in the third case.

Prophylactic antibiotics are prescribed infrequently by dentists during dental cleaning in cases of gingival bleeding. The need for generalising this practice might be considered, in the light of this presentation.

[1] Principles and Practice of Infectious Disease, New York, Willey 1979, pp 780-785)

24.

Giant Cavernous Angioma of The Cerebello-Pontine Angle

D.J. MORASSUTTI, B.G. BENOIT, B. LACH and N.A. RUSSELL (Ottawa, Ontario)

Extra-axial cavernous angiomas of the C/P angle are extremely rare. They are not angiographically distinct, and are usually misdiagnosed as acoustic neuromas or meningiomas. Despite their vascular nature, these lesions may be totally removed with minimal morbidity. We present the case of the largest reported cavernous angioma of the C/P angle, measuring 5 x 3 x 4 cms.

A 65-year-old woman presented with ataxia, dysarthria, and right hemiparesis. Studies revealed a large well-demarcated, enhancing hyperdense mass of the right C/P angle, extending up through the incisura. The angiographic tumor blush was consistant with a tentorial meningioma. Obstructive hydrocephalus was treated by V/P shunting, which resulted in considerable functional improvement and return to independent living. Tumor removal was deferred initially, because of slow symptom evolution, improvement with shunting, and anticipated major technical difficulties. One year later, original symptoms recurred, and she now exhibited new cranial neuropathies (N. 5, 7, 8, 9, 10). A scan showed tumor enlargement. Through a suboccipital-transtentorial approach, a large cavernous angioma was found, seemingly arising from the edge of Meckel's cave. Despite its size and vascularity, the lesion was totally removed. Only a trochlear paresis, and minimal gait disturbance persist.

The literature on cavernous angiomas of the C/P angle is sparse: only 6 cases have been previously reported. They cause symptoms similar to those of acoustic neuroma or meningioma, but usually progress more rapidly. They are often angiographically occult, and are almost never correctly diagnosed before operation. our experience with this case revealed that a good surgical plane can be developed, bleeding is minimal, and complete removal can be safely achieved using conventional microsurgical techniques.

25.

A Neurotrauma Assessment Record

D. KONDIZIOLKA and M. SCHWARTZ (Toronto, Ontario)

A Neurotrauma assessment record has been designed to aid in the data collection and clinical documentation of patients with multiple injuries. It obviates the narrative record of the history and physical examination. It ensures more complete recording of information during initial patient assessment, allows easy transfer to computerized data bases and may assist academic centres in performing clinical research.

The record collects data concerning patient demography, present trauma history, airway and hemodynamic parameters, systemic injuries, Glasgow Coma Scale (GCS), brain, spinal cord and peripheral nerve exams, radiographs and CT scans. It requires the clinician to specify surgical treatment planning and to make a diagnostic summary. Diagrams are provided to mark injuries and regions of sensory loss. The physician need only circle the correct listed answer or write a focused comment. The form occupies two sides of a page.

The form has been validated by reviewing the narrative records of 100 consecutive polytraumatized patients and transcribing their information to the form. No problems in recording have been encountered by surprising lapses in the records have emerged. Eight of 55 patients with head injuries lacked sufficient description to calculate the GCS. Five of 20 patients with spinal injuries had no recorded rectal exam. A study is now proceeding using the form and a second quality control review will follow.

Similar assessment forms for the use of orthopedic and general surgery are being developed.

26. **Withdrawn**

Cerebrovascular Disease (Platform)

THURSDAY, JUNE 16TH - P.M.

27.

Hemodynamic and Metabolic Effects of Severe Extracranial Carotid Disease

RICHARD LEBLANC (Montreal, Quebec)

Cerebral blood flow (CBF), cerebral blood volume (CBV), the CBF/CBV ratio - an index of hemodynamic reserve capacity - the rate of oxygen metabolism ($CMRO_2$), and the fractional extraction of oxygen by the brain (OEF) were studied by positron emission tomography (PET) in the cortical territory of both internal carotid arteries in 15 cases of transiently symptomatic or progressive extracranial atherosclerotic carotid disease. None of the patients had a major stroke or had a significant neurological deficit except 1 whose damaged hemisphere is excluded from study. All were asymptomatic at the time of PET scanning. Values were obtained in the middle cerebral artery (MCA) distribution, and in the anterior and posterior watershed regions. Eight cases had unilateral carotid stenosis of 80% or greater and 7 had unilateral or bilateral occlusion of the origin of the internal carotid artery. Results obtained in patients were compared, using Student's t-test, to those obtained in neurologically normal, elderly volunteers.

Patients with carotid stenosis had a significantly decreased CBF ($p<.025$) and CBF/CBV ratio ($p<.025$) selectively in the ipsilateral anterior watershed region. This was accompanied by a trend toward elevated OEF and declining $CMRO_2$ values. Patients with carotid occlusion had significantly decreased CBF, ($p<.005$), decreased CBF/CBV ratio ($p<.005$) and decreased $CMRO_2$ ($p<.025$) in the ipsilateral anterior watershed and MCA territories. Similar changes were present in the opposite hemisphere of patients with bilateral carotid disease.

These results indicate that severe carotid stenosis is associated with hypoperfusion and diminished hemodynamic reserve capacity in the anterior watershed region, and that carotid occlusion produces more widespread hypoperfusion and metabolic depression. Therapeutic efforts should be directed at preventing the progression of stenosis to occlusion, and PET may identify patients with carotid stenosis who are at risk of further ischemic events.

28.

Trans-Cerebral Venous Perfusion of Verapamil in the Treatment of Acute Stroke

Y.L. YAMAMOTO, T. UEDA and M. DIKSIC (Montreal, Quebec)

We recently established for the first time that the cerebral venous system of rats with focal ischemia can tolerate up to 150 mmHg perfusion pressure without any change of blood-brain barrier (BBB) permeability or regional cerebral blood flow (RCBF) (Ueda et al., 1988). We outline here the effect of the calcium channel blocker verapamil administered at various perfusion pressures into cerebral veins in focal ischemic rats. The results of this transvenous perfusion of the brain (TVPOB) are compared with those achieved with systematic administration of verapamil in the same ischemic model.

Method - Twenty-four rats with occlusion of the middle cerebral artery were used in this study. Animals were divided into four groups of six. Group A rats received no medication. The other three groups received verapamil (0.1 mg/kg/2hrs): the drug was administered to group B intravenously, to group C TVPOB at 100 mmHg and to group D TVPOB at 150 mmHg perfusion pressures. The perfusion of saline in the control of animals or of Verapamil in groups B, C, and D started one hour after the MCA occlusion and lasted for 2 hours. The animals were killed 3 hours post-occlusion and the brain studied for RCBF and BBB changes using double-tracer autoradiography with ^{18}F-FAP and ^{14}C-AIB as tracers.

Results - As compared to group A, group C showed a significant increase of RCBF (88%; $p<0.01$) in the parietal cortex only. Group D showed an extensive and significant increase of RCBF in the ischemic cortical areas (70% - 100%; $p<0.01$). Group B showed no significant changes of RCBF as compared to group A. There was no change of BBB permeability in any group.

Comments - Our results indicate that in rats that had undergone MCA occlusion the TVPOB of verapamil at 150 mmHg perfusion pressure resulted in an extensive and remarkable improvement of RCBF in the ischemic cortical and subcortical areas without any change of RCBF in the contralateral hemisphere. Since the cerebral venous system has a minimum atherosclerotic process and TVPOB is a simple surgical procedure, we are investigating further this promising new treatment for acute cerebral ischemia. Supported by MRC (MT-3174).

29.

A Double-Blind, Placebo-Controlled Trial of a 21-Aminosteroid in the Prophylaxis of Chronic Cerebral Vasospasm in A Primate Model: Clinical Radiological and Pharmacological Studies

D.E. STEINKE, B.K.A. WEIR, J.M. FINDLAY, D. COOK, C. KRUEGER, M. GRACE and T. TANABE (Edmonton, Alberta)

This study was designed as a randomized, double-blind, placebo-controlled trial. The primary objective was to evaluate the efficacy of the 21-aminosteroid U74006F, in the prophylaxis of chronic cerebral vasospasm (VSP) following subarachnoid hemorrhage (SAH). Thirty

female cynomolgous monkeys were divided by restricted randomization into 2 groups of 15. The treatment groups were then further subdivided with 5 animals from each placed into subgroup 1. Subgroups 2 and 3 were made up in a similar fashion. On Day 0 all animals underwent baseline angiography followed by a right frontotemporal craniotomy and experimental SAH. On Days 1-6 the animals received an intravenous injection of either U74006F or placebo every 8 hours. In the event that a delayed ischemic deficit occurred, a Magnet Resonance Image was obtained. On Day 7 angiography was repeated and the animals were sacrificed. The degree of VSP was determined based on angiographic and pathologic criteria. Animals in subgroup 1 underwent perfusion-fixation and had their cerebral vessels examined with scanning and transmission electron microscopy. The animals of subgroup 2 had cortical biopsies taken and middle cerebral arteries harvested prior to sacrifice. Utilizing High Performance Liquid Chromatography, these tissues were examined for the presence of high energy phosphates. The cerebral vessels of monkeys in subgroup 3 were investigated pharmacologically. The effect of SAH on endothelium-dependent relaxation was evaluated and the ability of U74006F to preserve endothelium-dependent relaxation factor activity ascertained. The results will be presented.

30.

A Double Blinded Randomized Trial of PY108-068 In Acute Ischemic Cerebral Infarction

W.J. OCZKOWSKI, V.C. HACHINSKI, J. BOGOUSSLAVSKY, H.J.M. BARNETT and S.G. CARRUTHERS (Hamilton and London, Ontario; Lausanne, Switzerland)

A double blinded randomized trial of the calcium channel antagonist PY108-068 was completed in patients with acute ischemic cerebral infarction.

Nine patients received PY108-068 and ten patients received placebo medication within 48 hrs of stroke onset. Treatment was given orally, 150 mg/day, for a total of 21 days.

The mean age of the treated patients was 63.7 years (4 males, 5 females), control patients 64.4 years (7 males, 3 females). In the treated group there were 6 left, 3 right hemispheric infarctions; control group 5 left, 5 right hemispheric infarctions; most MCA.

There was one death in the treated group from sudden cardiac death on day 12; one death in the control group from cerebral herniation. Two patients in the control group had myocardial infarctions during the study period. Two patients in the treated group had episodes of hypotension during the first day of treatment.

At stroke onset the mean Toronto Stroke Scale scores were 67 and 90 in the treated and control groups respectively. At week 12 the mean scores were 22.5 and 34.7 in the treated and control groups respectively. There was a parallel improvement in both groups with no significant difference in outcome (p. 0.05).

At stroke onset the mean Barthel functional scores were 32.8 and 33 in the treated and control groups respectively. At week 12 the mean scores were 90 and 78.8 in the treated and control groups respectively. There was a trend in favour of the treated group but it did not reach significance at the 5% level.

The drug was found to be safe when administered to patients with acute ischemic cerebral infarction.

31.

Calcium Channel Activation in Models of Cerebral Ischemia

A. HAKIM, A. GJEDDE, L. BERGER and D. POPOW (Montreal, Quebec)

The ischemic penumbra is defined as a peri-infarct zone where neurotransmission is interrupted but membrane transport is preserved, maintaining the cell in a temporary state of "reversible activation". It is important to define the metabolic functions of the penumbra further since it is a reversibly injured region that may respond to therapy resulting in improved neurologic function.

We developed an autoradiographic technique for the in vivo quantitative evaluation of calcium channel activity after the onset of focal cerebral ischemia in the rat. Rats were subjected to occlusion of the left middle cerebral and ipsilateral common carotid arteries. CBF measurement, autoradiographically 4 hours after occlusion, showed severe hypoperfusion (CBF mean ± SEM 11 + 1 ml/100g/min) in the lateral caudate and moderate hypoperfusion (CBF 28±7) in the ipsilateral cortex. In a similarly treated but separate group of rats ^{3}H-nimodipine (NEN, specific activity 144.6 Ci/mmol), 250 μCi was injected 3.5 hours after the onset of ischemia and binding potential measured 30 min. later. Compared to ^{3}H-nimodipine binding in the contralateral hemisphere, binding was quite low in the lateral caudate where perfusion was severely decreased but in the ipsilateral cortex the binding potential was increased 480%. This implies that the calcium channels in the regions with moderate ischemia are activated. Since CBF after a stroke is quite variable, measurement of nimodipine binding may be a good model to estimate the presence of tissue that may respond to therapy.

32.

Stroke in two Families with Heterozygous C2 Deficiency

D. SIMARD and J.P. MATHIEU (Quebec City, Quebec)

Numerous studies reported a correlation between C2 deficiencies, autoimmune or non-autoimmune diseases. We are reporting two families with an heterozygous C2 deficiency picture associated with documented strokes in at least two members.

A 31 year old woman (DV) had a second episode of hemispheric stroke and a 42 year old man (JPR) suffered a massive vertebrobasilar infarction. Assessments of risks factors and tests for autoimmune diseases including clinical evaluation, antinuclear antibodies, cryoglobulins, direct and indirect Coombs, VDRL, rheumatoid factor, protein electrophoresis and immunoglobulins dosages were all negative.

DV, a 28 year old woman then, suffered in 1983 a right hemispheric infarction confirmed with CT scan. In 1986 still complaining of a left sided residual neurological deficit, she developed right sided neurological symptoms. Standard and double infusion CT scans were then normal as well as the cerebral angiogram. No mitral valve prolapsus could be detected both clinically and echocardiographically. Her complement studies revealed a diminished CH50 and C2 but normal C3 and C4. A year later the C2 was still more than 50% lower than normal. HLA studies brought out the following haplotype: A3, A25, B18, Dr1, Dr2.

Her siblings demonstrated a familial C2 deficiency.

JPR suffered a vertebrobasilar infarction which left him with akinetic mutism. An early CT scan was normal but the angiogram revealed a complete basilar trunk occlusion and a tight left internal carotid stenosis. He died several months later of respiratory insufficiency. His complement levels showed a diminish CH50 and C2. Three months later the CH50 was back to normal but the C2 was still 50% below normal. HLA studies showed HLA, A25, A30, B18, D2. His family was then studied and also demonstrated a familial C2 deficiency.

The two families showed heterozygous C2 deficiency, HLA Haplotypes correlating the index patients, and also several vascular problems.

This is the first report of stroke in two families with heterozygous C2 deficiency.

33.

Carotid Endarterectomy: Objective Identification of a High Risk Group by Intra-operative Monitoring

G.G. FERGUSON and W.T. BLUME (London, Ontario)

A series of 371 consecutive endarterectomies in which an internal shunt was used only 4 times has been reviewed in relation to the findings on intra-operative monitoring and the clinical outcome. The purpose was to evaluate the clinical significance of the changes observed during monitoring, and thus to define its usefulness in assessing the need for internal shunts during surgery.

In 292 cases with continuous intra-operative EEG monitoring, a significant change occurred in 72 or 25% (moderate 43, severe 29). In 276 cases with carotid 'stump' pressure measurements, 14 had mean 'stump' pressures less than 25 mmHg. In 27 cases with CBF measurements, 8 had mean flows less than 20 mls/100g/min.

Five patients (1.3%) awoke with major deficits; two (0.5%) of which were permanently disabling. Four of these patients had severe EEG changes; two had mean 'stump' pressures less than 25 mmHg. All 5 had widely patent endarterectomy sites on immediate post-operative angiography, but two of these had evidence of embolization. The risk of stroke was 0.4% if there was no EEG change or the change was moderate, but was 14% if the change was severe. The risk of stroke was also 0.4% if mean 'stump' pressure was greater than 25 mmHg, but 14% if less. None of the 27 cases with CBF measurements had a post-operative deficit.

A group of patients undergoing carotid endarterectomy who have a relatively high risk of intra-operative stroke has been objectively identified with intra-operative monitoring techniques, consisting of those with either a severe EEG change or mean carotid 'stump' pressures less than 25 mmHg. Internal shunts may reduce the risk of intra-operative stroke in this group, although this has yet to be proven.

34.

Recurrent Stenosis After Carotid Endarterectomy - Risk Factor Analysis

J. D'ALTON, B. BENOIT, N. RUSSELL, C. SKINNER and N. SIMMONS (Ottawa, Ontario)

The efficacy of carotid endarterectomy in the treatment of patients with symptomatic carotid stenosis to controversial. A multi-centre study to evaluate this procedure is currently in progress.

We prospectively followed 171 patients who had this operation, for up to 1200 days, to determine the incidence of re-stenosis and to define the risk factors which might contribute to recurrent disease. Mean age was 67.6 and 63.7% were males. Patients were interviewed at 3 monthly intervals and had a carotid doppler study.

Forty-six (27%) developed recurrent stenosis $\geq$ 50% and 7 (4%) an occlusion during the follow-up period. No significant difference was found in the incidence of hypertension, smoking, diabetes mellitus or coronary artery disease between those who re-stenosed and the others. Mortality was 12% and late stroke 0.8% in the no stenosis group, 8.7% and 2% in the re-stenosis group and 0% and 33% in the occlusion group.

Recurrent stenosis develops in a significant number of patients after carotid endarterectomy. Analysis of risk factors fails to show a difference from those whose vessels remain patent. The associated stroke risk is low.

35.

Is Internal Carotid Artery Dissection a Major Cause of Idiopathic Stroke in Children?

P. HUMPHREYS, M. RIDING, P. JACOB, D. KEENE, S. PARNES and S. WHITING (Ottawa, Ontario)

We have retrospectively reviewed all cases of non-hemorrhagic stroke in children aged 28 days to 18 years treated at the Children's Hospital of Eastern Ontario between 1979-87 inclusive. Of 24 cases ascertained, 14 had defined causes, including congenital heart disease (3), cardiomyopathy (1), neck vessel injury (3), air/fat embolism (1), focal cerebral vasculitis (2), fever/dehydration (1), complex migraine (2), and mitochondrial encephalopathy (1). The remaining 10 patients were either said to have "moya-moya" disease (2) or an "idiopathic" stroke (8). Extensive review of the clinical and radiologic findings in these 10 patients showed that 8/10 (33% of total stroke patients), including one "moya-moya" case had common features suggesting a similar pathologic process. 7/8 were female (aged 4-14); 6/8 had symptoms involving the left hemisphere. All had the abrupt onset of pure motor hemiplegia, usually during exercise (6/8). The patients with left hemisphere lesions also had major expressive speech difficulties. 7/8 children had CT findings compatible with infarction in the territory of the ipsilateral lenticulostiate arteries; 1/8 had the same lesion plus infarction of part of the peripheral middle cerebral territory. All 8 patients had angiographic findings compatible with dissection of the supraclinoid portion of the internal carotid and its branches; discrete narrowing of internal carotid and middle cerebral $\pm$ occlusion of anterior cerebral $\pm$ double lumen phenomenon. All 8 patients have survived, seven having significant residual deficits. We suggest that non-fatal internal carotid artery dissection is one of the most common causes of non-hemorrhagic stroke in children.

36.

Functional Recovery After Decompressive Craniectomy for Cerebral Infarction

D.S. KONDZIOLKA and M. FAZL (Toronto, Ontario)

Continuing controversy exists concerning the benefits of decompressive craniectomy in the treatment of lesions causing increased intracranial pressure (ICP) and brain edema. Poor results have been observed in patients following closed head trauma. Laboratory work has shown a decrease in ICP after craniectomy, but also a detrimental enhancement in the formation of underlying brain edema. We aim to define a group of patients with massive supratentorial infarction, who may benefit from craniectomy.

Five patients over a three-year period, with acute supratentorial cerebral infarction, were treated with fronto-temporal craniectomy after progression into coma from trans-tentorial herniation. Patient age ranged from 32 to 51 years. The etiology of infarction included two cases of carotid dissection, two cases of subarachnoid hemorrhage and one case of embolic stroke. Initial therapy with intubation, hyperventilation and mannitol was followed immediately by craniectomy, in cases where the patient developed a fixed and dilated pupil in association with hemiparesis and coma. Although in all cases, normal pupillary reactivity was restored immediately post-operatively, general clinical improvement in four patients was slow. The effect of craniectomy rests in lowering ICP, relieving supratentorial herniation and possibly augmenting cerebral blood flow to the ischemic penumbra, although this has never been proven.

Our cases define a young population who may be more prone to developing brain swelling after infarction, as a result of less cerebral atrophy, smaller ventricles and perhaps a greater edema response. At 9 to 36 months follow up, all patients are alive and walking, despite a paresis appropriate to their original stroke. Two have returned to work. In patients with massive cerebral infarction causing coma and impending death, supratentorial craniectomy may not only be a life saving procedure, but one associated with good functional recovery.

37.

Post-Traumatic Vertebrobasilar Ischemia: Immediate and Delayed Events

M.G. BEAUDRY and J.D. SPENCE (London, Ontario)

Recent cervical injury, e.g. from chiropractic manipulation, is a known cause of vertebrobasilar (VB) ischemia. We describe 30 patients

with delayed VB symptomatology occurring months to years (Mean = 13.1 months; SD = 13.6 months; range = 2 weeks-5 years) after trauma, most (28/30) after a motor vehicle accident (MVA). We excluded isolated vertigo or loss of consciousness (LOC). The mean age was 41. Only 5 patients initially had LOC and/or amnesia > 1 hour; 15 had no LOC. 9 had immediate symptoms after trauma, 8 of which later developed VB episodes of a different nature. In follow-up 7 patients had mild-moderate and 2 severe sequelae, 5 as a result of a delayed event.

Patients were classified as: A) definite - 10 pts, B) probable - 11 pts, C) possible - 9 pts. In each group severity of initial trauma and likelihood of immediate VB signs and symptoms were comparable; group A & B had more prolonged initial LOC. Neck movement precipitated delayed events in at least 10 cases.

CT or MRI were abnormal in 2 pts including one case of pontine tegmental hemorrhage. Angiography was performed in 24/30 pts (mean 1.7 years after trauma) often during an asymptomatic period; 5 pts had abnormalities attributable to trauma.

Previous cervical injury from MVA is an under-reported cause of VB ischemia. We hypothesize two mechanisms: 1) vasospasm 2) platelet emboli related to intimal damage and/or dissection. Both may be related to arterial wall injury at the time of injury.

38.

Ictus Anosognosique et Epilepsie Anosognosique

F. GRAND'MAISON, J. REIHER, M.L. LEBEL and J. RIVEST (Sherbrooke, Québec)

A partir d'observations récentes, nous nous devons d'annoter un chapitre encore méconnu de la séméiologie neurologique.

L'anosognosie, manifestation caractéristique des lésions pariétales de l'hémisphère mineur, est généralement durable. Qu'une anosognosie puisse survenir de façon soudaine, transitoire et épisodique, relève de l'inédit et mérite d'être rapporté.

Chez cinq malades, des épisodes d'hémiparésie gauche et d'anosognosie transitoire sont á rapprocher de l'ischémie cérébrale transitoire. Chez le sixième malade, des manifestations identiques, néanmoins précédées de clonies hémicorporelles gauches, elles aussi ignorées malgré un état de conscience par ailleurs préservé, tiennent d'une perturbation épileptique critique et post-critique de l'hémisphère mineur; à pareille perturbation, et à elle seule, convient l'appellation «épilepsie anosognosique», contrairement á l'usage impropre qu'en fait Schwab dans sa description princeps.

L'expression "ictus anosognosique", plus générique, convient davantage à désigner l'anosognosie transitoire, quel qu'en soit le principe physiopathologique. A côté de l'ischémie transitoire et de l'épilepsie partielle identifiées chez ces six malades, d'autres conditions incluant la migraine et les «tumor attacks» de Ross pourraient en effet trouver dans l'ictus anosognosique une autre forme inusitée d'expression clinique.

Reconnaître d'urgence l'anosognosie transitoire malgré le déni déconcertant du malade s'impose. La diagnostiquer sans délai, c'est assurer la mise en oeuvre précoce d'une thérapie spécifique, et la prévention de déficits majeurs potentiellement durables.

Cerebrovascular Disease (Poster)

FRIDAY, JUNE 17TH - P.M.

39.

Physiological Effects of the Partial Treatment of Large Cerebral Arteriovenous Malformations

R. LEBLANC, J. THÉRON, J.L. TYLER, Y.L. YAMAMOTO and A. HAKIM (Montreal, Quebec)

Six patients with supratentorial arteriovenous malformations (AVM) larger than 6 cm were studied with positron emission tomography (PET). Cerebral blood flow (CBF), cerebral blood volume (CBV), the CBV/CBF ratio, the fraction of oxygen extracted from arterial blood by the brain (OEF) and oxygen and glucose metabolism ($CMRO_2$ and CMRG1) were evaluated in the cortex, excluding the area of the malformation, before and after partial embolization of the AVM. Results obtained in patients were compared to those obtained in 20 healthy young volunteers. A value beyond two standard deviations from the mean value of the control group is considered significant. In situations of relative ischemia, as cerebral perfusion pressure (CPP) falls the CBV can rise as resistance vessels dilate to maximize the area available for nutrient exchange, and the CBV/CBF ratio, which is mathematically equivalent to cerebrovascular transit time, rises to indicate prolonged cerebral circulation.

Prior to embolization patients had increased CBV and increased CBV/CBF ratios, indicating diminished cerebral perfusion pressure and prolonged cerebrovascular transit time, in cortical areas remote from the AVM itself. This was matched by a decreased CMRG1 indicating glucose hypometabolism, but the $CMRO_2$ was in the normal range. Partial embolization resulted in improved hemodynamic function manifested by a shortened cerebrovascular transit time in areas remote from the AVM in three cases. This was not, however, matched by improved glucose metabolism.

These data suggest that diversion of blood through AVMs may result in reduced CPP, prolonged cerebrovascular transit time, and glucose hypometabolism in areas remote from the lesion. Partial embolization may improve hemodynamic function in some cases but this is not consistently matched by improved glucose utilization. The aim of treatment of cerebral AVMs remains, therefore, complete resection or obliteration.

40.

Intracranial Haemodynamics in Cluster Headache

M.J. GAWEL and A. KRAJEWSKI (Toronto, Ontario)

It is now possible to measure blood flow velocity in intracranial vessels using transcranial Doppler. Previous reports of Schroth and Russell have confirmed asymmetries in the supratrochlear arteries using conventional Doppler.

We measured Doppler flow velocities in the middle cerebral artery, proximal (MCAP) and mid-portion (MCAM), in the posterior cerebral (PCA) and anterior cerebral (ACA) arteries in 42 cluster headache patients and 44 controls. Thirty-two patients had paroxysmal cluster and 10 were chronic. Seven were in remission and 35 were active.

There was significantly more inter-hemispheric asymmetry in the cluster group than the controls (MCA control 8.86 cm/sec; cluster 16.78 cm/sec – p 0.005).

Within the cluster group there was a significantly increased velocity in the MCA and PCA in the side usually involved in the headache (MCA headache side 100.3+/−23 cm/sec; other side 91.8+/−22.0 cm/sec; p 0.03). The velocity in the ACA was significantly slower.

We postulate that the increased velocity in the headache side is due to a narrowing of the lumen of that artery caused by neurogenic inflammation. Recently, Moskowitz has demonstrated unilateral neurogenic inflammation in the cat caused by unilateral stimulation of the trigeminal nerve. Our hypothesis is that this neurogenic inflammation is due to an episodic dysfunction in the fifth nerve nucleus. It has been shown that Doppler velocities fall in the MCA during an attack, presumably due to dilatation of the vessel walls. Such a dilatation of an inflamed vessel may form the background of the pain experienced. The efficacy of steroids and calcium blockers in cluster headaches would fit well with this hypothesis.

41.

Regional Lipid Peroxidation and Superoxide Dismutase Activity Following Transient Forebrain Ischemia

G.R. SUTHERLAND, R. BOSE, J. PEELING and C. PINSKY (Winnipeg, Manitoba)

Pre- and Post-ischemic lipid peroxidation [spectrophotometric assay of thiobarbituric acid reactive substances expressed as malondialdehyde generated (nM/hr/gm)] and superoxide dismutase (SODase) activity [nitro blue tetrazolium assay (units/gm)] were evaluated in 20 age-matched rats. Five control rats were decapitated and the hippocampus, frontal lobes, parietal/occipital lobes and cerebellum were dissected. The remaining rats underwent temporary forebrain ischemia [bilateral carotid occlusion and controlled hypotension (50 torr) for 10 minutes]. At 1 hr, 24 hr, and 7 days post-ischemia, 5 animals were sacrificed and tissue samples obtained as above.

Lipid peroxidation was significantly higher in the 1 hr and 24 hr post-ischemic cortical specimens and had reverted towards control values by the seventh day [frontal 62±3 (control), 104±9 (1 hr), 102±4 (24 hr), 80±18 (7 days); parietal/occipital 69±3 (control), 97±6 (1 hr), 102±13 (24 hr), 87±10 (7 days)]. The other brain regions showed no significant change in post-ischemic lipid peroxidation. The SODase activity continued to increase up to the seventh day:

	Frontal	Parietal/ Occipital	Cerebellum	Hippocampus
Control	4090± 605	3966± 630	2702± 326	1205± 749
1 hr	4763±1713	5238±1260	4225±1277	4887±1302
24 hr	10927± 456	10865± 985	10121± 584	11459± 606
7 days	18140± 362	19738±1033	16876± 396	17471± 336

The hippocampus, the region most vulnerable to ischemia showed the lowest basal SODase activity. By 7 days, regional differences in activity had disappeared.

These data are evidence for ongoing free radical generation and continuing global compensation following transient cerebral ischemia. Early intervention with free radical scavengers could compensate for the delay in the activation of primary cellular defense mechanisms (SODase) and thereby inhibit the lipid peroxidation that follows ischemia.

(Supported by Canadian Heart Foundation)

42.

Reversible Myocardial Damage Following Acute Brain Swelling. Quantitative Evaluation

A. KOLIN, A. BREZINA, J.A. KELLEN, A.J. LEWIS and J.W. NORRIS (Toronto, Ontario)

Unilateral carotid ligation in gerbils sufficient to produce cerebral edema or infarction causes reversible myocardial damage demonstrable by succinic dehydrogenase histochemistry and release of myocardial creatine kinase (A. Kolin et al — Stroke 18, 280, 1987). Catecholamines seem to be the link between cerebral and heart changes.

To obtain quantitative data of myocardial damage we measured accumulated neutral fat in myocardium by electron microscopy morphometry (expressed as % of muscle fiber area occupied by fat droplets) and by a biochemical method for triglycerides. We used the same gerbil model and compared results obtained in 3 gerbil groups (N = 5 each) — sham-operated, carotid-ligated with and without metoprolol (Betaloc-Astra) pretreatment — 16 hours after operation. No signs of irreversible myocardial damage were found. A significant increase in myocardial triglycerides was found in carotid-ligated animals both biochemically ($p<0.005$) and by morphometry ($p<0.025$). Metoprolol pretreatment decreased the myocardial damage measured by both methods ($p<0.025$; $p<0.025$).

Our results indicate that myocardial damage caused by acute brain lesion can be prevented by beta-adrenergic blockade, and can be quantitated by measuring accumulated fat in muscle fibers by biochemical and EM morphometric methods.

43.

Tolerance of the Cerebral Venous System of Focal Cerebral Ischemic Rats to Retrograde Perfusion Pressure Studied by Double-Tracer Autoradiography

T. UEDA, Y.L. YAMAMOTO, E. TAKARA and M. DIKSIC (Montreal, Quebec)

A sudden increase in the arterial blood pressure can cause permeability changes in the cerebral small vessels, including the venules (Haggendal et al 1972; Auer 1978). The tolerance of the cerebral venous system to retrograde perfusion pressure into the cerebral vein in focal cerebral ischemic tissue remains unknown, however. We therefore examined the tolerance of the cerebral venous system to retrograde perfusion pressure into the cerebral vein in focal ischemic rats by quantitative double-tracer autoradiography.

Method — Twenty-seven rats were used for this study. The main trunk of the inferior cerebral vein, anatomically comparable to Labbe's vein in humans, was cannulated and perfused with autologous arterial blood at venous perfusion pressures of 0 (sham), 100, 150, 170, and 200 mmHg, respectively. The retrograde transvenous perfusion was started 1 hour after occlusion of the middle cerebral artery (MCA) and ended 3 hours after MCA occlusion. Double-tracer autoradiography was used to measure LCBF and blood-brain barrier (BBB) permeability, using ^{18}F-FAP and ^{14}C-AIB as tracers.

Results — The rats with perfusion pressure below 150 mmHg exhibited no significant changes of LCBF and BBB permeability. However, the rats with perfusion pressure above 170 mmHg showed significant ($p<0.05$) changes of the BBB permeability in the superficial cortical layer with slight reduction of LCBF. In the 200 mmHg perfusion group BBB permeability change extended to the entire cortical zone and significant LCBV reduction ($p<0.05$) occurred.

Comments — Our results indicate for the first time that the cerebral venous system in rats can tolerate up to 150 mmHg retrograde perfusion pressure into the cerebral venous system without any BBB permeability or LCBF changes. However, there is a progressive BBB permeability change and LCBF reduction once the pressure exceeds 170 mmHg. Our new method makes it possible to deliver cytoprotective agents into the ischemic tissue more efficiently.

(Supported by MRC of Canada (MT-3174)).

44.

Effects of Oxyhemoglobin and Removal of the Endothelium on Responses of Canine Cerebral Arteries to Vasodilator Drugs

T. TSUJI, B.K.A. WEIR, C.A. KRUEGER and D.A. COOK (Edmonton, Alberta)

Oxyhemoglobin (OxyHb) appears to act directly on vascular smooth muscle to cause contraction and to inhibit endothelium-dependent relaxation. Since endothelial damage has been demonstrated in cerebral vessels after subarachnoid hemorrhage (SAH), it is possible that OxyHb released from lysed erythrocytes may be involved in the production of delayed cerebrovascular spasm by its interference with endothelium-derived relaxing factor. We have examined this possibility using the stainless-steel cannula inserting method to measure relaxant responses of canine basilar artery. Using this system, relaxant effects can be measured without the need for preconstriction. Endothe-

lial function was impaired by infusion of saponin. In preparations with intact endothelium administration of OxyHb gave a vasoconstriction, acetylcholine produced a small vasodilation followed by a vasoconstriction, while the calcium ionophore A23187, thimerosol and sodium nitroprusside produced a dose-dependent vasodilation. After treatment with OxyHb the vasoconstrictor component of the acetylcholine response and the dilation produced by sodium nitroprusside were enhanced somewhat, while the vasodilator responses to A23187 and thimerosol were inhibited. These same observations were further enhanced after endothelial removal with saponin. These data suggest that OxyHb administration works in concert with endothelial damage, and is consistent with a role for this mechanism in the pathogenesis of the vasospasm which develops after SAH.

(This work was supported by the Alberta Heart Foundation and the AHFMR).

45.

Spontaneous Midbrain Hemorrhage

R.S. FINGEROTE, A. SHUAIB and A.K.W. BROWNELL (Calgary, Alberta)

In the past, spontaneous midbrain hemorrhages (MBH) were considered rare. With widespread availability of cranial computerized tomography (CT) scanning, MBH is being diagnosed more frequently and may account for a certain percentage of "idiopathic 3rd nerve palsies" and "brain stem infarction".

We report 5 cases of MBH, seen over a 2 year period at the Calgary General Hospital and Foothills Provincial General Hospital in Calgary. Patient ages ranged from 17-56 years. Headache was present in all patients. Neurological signs observed included partial to complete 3rd nerve palsies in five, Parinaud's syndrome in one, ataxia of gait in two, mild hemiparesis in one, and unilateral asterixis in one. No patient had an altered level of consciousness or hypertension at presentation. CT demonstrated MBH in all cases with extension into the pons in one case, the thalamus and third ventricle in one case and the hypothalmus in one case. In all, the diagnosis of MBH had not been considered prior to CT scanning. Complete cerebral angiography was noncontributory in all cases. In all cases, there was significant though incomplete recovery. All patients were discharged within 15 days of admission. Follow-up CTs showed significant resolution of the hemorrhages.

MBH appears more common than previously suspected. The diagnosis may not be clinically obvious and is made only following investigation by CT or magnetic resonance imaging. Angiography is usually normal and prognosis for survival and recovery is good.

46.

Cerebral Granular Pericytes and Aging

B.J. JEYNES (St. John's, Newfoundland)

Cerebral granular pericytes may play a significant role in the functioning of the blood-brain barrier. Aside from their putative phagocytic role, little is understood about their normal biology or their role in cerebrovascular related diseases. In this investigation we examined their densities and certain of their morphologic characteristics as a function of age in a rabbit animal model. The brains from neonate, middle-aged and old rabbits were fixed by perfusion and processed for either methacrylate embedding or standard electron microscopy. Whole coronal slices of the left side of the brain were embedded for methacrylate processing at three levels midway through the brain. Semi-thin (1 m) sections were cut and stained with P.A.S. Counts of P.A.S. positive granular pericytes were made for each whole section at each age level and the total area for each section was recorded. Cubic millimeter samples from the opposite half of each brain were removed randomly and processed for electron microscopy. We observed a significant increase in the density of granular pericytes at middle-age when compared to the comparable densities of neonate and old animals. Morphologic evidence of an age-dependent variability of granule characteristics was observed. These results support the hypothesis that cerebral granular pericytes may alter their numbers according to changing metabolic demands over a life-span under normal conditions. The age-dependant variability in granule morphology may reflect aging changes in the quantities and qualities of anabolic and/or catabolic materials traversing the blood-brain barrier.

47.

Systemic Administration of the Glutamate Antagonist MK-801 Fails to Protect Hippocampal Neurons from Brief Periods of Forebrain Ischemia

W. WANG, D. VECCHIO, W. PULSINELLI and A. BUCHAN (New York, U.S.A.)

The excitatory NMDA receptor has been proposed as a mediator of neuronal injury in a wide variety of disorders, particularly stroke. NMDA receptor antagonists might prevent neuronal injury and one such compound MK-801 has been shown to protect hippocampal neurons against injury from transient forebrain ischemia in the gerbil. This neuroprotective effect of MK-801 was therefore tested using transient forebrain ischemia in the rat.

Male Wistar rats were injected with either MK-801 or physiological saline intraperitoneally one hour prior to forebrain ischemia. In the first experiment animals sustained fifteen minutes of ischemia and in the second, five minutes of ischemia. Cerebral blood flow was restored in animals that met full ischemia criteria. Survivors were allowed to reperfuse for 72 hours prior to perfusion-fixation. Histological analysis of hippocampal CA1 zone was performed and a grade determined (0 = normal, 1 < 10%, 2 = 10-50%, and 3 > 50% of CA1 neurons damaged).

Mean Grade of Hippocampal CA1 Neuron Injury
(Mean Grade ± SD)

	N	0.9% saline	N	MK-801
5′ ischemia	n = 12	2.06 (±0.6)	n = 13	2.04 (±1.0)
15′ ischemia	n = 5	3.0 (±0.0)	n = 6	2.88 (±0.3)

Fifteen minutes of forebrain ischemia produced consistent CA1 damage that was equivalent for the MK-801 and saline-treated animals. Damage was more variable in the five minute animals but the drug failed to influence the outcome from even this brief period of ischemia.

48.

Anévrysmes intracrâniens familiaux: étude de 9 familles saguenéennes

L. CANTIN, J. MATHIEU, M. DEBRAEKELEER et A. VIGNEAULT (Chicoutimi, Quebec)

Les auteurs ont identifié 22 individus (9 hommes, 13 femmes) porteurs d'anévrysmes sacculaires intracrâniens et issus de 9 familles résidant au Saguenay-Lac-Saint-Jean, région relativement isolée au nord-est du Québec. Parmi ces 9 familles, 8 fratries ont deux individus ou plus porteurs d'anévrysmes intracrâniens.

La reconstruction généalogique de ces 9 familles et de trois groupes témoins appariés selon la paroisse et la date de mariage, l'origine des migrants et le statut socio-économique a été effectuée sur une profondeur de 7 générations en utilisant le registre de population du Saguenay-Lac-Saint-Jean (SOREP) et divers registres et mariages couvrant tout l'est du Québec.

Le coefficient d'apparentement (Phi) est nettement plus élevé chez les familles atteintes que chez les groupes témoins alors que le coefficient de consanguinité (F) est similaire dans tous les groupes. La reconstruction généalogique de ces 9 familles a permis d'identifier deux couples ancêtres communs. Le premier couple, commun à la majorité des familles, s'est marié à Québec en 1660. L'autre couple ancêtre s'est installé à La Pocatière, sur la rive sud du Saint-Laurent, en 1700.

L'identification de couples ancêtres communs, la présence de deux (2) individus atteints ou plus au sein de plusieurs fratries, l'atteinte d'individus des deux sexes et l'absence d'anévrysme intracranien chez les ascendants directs suggèrent fortement la présence d'une mutation génétique de type autosomal récessif.

La concentration de ces familles au Saguenay-Lac-Saint-Jean pourrait être la conséquence de facteurs démographiques liés aux populations isolées de Charlevoix et du Saguenay-Lac-Saint-Jean. Cependant, la reconstruction généalogique permet de croire à une diffusion plus large de cette génopathie à l'ensemble du Québec.

49.

Cerebral Hyperperfusion Syndrome After Carotid Endarterectomy: A C.T. Scan Study

M.J. WONG and P. HARRISON (Vancouver, B.C.)

The cerebral hyperperfusion syndrome is a rare complication following carotid endarterectomy, performed for high grade carotid stenosis. The clinical triad of this syndrome was first reported in 1984. Patients present with severe headaches, focal seizures which are resistant to drug treatment and may go on to a delayed cerebral hemorrhage. Seizures occur between the 3rd and 11th post-operative day, but most manifest themselves by the 7th post-op day. Most patients have a transient neurological deficit followed by recovery; however a small percentage have a cerebral hemorrhage.

The pathogenesis of this syndrome is felt to be related to a hyperperfusion state. Chronic high grade stenosis may induce hypoperfusion, with maximal vasodilatation of small vessels to ensure adequate blood flow. This chronic vasodilated state results in a loss of autoregulation. When blood flow is restored after endarterectomy, the capillary bed is unprotected, resulting in cerebral edema and hemorrhage. This is analogous to the "break-through bleeding" that occurs after resection of a cerebral arteriovenous malformation.

Post-Mortem studies show edema with multiple percapillary microhemorrhages. Small arteries and arterioles show endothelial swelling and fibrinoid necrosis.

Previous studies report normal nuclide and C.T. brain scans apart from the terminal hemorrhage. EEG shows PLEDS.

We would like to present serial C.T. findings of this syndrome.

50.

Migraine Accompaniments and Cerebral Infarction

A. SHUAIB and M.A. LEE (Calgary, Alberta)

Migraine accompaniments refers to any migrainous phenomenon that occurs in the absence of migraine headache. The majority of patients with migraine accompaniment do not experience headache at any time but 13-20% of patients who do have cephalgic migraine may also at other times experience migraine accompaniment. Visual and sensory symptoms are commonly observed and these may last from a few minutes to several hours. Lasting symptoms with evidence of cerebral infarction on CT Scan have, however, not been previously reported.

We now report four patients (three females, one male) age 37-52 years who had a history of migraine accompaniment and who developed cerebral infarction. Common migraine not associated with the migraine accompaniment was seen in two patients and one patient had a history of classical migraine, but had experienced no headaches in the previous three years. Symptoms were visual in all four cases and in three the onset of cerebral infarction was clearly related to the aura. Cerebral infarctions were left occipital in two cases, left frontoparietal in one case and bilateral cerebellar and right parietal in one case. Recovery was good in three patients but the patient with the frontoparietal infarct continued to have a mild aphasia. The mechanism of cerebral infarction in migraine is poorly understood but may in part be related to vascular spasm. It is likely that a similar mechanism may also be responsible for cerebral infarction in cases with migraine accompaniment. Migraine accompaniments, therefore, may not be as benign an entity as has previously been considered.

51.

Man in the Barrel Syndrome

S. JARJOURA, A. LAMONTAGNE and S. KANTARDJIEFF (Sherbrooke, Québec)

"Man in the barrel syndrome" is a term used by Mohr to describe brachial diplegia with preserved motor function of the lower limbs (as if the patient's arms and trunk were constrained within a barrel).

Even if this syndrome has been reported to be a frequent sequella of cerebral hypoperfusion with distal field infarction, there are few detailed reports of it in the literature, specially of patients who have presented this syndrome after hypotensive coma and whose progressive recuperation is documented on video-cassette.

CT scans showed extensive cerebral hypodensities in both frontal areas, supporting the ischemic damage hypothesis. Somatosensory evoked potentials of the median nerves showed absent waves over frontal and centro-parietal areas after N17 on both sides.

CT scans and electrophysiological studies tend to demonstrate that this syndrome is secondary to bilateral motor cortex infarction, involving the watershed area, as postulated by Mohr and Sage.

General Neurology (Platform)

THURSDAY, JUNE 16TH — P.M.

52.

Brain Metals and Chronic Neurological Diseases

R.J. UITTI, A.H. RAJPUT, B. ROZDILSKY and W.K. YUEN (Saskatoon, Saskatchewan)

Several neurological disorders are known to be caused by deficiency or toxicity of different metals — Wilson's disease being a prominent example. In 1985 we reported that brain concentrations of copper in the substantia nigra and magnesium in the caudate nucleus and cerebellum were lower in idiopathic Parkinson's disease (PD) than in normal age and sex matched control brains. We have expanded our studies to include other chronic diseases to determine if those findings are specific for PD.

Using atomic absorption and atomic emission spectroscopy, concentrations of 24 metals were measured in four brain regions (frontal cortex, caudate nucleus, substantia nigra, and cerebellum) in 36 human brains. Regional metal concentrations were compared between 12 normal control brains and 24 chronic neurologically diseased brains (confirmed by a qualified neuropathologist). These included the following conditions: PD, motor neuron disease, senile parkinsonism, parkinsonism due to basal ganglia neurofibrillary tangle disease, Alzheimer's disease, multi-

ple sclerosis, Huntington's disease, and Down's syndrome/Alzheimer's disease.

Our results show that parkinsonian brains as a group have significantly lower concentrations of magnesium in the caudate nucleus and copper in the substantia nigra; no such abnormality was detected in other diseases. Brain metal contents did not correlate with any of the other chronic neurological diseases examined — including aluminum and Alzheimer's disease. The significance of parkinsonism and metal deficiency state in the brain remains to be established.

53.

Natural History and DNA Linkage Studies of NF-2

W. WERTELECKI, G.A. ROULEAU and D.W. SUPERNEAU (Mobile, U.S.A.)

We investigated a large kindred with NF-2 (formerly referred to as "central" or BANF). The main nosological landmarks were: postpuberal emergence of ependymomas (EP), meningiomas (MEN), acoustic neuromas (AN) and other central nervous system tumors (CNST). None of the patients met the diagnostic criteria of NF-1 (von Recklinghausen NF). Symptoms began between the ages of 15 and 55 years. With aging, 20 of 23 patients developed two or more CNST, of which 9 had only bilateral AN. Unusual intracranial calcifications were found in 9 of 11 patients. Intracranial calcifications probably are a prodromic sign of NF-2. We found no evidence that puberty, pregnancy or maternal inheritance had clinical effects and our data is inconclusive concerning cataracts in NF-2. Simultaneous analysis of **D22S1** and **IGLV** DNA markers for co-inheritance with NF-2 indicates that the locus of NF-2 is near the center of the long arm of chromosome 22. (22q11.1-22q13.1) Our studies demonstrate an etiologic relationship between a mutation of a gene on chromosome 22, NF-2 and the emergence of a variety of CNST. The natural history of NF-2 in this family is virtually identical to the family investigated by Gardner et al over a half century ago. In contrast, other investigators have reported multiple CNST including AN in association with peripheral nerve sheath tumors and even pigmentary skin changes. Thus, DNA studies, linkage studies require attention to the clinical categorization of families. Once the diagnosis of NF-2 is entertained, a complete assessment of intracranial, spinal structures and audiologic function are indicated. In contrast to Huntington chorea where treatment modalities remain limited, the negative effects of predictive DNA diagnostic testing of NF-2 are tempered by potential advantages that can accrue from presymptomatic diagnosis and early treatment.

54.

Clinical and Biochemical Profile of Neuroleptic Malignant Syndrome: A Study of 24 Cases

P.I. ROSEBUSH (Toronto, Ontario)

Neuroleptic malignant syndrome (NMS) is a fulminant, life-threatening reaction to neuroleptic medication that is reported to be associated with a mortality rate of 20-30%. I have had the opportunity to study 24 cases of NMS in detail over the past 6 years. The patients had a mean age of 43.8 years (range 17-92 years). Clinical features of the syndrome included: fever (100%); diaphoresis (100%); autonomic instability (100%); delirium (100%); mutism or hypophonia (96%); muscular rigidity (96%); bradykinesia (100%); tremulousness (92%); dystonic or choreiform movements (59%); incontinence (55%); and rash (30%). Laboratory findings included: elevated muscle enzymes (100%); hypoferraemia (96%); hypomagnesaemia (60%); hypocalcaemia (58%); proteinuria, usually with myoglobinuria (91%); and elevated CSF protein (37%). Extensive investigations in each case revealed no other medical condition which could account for the clinical and laboratory findings. The CSF was acellular in all cases, while diffuse slowing was found in all 7 patients who had EEG studies. All patients were treated with vigourous supportive therapy, which included intravenous fluids, antipyretic agents, and discontinuation of the neuroleptic medication. There were no fatalities on this regimen, with virtually all patients making a complete or almost complete recovery, the lone exception being a patient with AIDS, who remained quite ill.

NMS is a severe, fulminant illness with multiple associated metabolic abnormalities that with prompt recognition and vigourous supportive treatment need not carry the high mortality rate with which it has traditionally been associated.

55.

Late Onset Metachromatic Leukodystrophy in Consecutive Generations

G. FRANCIS, A. ABDOLLAH, B. YAMUT, P. HECHTMAN, D. ARNOLD, L. WOLFE, L. CHARRON, M. BOTEZ, S. CARPENTER and G. KARPATI (Montreal, Quebec)

Metachromatic Leukodystrophy (MLD) is an autosomal recessive disorder due to cerebroside sulfatase deficiency causing sulfatide accumulation in white matter.

We present results of studies on a non-consanguineous family with an affected member in two consecutive generations. The proband (age 19) had clinical onset at age 15 with features of dementia, spastic tetraparesis, cerebellar incoordination and mild sensory loss. His maternal uncle (age 42) had onset at age 20 manifest by spastic gait, progressive cerebellar signs and mild dementia.

Sural nerve biopsies from both patients showed conspicuous storage of metachromatically staining material in Schwann cells and macrophages. EMG studies revealed markedly slowed nerve conduction times with slowed SSEP. CSF protein was greatly increased. CT and MRI scans showed large confluent abnormalities in the cerebral white matter. Phosphorous magnetic resonance spectroscopy indicated elevated inorganic phosphate in muscle and reduced phosphodiesters in brain.

Leukocyte arylsulfatase activity in the proband was 4.5 nmole/mg protein/hr., uncle 2.6, mother 12.2, father 72.4, sister 120.4, brother 102.4 (normal = 215). Enzyme levels in unaffected members suggest all are heterozygotes. Only the mother had abnormal studies consisting of prolonged F wave and H reflex responses.

This family represents a rare occurrence of late onset MLD in consecutive generations.

56.

A Preliminary Clinical Trial of Orthoclone OKT*3 Treatment in Chronically Progressive Multiple Sclerosis

B.G. WEINSHENKER, B. BASS, G.C. EBERS and G.P.A. RICE (London, Ontario)

Orthoclone OKT*3, a pan-T cell monoclonal antibody is being studied in a preliminary trial in patients with chronically progressive multiple sclerosis (MS). OKT*3 is administered in 10 daily intravenous injections of 5 mg. Outcome is assessed using the Kurtzke functional and extended disability status scales, as well as alterations in magnetic resonance imaging (MRI) post treatment. We have entered 10 patients into our study and propose to treat an additional 5. One patient was withdrawn following an anaphylactic reaction on the first day. Treatment in the remainder was associated with a highly characteristic sequence of adverse side effects. On the first day, hypotension developed in all patients in association with nausea, vomiting and occasionally diarrhea. The subsequent hospital course was complicated by a generalized erythematous macular rash and fever in all patients, fol-

lowed in several cases by myalgias and arthralgias. All patients deteriorated functionally during the course of treatment, but most returned to their pretreatment level of disability by the conclusion of treatment. The first post treatment MRI (day 10) was unchanged by treatment with OKT*3.

At the meeting we will report the six month follow-up data on the patients.

57.

Effets cliniques, électrophysiologiques et endocriniens de la TRH en perfusion dans la sclérose latérale amyotrophique (SLA)

J. PUYMIRAT, B. GUEGUEN et P. RONDOT (Ste-Foy, Québec; Paris, France)

Des études récentes ont rapporté les effets bénéfiques de l'administration de l'hormone thyréotrope (TRH) chez des sujets atteints de SLA avec amélioration de la force musculaire et diminution de la spasticité. Nous rapportons les résultats d'un essai de traitement aigu par la TRH dans 8 cas de SLA avec appréciation des effets cliniques, électrophysiologiques et hormonaux. La TRH a été administrée par voie intraveineuse à raison de 500 mg perfusé en 3 heures. Les perfusions ont été en général bien tolérées en dehors de certains effets mineurs (frisson, tachycardie, tachypnée, myoclonies). Sur le plan clinique, une amélioration subjective a été observée chez 2 sujets. Sur le plan électrophysiologique, les tests de comparaisons multiples n'ont permis d'objectiver aucune modification significative de la réponse H. Sur le plan endocrinien, les taux de base de prolactine (PRL), HGH, FSH, LH, TSH, T_3, T_4 ne sont pas modifiés chez les patients atteints de SLA. Après la perfusion de TRH, il a été observé une rapide et nette augmentation du taux sanguin de PRL, HGH, de TSH. Alors que les taux de FSH, LH sont restés stables de même que les taux sanguins de T_4.

Notre étude n'est pas en faveur d'un effet bénéfique du TRH dans le SLA et montre l'importance du retentissement endocrinien de tel traitement.

58.

Postherpetic Neuralgia and Topical Capsaicin

C.P.N. WATSON, R.J. EVANS and V.R. WATT (Toronto, Ontario)

Topical 0.025% capsaicin was used to treat 32 patients with postherpetic neuralgia > 3 months duration. Twenty-two females and 10 males entered this open label study. Capsaicin ointment was applied four times daily for four weeks. Pain was assessed weekly by verbal intensity and visual analogue scales, and a daily pain diary. Patients were categorized as excellent, good, poor or unchanged. 55% of 21 patients had good (10) or excellent (2) relief. 77% of the 21 noticed at least some improvement in pain status. Post-capsaicin burning was a common untoward effect in most patients and in one-third was so unbearable that the trial was terminated prematurely. This treatment appears to be a useful modality in PHN, particularly in the elderly in whom oral medications are often poorly tolerated, however it does require supervision. A double-blind, controlled trial is now necessary.

General Neurology (Poster)

FRIDAY, JUNE 17TH - P.M.

59.

Longterm Follow-up of Acute Encephalitis - Herpes Simplex Cases Compared to Other Causes of Encephalitis.

A. KIRK, Y. PARNELL, D. LEE and W. BROWN (London, Ontario)

The records of 35 cases of acute encephalitis seen at the University Hospital in London over a 12 year period were examined with the object of comparing the long-term outcome of herpes simplex I cases to other causes of encephalitis. Eight cases were considered as herpes simplex positive based on autopsy (1), biopsy (2), or significant rises in antibody titres against HSVI (5). Another 14 cases showing no titre rise against HSVI or other viruses were classed as HSVI negative. Convalescent titres and biopsies were not obtained in another 11 cases classed here as "uncertain". Single cases of coxsackie B and varicella-zoster encephalitis were seen in the same twelve year period. The mean survivor follow-up period was approximately five years for both the HSV positive and HSV negative groups and nine months for the uncertain group.

Of the HSV positive group, two died early, four were institutionalized of whom three later died, two returned home, only one of whom was able to return to work. By contrast only one of the HSV negative patients died, the remainder returning home, half returning to work. All uncertain patients survived but half were unable to return to work. Two of the three HSV positive survivors had neuropsychological studies. These were normal in one while the other had a disabling amnestic syndrome and bi-temporal macrocystic encephalomalacia on MRI. Five of the thirteen HSV negative survivors were neuropsychologically normal, none having MRI residua of encephalitis. Of five other HSV negative patients contacted, three were reported by their families as completely recovered. The most disturbing feature was the high percentage of patients who never returned to their former jobs. As expected, HSVI cases fared much worse than the HSV negative and uncertain encephalititides.

60.

Antiphospholipid Antibodies and Neurologic Disease

C.L. BARCLAY, A. SHUAIB, W. MURPHY, K.M. HOYTE and D.G. PATRY (Calgary, Alberta)

Lupus anticoagulant and anticardiolypin antibodies are antiphospholipid antibodies which have been increasingly implicated as factors in the development of neurologic disease. Case reports have indicated an association of these antibodies with such diverse neurologic conditions as cerebral infarction, migraine headache, epilepsy, Guillain-Barre syndrome, myelopathy and chorea.

We present five patients with antiphospholipid antibodies who developed a wide range of neurologic problems. These patients presented to hospital between the spring of 1985 and the fall of 1987. All of them were female and they ranged in age from 26-48. Two had SLE. Their PTT's ranged from 37-56. Two of the five suffered from migraine headaches and seizures and one had migraine accompaniments. Three suffered cerebral infarctions. Angiograms in all three cases were consistent with thrombosis and none of the echocardiograms revealed an embolic source. Each of these patients received anticoagulants, although in one, treatment was stopped due to side effects. One of the three also received ASA. Only one suffered a recurrent infarction but this occurred before she was started on therapy.

A PTT is a useful, though not 100% sensitive screening test for antiphospholipid antibodies. It should be used routinely in the investigation of young adults with stroke or other neurologic conditions where indicated. If this were more widely done, the true extent of antiphospholipid antibody associated neurologic disease would become better understood and the most optimal form of treatment could be determined.

61.

Postherpetic Neuralgia Post Mortem

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C.P.N. WATSON, J. DECK, C. MORSEHEAD and D. VANDERKOOYS (Toronto, Ontario)

The purpose of this investigation was to study pathologically a case of a 58 year old man who had suffered from postherpetic neuralgia in the right T6, 7, 8 dermatomes for 5 years.

An autopsy was performed 12 hours after death. Specimens of spinal cord, dorsal roots, and dorsal root ganglia were obtained. The material was examined by light microscopy. The spinal cord was stained by immunohistochemistry for substance P, serotonin and dopamine-beta-hydroxylase, and also assessed for the presence of opiate receptors.

Light microscopy showed atrophy of the dorsal horn of the spinal cord at the appropriate level. Loss of all diameter fibres was found in the dorsal root. The dorsal root ganglia showed fibrosis at T8. No deficiency in serotonin, dopamine-beta-hydroxylase, or substance P was demonstrated in the atrophic dorsal horn. No difference in opiate receptors was determined on the affected side.

These pathological findings on light microscopy add new information to the few previously reported cases of long-term survivors with herpes zoster. Assays for neurotransmitters and opiate receptors have not previously been reported in this condition.

62.

Ultrastructure of Human Post-traumatic Syringomyelia

K. REDDY, M.R. DEL BIGIO and G.R. SUTHERLAND (Winnipeg, Manitoba)

Post-traumatic syringomyelia is well recognized as a clinical entity, but the pathogenesis of this condition is still in dispute. Studies of the ultrastructure of the syrinx cavity may help improve our understanding of the pathophysiology. No such detailed studies are available. We have treated a patient with post-traumatic syringomyelia by cordectomy, and have analyzed the cordectomy specimen by Light, Transmission and Scanning microscopy.

The syrinx cavity at the lower end, was found to be not in communication with the central canal, but a cluster of ependymal cells were found at the lower end of the cavity. The cavity was lined almost entirely by glial fibres, with some macrophages. Small areas of the lining was found to be formed by cells ultrastructurally similar to ependymal cells. Subependymal axons were rarely visualized. In the area surrounding the syrinx, the finding of perivascular spaces being filled with collagen was confirmed. No enlargement of the Virchow Robin spaces, or schwannosis were found, as previously reported. These findings, their similarities to the non-traumatic syrinx, and their relevance to the understanding of the pathogenesis of this entity, are discussed.

63.

Multiple Ocular Neuropathies Secondary to Sjogren's Syndrome

P. PELOSO, L.M. METZ, O. SUCHOWERSKY, M.J. FRITZLER and S.K. FIELD (Calgary, Alberta)

Central nervous system (CNS) manifestations may be present in 15-25% of patients with primary Sjogren's Syndrome (SS) but cranial neuropathies appear to be rare. There have been 22 reported cases of single cranial neuropathies and 2 cases of multiple unilateral cranial neuropathies. Patients with other CNS involvement also have a high incidence of abnormal visual and auditory evoked potentials (EP's). We present a patient with primary SS and bilateral multiple ocular neuropathies.

A 55 year old male presented in 1984 with pleuritic chest pain and pleural effusion. He was subsequently proven to have primary SS based on serology and positive salivery gland biopsy (Grade III). He had no other collagen vascular disease. He remained stable until July 1987 when his pulmonary function began to deteriorate. In October 1987 prednisone 20 mg daily was commenced with some improvement. One month later he developed bilateral retroorbital pain, bilateral lateral rectus palsies, impaired right superior rectus function, right ptosis, and mildly prolonged visual EP's bilaterally. Enhanced CT scanning with sellar and orbital views was normal. Cerebrospinal fluid was normal including cytology. Increasing his prednisone to 60 mg daily resulted in minimal improvement in his ocular findings at 4 weeks.

We believe this patients ocular neuropathies are secondary to SS as complete neurologic investigation did not reveal another etiology, and his SS was active at the time of onset of neurologic complaints.

Because SS may not be recognized in over half of patients prior to onset of neurologic complications, SS should be considered as a cause for multiple ocular palsies where they are otherwise unexplained.

64.

Sjogren's Syndrome Infrequently Mimics Multiple Sclerosis

L.M. METZ, M.J. FRITZLER and T.P. SELAND (Calgary, Alberta)

The diagnosis of multiple sclerosis (MS) has many pitfalls because it relies mainly on clinical criteria. Recent published data suggest that primary Sjogren's syndrome (SS) may mimic MS.

Patients with SS may have relapsing-remitting neurologic manifestations affecting any level of the neuraxis. They frequently have abnormal evoked potentials and oligoclonal bands in their cerebrospinal fluid (CSF). Such patients have been mistakenly thought to have MS because SS was either not recognized or was otherwise asymptomatic. Twenty such patients were reported from one centre.

At the University of Calgary MS clinic we screened 42 consecutive, unselected patients for SS in an attempt to estimate the frequency that SS is mistakenly diagnosed as MS. All patients had probable or definite MS according to the 1983 Poser criteria. Epidemiologically and clinically they were a typical sample of MS patients except for a slight female preponderence. Patients were screened for history of xerostomia, xerophthalmia and recurrent salivary gland enlargement. They all had serology (anti-Ro (SSA)) and anti-La (SSB)) and a Shirmer's test.

None of our patients were found to have SS. All patients have negative serology. Six patients complained of xerostomia or xerophthalmia but all were on anticholinergics. Ten patients had an abnormal Shirmer's test but 7 of these were on anticholinergics (includes 4 of 6 symptomatic patients).

We therefore conclude that in the setting of an MS specialty clinic SS is not frequently misdiagnosed as MS.

65.

Protracted Clinical Course of "Adult Onset" Metachromatic Leukodystrophy (MLD): Case Report

R.A. PURDY, B.J. DOANE, M.W. SPENCE, T.J. BENSTEAD, V. SANGALANG and W.J. MALONEY (Halifax, Nova Scotia)

Metachromatic Leukodystrophy (MLD) is a rare disorder in adults. By convention adult onset MLD presents after age 21, while juvenile onset MLD onsets between age 4-21, and late infantile MLD presents from 12-18 months to 4 years of age.

We report a 31 year old female who presented with a 13 year history of behavioral problems, including being expelled from school at age 18. She became progressively worse one year prior to presentation and was admitted to the Psychiatry Service for investigation of a possible schizophrenic disorder. At age 10 she was seen because of high arches but had no peripheral nerve symptoms throughout her life.

Neurological examination revealed a severe dementia frontal lobe release signs, high arches, absent ankle jerks and distal atrophy in her hands and feet. CT Scan demonstrated marked cerebral and cerebellar atrophy with symmetrical focal low density white matter lesions. EEG showed diffuse generalized slowing. EMG showed evidence of a diffuse motor-sensory neuropathy. The leukocyte aryl sulfatase levels were low and consistent with MLD. Sural nerve biopsy was consistent with MLD.

Cases presenting with symptoms in their teens have been considered as part of adult onset MLD if death occurred after age 21 suggesting these cases are different than the juvenile onset cases. This particular patient appears to have begun before age 10 with peripheral nerve dysfunction and at age 30 with severe progressive dementia which is still ongoing.

Detailed clinical, biochemical, electrophysiological, radiological, and pathological findings will be presented along with a discussion of the possible reasons for such a protracted course to date as well as the unusual CT findings.

66.

Neurological Manifestations of Kawasaki Disease in a Young Adult

E.J. ANGUS and M. MOEN (Detroit, U.S.A.)

Kawasaki disease or mucocutaneous lymph node syndrome is an acute febrile illness of unknown etiology which is most commonly recognized in young children.

We report a young adult patient who fulfilled the diagnostic criteria for Kawasaki disease, and who also had striking central nervous system involvement manifested by encephalopathy, aseptic meningitis, increased intracranial pressure, bilateral papilledema and bilateral sixth nerve palsies. Other clinical findings in this patient were consistent with Kawasaki disease including cervical adenopathy, hilar adenopathy, thrombocytosis, and coronary artery aneurysm. Therapy with acetazolamide resulted in resolution of signs and symptoms of increased intracranial pressure.

This case underlies the importance of considering this diagnosis in adults with increased intracranial pressure and negative CT scan.

67.

Postherpetic Neuralgia: 159 Cases

C.P.N. WATSON and R.J. EVANS (Toronto, Ontario)

159 patients with postherpetic neuralgia (PHN) were assessed in a prospective, longitudinal study designed to evaluate demography, clinical features, treatment results and long-term status. PHN was commonest in females and increased in incidence and severity with age. There was a predilection for involvement of the ophthalmic division of the trigeminal nerve and for mid-thoracic dermatomes. Pain was most commonly a combination of steady burning with superimposed jabbing. Scarring, hyperaesthesia, dysaesthesia and sensory loss were common findings and the latter commonly exceeded the area of the skin lesions. Allodynia and hyperpathia were less common. Our largest experiences and most successful results were with the antidepressants amitriptyline and nortriptyline. A variety of other pharmacological agents and treatment approaches were less successful. A number of patients with longstanding PHN continued to improve with time.

68.

Neurological Complications of Systemic Lupus Erythematosus (SLE)

W.P. OLSZYNSKI, J.T. SIBLEY, W.E. DeCOTEAU and M.B.M. SUNDARAM (Saskatoon, Saskatchewan)

188 patients with SLE were registered in the data bank of our hospital between 1973 and 1986 (males - 29, females - 159; mean age - 37 years; mean follow-up from diagnosis - 7.8 years). Of these, 50 (26%) had neurological dysfunction.

Seizures (n.14): Attacks were generalized in 10 patients and partial in 4. In 9 cases, seizures occurred before or at the time of diagnois of SLE. Nine patients had only single seizures and attacks were infrequent in the remaining 5. Anticonvulsants were used in 10 patients and they did not aggravate lupus activity in any of them. Also, there was no worsening of other systemic clinical features or laboratory findings in any patient at the time of seizures.

Encephalopathy (n.18): common features included hallucinations, delusions and confusion. 14 patients had single bouts and 4 suffered recurrent attacks. Corticosteroids were not responsible for any of the episodes.

Others: Cerebral stroke (n.6), probable brain stem dysfunction with diplopia (n.11) and polyneuropathy (n.17) were also seen. 7 of 17 patients with polyneuropathy also had CNS dysfunction.

Conclusions: Neurological compliations are common during the course of SLE. Seizures and encephalopathy in the majority of cases appear to run self limited course and occur in the absence of multisystem flare-up. In this series, anticonvulsants did not aggravate lupus activity and corticosteroids were not responsible for psychosis.

Movement Disorders (Platform)

THURSDAY, JUNE 16TH - P.M.

69.

Progabide, A GABA Agonist, In The Treatment of Dystonic Torticollis

O. SUCHOWERSKY, R. FROSS, J. TSUI, G. ROHS and D.B. CALNE (Calgary, Alberta; San Francisco, U.S.A.; Vancouver, B.C.)

GABA is a major neurotransmitter of the outflow tracts in the striatum. As dystonia may be associated with striatal lesions, loss of GABAergic outflow may contribute to the motor disturbance. Progabide is a benzylidene derivative which acts as a GABA agonist, and may be potentially useful in treatment of dystonia. We performed a preliminary study to test efficacy and safety of this drug in spasmodic torticollis, a focal dystonia.

Twelve patients with torticollis were studied using a placebo-controlled dose ranging study. Five study days, at least 24 hrs apart, were chosen and patients were given increasing doses of progabide (900, 1500, 2100, or 2700 mg) in a single morning dose. A placebo was interspersed at random in the dosing schedule. Patients were closely monitored for 24 hrs following drug administration. A clinical score was assigned using the UBC Torticollis Evaluation Scale at regular intervals and all patients were videotaped. These were evaluated in a blinded manner. Biochemical and hematological indicies were monitored at the beginning and end of each 24 hr period.

Eleven patients completed the study. One improved both objectively and subjectively, and one reported mild subjective improvement. When all scores were analyzed no significant difference was found between placebo and drug effect. Adverse effects included visual blurring, lightheadedness, dizziness, confusion, nausea and mild ataxia. These were usually mild, but in one patient caused study termination. No hematalogical or biochemical changes occurred.

This study demonstrates the safety and tolerability of single doses of progabide in the maximum single dose range of 33-44 mg/kg. No acute benefits of the GABA agonist were seen. However, this does not reflect on what might occur with chronic dosing, and we feel that a long-term study to determine possible benefits in the treatment of dystonia is justified.

70.

Role of Dopamine D_1 Receptors in Treatment of Parkinson's Disease

P.J. BÉDARD and R. BOUCHER (Québec (Québec))

Treatment of Parkinson's disease is based on the replacement of the action of dopamine on striatal dopamine receptors. These receptors can be classified as DA_1 or DA_2 on the bais of their link with adenylate cyclase (Kebabian and Calne, Nature 1979, 130, 479). Agents which act on both receptors such as L-DOPA appear more likely than the pure D_2 agonist (such as bromocriptine) to induce dyskinesia. The latter however appear less powerful when given alone and tend to lose their efficacy more rapidly. Recently, selective agonists and antagonists of the D_1 receptor have become available. No extensive clinical trial has yet been conducted with these agents. When given alone to monkeys rendered parkinsonian by the toxin MPTP, the agonist SKF 38393, 5 mg/kg i.v. is without any visible effect on motility. Moreover it does not appear to potentiate the action of a D_2 agonists. However another D_1 agonist CY 208243, 0.5 mg/kg s.c. (Sandoz) can by itself induce a significant increase in locomotor activity without dyskinesia. When given together with a D_2 agonist (Quinpirole, Lilly) 0.5 mg/kg i.p., it markedly potentiates the locomotor response as well as the dyskinesia induced by the latter. Surprisingly the selective D_1 antagonist SCH 23390 (Schering) is able to block antiparkinsonian activity of combined D_1 and D_2 agonists as well as of mixed agonists. The above results suggest that full expression of the dopaminergic response requires the simultaneous activation of both receptors. Careful titration of the agonists of the two receptors may provide optimal therapeutic efficacy.

71.

Paradoxical Effect of Low-Dose Bromocriptine on Tardive Dyskinesia (TD)

E. POURCHER and P. BEDARD (Québec City, Québec)

To test the clinical usefullness of the presynaptic high-affinity D2 autoreceptor concept, Bromocriptine a D2 agonist, was given in low-dose (less than or equal to 5 mg a day) in a double blind study to 20 psychiatric patients presenting a tardive dyskinesia (TD) as a late side effect of their neuroleptic treatment.

In 60% of patients, TD significantly improved although in a delayed and transient manner.

Dividing the 20 subjects in sub-groups according to an "organicity index" (addition of risk factors such as age, vascular factors, encephalopathic antecedents and physical neurological signs) allows a more significant different distribution of the results.

The autoreceptor concept and "Supersensitivity" hypothesis for TD are then discussed.

72.

Numerical Analysis of Substantia Nigra Cells in General Population

A.H. RAJPUT, B. THIESSEN, D. MUNOZ, W. LAVERTY and H. DESAI (Saskatoon, Saskatchewan)

The clinical features of idiopathic Parkinson's disease (IPD) become evident only after 70% or more of substantia nigra (SN) cells have degenerated. Understanding the basis of SN neuronal atrophy is therefore crucial in identifying the etiology of IPD. Several recent reports indicate that the cause of IPD is some environmental factor(s). We have observed that IPD beginning at an early age is most likely to occur in those growing up in rural Saskatchewan. We are reporting on SN neuronal count in 48 neurologically normal individuals. All the counts were done at the same midbrain level by one of us and the cell count was adjusted for the tissue slide thickness for the purpose of comparison. With the advancing age, there was progressive SN cell loss but by itself, it was not sufficient to produce IPD. Those cases that had lived 80% or greater portion of life in rural communities had lower SN cell count than the urban residents. These differences were evident during first four decades of life and by age 75 years the cell counts were similar. When only the 5th percentile cases were considered, the rural subgroup by age 20 years, had SN cell loss of 70% compared to the expected normal. It is concluded that the rural Saskatchewan residents are predisposed to SN cell loss at an early age. The offending agent (or factor) remains to be determined. Attempts focused at rural environments, we feel, would be rewarding in identifying the cause of IPD.

73.

Somatostatin, Neuropeptide Y and Vasoactive Intestinal Peptide in Huntington's Disease: No Relationship Between Neuropeptide Levels and Degrees of Tissue Atrophy

M.F. MAZUREK, M.F. BEAL, D.W. ELLISON and J.B. MARTIN (Hamilton, Ontario and Boston, U.S.A.)

Concentrations of somatostatin (SS), neuropeptide Y (NPY) and vasoactive intestinal polypeptide (VIP) are elevated in postmortem striatal tissue dissected from the brains of patients dying with Huntington's disease (HD). These increased tissue levels might reflect: (1) a simple concentration effect, owing to the fact that the afferent neuronal terminals and aspiny striatal neurons within which these neuropeptides are contained are relatively spared in the HD, while the surrounding striatal matrix undergoes extensive atrophy; or (2) increased absolute levels of SS, NPY and VIP in HD striatum. We have addressed this issue by examining levels of SS, NPY and VIP in postmortem brain tissue dissected from 12 controls and 24 patients with HD, as defined by the family history, clinical presentation and neuropathological findings. The HD cases were subdivided into those with mild-to-moderate striatal atrophy (Grades I and II by the criteria of Von Sattel et al) and those with severe atrophy of the striatum (Grade III and IV). Concentrations of all 3 neuropeptides were increased 2- to 4-fold in HD caudate and putamen, and 1.5- to 3-fold in HD accumbens. There were no differences in levels of any of the 3 peptides between mild-to-moderate and severe cases.

These results suggest that the increased striatal concentrations of somatostatin, NPY and VIP found in HD striatum may not simply reflect a relative preservation in the face of atrophy of the surrounding striatal matrix, but may actually represent increased absolute levels of these peptides.

Movement Disorders (Poster)

FRIDAY, JUNE 17TH - P.M.

74.

Evidence that the Substantia Nigra is a Site for the Therapeutic Action of L-Dopa

G.S. ROBERTSON and H.A. ROBERTSON (Halifax, Nova Scotia)

L-Dopa is believed to exert its effects in Parkinson's disease (PD) by replenishing dopamine (DA) levels in the corpus striatum. Decarboxylation is thought to occur in the terminals of surviving nigrostriatal neurons. However, dendrites of dopamine neurons are also capable of releasing DA which may modulate striatal output in the substantia nigra pars reticulata (SNR) by interacting with D1 DA receptors. The D1

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receptors in the SNR are located on the terminals of the striatonigral pathway where they facilitate GABA release when stimulated by dendritically-released DA. Consequently, L-Dopa may be alleviating the symptoms of PD by restoring DA levels in the substantia nigra (SN). To address this possibility, the effect of L-Dopa on DA levels in the SN were studied in an animal model of PD.

Rats were unilaterally lesioned using 6-hydroxydopamine (6-OHDA). Animals that rotated over 400 times/hr following apomorphine were included in the study. Rats received either carbidopa (25 mg/kg, i.p.) followed one hour later by L-Dopa (25 mg/kg, i.p.) or the carbidopa followed by saline. Animals were killed 1, 2 or 3 hrs after the L-Dopa or saline. Striatum and SN were dissected and DA and DOPAC content was determined by HPLC.

At 1 hour after L-Dopa, DA and DOPAC levels were elevated in the striatum and the SN ipsilateral to the 6-OHDA lesion relative to vehicle controls. However, at 2 hours the DA content in the striatum was reduced by half while the levels in the SN were the same as that at 1 hour. At 3 hours the DA content in the denervated striatum was nearly back to preinjection levels while the DA content in the lesioned SN was the same as that at 1 hour. These results suggest that the striatum may initially mediate L-Dopa turning but after 2 hours, the SN maintains circling. Hence, in PD, L-Dopa may be exerting a therapeutic effect by elevating both striatal and SN DA levels.

Supported by the Parkinson Foundation of Canada, Sandoz (Canada) and the MRC.

75.

Effets de l'étirement musculaire prolongé dans le traitement de la spasticité chronique des muscles adducteurs de la hanche

S. CLAUDE, F. MALOUIN, C.L. RICHARDS, F. DUMAS and J.P. BOUCHARD (Québec, Québec)

Le but de ce travail est d'étudier l'effet d'un étirement musculaire prolongé (EMP) des adducteurs (ADD) de la hanche chez des sujets présentant une spasticité chronique des ADD se manifestant par une démarche en adduction et rotation interne des membres inférieurs. La force et/ou l'activité électromyographique (EMG) sont mesurées lors de contractions statiques des abducteurs (ABD) et de mouvements d'abductions passives (abd P) et actives (abd A).

Sept adultes paraparétiques, dont 5 ataxiques de forme spastique récessive (ARSACS) et 2 paralytiques cérébraux (diplégie spastique) ont été évalués avant et après 30 min de repos (contrôle) puis 30 min d'EMP. Celui-ci est réalisé en décubitus dorsal avec un appareil d'abduction bilatérale. Le sujet étant couché sur le dos, son pied attaché sur une planche à roulettes, un dynamomètre manuel maintenu par l'évaluateur mesure la force obtenue lors des contractions statiques maximales des ABD et la résistance (R) lors des mouvements d'abd P. L'EMG des muscles étirés (ADD) et de leurs antagonistes (ABD) est détectée par des électrodes de surface lors des abd P, des abd A et des contractions statiques. L'amplitude du mouvement est mesurée par un électrogoniomètre (EGM). En abd P, la vitesse est standardisée par une cadence verbale et, en abd A, le sujet effectue le mouvement à sa vitesse maximale. Les signaux de force, d'EMG et d'EGM sont envoyés simultanément à un ordinateur IBM-PC pour transformation et analyse.

En statique et en abd A, aucun des paramètres analysés n'est modifié par l'EMP. Par contre, en abd P, la R est diminuée chez 4 sujets (19% à 34% par rapport au pré-test) et l'EMG des ADD chez 2 de ces sujets (30% et 47%). Ceci suggère que l'EMP agirait à 2 niveaux dans le traitement de la spasticité chronique des ADD: sur l'activation musculaire réflexe et sur les structures passives musculo-tendineuses. Par ailleurs, le fait que l'activation volontaire des ABD ne soit pas facilitée par une séance d'EMP pourrait indiquer qu'il est nécessaire de répéter l'EMP pour agir sur l'activation volontaire et améliorer la marche. Enfin, chez certains sujets, la spasticité n'est pas réduite par une séance d'EMP de 30 minutes.

76.

Action and Resting Tremor in Two Patients with Complicated Migraine

S. HOUDE and M. VEILLEUX (Sherbrooke, Québec)

Recently, Fisher reported unusual vascular events in the territory of the posterior cerebral artery in 10 patients who had a presumed diagnosis of complicated migraine. Interestingly, seven of them had a movement disorder as a long-lasting neurologic sequela. We report two women, aged 23 and 29 years, who presented a sudden onset of arm tremor which occurred in association with a severe throbbing headache, a cloudiness of vision, and motor and sensory deficits. The latter symptoms abated over a period of 6-8 weeks, but an action and resting tremor persisted for 6-12 months. There was no family history of movement disorder and none of the patients were on medication prior to the onset of tremor. Investigations including electroencephalogram, head CT scan, cerebrospinal fluid studies, multi-modality evoked potentials, electrocardiogram, thyroid function tests, serum copper and ceruloplasmin, sedimentation rate and antinuclear antibodies were normal. A presumed diagnosis of complicated migraine was made on the basis of clinical history, past history of vascular headaches, and exclusion of multiple sclerosis and systemic diseases. Action and resting tremor can be occasionally seen as a long-lasting neurologic sequela in young patients with complicated migraine.

77.

Parkinson's Disease and Cerebral Astrocytoma In A Patient with Waldenstrom's Macroglobinemia; Is There An Association?

A. SHUAIB, G.M. KLEIN, M. LONG, W. BLAHEY and C.L. DEWAR (Calgary, Alberta)

We report a patient with Waldenstrom's Macroglobinemia (WM) whose clinical course was complicated by the development of Parkinson's disease (PD) and Cerebral Astrocytoma. PD developed four months after the onset of WM, and seemed to respond well to plasmapheresis used for the treatment of hyperviscosity from WM. Cerebral Astrocytoma became obvious two years after onset of WM, and led to the patient's demise within six weeks. We review the association of WM and Cerebral Astrocytoma and explore mechanisms that may explain this. Finally, the role of hyperviscosity and WM is reviewed in relation to neurodegenerative disorders.

Child Neurology (Platform)

THURSDAY, JUNE 16TH - P.M.

78.

Coma Scales In Pediatric Practice

J.Y. YAGER, B. JOHNSTON and S.S. SESHIA (Winnipeg, Manitoba)

The Glasgow Coma Scale (GCS) is considered to be the gold standard for assessing adults comatose after head injury. There is good inter-observer (I-O) agreement in this situation. The GCS is not readily applicable to young children and other coma "scales" have been proposed: (i) 0 to 4 grade (Seshia et al 1977), (ii) Simpson and Reilly (SR) Scale (1982), (iii) CCS scale (Raimondi and Hirschauer 1984), (iv) Jacobi scale (1982) and (v) COHMC scale (1984). The objective of our study was to assess I-O agreement associated with the use of coma scales in children since this has not been tested before.

Sixteen comatose children were examined independently by JYY and SSS in the Pediatric Intensive Care Unit of the Children's Hospital, Winnipeg between September 1986 and December 1987. Each child was examined by both observers within a half an hour period. Data sheets that listed the items in the six coma scales were then filled in a double-blinded fashion. A disagreement rate (DR) was calculated (Teasdale et al 1978). Practical and ethical considerations limited the number of observers for the study.

The DR for the various items in the different scales ranged from a high of 0.18 to a low of 0.03. The DR exceeded 0.10 for the CCS verbal, COHMC brainstem, COHMC cortical, GCS verbal and Jacobi verbal responses.

Our study suggests that there is generally good I-O agreement for the items in all the scales assessed. The DR was most marked for the items in the COHMC scale. Of the verbal responses in the various scales, there was least DR with that in the SR scale. Furthermore, there was less DR for motor responses in the SR scale as compared to motor responses in the GCS suggesting that the SR scale might be better for the pediatric age group than the GCS.

Acknowledgement: Funded by Health & Welfare Canada

79.

Neonatal Dural Sinus Thrombosis

M.I. SHEVELL, K. SILVER, A.M. O'GORMAN, G.V. WATTERS and J.L. MONTES (Montreal, Quebec)

Dural sinus thrombosis (DST) in the newborn has been infrequently documented and its clinical presentation remains obscure. Seventeen patients with DST diagnosed in the neonatal period were retrospectively identified and reviewed. Diagnosis in each patient was on the basis of a non-infused CT scan which showed dense intracranial sinuses with concommitant small ventricles. Two patients had ancillary studies (cerebral angiography and nuclear flow scan) which confirmed the diagnosis.

All the patients were full term infants. Only four had evidence of perinatal asphyxia. Three patients were identified as having associated medical conditions known to predispose to DST (two with polycythemia and one with congenital heart disease). None of the patients tested had a hypercoagulable state identifiable. Neonatal seizures were the initial presentation in 15 patients. Seizure onset was predominantly in the first week of life. Follow-up was available in all 17 patients and ranged up to six years. Only three patients had seizures beyond the neonatal period. In 11 of 12 patients with no history of perinatal asphyxia, neuro-developmental outcome was normal. Two of four infants with perinatal asphyxia had neurologic sequelae.

DST represents an important and under recognized cause of neonatal seizures in term infants. In the absence of perinatal asphyxia, normal neurodevelopmental outcome is likely and the risk of seizure recurrence is low.

80.

The Prediction of Outcome Following Perinatal Asphyxia: The Value of Non-invasive Assessment of Cerebral Structure and Function

B.A. LUPTON, E.H. ROLAND, M.F. WHITFIELD, O. FLODMARK, P.K.H. WONG and A. HILL (Vancouver, British Columbia)

Non-invasive investigations of cerebral structure and function in the term newborn are a potentially useful adjunct to clinical examination for the assessment of brain injury following hypoxic-ischemic (HI) insult. Available techniques include measurement of intracranial pressure (ICP), visual evoked potential (VEP), brainstem auditory evoked response (BAER), cerebral blood flow velocity (CBFV) expressed as pulsatility index (PI) or area under the velocity curve (AUC) and ultrasound (US) and CT scanning. This study reviews the relative value of these investigations in the assessment of HI brain injury.

The studies were performed during the first five days of life in 37 asphyxiated term newborns with HI encephalopathy. The results were correlated with neurological outcome at 18 months of age. The predictive accuracy of each test was determined for 1) the presence of abnormality of any severity or 2) severe neurological abnormality or death. The predictive accuracy for each test is shown in the Table.

	Predictive accuracy (%)						
Outcome	ICP	CT	BAER	VEP	US	CBFV (PI)	CBFV (AUC)
Abn. of any severity	83%	72%	86%	80%	75%	83%	97%
Severe abn. or death	97%	97%	89%	88%	72%	83%	84%

There were differences in the predictive accuracies of each test which, in some instances, reached statistical significance. The presence, but not the extent, of neurological abnormality was predicted most accurately by measurement of CBFV (AUC). However, CT scanning and ICP measurements were the most accurate predictors of severe brain injury.

The above data demonstrate the value of selected non-invasive techniques for the assessment of HI cerebral injury in the term newborn and for the prediction of outcome.

81.

Prospective Study of Acute Bacterial Meningitis: Clinical and Electrophysiological Findings at Follow-up

M.G. PIKE, K. FARRELL, D.A. CABRAL, O. FLODMARK, D. SPEERT and P.K.H. WONG (Vancouver, British Columbia)

Forty-one children with acute bacterial meningitis were studied prospectively during the acute illness with clinical examination, CT head scan, electroencephalogram (EEG), brain stem auditory evoked response (BAER) and visual evoked potential mapping (VEPM). These were repeated in 30 children 4-29 months after the illness at a mean age of 3.24 years (range 0.9-13.6 years). Two of the 41 children died during the acute illness. Eighteen of the 30 children followed up had a neurological or cognitive deficit. In 5 of these, the deficit had been present prior to meningitis. Thus, 15 children had a poor outcome as a result of their meningitis and 12 children had a good outcome.

Age at onset of illness, sex ratio, causative organisms and duration of illness prior to treatment were similar in both groups. EEG, VEPM and BAER abnormalities and CT evidence of sub-dural effusion and ventricular dilatation during the acute illness were also equally prevalent in the two outcome groups. There was a significantly higher incidence of seizures during the acute illness in the poor outcome group (11/15 v 3/12, $p<0.02$). Focal neurological signs during the acute illness (8 patients) and initial CT evidence of cerebral edema, cisternal pus or cerebral infarction (7 patients) were invariably associated with abnormal outcome. VEPM abnormalities were present at follow-up in 9 out of 10 normal patients studied and 7 out of 10 abnormal patients.

These data reinforce the value of clinical assessment in the evaluation of children with acute bacterial meningitis and emphasize the prognostic relevance of seizures which probably reflect vasculitis-induced ischemia in most cases. The prevalence of abnormal VEPM's among apparently normal children at follow-up may be associated with subtle cognitive deficit and neuropsychological assessment of these children is planned at a later stage.

82.

Significant Differences In the Pharmacology of Chewable Versus Regular Carbamazepine

P.R. CAMFIELD, P.A. HWANG, C.S. CAMFIELD, S. SOLDIN, A. FRASER and A. L-QUDAH (Halifax & Toronto, Ontario)

We report the first comparison of Chewable and Regular Carbamazepine (CBZ) tablets in children with epilepsy. 15 children taking chronic monotherapy CBZ participated. In month 1 children received regular CBZ, in month 2 the same dose of Chewable CBZ. Once/week tasting predose CBZ and CBZ epoxide serum levels were determined. At the end of each month beginning predose, serum levels were obtained every 2 hrs. for 12 hrs. CBZ and CBZ epoxide were quantitated by HPLC in both centres. Overall weekly levels showed no consistent differences between the 2 months and seizure control was similar without side effects. 12 hr. curves in 10 children treated with BID doses showed 3 patterns. In 5/10 chewable CBZ produced significantly higher peak CBZ levels (ave. 26% higher than peak with regular CBZ). 2/10 had higher peaks with regular CBZ (ave 17%). 1 child had the same curve with both and 2 had very flat curves without peaks. 12 hr. curves in 5 treated TID were variable in shape. 3 showed higher peaks with regular CBZ (ave. 24% higher) and 2 slightly higher with chewable (6%). CBZ epoxide levels did not vary significantly in any patient throughout the 12 hr. curves despite wide fluctations in CBZ levels. For most CBZ epoxide/CBZ level was similar for chewable and regular CBZ averaging 16.5% with range 10-30%.

In conclusion regular and chewable CBZ often have unpredictable differences in peak but not through levels of CBZ suggesting that peak level side effects with one form of CBZ might be alleviated by changing to the other. For children on monotherapy CBZ epoxide levels remain constant through the day and appear to be of limited usefulness.

83.

Craniosynostosis - Review of Surgical Treatment in Southern Alberta

S.T. MYLES, H. JABER and D. COCHRANE (Calgary, Alberta; Vancouver, British Columbia)

Craniosynostosis, or premature closure of a cranial suture, has been described since ancient times and was first classified by Virchow in 1851. Numerous publications since have dealt with many aspects of the problem, including the indications for surgery, timing and best type of surgical procedure.

We have reviewed our experience with the surgical treatment of children with craniosynostosis in Southern Alberta in the past 15 years, from January, 1972 to December, 1987. In the first 10 years, all surgical procedures were done at Foothills Hospital, while in the past 5 years all were performed at Alberta Children's Hospital in Calgary.

A total of 140 operations were done on 120 children.

Fifty-six percent of operations were done for sagittal synostosis, 8.1% for lambdoid suture closure, 6% for metopic synostosis, while the remaining 29.9% had coronal suture involvement as part of the clinical syndrome. Right coronal suture involvement was much more common that left.

The diagnosis was made on clinical grounds and was supported by appropriate radiographic studies.

Surgery was advised for cosmetic reasons when only the sagittal or metopic sutures were involved, and in the children with unilateral coronal or lambdoid synostosis. In the others, including a subgroup with involvement of lambdoid suture and skull base, surgery was advised to allow for normal brain growth.

Surgical treatment at age 2 to 3 months consistently produced the best cosmetic results, with more than 95% judged satisfactory. The timing of surgery seemed more important in determining outcome than the type of procedure performed. In the complex group, forehead release produced better results than forehead advancement, if the procedure was done before 3 months of age.

There were 2 post-operative deaths for a mortality rate of 1.4%. The overall morbidity rate was 3.6%, with 3 complications in the first 55 patients and 2 in the next 65.

84.

Indications For Surgical Treatment Of The Sturge-Weber Syndrome

M.-A. BEAULIEU, F. ANDERMANN, T. RASMUSSEN, A. OLIVIER, J.-G. VILLEMURE and J. MONTES (Montréal, Québec)

The severity of the epileptic problem in patients with Sturge-Weber syndrome is quite variable. While in some patients it may not be sufficiently severe to warrant surgical treatment, in other patients the epileptic disorder leads to deterioration, hemiparesis and other defects, and surgical treatment should be considered.

Investigations are aimed at recognition of the localization and type of the epileptogenic abnormality leading to removal of the epileptogenic area when possible. A variety of other approaches may be appropriate; they include callosotomy, modified functional hemispherectomy or removal of the epileptogenic area not including the anatomical lesion.

Twenty-two patients have been treated surgically in the last 31 years (mean 14 years). Of these patients, ten had pial angiomatosis only. Complete or near complete cessation of attacks (up to 10% as many attacks as pre-op) was found in 12/22 (54%) of patients. Significant improvement (40-90% reduction in seizure frequency) was found in 3/22 (13%) and 7/22 (31.8%) had only a slight or no improvement.

As patients with Sturge-Weber are followed, the possibility of clinical deterioration must be kept in mind and the possibility of help from surgical treatment considered.

85.

The Survival and Functional Status of Children with Brain Tumors: A Clinical Study of 150 Children (Hôpital de l'Enfant-Jésus, Québec), 1970-1987

J.-F. LEMAY, L. BAILLARGEON, J.-P. BOUCHARD, J. FRANCOEUR, F. GAGNE and S. VERRET (Québec City, Québec)

Approximately 20% of all childhood cancers are primary brain tumors. The majority of these children benefit from therapy, either surgery, radiotherapy, chemotherapy or a combination of these. The survival of these patients is fairly well known. However the functional status of these children has been very little evaluated; this is the purpose of the present study.

During the period 1970 to 1986, 150 patients, 0 to 19 years of age with primary intracranial tumors were diagnosed and treated at l'hôpital de l'Enfant-Jésus in Québec City, Canada. Follow-up was conducted in every child until death or December 1987.

The clinical pictures were reviewed and will be presented. The most common histological type of brain tumors were astrocytomas (40%) and medulloblastomas (21%). Seventy-seven patients (51%) had survived their tumors for one to seventeen years (median, 7 years). The five-year survival was established.

Among survivors, the functional status was evaluated according to a modification of the scale employed by Bloom. Sixty-seven patients (87%) had mild or no deficit. Moderate or severe functional deficits were present in 10 patients (13%). The different factors influencing the function were evaluated and will be discussed.

We conclude that in spite of this severe condition, the survivors of childhood brain tumors have an acceptable quality of life.

86.

Diuretic Therapy For Infantile Hydrocephalus

H.Z. DARWISH, M. STRETTON and S.T. MYLES (Calgary, Alberta)

The management protocol of hydrocephalus with Furosemide and Acetazolamide was established by Shinnar et al (J Peds 1985) in the effort to avoid the significant morbidity associated with shunt procedures. They hypothesized that the time gained during therapy allows for cranial suture fibrosis to develop. This forces a new equilibrium leading to better reabsorption of CSF after withdrawal of treatment. We used this protocol to manage 18 infants with hydrocephalus. The mean age at initiation of treatment was 96±84 days with a range of 1 week to 8 months. The etiology was SEH-IVH in 10, congenital malformation in 5, and bacterial meningitis in 3. Therapy was successful in 4/7 infants on whom it was begun at less than 35 days of age, and in 10/11 who were older than 35 days. The type of hydrocephalus and its etiology did not correlate with response.

After therapy was begun, average velocity of head growth was 0.44±0.17 cms/week in the 4 neonates who responded and 1.1±0.1 cm/wk in the 3 failures. In the 10 infants successfully treated after 35 days of age, the average velocity was 0.18±0.16 cm/wk, whereas in the 1 failure it was 0.5 cms/week. In 2/14 responders an increase in velocity occurred on withdrawal of therapy. Treatment was successfully withdrawn in 12, after a mean of 19±13 weeks. Management of hydrocephalus in the infant under 1 year with combined Acetazolamide and Furosemide was effective in 78%. This therapy may be safely withdrawn in some after a "few" months of therapy. Head growth velocity in the 3 weeks after treatment correlated well with outcome but ventricular size did not.

87.

Leigh's Disease: Clinical, Biochemical and Pathological Correlations in 15 Children

D.D.R. EISENSTAT, L.E. BECKER, B.H. ROBINSON and W.G. SHERWOOD (Toronto, Ontario)

Fifteen children with histopathological criteria of Leigh's disease (subacute necrotizing encephalomyelopathy) presented between 1970-1987. The patient population consisted of 10 males and 5 females; 10 (67%) presented prior to the age of 6 months. Common clinical manifestations included: psychomotor retardation (80%), hypotonia (73%), seizure disorder (60%), failure to thrive (53%), metabolic acidosis (47%), tachypnea (47%), apneic spells (40%), diminished level of consciousness (40%) and hepatomegaly (33%). Computed tomography in 7 children demonstrated cerebral atrophy (3), decreased white matter density (3) and brainstem changes (2).

Neuropathological examination revealed lesions in the brainstem (80%), basal ganglia (73%), thalamus (67%), spinal cord dorsal columns (47%), cerebral white matter (33%) and mamillary bodies (20%). Abnormalities in liver, cardiac and skeletal muscle were also shown.

Mitochondrial respiratory chain enzymes were assayed in 7 patients. Three patients had pyruvate dehydrogenase (PDH) complex deficiencies; pyruvate decarboxylase ($PDH\text{-}E_1$) was found in 2 and dihydrolipoyl dehydrogenase ($PDH\text{-}E_3$) deficiency in another. One child had decreased phosphoenol pyruvate carboxykinase (PEPCK) activity. Definite uroporphyrinogen synthetase deficiency was present in a child who died suddenly and unexpectedly. Muscle biopsy revealed diminished cytochrome C oxidase in a patient with $PDH\text{-}E_1$ deficiency.

We propose that in Leigh's encephalomyelopathy, a variety of biochemical abnormalities may lead to the same final neuropathological alteration.

88.

A Comparison of Propanolol and Amitriptyline in the Prophylactic Treatment of Migraine in Children and Adolescents

P. HUMPHREYS, P. MCGRATH, D. KEENE, P. JACOB, J. GOODMAN and P. FIRESTONE (Ottawa, Ontario)

We undertook a double-blind randomized study comparing the efficacy of propanolol, amitriptyline and placebo in the prevention of migraine headaches in children employing a three group non-cross-over design. The study sequence included a 4 week baseline period of headache documentation, an 8 week treatment period, a 2 week withdrawal period and 14 weeks of follow-up. Of 39 children entering the treatment phase, 10 dropped out during the remaining phases, usually because of persistent headache activity despite treatment, less often because of apparent drug-related side-effects. During the treatment phase, all three groups, placebo included, showed a steady decline in headache activity with no significant difference between the three groups. This improvement was maintained during the drug withdrawal and follow-up phases in the propanolol and amitriptyline groups, with further improvement (off medication) in the case of amitriptyline. The placebo group had a rebound of headache activity during follow-up to the baseline level. During the follow-up observation periods, the difference between the drug groups and placebo group progressively approached statistical significance. We conclude that; 1) the results of controlled trials of migraine prophylactic agents in children may be masked by a strong placebo effect, and 2) the therapeutic benefit of amitriptyline (and possibly also propanolol) in the prevention of migraine headache may persist for weeks to months after cessation of treatment.

Child Neurology (Poster)

FRIDAY, JUNE 17TH - P.M.

89.

Childhood Cataracts: A Review of 97 Cases

M.G. PIKE, J.E. JAN and P.K. WONG (Vancouver, British Columbia)

Ninety-seven children born between 1954 and 1986 and presenting to the Visually Impaired Program, Vancouver, B.C. with a primary ophthalmological diagnosis of cataracts were studied. All children were fully evaluated ophthalmologically, neurologically and developmentally and their prenatal, perinatal, medical and family histories were reviewed. To our knowledge this is the largest multidisciplinary study of children with cataracts.

The cataracts were thought to be congenital in 91 children and of later onset in 6 children. Causal factors included congenital rubella (31), other intrauterine infections (4), dominantly inherited (20), recessive (2), various syndromes (9), trauma (1) and unknown (30).

Mild hypotonia and inco-ordination were common findings on examination and are frequently present in children with visual impairment of any kind. Markedly abnormal neurological findings were noted in 25 out of 31 children with rubella syndrome and in 13 out of 30 patients with cataracts of unknown cause, but were entirely absent in the group of children with dominantly inherited cataracts. Where congenital cataracts of unknown cause occur with a negative family history, a normal neurological examination suggests a newly mutated dominant disorder. Detailed metabolic investigations in such children, though clearly important, are usually negative.

The neurological profiles of children with cataracts in the various aetiological groups will be presented. Visual outcome over the 30 year study period and its relationship to age at surgery will be discussed.

90.

Clinical Profile, Prognostic Factors, Role of Hemispherectomy In Sturge-Weber-Dimitri Syndrome:

A.O. OGUNMEKAN, P.A. HWANG and H.J. HOFFMAN (Toronto, Ontario)

We report on 12 patients operated on with Sturge-Weber-Dimitri Syndrome between January 1975 and December 1987.

10 patients had hemispherectomy and 2 had occipital lobectomy for intractable seizures. The seizure type in all patients was simple partial motor seizure except one who had complex partial seizures. All operations were performed between the ages of three months and twenty months except in two patients who were operated on at the age of 8 and 9 years. The onset of seizures in both subtotal and total hemispherectomies were between the ages of two and five months except in one patient at 15 months. Nine out of twelve (75%) operated patients had associated glaucoma ipsilateral to the skin lesions requiring therapy. There were no post operative deaths. Post operative shunt procedures were performed in three out of twelve (25%). Post operative seizure control ≥ one year was achieved in eleven out of twelve patients (six were on no medication (Grade I) and five were on medication with no seizures (Grade II)). The last patient is on medication with no seizures but follow-up not up to a year. Intellectual development was maintained after operation on follow-up in all except in two who were severely retarded and had operation late at age 8 and 9 years.

We conclude that patients with Sturge-Weber-Dimitri syndrome who have simple partial motor seizures in the first six months of life should be evaluated for early hemispherectomy.

91.

Neonatal Guillain-Barré Syndrome

A.A. AL-QUDAH, E.G. MURPHY and E. SHAHAR (Toronto, Ontario)

Guillain-Barré syndrome (GBS) has not been reported in the neonatal period. This full-term female newborn with a history of decreased fetal movements late in pregnancy, was delivered by C-section due to breech presentation. Apgar scores were normal. Examination revealed a bright looking neonate with generalized hypotonia and paucity of lower limb movements. Deep tendon reflexes were diminished in the upper limbs and absent in the lower limbs. CSF analysis at 3 weeks disclosed a protein of 0.4 gm/L (normal) and less than 3 WBC X 10^6/L. Nerve conduction studies which were abnormal at 3 weeks of age, showed subsequent progressive recovery (Table). EMG studies at 5 weeks demonstrated denervation and reinnervation and at 10 weeks became normal. Progressive clinical improvement was noted since age 2 weeks and subsequent neurological and developmental assessments at age 5.5 and 8 months were normal.

The clinical course of this infant along with the ancillary investigations are consistent with the diagnosis of GBS. CSF protein which was measured during the recovery phase may merely reflect the clinical improvement. Our patient, as the youngest reported case of GBS, represents a benign entity to be considered in the differential diagnosis of the floppy neonate.

Table: Serial Motor Nerve Conduction (N.C.) Studies From 3 weeks to 22 weeks of age

Age in Weeks		3	5	10	22
left post tibial nerve	- N.C. Velocity (M/sec)	7.2	12	18.5	29.4
	- Amplitude (mv)	0.3	1.5	2	5
left median nerve	- N.C. Velocity (M/sec)	15.8	15	21.6	25.9
	- Amplitude (mv)	1.5	1	4.5	5.2

92.

Neuronal Intranuclear Hyaline Inclusion Disease Presenting with Cerebellar Ataxia and Seizures

J.E. WARK, L-C. ANG, L.E. BECKER and R.H.A. HASLAM (Toronto, Ontario)

Born to a Finnish father and an Anglo-Saxon mother after first-trimester spotting, the subject had normal early milestones and documented normal gait at 28 months. A severe tremor, worse with intention, emerged at 33 months; brief seizures in which his head snapped back and his eyes rolled up began at 37 months of age. By 51 months, seizures and tremor were worse, he was unable to sit, stand, or talk, and he exhibited increasing drowsiness and lethargy. The EEG progressed from infrequent polyspike and wave discharges to frequent, multifocal spikes and sharp waves. By 43 months, cerebellar and brain stem atrophy were seen on CT and MRI, respectively. At 51 months of age, he was found unresponsive and could not be resuscitated.

At autopsy, there was bilateral, acute, pulmonary edema. In the CNS, marked cerebellar atrophy was seen. Microscopic examination confirmed loss of Purkinje and granular cells with marked gliosis. Widespread intranuclear hyaline inclusions measuring 4-10 μm were seen in the remaining Purkinje cells as well as the neurons of the dentate nuclei, inferior olives, substantia nigra, locus ceruleus, hypothalamus, and the autonomic ganglia outside the CNS. Ultrastructurally, these inclusions consisted of a mesh of straight filamentous material and are similar to those first described in 1972 by Wagener et al. Our case showed eosinophilic inclusions in hepatocytes, previously only seen intranuclearly, but here present in the cytoplasm. Of the 13 other cases in the literature, two were twins of Finnish descent. Neuronal intranuclear hyaline inclusion disease should be considered in the differential diagnosis of olivo-ponto-cerebellar atrophy.

93.

Fulminant Meningitis is Childhood - A Clinical and Pathological Review

J.M. TAPPER and L.E. BECKER (Toronto, Ontario)

A retrospective study over a 10-year period utilizing medical and autopsy records, assessed the clinical and pathologic features of 18 children presenting at The Hospital for Sick Children with fulminant meningitis (FM). The clinical charts of the first twenty children in 1982 who survived bacterial meningitis were also reviewed. The average number of patients with FM was 2-3 per year (5% of all cases with meningitis). The mean age at presentation was 26 months for FM and 19 months for survivors of meningitis (SM). Children with FM had more seizures, focal neurological signs, coma and papilloedema at the time of presentation. Of all patients with meningitis, 40% had signs of hippocampal uncal herniation prior to lumbar puncture. At autopsy, all patients had significant cerebral edema with 80% demonstrating uncal and/or cerebellar tonsillar herniation. In pneumococcal meningitis, there was more purulent exudate, vasculitis, infarction, and edema. Pneumococcus was present in 28% of patients with FM compared to 15% of SM. In meningococcal septicemia, meningitis may be minimal but septic shock results in rapid clinical deterioration. The clinical course of patients with FM is short, with 40% of cases presenting with brain death. Children with FM are an important subgroup of those with bacterial meningitis for whom more effective treatment must be sought.

94.

Polygenic Inheritance of Non-syndromic Macrocrania

G.V. WATTERS, L. ARBOUR and F.C. FRASER (Montreal, Quebec)

Several studies have suggested that non-syndromic macrocrania, with or without developmental delay, shows autosomal dominant

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inheritance. If this were so, the distribution of head circumference (HC) of parents and sibs of macrocranic children should be bimodal. To test this hypothesis, probands with macrocrania (HC>2 S.D), with or without developmental delay, referred to Neurology or Genetics at The Montreal Children's Hospital were selected, and the HCs of their parents and sibs were measured. Probands with syndromes or West Indian origins were excluded (the latter may normally have above average HCs). HCs were standardized for age and sex. The mean HC of parents and sibs of probands was 1.5 standard deviations above the mean, with no indication of bimodality. Enlarged CSF space did not correlate with psychomotor delay, but history of obstetrical difficulty did. Recurrence rate of psychomotor delay in sibs was low.

These findings suggest that non-syndromic macrocrania has a polygenic basis and that the "dominant" pedigrees reported by others resulted from the imposition of an artificial threshold of abnormality, at +2 S.D above the mean, on a continuous distribution. Indeed, we could produce the same autosomal dominant appearance by applying the same threshold to our pedigrees — demonstrating that dominant macrocrania may be a statistical artefact.

It appears that the increased risk of perinatal brain damage is a major determinant of subsequent psychomotor delay.

95.

Malignant Breath-holding Spells in Children

E.H. ROLAND and A. HILL (Vancouver, British Columbia)

Breath-holding spells are common in early childhood and have an excellent prognosis. The diagnosis is based on a typical history. Thus, crying, as a result of a provoking factor e.g. anger, frustration or pain, is followed by prolonged apnea, which proceeds rapidly to cyanosis and eventually, loss of consciousness. Although breath-holding spells generally are considered benign and self-limited, we describe 5 children in whom such spells were clearly pathological in origin.

Three patients, each of whom had meningomyelocele, Arnold-Chiari malformation and shunted hydrocephalus, developed cyanotic episodes associated with a classical history of breath-holding spells during the first year of life. In each patient, crying was clearly precipitated by anger or pain and was followed rapidly by apnea, marked cyanosis and loss of consciousness, recovery from which required resuscitation. These episodes were frequent and continued beyond the age of 5-6 years when breath-holding spells usually cease. Tracheostomy, posterior fossa decompression and treatment with atropine and anticonvulsants were of no benefit. Neuropathological studies in one infant who died at twelve months of age demonstrated extensive gliosis and scarring of the brainstem.

Two other children, aged 10 and 18 months, had recurrent and typical cyanotic breath-holding spells and were neurologically normal. However, each infant had at least one episode of generalized tonic-clonic status epilepticus lasting longer than one hour, immediately following a typical cyanotic breath-holding episode. Treatment with intravenous anticonvulsant medication was required. Both infants recovered fully and subsequent electroencephalograms were normal. It appears most probable that cerebral hypoxemia associated with breath-holding triggered the prolonged seizures in these children, possibly as a result of a low seizure threshold.

These data suggest that although the vast majority of breath-holding spells are benign and require only parental reassurance, further investigation and treatment may be indicated in a minority of children, especially those in whom there is increasing frequency or severity of spells and/or other evidence of brainstem dysfunction.

96.

The Effects Of Gastrostomy In The Seizure Management Of Children With Severe Neurological Impairment

M.R. DELGADO, G. STRINGEL, J.D. COOK, N. NEWTON, B. PRATHER and L. BURDICK (Dallas, U.S.A.)

Chart review of 52 children with the diagnosis of severe static encephalopathy and seizure disorder and who had a gastrostomy (gt) in the last 5 years was undertaken. 19 patients were excluded from this study because the gt was done before their first visit to our Neurology clinic and there was no clear documentation of their seizures or anticonvulsants before the gt.

The information was obtained from hospital charts and parent interview of 33 patients. There were 14 females and 19 males with age of 7 mos. to 13 yrs. (X:5.1yr). 29 (88%) had spastic quadriparesis, 3 (9%) hypotonic quadriparesis, and 1 (3%) mixed quadriparesis. 11 (33.3%) patients had primary generalized seizures. 9 (27.3%) partial seizures, 6 (18.2%) partial with secondary generalization and 7 (21.2%) mixed type. Malnutrition, gastroesophageal reflux and aspiration were the main indications for the gt. 24 patients (73%) had a significant reduction in seizure frequency after gt. 30 patients (91%) had a reduction in the dose of the anticonvulsant medication. 24 patients (73%) had an increase in the serum level of the anticonvulsant after gt, with the same or lower dose that they were taking before the gt. The parents of 32 patients (97%) thought that their child was better off after gt and that it was easier to administer the medications. 27 parents (87%) said the seizures were better controlled after gt. Gt. not only improves the nutrition in children with severe neurological impairment, but greatly facilitates the administration of anticonvulsant medications with a subsequent improvement of seizure control.

97.

Arthrogryposis Multiplex Congenita: Clinical and Muscle Biopsy Findings

C. ADAMS, L.E. BECKER and E.G. MURPHY (Toronto, Ontario)

Thirteen cases of arthrogryposis multiplex congenita (AMC) without evidence of spinal muscular atrophy, congenital muscular dystrophy, or structural myopathy were reviewed. Family history, consanguinity, pregnancy, delivery, number and severity of contractures, and outcome were evaluated. Laboratory investigations included creatine kinase and electromyography. Muscle biopsy from an affected limb had been examined histochemically and by electron microscopy. Five biopsies showed fiber type 1 predominance and 3 had type 2 predominance. Patterns of fiber type predominance may have resulted from altered neural influence leading to impaired maturation of type 1 or 2 motor units. Nine patients had been followed for 3 to 8 years and had undergone a mean of 4 operations. Two were still not walking at age 8 years. For the six who were walking the mean age at walking was 4.7 years. There was no deterioration in power. We recommend muscle biopsy in AMC. Finding a probable neurogenic picture is valuable in predicting a non-deteriorating outcome. There also appears to be no increased family incidence.

98.

Dyskinesia Following Cardiovascular Surgery and Profound Hypothermia

W.J. LOGAN, G.A. TRUSLER and F.A. BURROWS (Toronto, Ontario)

Dyskinesia is one of the clinical syndromes that can be seen following cardiovascular surgery. It has been described in patients who had profound hypothermia as part of their operative management but the pathogenesis has not been elucidated. We reviewed 8 patients seen from 1983 through 1988 in an attempt to identify factors which might contribute to the development of this disorder.

Most of these patients were infants under the age of 2 years. They had a variety of cardiac abnormalities, but the most common was transposition of the great arteries. The dyskinesia became apparent on

recovery from the operation. It consisted of oral facial dyskinesia with facial grimacing and tongue thrusting and choreoathetoid movements particularly of the upper extremities. These movements responded to Haloperidol and gradually improved. Many of the cases had cortical blindness which generally improved rapidly.

In each case the anaesthetic management included profound hypothermia with the lowest temperature in this group being 15°C rectal and 7°C in the nasal pharnyx. Most, but not all had circulatory arrest induced at surgery. Perfusion time varied from 30 to 200 minutes. A variety of pharmacological agents were used in these cases including Dopamine. The most consistently utilized agent was Pancuronium.

Thus, dyskinesia following cardiovascular surgery appears to be a distinct syndrome which is seen when profound hypothermia has been employed. Pancuronium may also be a contributing factor.

99.

The Hopkins Syndrome: Poliomyelitis-Like Disease Associated with Bronchial Asthma

E. SHAHAR, C. ADAMS, C.E. NIESEN, P.A. HWANG and E.G. MURPHY (Toronto, Ontario)

Acute onset of poliomyelitis-like disease during the course of an attack of bronchial asthma is reported in two infants presenting at age 13-22 months. Both developed acute flaccid paralysis of one or both lower limbs with preserved sensation 7-8 days following the onset of the asthmatic episode. CSF and viral studies in the younger infant were unremarkable. CSF examination in the older patient revealed 18 WBC and a protein of 0.19 g/L rising to 0.81 g/L (N: 0.3-0.7 g/l) in subsequent studies. Enteroviruses were isolated from a nasal swab and stools in this patient. Both had absence of motor action potentials; the younger from the right lower limb (RLL) and the older from the left lower limb (LLL) also with decreased amplitude from the RLL suggestive of axonal involvement. Aside from minimal improvement of the RLL motion in the older patient where both limbs were involved, no further clinical or electrophysiologic improvement was noted in both within 4-5 months follow-up.

Acute onset of flaccid paralysis of extremities with absent motor action potentials and preserved sensation are highly suggestive of an anterior motor horn cell disease in these infants. The association between poliomyelitis-like disease and bronchial asthma is rare and therefore should be stressed regarding the long-standing severe motor handicaps. Although a thorough viral study is often disappointing, enteroviruses other than the poliovirus associated with acute respiratory illness may be found, and such infants should be intensively investigated.

100.

Spontaneous Intracranial Hemorrhage In Infancy Due To Idiopathic Vitamin K Deficiency: Natural History and Outcome

S. PHANCHAROEN, S. LIMUDOMPORN, C. MITRAKUL and N. SUWANWELA (Bangkok, Thailand)

This is a study of twenty-two infants with spontaneous intracranial hemorrhage admitted to the Pediatric Department, Chulalongkorn Hospital between January 1980 and December 1987, in which the cause of hemorrhage was Idiopathic Vitamin K Deficiency. The age range were two to eight weeks, 90.90% of the patients' birth weight were more than 2,500 grams and 86.36% were breast-fed. Acute onset of drowsiness, pallor and tensed anterior fontanel were the major clinical manifestations. All patients had hematocrit level below 30% and prolonged prothrombin time which returned to normal level after vitamin K1 and fresh frozen plasma administrations. Computerized axial tomography studied in fifteen patients (68%) revealed the incidence of subdural, subarachnoid and intracerebral hemorrhage as 73.33, 33.33 and 60.00% respectively. Craniectomy were performed in four patients due to their clinical deterioration from brain herniation and one died from brainstem dysfunction caused by the herniation. Convulsive disorders, microcephaly, delayed growth and development with motor deficit were common sequelae, especially in the intracerebral bleeding group (6 out of 8). The role of early surgical intervention in this group is still controversial.

101.

The Frequency of Central Nervous System Anomalies in Dysraphism, Neuroimaging Evaluation of 40 Unselected Affected Neonates

G.M. RONEN, B.C. CRAMER, F. MAROUN and W.D. HENEGHAN (St. John's, Newfoundland)

Dysraphic conditions remain an important cause of physical and neurodevelopmental handicaps. Post mortem studies have shown a variety of associated central nervous system (CNS) malformations and deformations. To assess the frequency of CNS anomalies in dysraphism, 40 affected neonates were examined. These were consecutively admitted to the only referral centre in the province of Newfoundland and Labrador, over a 4 year period. Evaluation was done by cranial ultrasound (100%), spinal ultrasound (90%), CT scan (30%) and myelogram (10%). Chiari I malformation was identified in 3 infants, Chiari II in 30, and Chiari III in 2. Four showed no abnormalities above or at the craniocervical junction and 1 case could not be precisely classified. Associated anomalies included ventricular dilation (90%); suspected cerebral cortical abnormalities (80%), (as determined by the shape of the cingulate gyrus and sylvian fissures); and caudally placed 4th ventricle (88%), of which over half were in the spinal canal. The cord-medullary junction was also down in 81%; as was the cerebellar peg in 86%. Atrophy of the spinal cord was suspected in 59% and syringomyelia in the cervical and thoracic region in 34%. These findings demonstrate a significant rate of serious associated anomalies in patients with dysraphic conditions and indicate the need for careful neuroimaging of all affected infants, particularly in view of possible earlier neurosurgical intervention.

102.

The Human Tail and Spinal Dysraphism

A.J. BELZBERG, S.T. MYLES and C. TREVENEN (Calgary, Alberta)

Recent publications have endeavoured to differentiate between the true, or vestigial, tail and the pseudo-tail by clinical and pathological examination, and have indicated the benign nature of the true tail. The true tail arises from the most distal remnant of the embryonic tail, and contains adipose, connective, muscle and nerve tissue, and is covered by skin. Pseudo-tails represent a variety of lesions having in common a lumbosacral protrusion and a superficial resemblance to vestigial tails. A review of the case reports indicate spina bifida to be the most frequent co-existing anomaly with both.

The term "spinal dysraphism" was used in 1940 by Lichtenstein to designate congenital abnormalities of the vertebral column and spinal cord, specifically incomplete fusion or malformation of structures in the dorsal midline. Occult spinal dysraphism is associated with cutaneous signs in more than 50% of instances.

Three cases of spinal dysraphism with tail-like cutaneous structures will be described and their radiological, operative and pathological findings presented. The classification of each of the appendages into true tail or pseudo-tail remains obscure. While the finding of these three tails was the subject of much curiosity, surgical treatment was clearly designed to adequately deal with the dysraphic state.

The presence of a tail-like appendage in the lumbosacral region should alert the clinician to the possibility of underlying spinal dysraphism. Preoperative assessment must include a complete neurological history and examination as well as CT or MRI imaging.

103. Withdrawn

104.

Choreoathetosis Following Cardiopulmonary Bypass: Clinical Characteristics, Treatment and Follow-up

P. JACOB, D. KEENE, P. HUMPHREYS, S. PARNES, S. WHITING, P. VLAD, O. TEIXEIRA and W. KEON (Ottawa, Ontario)

Little is known about the long-term outcome of patients presenting with choreoathetosis following cardiopulmonary bypass. Between 1984 and 1988, we had the opportunity to examine and follow 5 patients (3 boys, 2 girls) with severe choreoathetosis following cardiopulmonary bypass for correction of congenital heart disease. Two to 4 days following surgery, after an uneventful recovery, they presented a similar picture characterized by marked choreoathetosis, hypotonia and in older patients, difficulty with speech initiation and word finding. Age at surgery varied from 11 months to 4 1/2 years. All the patients were felt to be free of any motor or speech disability prior to the surgery. Post surgery evaluation revealed transient metabolic disturbances all of which were promptly corrected. CT scan in 5/6 patients showed mild dilatation of the ventricles and a slight increase of the sub-arachnoid space. In 1 case there was a slight decreased density in the thalamus and the palidum bilaterally. Follow-up observation ranging from 1 to 4 years showed only a slight improvement of the degree of disability despite trials of Haloperidol, Perphinazine, Tetrabenazine as well as benzodiazepines. Trihexyphenidyl worsened the symptoms. Contrary to what has been previously reported, our experience suggests that patients with post cardiopulmonary bypass choreoathetosis do relatively poorly, with major residual disabilities.

105.

Cortical Visual Impairment in Children

P.K.H. WONG and J.E. JAN (Vancouver, British Columbia)

We wish to report a retrospective review of 123 children with cortical visual impairment (CVI). Our aim was to investigate the clinical and behavioural characteristics of this group of children who have various non-ocular causes for their visual loss (see Whiting et al, Dev Med & Child Neurol 1985, 27:730-739).

The findings are as follows: a) there was even distribution of residual vision from total loss (11%), to normal acuity (21%); b) asphyxia was the most common etiology (46%), with the majority being neonatal asphyxia (53% term, 35% premature); c) occurrence of cerebral palsy, mental retardation and epilepsy was common; d) 58% of all children had no ocular findings, and optic atrophy was found in 26% (the majority was minimal in degree); e) there was complete or almost complete visual recovery in 16%, moderate recovery in 16%, minimal recovery in 25%, and no recovery in 34%; f) 33% were mobile to varying degrees, with 18% able to run, and 34% able to walk; g) 14% showed better vision with moving targets.

Subtypes of CVI may be identified based on clinical characteristics, as is our experience with visual evoked potential mapping. Accurate diagnosis is important particularly as it affects choice of appropriate rehabilitation and education for these handicapped children.

106.

Inter-Observer Variability In Assessing Comatose Children

J.Y. YAGER, B. JOHNSTON and S.S. SESHIA (Winnipeg, Manitoba)

Clinical data in the comatose child provide clues to diagnosis, clinical course and prognosis. Information in coma scales, such as the Glasgow Coma Scale is insufficient for diagnostic purposes. Furthermore, Levy et al (1981) did not find it useful to generate a score from such a scale for predicting the outcome of adults with non-traumatic coma. We have, therefore, used the approach of Plum and Posner since 1975 for assessing comatose children (Seshia et al 1977; 1983). In this study, we report on inter-observer (I-O) agreement for the items in the neurological examination.

Sixteen comatose children were examined independently by JYY and SSS in the PICU of Children's Hospital, Winnipeg between September 1986 and December 1987. Each child was examined by both observers within a half an hour period. No attempt was made to influence pre-existing ideas about definition or examination. Data were entered on separate proforma sheets. Disagreement rates (DR) were then calculated (Teasdale et al 1978). The number of observers was limited by practical and ethical consideration.

The DR was less than 0.10 for coma grade, fundi, corneal reflexes, gag, pupillary responses, respiration, recording of seizure time/type, temperature and blood pressure; the DR was 0.13 to 0.16 for extraocular movements (EOM), motor responses (MR) and deep reflexes. The greater DR for EOM and MR can be explained by the larger number of categories in them (Koran 1975). Disagreements were often clinically unimportant.

Our study suggests that there is good I-O agreement for the items in the neurological examination of the comatose child. Agreement may be improved by providing more exact definitions of the various responses, prior discussion about the neurological examination and by training. Funded by Health & Welfare, Canada.

107.

Is Hepatic Failure in Children Receiving Valproic Acid Always Drug-related?

R.E. APPLETON, K. FARRELL and J.E. DIMMICK (Vancouver, British Columbia)

The use of valproic acid (VPA) in children is limited by the severe hepatotoxicity associated with this drug. This toxic effect has been described most frequently in young, mentally-handicapped children and in those on polytherapy. We describe two unrelated children receiving VPA who died from hepatic failure probably related to an inherent metabolic abnormality.

The first patient was a boy who developed acute infantile hemiplegia with hemiconvulsions at nine months of age. AST activity was 118 units shortly after the initial episode of status. Myoclonic seizures were observed after three weeks and he was treated with VPA. He developed liver failure and died three months after the onset of the seizures. Autopsy demonstrated diffuse hepatic steatosis and necrosis. The older sister of the first patient had been found dead in her cot at nine months of age and autopsy had demonstrated marked hepatic steatosis. A younger sister developed hepatomegaly at six months of age and liver biopsy demonstrated moderate steatosis with minimal necrosis. At nine months of age she developed seizures. Although not treated with VPA, she also developed hepatic failure and died one week after the onset of the seizures. Despite intensive investigation, including a metabolic autopsy, the etiology of her hepatic disorder was not demonstrated. The second patient was a boy who presented with status epilepticus at nine months of age. He developed intractable myoclonic

seizures and, shortly after the addition of valproic acid, he developed hepatic failure and died. Autopsy demonstrated diffuse atrophy of the cerebral cortex and hepatic steatosis with fibrosis (Alpers' Disease). A younger brother has developed raised liver enzyme activity at six months of age.

Although patient 1 developed evidence of liver failure shortly after being exposed to VPA, hepatic steatosis was also observed in two of his siblings who were not exposed to VPA but who also died in the first year of life. Similarly, patient 2 was demonstrated to have a disorder associated with hepatic failure. This raises the possibility that some of the patients described in the literature with VPA associated liver failure may also have had an inherent hepatic disorder which was manifest when they were exposed to VPA.

108.

Subacute Measles Encephalitis (SME) in the Immunocompromised Host: Clinical Features and Response to Interferon

E.H. ROLAND, R.W. ARMSTRONG, K. FARRELL and A. HILL (Vancouver, British Columbia)

Improvements in survival of children with acute lymphoblastic leukemia (ALL) have resulted in an increase in long-term complications relating to immunosuppression. In immunosuppressed patients, SME is a distinct neurological entity which is rapidly progressive and often fatal. We describe the clinical and laboratory observations in 3 children on maintenance chemotheraphy, who developed SME after being in remission from ALL for 2-4 years. Treatment with intravenous interferon in one patient was associated with long-term survival.

Clinical features included lethargy, fluctuating hemiparesis and focal motor seizures. All 3 patients developed severe, intractable epilepsia partialis continua, which persisted in 2 patients for 4-12 weeks until death despite aggressive anticonvulsant therapy. One patient had persistent pneumonitis and marked chorioretinitis with major involvement of the macular region resembling subacute sclerosing panencephalitis (which has not been described previously in SME). In each patient, the CSF cell count, protein and glucose were normal. However, there was increased CSF IgG synthesis index and oligoclonal bands. Infection with measles virus was confirmed by the presence of typical eosinophilic viral inclusions at autopsy in the brains of 2 patients, and was suggested by a rising titre of measles antibody in the serum of the patient who survived. This patient was treated for 10 days with high dose intravenous interferon. (15×10^6 units/kg/day). Side effects included transient fever and thrombocytopenia. Residual clinical abnormalities included hemiparesis, cognitive dysfunction and seizure, which were controlled with phenytoin. To our knowledge, this is the first case of long-term survival following treatment with interferon in a child with SME.

These data emphasize that SME should be considered in immunosuppressed children in whom there is sudden onset of focal neurological abnormalities, especially epilepsia partialis continua. Treatment with high dose intravenous interferon may be effective for this condition which generally has been considered rapidly progressive and fatal.

109.

A PET Study of Cerebral Glucose Metabolism in the Rigid Form of Juvenile Huntington's Disease (JHD)

P.M. MATTHEWS, A. EVANS, F. ANDERMANN and A. HAKIM (Montreal, Canada)

Local cerebral glucose metabolism was measured by PET using 2-deoxy- 2-fluoro^{18}- D-glucose (FDG) in the 7 year old daughter of a male with known Huntington's Disease (HD). The patient presented with a history of personality changes, dementia, a gait disturbance, and diffuse rigidity. Her EEG displayed epileptiform activity. A brain CT showed early caudate atrophy. Calculated cortical (40 μmol/100g/min) and white matter (18-27 μmol/100g/min) glucose utilization rates were within normal limits for adult controls. Glucose utilization in both the caudate (9 μmol/100g/min) and putamen (18.5 μmol/100g/min) were profoundly reduced bilaterally and symmetrically as has been previously observed in adult HD (AHD). Glucose metabolism in the anterior thalamus was normal, similar to that in the cortex. Unexpectedly, the posterior thalamus was hypometabolic (27.2 μmol/100g/min), whereas in AHD thalamic FDG uptake has been found consistently to be normal or increased (Ann. Neurol. 20:296-303, 1986). This finding correlates with previous pathological studies showing more widespread degenerative changes involving the thalamus in the juvenile form (Neurology 23:561-569, 1973). We speculate that the thalamic dysfunction may contribute to this patient's rapidly developing "sub-cortical" dementia of JHD.

110.

Prenatally Diagnosed Hydrocephalus: Factors Affecting Morbidity and Mortality

R.C. TURLIUK, R.F. DEL MAESTRO and R. NATALE (London, Ontario)

A retrospective review was done in a series of 13 children whose diagnosis were made prenatally by ultrasound and were born from 1979 to 1985. These children were born in a hospital where a multi-disciplinary team collaborated in their management in the perinatal period. The purpose of the study was to determine prenatal and postnatal factors that might affect subsequent physical handicap, neurodevelopment and hospitalizations. Ten neonates were operated upon in the first 2 weeks of life and initially had either a ventriculoperitoneal or ventriculoatrial (1) shunt. Three neonates were not shunted; 2 died in the first 12 hours of life and the other died at age 6 weeks. Of the 10 neonates shunted, 1 child was lost to follow-up when the family moved from the region at age 5 months. Nine neonates were followed from 10 months to 7.8 years (median 3.8 years). These children were followed in specialized clinics and were offered stimulation and special education programs to optimize development. Two of the children presented to hospital after deterioration over several hours prior to admission and died at age 10 and 13 months. One of the children had a congenital heart anomaly previously operated on at 3 weeks of age.

Overall, physical limitations include meningomyelocele effects in certain patients, cerebellar symptoms, blindness, and presence of non-neurologic lesions at birth. Neurodevelopment ranged from severely restricted to no detectable abnormality. Hospitalization included numerous admissions for shunt assessment, revision and respiratory problems. Prenatal factors influencing outcome included genetic predisposition to hydrocephaly, respiratory maturation and degree of ventricular dilatation. Postnatal factors included shunt obstruction, and respiratory factors.

The authors conclude that a prospective study is needed involving a multidisciplinary collaborative team in the prenatal period, that would identify factors that are predictive of outcome.

Neurophysiology (Platform)

THURSDAY, JUNE 16TH - P.M.

111.

Magnetic Stimulation of the Human Nervous System

B. BROUWER and P. ASHBY (Toronto, Ontario)

Neural structures in man can be excited using an intense, rapidly changing magnetic field. We examined the effects of altering the orientation of the stimulating coil relative to the peripheral nerves in the forearm. It was evident that orthogonal placement of the coil along the forearm axis produced the most selective stimulation of the median nerve. However, the most effective placement in terms of response magnitude at any given intensity was obtained by laying the coil flat. In this orientation it was possible to obtain supramaximal stimulation of the median nerve at the wrist and proximal to the elbow, but not at mid forearm indicating that the induced current falls off rapidly with an increase in depth of even a few mm.

We also explored the motor responses to stimulation over the scalp and the effects of voluntary contraction on them. Stimulating with the coil over the motor cortex elicited responses in both upper and lower limb muscles. Although the recruitment thresholds were somewhat variable across subjects, the tendency was that the hand muscles were activated at lower stimulus intensities. These activation thresholds were shown to be strongly influenced by voluntary contraction; the mechanisms of which we studied in greater detail. The post synaptic potentials (PSPs) produced by magnetic stimulation of the brain were derived from poststimulus time histograms of single motor unit firings. These PSPs were not increased by greater voluntary contraction suggesting that the enhanced response to magnetic stimulation does not result from summation at the cortex, but rather, from an increase in the excitability of spinal motoneurons.

112.

Technically Satisfactory Electrophysiological Evoked Potential Monitoring During Carotid Endarterectomy Surgery

H. SCHUTZ, C.H. TATOR, V. MRAZ, F. WILEY, G. SAWA and R.D. LINDEN (Mississauga & Toronto, Ontario)

Carotid endarterectomy (CE) surgery has an associated risk of brain ischemia. Somatosensory evoked potentials (SSEP) have been recommended as a tool for early detection of this portend event. The purpose of this paper is to present our method of intraoperative monitoring and to describe our results using this technique.

Thirty-nine patients had CE performed with intraoperative monitoring of SSEPs. All patients had preoperative SSEPs recorded. SSEPs were elicited by electrical stimulation of the median nerve at the wrist. Stimuli (250 usec. duration) were delivered at a presentation rate of 4.72/s. Electrodes were attached to the skin overlying Erb's point, Fz, C3', C4' and to the skin overlying the fifth cervical vertebrae. Preoperatively, 1000 stimuli were recorded in each trial. Intraoperatively, 200 stimuli were recorded in each trial. The system bandpass was 30-3000 H_z and the sweeptime was 50 ms.

All cases were successfully monitored. Preoperative testing decreases the intraoperative set-up time. Four cases had shunts inserted because of changes in the scalp N20 potentials. An increase in latency greater than 5 ms and amplitude decrease greater than 50% was considered significant. One patient had a change in the cortical potential after the clamp had been released. In our series of monitored patients there have been no postoperative neurological deficits. One false-negative result was observed caused by a technical error.

Intraoperative monitoring of SSEPs can be performed successfully during all CF surgeries. This technique is a useful tool in the monitoring of cerebral ischemia. Muscle relaxant administration results in the acquiring of a high-signal-to-noise ratio, therefore decreasing the number of averages required.

113.

Neuroanatomical Spinal Cord Substrates of Motor Evoked Potentials and Cerebellar Evoked Potentials

F. GENTILI, F. SHICHIJO and G. NIZNIK (Toronto, Ontario)

There is an increasing interest in the use of evoked potentials to evaluate and monitor spinal cord function during spinal surgery. Recently, it has been suggested that motor evoked potentials (MEPs) and cerebellar evoked potentials (CEPs) are a more reliable monitor of motor function than sensory evoked potentials. The purpose of the present study was to determine the neuroanatomical substrate of both MEPs and CEPs utilizing selective spinal cord lesions. Forty (40) adult mongrel cats were used. With the animals anaesthesized with Ketamine and intubated, stimulating electrodes were placed transcutaneously over the motor cortex or the cerebellum with the cathode electrode on the hard palate. A wide laminectomy was made at T12/13 and epidural electrodes were placed at T7 and L3. The peripheral nerve responses were recorded form L7 dorsal and ventral nerve roots after a L6/7 laminectomy, and from the sciatic nerves in the popliteal fossa. Baseline and immediately followed selective spinal tract lesions at T12. The major negative wave of the MEP and CEP recorded from epidural electrodes showed only minor attenuation by lesions in the dorsal half of the cord. By contrast, the amplitude of the late components of the MEP was significantly reduced. Lesions in the ventral half of the cord resulted in significant attenuation of the major negative wave of both MEP and CEP. After a complete section of the spinal cord, but sparing the dorsal columns, the MEP responses were abolished. By contrast, the late components of the CEP response on epidural recording and the responses from the dorsal nerve root and sciatic nerve were preserve. The results from this study suggests that, in the cat, MEPs are conducted orthodromically through both the pyramidal and extrapyramidal motor pathways in both the dorsal and ventral quadrants of the cord. CEPs on the other hand, appear to be conducted not only orthodromically through the pyramidal and extrapyramidal motor pathways, but also antidromically through the dorsal columns. Our findings suggest that the current belief that motor evoked potentials reflect activity primarily in the dorsal lateral quadrant of the spinal cord will have to be re-evaluated.

114.

Motor Evoked Potential Elicited by Magnetic Stimulation of the Awake Human Cortex

A.A. EISEN, S. BOHLEGA, A.S. BUCHMAN, K.M. MURPHY, M. HOIRCH and D. FAIRHOLM (Vancouver, British Columbia)

The motor cortex was stimulated using a Dantec 16E06 magnetic stimulator in 13 awake, normal subjects. Motor evoked potentials (MEPs) were recorded from the thenar muscles without untoward effects. An initial "priming" stimulus was followed by a test stimulus of 70% maximum output of the stimulator. MEP latency measured 21.4 ± 1.3 msec (range 19.4 - 23.2 msec). Amplitude measured 3.3 ± 2.2 mV (range 1.1 - 7.9 mV) which was 29.4% ± 18.4% (range 14% - 79%) of the thenar M wave evoked by electrical stimulation at the wrist, measuring 12.0 ± 2.6 mV. Central motor conduction time was 7.3 ± 1.2 msec (range 6.8 - 9.3 msec). This was calculated using the difference between the latency of the cortical evoked thenar MEP and ((median F-wave latency -1 + M wave latency)/2). In ALS patients the MEP may be reduced in amplitude or unobtainable. In MS the MEP latency may be markedly prolonged at a time when the somatosensory evoked potential from the same arm is normal.

Magnetic MEPs were studied for use in monitoring spinal cord function during surgery. They were easily obtained before induction of anesthesia. However, even at stage 1 anesthesia cortical MEPs could not be obtained although peripheral evoked MEPs were still present. Initial studies in dogs utilizing various anesthetics showed similar results. It appears that magnetically elicited MEPs cannot be used during general anesthesia to monitor motor function.

115.

How Useful are F-wave Studies in Detecting Early Abnormalities in the Guillain-Barré Syndrome?

W.T. NOLAN and J.D. STEWART (Montreal, Quebec)

Early in the course of Guillain-Barré syndrome (GBS), 10-20% of patients have normal standard nerve conduction studies (NCS). It has been suggested that F-wave studies will increase the electrodiagnostic yield because this technique can show slowing of proximal conduction. Several studies have addressed this application of F-waves, but the conclusions are unsatisfactory for various reasons; the best study reported abnormal F-waves in all of 21 patients with early GBS.[1]

We report 38 patients who met standard criteria for the diagnosis of GBS, and who were all evaluated electrophysiologically within the first 2 weeks of their illness with a standardized protocol: median nerve motor, F-wave, sensory; tibial motor and F-wave; sural sensory.

Results: 31/38 (82%) had abnormal F-waves; 32/28 (84%) had abnormal NCS. Of the 6 patients with normal NCS, 3 had abnormal F-waves - resulting in a total of 35/38 (92%) patients with abnormal electrodiagnostic tests. The 3 patients with normal tests all later developed abnormalities of NCS and/or F-waves.

Conclusion: F-wave abnormalities were found in about the same frequency as abnormalities in standard nerve conductions in early GBS. However, doing **both** tests will increase the diagnostic yield from about 80% to 90%.

[1] Ambler Z, Stalberg E, Flink R et al: Ceskoslovenska Neurologie a Neurochirurgie 48; 81: 215-250. 1985.

116.

Latent Transcarpal Median Sensory Conduction Abnormalities in Mild Carpal Tunnel Syndrome

J. DE LÉAN (Québec City, Québec)

The major slowing of nerve conduction in the carpal tunnel syndrome (CTS) is located in the palm to wrist segment. The aim of this study was to develop a reliable, sensitive and accessible approach for detecting minimal slowing of median sensory nerve conduction velocity which escapes conventional electrodiagnostic techniques.

The author has designed a sensory amplifier with an integrated stimulus artefact suppressor. This custom-built amplifier has a fast recovery time (<500 μsec), a low input voltage noise (< 0.3 μV RMS), a high common mode rejection ratio (>122 dB) and a high input impedance (>100 MΩ).

On stimulation of digits II and III, evoked sensory nerve action potentials simultaneously were recorded at the palm and at the wrist. Recording electrodes were placed perpendicular to the nerve and the latency was measured to the time of the initial positive-to-negative deflection. Distances were determined with a ruler. Limb temperature was kept over 32°C. Median nerve conduction velocity was estimated from digit to palm and from palm to wrist in 80 healthy hands and 253 hands with a presumptive diagnosis of CTS.

In the hands of healthy subjects, the transcarpal and the digital conduction velocities were respectively 49.4 m/sec ± 4.7 m/sec and 51.8 m/sec ± 5.1 m/sec.

According to conventional criteria, 131 of the 253 hands from those suspected of CTS were tough to have median nerve compression at the wrist. When median transcarpal conduction velocity was taken into account, the diagnostic yield increased by 18.1%.

The described technique provides a simple, sensitive and acceptable method of diagnosing mild CTS as well as an interesting alternative to other electrodiagnostic methods.

117.

Median Nerve Somatosensory Evoked Potential (SEP) Grading System Accurately Predicts Outcome in Comatose Patients

D.A. HOULDEN, CHEN LI, M.L. SCHWARTZ, M. SEGUIN, D.W. ROWED and M. FAZL (Toronto, Ontario)

In the past, multimodality cortical evoked potentials have served to predict outcome in comatose patients. Pavot et al[1] described an SEP grading system which accurately predicted outcome in stroke patients. Our simplified median nerve SEP grading system afforded early, accurate prediction of outcome in 88 comatose patients, 71 with cerebral trauma.

The amplitude of the cortically generated P22 waveform recorded from the contralateral somatosensory cortex-FZ and the interpeak latency (IPL) between the cervical SEP (C2 vertebra-FZ) and the cephalically recorded N20 were determined from normal subjects following median nerve stimulation.

Six median nerve SEP grades were devised to categorize coma patients into six SEP groups. The SEP determinations were made 3 to 22 days after the onset of coma. The SEP grades were based on the presence or absence of N20 and all other subsequent waveforms, P22 amplitude and cervical SEP-N20 IPL.

All 13 patients in SEP grade 1 (bilaterally absent N20 and all other subsequent waveforms in the presence of normal cervical SEP's) either died or remained in a vegetative state up to six months after trauma. In contrast, of 9 patients in SEP grade 6 (bilaterally normal N20 and all other subsequent waveforms, P22 amplitude and cervical SEP-N20 IPL) seven patients had good-excellent gait, mobility, and activities of daily living and excellent hand function[1] by six months after trauma. The two remaining patients died of extracranial causes. For 34 patients in SEP grades two and five, prediction was as definitive at early follow-up assessments. Accordingly, follow-up is continuing.

[1] Pavot AP et al: The prognostic value of somatosensory evoked potentials in cerebrovascular accidents. Electromyogr Clin Neurophysiol 26:333-340, 1986.

118.

The Retinal Nerve Fiber Layer, Neuroretinal Rim Area and Visual Evoked Potentials In Multiple Sclerosis

D.J. MacFADYEN, S.M. DRANCE, G.R. DOUGLAS, P.J. AIRAKSINEN, D.K. MAWSON and D.W. PATY (Saskatoon, Saskatchewan; Vancouver, British Columbia; Oulu, Finland)

In a prospective study of 57 patients with clinically definite, probable or possible multiple sclerosis (MS) half of whom had a history of optic neuritis, retinal nerve fiber layer (RNFL) defects and the neuroretinal rim (NRR) area were quantitatively determined and compared with the visual evoked potential (VEP). An abnormal VEP latency was present in 63% of all patients (definite and probable = 68%, possible = 50%). Local or diffuse RNFL defects occurred in 54% of all patients (definite and probable = 54%, possible = 50%). The NRR area was abnormally small in 30% of all patients (definite and probable = 32%, possible = 25%). Abnormalities in one or more of the VEP, RNFL or NRR area occurred in 86% or all patients (definite and probable = 90%, possible = 75%), thus considerably increasing the yield of optic nerve abnormalities over that of the VEP alone. The predominance and extent of the diffuse RNFL defects, which are axonal abnormalities, suggest a more diffuse optic nerve pathology in MS than can be accounted for by a "plaque" pathology and indicate that extensive axonal loss commonly occurs in the optic nerves of MS.

119.

Color Vision (FM 100-Hue) and The Visual Evoked Potential In Multiple Sclerosis

D.J. MacFADYEN, S.M. DRANCE, G.R. DOUGLAS, I.A. CHISHOLM, J.F. KOZAK and E. BLAU (Saskatoon, Saskatchewan; Vancouver, British Columbia)

In a prospective study of two groups of multiple sclerosis (MS) patients (57 in Vancouver and 78 in Saskatoon) visual evoked potentials (VEP), FM 100-Hue color vision (CV) and automated perimetry were performed. Retinal nerve fiber layer (RNFL) photography and neuroretinal rim (NRR) area measurement via disc photography were done in the Vancouver group (Vanc). The two groups were very similar in age and disease duration but the Saskatoon group (Sktn) was more disabled by their disease. In patients with definite or probable MS with or without a history of optic neuritis (ON) the VEP was more often abnormal than the CV (68%/43%). An abnormality in VEP or CV was found in 95% of Vanc definite or probable MS patients (100% of Sktn) with a history of ON and in 75% of those with no history of ON (59% of Sktn). An abnormal red-green color axis occurred in only 8 (4%) of all definite or probable MS eyes and an abnormal blue-yellow axis occurred in 11 (6%). Ten of these 19 eyes with an abnormal color axis had an abnormal CV score. In both control eyes (n = 30) and MS eyes the most consistent error scores were in the "blue" quadrant of the FM 100-Hue color circle. Of all eyes with an abnormal VEP 42% had an abnormal CV score and of those with an abnormal CV score 68% had an abnormal VEP. The VEP was abnormal in 65% of all eyes with an abnormal RNFL and the CV score abnormal in 33% of these eyes. In all eyes with an abnormal NRR area the VEP was abnormal in 52% and the CV score in 36%. Abnormal color vision in MS probably reflects a different pathology than the demyelination responsible for the VEP latency abnormality and the absence of a specific red-green deficiency suggests that the maculopapillary fibers are not selectively vulnerable in MS.

120.

Automated Perimetry and The Visual Evoked Potential In Multiple Sclerosis

D.J. MacFADYEN, S.M. DRANCE, G.R. DOUGLAS, I.A. CHISHOLM, K. WIJSMAN and E. BLAU (Saskatoon, Saskatchewan; Vancouver, British Columbia)

In a prospective study of two groups of multiple sclerosis (MS) patients (57 in Vancouver, 78 in Saskatoon) visual evoked potentials (VEP), FM 100-Hue color vision (CV) and automated perimetry were performed. Retinal nerve fiber layer (RNFL) photography and neuroretinal rim (NRR) area measurement via disc photography were done in Vancouver (Vanc) group. Perimetric studies in all patients in the Vanc group were by Competer and, in 44 patients, also by Octopus (program G1). In the Saskatoon group (Sktn) all patients were examined by Octopus program 31. The two groups were very similar in age and disease duration but the Sktn group was more disabled by its MS and had a higher incidence of reduced visual acuity. A normal Competer "P"value was determined to be 444 (P = 0.05) in 20 normal eyes. Octopus G1 normal parameters were as in the program and Octopus 31 normal mean deviation (MD) in 30 normal eyes was found to be 3.2 (p = 0.05). In all probable or definite MS patients with a history of optic neuritis (ON) the VEP was abnormal slightly more often than the perimetry: Vanc VEP = 74%, Competer "P" = 65%, MD(G1) = 67%; Sktn VEP = 88%, Octopus 31 MD = 81%. In definite or probable MS patients with no history of ON the VEP was also slightly more sensitive than the perimetry except in the case of MD(G1): Vanc VEP abnormal in 46%, Competer "P" in 41%; Sktn VEP was abnormal in 52%, Octopus 31% MD in 50%. In general, large or deep scotomata were uncommon. The corrected loss variance (CLV) in the G1 examined eyes is a statistical measure of localized defects and in Vanc definite and probable eyes it was abnormal in 39%. Of all eyes with an abnormal VEP 45% had an abnormal "P", 52% an abnormal MD(G1) and 73% and abnormal Octopus 31 MD. It is not clear whether the above perimetric abnormalities are the result of demyelination or axonal loss but they are notably diffuse/ multifocal.

Neurophysiology (Poster)

FRIDAY, JUNE 17TH — P.M.

121.

Carpal Tunnel Syndrome: Clinical and Electromyographic Correlation of Palmar Stimulation

M.L. D'AMOUR, F. DELISLE, D. BISSOON-DOYAL, S. LAUZIER, L.H. LEBRUN and S. GAGNON (Montreal, Québec)

Palmar stimulation is said to be one of the most sensitive techniques used in the detection of mild compression of the median nerve at the carpal tunnel. However, few studies have evaluated the method in regard to clinical findings.

Twenty-five patients with symptoms suggestive of carpal tunnel syndrome were studied. Clinical and electromyographic (EMG) data were compared with those of 25 normal subjects. Nocturnal hand paresthesias occurred in 24/25 patients; Phalen's sign was positive in 19/25 cases, Tinel's in 14/25; 11/25 experienced a sensory deficit in the median nerve distribution.

Median nerve conduction values for different segments in patients and normal subjects respectively were as follows: Motor distal latency: 4.96±1.0, 3.2±.46 msec ($p<.005$); Sensory conduction velocity from middle finger to wrist: 44.5±17.5, 61.9±7.6 M/sec ($P<.005$); from middle finger to palm 45.8±18.8, 60.5±6.3 M/sec ($p<.005$); from Palm to wrist: 41.2±11.7, 64±6.9 M/sec ($<.0005$).

The patient group differs greatly from the control group, especially with respect to the palm to wrist segment.

However, 8 of the 25 patients had a normal palm to wrist conduction velocity: 7/8 reported nocturnal paresthesias and 3/8 revealed a Phalen sign or a sensory deficit in the median nerve distribution. Of the latter, one had a prolonged conduction in the finger to wrist segment, and another in finger to palm segment. Both had a motor distal latency at the upper limit of normal (4.1 and 4.4 msec).

These findings suggest that the palmar stimulation technique is more sensitive when used to detect mild compression of the median nerve at the carpal tunnel, but it has limitations when analyzing individual patients.

122.

Etude Electromyographique Dynamique du Plancher Pelvien dans la Constipation: Importance de l'EMG à l'Aiguille

M.L. LEBEL et F. GRAND'MAISON (Sherbrooke, Québec)

L'électromyographie dynamique du plancher pelvien complète le bilan radiologique et manométrique de la constipation opiniâtre. Elle permet de mieux étudier «l'anisme» ou «syndrome du plancher pelvien spastique». Une absence de relaxation, voire même une contraction paradoxale du muscle puborectal (PR) et du sphincter anal externe (SE) lors de la défécation simulée en sont les manifestations électromyographiques cardinales.

Pareille conclusion reposant sur des données recueillies à partir d'électrodes de surface nous parait cependant sujette à caution. Sou-

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cieux d'identifier l'activité musculaire propre au puborectal et au sphincter anal externe, il nous a paru préférable d'utiliser des électrodes-aiguilles, malgré l'inconfort inhérent à leur emploi.

Chez deux de nos 38 malades investigués par électromyographie à l'aiguille pour désordres de défécation, nous avons retrouvé une dissociation majeure entre l'activité du PR et du SE, comme il est impossible d'en documenter avec un enregistrement de surface.

Dans ces deux cas, lors de la défécation simulée, l'inhibition habituelle de l'activité du PR s'est accompagnée d'une contraction paradoxale du SE. La signification de cette dissociation PR/SE nous échappe pour le moment; sa survenue souligne néanmoins l'importance de l'enregistrement sélectif à l'aiguille de ces muscles chez un plus grand nombre de malades et chez des sujets témoins.

Cette étude illustre la supériorité de l'enregistrement à l'aiguille sur les tracés de surface dans l'investigation d'une constipation opiniâtre.

123.

Dynamic Modeling of Scalp Recorded Neuro-electric and Neuro-magnetic Activity in Epilepsy

F. RICHER, A. ACHIM, C. ALAIN, J.-M. SAINT-HILAIRE (Montreal, Quebec)

The localization of intracerebral sources of scalp recorded activity is difficult when several sources overlap in time. Dynamic modeling of multiple dipolar sources has been developed to help resolve such situations. Its purpose is to explain the data variance across time and recording sites by the combined activity of spatially distinct dipolar sources.

We applied the technique to sequentially acquired single-channel magnetoencephalographic (MEG) records and 32-channels referential EEG records of interictal spikes from patients with partial complex epilepsy. The sources thus identified were compared to localizations obtained from depth electrodes (SEEG).

Given that the bipolar SEEG responds mostly to sources very close to the pair of electrode contacts, our preliminary results show acceptable correspondence between a subset of the sources identified by dynamic modeling and the localizations obtained from depth electrode recordings during ictal activity or REM sleep interictal spikes.

This suggests that, even in cases where the standard visual inspection of bipolar scalp EEG provides poor or no localization, quantitative modeling of the situation that produces the records can contribute usefully to localizing the sources of epileptogenic activity, especially when a large number of recording sites is used. The better spatial definition of MEG signals and their simpler underlying model (insensitivity to the radial component of sources) make MEG a useful addition to EEG.

124.

Intraoperative Monitoring of Somatosensory Evoked Potentials Revisited

R.D. LINDEN, C.H. TATOR, H. SCHUTZ, M.G. FEHLINGS (Toronto, Ontario)

Intraoperative monitoring of spinal cord function with somatosensory evoked potentials (SSEP) has been reported to be of limited use. Both false-negative and false-positive results have been documented. However, with improved techniques, SSEPs, may now be recorded reliably in all cases, and therefore, their intraoperative clinical usefulness should be re-examined. The purpose of this paper is to describe four cases wherein the intraoperative SSEPs disappeared, the surgical approach was altered, and the patient after surgery had preserved neurologic function. Each patient was operated on for cervical lesions (2 tumors, 2 degenerative spinal disease). Depending on the level of the lesion, either upper limb or lower limb SSEPs were recorded. Upper limb SSEPs were elicited by stimulating the median nerve at the wrist and lower limb SSEPs were elicited by stimulating the posterior tibial nerve at the ankle. Stimuli (250 usec) were delivered at a presentation rate of 4.72/s. To record lower limb SSEPs, electrodes were attached to the skin overlying the popliteal fossa, L3, T12 and to the scalp at Cz′ and Fpz′. To record upper limb SSEPs, electrodes were attached to the skin overlying Erb's point, Fz, C3′, C4′ and to the skin below the operative site. The system bandpass was 30-3000 Hz and the sweeptime was 50 ms. In each of the four cases a change in the SSEPs recorded above the operative site was observed induced by an operative manipulation. A change in the surgical approach resulted in an improvement in the recorded waveforms. These data indicate the clinical usefulness of the intraoperative recording of SSEPs. Therefore, until methods have been developed to monitor both the motor and somatosensory components of the cord, SSEPs should be recorded as a test for global spinal cord function intraoperatively.

125.

Interictal EEG in Epilepsy

T. HOGAN, M.B.M. SUNDARAM and R. UITTI (Saskatoon, Saskatchewan)

We investigated the yield of epileptiform discharges (ED) in standard interictal EEG and various factors affecting the yield. 347 records from 347 consecutive patients with seizure(s) referred over a 6 month period were analysed (mean age — 29 years). Cases with febrile and alcohol withdrawal seizures were excluded. Seizures were partial (± secondary generalisation) in 189, generalised from onset in 134 and unclassified in 24.

ED occurred in 47% of EEGs and nonspecific changes were seen in additional 19%. Incidence of ED was similar in children (16 years or less; 53%) and adults (49%). 55% of records from patients with partial seizures and 44% from those with generalised attacks contained ED ($p<0.01$). Yield of ED increased with seizure frequency in the preceding year: 31% in those with no or single attack; 50% in patients with 2-12 seizures and 70% in those with >12 attacks. Of the recordings done within 2 days of a seizure, 67% contained ED; 46% of EEGs done between 3 to 7 days after seizure and 41% of those done after 7 days showed ED.

Conclusions: Standard interictal EEG is more likely to show ED in patients with partial seizures and when done within 2 days of a seizure. Age does not seem to influence the yield.

126.

Predictive Value of BAER Discriminant Analysis in the Diagnosis of Suspected Multiple Sclerosis

M. JAVIDAN, D.R. MCLEAN, A. FARID and K.G. WARREN (Edmonton, Alberta)

Brainstem Auditory Evoked Response (BAER) is considered to be the least sensitive evoked potential modality in the diagnosis of multiple sclerosis (M.S.). We previously reported the value of discriminant analysis in analysing BAER in M.S. patients. In our previous study, the BAER response from 34 normal controls and 98 definite M.S. patients were analysed. Stepwise discriminant analysis identified the most discriminating BAER variables and a formula consisting of those variables allowed compution of a final score to classify BAER as normal or abnormal. Using this technique, 79% of M.S. patients and normal controls were correctly classified.

This discriminant formula was utilized to analyse BAERs from 56 possible and 59 probable M.S. patients. In patients with possible M.S.,

the BAER was abnormal in 10 (18%) using traditional interpretation methods and was abnormal in 33 (59%) using discriminant function. Two abnormal cases by traditional interpretation were reclassified as normal. In patients with probable M.S., the abnormal patients increased from 23 (40%) to 43 (74%) by using discriminant function. One abnormal case by traditional interpretation was reclassified as normal using discriminant function.

32% of the 25 possible M.S. patients with abnormal BAER identified by discriminant function had abnormal VEP and/or SEP. 13 of these patients (52%) were subsequently reclassified clinically M.S. at follow-up. 64% of the 22 probable M.S. patients with abnormal BAER identified by discriminant function had an abnormal VEP/SEP. 12 of these patients (55%) were subsequently reclassified as clinically definite M.S. at follow-up.

Analysis of BAER by discriminant function improves the sensitivity of this test and increases the usefulness of BAER in establishing the diagnosis of possible and probable M.S. patients.

Neurobiology (Platform)

FRIDAY, JUNE 17TH - P.M.

127.

A Calmodulin Antagonist retards the Development of Kindling and reduces the Production of c-fos protein following a Kindling Stimulus

D.G. HERRERA, M.R. PETERSON and H.A. ROBERTSON (Halifax, Nova Scotia)

We know that permanent changes can occur in brain. Examples are memory and such long-term electrophysiological changes as kindling. There has never been an adequate explanation for these long-term changes in brain though it is now generally thought that they involve protein synthesis. For example, it is fairly certain that electrophysiological kindling, produced by daily stimulation of some limbic structure, requires protein production. The problem here is that we know that proteins have very limited half-lives, in the order of hours or days but certainly not the months, years or even decades necessary to explain long-term events such as kindling or memory. Only the genetic material has such longevity. We have recently shown that kindling stimuli are accompanied by activation of the proto-oncogene c-fos in the dentate gyrus. This proto-oncogene may be a master-switch, regulating protein production. However, there is only circumstantial evidence suggesting that c-fos is involved in kindling. In cultured cells, the activation of c-fos production is dependent on calcium influx and activation of calmodulin. We therefore studied the effects of the specific calmodulin inhibitor W7 on both kindling and the production of c-fos protein. Here we report that the calmodulin antagonist W7 retards the development of kindled seizures and reduces the production of c-fos protein.

Rats were given saline or W7 (N6-aminohexyl-5-chloro-naphthalene-sulphonamide) (15 mg/kg, i.p.) followed by a kindling stimulation through a bipolar electrode implanted in the amygdala. This dose of W7 completely eliminated c-fos protein accumulation in the dentate gyrus. Similar doses also significantly retarded the development of kindled seizures.

These results add to the evidence which suggest that activation of the proto-oncogene c-fos is involved in long-term changes in brain.

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128.

Neuro-Behavioral Effects of Intrathecal Somatostatinergic Therapy in Subhuman Primates

R. LeBLANC, S. GAUTHIER, M. GAUVIN, R. QUIRION, R. PALMOUR and H. MASSON (Montreal, Quebec)

Somatostatin (SS) is a peptide neurotransmitter widely distributed within the cerebral cortex of primates. Cortical deficiencies of SS have been noted in patients with Alzheimer's disease (AD), neuronal tangles have been identified in somatostatinergic neurons, reductions in SS correlate with senile plaque counts and loss of SS in cerebral cortex has been correlated with glucose hypometabolism in patients with AD. It has been postulated, therefore, that SS deficiency may be of etiological importance in AD. It has been suggested that SS delivered directly into the intracranial cerebrospinal fluid might be helpful in the treatment of patients with AD but the safety of such a treatment strategy has not been demonstrated. We have studied the neuro-behavioural effects of the intracranial-intrathecal administration of SS in subhuman primates to document possible dose-related side effects of such a treatment.

Somatostatin and its longer acting analogue Sandostatin^{R} (SMS 201-995) was infused into the prepontine cisterna of seven monkeys through a catheter placed in the cisterna magna and connected to an Infusaid infusion pump. Acute bolus infusions of up to 50 μg/kg produced no abnormal neuro-behavioural effects. Chronic infusions of Sandostatin produced marked neuro-behavioural changes characterized by truncal ataxia, dysmetria and severe bradykinesia with normal level of consciousness, occurring 24-36 hours after the initiation of infusion of 16 μg/kg/day and at two weeks after the initiation of infusion of 4 μg/kg/day. These effects were promptly reversed by the subcutaneous injection of apomorphine, a dopaminergic agonist. We conclude that the chronic intracranial-intrathecal infusion of somatostatin analogues can produce marked toxic effects in primates possibly by interfering with dopaminergic mechanisms. Further studies of somatostatinergic replacement therapy are required before such a treatment can be offered to patients with Alzheimer's disease.

129.

Does Chronic Treatment with SKF 38393 potentiate the action of Bromocriptine in Parkinsonian MPTP-Treated Monkeys?

C. ROUILLARD, P.J. BÉDARD, R. BOUCHER and T. DiPAOLO (Québec, Québec)

The neurotoxin 1-methyl-4-phenyl-1,2,3,6 tetrahydropyridine (MPTP) causes destruction of nigrostriatal dopamine (DA) neurons and symptoms resembling Parkinson's disease in humans and subhumans primates. We have already reported different effects of chronic treatments with various DA agonists in MPTP-treated monkeys (Bédard et al., **Brain Res.**, 379-294; Bédard et al., **Soc. Neur. Abs.**, 17:567). MPTP induces an increase of 30% in the number of [^{3}H]-spiperone binding sites (Bmax) in caudate nucleus and putamen which is reduced by chronic treatment with L-DOPA, bromocriptine (BRC) (a D_2 agonist) or SKF 38393 (SKF) (a selective D_1 agonist). No dyskinesia were seen in monkeys on BRC or SKF as opposed to the L-DOPA treated animals where the dyskinetic response appeared to increase with time. However, SKF alone was ineffective in relieving the parkinsonian symptoms. In the present study, we have investigated the behavioural and biochemical effects of chronic treatment with BRC and BRC + SKF. Eight ovariectomized MPTP-treated monkeys were divided in two groups and treated orally during 7 weeks with BRC (5 mg/kg) or BRC (5 mg/kg) + SKF (5 mg/kg). No dyskinesia was seen in either group and there was no difference in motility. They were sacrificed three days after the last dose. Only one animal in each group had a decrease of DA and DA metabolites of less than 90% in the caudate nucleus and putamen and they were not considered for calculation of the mean values. No difference in [^{3}H]-spiperone dissociation constant was observed between the two groups. The Bmax was lower in the caudate nucleus of monkeys treated with BRC than in those treated with BRC + SKF. In fact, the

BRC-treated group had a mean value of the number D_2 binding sites which is very close to that of intact monkeys while that of BRC + SKF-treated group was intermediate between intact animals and MPTP-denervated ones. These results demonstrate that chronic treatment with selective D_1 and D_2 dopamine agonist alone or in combination can modulate differently the adaptation of the nigrostriatal system to denervation. Supported by the MRC and the Parkinson Foundation of Canada.

130.

Dopaminergic Innervation of the Pallidum and Subthalamic Nucleus in Primates: A Tyrosine Hydroxylase Immunohistochemical Study

B. LAVOIE, Y. SMITH and A. PARENT (Québec City, Québec)

Light and electron microscopic immunohistochemical studies of the basal ganglia in the squirrel monkey (*Saimiri sciureus*) with an antiserum raised against tyrosine hydroxylase (TH) revealed a massive and differential dopaminergic innervation of the globus pallidus (GP) with only a small input to the subthalamic nucleus (STH). At light microscopic level, axons of TH-immunoreactive neurons of the substantia nigra pars compacta were seen to form a massive bundle ascending through the field H of Forel. The dopaminergic innervation of GP derived mostly from two fascicles that detached themselves from this main bundle and reached their target by coursing along the two major output pathways of GP: the lenticular fasciculus caudally and the ansa lenticularis rostrally. Caudally, the TH fibers in the lenticular fasciculus coursed along the dorsal surface of STH. Some fibers were seen to penetrate STH itself where they arborized exclusively within the dorsomedial third of the structure. More laterally, the fibers traversed the internal capsule and invaded GP from its dorsal surface. Rostrally, a larger contingent of TH fibers swept laterally along the ansa lenticularis to invade GP from it ventral surface. Within GP itself TH fibers were significantly more numerous in the internal (GPi) than in the external (GPe) pallidal segment. They formed numerous small plexuses distributed over the entire dorsoventral extent of GPi, whereas GPe displayed only few short fibers that were uniformly scattered throughout its dorsal portion. However, a very dense field of TH-positive terminals occurred ventrally in the cauldalmost portion of GPe. At electron microscopic level, numerous nonmyelinated and some myelinated TH-immunoreactive fibers were visualized in both GPe and GPi. TH-positive varicosities were seen in close contact with dendrites of pallidal neurons in the form of synapse en passage, but typical junctional appositions were rarely seen. These findings suggest that, in addition to their potent influence at striatal levels, the nigrofugal dopaminergic fibers in primates may modulate directly the activity of pallidal neurons, particularly those of the internal segment of the globus pallidus. (Supported by MRC, FRSQ and FCAR).

131.

Ultrastructure de l'innervation à sérotonine (5-HT) du néostriatum chez le rat adulte

J.-J. SOGHOMONIAN, K.C. WATKINS et L. DESCARRIES (Montréal, Québec)

La radioautographie (RAG: capture de [^{3}H]5-HT injectée par voie cérébroventriculaire) et l'immunocytochimie (IMMUNO: antisérum dirigé contre un conjugué 5-HT- glutaraldéhydeprotéine, courtoisie de M. Geffard) ont été utilisées en parallèle pour identifier et examiner des terminaisons (varicosités) axonales 5-HT du néostriatum en microscopie électronique. Ces varicosités, définies comme telles par la présence de vésicules synaptiques agglomérées, ont été visualisées sur coupe fines isolées dans le cas de la RAG et sériées dans le cas de l'IMMUNO. Les deux approches ont donné des résultats concordants. Les varicosités néostriatales 5-HT sont généralement petites (0.5μm de diamètre moyen) et leur contenu vésiculaire souvent pléomorphique. Lorsqu'elles montrent une spécialisation membranaire (complexe de jonction), celle-ci s'avère asymétrique et le partenaire synaptique est toujours une épine ou un axe dendritique. De telles varicosités 5-HT synaptiques sont cependant peu nombreuses: même en coupes fines sériées, 10% seulement des terminaisons immunopositives montrent un complexe de jonction comparativement à 70% des terminaisons immunonégatives du neuropile environnant. Diverses structures se retrouvent directement apposées aux varicosités 5-HT jonctionnelles ou non, notamment d'autres terminaisons axonales, des épines ou des axes dendritiques et, rarement, des corps cellulaires. Ces données prouvent que l'innervation 5-HT néostriatale est à forte prédominance non jonctionnelle et suggèrent une multiplicité de cibles cellulaires possibles pour l'action de la 5-HT dans cette partie du cerveau (Subventionné par le CRM et le FRSQ).

132.

Horizontal Limb of the Diagonal Band and Nucleus Basalis Cholinergic Neurons Project to Defined Cortical Areas in the Rat

M. PIOTTE, R. EGIZII, G.E. LUCIER and A.C. CUELLO (Montreal, Quebec; Calgary, Alberta)

The cholinergic neurons forming the horizontal limb of the diagonal band (HDB) and those belonging to the nucleus basalis magnocellularis (NBM) merge at the rostral NBM level. Furthermore, both nuclear groups project to the neocortex. In an attempt to further delineate these two neuronal groups their respective cholinergic cortical projection pattern was examined. For this, we employed a double labeling technique combining horseradish peroxidase (HRP) retrograde tracing with choline acetyltransferase (ChAT) immunocytochemistry. A small piece (<1mm in diameter) of a polyacrylamide slow-release gel containing 15% HRP was stereotaxically inserted beneath the brain surface of adult male Wistar rats (250-320 g) in each of the following cortical areas: frontal, parietal, temporal, occipital and cingulate (Zilles, K., The Cortex of the Rat, A Stereotaxic Atlas, 1985). Seventy-two hours later animals were perfused, brains removed and 40 μm thick serial frozen sections of cortical implant sites, NBM and HDB were cut with a sledge microtome. All sections were processed for HRP histochemistry followed by ChAT immunocytochemistry for NBM and HDB sections only. The material was then examined under a light microscope to which a camera lucida drawing tube was attached. This study revealed that the highest incidence of ChAT-positive perikarya occurred in the NBM after parietal cortical implants, followed by occipital, cingulate, temporal and frontal cortical implants in decreasing order. The projection pattern of double-labeled NBM neurons will be compared with that of the HDB double-labeled neurons. Results will be discussed in relation to the search for suitable animal models to study the cholinergic deficit associated with Alzheimer's disease.

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133.

Nerve Growth Factor and Sensory Neurons

V.M.K. VERGE, P.M. RICHARDSON and R.J. RIOPELLE (Montreal, Quebec; Kingston, Ontario)

Radioautography following incubation of tissue sections with radioiodinated nerve growth factor (NGF) has been used to detect and quantify NGF receptors on several neuronal populations in rats. Studies with primary sensory neurons reveal two classes of receptor which are half-maximally saturated by approximately 20 picomolar and 2

nanomolar concentrations of NGF. Heavily labelled perikarya contain more than 100,000 high-affinity receptors. 40-50% of the neurons in a rat lumbar dorsal root ganglion (DRG) have high-affinity receptors and are thus responsive to NGF at endogenous concentrations. Although many receptor-bearing sensory neurons are immunoreactive for substance P and other neuropeptides, no rigorous co-expression of the NGF receptor and any single peptide has yet been discovered. Several weeks following sciatic nerve transection, the density of high-affinity receptors on DRG neurons is less than one half normal values. The capacity of sensory axons to take up NGF and transport it to their cell bodies is also diminished by nerve injury. These responses to axonal transection could represent selective death of neurons with NGF receptors or a down-regulation of receptors within individual neurons.

Why some but not all sensory neurons have NGF receptors is unknown. The loss of NGF receptors on injured sensory neurons raises questions about the regulation of receptor synthesis and the possible functions of NGF in neural injury.

134.

Direction-dependent modulation of SI afferent input prior to the onset of movement in the monkey

W. JIANG, E.C. CHAPMAN and Y. LAMARRE (Montréal, Canada)

Somatosensory transmission to primary somatosensory cortex (SI), as tested with evoked potentials, has previously been shown to be diminished during voluntary movement. The depth of modulation does not vary with the direction of movement, indicating that the effect is non-specific (Jiang et al., Abstr. Soc. Neurosci. 13: 673, 1987). This finding is somewhat surprising since the neural structures which are presumed to be involved in mediating these effects, including motor cortex, have directional discharge patterns. To further investigate this question, we have recorded the responses of single neurones in SI cortex to air puff stimulation before the onset of the elbow flexion and extension movement.

A monkey, macaca mulatta, was trained to perform rapid flexion and extension movements of the elbow. An air puff (50 ms) was applied to the cell's receptive field on the forearm with different delays before the onset of movement. Out of 35 cells tested, 31 demonstrated a significant decrease in their evoked discharge beginning about 100 ms before the onset of elbow displacement. Thirteen out of 31 (42%) demonstrated a greater inhibition ($p<0.02$) in one direction than in the other. This observation supports the idea that the efference copy from motor cortex may be involved in mediating these effects. Supported by the Canadian MRC and the FRSQ.

135.

The Effect of Nimodipine and Dextran on Spinal Cord Blood Flow and Axonal Function After Experimental Spinal Cord Injury

M.G. FEHLINGS, C.H. TATOR and R.D. LINDEN (Toronto, Ontario)

Posttraumatic ischemia is important in the pathogenesis of acute spinal cord injury (SCI). The present study evaluated whether the combination of the calcium channel blocker nimodipine (NIM) and dextran 40 (D40) could improve SCBF, measured by hydrogen clearance technique and axonal function as assessed by motor and somatosensory evoked potentials (MEP and SSEP) after SCI in the rat. Adult rats received a 53g clip compression injury of the cord at T1. The rats were randomly and blindly allocated to one of the following six treatment groups ($n=5$ each): placebo (P) and saline (S); P and D40; NIM 0.02 mg/kg and S; NIM 0.02 mg/kg and D40; NIM 0.05 mg/kg and S; and NIM 0.05 mg/kg and D40. At one hour after SCI, the drugs were administered by infusion for one hour. The following were recorded pre-SCI, one hour following SCI, at the end of drug infusion, and at one and two hours following infusion: SCBF at C6, T1, and T10; MEPs from the cord at T10 (MEP-C) and from the sciatic nerve (MEP-N); spinal evoked potentials (SEP) from the cord at T10; SSEPs from cortex; and hematocrit.

The preinjury physiological parameters, including the SCBF at T1 (56.84 + 4.51 ml/100g/min), were not significantly different ($p>0.05$) between the treatment groups. Following SCI, there was a significant decrease in the SCBF at T1 (24.55 + 2.99 ml/100g/min; $p=0.0001$) as well as significant changes in the MEP-C ($p=0.0001$), MEP-N ($p=0.0001$) and the SSEP ($p=0.002$). The only treatment which increased the SCBF at T1 (43.69 + 6.09 ml/100g/min; $p=0.003$) and concomitantly improved the MEP-C ($p=0.0001$), MEP-N ($p=0.0372$) and SSEP ($p=0.0013$) was NIM 0.02 mg/kg and D40. Furthermore there was a significant correlation between changes in SCBF and the MEP-C ($r=0.49$; $p=0.0001$) and SSEP ($r=0.67$; $p=0.0001$) amplitude. These data show, for the first time, that correction of posttraumatic cord ischemia with NIM and D40 results in a significant improvement in axonal function.

136.

Analgesia induced by N-acetylserotonin in the central nervous system

G.M. BROWN, S. PSARAKIS and L.J. GROTA (Hamilton, Ontario; Rochester, U.S.A.)

N-acetylserotonin (NAS), a naturally occurring derivative of serotonin which is a precursor of melatonin in the pineal gland, also occurs in other regions of the central nervous system (CNS). Moreover tritiated NAS has been shown to bind to both serotonin and non-serotonin sites in the CNS. The observation that NAS is similar in structure to the analgesic dipeptide 5-acetyl-5-hydroxytryptophyl-5-hydroxytryptophan (5-HTP-ACETYL-DP) prompted studies to determine whether NAS also had analgesic action. Using the rat tail-flick model, we initially replicated work showing that intraventricular (IVC) injection of 5-HTP-ACETYL-DP was capable of inducing analgesia in the rat. We then showed that IVC-NAS, given in the same dosage, elicited analgesia which had the same prolonged time course as the dipeptide. This effect proved to be structurally specific as it required the presence of both an acetyl group on the terminal side chain amine as well as a hydroxyl group on the C-5 position of the indole ring. Substitution of the C-5 hydroxyl by a methoxyl group (melatonin) abolished the analgesic effect. Similarly, removing the N-acetyl substitution (serotonin) eliminated the analgesia. In contrast to IVC-NAS, NAS, given peripherally in a 1000 fold higher dose, had no analgesic effect. IVC injection of highly specific antiserum to NAS induced hyperalgesia. Furthermore, an interaction was found between NAS and opiate systems. We demonstrated that while naloxone, the opiate antagonist, has no hyperalgesic properties of itself under our experimental conditions, it did counteract the analgesia induced by NAS. Similarly, NAS antiserum reversed the analgesia induced by the opiate morphine. This work provides evidence suggesting that NAS is an endogenously active substance within the CNS pain network.

137.

Acute Effects of Lithium on Dopaminergic Responses: Iontophoretic Studies in the Rat Visual Cortex

E. GOTTBERG, B. MONTREUIL and T.A. READER (Montréal, Québec)

The interactions between lithium and cortical dopaminergic receptors were investigated using the iontophoretic technique to record and apply dopaminergic compounds, GABA, acetylcholine and LiCl on

neurons in the primary visual cortex of the rat. The main response to dopamine (DA) or to the D_1 agonist (±)SKF38393 on spontaneously-active (SA) or visually-driven (VD) units was a prolonged decrease in firing and a reduction in the responsiveness to pulses of acetylcholine. The D_1 antagonist SCH23390, applied iontophoretically or intravenously, blocked or attenuated the inhibitory responses to both DA and (±)SKF38393. The D_2 agonist quinpirole (LY171555) produced but slight excitations or had no effects on both VD and SA units. The concomitant application of lithium blocked the inhibitory responses to DA and to (±)SKF38393 but did not modify the responsiveness to LY171555. In addition, the DA- and (±)SKF38393- induced decreases in responsiveness to acetylocholine were also suppressed by lithium. These effects were on dopaminergic mechanisms, since the excitatory responses to acetylcholine alone as well as the inhibitions caused by GABA were unchanged by the application of lithium. These results imply that the modifications in sensitivity to dopaminergic agents induced by lithium are mediated by dopamine D_1 receptors and are discussed in relation to adenylate-cyclase.

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138.

How Do Heparan Sulphate Proteoglycans Promote Neurite Outgrowth?

R.J. RIOPELLE, K.E. DOW and J.C. RODER (Kingston & Toronto, Ontario)

Embryonic neurons *in vitro* synthesize proteoglycans, some of which are cell-bound and some of which are released into the extracellular environment. The following evidence suggests that released heparan sulphate proteoglycans (HSPG's) promote neurite outgrowth when bound to laminin, and that the neuronal receptor for these HSPG's is a cell adhesion molecule. (1) In the presence of an inhibitor of proteoglycan assembly (βD-xyloside), neurite outgrowth is partially inhibited in a time-dependent fashion. (2) The neurite-promoting activity of neuron-conditioned medium (CM) is removed by digestion of CM with heparitinase. (3) The kinetics and magnitude of partial inhibition of neurite outgrowth by βD-xyloside and by the monoclonal antibody HNK-1 (Leu 7) which recognizes a carbonhydrate epitope on cell adhesion glycoproteins are identical, whether the inhibitor or the monoclonal antibody is used alone or together. (4) Heparitinase digestion of CM which removes neurite-promoting activity of CM also eliminates the inhibitory effect of HNK-1 (Leu 7).

The following evidence suggests that HSPG's which are intimately associated with the neuronal cell surface can promote neurite outgrowth on laminin in conditions where the neurite-promoting influence of released HSPG's is eliminated. (1) Antibody to HSPG partially inhibits neurite outgrowth. (2) Heparitinase digestion of the neuronal cell surface partially inhibits neurite outgrowth. (3) Neurite outgrowth is partially inhibited by glycosaminoglycan (GAG) side chains of HS. (4) Heparitinase digestion of the neuronal cell surface partially inhibits neurite outgrowth and eliminates the inhibitory influence of HS GAG chains.

Laminin promotes neurite outgrowth by providing an adhesion site (CSAT), a neurite-promoting site, and a distinct site for binding of HSPG's with neurite-promoting activity. Receptor sites on the neuronal cell surface that can mediate adhesion and/or neurite outgrowth include integrins, a high-affinity laminin receptor, cell adhesion molecules with binding sites for HSPG's, and membrane-associated HSPG's.

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Neurobiology (Poster)
THURSDAY, JUNE 16TH — P.M.

139.

The Effect of An Applied Direct Current Field on Injured Spinal Cord Axons: A Morphometric Analysis

M.G. FEHLINGS, C.H. TATOR and T.H. WONG (Toronto, Ontario)

There is evidence that direct current (DC) stimulation promotes neurological recovery in adult rats with spinal cord injury (SCI). To examine the effect of DC stimulation on axonal counts at the injury site, we conducted a morphometric analysis of axons at the site of SCI in rats treated with a DC field. Adult rats received a 17 g (n = 10) or 53 g (n = 15) clip compression injury of the cord at T1 and were treated with either a sham (O uA) or a functioning (14 uA) stimulator for 8 weeks. Serial 1 uM epon-embedded cross-sections of the cord injury site were stained with toluidine blue. At 1000X magnification, the number, size, distance from the pia, and myelination index of axons in the cord were analyzed on line with a digitizing pad and computer. Five normal control rats were also evaluated.

The number of axons in the normal spinal cord was 458,000±50,000. There was a significant relationship between the severity of SCI and the number of axons at the injury site ($p<0.0001$). After the 17 g injury, there was no significant difference in the number of axons between control (52,000±23,200) and treated (55,100±23,200) rats. However, after the 53 g injury, treated rats (51,700±8,300) had significantly more ($p<0.05$) axons than controls (25,300±8,500). Both the 17 and 53 g injuries caused preferential destruction of large calibre axons. Indeed, the mean axon diameter in normal cord was 1.94±0.07 uM and in injured cord (pooled data from 17 and 53 g lesions) was 1.35±0.10 uM ($p<0.0001$). Post hoc analysis showed that the axon diameter of treated rats with 17 g (1.46±0.01 uM) or 53 g (1.39±0.01 uM) injuries was significantly greater than that of 17 g (1.31±0.02 uM) or 53 g (1.17±0.02 uM) controls.

These data, for the first time, show that the application of a DC field increases the number and calibre of axons at the injury site and enhances the survival or regrowth of axons following SCI in the rat.

140.

Visualization of Epidermal Growth Factor (EGF) and Insulin-Like Growth Factor I (IGF-I) Binding Sites in Rat Forebrain

J.-G. CHABOT, D. ARAUJO, N.P.V. NAIR and R. QUIRION (Verdun, Quebec)

Recent studies have indicated that EGF and IFG-I may act as neurotrophic and/or neuromodulator substances in mammalian brain. Thus, we have used an *in vitro* receptor autoradiographic method to study the comparative distribution of specific binding sites for EGF and IGF-I in rat forebrain during ontogeny and in adulthood. Forebrain sections of fetal (E1), neonatal (P1, P3) and adult (3 month-old) rats are prepared as described previously (Quirion et al, PNAS 78: 5881, 1981) and then incubated for 60 min at 25°C with 200 pM (^{125}I)EGF or 50 pM (^{125}I)IGF-I in their respective buffers. At the end of the incubation, slides are rinsed in respective ice-cold buffer, rapidly dried and juxtaposed against tritium-labeled sensitive film. Non-specific binding for both ligands is defined in the presence of an excess (100 nM) of unlabelled EGF and IGF-I, respectively. Our data indicate that the distribution of EGF and IGF-I binding sites is discrete in rat forebrain and also undergoes modifications during brain development. EGF binding sites are mostly concentrated in cortical areas at E1 and P3, although lower amounts of sites are seen in sub-cortical regions. However, only very low amounts

of sites are found in all these areas in adult forebrain. IGF-I binding sites are more widely distributed during ontogeny and adulthood. The highest amount of sites is concentrated in cortical and hippocampal areas at P1. In contrast to EGF binding, high levels of specific IGF-I binding sites are present in various cortical and sub-cortical regions in adult rat forebrain. These data clearly indicate the differential ontogeny of EGF and IGF-I binding sites in rat forebrain. This could be relevant for the respective role of these two growth factors in the development and maintenance of neuronal function.

141.

Abnormal Responses of Pallidal Neurons to Passive Limb Movement and to Striatal Stimulation in Monkeys Rendered Parkinsonian by MPTP

L. TREMBLAY, M. FILION and P.J. BÉDARD (Quebec, Quebec)

The neurotoxin MPTP(1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is thought to induce parkinsonism in primates mainly by destroying dopaminergic neurons of the substantia nigra. These neurons send fibers at several levels within the basal ganglia. They release dopamine mostly in the striatum but also in the substantia nigra itself, in both segments of the globus pallidus, and in the subthalamic nucleus. We therefore studied the effects of the MPTP-induced dopaminergic deficiency at the output of the basal ganglia. We recorded single unit activities in the medial (internal) segment of the globus pallidus. Our goal was to identify abnormal responses to passive limb movements and to electrical stimulation of the striatum in waking monkeys with MPTP-induced parkinsonism. Cell counts showed that at least 90% of nigral neurons of the compacta-type were degenerated in these animals. In three intact monkeys, few pallidal neurons (16%) responded to joint rotation, and then almost exclusively to only one contralateral joint and in only one direction. In the parkinsonian monkeys, however, more neurons responded (65%), often more vigorously, to the same stimulation. In many of these neurons the responses were elicited by movement about more than one joint, of both upper and lower limbs, of ipsi- and contralateral sides, and in more than one direction. This increase of responsiveness and decrease of selectivity in the parkinsonian monkeys was also the case of pallidal responses to electrical stimulation of the striatum. In the parkinsonian monkeys, more neurons of the medial segment of the globus pallidus responded to electrical stimulation of the ipsi- and contralateral striatum at the same intensity as in intact monkeys. The duration of responses was longer and often consisted of a series of inhibitory-excitatory oscillations. More stimulations sites were effective in the parkinsonian monkeys and, especially, the responses to contralateral striatal stimulation were more frequent. These results suggest that dopaminergic mechanisms regulate gain and selectivity in the basal ganglia. In parkinsonism, the lack of dopamine appears to leave the system strongly responsive to any signals, without selectivity. This response to noise is very likely to affect the motor periphery and to produce muscular rigidity. The high gain in the system is likely to favor oscillations: tremor. And finally, being unable to select the appropriate input signals, the basal ganglia are unable to facilitate the execution of learned motor behaviors, hence akinesia.

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142.

Hormonal Modulation of Striatal D-1 Dopamine Receptors; Relationship with Estradiol Receptor

D. LÉVESQUE, G. PELLETIER and T. DI PAOLO (Quebec, Quebec)

It is well known that striatal D-2 dopamine (DA) receptors are modulated by estrogens. It has been shown that chronic estradiol treatment leads to an increased density of rat striatal D-2 DA receptors. Until now, no mechanism has been established to explain the estrogen action on the forebrain DA systems. Neither cell bodies of the DA fibers nor DA-sensitive neurons in the basal ganglia concentrate [^{3}H]-estradiol intracellularly. This study illustrates new data of striatal D-1 DA receptors modulation by estrogens and its relationship with estradiol receptors. First, we have investigated the striatal DA D-1 receptor with [^{3}H]SCH-23390 binding, a highly selective D-1 antagonist in, intact male, intact female, ovariectomized female, hypophysectomized male and after a chronic estrogen treatment (10 μg of 17ß-estradiol, b.i.d., s.c., for two weeks) of ovariectomized rats. D1-DA receptors were investigated by autoradiography of [^{3}H]SCH-23390 binding and with binding experiments in membrane preparations. Estradiol receptor mRNA was mapped with a novel *in situ* hybridization technique performed on rat brain slices. The chronic estradiol treatment increases D-1 DA receptor density while ovariectomy decreased it. Autoradiographic experiments illustrate that this effect is homogeneously distributed in the striatum contrarily to that observed for D-2 DA receptors. Our results demonstrate, as for D-2 DA receptors, that D-1 DA receptors are modulated by hormones under physiological and pharmacological conditions. However, the regulation of these two DA receptors shows differences. Furthermore, the *in situ* hybridization technique has revealed the presence of estradiol receptor mRNA in the striatum with a lateral-medial receptor gradient similar to DA D-2 receptors. This indicates that estrogen modulation of striatal DA receptors could be related to its action on estrogen receptors.

(Supported by the MRC).

143.

Modulation by Estradiol of D-2 Dopamine Agonist Binding Sites in the Striatum

D. LÉVESQUE and T. DI PAOLO (Quebec, Quebec)

17ß-estradiol (E_2) at a physiological dose acutely increases dopamine (DA) turnover in the rat striatum and nucleus accumbens (Di Paolo et al, Eur J Pharmacol 117: 197, 1985). This increase was observed 30 min after the steroid injection and coincided with the maximal induction of postural deviation of rats with an unilateral lesion of the entopeduncular nucleus. Similarly, a small dose of E_2 at a physiological concentration can increase dyskinesia and homovanillac acid (HVA) cerebral fluid concentrations in monkeys (Bédard et al, 1985; Neurosci Lett 58: 327, 1985). The aim of this study was to investigate the effect of an acute physiological dose of E_2 on striatal DA agonist binding sites of ovariectomized rats in order to elucidate the possible mechanism of the short term effect of E_2. Ovariectomized female rats injected with E_2 (100 ng sc.) showed an increase of the DA metabolites dihydroxyphenylacetic acid (DOPAC) and HVA with no change of DA concentrations in the striatum. This increase was observed as soon as 15 min following the injection while the plasma E_2 reached a peak of 78 pg/ml after 5 min and was significantly elevated until 45 min to ultimately return to control values at 60 min. Plasma prolactin levels remained unchanged after this injection of estradiol. We observed no change of the inhibition constants of high and low affinity D-2 DA agonist binding sites and of the sum of high + low agonist DAergic agonist binding densities as detected by apomorphine competition of [^{3}H]spiperone binding. By contrast, a conversion of high into low agonist affinity binding states was seen at 15 min (38.6% of conversion, $p<0.05$) and 30 min (40.% of conversion, $p<0.01$) after the acute physiological steroid injection. Thus, E_2, is able to rapidly increase DA turnover and modulate striatal agonist affinity states of the D-2 DA receptor. This steroid effect is probably non-genomic, presynaptic and may involve a membrane effect at the DA autoreceptor level.

(Supported by the MRC.)

144.

Concentration-Dependent Effects of Ammonium Ions on Synaptic Transmission in the Rat Hippocampal Slice

P. FAN and J.C. SZERB (Halifax, Nova Scotia)

While the role of hyperammonemia in the etiology of hepatic encephalopathy is generally accepted, the mechanism by which ammonium ions (NH_4^+) interfere with neuronal function is still controversial. The purpose of this study was to establish the effects of different concentrations of NH_4^+ on pre- and post-synaptic events associated with transmission from Schaffer collateral/commissural fibers to CA1 pyramidal neurons in hippocampal slices. The changes in the size of the presynaptic volley, the maximal slope of the field EPSP (fEPSP) and the population spike amplitude (pop. spike) were followed during three 30 min periods before, during and after the application of NH_4Cl. At a threshold concentration of 1.0 mM NH_4^+ reversibly reduced the fEPSP by 50% and pop.spike by 85%, while decreasing the presynaptic volley by only 10%, while in 3 mM NH_4^+ the latter decreased by 25%. By varying the intensity of stimulation, input/output relationships were established between presynaptic volley and fEPSP and between fEPSP and pop.spike NH_4^+ (1.0 mM) significantly decreased the slope of prevolley/fEPSP relationship, without affecting that of fEPSP/pop.spike. At 1.5 mM, NH_4^+ increased the slope of the fEPSP/pop.spike curve and shifted it to the left. Results suggest that NH_4^+ at the lowest effective concentration interferes primarily with excitatory transmission, probably by decreasing the release of the transmitter glutamate. At somewhat higher concentration, it increases the excitability of the postsynaptic neuron, either by reducing the IPSP or by releasing K^+. At even higher concentrations it interferes with axonal conduction or excitability. Since all of these effects can be seen at a rather narrow concentration range of NH_4^+, it is likely that they also can occur *in vivo* in hepatic encephalopathy.

(Supported by the MRC).

145.

Temperature Dependence of Rapid Organelle Transport in Primate Myelinated Axons

J. LAZAREFF and R.S. SMITH (Edmonton, Alberta)

The properties of rapid anterograde and retrograde axonal transport are well described in lower vertebrates, but there is little information on the operation of these transport systems in primates. In the present work we describe the temperature dependence of the velocity of optically detected organelles in myelinated axons of the monkey.

Sciatic nerves were obtained from adult *Macaca fascicularis* at the time of their sacrifice in other non-related experiments. Single myelinated axons were isolated from fascicles of nerve and were mounted in a glass observation chamber. Axons were viewed by differential interference-contrast video microscopy. The television image was enhanced in real time by digital spatial filtering, noise reduction and background substraction to allow the detection of sub-resolution rapidly transported organelles. The temperature of the microscope and specimen was varied over the range 16-41°C. Organelles were classified as small (sub-resolution) or large (dimensions above the resolution limit).

Mean organelle velocities in any of the categories of anterograde or retrograde transport were statistically different in different individual axons. Common features of organelle transport were: small organelles (anterograde and retrograde) showed exponentially increasing velocity with temperature (Q_{10} approx. 2.0) with statistically similar velocities at 37°C (approx. 340mm/24h). Large retrogradely transported organelles also showed an exponentially increasing velocity with temperature with a mean velocity at 37°C of approx. 170mm/24h. Large anterogradely moving organelles showed no statistically significant change in velocity with temperature over the range investigated. The results suggest that the mechanism of transport of large anterogradely moving organelles is substantially different from those causing the anterograde or retrograde transport of other classes of organelles.

146.

Organization of Efferent Projections of the Subthalamic Nucleus in Primates

L.-N. HAZRATI, Y. SMITH and A. PARENT (Quebec City, Quebec)

The lectin *Phaseolus vulgaris* leucoagglutinin (PHA-L) was used as an anterograde tracer to study the patterns of termination of the subthalamofugal fibers in the squirrel monkey (*Saimiri sciureus*). Small microiontophoretic injections of PHA-L in the core of the subthalamic nucleus (STH) led to profuse fiber labeling in the ipsilateral globus pallidus (GP). The coarse and smooth labeled fibers that arose from the injection site traversed the internal capsule via the subthalamic fasciculus and invaded both the internal (GPi) and external (GPe) pallidal segments where they formed up to 4 distinct bands lying parallel to the medullary laminae. These bands were most commonly found on each side of the internal medullary lamina and along the inner surface of the external medullary lamina. They were composed of a multitude of short and varicosed axon collaterals branching at right angle of the main fiber and arborizing along the major axis of the long dendrites of pallidal neurons. Other labelled axons were visualized in smaller number in the putamen and caudate nucleus. In contrast to the fibers in GP, however, the axons continuing their route into the striatum were extremely long, linear and branched only infrequently. A small contingent of fibers also descended along the dorsal surface of the cerebral peduncle to arborize principally in the pars reticulata of the substantia nigra. These fibers formed small, diffused plexuses at the basis of the substantia nigra, but some fibers also ascended along the typical cell columns of the pars compacta that impinged deeply within the pars reticulata. In cases in which only the medical tip of STH was injected, the labeled fibers were mostly confined to the rostral pole of GP and the ventral pallidal area. At these levels the labeled fibers formed diffused plexuses rather than well-defined bands. Hence, the pattern of fiber labeling in GP varied markedly according to the location and extend of STH injection sites. The fact that PHA-L injections in the striatum also produced complex band-like fiber labeling in GP indicates that the terminal aborizations of the subthalamopallidal and striatopallidal fibers in GP are organized according to a highly specific and complementary pattern in primates.

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147.

Magnetic Resonance Micro-Imaging of Experimental Spinal Cord Injury in the Rat

E. DUNCAN, C. LEMAIRE, R. STRUCK, R. ARMSTRONG, C. TATOR and D. LINDEN (Toronto, Ontario)

The technique of magnetic resonance imaging (MRI) is unaffected by the bony vertebral column and, therefore, has become the modality of choice for diagnostic imaging of the spinal cord. However, the technique is relatively insensitive and this may limit the resolution of small structures.

This laboratory uses a well established model of experimental spinal cord injury in the rat. An extradural compression injury is made at the C8/T1 cord level using a modified aneurysm clip. However, the small diameter of the rat spinal cord and the limited length of cord examined limits the volume of tissue from which an MR signal may be acquired.

To allow the MRI characterization of this model we have developed a MR micro-imaging technique which produces high resolution images of rat spinal cord.

The images were obtained using a General Electric CSI magnetic resonance spectroscopy/imaging unit with a 2 Tesla superconducting magnet. Images were acquired using a partial saturation spin echo sequence (TE = 60 ms, TR = 500 ms), 4 accumulations per image, using a surface coil. Formalin fixed tissue blocks containing the cervical and upper thoracic spinal cord were imaged. A field of view of 3.0 x 3.3 cm was obtained. The image was 512 x 512 pixels with a resulting resolution of approximately 60 microm per pixel edge.

In the normal cord there was excellent resolution of the grey/white junction and fine detail, such as the subarachnoid space and nerve root, was visualized. In the injured cord there was loss of the grey/white junction and details of the injury site, such as haematoma, were identified. Thus, MR micro-imaging may be used to study experimental spinal cord injury in a small animal model.

148.

5α-dihydrotestosterone Acutely Affects Rat Striatum Biogenic Amines Metabolism

M. MORISSETTE and T. DI PAOLO (Quebec, Quebec)

Recently, we have shown that a physiological dose of progesterone or 17ß-estradiol acutely increases biogenic amine metabolism in rat striatum. The effect of 5α-dihydrotestosterone (5α-DHT) is much less documented. We thus investigated the effect of an acute dose of 5α-DHT on dopamine (DA) and serotonin (5-HT) metabolism in the striatum of ovariectomized female rats (OVX). Biogenic amines and their metabolites were measured by HPLC with electrochemical detection. OVX rats injected with 5α-DHT (150 μg, s.c.) showed a decrease in striatal DA levels after 30 min (−14% at 45 min, $p<0.01$) with a return to control values 240 min after the steroid injection. The DA metabolite dihydroxyphenylacetic acid (DOPAC) concentrations increase 45 min after the steroid injection (+16%, $p<0.05$) followed by a return to control values at 90 min and a decrease at 180 min while the other DA metabolite homovanillic acid (HVA) concentrations show an increase at 45, 60 and 120 min (+28%, $p<0.01$) after the 5α-DHT injection. DOPAC/DA and HVA/DA ratios are increased at 45 min (DOPAC/DA: +37%, $p<0.01$; HVA/DA: +59%, $p<0.01$) followed by a return to control values at 120 min (150 min for HVA/DA). Striatum 5-HT levels show a decrease at 120 and 240 min after the 5α-DHT injection. The 5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA) concentration is decreased at 15 min and remains low up to 240 min. The 5-HIAA/5-HT ratio remains unchanged up to 240 min where it is increased (+24%, $p<0.05$). Plasma 5α-DHT concentrations are significantly elevated at 30 min and increase gradually to reach a peak 120 min after injection. Thus, 5α-DHT can acutely modulate biogenic amine activity in the rat striatum.

(Supported by MRC).

149.

Blood-Brain Barrier Breakdown Induced by Ethanol and Sodium Pentobarbital

C.R. FARRELL and P.A. STEWART (Toronto, Ontario)

We examined the effects of acute ethanol and sodium pentobarbital on the permeability of the blood-brain barrier (BBB) to circulating protein. The enzyme horseradish peroxidase is unable to cross the normal BBB but leaks into the brain when the barrier is damaged. Using this tracer we assessed the barrier in three ways. Total peroxidase activity was measured spectrophotometrically in cortical extracts to provide a quantitative estimate of barrier damage. Sites of vascular leakage were visualized and quantitated by reacting slices of brain to produce a coloured reaction product. Leakage sites were further examined in the electron microscope to determine the ultrastructural changes in capillary walls that underlie barrier loss. Anesthetic doses of sodium pentobarbital had no effect on the BBB, but at high doses a small increase in cortical horseradish peroxidase activity was observed. In the presence of ethanol sub-anesthetic doses of sodium pentobarbital did not affect barrier permeability. However, pentobarbital anesthesia plus ethanol compromised the integrity of the BBB at focal sites within the microvasculature. High doses of ethanol alone caused barrier breakdown of a similar magnitude. Within leaking segments a proportion of endothelial cells had lysed cell membranes allowing tracer to infiltrate endothelial cells and penetrate the basal lamina. This was accompanied by edema of adjacent astrocytic end-feet. These results indicate that high doses of ethanol break down the BBB at focal sites and that when the additional stress of pentobarbital anesthesia is present, much less ethanol is required to achieve barrier breakdown of the same magnitude. The acute effects of ethanol on the BBB in the presence of other possible stress factors should be further investigated.

150.

Quantification of the Noradrenaline (NA) Innervation in the Hippocampus of Adult Rat

S. OLESKEVICH and L. DESCARRIES (Montreal, Quebec)

The hippocampal formation receives a relatively dense noradrenaline (NA) innervation in adult rat. To quantify this innervation, we used a radioautographic technique which makes it possible to identify and count these axon terminals (varicosities) in rat cerebral hemisphere slices incubated with [^{3}H]NA (1 μM) in presence of an inhibitor of monoamine oxidase. The slices were then fixed with glutaraldehyde, postfixed with osmic acid vapours, embedded in Epon and radioautographed as 4 μm-thick sections. The labeled varicosites were visualized as small silver grain aggregates, and counted using a computer-assisted image analyzer. Three horizontal levels, equidistant along the ventro-dorsal axis, were studied. Rectangular counting windows, aligned in rows, were positioned in such a way as to sample the different layers in every anatomical subdivision of the hippocampus. The initial counts per surface unit of section (mm^2) are to be transformed by two experimentally determined factors to correct for incomplete detection at the chosen radioautographic exposure time and from the examined tissue thickness. Subsequent application of a sterological formula taking into account the average diameter of hippocampal NA varicosities (measured in electron microscope radioautographs), will yield final values of regional and laminar innervation density expressed in number of varicosities par mm^3 of tissue.

(Supported by MRC and FRSQ).

151.

Immunocytochemical Mapping of Nuclear T3 Receptors Using a Monoclonal Antibody in the Developing and Adult Rat Brain

L. MIN and J.H. DUSSAULT (Ste. Foy, Quebec)

By using a monoclonal antibody raised against rat nuclear T3 receptors (NTR), the immunocytochemical localization of NTR has been achieved in the developing and adult rat brain. In 16-day-old embryo, only weakly NTR-immunostaining neurons were detected in the globus pallidus (GP), amygdala (AA) and hypothalamus areas. In the 18-day-old embryo, the NTR-immunostaining neurons were increased in both density and intensity. The NTR-staining neurons were mainly distributed in the striatum, GP, AA, thalamus (TH) and hypothalamus areas.

Thereafter, the number of NTR staining neurons was progressively increased in cerebral cortex and in the regions previously described. After birth, the highest density of NTR-staining cells was found in the 6-day-old rat. The high density of the medium to strongly NTR-staining neurons was seen in cerebral cortex (lamina II and III, particularly in cingulate and interhemispheris cortex), nucleus habenula medialis (Hbm), amygdal area and some nuclei of the hypothalamus (nucleus (N) paraventricularis, N. dorsomedialis, N. ventromedialis, N. supraopticus and N. preopticus). Moderate density was found in the hippocampus dentate gyrus, most parts of the thalamus, some parts of cerebral cortex (piriform and suprarhinal cortex) while only a few of the weakly to median staining cells were observed in the cerebellum (only in the Purkinje's cells) and the brain stem. In 14-day-old the density and intensity of NTR-immunoreactivity were slightly decreased except in the hippocampus and cerebellar cortex. In the adult brain, the distribution was similar to that in the 14-day-old, but the number of NTR-staining cells in the cerebrellar cortex (particular in granular layer) was evidently increased. These studies provide a map of the NTR in the developing, adult brain and indicated that the NTR is selectively concentrated in certain regions in both developing and adult brain.

152.

Influence des facteurs neuronotrophiques sur la différenciation des neurones cholinergiques centraux de rat en culture cellulaire

R. GARZA, J. PUYMIRAT et J.H. DUSSAULT (Ste-Foy, Québec)

Le déficit cholinergique central est une donnée actuellement bien établie dans la maladie d'Alzheimer (A.D.). Cependant le(s) mécanisme(s) de cette dégénérescence demeure actuellement inconnu. Parmi les diverses hypothèses, l'une d'entre elles ferait jouer un rôle à certains facteurs neuronotrophiques sur la differenciation des neurones cholinergiques centraux de rat dans un système de culture cellulaire. Ainsi nous avons pu montrer le rôle de la triiodothyronine sur la différenciation morphologique (taille des corps cellulaires, élongation neuritique/et biochimique (activités de la ChAT de l'AChE) des neurones cholinergiques centraux. Par contre d'autres facteurs neuronotrophiques sont sans effet: c'est le cas du fibroblaste Growth Factor (FGF), de la laminine. Enfin, l'étude de milieux conditionnés par des astrocytes centraux montre la sécrétion par les astrocytes de facteur(s) responsable(s) d'une élongation des neurites des neurones cholinergiques.

Cette étude montre le rôle de la LT3 et des atrocytes sur la maturation des neurones cholinergiques centraux et ouvre la voie à l'étude du rôle de ces facteurs sur les neurones cholinergiques dans le cerveau adulte.

153.

The Contribution of the Basolateral Amygdala and the Pyriform Cortex to Neophobic Behavior in Rats

N. BEAULIEU, A. SKYDEL, M. PETRIDES (Montreal, Quebec)

The present studies investigated the effects of bilateral lesions restricted to the pyriform cortex (PC) or to the basolateral amygdala (BLA) on reactivity to a novel gustatory stimulus and a novel object. In testing the neophobic response to a gustatory stimulus, the animals were maintained on a water-deprivation schedule with 20 min. free access to water for 3 consecutive days. On day 4, they were exposed for the first time to a .01% quinine solution for 20 min. On days 5 and 6, they were again allowed 20 min. access to water and, on day 7, they were re-exposed to the quinine solution. Normal animals increased significantly their consumption on the second exposure to the quinine solution, suggesting a neophobic response on first exposure to the solution. The intake of the two operated groups was the same on both exposures, indicating a lack of neophobia. To examine the neophobic response to a novel object, the animals were initially allowed to explore an open field for 10 min. Following a 2 min. interval, they were exposed to the open field for another 10 min. but now with an object present in one of the corners of the field (corner A). After a 2 min. interval, the animal was re-exposed to the field and the object for another 10 min. The two groups of operated animals spent more time in corner A during the first 10 min. session with the object than did normal animals, indicating a lack of neophobia to the object on first exposure to it.

The results of these experiments indicate that both the PC and the BLA play a major role in an animal's reactivity to a novel stimulus, although the contribution of these two neural structures may not be of the same nature.

154.

The Organization and Development of the Noradrenergic Projections to the Rat Cerebellar Cortex Studied by Tyrosine Hydroxylase Immunocytochemistry

G. BROCHU and R. HAWKES (Quebec, Quebec City)

The mammalian cerebellar cortex has an elaborate topographical organization that can be demonstrated by electrophysiological and biochemical methods. Immunological techniques have also proved effective to investigate the global organization of cerebellar cortex. For example, monoclonal antibody mabQ113 recognizes a subset of Purkinje cells distributed in parasagittal bands. It has been shown that the mossy and climbing fiber afferents are organized in bands with the same structural boundaries as the mabQ113 antigenic compartments. The third class of cerebellar afferents are the noradrenergic projections, arising primarily from the locus coeruleus. These can be revealed by using tyrosine hydroxylase (TH) immunocytochemistry. We have used a commercial antibody against TH and mabQ113 to explore whether the noradrenergic projections from the locus coeruleus to the cerebellar cortex correspond to the antigenic Q113 compartments. Immunoreactive profiles are seen in all laminae of the adult rat cerebellar cortex. No evidence of compartmentation was found: an homogenous distribution of stained profiles was observed in both frontal and sagittal planes. Developmental studies were carried out to study the distribution and form of noradrenergic growth cones as a function of cerebellar lamination. Stained axons and growth cones were seen from birth in the white matter and the developing granular and molecular layers, but never in the external granular layer. Growth cone morphology varies as a function of age and laminar distribution and may reflect specific responses to cues in the target fields.

155.

Metabolic Compartmentation of the Cerebellar Cortex Revealed by the Enzyme Cytochrome Oxidase

N. LECLERC, L. DORÉ, L. TREMBLAY and R. HAWKES (Quebec, Quebec City)

The mammalian cerebellar cortex is subdivided in functional modules revealed by electrophysiological, histochemical and immunocytochemical techniques. These different chemoarchitectonic compartments respect the same structural boundaries. For example, in the adult rat cerebellar cortex, it has been demonstrated that the modular distribution of the enzymes 5'-nucleotidase and acetylcholinesterase corresponds precisely to the immunocytochemical Purkinje cell compartments recognized by a monclonal antibody mabQ113. Micromapping methods have demonstrated that the cutaneous projections to the rat cerebellar cortex are represented by a fractured mosaic reminiscent of the chemoarchitectonic zonation. To explore the functional correlates of

chemical zonation, we have used the enzyme cytochrome oxidase (CO), reported to be a reliable marker for the functional activity of the neurons in the visual cortex. Surprisingly, in the adult rat cerebellar cortex staining for CO reveals a compartmental organization of the neuronal metabolic activity: the high CO-activity bands coincide with the mabQ113-compartments and the weak CO-bands with mabQ113+ compartments. This suggests that the mabQ113-Purkinje cells are more active than the mabQ113+. Two strategies have been employed to investigate the role of the afferent inputs that terminate in the respective histochemical compartments: in one neuronal activity was suppressed by deafferentation of the forelimb and the vibrissae, a strong somatosensory cerebellar input, and in the other the neurons were activated by daily cutaneous electrical stimulation of the forelimb. No modification of the neuronal CO was detectable. Furthermore, developmental studies strongly suggest that the different CO levels are stable. Within the first few post-natal days preceding synaptogenesis, we can already distinguish two subsets of Purkinje cells, one showing high CO activity and another showing low activity. Thus, it appears that although CO activity varies between compartments, the levels are determined intrinsically rather than induced as a response to neuronal patterns of use.

156.

Differential Regulation by Dexamethasone of Glucocorticoid Receptor Gene Expression in Primary Cultures of Neurons Derived from Foetal Rat Cerebral Cortex and Hypothalamus

M.-C. PEPIN and N. BARDEN (Quebec, Quebec)

The glucocorticorticoid receptor (GR) is an essential protein which mediates the action of glucocorticod hormones. Since the intracellular concentration of GR may be important for the modulation of glucocorticoid action, we have investigated the regulation, by dexamethasone, of GR gene expression in primary cultures of rat cerebral cortex and hypothalamus.

Female Sprague-Dawley rats were mated and foetuses were removed between days 16 and 18 of gestation and placed in sterile phosphate-buffered saline supplemented with D-glucose. The hypothalamus and cerebral cortex was excised under a dissecting microscope and mechanically dissociated. Cells were cultured in a serum-free and antibiotic-free chemically defined medium (DMEM: F12, 50:50) supplemented with glutamine, insulin, selenium, transferrin, putrescine and progesterone. After 15 days in culture, the cells were washed and the incubated for various times in the same medium containing dexamethasone (10^{-7} M). Cells were scraped off the wells, their RNA content isolated and deposited on nylon filters. The filters were hybridized with a ^{32}P-labelled RNA probe complementary to a 2.2 Kb fragment of the glucocorticoid receptor mRNA. Actin mRNA concentration, determined by hybridization of a replicate dot blot with a ^{32}P-labelled actin cRNA probe, was used as internal standard. In cells derived from cerebral cortex, dexamethasone caused a rapid, but transient, increase in GR mRNA concentrations. This initial increase was followed, at times greater than 24 h, by a more sustained increase which was maintained for up to at least 72 h of incubation. The GR mRNA content of hypothalamic cells did not show this biphasic stimulation and, in fact, appeared to be decreased by dexamethasone. These results show that the regulation of GR mRNA concentrations by dexamethasone is not the same in hypothalamic and cerebral cortex cells. This fact that could be related to the role of hypothalamic, but not cortical, neurons in the negative feedback regulation of the hypothalamic-pituitary-adrenal axis by glucocorticoids.

157.

Possible Abuse Potential of Glutamate Receptor Antagonists

D. CORBETT (St. John's, Newfoundland)

Extracellular levels of glutamate increase during pathological conditions such as cerebral ischemia and epilepsy. High levels of glutamate have neurotoxic effects on brain cells especially in limbic structures (e.g. hippocampus). The N-methyl-D-aspartate antagonist, MK-801 has been found to protect the brain against damage in animal models of cerebral ischemia. However, MK-801 has a similar chemical structure to ketamine and phencyclidine, drugs which are abused by humans. In order to examine the abuse potential of MK-801 I looked to see if this drug would facilitate responding for rewarding electrical brain stimulation (self-stimulation). Self-stimulation is facilitated by all drugs of abuse (e.g. cocaine, amphetamine, heroin, etc.) and thus can serve as a useful tool for screening compounds which may be abused.

Rats with electrodes aimed at the medial forebrain bundle were trained to press a lever to self-administer electrical brain stimulation consisting of .1 msec, cathodal pulses delivered in .5 sec trains at frequencies ranging from 16-100 Hz. Current intensities were adjusted to provide sustained responding and then were held constant. Once the self-stimulation behavior had stabilized, separate groups of rats were injected with one of several doses of ketamine (20 and 40 mg/kg) or MK-801 (.01, .1 and 1.0 mg/kg). Both drugs facilitated self-stimulation although ketamine initially produced considerable sedation. The pattern of facilitation observed with MK-801 was similar to that observed with amphetamine.

These results suggest that MK-801 and other excitatory amino acid antagonists may have abuse potential in humans, especially if they are used chronically to protect against ischemic damage or in the treatment of epilepsy.

158.

Effect of Cholinomimetic Drugs on the Behavior of Cortically Devascularized Rats in a Passive Avoidance Paradigm

L. GAROFALO, P.J. ELLIOTT and A.C. CUELLO (Montreal, Quebec)

In neurodegenerative disorders such as Alzheimer's disease, memory impairments are generally associated with cholinergic deficits involving the basal forebrain-cortical pathway. We have shown that, in mature rats, unilateral devascularizing lesions of the cortex result in biochemical (decreased ChAT activity) and morphological (cell shrinkage or loss) retrograde degenerative changes in the nucleus basalis magnocellularis (NBM) 30 days following lesioning. In addition, these animals showed a decreased performance in memory testing paradigms such as the Morris water maze and passive avoidance. We were interested in examining whether cholinomimetic drugs could improve the memory deficits observed in our model of retrograde neuronal degeneration. Eighty mature (325-350 gr) male Wistar rats were used in this study. Half were sham operated while the other half were cortically lesioned unilaterally by disrupting the pia-arachnoid vasculature. Thirty days following surgery the animals were tested in a passive avoidance paradigm. Immediately following the acquisition of a one-trial passive avoidance task the sham operated and lesioned rats were injected intraperitoneally with either: saline (1 ml/kg), an antichlinesterase, physostigmine (0.03 mg/kg) or various cholinergic agonists: arecoline (1 mg/kg), pilocarpine (4 mg/kg) or oxotremorine (0.1 mg/kg), [n = 8 for all groups]. All animals were retested 5 days following drug treatment. No significant differences were observed in the latency to enter the dark side of the passive avoidance box between the sham vehicle treated and sham drug treated rats. However, we have found that all of the cholinergic drugs enhanced the 5 day retention of passive avoidance of cortically lesioned rats when compared to their vehicle treated counterparts. This study lends further support for a cholinergic role in memory.

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159.

Récupération de la Fonction Motrice Après Lésion des Noyaux Profonds du Cervelet Chez le Singe

K. AMRANI, M.T. PARENT et Y. LAMARRE (Montréal, Quebec)

Le rôle des noyaux profonds du cervelet dans la planification, l'initiation et le contrôle du mouvement volontaire est mis en évidence par plusieurs travaux. En effet, la lésion des noyaux dentelé et interposé occasionne un dysfonctionnement sévère de l'acte moteur. Un tel déficit n'est cependant pas définitif, un phénomène de récupération, rapide et progressif, intervient pour restaurer la fonction motrice. Quels sont les mécanismes de cette récupération? Nous proposons l'hypothèse que le côté opposé du cervelet serait en partie responsable de la récupération. Le présent travail limite son étude au «pointage» qui mobilise principalement la musculature proximale. Une telle limite méthodologique permet une évaluation plus claire de la chute de performance et de la récupération de ce comportement de base.

Un signe, macaca, est entrainé à ramasser un morceau de nourriture sur un disque rotatif qui tourne à 4 vitesses différentes. Plusieurs niveaux cibles sont disposés sur le disque pour favoriser une évaluation plus évidente du «pointage» et de son ajustement sur la cible d'une rotation à une autre. Les deux membres supérieurs sont testés alternativement à partir d'une performance stable de 80% (environ 150 essais) pour la vitesse 0.8 rotations par seconde. La préparation chronique de l'animal permet de procéder aux enregistrements électrophysiologiques et à l'électrocoagulation des noyaux sans anesthésie afin de perturber au minimum les performances motrices. Les noyaux Dentelés et Interposés sont été repérés par enregistrement électrophysiologique et par radiographie pour procéder aux lésions électrolytiques. *Une première lésion* des noyaux Dentelé et Interposé droits a permi d'observer une chute de performance droite à 30% et une récupération à 85% sur 8 jours; aucun déficit du membre gauche. *Une deuxième lésion* des mêmes noyaux à gauche met en évidence une double chute: à gauche à 35% et de nouveau à droite à 55%. Un récupération bilatérale près que à 100% a été observée au bout de 3 semaines. Le contrôle histologique a montré que la destruction des noyaux par les microlésions n'est pas totale, elle avoisinerait 60%. La récupération globale qui s'est effectuée et qui avoisine 100% pourrait s'expliquer par la présence des parties intactes des noyaux. Les résultats obtenus montrent qu'une lésion du coté gauche du cervelet a provoqué une chute de performance du membre supérieur droit, c'est-à-dire au membre contralatéral. Ce résultat va dans le sens de notre hypothèse en établissant qu'une relation fonctionnelle existe entre les deux hemisphères du cervelet. Une telle relation favoriserait, au moins en partie, le mécanisme de récuperation par des voies contralatérales.

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160.

Mathematical Modelling of the Contribution of Arterial Diameter Pulse to the Configuration of the Intracranial Pulse Wave

P. KLASSEN, E. SCHWEDYK and E.R. CARDOSO (Winnipeg, Manitoba)

Previous studies have traditionally taken the systemic arterial pulse wave as the input signal responsible for the generation of the intracranial pulse wave (ICPW). The ICPW however, depends not only on the input pressure wave but also on the filtering effect of the arterial wall characteristics and the properties of the intra-cranial compartment. A mathematical model has been derived which takes this into account.

The model considers a single artery enclosed within a fluid-filled elastic container that simulates the intracranial compartment. Model parameters are obtained from the pressure-volume characteristics of the vessel and container. The input signal, intraluminal arterial pulse pressure (ΔPi) is related to the output pulse pressure (ΔPo) by

$$\Delta Po = A\,(MPi - MPo + 1)^{K-1}\,\Delta Pi$$

where Po also depends on the mean outer container pressure (MPo), and the mean intraluminal arterial pressure (MPi).

Experimental validation of the theoretical model was carried out on *in vivo* segments of abdominal aorta of 6 adult cats, enclosed in a biological container. MPi and ΔPi were measured from an aortic catheter. MPo and ΔPo were obtained from a catheter introduced into the outer container. Alterations of MPi were produced by sustained Valsalva maneuvers, while ΔPi changes were induced by application of a clamp to the proximal portion of the aorta.

The experimental findings confirmed the values predicted by the mathematical model. The results can be extra-polated to the cerebral circulation, providing a better understanding of the arterial contribution to the configuration of the ICPW.

161.

Comparison Between Water Content of Fresh and Preserved Cerebral Tissue

A.M. KAUFMANN and E.R. CARDOSO (Winnipeg, Manitoba)

We investigated the effects of formaldehyde fixation and deep freezing upon cerebral water content, in order to devise a method to preserve brain samples without altering their water content. This would overcome errors related to tissue water evaporation during transportation of human cerebral samples.

Specific gravity and water content were determined by the gravimetric technique. Cerebral samples from anesthetized adult mice were either immediately immersed in the gravimetric column, or first preserved by one of two methods:

(i) fixation in 2.5 to 40% formaldehyde,
(ii) rapid freezing in liquid Nitrogen followed by deep-freeze storage at −80°C.

The specific gravity and water content of fresh and preserved cerebral samples were compared statistically.

The mean water content of fresh cerebral tissue was 73.71 ± 0.13 ($n = 65$). There was a linear correlation ($r = 0.997$) between the specific gravity of fixed samples ($n = 35$) and the concentration of formaldehyde solution, indicating that cerebral water content of fixed samples is dependent upon the concentration of the storage solution. Conversely, there was no significant difference between the water content of fresh samples and those frozen for up to 90 days ($n = 122$).

The effect of freezing upon edematous cerebral tissue was also studied. Water content of 48 cerebral samples from water intoxicated mice was either measured immediately or after freezing in liquid Nitrogen. Results from frozen and fresh samples from the same animal were compared and no significant difference was found.

Our findings indicate that storage of cerebral samples in liquid Nitrogen, with or without subsequent deep-freezing, preserves water content of normal and edematous cerebral tissue, thereby allowing accurate measurements at a later time.

162.

Parkinsonism and Pyridine Compounds

M.N. HASSAN, J. THAKAR and J.D. GRIMES (Ottawa, Ontario)

In recent years, attention has been focused on environmental factors in relation to the etiology of Parkinson's Disease. Since methyl-phenyl-tetrahydro-pyridine (MPTP) and its metabolite methyl-phenyl-pyridinium ion (MPP^+) produce parkinsonism in man and several animal species, other pyridine compounds are being evaluated for possible parkinsonian-inducing properties.

We have compared the behavioral and biochemical effects of MPTP, MPP^+, 4-phenylpyridine (4-PP) and 2-phenylpyridine (2-PP). Groups (n = 7) of C57 black mice were injected daily (IP, 30 mg/kg) with these compounds for 6 consecutive days. After drug administration, locomotor behavior was monitored for 2 hours in electronic meters. On day 7, the mice were sacrificed, the striata dissected and frozen for subsequent catecholamine determination. In other experiments, the effects of these compounds on energy production in isolated mitochondria from rat striatum and liver were evaluated.

After 2 days, mice treated with MPTP exhibited a progressive decrease in locomotor activity, and became virtually immobile by day 5. In contrast, animals treated with 2-PP and 4-PP showed decreases in locomotor activity of about 25% and 60%, respectively. Animals receiving 4-PP demonstrated marked immobility for up to 1 hour following each injection, but regained normal mobility after 6 to 8 hours. The *in vitro* studies demonstrated that MPTP (1 mM) has no significant effect on mitochondrial oxygen consumption. In contrast, MPP^+, 2-PP and 4-PP markedly inhibited the oxidation of the energy-producing substrates pyruvate/malate. The differences in the pharmacological profiles of these compounds, and their relevance to a parkinsonian model, will be presented.

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163.

Utilisation de biomatériaux comme implants intracérébraux

S. WOERLY, C. LAVALLÉE, R. GUIDOIN et R. MARCHAND (Québec, Québec)

Nous avons par le passé transplanté des cellules nerveuses embryonnaires dopaminergiques couplées à des matrices extracellulaires artificielles (MEC) constituées de gels très hydratés de collagène (hydrogels) autoformés *in situ* (Vitrogen, Coll. Corp., C.A.) dans des lésions cavitaires du striatum de rats dans le but (1) de remplacer la perte de microvolumes de tissu cérébral et (2) d'introduire au sein du site d'implantation une architecture extracellulaire tridimensionnelle. Nous avons montré que ces MEC assuraient la stabilisation de la greffe cellulaire, procuraient des surfaces de croissance pour les fibres nerveuses et neurogliales, se vascularisaient et s'intégraient progressivement au tissu hôte. Cependant les matrices de collagène étaient partiellement biodegradées *in situ* à plus ou moins long terme. Donc, afin d'implanter des MEC stables et permanentes pouvant assurer une architecture de soutien à la croissance de fibres nerveuses, nous avons préparé des hydrogels synthétiques de polyméthacrylate de glycol (PGMA), microporeux (40-60% d'eau) et macroporeux (60-80% d'eau) qui ont été complexés au collagène. Après 2 mois d'implantation dans le cortex cérébral du rat, les résultats histologiques démontraient la biocompatibilité des hydrogels ainsi que leur biostabilité. Parmi ceux-ci, les hydrogels contenant 70-80% d'eau étaient envahis par des cellules d'origine hétérogène et des fibres gliales. Dans certains cas, une capsule fibrinocollagèneuse s'était développée à l'interface tissu hôte/bioimplant. La microscopie électronique à balayage a permis de mettre en corrélation de façon qualitative le degré de porosité et la configuration interne des hydrogels avec l'importance et l'orientation de la cellularisation des implants. Ces biomatériaux ont montré leur non cytotoxicité après incorporation *in vitro* de neuroblastes dans la structure d'hydrogels macroporeux. Ces tests préliminaires pourraient être la base d'une nouvelle stratégie des greffes nerveuses comprenant (1) une étape *in vitro*: immobilisation de cellules nerveuses embryonnaires dans un réseau polymérisé de PGMA, et induction de leur différenciation conduisant à l'établissement de circuits nerveux dans le trois plans de l'espace. (2) une étape *in vivo*: introduction des *micro-unités d'implantation* dans un volume cible du parenchyme nerveux.

(Supporté par le FRSQ et le CRM).

164.

Présence d'une organisation fondamentale précoce dans le tronc cérébral en développement

M.-C. BÉLANGER, L. BERTRAND, S. WOERLY et R. MARCHAND (Québec, Québec)

Des études passées menées sur divers aspects du développement et sur l'organisation des structures neuronales adultes du tronc cérébral avaient mis en évidence l'existence d'un arrangement longitudinal des éléments neuronaux, tel que les colonnes somato-motrices, viscéro-motrices . . . et de faisceaux associés. Dans la présente étude, nous avons voulu explorer en détail la génèse de cette organisation fondamentale. Notre protocole répondait aux objectifs suivants: (1) vérifier l'existence précoce d'une organisation en colonne dans le tronc, (2) décrire les transformations histogénétiques qui conduisent à la morphologie adulte, (3) identifier les dérivés de chaque colonne et (4) vérifier s'il existe une relation entre les colonnes cellulaires et les faisceaux d'axones longitudinaux du tronc. Des rates ont été injectées de thymidine tritée au 11^e jour de la gestation, leurs embryons prélevés 2 heures après l'injection puis à toutes les 24 heures et préparés pour l'histologie et l'autoradiographie. Un atlas morphogénétique des groupes cellulaires *générés précocement, constitué à partir d'illustrations graphiques obtenues* à la caméra lucida a servi de base à notre étude.

Nous avons pu confirmer la présence de colonnes longitudinales complexes impliquant, non seulement des colonnes somato-motrices et viscéro-motrices, mais aussi d'autres groupes cellulaires compris entre le mésencéphale et la moelle épinière. En outre, nous avons noté que plusieurs des groupes cellulaires appartenant à une même colonne étaient chez l'adulte en interrelation axonale. Nous entrevoyons ici un mécanisme de mise en place des structures du tronc qui favoriserait l'élaboration d'un plan précis de communication axonale. En effet, la prolifération d'un secteur de la zone germinale du tube neural est à l'origine de colonnes cellulaires qui représenteraient des voies préstructurées pour la migration ultérieure des grands faisceaux. L'absence ou un défaut dans l'organisation ou l'ordre d'apparition des structures longitudinales du tronc pourraient conduire à des hétérotopies neuronales intraaxiales, elles-mêmes responsables de certaines anomalies morphologiques associées à des syndromes neurologiques congénitaux tel que aplasies ou désorganisationde noyaux du tronc ou encore variations du trajet des faisceaux longitudinaux.

«Recherche subventionnée par le CRM et le FRSQ.»

165.

MHC-Class II Expression by Human Adult Astrocytes in Tissue Culture

Y. GRENIER, T. RUYS, Y. ROBITAILLE, A. OLIVIER and J. ANTEL (Montreal, Quebec)

Human adult astrocytes surrounding inflammatory and neoplastic lesions are reported to express MHC-class II antigens to a larger extent than astrocytes in «normal» tissue, suggesting that MHC-class II antigen expression is linked to the extent of astrocytic cell reactivity. In this study we have attempted to correlate MHC-class <II antigen expression with the morphologic features of human adult astrocytes maintained in tissue culture (DMEM plus 10% fetal calf serum). The astrocytes were derived from surgically resected tissue (epilepsy surgery). Cultures were analyzed by double immunostaining with acute glial fibrillary acidic (GFAP) and anti MHC class II (SJ465) antibodies. Astrocytes (GFAP + cells) were morphologically categorized as fibrillary, protoplasmic, gemistocytic, or undifferentiated based on criteria which included cell size, nuclear atypy, and extent of cell process extension. We found that about 20% of astrocytes expressed class II antigen, with no correlation being observed with morphologic subtype. Addition of γinterferon (10-1000 units per ml) produced only small variation in the

proportion of class II + astrocytes while markedly enhancing class II antigen expression by non-glial cells (endothelial, microglia-macrophage) contained in the cultures. Whether the culture conditions used (presence of fetal calf serum) or individual donor differences influence the degree of MHC-class II antigen expression by astrocytes in culture is currently being tested.

Neuro-oncology (Platform)

FRIDAY, JUNE 17TH, 1988 — P.M.

166.

Magnetic Resonance Image Guided Stereotaxis

E.J. DOLAN, J. GORECKI, R.R. TASKER and W. KUCHARCZYK (Toronto, Ontario)

Magnetic resonance imaging (MRI) is a new technique whose efficacy for stereotaxis has not yet been proven.

In a series of biopsies we have correlated the CT and MRI target coordinates utilizing an MRI compatible Leksell frame and a GE Signa 1.5 magnetic resonance scanner.

Correlating the MRI and CT images with monitoring and the histopathology of the serial biopsies taken along the biopsy trajectory allows correlation between the imaging characteristics and electrical characteristics of the tissue.

The MRI and CT coordinates were identical within the limits of the Leksell frame. The advantage of MRI is the ease with which a trajectory for biopsy can be obtained to avoid important structures. Post-biopsy MRI clearly shows the biopsy tract, and sites of biopsy. The main disadvantage is the 45 minute scan time for the MRI compared with 15 minutes for the CT.

Impedance measurements showed white matter (500-600 ohms) to have values less than gray matter (600-700 ohms). Basal ganglia and thalamus were lower at 450-550 ohms with cerebral spinal fluid at 300-400 ohms. Impedance values rose at the edge of T2 (MRI) lesions related to gliosis or tumour cell infiltration. Decreased signal areas on T1-MRI or CT always showed a fall in impedance. The enhancing rim on CT showed either a fall or rise. Impedance changes were more pronounced in more malignant tumours.

MRI targeting is highly accurate, and enables preselection of biopsy trajectories, and excellent post-operative visualization of biopsy trajectory. Impedance monitoring is a valuable abjunct, and some preliminary correlations with tumour characteristics can be made.

167.

Nuclear Magnetic Resonance Studies of Human Cerebral Tumors

J.F. MEGYESI and R.F. DEL MAESTRO (London, Ontario)

Altered vascular permeability leads to edema in and around human cerebral tumors. Nuclear magnetic resonance (NMR) spectroscopy has been used to measure the properties of water molecules in edematous tissue. The parameters measured are the spin-lattice relaxation time (Tl) and the spin-spin relaxation time (T2), both of which are elevated in a cultured glioma cell line (C6) and in experimentally induced murine intracranial tumors.

NMR relaxometry was used to analyse tissue samples removed from patients at the time of surgery for intracranial neoplasms. Where possible, the following specimans were obtained: viable tumor tissue, necrotic tumor centre, and in cases of wide resection margins, peritumor tissue and tissue that appeared grossly normal. Histologically proven tumors that underwent analysis included glioblastoma multiform (10 cases), metastatic lesions (6 cases) and meningioma (4 cases). Cortical matter, removed at the time of epilepsy surgery (4 cases), was taken to be representative of a normal control.

Both glioblastoma multiforme and metastatic tumors showed significantly elevated T1 and T2 relaxation times relative to epilepsy specimens. Furthermore, relaxation times for glioblastoma multiforme were elevated above those of the other two tumor categories. Changes in brain tumor cell microenvironments may lead to the varying amounts and altered properties of water in different tumor types.

168.

^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) Spectroscopy of Plasma from Patients with Primary Intracranial Neoplasms

G.R. SUTHERLAND, J. PEELING and K. MARAT (Winnipeg, Manitoba)

Proton (^{1}H) NMR spectroscopy has recently been used to study the plasma of patients with systemic cancer. It was initially shown that the NMR peaks of methyl and methylene groups in the lipid residues of plasma lipoproteins are significantly narrower in patients with cancer compared to healthy controls. In this study, we evaluated the plasma from patients with malignant (n = 23) and benign (n = 17) primary intracranial neoplasms and from healthy control subjects (n = 16) using ^{1}H and ^{13}C NMR spectroscopy. Plasma samples were obtained from fasted subjects prior to initiation of any treatment and stored at 4°C until NMR measurements were performed. The NMR spectra were obtained using a Bruker AM-300 spectrometer operating at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C at a temperature of 27°C.

Although the NMR linewidths for patients with malignant neoplasms (27.2 ± .9; range 18.4-34.9 Hz) are significantly smaller than for patients with benign neoplasms (29.6 ± .7; range 22.9-34.4 Hz) or healthy controls (31.0 ± .6; range 27.1-34.3 Hz), there is considerable overlap among the three groups. Analysis of the ^{13}C spectra show the intensities of lipid peaks to be elevated in the spectra of patients with malignant neoplasms. Difference spectra (malignant-control) show that the plasma from patients with malignant neoplasms has elevated levels of fatty acids, both monounsaturated and polyunsaturated.

The considerable overlap between the study groups precludes the use of this method as a screening test for primary intracranial neoplasms. We hypothesize that the lipid residues arise from membranes shed from cells in growing neoplasms. Variability in the results may therefore reflect the known variability in cell kinetics within these tumors. An ability to follow indirectly the tumor's growth kinetics may be of considerable importance in elucidating the effects of primary intracranial neoplam therapy.

169.

Phosphorus Magnetic Resonance Spectroscopy and Characterization of Astrocytomas, Meningiomas and Pituitary Adenomas

J.F. EMRICH, E.A. SHOUBRIDGE, J-G. VILLEMURE, W. FEINDEL and D.L. ARNOLD (Montreal, Quebec)

The *in vivo* imaging of brain tumors can be performed with CT, angiography, PET and MRI. These techniques provide excellent anatomical localization (CT, angio, MRI), characterization of tumour edema (CT, MRI) and tumor metabolism (PET). To some degree, each of these modalities lacks specificity in identifying the nature of the tumour. Phosphorus magnetic resonance spectroscopy (MRS) allows non-invasive characterization of phosphate-containing compounds *in vivo* and subsequent determination of the energy state and intracellular pH of brain tumour cells. We have obtained localized phosphorus MR spectra from 10 normal brains, four low-grade astrocytomas, six glioblastomas, four meningiomas and three pituitary adenomas.

Compared to normal brain, spectra from low-grade astrocytomas showed a significant reduction of the phosphodiester (PDE) peak. Glioblastomas also showed a significant reduction of the PDE peak and, in addition, a high intracellular pH (pH_i). Compared to each other, there were no significant differences between low grade gliomas and glioblastomas. The spectra from meningiomas showed significant reduction in inorganic phosphate (P_i), PDE and phosphocreatine (PCr), as well as a more alkaline pH_i. Pituitary adenomas were characterized by a high phosphomonoester (PME) peak as well as significant reductions in P_i, PDE and PCr, and a more alkaline pH_i.

Although the number of tumours studied is small there appears to be a unique spectrum associated with astrocytomas, meningiomas, and pituitary adenomas. These findings can be useful in the preoperative identification of these tumours, particularly in the parasellar region.

170.

Subependymoma: A Review of 12 Surgical Cases

A.F. SADIKOT, J.-G. VILLEMURE, Y. ROBITAILLE and D. PENNEY (Montreal, Quebec)

Subependymomas are rare tumors, usually found incidently at autopsy in elderly men, as small neoplasms of the fourth ventricle. The larger, symptomatic cases arise predominantly in the fourth ventricle, although supratentorial cases and occastional cervical spinal tumors have been reported. We reviewed the surgical experience at the Montreal Neurological Institute over the last 25 years, finding 12 cases, including 10 arising from the fourth ventricle, one from the temporal lobe, and one of the cervico-medullary junction. The clinical presentation, radiologic findings, pathologic aspects, and surgical results are discussed. The utility of newer technologies, including magnetic resonance imaging and the Cavitron ultrasonic surgical aspirator (Cooper Medical), is emphasized. Two pedigrees of familial subependymoma were found in the series, including maternally related male cousins, and a father and son. Chromosomal banding performed on peripheral blood samples of 3 of the 4 familial cases revealed normal karyotype. Review of the site of origin and the histology of familial cases showed remarkable similarity. The significance of familial occurrence and overwhelming male predominance of this tumor is discussed.

171.

Phenotypic Characterization of Glioma Lymphocytic Infiltrates

J.-P. FARMER, N.R. CASHMAN, J.-G. VILLEMURE and J.P. ANTEL (Montréal, Quebec)

Lymphocytic infiltration is a characteristic pathologic finding in human gliomas. A positive correlation has been reported between the degree of this lymphocytic infiltration in glial tumors and the length of survival of patients harboring them, suggesting that the infiltrate may represent an attempt by the immune system to reject the neoplasm. Previous attempts at phenotyping the tumor infiltrating lymphocytes (TIL) utilized either an immunohistochemical technique which samples only a limited area of the tumor, or a technique in which the glioma TIL's are isolated in small numbers from the resected tumor and then expanded in mitogen and lymphokine-supplemented in-vitro culture prior to analysis; this latter technique may result in disproportionate expansion of selected lymphocyte subsets. We have developed a technique allowing establishment of the phenotypic profile of the extracted lymphocytes immediately after their isolation from glioma tissue, thus permitting a direct comparison of the TIL profile to that of freshly isolated autologous peripheral blood lymphocytes (PBL) also obtained at the time of craniotomy. TIL's are separated from myelin without use of trypsin by mechanical dissociation and density gradient centrifugation with Percoll. The mixed population of TIL's and tumor cells thus obtained is distinguished by double immunostaining with a fluorescein-conjugated monoclonal antibody directed against a common leukocyte surface antigen (H1e-1) and with mouse anti-T cell, T cell subset or macrophage antibodies coupled to an anti-mouse antibody conjugated to rhodamine. Initial data suggests that 30% of all isolated cells are of lymphoid origin, that 70% of cells of lymphocyte size as defined by FACS analysis express the leukocyte marker and that 75% of leukocytes are T cells. T cell subset analysis is currently being undertaken.

172.

Observations on Superselective Cerebral Arterial Low Dose Infusion of BCNU in High Grade Glioma

J.-G. VILLEMURE, D. MELANSON, R. LEBLANC, J. EMRICH, S. FONTAINE and J. THÉRON (Montréal, Québec)

Thirty-three patients suffering from histologically proven high grade glioma (3-4) were treated at time of recurrence, after surgery and radiotherapy, with superselective cerebral arterial low dose infusion of BCNU. There were 70 catheterization procedures: 35 in the supra-ophthalmic segments of the ICA, 34 in the MI portion of the MCA, 1 in the PCA. There were 55 BCNU treatments administered. BCNU was diluted in D5W and delivered by infusion pump over a three-hour period. Dosage of BCNU was 200 mgm/m^2 body surface in the first 8 patients and in the other patients 100 mg when given in MCA and 150 mg when given in ICA. The response rate was characterized as stabilization, improvement or worsening based on the patient clinical condition and on the tumor volume on infused CT scan done at 5 weeks post-treatment. Treatments were repeated at 5 weeks if the tumor volume (CT) had remained the same or improved. The response rate was 86%.. There were no thrombo-embolic complications related to technique. There was a 31% incidence of transient deterioration shortly after treatment that appears directly related to dosage. There was a 14% incidence of late permanent deterioration secondary to BCNU toxicity usually related to a cumulative dosage of BCNU. Of 24 evaluable patients, the overall survival is 71.5 weeks, with an average survival of 65 weeks for the patients who have died and 121 weeks for 4 survivors.

Better understanding of toxicity from BCNU, other schedule and dosage trials are necessary to further improve treatment in high grade glioma.

173.

Changes of Blood-Brain Barrier Permeability and Local Cerebral Blood Flow Following Intracarotid Administration of BCNU in Rats

S. NAGAHIRO, Y.L. YAMAMOTO, M. DIKSIC, S. MITSUKA, W. FEINDEL (Montreal, Quebec)

BCNU is one of the most effective agents for intreacarotid brain tumor chemotherapy. However, this treatment has definite dose limits because of its toxicity to the brain. To evaluate early toxicity and its causative factor, we studied in rats changes of blood-brain barrier (BBB) permeability and local cerebral blood flow (LCBF) measured by quantitative double-tracer autoradiography following intracarotid administration of BCNU.

Method — Thirty-six female Wistar rats, weighing 190-240 g, were divided into three groups receiving three different doses of BCNU (1 mg, 3 mg, 10 mg). The LD_{10} of BCNU with systemic administration in rats is known to be 13.1 mg/kg. BCNU was infused slowly for one hour through the carotid artery. BBB permeability and LCBF were measured with the quantitative autoradiographic method using the double tracers, ^{14}C-AIB and ^{18}F-FAP. The tracer studies were performed on Day 1 or Day 4-12 after administration of BCNU.

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Results — (1) In 13 rats in the 1 mg group, there were no changes of LCBF or BBB permeability. (2) In 15 rats in the 3 mg group, changes of BBB permability were seen in 3 of 5 rats (60%) on Day 1 in the ipsilateral hippocampus and caudate nucleus, and in 7 of 9 rats (78%) on Day 4-12, mainly in the hypothalamus. Histological changes, which occurred mainly in the ipsilateral hypothalamus with hemorrhage, were seen in only 4 of 10 rats (40%) on Day 4-12, and in none of 5 rats on Day 1. (3) Of 8 rats of the 10 mg group, 3 died from massive and multiple hemorrhages in the ipsilateral hemisphere within 10 days followng BCNU infusion. However, there were no histological changes in 3 rats on Day 1, when changes of BBB permeability and LCBF were ween in the ipsilateral hippo-campus, caudate and thalamic nuclei, and hypothalamus.

Conclusion — BBB permeability appears to be the most sensitive indicator for evaluating the toxicity of intracarotid BCNU treatment. Changes of BBB permability occurred in the ipsilateral hippocampus and caudate nucleus without any histological changes within 24 hours.

174.

The Influence of Ibuprofen on Patients with Peritumoral Edema

R.F. DEL MAESTRO and A.G. MATTAR (London, Ontario)

Ibuprofen has proven to be effective in decreasing microvascular permeability in a murine C6 astrocytoma cerebral tumor model. This open label prospective clinical study was carried out to assess the efficacy of ibuprofen on patients with known cerebral tumors and significant peritumoral edema. Patients included in the study had to be over 16 years of age, have convincing radiological evidence of a tumor with edema and have a Karnofsky performance rating between 30 and 90. Exclusion criteria included known intolerance to nonsteroidal anti-inflammatory drugs (NSAIDs). Treatment with NSAIDs or corticosteroids within 7 days of being included in the trial also resulted in exclusion. Patients accepted into the trial were treated for 7 days with ibuprofen (Motrin) 600 mg po qid and their Karnofsky rating was monitored daily. Fourteen patients were admitted to the trial however two patients were later excluded; one had been given and inadvertent dose of corticosteroids and another had coexistent carcinomatous meningitis. Of the 12 remaining patients 5 had improvement of at least one level on their Karnofsky rating scale and no patient deteriorated while on ibuprofen. These results suggest that ibuprofen may have some efficacy in the treatment of selected patients with symptoms related to peritumoral edema.

175.

Ibuprofen Inhibits Tumor Growth in the C6 Spheroid Implantation Glioma Model

C.L. FARRELL, J. MEGYESI and R.F. DEL MAESTRO (London, Ontario)

Spheroids of pure C6 astrocytoma cells implanted into brain develop into fully vascularized tumors with many of the growth and pathological characteristics of human gliomas. The effects of long term low and high dose ibuprofen on tumor growth and permeability were assessed in this experimental glioma model. In this experiment, rats were pretreated for 24 hours before implantation and then for 13 days following implantation of C6 spheroids with 24 mg/kg/day or 96 mg/kg/day ibuprofen. Tumor wet weights, dry weights and protein extravasation as measured by Evans Blue dye were measured. Protein extravasation into the tumor tissue did not appear to be reduced by the treatments when expressed as a per mg dry weight basis. The treatment significantly reduced the wet weight of the tumors in rats treated with high and low dose ibuprofen when compared to control humor treatment significantly decreased the dry weights of the tumors compared to tumors of control animals. It is hypothesized that ibuprofen inhibits eicosanoid dependant angiogenesis, thereby interfering with the tumor growth.

176.

Cerebral Mass Lesions and Platelet Sequestration

R.R. DEL MAESTRO, D.R. GRAVELLE, G.J. MORRISSEY, C.L. FARRELL and A.A. DRIEDGER (London, Ontario)

This experiment was undertaken to assess the sequestration of autologous indium labelled platelets in a number of different cerebral mass lesions. The hypothesis tested was that malignant primary and secondary tumours would accumulate platelets. Blood samples were removed from each patient, labelled with indium-lll and scans were obtained at 24 and 48 hours post-reinjection. Following the 48 hour platelet scan the patients red blood cells were labelled with technicium-99 and a blood pool scan carried out. The double labelling technique allowed the quantitation of corrected platelet count in tissue samples and subtraction of the blood pool data from the platelet scan to obtain an accurate assessment of platelet sequestration. At 72 hours after injection of autologous platelets operative procedures were carried out and tissue specimens processed for histopathology and quantitative platelet determination. Platelet scans were positive in 7 of 9 cases of malignant glial tumors and tumor tissue quantitatively contained more platelets than normal cortex or white matter. Four of 7 secondary tumors were positive and 1 of 3 meningiomas. A number of other mass lesions have also been assessed and only 2 cases of cavernous angioma were positive. Platelet sequestration appears to be common in malignant tumors and cavernous angiomas and this may be related to the adhesion of platelets to abnormal endothelial cells in these disease processes.

177.

Complications of Interstitial Brachytherapy in Patients with Malignant Astrocytomas

M. BERNSTEIN, N. LAPERRIERE, S. McKENZIE and P. LEUNG (Toronto, Ontario)

Interstitial brachytherapy is a promising treatment for patients with malignant astrocytomas. This modality of therapy is currently under investigation in Toronto in both a phase III randomized study for newly diagnosed patients with these tumours, and as well in a phase II setting for patients with recurrent malignant astrocytomas who are not participating in the phase III study. At the time of this writing, 20 patients have been treated with interstitial radiation — 11 on the phase III study and nine for recurrent disease on the phase II study. Patients are being followed with regular neurological examination, CT scan, MRI, neuropsychological evaluation and quality of life analysis. It is too early to comment on the efficacy of this therapy but one can document several devastating and interesting complications.

Of the 20 patients treated with interstitial radiation, a total of 12 complications occurred in a total of 7 patients. Only 1 complication occurred in a patient being treated for recurrent disease whereas 11 complications occurred in 6 patients in the phase III study for newly diagnosed tumours. The complications are as follows: one middle cerebral artery occlusion, one brain abscess, one case of severe facial pain, one mild scalp infection, two cases of systemic tumor metastases, three cases of acute neurological deterioration with complete recovery, and three cases of radiation necrosis requiring repeat craniotomy. The pathogenesis and potential methods of prophylaxis of these complications are addressed.

Neuro-oncology (Poster)

THURSDAY, JUNE 16TH - P.M.

178.

Paraneoplastic Encephalomyelitis and Subacute Pandysautonomia Due to Occult Atypical Carcinoid Tumor of the Lung

M. VEILLEUX, P. NAUD and J.B. LAMARCHE (Sherbrooke, Quebec)

Encephalomyelitis and subacute pandysautomia are rare paraneoplastic complications of bronchial carcinoma and have been seldom reported as a non-metastatic manifestation of an occult carcinoma. A 72-year-old man had a 6-month history of orthostatic hypotension and a recent onset of lethargy and sphincter disturbance. Investigations were normal except for diffuse slowing of the background activity on the EEG, mononuclear pleocytosis and increased protein in the CSF. Chest X-rays were normal, and head CT scan was normal except for mild, diffuse cerebral atrophy. Tests of autonomic function revealed low plasma norepinephrine level, a marked drop of blood pressure (BP) to vertical tilt and Valsalva maneuver, and a marked rise of BP to norepinephrine infusion. A few days prior to death, the patient became hypothermic and presented repated episodes of respiratory arrest associated with atrioventricular block on the EKG. Autopsy revealed an atypical carcinoid tumor in a few tracheobronchial lymph nodes, widespread lymphocytic infiltrates and loss of neurons in the cerebral and brainstem gray matter, the spinal cord, and the paravertebral sympathetic ganglia as well as microglial and astrocytic proliferation in the central nervous system.

179.

Intraparenchymal Epithelial (Enteric) Cyst of the Medulla Oblongata. Radiological Ultrastructural and Immunohistochemical Features

B. LACH, N. RUSSELL and B. BENOIT (Ottawa, Ontario)

Intraparenchymal epithelial cysts of the brain are extremely rare. Only a few examples have been described and a very limited immunohistochemical, ultrastructural and radiological data are available.

We report a unilocular cyst located within the substance of the medulla oblongata of a 67 year old woman with a history of ataxia, tinnitus and hypoesthesia of the left hand and foot. Neurological examination also revealed nystagmus toward the side of the gaze. CT-scan examination was inconclusive. MRI disclosed a large rounded cyst replacing most of the parenchyma of the medulla oblongata at the ponto-medullary junction. At surgery, the cyst was located in the parenchyma of the brain stem and separated from the IVth ventricle by a thin membrane. The wall of the cyst with the floor of the IVth ventricle was biopsied and a fenestration procedure carried out.

Light microscopic examination of the wall of the cyst revealed an attenuated single layer of epithelial cells resting on a prominent basal lamina. The cells were positive for cytokeratin, keratin, epithelial membrane antigen and Ulex Europeus lectin. Immunostains for S-100, neuron-specific enolase and glial fibrillary acidic protein were negative in the epithelium of the cyst but positive in the adjacent ependyma of the IVth ventricle. Neither the ependyma nor the epithelium showed the positivity for Leu 7, M 1 or vimentin. Ultrastructural study of the lining of the cyst revealed a single layer of flattened, elongated cells displaying desmosomal junctions and tonofilaments, short microvilli and surface coating material corresponding to glycocalix.

Our immunohistochemical and ultrastructural studies indicate the endodermal origin of the cyst routinely mislabelled as ependymal or neuroectodermal cyst. Furthermore, this case demonstrates unsurpassible value of magnetic nuclear resonance in the correct pre-operative diagnosis of intraparenchymal cystic lesions.

180.

Anterior Decompression and Fixation for Symptomatic Spinal Metastases

R.G. PERRIN and R.J. McBROOM (Toronto, Ontario)

Spinal stabilization is of critical concern in planning the treatment for patients with symptomatic spinal metastases. The necessity for stabilization can be anticipated in patients with: 1) progressive vertebral collapse; 2) frank pathological fracture - dislocation; 3) extensive spinal decompression.

Anterior decompression for symptomatic spinal metastases involves vertebral corporectomy and requires spinal stabilization as a matter of course.

A variety of methods and materials have been used to secure spinal stabilization after anterior decompression procedures including bone graft (from iliac crest, tibia and fibula) and acrylic incorporated about various fixation devices bridging the decompression defect (including screws, Steinmann pins, Harrington rods, and Knodt rods).

We have utilized a contoured stainless steel plate and screws supplemented with methylmethacrylate forming a block replacement for the decompressed spinal segment(s).

Sixty patients with symptomatic spinal metastases have been treated with anterior decompression and stabilization using the method described. There have been two fixation failures.

Advantages of our method include: 1) simplicity and ease of insertion; 2) custom design to fill any size gap and with the option to extend fixation for one or two levels; 3) conformity to the size and shape of the spinal column without compromising paraspinal structures; 4) availability of materials in virtually all hospitals.

181.

An Update on Photodynamic Therapy of Primary Malignant Brain Tumors

P. MULLER and B. WILSON (Toronto, Ontario)

We are updating our experience with intraoperative PDT in 32 patients with malignant supratentorial gliomas; in 19 cases the tumor was recurrent. There were 20 males and 12 females with an age range of 17-73 [mean = 45] years. The first 8 patients in this series received HPD [Photofrin I] and the next 24 received DHE [Photofrin II]. A photo-illuminating device, of the authors' design, was coupled to an argon dye pump laser in order to deliver light at 630nm to a tumor cavity created by radical tumor resection and/or tumor cyst drainage. The total light energy delivered ranged from 440 to 3888 Joules and the light energy density ranged from 8 to 68 J/cm^2.

There were 2 post-operative deaths. Follow-up has ranged from 1 to 3 years. In the interval between PDT and death, the deaths per observation year was 1.02 for the whole group and 0.94 when the 2 postoperative deaths are excluded. In the interval between first diagnosis and death, the death rate was 0.47. The median post-PDT survival time was 29 weeks with 28% surviving >1 year and 6% surviving >2 years. The median survival time from first diagnosis [1st operation] was 67 weeks with 60% surviving >1 year and 22% surviving >2 years.

In six patients the tumor disappeared on CT scan post-PDT. Only 2 of the 6 patients had post-PDT radiotherapy. Of the 6 cases 5 have had tumor recurrence and 4 have died. In 4 patients the area of original tumor remained stable or decreased; in spite of which, tumor developed remote from the site of treatment suggesting that light penetration was inadequate.

Photodynamic therapy of malignant brain tumors using surface or cavitary photo-illumination can be carried out with acceptable risk and appears to be active against some gliomas.

182.

Carcinomatous Meningitis Following Surgical Intervention of Cerebral Tumors

J.F. MEGYESI and R.F. DEL MAESTRO (London, Ontario)

The occurrence of carcinomatous meningitis following surgical intervention of cerebral neoplasms was noted in a number of patients. To elucidate any relationship between operation and the occurrence of carcinomatous meningitis, a retrospective study was undertaken. Six hundred and eighty-three patients were operated on for cerebral tumors by the neurosurgical service at Victoria Hospital, London, Ontario, Canada from 1981 to 1987. Primary gliomas accounted for 26% of cases while metastatic lesions accounted for 21%. Of the known cases of metastatic primaries, 58 were from lung, 22 were from malignant melanoma, 7 were from kidney and 6 were from breast.

During the same period, twenty-four cases of carcinomatous meningitis were seen. Of these, 16 (67%) were classical cases of arcinomatous meningitis with seeding of the cerebrospinal fluid (CSF) directly from a non-intracranial primary lesion (10 breast, 3 lung, 1 prostate, 1 lymphoma, 1 unknown). The other 8 (33%) were cases of carcinomatous meningitis that occurred after a cerebral tumor had undergone surgical intervention. Of these eight cases, three were carcinomatous meningitis after surgery for glioblastoma multiforme, one after surgery for medulloblastoma and four were after surgery for metastatic lesions to brain (2 malignant melanoma, 1 lung, 1 renal). The median time for the development of carcinomatous meningitis after surgery was 7 months (range: 2-12 months). Seeding of the CSF by tumor cells at the time of surgical intervention may occur and special care should be taken at the time of operation to decrease the possibility of it.

Supported by the Brain Research Fund Foundation.

183.

Symptomatic Exophytic Subependymoma of the Spinal Cord

B. LACH, N. RUSSELL and B. BENOIT (Ottawa, Ontario)

Subependymomas are uncommon tumors usually located around the ventricular system. Only five cases have been reported in the spinal cord, all intramedullary and showing characteristic morphological appearance. We present a patient with subependymoma of the spinal cord, infiltrating leptomeninges and spinal roots, and showing unusual ultrastructural features.

A 76 year old woman had a two-year history of progressive left arm weakness and urinary incontinence. Myelogram showed an extramedullary intradural mass. Laminectomy revealed a well demarcated tumor involving the roots and leptomeninges on the left side of the spinal cord at C_7 to T_1 levels. The tumor was attached by a thin stalk to the posterior aspect of the spinal cord and was easily accessible for a total gross removal. The patient was discharged home and re-admitted eight months later with recurrence of symptoms. In addition, she had spastic weakness of the right leg. Repeated myelogram revealed marked swelling of the spinal cord that extended from C_4 to T_4. At the laminectomy, intramedullary very well demarcated tumor was discovered and removed. There is no sign of recurrence one year later.

Light microscopic and immunohistochemical examination of the extramedullary tumor from the first surgery, revealed a typical example of subependymoma, with many cells positive for GFAP and vimentin. Formation of small rosettes lined by villi and cilia; multiple astrocytic processes full of intermediate filaments as well as zonula adherenses and gap junctions were found ultrastructurally. Intramedullary tumor from the second resection showed predominantly large, GFAP-positive astrocytic cells and no light microscopic features of ependymoma or subependymoma. However, ultrastructural examination revealed frequent intracellular lamina with cili and villi and intercellular junctions. Although the tumor showed an unusual, large-cell component in the re-operation, the neoplastic cells still preserved ependymal and astrocytic features characteristic of subependymoma. In view of the good prognosis in subependymoma, this case underlines the importance of electronmicroscopy in the correct diagnosis and management of spinal cord gliomas.

184.

Investigation of an Inhibitor of Lipid Peroxidation in the C6 Astrocytoma Implantation Model

J.F. MEGYESI, C.L. FARRELL and R.F. DEL MAESTRO (London, Ontario)

Lipid peroxidation reactions are an important component of the inflammatory response. Inhibition of these reactions may reduce free radical induced cell membrane damage and vascular permeability changes. The role played by lipid peroxidation reactions in cerebral tumor growth and protein extravasation has not been defined. A potent *in vitro* inhibitor of lipid peroxidation, 21-[4-(2,6-di-1-pyrrolidinyl-4-pyrimidinyl)-1-piperazinyl]-16α-metylpregna-1,4,9(11)-triene-3,20-dione monomethane sulfonate (U74006F), has been used to assess its influence on both tumor growth and protein extravasation in the rat C6 astrocytoma implantation model. Following spheroid implantation, rats were treated with one of three U74006F regimens, as well a a control group. Tumor wet weights, dry weights and protein flux as measured by Evans blue dye extravasation were evaluated. Neither wet weights nor dry weights of any of the three treatment groups was significantly lower when compared to control tumor wet weights and dry weights. Protein dye extravasation did not appear to be significantly reduced by any of the treatments when expresed as a per milligram dry weight basis. It is concluded that U74006F did not significantly decrease tumor growth or permeability in the C6 astrocytoma spheroid implantation model.

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Neuropsychology (Platform)

FRIDAY, JUNE 17TH - P.M.

185.

Intracerebroventricular Bethanechol Chloride in Alzheimer's Disease: Dose-Related Response in a Patient

R. BOUCHARD, L. GAUTHIER, S. GAUTHIER and R. LEBLANC (Québec and Montréal, Québec)

As part of a multicenter study, transmitter-replacement therapy has been tried in nine patients, using intracerebroventricular infusion of bethanechol chloride (urecoline) a cholinergic agonist. The clinical and laboratory data as well as the brain biopsy findings have already been reported. Each patient was submitted to a six-month double-blind cross-over trial. The full results will be published with the multicenter trial group but overall no significant improvement was noted at the dose used (0,3mg/day), except for a slight increase in the Mini Mental State. After the trial each patient was free to continue the treatment.

We report on a patient whom we consider a dose-related responder to that therapy. He is 69 yars old, has had a clinical diagnosis of Alzheimer's disease (AD) for six years, and is under treatment for two years. After the double-blind trial, the dose of urecholine was progressively increased over a period of four months by 40%. This increase was associated with improvement of the functional independance level as measured by serial ADL assessments and the Rapid Disability

Rating Scale and this was corroborated by all members of the family. However, objective neuropsychological tests did not show improvement.

After six months of stabilization at the same dose, the patient began to deteriorate slowly and 16 months after the end of the initial trial, he has returned to his previous level of autonomy. This suggests a progression of the disase or a decreased sensitivity to the drug. Cholinergic agonists may be effective in some patients with relative preservation of post-synaptic receptors, but high doses may be necessary. There is also hope with more selective muscarinic post-synaptic agonists which are now being studied in animals. The relative value of ADL assessments and objective neuropsychological tests will be discussed.

186.

Tetrahydroaminoacridine (THA) avec Lécithine dans la maladie d'Alzheimer (MA)

S. GAUTHIER, H. MASSON, L. GAUTHIER, Y. BACHER, R. BECKER, H. BERGMAN, R. CHARBONNEAU, B. COLLIER, D. DASTOOR, D. GAYTON, C. KISSEL, M. KRIEGER, S. KUSHNIR, N.P.V. NAIR, L. NEIRINCK, J. RATNER, M. ST-MARTIN, S. SUISSA, Y. TESFAYE, S. VIDA, R. BOUCHARD, J. MORIN, A. LAMONTAGNE, P. BAILEY and J. KENNEDY (Montreal, Quebec City and Sherbrooke, Quebec; St-John's, New Brunswick; Vancouver, British Columbia)

Cinquante-et-une personnes avec MA probable ou définitive aux stades 4 ou 5 à l'échelle de Reisberg ont reçu en simple insu Lécithine 2.4 gr. tid et THA à doses progressives de 25 à 150 mg die. Malgré l'emploi de glycopyrrolate 1 mg tid, des effets secondaires autonomiques furent notés chez 80% des sujets et une élévation réversible des SGOT, SGPT, LDH et/ou phosphatase alcaline chez 34%, à des doses aussi faibles que 25 mg die. Dix-neuf ont complété six semaines de traitement et ont montré en utilisant le signed- rank test une amélioration significative du pointage au Mini Mental State après quatre semaines de THA et des activités de la vie quotidienne sur la Rapid Disability Rating Scale après six semaines de THA. Il n'y a pas eu de détérioration de l'humeur selon l'échelle de dépression gériatrique. Une amélioration des symptômes de la MA est donc possible par inhibition de l'acétylcholinestérase mais avec une toxicité non négligeable.

187.

Familial Alzheimer Disease: Molecular Genetic Studies

P. ST GEORGE-HISLOP, J. GUSELLA, D. GAUVREAU, J. NALBANTOGLU, G. LACOSTE-ROYAL, D. GAUTRIN, Y. ROBITAILLE, R. BOUCHARD, A. CLARK, D. SADOVNICK, H. KARLINSKY and D. CRAPPER McLACHLAN (Boston, U.S.A.; Montreal and Quebec City, Quebec; Calgary, Alberta; Vancouver, British Columbia; Toronto, Ontario)

We have recently shown that the genetic defect responsible for the autosomal dominant form of Familial Alzheimer Disease (FAD) in 4 large FAD pedigrees is linked to two DNA markers (D21S1/D21S11 and D21S16) on the proximal long arm of chromosome 21. The recent cloning and mapping of the gene coding for the amyloid B-protein precursor to the same region of chromosome 21 has lead to the hypothesis that this gene may be the site of the FAD mutation. The following observations exclude the amyloid B-protein gene as the site of the FAD mutation: (1) the FAD mutation is not tightly linked to RFLPs in the amyloid B-protein gene; (2) there is no allelic association between sporadic AD and RFLPs in this gene; (3) contrary to previous reports no gene triplication or alteration in mRNA size is observed in brain or peripheral tissues from 63 AD cases.

Additional DNA markers from the proximal long arm of chromosome 21 have been isolated, and additional families with FAD are being sought in order to: (1) better define the location of the FAD gene; and (2) to addres the question of non-allelic heterogeneity in FAD. The results of these investigations carried out by the Canadian Alzheimer Collaborative study group will be presented.

188.

L'apraxie Constructive dans la Démence de type Alzheimer

C. RAINVILLE and B. CARDU (Montréal, Québec)

Avec l'amnésie de fixation et la désorientation temporo-spatiale, l'apraxie constructive est l'une des premières manifestations de la démence de type Alzheimer [DTA] (Rosen 1983a, b). La sévérité du désordre serait représentative du niveau d'évolution de la maladie (Ajuriaguerra et coll. 1960, 1965, 1978).

Le présent travail se propose d'étudier la nature des désordres constructifs en tentant de dégager et de caractériser des niveaux de performance dans la diversité des productions graphiques. Sur la base des caractéristiques graphiques, on tente également d'identifier ce qui distingue le vieillissement normal du vieillissement pathologique (DTA).

Un groupe de 21 sujets (Ss) ayant une DTA, en début d'évolution, ainsi qu'un groupe témoin de 21 Ss appariés, ont été soumis à des tâches classiques de praxies constructives. Les Ss devaient tantôt dessiner, tantôt copier, des figures géométriques et des figures concrètes. Par ailleurs, ils devaient copier la figure de Rey et des figures composées de deux carrés contigus, orientés différemment l'un par rapport à l'autre.

Il se dégage des résultats une perte plus marquée dans le dessin. Une analyse hiérarchique suggère que la désintégration procède des aspects les plus complexes vers les moins complexes, selon un schéma relativement constant. L'analyse qualitative met en évidence certains traits propres à chacun des groupes.

189.

Multivariate Analyses Permit a Morphometric Definition of Alzheimer's Disease Distinct From Normal Aging

M.J. BALL and P.H. FEWSTER (London, Ontario)

Neuropathological examination remains the most definitive investigation for confirming a clinical diagnosis of senile dementia Alzheimer type. A systematic approach utilizing quantitative histology to distinguish brain changes in normal aging from those in Alzheimer patients has been attempted by workers in Britain (Tomlinson and Henderson, Aging *3*, 1976), the United States (Khachaturian, Arch. Neurol. 1985) and Canada (Ball et al, Lancet 1985). We have now developed a unique multivariate programme for the statistical analysis of grey matter lesions (neurofibrillary tangles, neuritic plaques, granulovacuolar degeneration, Hirano bodies, neuronal loss) in samples from the hippocampal formation, from ten regions of neocortex, and from the basal forebrain in the cerebra of 42 subjects (33 with Alzheimer dementia, 9 cognitively normal age-matched controls).

After a Z-transformation, the ordination method of Principal Components Analysis (Orlóci, 1978) summarized the data from the histopathological Indices onto two component axes. These first two parsimonious axes, representing 69.5% of total linear variance, proved sufficient to summarize a majority of the variation. Results of a classification method of cluster analysis (Ward, 1963) were then superimposed to enhance interpretation of the scattergram. Morphometric data from 383,283 neocortical and 1,009,589 hippocampal fields indicate Alzheimer cases comprise a group distinct from the aging cohort.

Multivariate models should henceforth enable identification techniques (e.g., Mahalonabis' generalized distance method) to determine the neuropathological diagnosis in unknown cases with a statistically calculated degree of certainty.

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190.

Cerebral Biopsy in 2 Cases of Binswanger's Disease: Clinical, neuropsychological and neuroimaging correlations

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Despite a plethora of reports of subcortical arteriosclerotic encephalopathy (SAE) of Binswanger in recent literature, there are still less than 50 pathologically studied cases, all at autopsy.

Two demented patients with leukoencephalopathy had cerebral biopsies. One was a 52 year old normotensive man with 8 year history of T.I.A.'s and dementia characterized on neuropsycological testing by signs of primarily frontal subcortical disease. Microscopic features include severe arteriosclerosis with microinfarcts of white matter, pallor of myelin and sparing of cortex and of subcortical U fibres. Serial CT scans and MRI studies and neuropsychological assessments will be presented.

A second case, in 54 year old male but with less than 2 year clinical history of dementia and similar neuropsychological CT and MRI abnormalities had no significant arteriosclerotic changes and normal myelin staining in his cerebral biopsy. These findings suggest that the disturbance and leukoencephalopathy may precede significant histological change or vascular pathology and also support the contention that arteriolar changes are not constant in SAE. It also supports the concept that the extensive pallor of white matter with sparing of the arcuate fibres should not be regarded as a disease entity but is probably the result of many causes other than arteriosclerosis such as hypoxia, with or without acidosis as postulated by Huang et al.

191.

Amytrophic Lateral Sclerosis/Parkinsonism-Dementia Complex and Progressive Supranuclear Palsy: Neurodegenerations Half A World Apart

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During 1963 Richardson, Steele and Olszewski in Toronto described patients with progressive palsy due to neurofibrillary degeneration in heterogenous system nuclei of the central nervous system. The syndrome, they termed progressive supranuclear palsy (PSP) occurs worldwide and is now identified to be a relatively common neurodegeneration of later life.

After 1972, Steele lived in Micronesia and since 1983 he has investigated the amyotrophic lateral sclerosis/parkinsonism-dementia complex (ALS/PDC) of the Mariana Islands; a neurodegeneration that Spencer attributes to neurotoxin(s) in the seeds of the indigenous false sago palm which Chamorros formerly prepared as food and used as medicine.

In this report the authors reviewed their collaborative experience since 1983 of 64 patients with ALS/PDC, compare the clinical and pathological features of PDC with those of PSP, and conclude that these two neuro-degenerative syndromes are so remarkably alike in some patients as to suggest a similar pathogenesis.

ALS/PDC is now less common but it remains an important paradigm for the study and understanding of neurodegenerative diseases elsewhere. The authors expect that observations about this disappearing disease on these distant Pacific islands will profoundly alter present views about neurotoxins and their role in neurodegenerative diseases and aging of the human nervous system.

192.

Etude d'un cas de dyslexie acquise

M.J. TAINTURIER, S. LUPIEN et A.R. LECOURS (Montréal, Québec)

Nous présentons l'analyse d'un cas d'**alexie associée à une aphasie de Broca** consécutive à l'ablation d'un méningiome de la gouttière olfactive gauche (syndrome de Foster-Kennedy) chez un homme droitier et francophone, alors âgé de 47 ans.

Notre corpus est constitué de 1026 paralexies produites par Monsieur B. en lecture à voix haute de 1306 stimuli. Les erreurs concernant principalement la lecture des néologismes, des mots grammaticaux et des verbes conjugués sans que les autres catégories ne soient épargnées pour autant. La plupart des paralexies verbales ont pu être assignées à l'une des catégories suivantes:

- **erreurs dites sémantiques**; le stimulus et la réponse entretiennent une relation de sens mais pas de relation de forme: **TABLE** est lu **CHAISE**;[2]
- **erreurs dites visuelles**; le stimulus et la réponse entretiennent une relation de forme mais pas de relation de sens: **BUFFFET** est lu **BUFFLE**;
- **erreurs dites morphologiques**; le stimulus et la réponse sont unis par un lien morphologique de nature dérivationelle ou flexionelle: **EPICIER** est lu **EPICERIE, BOUCHA** est lu **BOUCHERA**.

Certaines erreurs sont demeurées inclassifiables parce qu'aucun lien précis ne semblait unir le stimulus et la réponse (e.g., **FIEVRE** est lu **COMBIEN**).

Ce tableau correspond de façon prototypique au syndrome que les neuropsychologues cognitivistes ont pris coutume d'appeler la **dyslexie profonde**. Nous situerons notre cas (à notre connaissance le premier décrit de façon extensive chez un sujet francophone) dans le cadre des conceptions actuelles ayant trait à ce syndrome, en faisant état des modifications qu'il conviendrait selon nous d'y apporter à la lumière de nos observations.

193.

The Relationship Between Age and Aphasia Type

J. BOEGLIN, P. GOULET and Y. JOANETTE (Montréal, Québec)

It seems, for many clinicians (e.g., speech therapists, behavioral neurologists), that Broca's aphasics tend to be younger than Wernicke's, or that non-fluent aphasics are younger than fluent aphasics. In recent years, this "observation" has been both confirmed and invalidated by systematic studies. The importance of this question is not only clinical but also theoretical since different hypotheses have been advanced to account for this relationship (e.g., the "continuing lateralization hypothesis" of Brown and Jaffe (1975)). Thus the present study investigated the relationship between age and aphasia type. The experimental sample included 14 Broca's and 12 Wernicke's aphasics. Only those patients with an unequivocal diagnostic — as confirmed by a detailed examination — were included. All subjects were right-handed, and had suffered a unique unilateral vascular lesion of the left-hemisphere. There was no significant difference between groups as to male/female ratio and schooling. Results show that patients with Broca's aphasia were significantly younger than those with Wernicke's aphasia. These

results suggest that the previously reported difference in age between Broca and Wernicke aphasics is not accidental. However, by now, no study has controlled for all factors which might have an influence on such a difference (e.g., sex differences, taxonomy of aphasia used, handedness, lesion size, lesion location, schooling, family history of left-handedness, etiology, number of days after the onset of the lesion).

194.

Reaction Time and Movement Time in Normal Pressure Hydrocephalus

L. MARCHAND and T. BOTEZ (Montréal, Québec)

Since 1974 we have used repeated lumbar punctures (LP) as a predictive method for the shunting procedures in normal pressure hydrocephalus.

In the present study, 17 patients were divided into two groups. The first group was comprised of 10 subjects (age 68.7 ± 10.9) with the classic NPH syndrome confirmed by the existence of the clinical triad of Hakim and Adams as well as by radioisotopic cysternograms and CT scans. They were subjected to 3 LPs with withdrawal of 30 ml of CSF at 2 to 3 day intervals. In the second group, 7 patients (age 64.7 ± 7) with Alzheimer's disease or multiinfarct dementia underwent spinal-taps as described above. The visual simple reaction time (RT) and movement time (MT) were carried out before and after the set of LPs. This method does not induce practice effects.

The statistical (ANOVA) results showed a significant diminution of visual RT in group 1 in the post trial examination but no significant changes were noted in group 2. There was also a significant diminution in visual MT in group 1 whereas group 2 showed no significant changes.

To conclude, simple RT and MT assessment is a useful method for establishing whether or not repeatable withdrawals of CSF by LP improve the condition of NPH patients and in order to serve as a good predictive value for eventual shunting procedures.

195.

Visual Neglect and Idiopathic Parkinson's Disease

L. GAUTHIER, S. GAUTHIER and Y. JOANETTE (Montreal, Quebec)

Villardita et al (1983) reported the presence of visual neglect in left-sided and bilateral parkinsonians using a modified version of the Albert's cancellation test. Starkstein et al (1987) found a mild left hemispatial neglect in left parkinsonians (no controls) on a line bisection task. The present study aims to investigate further visual neglect in Idiopathic Parkinson's Disease (IPD) using a battery of detection tasks.

The performance of 30 right-handed IPD subjects (10 PDLeft, 10 PDRight, 10 PDBilateral) with normal visual fields and of 10 controls was compared. Tests included: Mini-Mental State (MMS), 3 cancellation tests: Albert, Bell and letters, line bisection, reading and drawings.

Results show no difference between the IPD groups for schooling and MMS. All 3 IPD groups demonstrate no significant evidence of visual neglect in all tests. PDB were slower on the Bell's cancellation test with distractors. Only one PDL subject shows neglect of the left space, however the subject also presents other cognitive impairments suggesting dementia type features.

In summary, our study does not confirm the presence of visual neglect in IPD. Caution is thus important before attributing this symptom to all left and bilateral parkinsonians since inattention and neglect could bring upon parkinsonians unwarranted functional limitations (eg. driving permit). Contributions of cortical and sub-cortical structures in directed attention towards extrapersonal space in view of the present results will be discussed.

196.

Memory Testing Following Amytal Injection: A Controlled Study with Unilateral Temporal Lobe Epileptics

I. ROULEAU, R. LABRECQUE, J.M. SAINT-HILAIRE, N. GIARD and G. BOUVIER (Montreal, Quebec)

The Amytal Test originally used by Wada and Rasmussen (1960) for the assessment of cerebral dominance for language was adapted by Milner to predict post-operative memory impairment after unilateral temporal lobectomy. It is now being used as a routine test in the pre-operative investigation of epileptic patients submitted to temporal lobectomy.

Besides its clinical use, the Amytal Test can be used as an interesting experimental tool for the understanding of the mechanisms involved in human amnesia. We designed an original test for memory assessment using a continuous recognition task of easily identifiable pictures. Recognition is assessed both under the effect of Amytal and after the effect has completely disappeared. Thus in addition to a retrograde memory measure, the protocol includes both short-term and long-term anterograde memory measures. This method enables us to test the three main hypothesis of the human amnesic syndrome (encoding, consolidation, retrieval).

Twenty epileptic patients with SEEG-confirmed temporal lobe foci were given right and left injections on successive days. Only the long-term memory measure for material presented under Amytal was significantly related to the presence of a contralateral temporal epileptogenic focus. Short-term memory deficits were observed equally often after ipsilateral and contralateral injection to the epileptogenic focus and no retrograde amnesia was observed. These results are consistent with the consolidation hypothesis.

Neuropsychology (Poster)

THURSDAY, JUNE 16TH — P.M.

197.

Prosopagnosia in a Right Hemispherectomized Patient

J. SERGENT and J.G. VILLEMURE (Montreal, Quebec)

Prospagnosia is a rare behavioural impairment characterized by an incapacity to recognize known persons by their faces. It usually results from bilateral damage in the mesial occipito-temporal areas. We present the case of a 34-year old woman who underwent complete right hemispherectomy at 13 and who displays a total inability to recognize relatives and celebrities by their faces. She has normal intelligence, and no alexia, object agnosia or achromatopsia. Except for a dense left hemianopsia, she presents no severe cognitive deficits other than prosopagnosia. A series of neuropsychological tests were carried out to examine the nature of her impairment. She shows a marked deficit in contrast sensitivity at low spatial frequencies, but has normal acuity. Although she can identify hundreds of objects visually, she has difficulty making discriminations within categories of objects presenting a close visual similarity to one another (green vegetables, cars, faces). Her impairment with faces is restricted to situations where the individuality of the face matters, as indicated by her capacity to tell the sex, approximate age, and emotion expressed by a face. Examination of perceptual processes through multidimensional scaling analysis reveals an incapacity to combine facial features into an integrated configuration that uniquely defines each face. The results suggest that her impairment is primarily perceptual rather than mnesic, and that she has difficulty encoding and storing facial information in a reliable manner. Some features of her neurological history will be presented that may

account for the atypical occurrence of prosopagnosia after hemispherectomy.

198.

Vocal Agnosia

S.E. BLACK, J. GORMAN, M. HOHOL and W.G. SNOW (Toronto, Ontario)

The neuropsychology of human voice recognition has received little attention, but recent evidence suggests that, like face identification, it is based on "holistic" pattern recognition, mediated by the right hemisphere. Although loss of voice recognition (vocal agnosia), has not been reported as a major complaint in right brain-damaged (RBD) subjects, these RBD subjects perform less well than left brain-damaged subjects both on face and voice identification tasks (Van Lancker and Kreiman, *Neuropsychologia*, 1987). On the other hand, vocal agnosia has been described in association with bitemporal or left temporal damage in patients with word deafness and/or auditory agnosia. Thus, the neuroanatomical basis of vocal agnosia remains unclear. We had the unique opportunity to study loss of both face and voice recognition in a 65-year-old, right-handed engineer, who developed severe prosopagnosia from a right temporal haemorrhage, two years after a left parieto-occipital stroke. Unable to recognize even his own face, the patient could readily identify family and acquaintances by their voices. One year later, he suddenly lost this ability. Comprehension of speech and environmental sound were also impaired initially but quickly improved. His vocal agnosia persisted causing him great distress. An MRI showed two resolving haematomas on the left in the hippocampus and in the superior and middle temporal gyri, in addition to the previous right temporal and left parieto-occipital lesions. We review the literature and present our neuropsychological investigations of this illustrative case. We conclude that, while RBD may cause some impairment in voice recognition, bilateral temporal lobe damage is necessary for severe vocal agnosia.

199.

Marqueurs linguistiques de la sénescence

R. BELAND and A.R. LECOURS (Montréal, Québec)

Une population de sujets normaux a été soumise à un protocole d'examen de l'aphasie (le Montréal-Toulouse, MT-86B modifié) dans le but d'obtenir des normes sur la performance des sujets en fonction de leur âge et de leur scolarité. Le MT-86 B modifié comprend différentes épreuves évaluant la fonction linquistique sur les versants oral et écrit et dans les modalités de production et de compréhension. Nous présenterons ici les résultats obtenus à cinq épreuves: 1) l'appariement mot/image et phrase/image 2) la répétition de mots, 3) la lecture à voix haute de mots, 4) la dénomination orale, et 5) la copie de mots.

Les 171 sujets sont répartis en trois groupes d'âge (0-49 ans, 50-69, 70 et +) et trois niveaux de scolarité (0-9 ans, 10-14, 15-24). L'analyse des performances obtenues à l'épreuve d'appariement mot/image et phrase/image dans laquelle le sujet doit pointer l'image correspondant au mot ou à la phrase entendue a montré que les scores moyens obtenus diffèrent significativement selon l'âge et la scolarité des sujets. Les sujets plus jeunes et/ou plus scolarisés obtiennent des résultats moyens supérieurs aux sujets plus âgés et/ou moins scolarisés. L'analyse montre qu'il n'y a pas d'interaction entre les deux variables âge et scolarité, chacune agissant de façon indépendante. Les baisses de performance reliées à l'âge apparaissent surtout dans la troisième groupe d'âge (70 ans et +). Des analyses semblables seront appliquées à chacune des quatre autres épreuves pour voir si ces tendances se maintiennent. Une analyse préliminaire semble indiquer que la variable scolarité joue un rôle majeur dans l'ensemble des performances. Ces premiers résultats mettent en évidence la nécessité de données normatives dès lors qu'on s'intéresse à l'évaluation de la fonction linguistique dans le vieillissement normal et pathologique.

200.

Neuropsychological Aspects of Normal Aging: Evidence for Subgroups

S. VALDOIS, Y. JOANETTE, J. COULOMBE, F. FONTAINE, R. LABRECQUE, A. POISSANT and B. SKA (Montreal, Quebec)

There is an increasing number of studies pointing to the fact that there may exist subgroups among patients with dementia of the Alzheimer type (DAT) as defined on the sole basis of their neuropsychological features. This might reflect sub-types of DATs that could coincide with genetical and/or epidemiological features. However, it could also be that sub-types of DATs reflect, partly or totally, the existence of subgroups, among the normal aged population, that are characterized by their neuropsychological patterns. The aim of this study is to look for the possibility of such subgroups among 75 normal volunteers aged between 55 and 85 submitted to a neuropsychological protocol comprising 20 tasks, each of them addressing a specific aspect of cognitive functioning in either memory, language, praxes or gnoses. Results show the existence of subgroups that are not age-determined. Thus, cognitively-based subgroups of DATs could reflect, in part, the existence of subgroups among the normal aged population.

201.

Réduction de la Disponibilité Lexicale chez la Personne Agée Normale

C. POULIOT, P. GOULET et Y. JOANETTE (Montréal, Québec)

L'objectif de cette étude consiste a vérifier, chez l'adulte, la présence de modifications avec l'âge des capacités d'accès au lexique et ce, par l'entremise d'une épreuve de disponibilité lexicale. Ce type d'épreuve, couramment utilisée en neuropsychologie, exige la production du plus grand nombre de mots différents à l'intérieur d'une période de temps donnée et respectant des critères formels (e.g., mots débutant par la lettre B) ou sémantiques (e.g., noms d'animaux). Comparativement à la production sur critères formels, l'évocation lexicale à partir de critères sémantiques est constamment plus efficace dans l'étude de Joanette et Goulet (sous presse) quelque soit le temps écoulé, alors que cette efficacité diminue en fonction du temps de production écoulé dans l'étude de Rosen (1980). Or les sujets de Joanette et Goulet sont plus jeunes que ceux de Rosen (57.1 ans W 83.6 ans). Il est donc possible qu'il existe, avec l'âge, une modification des mécanismes d'exploration sémantique les plus volontaires lesquels seraient surtout importants après une première période de production assurée par une activation plus automatique du lexique. Les performances de 17 sujets âgés entre 40 et 60 ans ont donc été comparées à celles de 17 sujets âgés entre 70 et 85 ans. L'analyse des résultats tient compte du nombre de mots produits pour chaque type de critères (formels et sémantiques) et pour chaque tranche de trente secondes qui compose la période de deux minutes de production allouée pour chaque critère. Cette analyse révèle une interaction significative entre les facteurs groupe et type de critères, non affectée par le facteur temps. Selon cette interaction, les sujets les plus âgés produisent moins de mots pour chaque type de critères mais ce, de façon plus marquée quand les critères sont formels. Conformément aux propos de Rosen, cette interaction souligne la moindre flexibilité (cognitive) qui marquerait le vieillissement. De plus, elle suggère qu'avec l'âge les difficultés d'accès aux **formes lexicales** seraient plus marquées que celles d'ordre strictement lexico-**sémantique**. Toutefois l'absence d'influence du facteur temps ne permet pas de conclure quant au degré de volition des processus affectés.

202.

The Two Forms of Visual Spatial Neglect

G. PLOURDE, Y. JOANETTE, F. FONTAINE, C. RENASEAU-LECLERC and L. LAPLANTE (Ottawa, Ontario; Montreal, Quebec)

The purpose of this study was to substantiate the possible distinction between a minor and a major form of visual neglect. In order to do so, 36 left- (LBD) and 41 right-brain-damaged (RBD) patients were evaluated with a line cancellation test. Distribution of frequency of omissions according to number of subjects revealed a unimodal distribution for LBD but a bimodal one for RBD: in other words, both LBD and RBD subjects could evidence a minor form of visual neglect but only RBD group did show both a minor and a major form, both of these forms being independent (bimodal distribution). Given these results, either there are indeed two forms of visual neglect, each of which would correspond to the specific functional lesion of given mechanisms (bilateral low-level versus unilateral right high-level mechanisms), or these two forms correspond to the same impaired mechanisms whose actualization could be enhanced by the presence of other functional impairment, such as anosognosia.

203.

L'Adaptation au Déplacement Prismatique: Indice non Cognitif de Sénescence ou de Sénilité?

Y. JOANETTE, S. VALDOIS, P. GOULET, G. MARTIN, J. COULOMBE et A. POISSANT (Montréal, Québec)

Cette étude a pour but de juger de la pertinence du coefficient d'adaptation à la vision prismatique comme indice non cognitif de sénescence ou de sénilité cérébrale. Il est généralement établi que l'évaluation globale du fonctionnement intellectuel, telle qu'appréciée par l'Ottawa-Wechsler met en évidence une baisse des performances avec l'âge dans le cas de sénescence normale et/ou pathologique. Cette tâche constitue donc un marqueur cognitif de sénescence cérébrale. Rien ne permet cependant d'affirmer que les premières manifestations de sénescence sont d'ordre strictement cognitif. Certaines études soutiennent notamment que l'adaptation au déplacement prismatique qui requiert une certaine plasticité cérébrale et l'intégrité du système nerveux central, peut constituer un indicateur de sénescence cérébrale (Rey et al, 1982).

Dans le cadre de la présente étude, 87 sujets (78 sujets normaux répartis en 4 groupes d'âge et 9 sujets déments) ont été soumis à une épreuve d'adaptation au déplacement prismatique et ont été évalués à l'Ottawa-Wechsler. L'analyse des résultats montre une baisse significative des scores pondérés de l'Ottawa-Wechsler en fonction de l'âge chez les sujets déments comme chez les sujets neurologiquement sains. Les performances en adaptation au déplacement prismatique témoignent, quant à elles, d'une tendance à une moindre adaptation dans le cas de démence seulement. Ces résultats suggèrent que les manifestations de sénescence cérébrale, normale et pathologique, sont avant tout d'ordre cognitif. L'utilisation du coefficient d'adaptation au déplacement prismatique pourrait constituer un indice de sénilité si la tendance relevée dans cette étude se voyait confirmée sur une population plus large.

204.

Neglect of Far Peripersonal Space

P.A. SHELTON and K.M. HEILMAN (Gainesville, U.S.A.)

The manifestations of neglect are usually restricted to a specific spatial field, most often left hemispace as defined by the mid-sagittal plane. However, lower vertical neglect has also been reported, and neglect of near peripersonal space has been reported in monkeys. Recently we had the opportunity to test a patient with bilateral inferior temporal lobe lesions who appeared to have both upper vertical neglect and neglect of far visual space.

We tested for neglect in three dimensions of extracorporeal space using a line bisection task. Stimuli were oriented horizontally, vertically and radially away from the patient in the transverse plane. Unlike controls, he misbisected vertical lines 5.78 ± 2.08 cm below midpoint and radial lines 7.10 ± 1.95 cm toward his body. There was also a gradient of response whereby his error decreased when lines were moved closer to his body. The error was 2.59 ± 2.03 cm for vertical and 2.18 ± 1.62 cm for radial lines in near peripersonal space. These findings suggest the processes mediating visual attention to stimuli and activating responses are organized in terms of proximity to the body in 3-dimensional space and that focal lesions may disrupt these processes.

205.

Difficulté des Cérébrolésés Droits à Compléter des Phrases: Inadéquacité Partielle ou Totale des Réponses

P. GOULET et Y. JOANETTE (Montréal, Québec)

L'hypothèse d'une contribution de l'hémisphère droit du droitier au langage découle entre autres de l'étude des performances verbales de cérébrolésés droits (CD) (Hannequin, Goulet et Joanette, 1987). Jon Eisenson (1960) est un des premiers à avoir entrepris ce type d'étude de manière systématique. Ce chercheur rapporte que les CD connaissent certaines difficultés à compléter par un mot les phrases lacunaires qu'on leur présente et ce, surtout quand le mot à fournir est abstrait. Or, cette étude n'a jamais été reprise. Par ailleurs, Millar et Whitaker (1983) émettent certaines critiques à son endroit dont la plus pertinente veut qu'on ne sache pas si les réponses émises par les cérébrolésés droits sont totalement inadéquates ou simplement inattendues par la grille de correction utilisée. L'objectif de la présente étude consiste donc à reprendre la démarche d'Eisenson en s'attardant sur la qualité des réponses émises. Les performances de 31 droitiers porteurs d'une lésion d'origine vasculaire unique et unilatérale de l'hémisphère droit ont donc été comparées à celles de sujets non porteurs de lésion cérébrale. Les sujets avaient à compléter des phrases exigeant la production d'un nom concret dans cinq cas (e.g., Le bûcheron coupe un _____) et l'évocation d'un nom abstrait dans cinq autres cas (e.g., En cette société de luxe, les gens recherchent le _____). Les performances des CD corrigées en fonction de réponses attendues sont significativement inférieures à celles des sujets contrôles uniquement pour les phrases exigeant des mots abstraits. De plus, il n'y a pas de différence significative entre les deux groupes de sujets quand les réponses inattendues mais adéquates sont aussi considérées correctes. Les réponses des CD ne sont donc pas totalement inappropriées, ce qui peut expliquer que leur "déficit" verbal soit moins marqué que celui observé à la suite de lésion de l'hémisphère gauche. Reste que les CD ont plus de difficulté à spécifier les termes les plus appropriés quand les phrases semblent être sémantiquement moins contraignantes.

206.

Traitement Sémantique des Mots Abstraits après Lésion de l'Hémisphère Droit chez le Droitier

P. GOULET et Y. JOANETTE (Montréal, Québec)

La neuropsychologie actuelle prétend que, chez le droitier, le traitement sémantique des mots abstraits est exclusif à l'hémisphère gauche du cerveau alors que les deux hémisphères contribueraient au traite-

ment sémantique des mots concrets. Ils existe cependant quelques rares indications à l'effet que l'hémisphère droit contribuerait aussi au traitement sémantique des mots abstraits (Eisenson, 1960; Joanette et Goulet, 1984; Gainotti et al, 1983; Chiarello, 1986; Brownell et al, 1984). Une façon de la vérifier consiste à déterminer si le traitement du sens des mots abstraits est perturbé chez les cérébrolésés droits ce qui jusqu'à présent n'a jamais été fait de manière systématique. La présente étude porte sur cette verification. Des triades de noms abstraits (e.g., qualité-propriété-obsession) contenant chacune deux synonymes ou quasi-synonymes et un élément distracteur ont été présentés à 14 droitiers porteurs d'une lésion vasculaire de l'hémisphère droit sans évidence d'une atteinte de l'hémisphère gauche, et à 14 sujets non porteurs de lésions cérébrales. Pour chaque triade, les sujets devaient associer les deux mots qui allaient "le mieux ensemble". Les résultats recueillis jusqu'à présent montrent que la légère différence qui existe entre les cérébrolésés droits (x: 24.14; s: 6.1) et les sujets contrôles (x: 25.21; s: 4.17) n'est pas statistiquement significative. Une telle absence de différence significative doit être considérée avec prudence. Néanmoins cette étude suggère qu'une lésion de l'hémisphère droit n'entrave pas a priori le traitement sémantique des mots abstraits. Elle suggère aussi qu'un hémisphère droit intact n'est pas toujours indispensable au traitement des mots abstraits quand celui-ci repose essentiellement sur un savoir sémantique systématiquement organisé à la manière d'un dictionnaire conceptuel.

207.

Capacités Lexico-Sémantiques des Droitiers Porteurs d'une Lésion Hémisphérique Droite

L. SABOURIN, P. GOULET et Y. JOANETTE (Montréal, Québec)

La présente étude s'intéresse aux capacités lexico-sémantiques des cérébrolésés droits droitiers (CD). Une façon d'aborder ce thème consiste à soumettre ces sujets à une épreuve de disponibilité lexicale (DP) exigeant la production, dans un temps limité, du plus grand nombre de mots différents respectant un critère donné (formels: lettre du début; sémantique: catégorie sémantique). Par le passé, cette démarche a donné lieu à des résultats contradictoires. Parmi les facteurs susceptibles de rendre compte de ces divergences il y a la nature des critères utilisés et le degré de productivité qui leur est associé (Borkowski et al, 1967). Cette étude propose donc de manipuler la nature des critères afin de déterminer l'influence de ce facteur tout en contrôlant le degré de productivité associé à chaque type de critère (formel W sémantique). Les performances en DP de 19 CD ont été comparées à celles de 18 sujets neurologiquement indemnes. L'analyse des résultats montre qu'il n'y a pas de différence significative entre les deux groupes de sujets pour les deux types de critères employés. Il est donc permis de croire que les moindres productions des CD relevées par d'autres chercheurs (Laine, 1987; Laine et Neimi, 1988) reposent sur le degré de productivité des critères utilisés plutôt que sur la nature de ces derniers. La mise en évidence d'un déficit lexico-sémantique chez les CD dépendrait alors de ce premier facteur.

208.

Jugement d'orientation de lignes: Différence qualitative des performances des personnes âgés normales et des déments de type Alzheimer

A. POISSANT, N. PERREAULT, S. VALDOIS, J. COULOMBE, B. SKA et Y. JOANETTE (Montréal, Québec)

Benton et al (1978) ont développé un test clinique de jugement d'orientation de lignes standardisé auprès d'une population âgée normale. Des études récentes utilisent cette épreuve parmi un ensemble d'épreuves neuropsychologiques afin de caractériser le vieillissement normal et pathologique. Malgré l'intérêt croissant pour cette tâche, aucun chercheur ne s'est interrogé sur la nature des erreurs que les sujets y font. Les performances de sujets âgés neurologiquement sains (N = 80) et de sujets (N = 10) atteints de démence de type Alzheimer (DTA) ont été soumises à une analyse qualitative détaillée. Les différents types d'erreurs (erreurs sur la verticale, erreurs sur les horizontales, erreurs de quadrants, etc.) ont été répertoriés et analysés (fréquence). Les résultats de cette analyse montrent que certaines erreurs se rencontrent chez tous les sujets, contrôles et DTAs, tandis que d'autres sont spécifiques des DTAs. Il ressort de cette étude que l'analyse qualitative des performances obtenues à l'épreuve d'orientation de lignes peut aider à différencier la personne âgée normale d'une DTA en début d'évolution.

Epilepsy (Platform)

FRIDAY, JUNE 17TH — P.M.

209.

Educational and Psychosocial Morbidity in Typical Absence Epilepsy

J. ZAIDE, K. FARRELL, R. ARMSTRONG and P.K.H. WONG (Vancouver, British Columbia)

Although normal children with typical absence seizures tend to have normal intelligence, studies involving adults who have had absence epilepsy during childhood have demonstrated that between one-third and one-half experience social maladjustment.

We examined twenty-six children with typical absence seizures and 3/sec spike and wave on EEG. The age at onset of the absence was 3.25-11.0 (mean 7.5) years. The seizures were controlled at the time of the examination. The patients were receiving ethosuximide (9), valproic acid (14) and/or carbamazepine (2) alone or in combination. Three patients were on no medication. The evaluation consisted of a comprehensive battery of neuropsychological tests, a review of the school reports, a structured parent interview, a general family questionnaire completed by a parent and parent's responses to a Child Behavior Checklist.

Intellectual scores were normally distributed (Verbal 98, Performance 100, Full Scale 98). The mean subtest scaled scores were uniform and all were within average limits. In contrast, 40 to 70% of children displayed deficits in one or more areas of verbal fluency, fine motor co-ordination, visual sequencing or visuoconstructive pencil skills. Seventeen of 26 children (65%) were experiencing difficulty at school, particularly in work organization, retention and concentration. The children tended to have greater difficulty with mathematics than with reading or writing. Ten of the 23 children assessed showed abnormalities in emotional function and four had been referred to a psychiatrist. There was no consistent pattern in the types of emotional difficulty. These included anxiety or somatization (3), depression (3) and aggressive behaviour or difficulties in conduct (4). Four children demonstrated a mild to moderate degree of attention deficit.

This study demonstrates that children of normal intelligence with absence epilepsy frequently experience school difficulties and have a high incidence of psychosocial morbidity. In many children, the neuropsychological profile was consistent with posterior frontal lobe dysfunction but the role of medication and subclinical seizures cannot be excluded.

210.

Cerebral Cavernous Angiomas

J.-P. FARMER, G.R. COSGROVE, J.-G. VILLEMURE, K. MEAGHER-VILLEMURE and D. MELANSON (Montreal, Quebec)

We have studied 31 patients with histologically verified intracerebral cavernous angiomas. Twenty-two patients were symptomatic, 9 were asymptomatic. All 22 patients experienced seizures. Three patients experienced intracranial hemorrhage and one had signs of a space-occupying lesion. Twenty-seven lesions were located in the neocortex, 3 were found in the brain stem and one was identified in the cerebellum. Lesions exhibited characteristic gross and microscopic features of cavernous angiomas. CT identified the location and extent of the lesion in 16 of 27 cases. Six of seven lesions demonstrated contrast enhancement and 10 of 27 scans harbored densities consistent with intracerebral calcium. Angiography was performed in 17 cases and was completely normal in 8. MRI revealed mixed signal intensity centrally with a ring of deceased signal intensity peripherally on T2 weighted images and was diagnostic in 5 cases. Surgical treatment offers an excellent prognosis for the cure of epilepsy in patients harboring such lesions.

211.

Comparison of Frontal and Temporal Lobe Epileptic Manifestations

J.M. SAINT-HILAIRE, N. GIARD, F. VEILLEUX, G. BERNIER, M. MERCIER, I. ROULEAU, A. TURMEL and G. BOUVIER (Montreal, Quebec)

To compare temporal with frontal lobe epileptic manifestations, we studied 52 seizures of temporal lobe patients (14 patients: 7 right, 7 left) which remained localized in one temporal lobe without diffusion to other lobes including the contralateral temporal lobe. All patients had depth electrodes in both frontal lobes as well as in both temporal lobes. We analyzed 259 manifestations including "aura" (127 right temporal and 132 left temporal). They were called "pure" temporal manifestations. At the same time we studied "pure" frontal lobe seizures that is seizures without diffusion outside the frontal lobes (11 patients, 20 seizures, 87 manifestations).

Consciousness is preserved in 74% of temporal lobe seizures. In "pure" frontal lobe seizures, preservation of consciousness is difficult to evaluate when analyzing the manifestations on video. The "pure" frontal seizures are of short duration (usually less than 30 seconds), but as far as we can see consciousness is altered in most of the seizures. No hallucinations were reported in the frontal patients and they were reported infrequently in the temporal cases (3%: taste and smell only). Emotions were noted in 7% of frontal manifestations and 11% of temporal. Visceromotor and viscerosensitive manifestations were more frequent in temporal (25%) while only 4.6% in frontal. But the most characteristic difference came from the motor manifestations (tonic, clonic or head and eyes deviation). The motor manifestations represented 60% of all "pure" frontal manifestations and only 1.5% of "pure" temporal manifestations. While head and eyes deviation accounted for 20.7% of all frontal manifestations (5/11 patients) none was recorded in temporal cases. Automatisms were equally represented in both localization (11.5%) in frontal and no oro-alimentary; 16.2% in temporals and mostly oro-alimentary). Behavior manifestations were slightly less frequent in frontals (11.5%) than in temporals (20%). Motionless staring happened in 1% of frontal and 2.7% of temporal manifestations.

212.

Clobazam in Refractory Epilepsy: Preliminary Results

N.H.H. OTTEN and N. PILLAY (Winnipeg, Manitoba)

Clobazam was initiated in an open trial as adjunct medication in 29 therapy-resistant epileptic patients ranging in age from 15-51 years. Assessment of adverse effects and efficacy were carried out through the maintenance of seizure records, electroencephalograms, physical examinations, personal interviews and laboratory tests.

All but 3 of the 29 patients had mixed seizures. Twenty-one had complex partial seizures, 19 of whom also had generalized seizures. The other 8 patients had a generalized seizure disorder (5 with tonic-clonic, 7 with atypical absence and 5 with atonic seizures). Doses required ranged from 10 to 75 mg (mean 40 mg/day). Length of therapy ranged from 3 to 30 months with a mean of 8 months. Six patients had minimal or no response, 5 had increased seizures, 5 with 50% reduction, and 13 (45%) with greater than 75% reduction, 4 of whom had complete control. Complete tolerance developed in 2 patients within 3 months while 3 patients exhibited partial tolerance requiring increased doses. Four of 7 patients with atypical absence had increased seizures while 2 had greater than 75% reduction. Temporary adverse effects (primarily sedation and lethargy) were noted in 18 patients (62%) requiring reduction of clobazam or other antiepileptic drugs in 11 patients. Six patients showed marked improvement in affect.

Patients with complex partial seizures appeared to receive the most benefit on clobazam while patients having primary generalized seizures, especially atypical absence, are more likely to deteriorate. Adverse effects occur early, are usually mild, and can be overcome by more slowly titrating the dose of clobazam or decreasing the doses of concurrent medications.

213.

Reoperation in Temporal Lobe Epilepsies

A. OLIVIER, T. TANAKA and F. ANDERMANN (Montreal, Quebec)

Out of a series of over 400 cases operated for temporal lobe epilepsy, 20 patients who continued to have seizures and subsequently had further removal of epileptogenic brain tissue were retrospectively evaluated. Following a first surgery there was no significant or substantial improvement in seizure tendency in these patients. In this series of temporal resection a total of 65% of the patients had preservation of the hippocampus and 35% had only a subtotal removal at the time of the first operation. Following a second operation and more radical removal of the hippocampus and in a few cases, additional corticectomy; 80% of the patients had a successful result (30% became seizure free, 15% had marked improvement, 35% had significant improvement and 20% had no improvement). The basis for improvement appears to be the more radical hippocampal resection. The results of these studies underline the role of the hippocampus in the occurrence of seizures and the importance of its adequate removal at the time of surgery.

214.

Surgical Outcome of Selective Cortectomies in Frontal Lobe Epilepsy. A Retrospective Study

A. TURMEL, G. BOUVIER, J.M. SAINT-HILAIRE and N. GIARD (Montreal Quebec)

Thirty-one (31) patients with chronic frontal lobe epilepsy resistant to medical treatment were operated during 1973-1986. Preoperative evaluation consisted of: 1) history of seizures; 2) scalp EEG; 3) cerebral angiogram; (4) CT scan (more recently NMR); 5) depth electrode recordings and 6) for some, neuropsychological evaluation.

Patients were treated according to depth electrode recordings: a) when epileptic discharges were well lateralized and localized to one frontal lobe, patients were subjected to selective cortectomies with or without anterior callosotomies (24 patients); b) when epileptic discharges were diffused at onset or localized to both frontal lobes, patients were subjected to callosotomies only (7 patients).

Results of selective cortectomies were evaluated according to the outcome classification of Engels, CLASS 1 — Seizure free (8 patients), CLASS 2 — Rare seizures (3 patients), CLASS III — Worthwhile

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improvement being 90% reduction in seizure frequency (5 patients), CLASS IV — No worthwhile improvement (8 patients).

Thus, 16 out of 24 patients benefited from this intervention. Selective frontal lobe cortectomy can be a worthwhile option for patients debilitated by chronic frontal lobe epilepsy.

215.

Adrenergic Stimulated Inositol Phospholid Metabolism in Human Epileptic Cortical Slices

F. DUBEAU, A. OLIVIER, J-G. VILLEMURE, R. LEBLANC, F. QUESNEY, F. ANDERMANN, E. ANDERMANN, M. DE ROODE, D. GUEVREMONT and A. SHERWIN (Montreal, Quebec)

Alpha-1 adrenergic receptors are known to stimulate membrane phosphoinositol (PI) turnover in neural tissues. There are strong arguments suggesting that this inositide-linked second messenger system is involved in cellular signal transduction and contributes to mobilization of Ca^{2+} from intracellular stores. This calcium gating effect may play an important role in the regulation of cortical neuronal excitability. We analysed the action of epinephrine (E), an adrenergic agonist, on the activation of PI breakdown in brain specimens obtained from 18 patients with intractable epilepsy. Electrographic recordings performed during surgery showed active spiking cortex in 13 patients while in 5 cases no surface epileptic activity was recorded (nonspiking). Tissues were rapidly dissected and fresh cortical slices (350μ) labeled with 2-(^{3}H) myoinositol and incubated with various concentrations of E (0-90μM). Tritiated inositol-1-phosphate (IP_1) accumulation was measured following ion exchange chromatography (Berridge, 1987). Basal and agonist stimulated IP_1 values were compared for each experiment. The maximal effect (Emax) and EC_{50} were calculated by linear regression. Preliminary results show a trend toward decrease efficacy (Emax) of agonist stimulated IP_1 accumulation in spiking cortex ($P<0.05$, one tailed t test): Spiking ($N=13$), Emax = 572±39 (mean % above basal ± SEM), $EC_{50}=3.6$ μM±0.7 and nonspiking ($N=5$), Emax = 743±93, $EC_{50}=5.6$ μM±1.3. The data is in keeping with our previous findings of a decreased number of cortical alpha-1 adrenoceptors in spiking human cortex. The central adrenergic system appears to play a role in the pathobiochemistry of human focal cortical epilepsy perhaps in an attempt to dampen the intensity and propagation of the epileptic discharge.

216.

Successful Desensitization of Patients With Carbamazepine Allergy

S.J. PURVES, S.A. HASHIMOTO and K.S. TSE (Vancouver, British Columbia)

Five patients with partial complex seizures and a history of diffuse dermatitis from previous carbamazepine (CBZ) treatment were subjected to a protocol of "desensitization" to CBZ because their seizures could not be well controlled by other drugs. The starting dose of CBZ 2.5 mg daily (given in a 1 mg/ml suspension) was doubled every 3 days along with the concomitant administration of an antihistamine, astemizole 1 mg daily. When a mild allergic reaction occurred, the CBZ dose was reduced to the previous, tolerated level and maintained for 6 days before further increases. A final therapeutic dose of 400-600 mg per day with a corresponding, adequate serum level of CBZ could be achieved in all four patients, resulting in a significant improvement in the control of their seizures. Improvement has been sustained for 2-4 years. No serious adverse reaction was encountered and no abnormality in hepatic function, serum chemistry and hematologic parameters was observed during and at the end of the desensitization protocol.

217.

Seizures in Patients Receiving Cyclosporin A

R.E. APPLETON, K. FARREL, P. TEALE and S.A. HASHIMOTO (Vancouver, British Columbia)

Cyclosporin A (CyA) is an immunosuppressive agent that is effective in the prevention of graft versus host disease and solid organ rejection. Coma, abnormal behaviour, seizures, aphasia, cerebellar dysfunction and tremor have been described in patients receiving this drug. The etiology of the seizures is unclear but hypomagnesaemia, elevated blood levels of aluminum, hypertension, the concurrent use of steroids or methotraxate and a possible effect of CyA have been postulated as possible mechanisms. We describe four patients (three children post-renal transplant and one adult post-bone marrow transplant) who developed seizures when receiving CyA.

Two patients presented initially with abnormalities in behaviour, became stuporose and were demonstrated to be in complex partial status epilepticus. Complex partial status epilepticus has not been described previously in patients receiving CyA. In one patient an electroencephalogram (EEG) recorded during the stupor demonstrated continuous spike and wave discharges arising from the right frontal lobe. Treatment with intravenous diazepam was associated with a cessation of the spike and wave discharges and a rapid return to an alert state. In a second patient, an EEG recorded during a period of abnormal behaviour demonstrated background slowing with bursts of sharp and slow wave activity arising independently from both frontal lobes. Treatment with intravenous lorazepam during a separate episode of abnormal behaviour was associated with an immediate return of normal behaviour. The other two patients presented with brief, generalised tonic/clonic seizures. The seizures were associated with hypomagnesaemia (4 patients), hypoalbuminaemia (3 patients), mild hypertension (4 patients) and low/normal blood cyclosporin levels (4 patients). All four patients were receiving corticosteroids. Interictal EEG's and computed tomography scans of the head were normal in the four patients.

Abnormalities of behavour and/or stupor in patients receiving CyA may be a manifestation of complex partial status epilepticus. Thus, electroencephalography should be performed at the time of the abnormal behaviour. The underlying basis for the seizures in our patients is not clear. Hypomagnesaemia and mild hypertension were present in all four patients but the cyclosporin blood levels were in the lower half of the therapeutic range.

218.

Analysis of Drug-Induced Abnormalities in Routine Electroencephalograms (EEG's)

D.F. WEAVER (Kingston, Ontario)

The influence of neuroactive drugs upon EEG patterns and upon the ultimate diagnostic usefulness of electroencephalography requires greater clarification. To ascertain the incidence and clinical relevance of drug-induced EEG alterations, a protocol for EEG analysis and classification was devised. From an overall study population of 20,786 EEG's, 9,219 EEG's, recorded from 7,140 patients, were randomly selected and analyzed. Employing the study protocol, drug-induced alterations were characterized and described. Enhanced beta activity (type 1 effect), attenuated alpha activity (type 2 effect), augmented theta activity (type 3 effect), and potentiation of paroxysmal potentials (type 4 effect) were the commonest forms of drug-induced alteration. Two hundred and sixty-two commonly used pharmacologic agents were studied; 99 (37.8%) of these agents demonstrated a capacity to induce EEG alterations. Benzodiazepines were the drugs most frequently implicated, being responsible for 15.6% of all drug induced alterations identified in this study. Of the 497 patients taking benzodiazepines, 92

(18.5%) had drug-induced EEG abnormalities. Phenothiazines, butyrophenones, hydantoins and barbiturates were other significant inducers of EEG abnormalities. Importantly, drug effects were also identified for non-neurologic, non-psychiatric drugs, including cimetidine and propantheline. Drug-induced EEG effects did not correlate proportionately with drug doses and may persist days after medication discontinuation. Drug-induced EEG alterations are frequent, and must be considered when interpreting EEG results in the context of the clinical setting.

219.

HMPAO-SPECT in Epilepsy

G.B. YOUNG, R.S. McLACHLAN, W.T. BLUME, A. DRIEDGER and W. VEZNIA (London, Ontario)

Hexamethylpropyleneamineoxime (HMPAO) is a lipophilic molecule which enters brain on first pass through the vasculature. When coupled with ^{99m}Tc, its brain penetration can be imaged using single photon emission computed tomography (SPECT).

We performed HMPAO-SPECT scans on 24 patients with partial seizures. Only 2 had demonstrable structural lesions on CT or MRI scans — one arteriovenous malformation and 1 low grade tumor. The 2 patients studied ictally showed increased uptake only at the clinical-EEG focus. Of the 2 studied immediately post-ictally, 1 had reduced activity at the presumed focus and 1 was normal. Only 6 of the 20 patients studied inter-ictally showed an abnormality: reduced uptake at the clinical-EEG focus. The patient with the arteriovenous malformation showed reduced uptake while the patient with tumor was normal.

Although the HMPAO-SPECT scan may prove useful when epileptic patients are studied ictally, it shows, at best, only modest sensitivity in the interictal state.

220.

Characterization of EEG Spikes

P.K.H. WONG and R. BENCIVENGA (Vancouver, British Columbia)

We report a method of analysis of interictal spikes that allowed differentiation of clinical subtypes of 24 children with benign Rolandic epilepsy of childhood (BREC), based on a formal non-parametric statistical procedure.

Earlier reports had suggested that the interictal spike of patients with BREC had a distinct character, and that visual analysis may be able to distinguish them from those children who had BREC seizures and EEG focus, but had some abnormal clinical findings: neurological or intellectual deficit, learning disability etc. (i.e. atypical group). Parameters derived from spikes of both "typical" and "atypical" cases (12 each) were subjected to the Classification and Regression Tree (CART) analysis. A classification rule was constructed yielding 80% accuracy based only on the location and amplitude of the negative and positive peaks.

This explorative method requires no assumption of data properties (i.e. normal distribution), is immune to correlation between variables, and is not influenced by non-contributory variables. It is ideally suited to the analysis of topographic EEG data.

Epilepsy (Poster)

THURSDAY, JUNE 16TH - P.M.

221.

Status Epilepticus and Seizure Enhancement: Relationship to Clobazam

N. PILLAY, N. OTTEN and L. FINLAY (Winnipeg, Manitoba)

The availability of clobazam, a 1,5 benzodiazepine, as an add-on drug for treatment of uncontrolled epilepsy has generated enthusiastic reports on its efficacy, but a paradoxical increase in seizures or precipitation of status epilepticus as unwanted effects of clobazam have not been emphasized.

Twenty-nine adult patient with refractory epilepsy received clobazam, as an adjunctive drug. Response was favourable in 18 patients, 16 of whom had complex partial seizures. Five of the 11 non-responders had profound and serious exacerbation of seizures. Except for one patient with complex partial and atonic seizures, the other 4 patients had a mixed primary generalized seizure disorder (atypical absence and generalized tonic-clonic). Of the latter group 2 patients also had daily atonic seizures.

Temporary benefit in seizure control was experienced by all 5 patients at the start of treatment, however, exacerbation of seizure frequency and severity appeared within 2-3 months of clobazam in the 4 patients with the generalized seizure disorder and after 8 months of treatment in the one patient who also had complex partial seizures. Convulsive and nonconvulsive status epilepticus was precipitated in one patient. Electrographic confirmation of augmented seizures was obtained in 3 patients with generalized epilepsy and all 3 showed stereotyped ictal patterns. Seizure control and functional improvement coincided with clobazam withdrawal.

We concluded that:

1. while therapeutic benefit in intractible, complex partial seizures was remarkable (16/18), precipitation of status epilepticus and potentiation of habitual seizures were serious drawbacks in a minority (5/29).
2. individuals with generalized absence seizures (4/7) were at greater risk for exacerbation.
3. the complications tended to appear within the first 3 months of treatment.
4. recognition of undesirable consequences should prompt clobazam withdrawal.

222.

Recurrent Nonconvulsive (Triphasic Wave) Stupor and Chronic Cerebellar Ataxia in Adult Coeliac Disease

N. PILLAY and C.M. DEL CAMPO (Winnipeg, Manitoba)

The incidence of neurological complications which can be quite diverse in adult coeliac disease (ACD) is about 10% (Finelli et al 1980). Cerebellar ataxia (CA) and seizures are not infrequent (Cooke and Smith 1966). We now report a patient with chronic CA and recurrent nonconvulsive triphasic wave stupor in ACD, a finding not previously described.

A 63 year old lady was initially admitted with unexplained stupor to the ICU in 1981. Facial twitchings were observed. The EEG was interpreted to show continuous epileptiform abnormality. She was treated with phenytoin. On recovery in 4 days she was found to have dysarthria, truncal and appendicular ataxia. The CA was apparently present since 1975. In 1984, she was admitted for the fifth time in stupor. On this admission mild liver dysfunction was detected. The suspected diagnosis of ACD was confirmed on jejunal biopsy. She had low vitamin E levels. There was no generalized fat malabsorption. The

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patient declined a liver biopsy. All presentations were stereotyped: gradual obtundation to stupor in 12-24 hours. Recovery was also slow over 2-4 days. Prior to establishing the primary diagnosis, follow-up and compliance to phenytoin treatment was suboptimal. Failure to adhere to recommended dietary measures led to another admission, also in stupor in 1986. All EEG recordings taken when she was stuporous were identical. Clear distinction between epileptiform and non-epileptiform triphasic waves was not possible in some recordings. However, several EEGs did show typical triphasic waves with frontal-occipital delay.

We propose that intermittent stupor in this patient is due to hepatic dysfunction which can be deceptively mild. The CA is secondary to vitamin E deficiency. Early recognition is essential for proper diagnosis and prompt initiation of specific therapy.

223.

Discontinuation of Medical Therapy in Seizure-Free Patients After Resective Surgery for Epilepsy

J. BRUNI (Toronto, Ontario)

The successful outcome of resective surgery for the treatment of partial seizures is in the range of 70-80 percent. Forty to 60 percent are seizure free. Few studies have addressed the issue of discontinuation of drug therapy after resective surgery. We report our observations in a series of 20 epileptic patients (15 males and 5 females) who were selected for surgery after clinical neuroradiologic, EEG, and neurophysiologic evaluations.

A unilateral temporal lobectomy was performed in 19 patients and a frontal resection was performed in 1 patient. Fifteen patients (75 percent) remained seizure free for two years when antiepileptic drug monotherapy was discontinued. After discontinuation of drug therapy, twelve of these 15 patients (80 percent) remained seizure free at time of follow up, range 2 to 3 years. Two patients required re-institution of drug monotherapy after a recurrent seizure and remained seizure free. One patient was reluctant to discontinue medication.

We conclude that post-operative patients who remain seizure-free on medical therapy post resective surgery for two years are candidates for gradual discontinuation of drug therapy.

224.

Frontal Lobe Epilepsy: A Surgical Series

P.M. DEMONTE, W.T. BLUME and J.P. GIRVIN (London, Ontario)

Frontal lobectomy for therapy-resistant epileptic seizures was performed in 36 patients (21% of epilepsy operations, 1974-1987).

Over a minimal follow up period of 6 months (mean 3.5 years) 12 (33%) are seizure-free, 8 (22%) are >90% improved, 10 (28%) are 50-90% improved, and 6 (17%) are not helped. Effectiveness for the 20 patients with tumors is similar to that of the 16 patients with other lesions. 19 of the 36 patients (53%) had grand mal, 18 (50%) had complex partial seizures with prominent motor components, and 15 (42%) had simple partial (motor) attacks. 15 patients (42%) had more than one type of seizure. Effectiveness of surgery correlated better with resectability of the lesion than with seizure type.

Surprisingly, outcome is no better for the 18 patients with EEG recorded seizures originating over the lobe to be resected ("resected lobe") than among the remaining patients. This included 16 patients without a recorded seizure, 1 with immediate bilateral ictal activity, and 1 with diffuse onset over the ipsilateral hemisphere.

Interictal EEG spike location better forecast surgical success: 12 of 13 patients (92%) whose spikes were confined to the resected lobe benefit from surgery while 6 of 8 (75%) with focal spikes beyond the resected lobe helped. Moreover, 6 of 13 patients (46%) whose spikes were confined to the resected lobe are seizure-free while only 2 of 14 (14%) with focal spikes outside the resected lobe are seizure-free. All 5 patients with generalised spike wave discharges improved.

225.

Gangliogliomas Associated with Complex Partial Seizures: An Epilepsy Surgery Series

S. GAYTAN-GARCIA, W.T. BLUME and J.C.E. KAUFMANN (London, Ontario)

Of 264 lobectomies and corticectomies, tumors were found in 94 (35%). Of these 94,8 (8.5%) ere gangliogliomas, all of which were found in the temporal lobe.

Complex partial seizures compatible with a temporal lobe origin occurred in 7 patients and a simple partial seizure of presumed temporal lobe origin in the 8th. Four patients had associated grand mal seizures. Median age of seizure onset was 19 months (mean = 5 years, 5 months; range = 5 months - 13 years). Median age of surgery was 14 years (mean = 19 years; range = 10 - 41 years).

Complex partial seizures arising from the tumorous temporal lobe were EEG-recorded in 5 of the 8 patients while the other 3 had subclinical EEG seizures in this region. All patients had focal temporal delta and spikes on at least one recording. A right occipitally originating seizure occurred in one patient. Generalised spike and waves occurred in 3, multiple independent spikes in 2, bitemporal spikes in 1 and non-specific abnormalities in 2 patients.

Pre-operative CT scans disclosed temporal lobe lesions in 7 of the 8 patients; of these calcification appeared in 2.

Follow up data and any distinguishing data will be presented.

This series of 8 temporal lobe gangliogliomas appears to be larger than any thusfar reported. Babb and Brown (1987) report 2 gangliogliomas among 129 temporal lobectomies while the reports of Mathieson (1975) and Falconer (1964) do not specifically mention gangliogliomata.

226.

Periodic Lateralized Epileptiform Discharges, Afterdischarges and Seizures

J. REIHER, J. RIVEST, M. VEILLEUX and C.P. LEDUC (Sherbrooke, Quebec)

Observations from a study of 202 EEG records in 80 patients have led us to propose an original classification of periodic lateralized epileptiform discharges (PLEDs) into two main categories.

PLEDs proper consist of uniform PLEDs separated by prolonged and variable intervals; and of those occurring with a metronomic periodicity, either intermittently or consistantly throughout the recording.

PLEDs plus include complex PLEDs with striking afterdischarges, occurring singly (monopleds) or in groups (diplopleds, tripleds, polypleds).

It is an acknowledged notion that the prevalence of seizures and of altered consciousness is very high in populations of patients with PLEDs. Our data calls for the following precisions:

1. Identification of PLEDs' afterdischarges as a marker separating PLEDs plus from PLEDs proper provides a better frame for a more meaningful categorization of clinical manifestations.
2. PLEDs plus superseding PLEDs proper signals clinical deterioration, the reverse clinical improvement.
3. Recorded seizures, or seizures within hours of the recording are much more prevalent with PLEDs plus.
4. Status epilepticus, often yielding only to I.V. Thiopental, are recorded exclusively in patients with PLEDs plus.
5. Afterdischarges, when present, call for close supervision, and vigorous treatment.

227.

Phenytoin Suspension: "Not Shaken, Not Stirred"

D. RANKINE and M. SADLER (St. John's, Newfoundland)

Occasional unsubstantiated statements in the literature contend that phenytoin (PHT) suspension preparations may lead to significant variations in dosing if the manufacturer's directions for agitation prior to measuring a dose are ignored. The present study was designed to measure changes in PHT concentrations over time in 2 commercially available products (Dilantin-125 and Dilantin-30; Parke-Davis Canada).

One 250 ml bottle of Dilantin-125 was thoroughly agitated and a 10 ml sample decanted as the 'reference' concentration. Over the next 3 weeks 10 ml samples were obtained once daily with care taken to *avoid* agitation of the parent bottle. An identical procedure was followed for the Dilantin-30 preparation except 15 ml samples were decanted daily for 16 days.

At the end of the study period the PHT concentration of each sample (after appropriate dilution) was measured by fluorescence polarization immunoassay (TDx Analyzer; Abbott Laboratories Ltd). The maximum variability of PHT concentration inherent to our technique was calculated to be ± 11%.

The Dilantin-125 derived samples from days 2-20 showed no PHT concentrtion that fell outside ± 11% of the 'reference' value; on days 21 and 22 PHT concentration fell to 60% and 73% of the 'reference' value, respectively. The Dilantin-30 derived samples had no PHT concentrations that fell outside ± 11% of the 'reference' value except on days 9 and 12 (80% and 86% of 'reference' value, respectively).

We conclude that PHT concentrations in PHT suspension are very uniform even if agitation is neglected. Episodes of PHT intoxication or subtherapeutic serum levels should not be ascribed to insufficient mixing of suspension but more likely are due to improper measurement of dose or other factors known to alter PHT serum levels.

228.

Frontal Lobe Epileptic Seizures Studied with Depth Electrodes

J.M. SAINT-HILAIRE, F. VEILLEUX, N. GIARD, G. BERNIER, M. MERCIER, I. ROULEAU and G. BOUVIER (Montreal, Quebec)

Thirty-one patients were operated for frontal lobe epilepsy in our program of University of Montreal (Hôpital Notre-Dame) from 1973 to 1985. All patients have been investigated with depth electrodes (SEEG). The implantation included at least 3 electrodes in each frontal lobe, exploring the mesial (SMA and cingular gyrus) as well as the external cortex, both temporal lobes and frequently the parietal lobes. Thirteen patients were selected for the present study. Two hundred and fifty-four clinical manifestations (63 seizures) were analysed in details on video exactly correlated with the anatomical structures involved by the epileptic discharge at the same instant.

Motor manifestations (66.1%) excluding motor generalization clearly outnumbered any other manifestations. Head and eyes deviations (homo or contralateral) represented 26.8% (10/13 patients) of all the manifestations. Tonic seizures (tonic extension or flexion of 4 limbs, elevation of superior limb uni or bilateral, tonic grimacing or spouting) accounted for 31.8% of manifestations. Automatisms (7.1%), emotions (5.1%), autonomic visceral (2.8%) were evidently less frequent. To correlate more precisely the manifestations with the involvement of the frontal lobes, we studied 30 seizures (87 manifestations, 11 patients) which remained localized in the frontal lobes without any diffusion in the other lobes. The type and frequency of these "pure frontal" manifestations remained the same as when the epileptic discharge diffused outside the frontal lobes. The only exception being motor generalization which never happened in "pure" frontal lobe and was seen in 46.5% of "diffused" frontal lobe seizures.

Although most of the seizures started on the mesial aspect of the frontal lobes (SMA or cingular gyrus) a large number of structures in both frontal lobes were always involved at the time of the appearance of the first clinical manifestations. Exact clinical correlation with anatomical structures was thus impossible.

229.

Morphea or Focal Scleroderma of the Brain: Intractable Epilepsy and Clinicopathological Correlation

F. DUBEAU, F. ANDERMANN, Y. ROBITAILLE, A. OLIVIER, R. WILKINSON and A. DELGADO-ESCUETA (Montréal, Québec; Los Angeles, U.S.A.)

We present a 45 year old man who at the age of 42, developed intractable partial complex seizures of focal onset arising in the left frontal lobe. At the age of 4 years, he sustained a severe abrasion of the forehead on that side, which healed with no apparent sequelae. In the third decade of life, a linear scar "en coup de sabre", gradually increasing in depth and extent, appeared over the left frontal region.

An abnormal signal obtained from the left frontal lobe by MRI. Ictal and interictal EEG discharges were recorded from the same area. A limited and later a more extensive surgical removal were undertaken leading to considerable improvement in seizures. The epileptogenic brain tissue removed at surgery showed chronic inflammatory changes with both peri-vascular infiltrates and scattered microglial nodules in deeper cortical laminae. There was also marked neuronal loss, gliosis and evidence for remote contusion.

Morphea or focal scleroderma is known to affect all layers of tissue from the skin to the underlying brain. To our knowledge, the pathological changes in the brain associated with the characteristic skin lesions have not been previously described. Focal scleroderma is known to be associated with electroencephalographic abnormalities or with controllable partial seizures but may also present, as in this case, with intractable epileptic attacks. The mechanism of the progressive process leading to the inflammatory changes described in this patient remains uncertain.

230.

Decoupures de Journeaux et Extraits de la Collection E.P. Chagnon. *Pour servir à l'histoire de la réhabilitation de l'épileptique à Montréal.*

G.M. REMILLARD (Montréal, Québec)

En 1904, G. Villeneuve aliéniste et neurologue, regrettait qu'il n'existait pas d'assistance publique pour les épileptiques dans la province de Québec et que la philantropie ne leur avait pas encore élevé d'établissements spéciaux. Il remarquait que pour un grand nombre, les parents, les amis, les pouvoirs publiques cherchaient à obtenir leur internement dans les établissements d'aliénés qui paraissaient leur seul refuge.

Le travail du dispensaire de neurologie de l'Hôpital Royal Victoria de Montréal ayant été divisé en février 1920, le soin des épileptiques au nombre de 12 ou 15 fut assigné à Arthur G. Morphy, assistant du département de neuropsychiatrie et une école industrielle "pour les épileptiques et les faibles d'esprit" était fondée et incorporée.

Après celle du Children Memorial Hospital, s'ouvrait à Montréal, en 1926, une école primaire à l'Hôpital Ste-Justine pour les petits estropiés, paralytiques, épileptiques, etc. S'ajoute au programme scolaire un enseignement professionnel (1928). Inauguration de la première colonie permanente d'été: le camps Le Grillon (1930). En 1932, l'école des petits infirmes s'appellera Ecole Victor Doré (108 infirmes et 37 épileptiques). 1933, fondation à Montréal au siège social de l'aide aux infirmes, des établissements Notre-Dame, incluant une école primaire, un cours de métier et une clinique médicale destinés exclusivement aux épileptiques éducables et subventionnés par l'Assistance Publique.

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1942, installation des établissements Notre-Dame, sur l'Ile-aux-Cerfs (70 épileptiques) à St-Charles sur Richelieu.

En 1946, s'ouvre le foyer Dieppe pour épileptiques éducables de la province de Québec complété grâce au travail de George A. Savoy, un homme d'affaires de St-Jean et président du Foyer Dieppe, ainsi que la générosité de plusieurs. De cette dernière institution naîtra en 1971, la Fondation Savoy.

Neuroradiology (Platform)

FRIDAY, JUNE 17TH - P.M.

231.

Intracranial Hemodynamics in Carotid Occlusion

A. KRAJEWSKI, L. CHADWICK and J.W. NORRIS (Toronto, Ontario)

Carotid endarterectomy in patients with asymptomatic carotid stenosis remains a highly-controversial topic. Although the severity and progression of of the stenosis correlate with ischemic cerebral events, at present there is no way to detect a high-risk subgroup which would justify surgery. However, allowing carotid stenosis to progress to occlusion has been termed failure of medical management.

To determine the contribution of the patent carotid artery to cerebral blood flow in 20 patients with unilateral carotid occlusion, we evaluated them using transcranial Doppler. Blood flow velocities in the middle cerebral artery during compression of the patent carotid artery were measured to evaluate the dependency of each hemisphere on the patent carotid. Cerebrovascular reactivity to CO_2 in each hemisphere was also determined using 5% CO_2 inhalation.

On the patent artery side, 10 hemispheres were totally dependent, 5 partially, and 5 were totally independent of the patent carotid. On the "occluded" side, 11 hemispheres were independent, 9 partially dependent and none was totally dependent. There was no difference in CO_2 reactivity between the two sides, but on the patent side CO_2 reactivity was inversely related ($r = -0.8$) to the degree of the stenosis when the hemisphere was highly dependent.

These tests of collateral blood supply may prove valuable in the decision to allow carotid stenosis to progress to occlusion or to perform prophylactic endarterectomy.

232.

Doppler Monitoring in Cerebral Trauma

A. KRAJEWSKI, C.Z. ZHU, M.L. SCHWARTZ and J.W. NORRIS (Toronto, Ontario)

Neurosurgical management of severe head injury patients is largely guided by monitoring of intracranial pressure (ICP), but this involves invasive surgical procedures.

To determine the efficacy of transcranial Doppler (TCD) as a non-invasive method of serially recording ICP we simultaneously recorded daily TCD readings in conjunction with ICP measurements available via a Richmond screw.

Ten patients were evaluated over periods varying from 3 days to 3 weeks. TCD recordings of middle cerebral artery (MCA) velocities showed close correlation with ICP readings. Rising MCA velocities often preceded a rise in ICP. Change in waveform shape was also a valuable predictor.

This pilot study indicates that TCD is a valuable adjunct to management of head injury patients and may replace ICP readings in some cases.

233.

Angioguided Stereotactic Biopsy. Results in 200 Supra Tentorial Brain Lesions

L. JASMIN, G. BOUVIER, C. MERCIER, F. ROBERT and J. LESAGE (Montréal, Québec)

Brain imaging obtained by CT or NMR has modified greatly our phisolophical approach to brain lesions. Some lesions, whether single or multiple, which are not polar or even located in functional brain areas, cannot be treated by open surgery. Stereotactic biopsy thus becomes a precious tool. 800 stereotactic biopsies were performed on 200 patients. A precise diagnosis was obtained on 90% of our patients. We encountered only one major complication. This very low rate of complications is directly related to the use of stereotactic-stereoscopic angiography.

When an histological diagnosis is needed, stereotactic biopsy is now the most reliable and harmless technique.

234.

Brain Arteriovenous Malformations: Analysis of the Angioarchitecture in Relationship to Hemorrhage

R. WILLINSKY, P. LASJAUNIAS, K. TERBRUGGE and P. PRUVOST (Le Kremlin Bicetre, France; Toronto, Ontario)

The authors studied the charts and angiograms of 178 patients with cerebral vascular lesions explored and/or treated at the Hopital de Bicetre between 1981 and 1986. The angiographic features of the arteriovenous malformations (AVMs) could be grouped into the following categories: arterial variations, arterial aneurysms, arterial infundibulum, arterial stenosis, venous variation, venous stenosis, venous ectasia, arteriovenous fistula, trans-cerebral vascularization and external carotid supply. The age and sex of the patients as well as the topography and angiographic features of the malformations were correlated with the incidence of hemorrhage. We found that deep and posterior fossa malformations were more likely to have bled. Arterial aneurysms and venous stenosis were the commonest features associated with hemorrhage. Furthermore, we found that older males (40-50 years) with associated aneurysms and younger females (20-30 years) with venous stenosis were more likely to have bled. Analysis of the angioarchitecture of brain AVMs is important for understanding of symptoms, predicting clinical outcome and thus directing treatment decisions.

235.

Cerebral Micro-arteriovenous Malformations: Review Of 13 Cases

R. WILLINSKY, P. LASJAUNIAS, J. COMOY, P. PRUVOST and K. TERBRUGGE (Le Kremlin-Bicetre, France; Toronto, Ontario)

From the authors series of 178 cerebral vascular malformations, 13 patients had arteriovenous malformations with a small nidus (less than 1 cm) or fistula, a single, pial normal-sized feeding artery and an early draining cortical vein. We call these micro-arteriovenous malformations (mAVMs). All 13 patients presented with an intracranial hematoma. 10 of the 13 patients had no previous symptoms related to the malformation. One patient had a previous bleed in the same location. In 11 patients the mAVM could be demonstrated angiographically, however, the hematoma represented a transient cause for the mAVM being occult in 2. In 2 patients, the malformations were only evident at surgery. All the mAVMs were superficial and 10 out of 13 were cortical. Since the nidus is small, and the feeding artery and draining vein is normal-sized, mAvms are by nature CT and MRI occult. 9 of the 13 patients were treated surgically

with no perioperative morbidity. These malformations are not reachable by an endovascular approach. Patients presenting with mAVM constitute a remarkable subgroup within the cerebral arteriovenous malformations, with a favorable prognosis following surgery. Micro AVMs have previously been unrecognized due to poor quality exams or studies done in the presence of the hematoma. They likely represent part of the group of lesions previously called occult or cryptic.

236.

Magnetic Resonance Imaging (MRI) Assessment of Hypothalamic Neurohypophyseal Secretion

J. KUCHARCZYK, W. KUCHARCZYK, I. BERRY, D. NORMAN and H. NEWTON (San Francisco, U.S.A.)

MRI of the pituitary fossa characteristically shows a well circumscribed area of high signal intensity in the posterior lobe on T_1-weighted (T_1W) images. In order to determine whether this pituitary "bright spot" might be functionally related to neurosecretory processes, we initially reviewed retrospectively 115 cases of suspected sella pathology. The high-intensity signal was visible in 44 of 47 patients with microadenomas, but in only 17 of 36 patients with macroadenomas. No "bright-spot" was detected in 3 of 4 patients with suprasellar lesions, in 1 stalk transection patient with diabetes insipidus, in 4 of 6 patients with an empty sella, or in any of 5 congenital pituitary dwarfs. Subsequently, a combination of MRI, electron microscopy and biochemical techniques were used in experimental animals to identify the chemical nature of the pituitary "bright spot". Histological sections of dog pituitary gland processed with lipid-specific markers showed intense staining in the posterior lobe but not the anterior lobe, thus documenting the location of fat in the posterior pituitary. Administration of vasoactive drugs known to influence vasopression secretion to anesthetized cats produced changes in the volume of the high intensity signal in the posterior pituitary. Subsequent electron microscopy showed a significant increase in posterior lobe glial cell lipid droplets and neurosecretory granules in dehydration stimulated cats. Considered together, these data suggest that the pituitary hyperintensity represents intracellular lipid signal in the glial cell pituicytes of the posterior lobe. The volume of the lipid signal may, in turn, reflect the state of hormonal release from the neurohypophysis.

237.

Pediatric Cerebrovascular Disease: Alterations of Regional Cerebral Blood Flow Detected by SPECT Scanning with 99mTc-HMPAO

E. SHAHAR, R. LAMBERT, E.K. COHEN, D.L. GILDAY, J.M. ASH and P.A. HWANG (Toronto, Ontario)

The regional cerebral blood flow (rCBF) as determined by 99mTc-HMPAO single-photon emission computerized tomography (SPECT) was studied in 10 infants and children presenting with acute cerebrovascular disorders at age 2 weeks - 16 years. 99mTc-HMPAO is a new available radiopharmaceutical with a superior brain uptake and prolonged regional distribution allowing tomographic imaging of rCBF using rather simple SPECT techniques. The rCBF patterns were correlated with the clinical presentation, EEG and radiological studies including head CT, MRI and angiography. All presented with acute onset of limb weakness accompanied in some with dysphasia, obtundation, seizures, cortical blindness and high temperature. An underlying etiology was found in 6 patients: congenital heart disease (3), CNS infection (1), head trauma (1), MELAS syndrome (1).

Alterations in rCBF were detected in all patients correlating with the clinical findings and EEG abnormalities as well as with the radiologic abnormalities in a vascular distribution mainly of the middle cerebral artery in 6 patients, and were more extensive in an additional infant. Early reduction of rCBF preceded the CT abnormalities in two patients and were the only positive radiologic tests in two other patients with normal CT despite focal clinical and EEG findings.

Thus, SPECT with 99mTc-HMPAO is a sensitive measure in early diagnosis and localization as well as in determination of the extent of rCBE impairment in acute-onset pediatric cerebrovascular diseases.

238.

Regional ^{1}H Nuclear Magnetic Resonance (NMR) Spectroscopy Following Transient Forebrain Ischemia

G.R. SUTHERLAND, J. PEELING, D. WONG, K. MARAT and R. BOSE (Winnipeg, Manitoba)

Post-ischemic changes were followed serially in 25 age- and weight-matched rats using ^{1}H NMR spectroscopy. Five rats (controls) were decapitated and the hippocampus, frontal lobes, parietal/occipital lobes and cerebellum were dissected. Perchloric acid extracts were obtained from each tissue sample and ^{1}H NMR spectra were obtained using a Bruker AM-300 spectrometer. The remaining rats underwent temporary forebrain ischemia [bilateral carotid occlusion and controlled hypotension (50 torr) for 10 mins]. At 10 mins, 1 hr, 24 hr, and 7 days post-ischemia, groups of 5 animals were sacrificed and tissue samples obtained, prepared, and analyzed as above.

Early post-ischemic neuronal inhibition was observed, the ratio (GABA + Ala)/(Glu + Asp) being significantly ($P<0.01$) higher at 10 mins compared to control values in frontal (235±6%), parietal/occipital (207±11%), and hippocampal (144±16%) tissues. These early changes reverted towards baseline values by 24 hrs. Such changes did not occur in the cerebellum. Significant persistent lactic acidosis was evident in the cortical and hippocampal regions, being maximum at 10 mins post-ischemia (frontal, 300±10%; occipital 260±5%; hippocampus 180±10% of control). Acetate (possibly reflecting membrane metabolism) was initially elevated, particularly in the hippocampus and cerebellum (470±70% and 210±28% of control, respectively), returning to control values by 24 hrs.

We conclude that forebrain ischemia evokes global prosencephalic inhibition with maximum changes observed in the cortex. This may reflect selective vulnerability/inhibition of neurons principally involved in excitation. Persistent elevated levels of lactate and acetate reflect ongoing tissue acidosis and its accompanying tissue injury.

Supported by: Canadian Heart Foundation

239.

The In-vitro Appearance of Endovascular Embolic Agents With Clinical Correlation

J.E. DION, E. SPICKLER, R. LUFKIN, F. VINUELA, G. DUCKWILER, T. RACHNER, P. LYLYK, T. LIN and J. BENTSON (Los Angeles, U.S.A.)

An in-vitro examination of embolic agents was undertaken to evaluate MR signal changes present in patients who have undergone endovascular embolic therapy for lesions such as AVM, aneurysm or tumor. Combinations of polyvinyl alcohol, avitene, Gelfoam, ethanol, I.B.C.A., barium impregnated silicone microspheres, metal coils and balloons containing contrast or Hema were imaged within plastic containers. Imaging sequences using a 0.3T MR scanner included spin echo T1 and T2 weighted images, and inversion recovery. Varying degrees of T1 shortening occurred with ethanol-particulate, and I.B.C.A. preparations. T2 shortening was present with Hema, Gelfoam, and silicone spheres. Other sequences tended to exaggerate the shortening effects shown with spin echo technique. Metal coils demonstrated local

field distortions. A review of the in-vitro model correlated with clinical MR case material will be presented. Recognizing the presence of embolic material within a lesion is important to avoid confusion with persistent flow void, hemorrhage or thrombus.

240.

MR In The Evaluation Of Endovascular Therapy Of Brain AVMs

J.E. DION, T. LIN, P. LYLYK, F. VINUELA, R. LUFKIN, E. SPICKLER and G. DUCKWILER (Los Angeles, U.S.A.)

MR studies on 25 patients with brain AVMs that underwent endovascular treatment was correlated with angiographic, clinical and surgical findings. An AVM nidus was clearly depicted on MRI in 19 cases. It was absent in 4 cases of pure A-V fistulae and was not noted in 2 dural AVMs located near the skull base. In the 4 cases of pure A-V fistulae, MR showed thrombosis or decrease in size of the draining veins after treatment. In all cases of pial AVMs in which the nidus was embolized, T2 weighted images showed the disappearance of part of the signal void previously noted and the appearance of areas of high signal intensity within the nidus and in a thin rim of surrounding tissue. These findings were consistent with slow blood flow, vascular occlusion and some vasogenic edema. In 11 cases, most of them following further embolization, more prominent parenchymal changes were noted: extensive edema and/or ischemic lesions. Only half of these patients developed mild focal neurological deficits mostly resolved by the time of surgery or within the first month of follow-up. MRI findings in association with clinical evaluation allowed optimal timing for subsequent embolization or surgery.

241.

Magnetic Resonance Imaging in Whiplash Injuries

R.N. RANAWAYA, D. STEINKE, J.D. MILLER and D.R. MCLEAN (Edmonton, Alberta)

Whiplash injuries frequently are a cause of prolonged disability and litigation.

In the majority of patients no bony or ligamentous injury is detected by routine radiological studies. Inspite of this, some of them subsequently develop significant longlasting disabling symptoms which include: neckache, headache, dizziness, auditory and visual symptoms, depression, inability to concentrate and memory disturbance.

Studies performed in monkeys with simulated whiplash have shown many soft tissue injuries in the neck which include: tearing of ligamentous and muscle fibres with subsequent swelling, bleeding into soft tissues and rupture of intervertebral discs without displacement.

This study was performed to see if magnetic resonance imaging of the neck can detect these abnormalities, and if so, whether the extent, level and severity of these injuries correlate with subsequent symptoms.

Ten unselected patients presenting to the Emergency room with acute whiplash injuries were seen by one of us (D.S) and a full neurological examination was performed. Routine cervical spine radiographs with tomograms or C.T. scan were performed where indicated. All patients had an M.R.I. scan of the neck performed within two weeks of injury using a 1.5 Tesla Phillips scanner with a surface coil.

All patients were followed up at 1 month and 6 months.

Neuroradiology (Poster)

THURSDAY, JUNE 16TH - P.M.

242.

Comparison of Computer Tomography and Magnetic Resonance Imaging in Children with Metachromatic Leukodystrophy

C.E. NIESEN, A.K. HOPE, E. COHEN, S. CHANG, J. CLARKE and D. MACGREGOR (Toronto, Ontario)

Computer tomography (CT) and magnetic resonance imaging (MRI) scans were performed in five different patients (ages 3-22) with metachromatic leukodystrophy to study the extent of white matter disease.

Four patients presented with delayed/deteriorating motor development. All five patients had abnormally low arylsulfatase A activity and one patient had multiple sulfatase deficiency. The onset of symptoms occurred less than five years of age in 4 patients; the fifth was asymptomatic.

CT scans done at time of diagnosis and at variable follow-up intervals in each patient demonstrated variable degrees of atrophy and low density periventricular white matter changes. MRI studies done in each patient showed similar atrophic change. White matter changes were readily appreciated as high signal on T2 weighted sequences. Periventricular areas were mainly affected and assumed an anterior/posterior distribution early in the disease or in milder cases. Patients with severe spasticity showed extensive altered white matter signal, often with infratentorial atrophy.

The extent and distribution of white matter changes in metachromatic leukodystrophy were much better demonstrated with MRI than CT, as suggested in previous anecdotal reports. Good correlation between clinical status and MRI findings was present.

243.

Regional Cerebral Blood Flow Threshold for Metabolic Changes in Cerebral Ischemia in Rats Studies by Triple-Tracer Autoradiography

Y.L. YAMAMOTO, H. NAKAI, M. DIKSIC and K.J. WORSLEY (Montreal, Quebec)

A concept of thresholds of ischemia has been developed relating various types of functional and metabolic disturbances to the level of remaining blood flow. The RCBF threshold of electrical functional failure for evoked potentials in baboons is reached at flow values of 20 ml/A (35% of CV) (Brantom et al 1977). The threshold of ion pump failure is 6-8 ml/A (14% of CV) (Astrup et al 1977). The threshold for tissue pH reduction measured by an extracellular microelectrode is 30 ml/A in rats (38% of CV) (Harris et al 1984).

We compare here the relationship between RCBF and tissue pH or RCGU in ischemic brain tissue in rats following occlusion of the middle cerebral artery. To eliminate animal-to-animal variability we use triple-tracer autoradiography, a technique we recently developed to obtain simultaneously three independent autoradiograms.

Method — Seven rats were fasted for 18 hours before the experiment. The middle cerebral artery was occluded under 2% halothane anesthesia. The rats were allowed to awake from anesthesia and the lower half of their body was immobilized with a loose-fitting plaster cast. Triple-tracer autoradiography was used to measure RCBF, tissue pH, and RCGU, using ^{18}F-4-FAP, ^{14}C-DMO, and ^{3}H-2-DG, respectively, as tracers.

Results — The threshold level of RCBF for tissue pH reduction was 49 ml/A (37% of CV). The threshold level of RCBF for RCGU hypermetabolism was 20 ml/A (15% of CV).

Comments — Our results indicate that the RCBF threshold for reduction of tissue pH coincides with the beginning of electrical functional failure for evoked potential (34%-37% of CV) and that the RCBF threshold for RCGU hypermetabolism almost coincides with ion pump failure (14%-15% of CV). The LCBF thresholds for both tissue pH and RCGU hypermetabolism are higher in hyperglycemic rats, which may relate to more deteriorating effects.

A = 100g/min; CV = control RCBF value

Supported by MRC of Canada (MT-3174).

244.

Laboratory Evaluation of Acute and Chronic Myelopathies

G. FRANCIS and C. TANSEY (Montreal, Quebec)

The diagnosis of myelopathic syndromes in neurology is frequently difficult, typically involving many studies including myelography. Many of the acute and chronic myelopathies with negative myelogram are felt to be demyelinating.

We have studied patients with acute/subacute (AM) or chronic progressive myelopathies (CPM) in whom myelogram were negative in order to determine the frequency of disease above the foramen magnum and confirm or refute a diagnosis of demyelinating disease.

Cranial MRI in AM (n = 12) showed lesions consistent with MS in 75% with abnormal CSF studies (elevated IgG or oligoclonal bands) in 75%, VER/BAER 30%, SSEP 60%.

CPM patients (n = 30) had cerebral MRI lesions in 75% with positive CSF in 55%, VER/BAER 30%, SSEP 50% and cranial CT only 10% positive. Ninety (90) percent of CPM patients had either positive MRI or abnormal CSF.

Using available lab studies, the vast majority of myelogram negative CPM patients fit diagnostic criteria for MS. One MRI negative CPM patient came to autopsy which showed only a thoracic focal demyelinating lesion. The situation with AM patients may be similar but follow-up is needed. To date, 4 of the 12 AM patients have developed definite MS; all had positive MRI.

Neuromuscular Diseases (Poster)

THURSDAY, JUNE 16th - P.M.

245.

Neuropathie sensori-motrice héréditaire avec ou sans agénésie du corps calleux: étude radiologique et clinique de 64 cas.

J. MATHIEU, F. BÉDARD, C. PRÉVOST et P. LANGEVIN (Chicoutimi, Québec, Ste-Foy, Québec)

Un syndrome autosomal récessif, retrouvé au sein d'une population originaire de Charlevoix et du Saguenay, caractérisé par une agénésie du corps calleux associé à une polyneuropathie sensori-motrice axonale, un retard intellectuel et quelques traits dysmorphiques a été décrit par Andermann et Andermann en 1971. Quelques cas isolés présentant un tableau clinique similaire mais sans anomalie calleuse ont aussi été rapportés. Les auteurs ont procédé à une étude radiologique et clinique de 64 individus porteurs de ce syndrome génétique et suivis à l'Hôpital de Chicoutimi.

Les résultats de la tomodensitométrie cérébrale révèlent une agénésie complète du corps calleux chez 37 patients (57,8%), une agénésie partielle chez 6 patients (9,4%) et la présence du corps calleux chez 21 patients (32,8%). La présence du corps calleux a été confirmée dans quelques cas par un examen en résonance magnétique. La tomodensitométrie cérébrale a permis également de mettre en évidence une fréquence élevée d'anomalies développementales ou dégénératives, en particulier l'atrophie de la fosse postérieure, malgré l'absence d'anomalie calleuse.

La présentation clinique et l'histoire naturelle de l'atteinte polynévritique, intellectuelle et comportementale semblent identiques chez les individus avec ou sans agénésie du corps calleux.

Des individus avec ou sans agénésie du corps calleux se retrouvent au sein d'une même famille et souvent au sein d'une même fratrie. Cette observation supporte l'hypothèse d'un syndrome génétique unique dont l'expression phénotypique la plus constante est la neuropathie sensori-motrice et non l'agénésie du corps calleux.

Ce syndrome récessif doit donc être soupçonné chez un enfant porteur d'une atteinte polynévritique et originaire de Charlevoix ou du Saguenay malgré la présence du corps calleux à la tomodensitométrie ou à l'examen en résonance magnétique. L'histoire familiale extensive et la recherche de traits dysmorphiques ou d'anomalies radiologiques mineures pourraient alors permettre une identification précoce de ce syndrome et un conseil génétique adéquat. Par ailleurs, l'absence d'anomalie calleuse observée chez plusieurs individus atteints réduit considérablement la pertinence du dépistage pré-natal par échographie.

246.

La Dystrophie Oculopharyngée au Québec: Nouvel Intérêt Clinique, Généalogique et Morphologique

J.-P. BOUCHARD, D. BRUNET, F. GAGNE et J. PUYMIRAT (Québec, Québec)

Il y a plus de 20 ans, A. Barbeau présentait au monde médical l'histoire de la dystrophie oculopharyngée au Québec. Il précisait cette maladie alors peu connue, et rattachait la totalité des familles nord-américaines décrites à un couple ancestral commun immigré au Canada français avant 1640.

A l'âge de la biologie moléculaire, un nouvel intérêt renaît pour cette maladie à transmission dominante pour l'identification de marqueurs et la localisation du gène responsable. L'apparition tardive des symptômes (ptose palpébrale d'abord et dysphagie, souvent après l'âge de 50 ans) exige en génétique une approche horizontale sur de larges effectifs. On compte plusieurs centaines de cas au Québec.

En 1980, F. Tomé et M. Fardeau décrivaient pour la première fois des inclusions intranucléaires dans quelques cas de dystrophie oculopharyngée de France. Depuis, de telles inclusions ont aussi été rapportées en Allemagne, en Hollande et en Italie dans le même syndrome. Nous confirmons chez quatre de nos cas étudiés en 1987 la présence d'amas de filaments tubulaires de 8 à 10 nm de diamètre dans des noyaux de muscles somatiques atteints. Trois spécimens ont été obtenus par biopsie au deltoide, et un à l'autopsie. Le muscle cricopharyngé (ou constricteur supérieur de l'oesophage) a été biopsié deux fois lors d'une myotomie pour corriger la dysphagie. Sauf dans un cas de muscle cricopharyngé très atrophique, les inclusions caractéristiques ont été retrouvées. Leur signification n'est pas claire, et nous collaborons pour l'identification biochimique de ce matériel dont la localisation intranucléaire est déjà fort intrigante.

247.

Pairs of Patients with ALS Sharing a Common Past Environment

A.A. EISEN, A.S. BUCHMAN, M. HOIRCH, M.T. SCHECHTER and S.B. SHEPS (Vancouver, British Columbia)

The worldwide incidence of ALS is constant except for a few pockets of increased incidence such as Guam. Recent evidence has implicated prior environmental toxic exposure as causative in the ALS-Parkinsonian-Dementia complex on Guam.

The distribution and characteristics of ALS in British Columbia were studied longitudinally in 121 patients between 1980-1987. The minimal annual incidence between 1981-1984 was 0.99/100,000. No significant regional clustering was identified using census districts. However, four pairs of patients were identified, who although unrelated, had known one another and lived in close proximity for 2 or more years, 15-40 years before developing ALS. Another patient who developed ALS at age 36, lived for 2 years, starting at age 11, in Western New Guinea, a high incidence focus of ALS.

Despite the difficulties of space and time clustering, these observations support the hypothesis that Western ALS may result from previous environmental exposure many years before the disease becomes clinically overt.

248.

Peripheral Nerve and Vascular Involvement in Myophosphorylase Deficiency (McArdle's Disease)

R.W. BYARD, B. LACH and D. PRESTON (Ottawa, Ontario)

Deficiency of muscle phosphorylase (Type V glycogenosis or McArdle's Disease) is a metabolic myopathy characterized by glycogen accumulation in skeletal muscles. We present a case of myophosphorylase deficiency in which glycogen excess was present in both, striated muscles and other tissues.

A 60 year old male with a history of muscle weakness since childhood was admitted to hospital with atypical chest pain. His brother had biopsy proven myophosphorylase deficiency. His parents and other 7 siblings had no history of medical problems. Examination revealed slight upper and lower limb muscle wasting. Electromyographic findings were consistent with a mild myopathy. He had marked exercise-induced myalgia and refused to complete an exercise test. His serum creatine phosphokinase was persistently elevated. Muscle biopsy showed an essentially normal morphology with only occasional very small subsarcolemmal vacuoles. Enzyme histochemistry revealed the absence of myophosphorylase in striated muscles. Electronmicroscopy demonstrated storage of free and lysosomal glycogen in the striated muscles, axons and Schwann cells as well as vascular smooth muscles and endothelial cells. It was not possible to ascertain whether the underlying mechanism was related to nonspecific uptake of glycogen by cells of tissues other than striated muscle or to a more generalized deficiency of phosphorylase. However, the reaction for myophosphorylase appeared to be weaker in smooth muscles and peripheral nerves in this patient compared to controls. The presence of endothelial glycogen accumulation, necrosis of some endothelial cells and thickening of the basal lamina of capillaries possibly contributed to muscle ischemia and played an additional role in this patient's symptomatology.

In conclusion, the finding of glycogen deposition in non-skeletal muscle tissue shows that Type V glycogenosis may be a more heterogenous disorder than was previously considered.

249.

Conjugal Inflammatory Muscle Disease: Coincidence or Evidence of a Common Environmental Factor?

G.M. KLEIN, A.K.W. BROWNELL, M.H. ATKINSON and C.J. PENNEY (Calgary, Alberta)

Inflammatory muscle disease is a very rare entity, with an incidence of 0.5 per 100,000 population. Case clustering of a disease this rare is highly unusual.

We had the opportunity to investigate both members of a married couple who presented to us with inflammatory muscle disease. Mrs. S. presented first. A diagnosis of dermatomyositis was made on the basis of a skin rash, proximal muscle weakness, a creatine phosphokinase (CPK) of 976 I.U., and a muscle biopsy showing mild active inflammatory myopathy. Later, a colonic carcinoma was identified. Mr. S. presented later with proximal muscle weakness. A CPK of 519 I.U., and a muscle biopsy showing active and chronic inflammatory myopathy confirmed polymyositis. A diagnosis of Sjogren's syndrome was also made.

We feel that a common environmental agent may have triggered inflammatory muscle disease in two individuals who were pre-disposed to it. Exposure to toxoplasmosis may be responsible. Other toxic or infectious etiologies are considered less likely.

250.

Adult Nemaline Rod Myopathy: Clinical Profile

M. YEUNG, A. SHUAIB and A.K.W. BROWNELL (Calgary, Alberta)

Nemaline Rod Myopathy (NRM) was described initially by Shy et al in 1963 as a congenital non-progressive disease. A second variety of NRM presenting in the adult, was subsequently described by A.G. Engel. Since only 17 cases of the adult variety have been published, the full clinical spectrum of the disease in adults, is unclear.

We now report six further cases of adult NRM, seen over a ten year time period at a university hospital. There were four females and two males. Age range at the time of presentation, was from 34-76 (mean 52.1) years and duration of symptoms before diagnosis was made, ranged from 4 months to 16 (mean 3.5) years. Mild to moderate weakness was seen in all cases; mild to moderate muscle atrophy was evident in five of six cases. Progression of weakness, although gradual, occurred in all cases. Associated diseases included severe chronic obstructive pulmonary disease (COPD) (1) and epilepsy (1). The single death was secondary to COPD. The clinical findings in our cases as well as previously reported cases of adult NRM will be reviewed, in order to better define the clinical features and course of this unusual myopathy of adult life.

251.

Mesure des Anticorps Contre le Recepteur de l'Acétylcholine dans la Myasthénie

J. OGER, R. KAUFMAN et K. YU (Vancouver, British Columbia)

Nous avons mesuré les anticorps contre le récepteur de l'acétylcholine d'origine humaine (A-RAch) dans la myasthénie et évalué les avantages de cette technique:

Comme outil diagnostique le test qualitatif a donné les résultats positifs suivants: 35/83 (42%) pour la myasthénie purement oculaire, 56/62 (90%) pour la myasthénie généralisée en phase active, 13/26 (50%) pour la myasthénie généralisée en phase de rémission. Parmi les 105 malades testés ayant un autre diagnostique nous avons trouvé 3 (3%) échantillons positifs: 2 pourraient avoir une myasthénie (traitement par penicillamine et suspicion de botulisme), le 3ième avait une maladie épileptique. Parmi les 50 sujets controles aucun n'était positif.

Nous utilisons aussi un test quantitatif (limite de détection 0.1nmole/l.) Celui-ci n'a pas révélé de différence entre malades différant seulement par la gravité de leur maladie. Par contre nous avons pu confirmer par des mesures mensuelles sur 4 malades que la quantité d'anticorps diminue quand la maladie est en rémission et que les anticorps augmentent lorsque la maladie redevient active. Ceci ne semble pas vérifié pendant les premiers mois de la maladie.

Finalement nous avons mesuré la quantité d'anticorps secrétée en culture par les lymphocytes isolés du sang. Le niveau de détection est de 1 femtomole d'anticorps. Parmi 32 malades ayant des A-RAch dans leur serum 18 d'entre eux secrétaient en culture. Ces malades semblent

avoir une durée d'évoluton moins longue que les non-sécréteurs. Aucun des 19 controles testés ne sécrétait en culture.

Nous avons confirmé l'intérêt de la mesure des A-RAch pour le diagnostic, la surveillance et la compréhension de la pathophysiologie de la myasthénie.

252. Withdrawn

Read By Title Only

253.

Lumbar Discectomy For Sequestrated Discs, Without Recurrences: A Must.

A. GODON (Montréal, Québec)

Surgery of lumbosacral discs in 1988, must concern itself with the extractions of the sequestrated disc responsible for the sciatic nerve root compression and its neurological consequences.

Surgery is directed to the one-level sequestrated disc, where neurological, neuroradiological and electrophysiological correlations are of the first order.

We review here the 155 cases that we have operated between 1982 and the end of 1986 (five years), W.C.B. cases and non W.C.B. cases.

A progressively very rigorous microsurgical technique was evolved over these five years, in trying to prevent and circumvent late recurrences years down the road.

100% of non W.C.B. cases and 76% of W.C.B. cases have now returned to productive employment.

A high incidence of concurrent lateral spinal stenosis at the same level in 30% to 60% of cases according to statistics, has to be dealt with seriously.

Recurrences at the same level years later attest to an iatrogenic problem of incomplete or partially inadequate surgery. We can prevent this through the use of the microscope, radical emptying of the disc space, protection of all adjacent microvascular and micronervous and bony structures, delicate and complete treatment of the lateral spinal stenosis, detailed exploration of the sciatic root at the end of surgery, all without creating post-operative instability.

Complications which occurred in our series are reviewed, with their treatment and prevention.

We conclude by insisting on the importance of proper usage of the lumbosacral spine and its musculature constantly, to prevent the recurrence of sciatica at the same level or at other levels.

Now resolved in 1988: the sciatica. Unresolved: the problem of persistent and often bothersome secondary lumbosacral instability.

254.

Trismus In A Patient With A Pontine Hemangioma

A. ABDOLLAH, D. GENDRON and G. FRANCIS (Montreal, Quebec)

We report a 27 year old primiparous woman who presented at 3 months gestation with sudden headache and right sided weakness. Examination pointed to a brainstem lesion. Magnetic resonance imaging revealed a large mixed-signal lesion extending from the left inferior pons to the cerebral peduncles characteristic of a cavernous hemangioma. The patient's symptoms and signs slowly resolved but incompletely.

Three months after presentation, the patient complained of difficulty opening her mouth. Clinical and radiological evaluation revealed no mouth or temporomandibular joint abnormalities. On jaw closure, both masseters were felt contracting and paradoxically on jaw opening, the left one contracted. The jaw jerk was brisk.

Electromyographic recording of both masseters were obtained. On jaw closure, contractions of the masseters were recorded, chronic denervation being present in the left masseter. On jaw opening, the right masseter became silent, whereas the left masseter displayed motor unit activity which was even more prominent then on jaw closure, the same motor units being recruited on jaw opening and closure.

Trismus, in the setting of a brainstem lesion has not been hitherto described. Pathophysiological mechanisms are unknown. Hypotheses will be discussed.

255.

Physical Activity and Cerebral Ischemia in the Mongolian Gerbil

B. TRANMER, O. KEMPSKI, K. WEBER and A. BAETHMANN (Calgary, Alberta; Munich, F.R.G.)

More so than ever, physical fitness is being stressed. It has been suggested that exercise may protect against heart attack, hypertension, and stroke. In preliminary studies, it was observed that physically active gerbils tolerated cerebral ischemia better than inactive gerbils. To further test this observation a series of experiments were designed in which exercised gerbils and inactive gerbils were subjected to cerebral ischemia and then survival weight loss, and hippocampal morphology were compared.

METHODS: In Experiment 1, adult male gerbils (60-80g) were subjected to bilateral carotid occlusion for 20 minutes under halothane anaesthesia. Exercised (running-wheel cages) and inactive (small cages) gerbils were followed for 14 days post ischemia for daily weight loss, survival, and then quantitative histology was performed after perfusion fixation of the brains. In Experiment 2, the gerbils (exercised and inactive) were exposed to bilateral carotid conclusion for 15 minutes, observed for 4 days, then sacrificed for quantitative histology of the hippocampus.

RESULTS: In Experiment 1, the survival (100%), and maximum weight loss (13+/-1%) of the exercised gerbils (N=9) were significantly better than in the inactive group (N=24) (21% survival and 26+/-3% weight loss). In Experiment 2, the histology of the CA1 sector of the hippocampus revealed significantly more neuronal loss in the inactive group (N=9) than in the exercised group (N=9).

The results demonstrate that physical activity provides a marked degree of protection in gerbils subjected to cerebral ischemia. The mechanism of this protection is not known, but these findings may lead to further understanding of the relationship between systemic and cerebral processes.

256.

Etude de l'activité acétycholinesterasique (AChE) et des concentrations en somatostatine (SRIF) dans le liquide cephalo rachidien (LCR) de patients atteints de démences de type Alzheimer

J. PUYMIRAT, C. BIANCO, S. GOMEZ, D. VALADE, C. JEANNIN et P. RONDOT (Ste-Foy, Québec; Paris, France)

Nous avons mesuré l'activité de l'AChE et les concentrations en SRIF dans le LCR de 83 sujets (18 contrôles, 65 patients déments). L'activité de l'AChE est réduite dan le LCR de patients atteints de SDAT/AD mais de manière plus importante dans les démences séniles (33%) que dans les démences pré-séniles (17%). L'activité AChE est effondrée (65%) dans le LCR de patients atteints (8) de Creuzfelt-Jakob et a été trouvée inchangée dans le LCR de patients atteints d'hydrocéphalie à pression normale, de Chorée de Huntingon, de démences vasculaires.

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Les concentrations de SRIF sont significativement réduites (40%) dans le LCR de patients atteints de démence de type Alzheimer (SDAT/AD). L'étude des formes moléculaires de SRIF dans Le LCR de SDAT/AD montre une augmentation significative de la prépro SRIF (15 kd) et une diminution de la forme mature (SRIF. 14): Les concentrations de SRIF ne sont pas modifiées dans les démences vasculaires, la Chorée de Huntington. Enfin, la comparaison des valeurs d'AChE et de SRIF dans le LCR à celles de ChAT et de SRIF dans le cerveau déterminées en post-mortem chez les mêmes patients révèle que la SRIF dans le LCR pourrait refléter l'activité des neurones à SRIF du cerveau, alors que l'AChE dans le LCR ne semble pas réfléter l'activité cholinergique du cerveau.

Cette étude indique que la détermination des taux de SRIF et surtout de la forme 15 KD dans le LCR pourrait-être un bon marqueur de la démence de type Alzheimer.

257.

Brain Stem Cavernous Angioma Mimicking Tumor: Magnetic Resonance Contribution

J.-G. VILLEMURE and R. LEBLANC (Montréal, Québec)

We are presenting 4 cases which on the basis of their clinical findings and radiological investigation were diagnosed as having a brain stem tumor. These patients eventually underwent Magnetic Resonance Imaging (MR) which did show a brain stem lesion having the characteristics of cavernous angioma. There were 2 males and 2 females. The age at onset of symptoms was 23, 24, 28 and 33 years old. The initial symptomatology was acute in 2 patients and referred as a stroke initially, to then show a fluctuating but stepwise deterioration thereafter. In 2 patients, the initial symptomatology was secondary to obstructive hydrocephalus and manifested with diplopia and ataxia. All had brain CT scan which demonstrated a mass lesion within the brain stem; this did not necessarily enhance with contrast infusion. The vertebral angiogram did confirm a mass effect but did not show abnormal vascularisation. Two patients were treated with conventional radiotherapy (5600 and 400 rads respectively) for their suspected tumor and continued to show deterioration. Magnetic Resonance Imaging was obtained in the 4 patients using the 0.5 and 1.5 Tesla superconductive magnets (Philips Gyroscan). The findings were those of a lesion with mixed intensity signal on the T2 weighted images, with lack of signal at the periphery, characteristics of cavernous angioma; this differs from the homogeneous signal intensity seen in proven brain stem glioma.

These cases emphasize the value of Magnetic Resonance Imaging in the diagnosis of brain stem lesions.

258.

Hereditary Motor and Sensory Neuropathy With Neuromyotonia

A.F. HAHN, S. STEWART, C.F. BOLTON and A. PARKES (London, Ontario)

We have investigated a family with this rare disorder.

The two affected members, siblings, a 15-year-old boy and an 11-year-old girl, experienced muscle stiffness and cramping during exercise. Voluntary muscle contraction set off a prolonged spasm, followed by myokymia and fasciculations. There was delayed grip release and focal tonic contraction of the tongue with percussion, followed by fasciculations. The distal muscles were weak and moderately wasted. Sensation and sweating were normal. Nerve conduction studies indicated a mild axonal motor and sensory polyneuropathy. Needle electromyography of the tongue and limb muscles revealed frequent, high voltage discharges, most commonly neuromyotonic, but occasionally myokymic, with fibrillation potentials and positive sharp waves. The abnormal potentials were provoked by voluntary contraction but not electrical or mechanical nerve stimulation, or needle movement within the muscle, or direct percussion of the muscle. They were generally inhibited by cooling the limb and were totally eliminated by regional curare block. The motor unit potentials suggested chronic denervation, which was confirmed by muscle biopsy.

The clinical and electromyographic manifestations were markedly improved by carbamazepine, dilantin or tocainide. This suggest that the altered physiology of motor nerve fibers may relate to an abnormality of ion channels in the axonal membrane.

259.

Partially Sequestered Fourth Ventricle: CT and MR Diagnosis Of An Unusual Entity

V.G. WAGLE, J.-G. VILLEMURE and D. MELANSON (Hartford, U.S.A.; Montréal, Québec)

Encystment of the fourth ventricle, due to occlusion of the aqueduct as the foramina of Magendie and Luschka has been described previously. However, partial sequestration such as that encountered in our two cases is a rare entity and has been described only once. In our two cases, the aqueduct of Sylvius was occluded, but the basal foramina (Magendie and Luschka) were patent. We present this partial sequestration or communicating hydrocephalus of the fourth ventricle on the basis of MRI and CT findings.

260.

Dural AVM's Of Posterior Fossa: Clinical Presentation and Endovascular Treatment

M. HEBERT, A. BERENSTEIN and I.S. CHOI (Québec, Québec; New York, U.S.A.)

A review of 34 cases of dural AVM of "posterior fossa" have been done. Thirty-three have been embolized with glue or particules or both. Two cases had combined treatment (endovascular and surgery).

Each cases has been analysed regarding clinical presentation, localisation (clival, falx, torcular) angiographics aspects, clinical testing, endovascular treatment (single or multiple) complication and results.

It appears that the endovascular treatment with glue when there is no contrindication give better results and less recurrence than particules alone.