XX Canadian Congress of Neurological Sciences Abstracts of the Scientific Program

Platform Presentations

1.

Neurotoxic Complications of Contrast CT in Children

R. HASLAM, D. D. COCHRANE, G. AMUNDSON and R. JOHNS (Calgary, Alberta)

Computed cranial tomography (CT) has been considered a safe and accurate method for studying intracranial lesions in children. As a diagnostic adjunct, radiographic contrast material is administered intravenously (IV) to enhance and further characterize lesions such as vascular malformations. Traditional ionic contrast agents can penetrate the blood brain barrier (BBB) and exert an adverse effect due to hyperosmolality, lipid solubility and neurotoxic properties when administered intra-arterially. Contrast agents given IV are generally considered non-neurotoxic.

We report 3 children with brain tumors who rapidly deteriorated following CT with infusion. All had evidence of papilledema but were alert and responsive prior to CT. A patient dose of 2-2.5 ml/kg IV Renografin-60 (diatrizoate meglumine 52% and diatrizoate sodium 8%) was used. Within 6 to 8 hours each child showed progressive lethargy, disorientation, bradycardia, hypertension and generalized seizures (2). One child died.

Zamani et al showed that 4 ml/kg IV diatrizoate meglumine-60 disrupted the BBB in some normal dogs. Focal seizures have recently been reported in adults with cerebral metastases following contrast CT. It is likely that the neurological deterioration in the reported children resulted from the osmotic effects of contrast material on cerebral tissue. As contrast enhanced CT may produce grave neurological complications in children with brain tumors, the study should be reserved for those where the probability of additional significant diagnostic yield exists. The utilization of the new non-ionic or low osmolality contrast agents may decrease the morbidity and mortality associated with this procedure.

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2.

Photoradiation Therapy of 9L-Gliosarcoma in Rats: Hematoporphyrin Derivative (Types I and II) Followed By Laser Energy

M-K. CHENG, J. McKEAN, B. MIELKE, J. TULIP and D. BOISVERT (Edmonton, Alberta)

Photoradiation therapy (PRT) was applied on one or more occasions in 9L-gliosarcoma rats, consisting in the injection of HpD (photofrin) type I or II and exposure to single-fibre laser energy 24, 48, or 72 h later. In brain tumors examined 72 h after laser exposure (n = 48), necrotic foci were most numerous in rats exposed to laser energy 24 h after HpD and were significantly commoner after HpD II (88%) than after HpD I (40%). In a further 42 rats brain tumor, after the use of HpD I or II and the application of laser energy once (7 or 14 days after inception of the tumor) or twice (days 7 and 14), neither the duration of survival of the rats nor the weight of the tumor was significantly different from control. Necrotic foci exceed 1/3 of the tumor area in 13 of the 80 treated rats with brain tumor; of these 13, 9 had received HpD II. In another group of flank rats (n = 11), multiple PRT (2 to 4 treatments) did not delay growth of the tumors; and in a fourth group, 11 of 12 PRT-treated tumors grew after transplantation into the brain, both groins, or peritoneal cavity of healthy recipients. We conclude that HpD II is a more effective photosensitizer than HpD I. However, the value of PRT will be limited until a lethal dose of laser energy can be delivered throughout a tumor without destroying vital healthy tissue.

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3.

Magnetic Resonance Imaging (MRI) in Temporal Lobe Epilepsy (TLE) — Pathological Correlations

R. S. McLACHLAN, R. L. NICHOLSON, S. BLACK, T. CARR, W. T. BLUME, J. P. GIRVIN, J. C. E. KAUFMANN and H. VINTERS (London, Ontario)

Magnetic resonance imaging is a noninvasive procedure which because of the absence of bone artifact, is particularly useful for imaging structures such as the temporal lobes which are adjacent to bone. Sixteen patients with refractory TLE and no known gross structural lesions who were being considered for surgical management had MRI (Technicare 0.15 Tesla Imager) as part of the surgical workup. Blind interpretation of the patients' MRIs, compared to those of a normal control group, revealed atrophic changes (temporal lobe, mesial temporal or hemisphere) and increases in spin-spin relaxation time (T_2) which were found to correlate with the electrographically determined seizure focus in 11 of 14 patients with these abnormalities. Eight of these patients have had temporal lobectomies (3 right, 5 left). Atrophic changes in the temporal lobe as demonstrated by MRI (i.e., small temporal lobe, mesial temporal atrophy) were confirmed at surgery in 7 of 8 patients, the other patient having no signs of atrophy either by MRI or direct observation in the operating room. However, the degree of atrophy seen with MRI did not correlate with that found by the surgeon nor was a correlation found with the histological abnormalities. Four patients had increased T_2 in the mesial temporal region on the resected side and one on the nonresected side. Increases in T_2 did not correlate with histological change or the maximum area of focal spiking on electrocortiocography.

Atrophic changes in the temporal lobes seen by MRI correlate qualitatively but not quantitatively with the gross findings at surgery but the significance, if any, of focal increases in T_2 in the mesial temporal region remains unclear.

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4.

Uneven Prevalence of Parkinson's Disease in the Province of Quebec

A. BARBEAU and M. ROY (Montreal, Quebec)

References generally quoted in the literature and in most textbooks indicate that Parkinson's disease is evenly distributed between various

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countries. However, closer scrutiny of the published results shows a 2 to 3 fold variation in mean annual age-adjusted mortality rates, for example between two highly developed countries like France (3.9/100,000) and the USA (1.6/100,000). In the USA itself, study of mortality data published in the early sixties, and reinterpreted now on a geographic basis, clearly indicates a decreasing prevalance gradient from North to South and from West to East. Thus, North-West USA has at least twice the prevalence of the South-East USA region. A similar West to East gradient is also reported by us for Canadian mortality rates.

Quebec (at 1.2 average annual age-adjusted mortality rate/100,000 population, one of the lowest in North America) is not uniform in its own distribution. We will present the result of a study of all reported cases of Parkinson's disease in the Province over the last five years, indicating that some hydrographic basins have prevalence rates at least twice the mean rate for the Eastern part of Canada, with an overall variation ratio of 1 to 6 between the lowest and highest prevalence basins. Highly punctual foci will also be described and analyzed, confirming the initial observation of Rajput and collaborators.

These studies support the hypothesis that environmental factors play a major role in the development of Parkinson's disease, in genetically susceptible individuals.

The cooperation of Dr. S. Gauthier is gratefully acknowledged. These studies are supported by the MRC and La Fondation Parkinson du Québec.

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5.

Clinical Events Following Neuroangiography: A Prospective Study

J. DION, P. GATES, A. J. FOX, H. J. M. BARNETT, R. J. BLOM and D. MOULIN (London, Ontario)

A prospective study of clinical events following neuroangiography was performed on approximately 1,000 consecutive patients. Each patient had neurological and laboratory examination 24 hours before, 24 and 72 hours after angiography. 98% of the procedures were transfemoral, using primarily 5 French catheters. When not contraindicated, 2,000 units of Heparin were injected upon entering the arterial system and reversed by protamine at the end. Overall event rate was approximately 10%. There were no deaths. Discernable hematomas occurred in 6.5% but needed treatment in only 0.3%. Neurological event rate was 3.5%: 0.5% occurred during or less than 30 minutes following the procedure; 0.6% between 30 minutes and 24 hours after; 1.2% between 24 and 48 hours; 1.1% between 48 and 72 hours. 2.4% represented repeat or worsening of pre-existing conditions while 1.1% were de novo events. All permanent ischemia (0.5%) fell into repeat or worsening category. Factors such as gender, age, indications, findings, duration of procedure and of compression, technical difficulty, etc. were recorded and evaluated. Cataloging all post angiographic events for 72 hours neither verifies nor excuses the angiography as the cause of deterioration. Our event rate compares favourably with that of other studies and confirms the low but definite risk of cerebral angiography, even with an extremely thorough clinical protocol.

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6.

Far-Field Potentials From Near-Nerve Recording

K. ODUSOTE, A. EISEN and M. HOIRCH (Vancouver, Canada)

Studies on peripheral nerve suggest that some or all the short latency, far-field potentials of the SEP arise from electro-physical changes in the surrounding volume conductor and that they are not neurally generated (Kimura et al: Neurology 33:1164, 1983). These experiments have been extended by recording far-field potentials from the median, ulnar, and radial nerves evoked by digital or mixed nerve stimulation. After locating the nerves at the elbow with a near-nerve needle (G1), sequential recordings were made with G2 placed variably from as far distally as the wrist to as far proximally as the shoulder. Positive far-field potentials with latencies compatible with the origin of the anterior and posterior interosseus nerves were recorded *distal* to the elbow in median and radial nerve recordings respectively. Two far-field potentials were recordable *proximal* to the elbow from all three nerves with latencies of about 9 and 11 msec. They were seen with shoulder, mastoid, knee, or scalp references. Their amplitudes were several times the size of far-field potentials recorded with surface electrodes. The results suggest: (1) that peripheral nerve far-field potentials reflect sites of branching, (2) that near-nerve recording enhances volume conducted far-field potentials. Both these observations have relevance to the clinical applications of SEP far-fields.

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7.

Comparative Neuropsychology, Dementia and Basal Ganglion Disease

M. FREEDMAN (Toronto, Ontario)

Experimental paradigms adopted from the animal literature were used to study the functional anatomical and neuropsychological basis of dementia in humans with basal ganglion disease. The tasks administered, delayed alternation (DA) and delayed response (DR), are sensitive to bilateral frontal lobe damage. However, DA deficits are more pronounced following orbitofrontal lesions, whereas DR is more impaired after dorsolateral frontal lesions. Analogous findings occur following ventrolateral and anterodorsal sector lesions, respectively, of the head of the caudate.

Idiopathic Parkinson's disease (PD) served as the model for basal ganglion dysfunction. Demented Parkinson's patients (n = 11) were compared to non-demented Parkinsonians (n = 6), normal controls (n = 20) and patients with Alzheimer's disease (AD) (n = 12). The demented Parkinsonians were significantly impaired only on DR, whereas the Alzheimer patients were impaired on DR and DA.

Although dysfunction of the frontal lobes (and/or their subcortical connections) is implicated in the pathophysiology of both PD and AD, the data suggest that the respective sites of involvement are different. Dorsolateral frontal systems appear primarily impaired in PD whereas both dorsolateral and orbitofrontal dysfunction are prominent in AD. It is proposed that different anatomical, physiological and/or biochemical systems underlie cognitive impairment in basal ganglion disorders as compared to Alzheimer's disease.

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8.

Calcium Channel Blockers Increase the Risk of Rebleeding in the Early Stages Post Subarachnoid Hemorrhage (SAH)

E. ARBIT, R. KAPLAN, A. GILLICH and S. BREM (Montreal, Quebec)

Calcium antagonists are the subject of much interest due to experimental and clinical evidence suggesting that they are effective in reversing the cerebral vasospasm induced by SAH. However, the local vasospasm that follows damage or rupture of a vessel, seems to have a protective effect of the clot, at least initially. This study addresses the question of whether CA^{++} antagonist enhance rebleeding by diminishing this protective vasoconstricion. In an experimental model simulating SAH (rats with a transsected middle cerebral artery) we studied various calcium antagonists. We have previously reported that the rate of blood pressure (BP) elevation is a crucial factor in recurrent hemorrhage using this model. In control animals (N = 6) the hemorrhage was allowed to cease spontaneously and the clot was challenged by increasing the B.P. with aramine. Rebleeding occurred at a mean pressure increment of 75.8 ± 6.6 mmHg. In six out of seven rats treated with verapamil rebleeding occurred spontaneously without any B.P. manipulation. When the new clot was subsequently challenged with aramine rebleeding occurred at 44.4 ± .0 mmHg. This is significantly ($p<0.01$) lower than the control group. Similar results were obtained with diltiazem HCL, our results imply that Ca^{++} channel blockers can increase the hazard of recurrent intracerebral hemorrhage in the face of even small increases in B.P. in the early post hemorrhagic period.

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9.

Pharmacological Characterization and Anatomical Localization of Adenosine Receptors and Transport Sites in Rat CNS and Interactions with Antidepressants

J. D. GEIGER (Winnipeg, Manitoba)

Adenosine receptors and transporter binding sites in rat CNS were examined using radio-ligand binding and autoradiographic techniques. Adenosine receptors were labelled with [^{3}H] cyclohexyladenosine ([^{3}H] CHA), and the potent nucleoside transport inhibitor, [^{3}H] nitrobenzylthioinosine ([^{3}H] NBI) was used to label the transporter sites. Various nucleosides and adenosine receptor agonists and antagonists were examined for their ability to displace [^{3}H] NBI from its binding site and it was noted that adenosine was the most potent nucleoside and that [^{3}H] NBI was not labelling adenosine receptors. The transport sites were heterogeneously distributed in the CNS with a pattern remarkably similar to adenosine deaminase containing neural systems. The similar distributions of adenosine receptors, transporter binding sites and adenosine deaminase in dorsal spinal cord suggests a role for adenosine in sensory neurotransmission.

Ten different antidepressants were tested for their ability to compete for the receptor and transporter sites. A competitive type of inhibition was observed for both binding sites, and a few of the drugs displaced the radio-ligands at clinically relevant concentrations. These studies support the recent postulate that adenosine may mediate some of the actions of antidepressants.

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10.

In Vitro Immunohistochemical Localization of Fibronectin, Laminin, Collagen Type IV and Procollagen Type III to Leptomeningeal Cells and Meningiomas

J. T. RUTKA, M. L. ROSENBLUM and S. J. DeARMOND (San Francisco, California)

The authors describe the previously unreported finding of the *in vitro* immunohistochemical localization of a number of glycoproteins of the extracellular matrix to arachnoid cells and meningiomas. Three cell lines derived from normal human leptomeninges and eight from meningiomas were studied using indirect immunofluorescence in order to evaluate the cellular expression of the following largely mesenchymal protein: fibronectin, laminin, collagen type IV and procollagen type III. All leptomeningeal cell lines stained intensely and uniformly for all matrix proteins. All meningioma cell lines, with the exception of one, also stained uniformly; however, there was considerable variability in the observed intensity of staining. Electron microscopy of the leptomeninges and meningiomas *in vitro* revealed abundant desmosomes and dense tonofilament formation. SDS-Polyacrylamide gel electrophoresis of the cell layers and DEHE-cellulose chromatography of the culture medium demonstrated procollagen types I and III production. The data shows conclusively that normal arachnoid cells *in vitro* synthesize several of the collagen subtypes. These cells are most likely responsible for the "fibrous response" observed in the leptomeninges following trauma, infection, or tumor infiltration. The similarities between leptomeningeal cells and meningiomas that were seen *in vitro*, by electron microscopy and by indirect immunofluorescence would support the notion that meningiomas are tumors of arachnoid cells. In addition, the co-existence of a unique mesenchymal glycoprotein profile and specialized epithelial intracellular junctions in the same cell type argues for a mixed neural crest-mesodermal origin of the leptomeninges. Finally, these results suggest that the cells of the leptomeninges may be important contributors to normal basement membrane formation both perivascularly and along the glial limitans externa within the central nervous system. Production and maintenance of a basement membrane between different cell types may play an important role in preserving the normal cytoarchitecture of the central nervous system, and preventing tumor growth.

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11.

Automatic Recognition of Single Stimulus Evoked Potential

G. P. MADHAVAN, H. De BRUIN and A. R. M. UPTON (Hamilton, Ontario)

The technique of averaging to extract evoked potentials assumes that the responses evoked by a series of identical stimuli will themselves be identical. It is well known that the effects of habituation, fatigue and the inherent variability of the CNS renders this assumption unrealistic most of the time. We have shown that adaptive noise cancellation can extract BSAEP without repetition of stimulus, giving the so-called Single Stimulus Evoked Potential (SSt EP) (Madhavan et al, 1984). Effective application of EP methodology in I.C.U. and neurosurgery can become practical as there is no lag-time necessitated by repetition of stimuli as in the case of the conventional averaging technique. Stimulus repetition being unnecessary, new evoked potentials like olfactory evoked potentials can become practical.

Monitoring in intensive care situations and during surgical procedures using evoked potentials demands prolonged attention of a neurologist or a well-trained technologist. A pattern recognition scheme which considerably reduces the demands put on the EP analyst has been developed by us (Madhavan et al., 1983). The syntactic method, used in the development of this scheme, not only classifies the EP as normal or abnormal but also builds up a description of the EP so classified in terms of peak locations (latencies and amplitudes). Tests on this classifier using BSAEP's have shown an accuracy of 83% which should be adequate for our application here.

A combination of this form of pattern recognition with single stimulus EP should find wide application in neurological practice and research. Some typical applications of this combined system are in the monitoring of changes in auditory, visual or somatosensory pathways during surgical procedures, feedback systems for control of intracranial pressure, barbiturate administration, etc.

Madhavan, G.P. et al., Proc. I.E.E.E. Int. Conf. SMC, Bombay, 1983: 637-640

Madhaven, G.P. et al., Proc. 6 Conf. I.E.E.E., EMBS, Los Angeles, 1984: 699-702.

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12.

Effects of Anticonvulsant Drugs on Rat CSF Indole and Catecholamine Metabolites

V. H. MacMILLAN (Toronto, Ontario)

Male Wistar rats were prepared with a permanent cannula in the cisterna magna which allowed for repeated sampling of CSF in the unanesthetized animal. After an initial CSF sampling (35 μL), Valproic acid (50, 100, 250, 500 mg/Kg), Diazepam (1, 5, 10 mg/Kg), Phenytoin (12.5, 25, 50 mg/Kg) or Phenobarbital (12.5, 25, 50 mg/Kg) were given intraperitoneally and followed by CSF sampling at 1, 2, 3, 6 and 24 hours. 5-hydroxyindoleacetic (5-HIAA) and homovanillic (HVA) acid contents of CSF samples were determined by HPLC- electrochemical detection methods. Valproic acid and Diazepam produced dose dependent increases of up to 700 - 800% in CSF contents of 5-HIAA and HVA; whereas, Phenytoin and phenobarbital produced minor and non-dose dependent increases of 20 - 30%. The results suggest that Valproic acid and Diazepam have an inhibitory action on the transport mechanism that removes organic acids from the CSF.

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13.

Cystic Meningiomas

J-L. CARON, C. WORTHINGTON and R. LeBLANC (Montréal, Quebec)

Six cases of intracranial meningiomas associated with cyst formation are reviewed and a previously undescribed type of cyst is reported.

Four men and two women aged 33 to 62 years had onset of symptoms 2 to 52 weeks before the histological diagnosis of syncytial meningioma. Four patients presented with a focal neurological deficit, 3 with seizures, 3 with headaches, and 2 with personality changes. CT scanning showed a cystic, enhancing supratentorial lesion in 5 cases so studied. Angiographic changes suggestive of meningioma were observed in only 3 cases, and correct pre-operative diagnosis was made in only half of the cases. In all cases the cyst fluid was xanthochromic, acellular and highly proteinaceous. A complete biochemical analysis was obtained in two cases and will be discussed. The relationship of the cyst, tumor and the subarachnoid space account for a variety of anatomical configurations and suggest several possible pathophysiological mechanisms in the formation of cysts associated with meningiomas.

Because it could not be demonstrated in three cases where it was specifically looked for, the absence of an external carotid supply to these lesions does not rule out cystic meningioma. Although the CT scan in three cases demonstrated an enhancing nodule in close association with meningeal structures, the CT appearance was suggestive of a malignant glioma or metastatic tumor. Therefore there is no definite radiological procedure that can be relied upon to establish the diagnosis of cystic meningioma. This underscores the importance of biopsy in the evaluation and treatment of cystic enhancing lesions of the brain.

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14.

Primitive Neuroectodermal Tumors

A. M. LOZANO, P. J. MULLER, J. BILBAO and W. TUCKER (Ottawa, Ontario) (Toronto, Ontario)

Primitive neuroectodermal tumors (PNET) are malignant tumors of the central nervous system which have a predominance of undifferential cells resembling the multipotential cells of the primitive neural tube. These tumors may differentiate along neuronal or glial lines. They have a tendency to occur in early life, are often cystic or hemorrhagic, are sharply demarcated from adjacent brain, are microscopically malignant in appearance and often have a prominent mesenchymal component.

From a review of 800 brain tumor biopsy specimens in the Tumor Registry of the Hospital for Sick Children, Toronto, Becker and Hinton (1983) found 247 examples of PNET in the paediatric population; 112 of which were infratentorial (medulloblastoma).

The St. Michael's Hospital Brain Tumor Registry in the years 1980-1983 contained data on 487 brain tumors in patients over the age of 18 years, 17% of which were infratentorial and 83% supratentorial. We identified 6 medulloblastomas in the infratentorial group and 3 other PNET in the supratentorial group. We are reporting the three cases of adult supratentorial PNET.

Their ages ranged from 20-49 years. All were treated with a combination of surgical resection and radiation therapy; two also underwent chemotherapy. One patient died 10 months after surgical treatment and the other 2 were alive at 1 and 2 years follow-up respectively. The histological features of these tumors as well as the theories of neurocytogenesis will be presented.

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15.

Superselective Arterial Administration of BCNU in High Grade Gliomas: Clinical Trial and Positron Emission Tomography Correlation (preliminary results)

J-G. VILLEMURE, J. THÉRON, L. Y. YAMAMOTO, M. DYKSIC, R. HAND, C. WORTHINGTON, J. TYLER, D. TROP, M. ABOU-MADI, D. ARCHER, L. MORIN, P. RAVUSSIN, R. LeBLANC, C. LUNEAU, L. PRESCOTT, S. GAUTHIER and W. FEINDEL (Montréal, Québec)

Superselective infusion of BCNU in a main cerebral artery (distal internal carotid, middle cerebral, or posterior communicating) should provide high and prolonged concentrations of the chemotherapeutic agent to the tumor with relative sparing of normal brain. Patients with histologically proven high grade gliomas who were status post operation and whole brain radiation were entered into this study at the time of clinical and/or radiological recurrence. Positron emission tomography was performed using intravenously administered ^{11}C-BCNU, and relative uptake was measured of the chemotherapeutic agent in tumor versus normal brain. Subsequently, the principle intracerebral vessel supplying the tumor was catheterized superselectively. A second PET scan was performed using ^{11}C-BCNU injected intraarterially through the superselective catheter. A therapeutic dose of BCNU (150 mg/m^2 BSA in D5W) was then administered via this route. There were 13 patients initially entered in this study. In 3 cases the procedure was abandoned due to complications of catheter placement. Four patients had two catheterizations and 6 had one. In the 14 cases in which patients received treatment 7 showed improvement, 5 showed no response, 2 died too early for follow-up, of whom 1 died of an unrelated cause. PET studies demonstrated a higher concentration of BCNU in tumor (mean of 75 times greater) with intraarterial infusion as compared to intravenous injection.

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16.

Familial Occurrence of Multiple Cerebral Vascular Malformations: Absence of Circulating Endothelial Growth Factor

J. TURNBULL, H. VINTERS, P. COSTELLO (London, Ontario)

Three brothers with multiple cerebral vascular malformations are described. One has symptoms referrable to a brain stem mass lesion. Symptomatic deterioration paralleled an increase in size of the lesion as judged by serial CT scans, and symptomatic improvement followed partial resection. The pathology revealed a vascular malformation (most consistent with arteriovenous malformation). He also had three subcutaneous nodules excised, all compatible with cavernous hemangiomata. The two other brothers had similar lesions on CT head scan. One has epilepsy, deafness, and hydrocephalus, while the other is asymptomatic. We postulated that the lesions could be caused by an endothelial abnormality or a circulating endothelial growth factor. The latter hypothesis was tested by exposing cultured endothelial cells (initially isolated from mouse or human brain microvessels) to media supplemented with serum from either the patients, or age and sex-matched controls, and measuring the effects of the sera on [^{3}H]-thymidine incorporation into DNA within the cells. In this system, there was no consistent difference in [^{3}H]-thymidine incorporation. We conclude that, if abnormal endothelial proliferation is the basis for a familial syndrome of vascular malformations such as we have described, the pathogenesis of the condition cannot be ascribed to a circulating factor that is mitogenic for microvascular endothelium.

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17.

Treatment of Tic Disorders with Clonazepam

L. VOULTERS, S. B. BRESSMAN and S. FAHN (New York, New York)

Haloperidol has been the mainstay of treatment for tic disorders over the last few years. However, it is now thought that up to 50% of patients either do not respond or develop intolerable side effects to haloperidol, precluding its continued use. In addition, there is still a concern about the long term effects of prolonged use of this antidopaminergic agent. There has therefore been a search for safer and more effective alternative drugs to treat tics.

We have conducted an open trial on 25 patients (19 male, 6 female) with tic disorders, either Tourette's syndrome (15 patients) or chronic motor tics (10 patients). Ages at time of treatment were from 6 years to 60 years (Mean 24.4 yrs.). Duration of disease ranged from 2 years to 43 years (Mean 15.2 yrs.).

All patients took clonazepam for a minimum of 3 months and average dose given was 2.5 mg daily. Follow-up was from 3 months to over 4 years and patients were evaluated using a global assessment. 17 patients (68%) had a significant response to clonazepam, defined as >50%

suppression in tics, sustained for at least 3 months. Side effects, most commonly drowsiness and occasionally behavioural changes were moderate or severe in 7 patients (28%) of which 4 in the good response group had to discontinue the drug.

Clonazepam thus compares favorably with haloperidol, pimozide, fluphenazine, tetrabenazine and clonidine, the drugs most commonly used in tic disorders with reported efficacies ranging from 40% — 70%.

We therefore conclude that clonazepam is an effective and safe drug and should be considered as a first line treatment for tic disorders.

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18.

The Diurnal Variation of Carbamazepine and Carbamazepine-10, 11-Epoxide Concentration of Saliva in Children with Epilepsy

O. EEG-OLOFSSON, E. BÄCKMAN, A. BERTLER and G. DAHLSTRÖM (Linköping, Sweden)

The aim of this study was to analyse the diurnal variation of the concentration of CBZ and CBZ-10, 11-epoxide in saliva of 33 mentally normal children treated with Tegretol. The diurnal variation of CBZ and its metabolite was considerable, with fluctuations between 30 and 115 per cent of the mean value.

The advantage of sampling saliva is that a great number of samples can be taken during twentyfour hours without blood losses and without exposing the child to repeated discomfort through venipuncture or finger pricks. Saliva samples also make controls at home possible, as the child with help of the parents can handle the sampling himself.

The concentration of CBZ and its epoxide in saliva mirrors the pharmacologically active fraction of plasma and is equivalent to the cerebrospinal fluid concentration.

One single sample of plasma or saliva taken drug fasting in the morning is not enough for estimating the adequate dose intake of CBA. The recommendation is to take both a fasting sample and another sample three hours after drug intake in the morning. It is possible that side effects as fatigue, diplopia, ataxia and vertigo will not vanish when changing from b.i.d. to t.i.d. A reduction of the dose is required, and usually a b.i.d. procedure can still be used.

As relatively great fluctuations during the twentyfour hours of the saliva concentrations of CBZ is found, a levelling could be obtained using a slow-release formula of CBZ.

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19.

Pergolide in the Management of Advanced Parkinson's Disease

J. D. GRIMES, M. N. HASSAN, L. D. SITWELL, P. GRAY and L. W. PAYNE (Ottawa, Ontario)

Dopamine agonists benefit many patients with advanced Parkinson's Disease (PD). Pergolide mesylate, a synthetic ergoline, is about 10 times as potent as bromocriptine. Twenty patients with advanced PD (mean duration 9.2 years) complicated by fluctuations (19 patients) and dyskinesias (15 patients) were treated with Pergolide in a double-blind placebo controlled study. Pergolide therapy was initiated at a dose of 0.1 mg daily and increased until clinical benefit was achieved, adverse effects developed, or a maximum daily dose of 5 mg was reached. Sinemet therapy was reduced if dyskinesias increased.

Ten of the 20 patients received active drug. The mean daily dose of Pergolide was 4.0 (range 3.25-5) mg. Dyskinesias increased in 7 patients and were improved with a mean daily Sinemet reduction of 190 (range 50 to 375)mg. Activities of daily living improved 50%; PD severity score was reduced by 58% (78 to 33). Daily "off time" decreased by 43% (6.0 to 3.4 hours) and end of dose dystonia was improved in 5 of 7 patients. One patient dropped out early with nausea and dyskinesias; no significant changes occurred in laboratory studies.

A clear placebo effect was obvious in the other 10 patients. Improvement was documented in activities of daily living (16%), "off time" (24%) and PD severity score (20%). These patients have been started on active drug.

Pergolide is a potent anti-Parkinsononian agent. It is effective in end of dose failure and, when combined with Sinemet reduction, dyskinesias are significantly reduced. The drug is safe, with tolerable adverse effects.

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20.

Decreased Density of Benzodiazepine Receptors after Chronic Antidepressant Treatments

B. E. SURANYI-CADOTTE, T. V. DAM and R. QUIRION (Verdun, Quebec)

The benzodiazepine (BZ)/GABA system has been extensively implicated in the actions of anxiolytic drugs. In addition to the benzodiazepines, anxiolytic effects have also been clearly demonstrated for a number of antidepressant agents. The present study was undertaken to investigate whether an interaction with BZ receptors may be involved in the mechanism of action of antidepressant agents. Since the therapeutic effects of antidepressants cannot be ascribed to short-term neuroreceptor changes, we have studied the effects of chronic treatment with different classes of antidepressants on BZ receptors in rat brain. Rats received twice-daily i.p. injections of either saline or 10 mg/kg desipramine, zimelidine, bupropion or adinozolam for 21 days. Twenty-four hours after the last injection, animals were killed, and brains were removed and stored at −70°C for subsequent BZ receptor binding assays using ^{3}H-flunitrazepam. Specific ^{3}H-flunitrazepam binding to homogenates of rat brain was defined by 1 μM clonazepam and represented 80-85% of total binding. Scatchard analysis of ^{3}H-flunitrazepam binding revealed that chronic treatment with desipramine, zimelidine, bupropion and adinazolam significantly reduced BZ receptor density (B_{max}) by 58 to 75% below control values (for all drug-treated groups $p < 0.001$ compared to saline treated group). From these results it appears that long-term treatment with drugs which have markedly different acute pharmacological profiles, but which display antidepressant properties can reduce the density of BZ receptors. Overall, these data suggest that an interaction with BZ receptors should be considered as a possible mechanism of action of antidepressants.

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21.

Adrenoceptor Binding Studies in Cerebral Cortex: Role of Disulfide and Sulfhydryl Groups at the α−1 and α−2 Sites

T. A. READER, L. GRONDIN and R. BRIÈRE (Montréal, Québec)

The tritiated adrenergic antagonists Prazosin ([^{3}H] PRZ) and Idazoxan ([^{3}H] IDA) bind specifically and with high affinity to α1 and α2 adrenoceptors in membrane preparations from cerebral cortex. Saturation experiments performed to determine the density of receptors and their dissociation constants were analyzed by iterative modelling and the procedure of Hill. The specificity of the labelling was determined by displacement experiments: for [^{3}H] PRZ the potencies were phentolamine >> clonidine > yohimbine > benextramine >> adrenaline > phenylephrine. The displacement experiments with [^{3}H] IDA showed that phentolamine > yohimbine > clonidine > benextramine >> phenylephrine > adrenaline. Since receptors are of protein nature, we examined the role of disulfide (−SS−) bridges and sulfhydryl (−SH) groups in the specific fixation of [^{3}H] PRZ and [^{3}H] IDA to the α1 and α2 sites. Treatments of the membranes with the −SS− reactive DL-dithiothreitol (DTT) or the −SH alkylating agent N-ethylmaleimide (NEM), alone or in combination, decreased specific binding or both ligands, with only minor changes in the non-specific counts. The [^{3}H] IDA binding (α2−sites) was more sensitive to both DTT and NEM than the [^{3}H] PRZ sites (α1). The initial changes induced by alkylation (low doses of NEM) of the α2 site were due to an important decrease in the affinity for [^{3}H] IDA. This change in affinity caused by alkylation of a thiol group could explain the higher potency of benextramine at the α2−site. The results provide further evidence for the participation of −SS− and −SH groups in the binding site of α1 and α2 adrenoceptors in the cerebral cortex.

Supported by MRC; MA-6967 and the Savoy Foundation for Epilepsy.

. — 0092

22.

Localization of Neurotransmitter and Neuropeptide Receptors in Human Brain

R. QUIRION, M. DALPÉ, P. LEMOINE, P. ETIENNE, N. P. V. NAIR and S. GAUTHIER (Verdun, Québec) (Montréal, Québec)

Much evidence suggests the existence of multiple classes of neurotransmitter receptors in the brain. Visualization of receptor sites by autoradiography also strongly supports that concept. However, very little is currently known on neurotransmitter receptor distribution in human brain. Thus, we have investigated the *in vitro* receptor autoradiographic distribution of various transmitters in *whole* human brain hemisphere. At autopsy, the brain is cut in 4-5 mm-thick coronal sections that are rapidly frozen in 2-methyl butane at −40°C to avoid ice crystal formation and then kept at −80°C until used. For autoradiography, 20 μm-thick whole hemisphere sections are cut at −15°C using a large stage cryomicrotome, and mounted on gelatin-coated slides, dried and kept at −80°C until used. Sections are then processed for receptor autoradiography according to incubation conditions previously determined. The following receptor binding sites were investigated: opiate, substance P, substance K, cholecystokinin, serotonin, acetylcholine, somatostatin as well as binding sites for calcium channel antagonists. In normal brain, high densities of opiate, substance P, substance K, cholecystokinin, somatostatin, calcium channel antagonists and hemicholinium binding sites are present in caudate and putamen. Moderate densities of substance K binding sites are found in the globus pallidus. All other ligands do not reveal significant binding in the area. The claustrum is enriched in opiate, substance P, cholecystokinin and calcium channel antagonist binding sites. Frontal, parietal and temporal cortices are enriched in opiate, substance K, cholecystokinin, serotonin and hemicholinium binding sites. However the laminar distribution of the respective binding sites is different. Already, our preliminary data demonstrate the differential distribution of various neurotransmitter receptors in brain using a new technique: whole human brain hemisphere receptor autoradiography. We are currently investigating possible receptor alterations in Parkinson's and Alzheimer's Diseases.

. — 0094

23.

A Cross Canada Survey of Neurologists and Neurosurgeons on Controversial Issues in Epilepsy Management

M. W. JONES and J. BRUNI (Vancouver, B.C.) (Toronto, Ontario)

A standardized questionnaire incorporating 23 "Yes-No" type questions (and with discussion) was circulated to the Canadian Neuroscience Community. Questions dealt with driving and epilepsy, selected problematic cases of tumors, drugs of choice for various seizure types and a section on pregnancy and breast-feeding. 29% (39) of Neurosurgeons surveyed responded and 30% (120) of all Neurologists surveyed responded.

Selected Results: 91% of Neurologists and 89% of Neurosurgeons do not routinely report patients with epilepsy to the Motor Vehicles Branch. There was a split on the question of patients with simple partial seizures with full motor control being allowed to drive, with 55% of Neurologists saying Yes and 47% of Neurosurgeons saying Yes. If the same patient in the same situation was a professional truck driver, 69% of Neurologists felt he should not drive as did 82% of Neurosurgeons. 51% of Neurologists felt it was safe for a patient with myoclonic jerks only to drive, and 49% of Neurologists felt patients with auras only could drive. 82% of Neurologists and 92% of Neurosurgeons felt patients with "rum fits" should not drive, and 60% of Neurologists and 76% of Neurosurgeons felt these patients should be reported to the Motor Vehicles Branch. 29% of Neurologists and 44% of Neurosurgeons would not treat a patient with a single cryptogenic seizure with a normal EEG. 52% of Neurologists felt surgery for epilepsy was underutilized as a mode of treatment, and 17% were undecided. 62% of Neurologists felt mothers could breast-feed safely, whereas 30% they should not and 9% were undecided. The "ideal" antiepileptic drug for planned pregnancy was Tegretol in 62% respondents with Dilantin being scored at 21%.

Summary: It would seem from this survey, except for the one example of alcohol and seizures, there is a wide variance of opinion on a number of commonly encountered clinical problems. We will try to correlate these interesting findings with the present motor vehicle regulations for each province as relates to epilepsy and correlate the findings with what scientific literature is available on other aspects reviewed in this survey.

. — 0104

24.

In Vivo Studies of Dopamine Synthesis in Schizophrenia

A. J. STOESSL, T. A. HURWITZ, H. PARFITT, W. R. W. MARTIN, T. J. RUTH and M. J. ADAM (Vancouver, B.C.)

Dopamine synthesis in two males with untreated schizophrenia was studied using positron emission tomography (PET). One subject, age 19, had been ill for 8 months and the other, age 45, had been ill for 15 years. Both patients were assessed by two research psychiatrists using the Schedule of Affective Disorders and Schizophrenia (SADS) and both met DSM-III criteria for schizophrenia. Neither had received neuroleptic treatment at any time prior to PET.

Patients received pretreatment with 100 mg oral Carbidopa and were then scanned following the intravenous administration of 1.5-3 mCi of ^{18}F-6-fluorodopa, which is metabolized to fluorodopamine in nigrostriatal nerve terminals. The use of a high resolution, multislice PET camera allowed the generation of coronal images which facilitated accurate placement of regions of interest. In the schizophrenic patients, activity in the caudate and putamen was similar to that seen in normal subjects of comparable age. Activity in the left nucleus accumbens was likewise similar, but there was a moderate depression of activity in the right nucleus accumbens in both patients.

Although preliminary, these data suggest an imbalance of mesolimbic dopamine activity in schizophrenia. PET studies using fluorodopa and positron-emitting receptor ligands should prove useful in further investigations of mental illness.

. — 0107

25.

PET Studies of Glucose Metabolism in Huntington's Disease

A. J. STOESSL, M. R. HAYDEN, W. R. W. MARTIN, C. CLARK and B. D. PATE (Vancouver, B.C.)

Local cerebral glucose metabolism (LCMRG) was studied using positron emission tomography (PET) in ten patients with early Huntington's disease (HD) who had only mild caudate atrophy on CT. Using linear discriminant analysis, the HD group was clearly separated from normals with 100% correct classification. Mean caudate CMRG was 4.38 mg/100g/min, compared with 7.92 mg/100g/min in the normal subjects ($F_{1,13} = 37.0$, $p < .001$). There was no significant difference in thalamic CMRG between the two groups.

We have also studied seven clinically and radiologically normal subjects at risk for developing HD, using both PET and DNA marker techniques. In the single subject with PET evidence of caudate hypometabolism, DNA analysis revealed a 95% probability of developing HD. PET can provide important information regarding the duration of caudate hypometabolism prior to the onset of clinical features in HD, although its value as a predictive test is yet to be fully determined.

. — 0108

26.

Mechanism of Neurogenic Hypertension and Cardiac Arrhythmias in Animal Study

D. E. RICHARDSON and C. W. DEMPSEY (New Orleans, Louisiana)

Systemic blood pressure elevation and cardiac dysrhythmias often follow subarachnoid hemorrhage and head trauma. In an attempt to understand the neural mechanism involved and develop an appropriate

intervention, we have conducted an animal study in 16 cats and rabbits.

Systemic blood pressure elevation and abnormal EKG's can be reliably produced in both species by stimulating a pressor area in the inferior medial frontal lobes anterior to the preoptic area. Mean blood pressure increases of 50-100 mm Hg are regularly elicited by stimulating currents of 2-3 milliamperes, while at higher currents the EKG response dependably displays inverted T-waves, prolonged P-R intervals, and occasionally inverted QRS complexes and irregular pacing marked by bi- and tri-geminy.

The beta-blocker propranolol (0.15mg/kg I.V.) has been observed to attenuate both the baseline mean blood pressure as well as the rises that occur in response to the stimulation. The alpha-blocker pentolamine (similar dose) produces smaller, but similar effects upon blood pressure. But, alpha blockade has proved more reliable in restoring normal wave form to the EKG. Maximum correction is achieved by administering both drugs together. Animals so treated are protected against stimulating currents more than twice as high as the threshold values.

These studies would indicate that the blood pressure and cardiac changes following brain injury or subarachnoid hemorrhage may be the result of focal injury to the medial frontal lobes and produces its effect from a norepinephrine/epinephrine storm that can be prevented or treated.

. — 0112

27.

Hippocampal CA1 Neurons in Slices Acutely Maintained in Clonazepam Exhibit Hyperexcitability Upon Drug Withdrawal

M. F. DAVIES, S. SASAKI and P. L. CARLEN (Toronto, Ontario)

Rat hippocampal slices were bathed in artificial CSF containing 20 nM clonazepam (CLON) from 2 to 6 hours, then transferred to the recording chamber at 35°C. CA1 neurons were impaled with K Acetate or KCl electrodes in 20 nM CLON and control measurements made. In CLON, the cells were generally silent with no spontaneous epileptiform activity present. Upon drug withdrawal, hyperexcitability in the form of spontaneous paroxysmal depolarizations and 1 or 2 extra EPSPs after the initial EPSP with orthodromic stimulation were observed. These changes occurred within 5-30 minutes after solution change and the latency was dependent on the rate of solution exchange. The depolarizing current required to elicit 1 spike and the orthodromic threshold were decreased. The epileptiform activity observed is similar to that seen in slices taken from rats chronically fed high doses of clonazepam (Davies and Carlen, Soc. Neurosci. Abstr. *10*, p. 561, 1984.). Therefore acute exposure of hippocampal slices to a concentration seen in the CSF with chronic administration of high doses of clonazepam may cause a rapid adaptation to an increased inhibitory state within the tissue. This study demonstrates that withdrawal epileptiform phenomenon can be demonstrated in in vitro mammalian tissue after only a few hours exposure to an anticonvulsant.

Supported by the Medical Research Council of Canada and Canadian Geriatrics Society.

. — 0117

28.

EEG Abnormalities Including Epileptiform Activity in Rats Induced by Chronic High Dose Clonazepam Administration, Withdrawal or Benzodiazepine Blocker Administration

I. A. NAQUET, M. F. DAVIES, M. W. BURNHAM and P. L. CARLEN (Toronto, Ontario)

We investigated the electroencephalographic activity of high dose clonazepam (50 mg/kg) administered for one month to 20 rats with 10 controls, as well as acute drug withdrawal and the action of the benzodiazepine antagonist CGS-8216. Spontaneous electrical activity was measured in frontal cortex (FrC), amygdala (Amy), hippocampus (Hipp) and mesencephalic reticular formation (MRF). During the course of clonazepam administration abnormalities in all areas were seen and these changed with time. Behavioral tolerance to the sedative actions of clonazepam also was noted. The major abnormalities were increased amplitudes in Amy and Hipp. A decrease in amplitude in FrC and MRF were observed in 8 rats. Five rats demonstrated epileptiform discharges in FrC during the chronic drug administration in the 3rd and 4th weeks. These electrical abnormalities corresponded with behavioral changes. The animals were initially sedated and 14 showed excitable behavior between the 2nd and 3rd week. Upon acute withdrawal of clonazepam or by injection of CGS-8216 (25 mg/kg) epileptiform activity was seen in all brain areas. The animals were hyperexcitable with increased activity, sniffing, twitching and tremor. However, no motor seizures were observed. Power spectral analysis of these data will be presented.

The major conclusion is that prolonged high dose administration of clonazepam is associated with EEG epileptiform abnormalities without motor seizures. Acute drug withdrawal or blockage of benzodiazepine receptors greatly increased the frequency of observed epileptiform abnormalities.

Supported by the MRC and Ontario Mental Health Foundation.

. — 0118

29.

Radioautography for Nerve Growth Factor Receptors

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

A technique has been developed for the radioautographic localisation of receptors for nerve growth factor (NGF) within the mammalian central nervous system. Cryostat sections of the rat lumbar spinal cord were incubated with ^{125}I-iodinated NGF, rinsed briefly, and exposed to radiosensitive film (LKB Ultrofilm). Optimal concentrations of ^{125}I-NGF and conditions for incubation were established by preliminary counting of gamma activity bound to sections or membranes from the spinal cord. The dissociation equilibrium constant for spinal receptors (concentration for half-maximal saturation) was in the order of 10 ^{10}M and the receptors were densely concentrated in laminae I and II (Rexed) of the dorsal horn. Specificity was demonstrated by suppression of binding in the dorsal horn when excess unlabelled NGF was added to the incubation mixture. The results extend previous observations that NGF can be selectively internalised and retrogradely transported by spinal axons of primary sensory neurons. However, the function of such receptors is unknown as no endogenous ligand has yet been identified in the spinal cord. The method can now be used to study the cerebral distribution of NGF receptors and the response of NGF receptors in injury and disease.

This work was supported by the Multiple Sclerosis Society of Canada and Medical Research Council of Canada.

. — 0119

30.

Low-density Lipoprotein Initiates the Production of Neovascularization by Cultured Smooth Muscle Cells

H. ALPERN-ELRAN, S. BREM, G. A. HOOVER, S. McCORMICK, E. ARBIT and N. KALANT (Montréal, Québec)

In previous studies, we observed that neovascularization was induced by atheromatous plaques taken from patients at the time of carotid endarterectomy. Histologic examination revealed that this putative angiogenic factor, A.N.F., was produced by the cellular component of the plaque, and not by the calcific, necrotic, acellular areas. We therefore investigated the role of smooth muscle cells in the production of neovascularization.

Suspensions of cultured smooth muscle cells, derived from explants of the pig aorta, were injected into a corneal assay to test for neovascularization. These cells from the non-atheromatous aorta consistently failed to induce neovascularization (N = 10). Because of the important role of low density lipoproteins (LDL) in atherogenesis, we tested a second group of smooth muscle cells, prepared under identical conditions but incubated with LDL for 24 hours. When the LDL-treated cells were placed in the corneal assay, a brisk neovascular response was elicited in 89% (8/9) of the eyes.

LDL may trigger the production of a neovascular factor by smooth muscle cells, that could be important in the natural history of plaque development in patients with atherosclerosis.

. — 0122

31.

Angiogenesis in Human Brain Tumors: Inhibition by Copper Depletion

S. BREM, H. ALPERN-ELRAN, A. O'DONNELL and E. ARBIT (Montreal, Quebec)

The development of blood supply is a crucial step for the growth of solid tumors. Capillary endothelial proliferation is especially prominent in intracranial tumors. These tumors are a potent source of angiogenic factors. Recently copper ion has been shown to be an essential co-factor and possible regulator of angiogenesis.

To test the hypothesis that copper depletion could inhibit angiogenesis in vivo, we tested 425 tumor fragments from 10 patients haboring a spectrum of CNS neoplasms: astrocytoma (141 fragments), meningioma (76), acoustic schwannoma (75), medulloblastoma (47), choroid plexus papilloma (42), hemangioblastoma (44). Test fragments (208) were implanted in the corneas of rabbits placed on copperdeficient diets, supplemented with penicillamine, and 217 fragments were transplanted to normocopremic animals.

All ten CNS neoplasms stimulated a brisk neovascular response, regardless of histiotype. With reduction of the copper level, we observed that: 1) Angiogenesis was totally inhibited and failed to appear in 50% of the test fragments, as contrasted to 26% of the controls ($P < .025$); 2) In the remaining eyes with an angiogenic response, there was a) Reduction in the number of average vessels/cornea (test = 53, control = 70) b) Delay in the onset of vascularization after implantation (test = 5 days, control = 4 days) c) Reduction in the rate of vascular growth (test = 0.12 mm/day, control = 0.16 mm/day, $p < .025$).

It has been previously shown that inhibition of angiogenesis leads to the regression of experimental tumors. Our results indicate that copper depletion retards neovascularization induced by human brain tumors. By interfering with tumor angiogenesis, depletion of copper ion could serve as a new approach for the treatment of patients with human brain tumors.

This work is supported by the Cancer Research Society.

. — 0124

32.

Endarterectomy In Asymptomatic Carotid Disease

R. N. GOYAL, B. G. BENOIT and N. A. RUSSELL (Ottawa, Ontario)

The widely practiced procedure of carotid endarterectomy, is currently undergoing a period of more critical appraisal. The risk/benefit ratio of the operation in patients with symptomatic disease, has been defined with a reasonable degree of accuracy. However, such data is not as readily available for patients presenting with asymptomatic carotid disease. It has been estimated that the risk of major stroke without warning ischemic event, in this group of patients, may range up to 5 percent per year. The combined risk of angiography and surgery varies, but it is usually higher. However, most of the reported series pertain to operations performed on symptomatic carotid stenosis, whereas it has been our experience that the risk is less, for operations performed on an asymptomatic vessel.

In previous years, we have been carrying out prophylactic endarterectomies on a small, selected group of patients, with asymptomatic carotid disease. The majority of these patients had presented with asymptomatic stenosis, and were found at angiography to harbour a significant lesion on the contralateral side. The indications for operation on the asymptomatic carotid included degree and irregularity of the lesion, evaluation of collateral flow, assessment of associated risk factors, and other considerations.

Our series includes a total of 52 patients, operated upon between the years of 1976 to 1984. One patient experienced a post-operative T.I.A., and another died from a cerebral infarction, resulting in a risk level of 2 percent. Follow-up data will be presented.

Since a group of patients such as this, has already passed the small, but definite, risk of angiography, prior to the operation on their asymptomatic carotid artery, a low surgical morbidity and mortality rate begs the question whether or not these operations should continue to be performed. An "acceptable risk" for the combination surgery and angiography in asymptomatic patients, has been estimated to be approximately 3 percent. However, it may be possible to define a small subgroup of patients, including some of those who have one symptomatic side, who might benefit significantly from an endarterectomy on their asymptomatic carotid stenosis.

. — 0125

33.

Genetics of Primary Generalized Dystonia in British Columbia and Alberta

O. SUCHOWERSKY, D. B. CALNE and M. H. HAYDEN (Calgary, Alberta) (Vancouver, B.C.)

Primary generalized dystonia (PGD) is a rare disorder with a reported prevalence of 3 per million. Fifty percent of cases are genetic. Autosomal recessive (AR) and autosomal dominant (AD) forms are seen, the former being more common in the Ashkenazi Jewish population.

To study the genetics of primary generalized dystonia (PGD) in B.C. and Alberta, patients with PGD were ascertained by contacting physicians in both provinces and through the B.C. Genetics Registry. All cases were examined to verify the diagnosis. Detailed family histories were obtained and all available family members examined. 21 patients from 17 families were identified (prevalence = 4.2 per million). Of these, 9 families (53%) showed a hereditary pattern: 6 were AD, 1 was AR, and 2 indeterminate. In AD families, expression was variable with some members showing mild focal dystonia (torticollis, writer's cramp, spasmodic dysphonia), which was only apparent by examination. Two patients were of Ashkenazi Jewish origin and both of these were sporadic.

Our study shows that in familial PGD, the most common pattern of inheritance is AD. However, there is wide variability in the severity of the dystonia and careful examination is necessary to find all affected family members.

. — 0130

34.

The Aicardi Syndrome, Reassessed

H. Z. DARWISH, C. B. VAN ORMAN, R. H. A. HASLAM, H. B. SARNAT and S. COUPLAND (Calgary, Alberta)

Aicardi et al described a syndrome characterized by particular abnormalities in the fundus oculi, early infantile spasms, corpus callosum agenesis and associated anomalies. The syndrome is considered lethal in males and characterized by mental deficiency in females. We reviewed 5 girls who presented in a 4 year period and in 3 of the cases, an erroneous diagnosis was first made by an ophthalmologist or neurologist. The correct diagnosis was made at a mean age of 9 mths (range 2.5 - 19 mths). These children first came to medical attention because of seizure activity (4/5), but the greatest longterm problem has been their profound developmental delay. The seizures were mixed in type but always included flexion spasms. These were not typical infantile spasms because of sustained rigidity and laterilized features. The seizures had an early onset (mean 10 wks., range 4 - 15 wks) and were never completely controlled. ACTH was effective in one of two patients so treated. One patient died at 7 mos. with aspiration occurring during a seizure. The other 4 patients are alive; the oldest boy is now 5 yrs. and 10 months. There is diversity in the literature regarding the EEG abnormalities. We disagree with Fariello et al but in general concur with Bertoni et al and Aicardi and Chevrie's descriptions. Yet we found that the asynchrony emphasized by Aicardi was most usually present only at an early age and was quite variable in degree. Consistent lateralized epileptiform discharges were present in 3/5 infants. Sleep spindles were present at an early age in all patients but these were abnormal (lateralized, brief, low amplitude and/or poorly formed). We noted two features not previously highlighted: 1) the presence of bursts of large amplitude paroxysmal theta and 2) sustained bursts of paroxysmal beta. We believe these may arise from heterotopic tissue. In spite

of the remarkable abnormalities seen on ophthalmoscopy, the two ERGs done were normal consistent with previous pathological descriptions suggesting that the lacunae in the fundus are limited to the choroid layer and do not affect retinal ganglion cells. CTs were always remarkably abnormal. In addition to absence of the corpus callosum, variable cerebellar hypoplasia, and irregular midline cystic structures, they always consistently showed bizarre asymmetric lateral ventricles. We believe these features, when seen together on CT, are rather specific for the Aicardi syndrome.

. — 0134

35.

Intravenous DSA for Carotid Artery Disease

R. DEL CARPIO O'DONOVAN, B. BENOIT and N. RUSSELL (Ottawa, Ontario)

Intravenous digital subtraction angiography (DSA) was carried out in 122 patients who presented with suspected ischemic cerebrovascular disease to the Ottawa Civic Hospital during our first six months of operation, between July and December 1984.

107 of these were out-patients (87%).

Of the 244 carotids examined 59 were abnormal, 44 showed significant stenosis (greater than 50%) and 15 showed complete occlusion.

DSA was originally conceived as a screening procedure, however it has become the final diagnostic examination in some patients. 21 carotids were studied by conventional angiography and in 16 the DSA findings concurred. Comparison with Doppler indicated 75% consistency. Correlation with surgical findings will be assessed. Only 1 major complication occurred which required hospitalization.

. — 0136

36.

Apnea Testing

M. J. STRONG and G. B. YOUNG (London, Ontario)

In apnea testing, continuous oxygen administration usually prevents hypoxemia while $PaCO_2$ levels rise. Simple observations for respirations could miss small volume breaths or mistake some upper torso movements for respiratory effort. We studied 12 patients who met Canadian (1), British (2) and American (3) criteria for brain death, to investigate the role of blood gas testing in the diagnosis of apnea.

Thirteen ten minute apnea tests were performed without preoxygenation with O_2 delivered via trachial cannula at 6 l/min. Initial mean $PaCO_2$ was 34.23 ± 12.96 mmHg. with some patients showing significant hypercapnia, and body temperature ranged from 35 - 38°C. We have found a $\Delta PaCO_2$ of 3.18 ± .42 mmHg/min (mean ± S.E.M.) ($p < 0.005$) and ΔpH of 0.024 ± 0.003/min ($p < 0.005$). Mean ΔPaO_2 during the procedure was 2.85 ± 1.38 mmHg (not significant). We suggest therefore that in conjunction with careful observation for respiratory effort, and in the absence of preoxygenation or hyperventilation to decrease $PaCO_2$ levels, blood gas determinations be done at the beginning and end of apnea testing. A $\Delta PaCO_2$ of 3.18 ± 0.42 mmHg/min or ΔpH of 0.024 ± 0.003/min is of confirmatory value in demonstrating absent respirations.

References

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. — 0154

37.

Polyneuropathy in Critical Illness: Analysis of Etiologic Factors

D. W. ZOCHODNE, C. F. BOLTON, G. A. WELLS, J. J. GILBERT, J. D. BROWN and W. J. SIBBALD (London, Ontario)

Polyneuropathy has been identified in patients with multi-organ failure, sepsis, and prolonged ventilator dependence (Bolton CF, Gilbert JJ, Hahn AF, Sibbald WJ, J. Neurol. Neurosurg. Psychiatry 1984; 47: 1223-1231). We studied 19 critically ill patients with mild (8), moderate (5) and severe (6) electrophysiologic or pathologic evidence of polyneuropathy. Difficulty in weaning from assisted ventilation prompted investigation. Clinical signs included weakness (11), wasting (4), fasciculations (2) sensory loss (4) and absent or depressed deep tendon reflexes (14). Electromyography revealed widespread denervation. Autopsy in eight of eleven patients who died disclosed axonal degeneration with denervation atrophy of respiratory and limb muscles. Polyneuropathy could not be attributed to specific drugs, infecting organisms or hypophosphatemia from hyperalimentation. An analysis of variance also demonstrated that the degree of severity did not correlate with any of the following: age, duration of illness, indices of nonspecific nutritional deficiency, use of TPN, serum glucose, hypoxemia, hypotension, renal dysfunction or hepatic enzyme elevation. Between admission and diagnosis, serum creatinine and creatinine excretion fell and serum akaline phosphatose rose. Our study further delineates the features of this polyneuropathy and rules out several obvious causes.

. — 0159

38.

Prevalence of Risk Factors for Stroke in Families of Patients with Cerebral Infarct and Transient Ischemic Attacks

J. F. DIAZ, V. C. HACHINSKI, L. PEDERSON and A. DONALD (London, Ontario)

Hypertension, heart disease and diabetes are not only the major risk factors for stroke, but also aggregate in families. However, it is unknown whether relatives of patients with specific types of stroke have an increased frequency of these conditions.

A total of 79 patients' relatives and 57 spouses' relatives, representing about 70% of their living parents and siblings, answered a self-administered questionnaire verified by information from their family physicians. The percentage of relatives reporting medical history of stroke and its major risk factor in each group was:

	Patients'	Spouses'
Hypertension	36.7	25.5
Angina	11.8	9.1
Abnormal EEG	11.4	3.6
Heart Attack	8.5	5.5
Diabetes	7.6	1.8
Stroke	6.6	3.6

Although none of the differences were statistically significant, various combinations of two or three diseases occurred in 23.7% of the patients' relatives as compared to only 3.6% of the spouses' relatives ($P<0.01$). These results suggest that the excess of risk for stroke among relatives of patients with cerebral infarction and TIA might be accounted for by the presence of *multiple* risk factors. Screening procedures, such as blood pressure measurement, ECG, biochemical tests, and auscultation for neck bruits, may be effective approach to identifying an additional number of undetected or uncontrolled cases at risk in these families.

Supported by: The Ministry of Health of Ontario.

. — 0162

39.

Altered Sympathetic Activity After Experimental Stroke

K. E. SMITH, J. CIRIELLO, V. C. HACHINSKI and C. GIBSON (London, Ontario)

It has been previously been shown in an intensive care stroke unit that stroke patients have increased cardiac arrhythmias, serum cardiac enzymes and plasma norepinephrine levels. Taken together, these data suggest an increased activity of the sympathetic nervous system. In the present series of experiments, we investigated, employing an experimental stroke model in the cat, the effect of middle cerebral artery (MCA) occlusion on somatosympathetic reflexes and plasma catecholamines. Electrical stimulation (0.5-1.5 mA, 2 ms, 1 Hz) of the sciatic

nerve evoked early and late reflex responses in either the T_2, T_3 or inferior cardiac nerve with peak latencies of 10-45 ms and 55-90 ms, respectively. After occlusion of the MCA, the amplitude of the late component was significantly increased ($57 \pm 11\%$; $p < 0.05$) whereas the early component was unaltered. In addition, the plasma levels of norepinephrine (44%) and dopamine (45%) were significantly ($p < 0.02$) increased. These changes were observed in all animals in which the insular cortex was involved in the infarcted area. These data suggest that the sudden withdrawal of inhibitory inputs from the damaged cortex to cardiovascular control centres in the brain stem and spinal cord results in altered sympathetic activity after experimental stroke.

Supported by: The Heart & Stroke Foundation of Ontario.

. — 0163

40.

Cognitive Induction of Sensory-Motor Rearrangement: Experimental Findings and Clinical Speculations

G. M. JONES (Montreal, Quebec)

It is now known that the adult central nervous system is susceptible to substantial alteration of reflex function when this is called for by relevant demands imposed by the external environment. Thus the "involuntary" vestibulo-ocular reflex (VOR) can readily be remodelled by optical rearrangement of relations between visual and vestibular responses to head rotation; and similar plastic modifiability has since been demonstrated in other sensory-motor systems; e.g. the ocular saccadic system, the accomodation-vergence system, and most recently even the monosynaptic myotatic reflex. In contrast to this form of long term plastic remodelling of such reflexes, it also proves possible to modulate their on-going activity by cognitive intent. For example during head rotation the VOR can, without any practice, be virtually abolished simply by trying to "look" at an *imagined* head-fixed target in the dark. But this in itself produces sensory-motor rearrangement (SMR), by altering the ratio of (ocular) motor output relative to the sensory (vestibular) input. The present experiments demonstrate that persistent application of this form of *mentally* induced SMR produces similar plastic remodelling of the reflex to that induced by real visual-vestibular conflict. Thus the determined application of relevant mental effort can not only "sculpture" reflex action for achievement of the immediately intended behavioural goal; it can also produce lasting plastic change in its inherent function.

Speculating on applied implications of these findings, perhaps the cognitive activation of mental exercises based on relevant mental imagery may offer an opportunity for early rehabilitative treatment of the transiently paralysed neurological patient.

. — 0166

41.

Magnetic Resonance Imaging (MRI) In Cerebrovascular Disease

A. KERTESZ, S. E. BLACK, P. COOPER, S. STEWART, I. NICHOLSON and T. CARR (London, Ontario)

A prospective study comparing MRI imaging with CT scans in the management of cerebrovascular disease was carried out in 150 patients. The scans were evaluated independently by two neurologists, who also assessed the patients clinically. One had only the MRI image, while the other had both CT and MRI. Rating scales for diagnosis, localization, value in decision making and relative overall contribution were evaluated. Results indicated that MRI was positive in 24 hrs. in 92% vs 46% in CT. 72 hours scans were equally positive. MRI sensitivity (69%) was greater than CT (46%) when all first week scans were considered. Only 2% of the MRI scans were "false" negative with positive CT. The negative scans were mostly brain stem strokes or technically inadequate MRI series. The earliest lesion seen is an increased signal in the T2 weighed Spin Echo (SE) sequence. Serial imaging shows the persistence of increased signal at the periphery of the infarct as a "halo" that appears larger than the extent of the infarct on CT. This is thought to represent gliosis on the basis of pathological correlation. Inversion Recovery (IR) sequences provide accurate anatomical localization by distinguishing cortex and subcortical grey matter.

MRI was considered to provide greater information in localization, and higher overall value, except in intracerebral hemorrhage, where CT is slightly more superior. SE and IR techniques were complimentary and both are needed to use the full diagnostic potential of MRI. Illustrative comparisons will be presented.

. — 0172

42.

Newborn Seizures — First Dose and Maintenance Therapy

P. LANGEVIN, C. MORIN, C. CARRIER, J. PICHETTE and M. MASSON (Ste Foy, Québec)

Seizures are one of the most important problems in neurology of the newborn. Their frequency is difficult to establish as clinical symptoms are often subtle. There is no unanimity regarding the treatment of choice. Even when therapeutic intervention is urgent this is often not initiated effectively.

Frequently the first dose is inadequate and therapeutic levels are not rapidly attained. Unfortunately long term sequelae may be associated with inadequate early control.

Between 1981-1984 we studied 22 newborns with a gestational age of 25 to 42 weeks. We administered a single high dose of phenobarbital (20-25mg/kg) IM or IV, and obtained adequate and stable therapeutic blood levels of the drug from the 12th hour to the fifth day following treatment.

Moreover with this dose it did not seem necessary to introduce maintenance therapy which may be associated with possible deleterious effects. The more premature the child, the higher the first dose should be.

We think this method is simple, safe and effective.

. — 0173

43.

Surgery for Intractable Seizures in Infants and Children

J. KOBAYASHI, A. WONG, P. HWANG, E. G. MURPHY and H. HOFFMAN (Toronto, Ontario)

Between 1974 and 1985 60 children (age range 2.5 months to 18.6 years with a mean of 11.1 years) had surgery for epilepsy resistant to multiple antiepileptic drugs. There were 39 males and 21 females with seizure duration ranging from 7 days to 17 years with a mean of 4 years. Twenty-three of the patients had complex partial seizures, 26 had complex partial seizures with secondary generalized tonic-clonic seizures, 6 had mixed complex partial and simple partial seizures and 5 had simple partial seizures only. All had detailed pre-operative assessments including EEGs and radiological studies. The majority had WADA tests, psychometric evaluation and intraoperative electrocorticography.

Forty-one patients had temporal lobectomies with 29 (78.5%) showing marked improvement, ie., seizure-free or > 50% reduction in seizures. Eight had extratemporal resections; 4 (50%) were markedly improved. Seven had hemispherectomies; 4 (67%) were markedly improved. Four had corpus callosum sections; 1 (25%) was improved. There was 1 death (1.6%). The follow up period was an average of 4 years (range 1.0 to 14.5 years).

In conclusion, surgery in carefully selected cases, especially those with temporal lobe epilepsy, is an effective mode of therapy for intractable seizures in childhood.

. — 0174

44.

Correlation of the Size of Infarction with Cerebral Perfusion and Metabolism. A Positron Emission Tomography (PET) Study

A. HAKIM, R. POKRUPA, M. DIKSIC, A. EVANS, C. THOMPSON, E. MEYER, Y. L. YAMAMOTO and W. FEINDEL (Montreal, Quebec)

Nine patients were studied within 48 hours of their stroke by PET including determination of cerebral blood flow (CBF), cerebral meta-

bolic rate of oxygen ($CMRO_2$), cerebral blood volume (CBV), cerebral metabolic rate for glucose (CMRGlu) and cerebral pH (CpH). The cortical rim in the involved hemisphere was subdivided to permit an analysis of these functions within a region I committed to infarction, an adjacent penumbra region A and a remote region R. The contralateral uninvolved cortical rim C was used for comparison.

Our data show that in patients with hypoperfused infarcts (6 patients), CBF in region A was 14.2 ± 2.5 mls/100g/min and satisfied published criteria for penumbral blood flow. The size of the region I depended on events in the penumbra region. Larger infarcts were associated with smaller CBV responses in the penumbra. As well, more intense anaerobic glycolysis in the penumbra region, evidenced by elevated CMRGlu/$CMRO_2$ ratios, was noted around larger infarcts. Finally, an infarct was larger if the penumbra region was more acidotic.

These findings point to complex interactions between the early cerebral responses to ischemic injury and the resulting size of infarction. It may be possible, if these findings are confirmed, to design and test therapy aimed at reducing the size of cerebral infarction.

Supported in part by the Medical Research Council of Canada and the Canadian and Quebec Heart Foundations.

. — 0177

45.

Disturbances of Oxygen and Glucose Metabolism in Acute Human Cerebral Infarction Studied by Positron Emission Tomography

R. POKRUPA, A. HAKIM, Y. L. YAMAMOTO, A. EVANS, M. DIKSIC, E. MEYER and W. FEINDEL (Montreal, Quebec)

Nine patients were studied within 48 hours of ischemic cerebral infarction with PET using $^{15}O_2$, ^{18}FDG, and $C^{15}O_2$, to obtain local cerebral metabolism of oxygen ($CMRO_2$) and glucose (CMRGlu), both in μM/100g/min and cerebral blood flow (CBF) in ml/100g/min. A peripheral "cortical rim" was defined on the $CMRO_2$ scan in nine cases and the remaining functional maps were topographically superimposed on this, allowing the various functions to be regionally correlated. Furthermore, $CMRO_2$ was used as a marker of metabolic cell injury in regions showing $CMRO_2$ below 67μM/100g/min (I) considered infarcted. Regions adjacent to the region of infarction (A) were considered to be "penumbra". For comparison purposes, remote regions (R) within the ipsilateral hemisphere and the cortical rim from the contralateral hemisphere (C) were used.

In the contralateral hemisphere of the nine patients, CBF was 25.2 ± 0.8 and CMRGlu/$CMRO_2$ ratio was 0.22 ± 0.02 (mean ± SEM). For region A, these same values were 17.8 ± 2.5 and 0.21 ± 0.03 respectively. For the region I the cerebral blood flow and the ratio of CMRGlu/$CMRO_2$ were related by the equation CMRGlu/$CMRO_2$ = 0.017 x CBF + 0.128, with a correlation coefficient of 0.85 ($p < 0.05$). No significant correlation was noted between CBF and CMRGlu/$CMRO_2$ in the regions (A), (R) or (C). The association for the infarct region shown here suggests that in the acute stage infarcts show anaerobic glycolysis proportionate to the degree of reperfusion. This may shed light on effects of reperfusion of infarcts on cerebral metabolism and ultimately clinical recovery.

Supported in part by the Medical Reseach Council of Canada and the Canadian and Quebec Heart Foundations.

. — 0179

46.

Temporal Lobe Gangliogliomas

E. VENTUREYRA, B. K. MALLYA and D. KEENE (Ottawa, Ontario)

Six cases of gangliogliomas in the temporal lobe were treated at the Children's Hospital of Eastern Ontario between 1980 and 1984. The age ranged from 8 to 17 years and there were five males and one female. The only presenting feature in all the cases were cerebral seizures, partial complex in nature (five), and generalized tonic-clonic (one). All patients were evaluated pre-operatively with scalp EEG's, CT Scan, Neuropsychological testing, Cerebral angiogram, WADA test, and assessment of visual fields. All patients underwent surgical excision of both the tumour and the epileptogenic focus, in addition to tumour removal a partial temporal lobectomy (5 cm) was carried-out in four patients.

The tumour was located in the right temporal lobe (four), and in the left temporal lobe (two). Surgical intervention was carried-out with pre and post resection electrocorticography with depth electrodes and microsurgical technique. Post-operative complications in particular, (visual field defects), were not encountered. Follow-up CT Scan confirmed total excision of the tumour (five) and gross subtotal excision (one). Following surgery five patients were started on single antiseizure medication, Tegretol (four), and Dilantin (one). A combination of medication was used in one case. In addition to surgery two patients required Cobalt radiation because of presence of malignant features in the astrocytic portion of the tumour. The follow-up period ranged from 6 months to 5 years. All patients are alive and well and five remained seizure free. From this study it is concluded that Pediatric patients with focal seizures or seizures which are not well controlled by medication should be further investigated. Ganglioglioma should be considered in the differential diagnosis of temporal lobe masses. Electrocorticography and microsurgical techniques were found particularly useful in this group of patients. Clinical, radiological and surgical aspects will be discussed.

. — 0181

47.

Modulation of Somatosensory Transmission in the Dorsal Column Nuclei by Stimulation of the Vestibular Nuclei

L. L. COOPER and J. O. DOSTROVSKY (Toronto, Ontario)

Previous studies have shown that stimulation of several brainstem nuclei inhibits the somatosensory responses of dorsal column nuclei (DCN) neurons but the effect of stimulating the vestibular nuclei (VN) has not been examined despite the fact that VN stimulation has been shown to alter the excitability of the central terminals of spinal primary afferents. In the present experiments extracellular single unit neuronal recordings were obtained in the DCN of chloralose anesthetized cats. Stimulating electrodes were placed bilaterally in the VN and the contralateral thalamus. The effect of stimulating the VN (100 ms train, 500 Hz, 0.1 ms pulses, 30-400μA) was determined on the just suprathreshold response of DCN neurons evoked by electrical stimulation of their receptive field delivered 30 ms after the termination of the stimulus train delivered to the VN. Ipsilateral VN (iVN) stimulation inhibited the somatosensory responses of 15 of 22 DCN neurons including 3 which projected to the thalamus. 80% of the neurons inhibited by iVN stimulation were also inhibited by contralateral VN (cVN) stimulation. The stimulating currents effective in inhibiting these neurons were approximately equal for the iVN and the cVN. No DCN neurons were found which could be inhibited by cVN stimulation and not also by iVN stimulation. These results suggest that the VN can modulate the transmission of somatosensory information in the DCN.

Supported by the Canadian Medical Research Council.

. — 0182

48.

Behavioral and Biochemical Comparison of Repeated Administration of Bromocriptine and L-DOPA in 6-OHDA Lesioned Rats and in MPTP-Treated Parkinsonian Monkeys

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

Chronic treatment of parkinsonian patients with dopamine precursors or agonists often lead to development of dyskinetic movements. The present study was designed behaviorally (circling and dyskinesia) and biochemically (^{3}H-spiroperidol binding) to study the effects of repeated administration of Bromocriptine (BRC) and L-DOPA. In the first part of the study, rats bearing a unilateral lesion of the nigrostriatal pathway performed with 6-OHDA received 8 injections of BRC (10 mg/kg i.p.) or L-DOPA (100 mg/kg i.p. + benserazide 50 mg/kg i.p. ½ hour before). Each injection was separated by 48 hours. Similar groups receiving only the first and the last injection of BRC and L-DOPA

agonist were run in parallel. Groups of rats receiving eight injections of BRC and L-DOPA showed a progressive and significant increase in contraversive circling but not those receiving two injections. Seventy-two hours after the last injection, the animals were sacrificed by decapitation and striata rapidly removed for subsequent binding studies. In BRC-treated rats, there was a significant decrease in the density of the dopamine receptors on the intact side, while it remained unchanged on the lesioned side. By contrast, chronic L-DOPA induced an increase in Bmax on the lesioned side, while the decrease on the intact side was not significant. In the second part of the study, 5 female macaque monkeys were treated with MPTP (0.33 to 3.0 mg/kg) until a severe parkinsonian syndrome appeared. Two of them were treated daily orally with Sinemet 100/25 to 200/50 for four and a half months and two others were treated with BRC 10 to 20 mg. Dyskinesia appeared after 15 days of treatment only in the monkeys treated with Sinemet. Binding studies indicated a greater striatal dopamine receptor density in Sinemet-treated monkeys than in BRC-treated ones. Our results therefore suggest that although both drugs can induce an increase in some behavioral responses after repeated administration, they do so by different mechanisms. BRC seems to act by desensitizing the intact striata while L-DOPA further increases the density of striatal dopamine receptors on the lesioned side.

Supported by MRC of Canada and Parkinson Foundation of Canada.

. — 0183

49.

Neuropeptide Y in Striatum: A Morphological, Hodological and Co-Localization Study

Y. SMITH, J. DUMAS, A. PARENT (Québec, Québec) (Ste Foy, Québec)

The distribution of the neuropeptide Y (NPY), a new member of pancreatic polypeptide family, in the striatum of squirrel monkey and cat, was studied by means of indirect immunofluorescence and PAP methods.

The density of NPY-immunoreactive cells is greater in caudate nucleus (CD) than in putamen (PUT) of squirrel monkey and it increases markedly along the rostrocaudal extent of the striatum. In rostral CD and PUT the densities are 23 cells/mm^2 and 14 cells/mm^2, whereas the values for caudal CD and PUT are 35 cells/mm^2 and 20 cells/mm^2. Striatal NPY-positive neurons in both CD and PUT are either fusiform, triangular or globular with a maximum diameter of 19 ± 3.59μ (mean ± S.D.; N = 2407). The cross-sectional area of PUT cells is slightly larger than that of CD cells (148.37 vs 145.37μ^2) and, in both CD and PUT, the values of cross-sectional areas obtained for neurons located rostrally are greater than those of caudal neurons. Furthermore, double-immunostaining experiments reveal that, in primates, the vast majority of NPY-positive striatal neurons also contain somatostatin. Finally, experiments combining the use of the retrograde marker HRP injected in substantia nigra, pallidum and cerebral cortex of cats with immunohistochemical methods for the visualization of NPY indicate that the NPY-containing striatal neurons do not project outside the striatum.

These results reveal that, in mammalian basal ganglia, the NPY-immunoreactive neurons represent a subpopulation of medium-sized striatal neurons that are intrinsically organized and also contain somatostatin.

This research was supported by the MRC. The NPY and SRIF antisera were kindly provided by Drs G. Pelletier and R.G. Benoît.

. — 0184

50.

Anticonvulsant Drugs, Cognitive Function, and Behaviour

M.R. TRIMBLE (London, England)

Amongst the undesirable complications of prolonged anticonvulsant medication would appear to be changes of cognitive function and behaviour. There have been few investigations in these areas, but at the National Hospitals a number of studies have been carried out over the past nine years in which cognitive function has been measured by psychological testing, and behaviour by standard rating scales for psychopathology in epileptic patients undergoing changes of drug therapy. In this presentation it is intended to outline these studies, and to note in particular the adverse consequences of polytherapy. Studies in which patients treated with monotherapy have been undertaken and their data will be discussed indicating differences in the profiles of the different anticonvulsant drugs, with regards to their impact on cognitive function and behaviour.

Finally, differences between studies in children and adults will be noted. The data collected will be discussed in the light of the known literature and conclusions drawn.

. — 0186

51.

Visual Evoked Potentials (VEPs) in Normal Preterm and Term Neonates

M. J. TAYLOR, R. MENZIES and H. E. WHYTE (Toronto, Ontario)

VEPs have been shown to change with CNS maturation in children, yet few studies have documented maturational changes in the premature infant. Using LED goggles, VEPs were studied in forty neurologically normal infants of 23-42 weeks gestational age (g.a.) within the first three days of life. Six of these (23-27 wks g.a.) have also been followed longitudinally with weekly then biweekly testing.

The 23 wk g.a. neonates have no identifiable waves. In all infants over 24 wks a negative wave is seen with a latency of 308 ms + 21 ms (N300); with the infants 24-27 wks g.a. only this negative wave is seen. After 28 wks a late positive wave appears (P400), but with a variable morphology and latency. After 32 wks an early positive wave begins to emerge with a latency of 220 ms + 22 ms (P200); it is present in all infants 37 wks g.a. or older.

The consistency of N300 across the ages studied suggests that it might arise from the basilar dendrites in the visual cortex, which undergo little further development between 24 wks and term. The P200 is suggested to arise from the apical dendrites which develop only in the last trimester, explaining the emergence of P200 after 32 wks. The infants followed longitudinally show a more rapid development of the VEPs compared to the cross-sectional data, having a full-term VEP when only at 29-34 wks g.a., or 3-6 wks old. This study suggests that VEPs could be used to confirm g.a. and to monitor sensory system maturation in prematures. These data will also be used as a basis for future studies in the neurologically abnormal neonate.

. — 0193

52.

Auditory Brainstem Responses in Comatose Children

L. J. DeMEIRLEIR and M. J. TAYLOR (Toronto, Ontario)

Auditory brainstem responses (ABRs) were studied in 65 comatose children (10 days - 17 yrs) to determine their value as predictors of final outcome. Patients with audiological abnormalities were excluded. The patients were divided into the following groups: 11 head trauma, 16 hypoxic and 8 toxic-metabolic encephalopathies, 12 CNS infection, 4 Reye's syndrome and 14 miscellaneous etiologies (eg., status epilepticus).

The ABRs, done shortly after admission, were analysed with respect to initial neurological status and final outcome. In 17 patients with asymmetrical ABRs, the more abnormal was considered. Of the 36 patients with initial Glasgow coma scale scores of <7, only 19/36 had severely abnormal ABRs with partial or complete absence of waves; 16 of these died. 10/36 (4 head trauma, 4 hypoxic, 1 toxic, 1 infection) had normal ABRs; 5 died, 4 were neurologically abnormal and 1 was normal on follow-up. Of the total group, 25/65 had normal ABRs, but their outcomes were evenly divided among normal, mild or severe deficits and death. Latency prolongation was seen in 14/65 with a range in clinical severity, but again, there was no correlation with final outcome (6 died, 1 was normal, 7 were neurologically abnormal). In 18/65 the ABRs were compatible with brain death (absent waves or only waves I and II), 14 died and 4 survived with neurological sequelae. On repeat testing (done in 22 children) if the ABRs were normal the outcome was favourable and if the ABRs deteriorated the prognosis was poor.

Our data do not support previous investigations in comatose patients that reported that the presence of all ABR waves signified a good prognosis, but we do confirm that loss of ABR components indicates poor neurological outcome. ABRs recorded on only one occasion are not very helpful in predicting neurological sequelae; repeat testing improves the prognostic power of this measure.

. — 0195

53.

Cherry Red Spot Myoclonus Syndrome in a 16 year old Boy

G. V. WATTERS, L. WOLFE, S. CARPENTER, T. KIRKHAM and B. ROSENBLATT (Montreal, Quebec)

At age 7, because of school difficulties, the patient was assessed. On the WISC, his performance scale score was low while the verbal scale score was normal. The only abnormalities on examination were cherry red spots and mildly deficient tandem gait. At age 9, he had lateral and upgaze nystagmus and a year later limb tremulousness and unsteady gait in the morning after nocturnal myoclonic attacks. Mild fluctuating spasticity in his legs over the next year evolved to produce a shuffling, spastic, ataxic gait. By age 13, he had nocturnal tonic-clonic seizures and brief seizures in the day. Myoclonic jerks occurred in the arms by day and massive body jerks occurred at night. Myoclonus was worsened by action or anxiety. He complained of pain in his limbs and back. By age 14, wheelchair bound, he had deficient occular pursuit and gaze paretic nystagmus. Startle and action myoclonus and vision worsened and dysmetria, scanning speech, tremulousness and spasticity all increased. At present, at age 16, though totally dependent, his thinking is clear and his appearance normal.

Urine TLC and HPLC for oligosaccharides showed a distinctive pattern. Neuraminidase activity was deficient in fibroblasts and beta galactosidase was normal. Psychological assessment at age 8 and 14 showed a decline in performance items with relative preservation of verbal skills. CT-Scans at age 9, 11 and 14 were normal. EEGs from age 7 through 15 had spike wave discharges early but later only low voltage activity with little alpha. EMG, ABR, EKG, and echocardiograms have been normal while SEP and VER have been abnormal. Height has been at the 5th percentile since early in life, and head circumference at the third to twentieth percentile.

Eight years from onset, this 16 year-old boy with some unique biochemical features retained normal appearance, good understanding, but had major disabilities including myoclonus, visuomotor deficits, and gait abnormalities similar to others reported with this syndrome.

. — 0197

54.

Effects of Weightlessness on an Otolith-Spinal Reflex

D. WATT, K. E. MONEY (Montreal, Quebec) (Ottawa, Ontario)

In our natural environment, the vestibular otolith organs sense linear accelerations and gravity. During orbital space flight, the loss of the gravitational component must result in unusual otolith signals during familiar motor acts.

In the present experiment, sudden, unexpected falls were used to elicit otolith-spinal reflexes. Four Spacelab-1 scientist astronauts were drop-tested repeatedly before, during and after their 9 day mission. On-orbit, elastic cords running from a torso harness to the floor substituted for gravity. Two bursts of electromyographic (EMG) activity were recorded from gastrocnemius-soleus, an early one which is otolith-spinal in origin, and a later one concerned with landing on the ground. EMG responses were rectified and averaged, and mean amplitudes determined within certain latencies.

The size of the first part of the early burst, which is assumed to represent the most direct otolith-spinal response, decreased immediately on reaching orbit. It continued to decline throughout the flight, with most of the fall-off occurring in the first 24 hours. On landing, the response returned immediately to normal.

By demonstrating that otolith-spinal reflexes progressively decrease in weightlessness, this experiment suggests that the otolith organs are gradually ignored by the nervous system during space flight, rather than having their abnormal activity corrected or reinterpreted.

. — 0200

55.

Better Clinical Assessment of Vestibulo-Ocular Reflex (VOR) Function

B. N. SEGAL and A. KATSARKAS (Montreal, Quebec)

To see clearly during rapid head movements, the vestibular system must stabilize the eyes in space by compensatory eye movements that are equal and opposite to head movement. However, compensatory movements that occur during a typical vestibular function test are not always perfect, being very dependent on mental activity and on what the subject is trying to do. Such variability complicates clinical testing of VOR function.

To reduce such variability, we are examining vestibular function with a BRIEF natural task that calls for visual stabilization during head movement. A subject is seated on a rotating chair with head fixed to the chair by a helmet. The subject is asked to look at a target, all lights are extinguished, the chair is rapidly turned to a new position while the subject tries to look at the imagined target, the lights are turned on again, and the target is refixated. If stabilization is perfect, the eye will be on target; if it is deficient, a corrective saccade will occur whose size indicates the degree of inaccuracy. Estimates of VOR gain, based on eye position before and after refixation, are then readily made (Exp. Brain Res. 56: 149-153, 1984).

Preliminary results have shown that vestibular function is much less variable during this test than others, by at least a factor of three. Thus this test has the potential to better examine clinical vestibular dysfunction.

. — 0203

56.

Group Rehabilitation as an Adjunct to Medical Therapy in Idiopathic Parkinson's Disease

L. GAUTHIER and S. GAUTHIER (Montreal, Quebec)

The medical treatment of Idiopathic Parkinson's Disease (IPD) improved the quality of life and survival of these patients. But as the illness progresses, impairments in daily living activities occur. A group rehabilitation program, in order to improve and/or maintain the functional status of these patients was initiated and funded by Health and Welfare Canada. The research protocol was repeated with 4 groups: blind pre-treatment evaluations, random assignment to experimental-therapy (E) or to control-no therapy (C) group, blind post-evaluations after the program, at 6 months and one year. Subjects suffered from IPD since at least one year, were at stages 2, 3 or 4 of Hoehn and Yahr scale, lived at home and signed consent form.

Briefly, the results show us that:

— there was no significant difference between the E and C groups with respect to the duration of the disease and of the DOPA treatment (T-test, Mann-Whitney U).

— on the Barthel Index of Activities of daily living: the E group maintained their functional status after one year. The C group showed a significant deterioration after one year ($p < .05$, T-test and Wilcoxon).

— on the Extra-pyramidal symptoms rating scale:

- at 6 months, there was a significant decrease in the E group of the following motor symptoms: expressive automatic movement, bradykinesia, rigidity, gait and posture, akathisia as well as parkinsonism's staging (Sign test).
- at 1 year, there was a significant decrease in the E group of the following symptoms: expressive automatic movement, bradykinesia and tremor (T-test, Wilcoxon).

Methodology, evaluations, group therapy program and other results will be presented in detail.

. — 0205

57.

The Direction-Related Discharge of Cerebellar Neurons During Visually Guided Arm Movements

A. M. SMITH, P. FORTIER and J. F. KALASKA (Montréal, Québec)

The influence of movement direction and direction of applied load on neuronal activity in the cerebellum of monkeys is under current investigation. To date one monkey has been trained to make prompt movements from a common actively maintained starting position to one of 8 targets located at equal distances of 8 cm and arranged circumferentially about a circular perimeter at 45 degree intervals. Movement was triggered by the illumination of one of the 8 target lights and an accurate displacement of a suspended handle to the target was required with 500 ms. In addition the animals were required to maintain the handle within a 1 cm radius of the target for 1 sec. to obtain a liquid reward. The position of the handle was computed by an ultrasonic emitter located in the handle transmitting a signal to two rows of orthogonally arranged microphones at a frequency of 100 Hz.

The preliminary results are based on a small sample of neurons including 19 Purkinje cells from the cerebellar cortex identified by their complex spikes, 27 units from nucleus Interpositus and 35 units from the Dentate nucleus. Cells with modulated discharge in all three regions showed graded activity changes related to the direction of arm movement and included 63% of Purkinje cells, 73% of Interpositus cells and 78% of Dentate neurons. The direction-related discharge of Dentate neurons appeared qualitatively different from the other two regions and frequently involved varying degrees of excitation in all directions. In contrast, Purkinje cells and Interpositus neurons more often demonstrated an excitation in a preferred orientation and an inhibition during the reciprocal movement. The responses from cerebellar neurons appeared to be more broadly tuned than those obtained from motor cortex neurons under similar conditions. In general, the changes in load had little effect upon the activity of all three groups of cerebellar neurons suggesting that the discharge of cerebellar cells is less specifically related to inferred individual muscle contractions than units recorded in the motor cortex.

This research was supported by the Medical Research Council of Canada.

. — 0206

58.

Motor Programming in the Absence of Sensory Afferents in Man

R. FORGET and Y. LAMARRE (Montréal, Québec)

Motor control has been assessed in 3 patients deprived of cutaneous and proprioceptive afferents following sensory polyneuropathies where the motor nerve fibers were not affected. The functional deficit of these patients varied with the degree of sensory involvement. In one particular case (G.L.), a 36 year old female functionally deafferented for the last 5 years, there was a total loss of touch, vibration, pressure, and kinesthetic senses in the four limbs. Tendon reflexes were absent. The motor fibers were not affected and the results of electrophysiological tests and nerve biopsy confirmed the above clinical findings. In a standardized functional motor test, G.L. performed more than 8 standard deviations below the normal mean. Although her strength was within the normal limits, she was unable to maintain a small isometric force at a constant level for more than 2 seconds in the absence of visual feedback. Analysis of the biceps and lateral triceps EMG activity during rapid elbow flexions toward a target showed that she was able to generate an EMG activity in the antagonist to decelerate the limb. However, even with visual feedback of her performance, most movements lacked the precision found in ten normal subjects. This deficit was shown to be attributable to improper adjustment of the size and timing of the antagonist burst. Without visual feedback the performance was worse and the movement did not end in the target zone in the majority of trials. These findings show the importance of sensory afferents in updating the central motor programs even during the performance of a simple motor task of the arm.

. — 0207

59.

Angiotensin II Excites Solitary Tract Neurones Involved in Control of Respiration in the Cat

J. L. HENRY and B. J. SESSLE (Montreal, Quebec) (Toronto, Ontario)

Angiotensin II has been implicated as a chemical mediator of synaptic transmission in the mammalian central nervous system. Angiotensin II and its precursors, degrading enzymes and binding sites are found in high concentration in specific regions especially the solitary tract nuclei. Its effects on respiration after central administration prompted the present experiments, which were done to determine whether angiotensin II has effects on solitary tract neurones involved in respiratory control. Adult cats were anaesthetized with chloralose and paralyzed with pancuronium bromide. Extracellular single unit spikes were recorded from one barrel of multibarrelled micropipettes. Barrels for iontophoresis contained angiotensin II (1 mM in 165 mM NaCl at pH 5.5, Peninsula Laboratories) and Na-L-glutamate (1M, pH 7.4). All neurones were classified according to Sessle et al (Brain Res. *216*: 146, 1981) as respiratory neurones (n = 29; fired rhythmically in phase with phrenic nerve activity) or as interneurones implicated in respiratory tract reflexes (n = 7; no rhythmic activity, but responded orthodromically to electrical stimulation of vagal and/or superior laryngeal nerves). Glutamate responses were typical of the fast excitation described elsewhere. Angiotensin II excited 7 respiratory and 4 reflex interneurones. Other neurones were unaffected, except for two respiratory neurones which underwent a very slow depression that did not reverse and could have been an artifactual decrease in activity unrelated to peptide action. Angiotensin-induced excitation began with 15-30 sec. of the beginning of current ejection and increased in magnitude throughout the period of ejection; recovery usually took 1-5 min after ejection was stopped. Our results provide physiological evidence to support the possibility that angiotension II may be a chemical mediator of synaptic transmission in the solitary tract nuclei, in pathways related to respiratory control.

Supported by the Canadian Medical Research Council.

. — 0213

60.

Pregnancy Outcome in Relation to Maternal Plasma Antiepileptic (AED) Levels and Folate

L. DANSKY, E. ANDERMANN, F. ANDERMANN, A. L. SHERWIN, D. ROSENBLATT, G. RÉMILLARD and R. A. KINCH (Montreal, Quebec)

In 105 pregnancies of epileptic women followed prospectively, there were 25 adverse outcomes (23.8%): 6 spontaneous abortions (5.7%) and 19 children with major congenital malformations (18.1%). In Trimester 1, primidone + other AEDs (n = 17) was associated with the highest frequency of adverse outcomes (58.8%). The frequency of major malformations increased linearly with increasing mean plasma phenytoin (PHT) levels (μg/ml) during pregnancy: PHT level ≤4 (n = 34), 11.8%; 5-9 (n = 29), 24.1%; 10-19 (n = 12), 41.7% ($p < 0.05$). In Trimester 1, spontaneous abortions were associated with higher mean ± SEM plasma PHT levels (n = 4; 14.6 ± 5.2), than those for normal outcomes (n = 23; 5.4 ± 0.7) ($p = 0.01$).

In 50 non-pregnant epileptic women, a negative correlation was found between total plasma AED levels, expressed as a score, and serum folate (SF) (Spearman rho = −0.43, $p < 0.005$), as well as red cell folate (RCF) (rho = −0.51, $p < 0.0005$). Twenty two patients on polytherapy had lower mean ± SEM SF (3.7 ± 0.5 ng/ml) than did 26 on monotherapy (5.0 ± 0.6) ($p = 0.05$). RCF was also reduced (398.8 ± 62.0 vs 609.7 ± 60.6, $p = 0.003$). RCF was lowest in women who took primidone + other AEDs (287.4 ± 48.5). Pregnant women showed similar results. In pregnancies with at least one subnormal SF level (n = 19), the frequency of adverse outcomes was 36.8% vs 10.7% for those with higher SF (n = 28) ($p < 0.05$). In Trimester 1 (n = 27), higher proportions of adverse outcomes were found for mean SF<4 (62.5%) vs ≥4 (15.8%) and mean RCF ≤ median levels of 385 (42.9%) vs >385 (15.4%) ($p < 0.025$). Mean RCF was lowest for spontaneous abortions (274.8 ± 15.2).

The results suggest a dose-response relationship between anticonvulsants, folate and adverse pregnancy outcome.

. — 0214

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61.

Indications for Seizure Monitoring

L. F. QUESNEY, P. GLOOR and F. ANDERMANN (Montreal, Quebec)

The main objective of seizure monitoring is to obtain a precise documentation of the electrographic and clinical features of patients' spontaneous attacks. The most common indications for seizure monitoring are:

(1) identification of seizure types.
(2) differentiation of epileptic from non-epileptic seizures.
(3) quantitative evaluation of seizure control.
(4) preoperative localization of seizure onset.

A summary of our experience at the MNH will be presented with special emphasis in the preoperative localization effectiveness of seizure monitoring in 50 epileptic patients who were surgical candidates. 311 seizures, mostly complex partial, were recorded in 30 of these patients. A localized EEG seizure onset was recorded in 147 (40%) of these episodes. 29 seizures (9.4%) exhibited a lateralized ictal EEG onset.

A few recommendations to increase the localization effectiveness of seizure monitoring will be offered.

. — 0216

62.

Elevation of Plasma Carbamazepine Epoxide Levels by Comedication with Valproate — A Useful Interaction

F. J. MIESNIKOWICZ and A. L. SHERWIN (Montreal, Quebec)

The plasma of patients receiving carbamazepine (CBZ) also contains its antiepileptic metabolite carbamazepine epoxide (CBZ-E). We employed a liquid chromatographic assay to simultaneously monitor CBZ and CBZ-E in groups of patients receiving either CBZ monotherapy, CBZ plus valproate (VPA) or polytherapy with phenytoin, phenobarbital or primidone (plus or minus VPA). Comparative plasma levels were as follows: (A) Monotherapy — CBZ, 7.9 ± 0.42 μg/ml (mean ± SEM); CBZ-E, 1.4 ± 0.07 (n = 30). (B) CBZ plus VPA — CBZ, 7.2 ± 0.60; CBZ-E, 3.2 ± 0.40 (n = 20). (C) Polytherapy including VPA — CBZ, 6.2 ± 0.54; CBZ-E, 3.8 ± 0.47 (n = 25). (D) Polytherapy excluding VPA — CBZ, 6.5 ± 0.44; CBZ-E, 1.7 ± 0.16 (n = 30). Comedication with VPA alone increased the mean CBZ-E plasma level more than two-fold ($p < 0.001$, t Test). In some cases CBZ-E levels equaled or even exceeded CBZ. The mean level of CBZ was unchanged suggesting a selective interference with CBZ-E clearance. Polytherapy which included VPA resulted in an even greater increase in CBZ-E, in contrast, no effect was observed when VPA was excluded. Polytherapy was associated with a modest but significant ($p < 0.01$) drop in mean CBZ level. Though CBZ-E can also give rise to CBZ side effects (Kutt et al, Epilepsia 25:674, 1984), this interaction may provide an alternative approach to improve efficacy in patients with carbamazepine resistant seizures or trigeminal neuralgia.

. — 0218

63.

The Syndrome of Focal Cortical Dysplasia, Macrogyria, and Intractable Epilepsy: A Study of Fifteen Patients

F. ANDERMANN, A. OLIVIER, D. MELANSON, T. STAUNTON and Y. ROBITAILLE (Montreal, Quebec)

Taylor and Falconer described focal cortical dysplasia in epileptogenic tissue removed at operation. The diagnosis can now be made by CT scanning. Areas of macrogyria or bands of thick smooth cortex associated with a few large sulci are found, often in the rolandic or sylvian areas. In three patients, these were bilateral and symmetrical. The patients have uncontrollable epilepsy from childhood or early life with a variety of seizure patterns which do not fit into any specific epileptic syndrome. Intelligence is usually low average. Mild congenital hemiplegia may be present with bilateral pyramidal changes in patients with bilateral lesions.

EEG abnormalities predominate in areas surrounding the zone of maximal structural abnormality, whereas the grossly abnormal areas do not appear to be capable of generating much epileptogenic discharge.

Removal of accessible epileptogenic tissue resulted in reduction of the severe seizure tendency in most of these patients, but complete seizure control cannot be obtained, probably because of the widespread distribution of the architectonic abnormalities.

There was blurred cortical lamination and very dense and poorly demarcated concentrations of giant dysplastic neurons associated with giant astrocytes and some white matter heterotopias.

These lesions resemble focal or partial lissencephaly and may be found also in megalencephaly, hemimegalencephaly, and as the neuropathological correlate of the linear nevus sebaceous syndrome. They have many overlapping features both clinically and pathologically with the so-called forme fruste of tuberous sclerosis.

Recognition of this clinico-pathological malformation syndrome has important prognostic and therapeutic significance.

. — 0222

64.

Applicability of Progressive Weight Bearing in Rehabilitation of Neurologically Impaired Gait

M. WAINBERG and H. BARBEAU (Montréal, Québec)

Rehabilitation of neurological disorders regularly involves locomotor training. In developing effective treatment rationals, experimental models have suggested new treatment strategies. Results from experimental studies on the adult spinal cat indicate that progressive weight support in combination with a treadmill training regimen can facilitate the recovery of normal locomotor function (S. Rossignol, H. Barbeau & C. Julien, 1985). Normative data is collected for healthy subjects for supported treadmill walking, and the current investigation studies the applicability of this strategy in neurological patients.

Cinematographic and electromyographic recordings were made of spastic paraparetic patients during free speed treadmill walking while full weight bearing (FWB) and with 20 and 40% of body weight externally supported (EWS). Preliminary data suggest that with increasing EWS, patients are more easily able to attain higher comfortable walking speeds (eg. in one case, 0.26 ms^{-1} at 20% EWS and 0.55 ms^{-1} at 40% EWS). With this increasing speed, cycle duration is significantly decreased ($p < .01$) and is related to the decrease of stance duration ($p < .01$). Stride length is increased over this range of increasing EWS and comfortable walking speeds. An important decrease in duration of proximal extensor activity has been noted in initial EMG analyses.

In light of this preliminary data, it may be suggested that by reducing extensor activity and normalizing the stance/swing ratio, progressive weight support locomotor training may be an effective treatment strategy in the rehabilitation of neurologically impaired gait. Further studies are currently in progress to test its applicability.

. — 0226.

65.

Influence of Partial Weight Bearing on Normal Human Gait: The Development of a Gait Retraining Strategy

L. FINCH and H. BARBEAU (Montréal, Québec)

Experimental studies on adult cats have demonstrated that locomotion can be restored following a treadmill training program combined with partial weight progressing to full weight bearing (S. Rossignol, H. Barbeau & C. Julien, 1985). These data form the basis from which knowledge can be applied to influence the rehabilitation of a neurological patient's gait pattern.

Knowledge of normal responses to partial weight bearing is a prerequisite to effective therapeutic decisions. The present investigation reports some preliminary findings of normal human gait under partial loads. These results may then be utilized in developing a training strategy for neurological patients.

Normal males walked on a treadmill at selected speeds with 70, 50 and 30 per cent of their body weight supported. Simultaneous surface EMGs and cinematographic data were collected throughout. All subjects to be comfortable needed to decrease progressively the treadmill speed at 30, 50 and 70 per cent weight support. Hence, to dissociate speed changes from weight changes the subjects also walked at the same selected speeds full weight bearing. Preliminary kinematic data from 4 subjects indicates that the cycle time increased by at least 10% at 50 and 70 per cent weight support above that attributed to the decrease in walking speed. However, the percent cycle duration of stance and swing were inverse of that normally seen; the percent stance decreased from 60 to 55 per cent while the swing increased from 40 to 45 per cent over all subjects studied. The EMG data from the hip, knee and ankle flexor and extensor muscles are being studied.

The majority of neurological cases have difficulty walking properly. A strategy of partial weight support decreasing the amount supported as parameters reach normative values seems possible based on these results. The feasibility of this strategy is being tested on a variety of neurological patients at this time.

. — 0228

66.

Predictive Validity of ABR and VEP Recording in Comatose Patients

S. G. COUPLAND and R. H. A. HASLAM (Calgary, Alberta)

The clinical utility of multimodal evoked potential (EP) recordings to predict neurological outcome for comatose patients has been well demonstrated. The timing of initial EP recordings and their predictive validity is still in question. We have investigated the visual and auditory EPs in a group of 20 comatose patients (mean age = 3.4 years) both upon admission and repeatedly up to 12 weeks following. Patients included those with head injury (N = 5), cardiorespiratory arrest (N = 5), birth asphyxia and hypoxic-ischemic encephalopathy (N = 7), Reye syndrome (N = 1), intraventricular hemorrhage (N = 1), and basilar artery thrombosis (N = 1). Initial neurological examination of patients included a clinical rating on the Glasgow Coma Scale (GCS). Monocular flash visual evoked potentials (VEPs) were recorded over both hemispheres and a 7-point scale of normality-abnormality was used to grade the VEP waveforms. Monaural auditory brainstem responses (ABRs) were obtained and a 9-point scale of normality-abnormality was used to grade the ABR waveforms. Follow-up neurological examinations were performed up to 12 months following admission and patients were then rated as to degree of neurological outcome.

Results of this investigation demonstrated no significant correlation between initial ABR or VEP results and Glasgow Coma Scale ratings. In addition, the GCS did not significantly correlate with subsequent neurological outcome. However, both the VEP and ABR results were found to be significantly related to neurological outcome. During the first 7 day period there was no statistically significant increase in predictive validity between the initial EP examination (on day 1) and subsequent EP recordings (done up to day 7). However, later EP recordings (done after the first week) were found to correlate more highly with subsequent neurological outcome.

. — 0235

Poster Presentations

67.

Une nouvelle méthode fluorochromique pour le diagnostic neuropathologique de mégacôlon aganglionnaire

H. B. SARNAT, C. L. TREVENEN, C. G. F. SEAGRAM et S. Z. RUBIN (Calgary, Alberta)

Le diagnostic histopathologique de mégacôlon aganglionnaire (la maladie de Hirschsprung) est souvent très difficile parce que les petits neurones des plexus myentériques et sous-muqueux sont difficiles à reconnaître dans les coupes de tissu colorées à l'hématoxyline-éosine, plus particulièrement dans les segments les plus distaux et chez le nouveau-né. Des techniques employant l'acétylcholinestérase et d'autres utilisant des anticorps contre les protéines neurofilamentaires ont été tâchées pour mieux identifier les petites cellules ganglionnaires, mais ces méthodes sont complexes et capricieuses. En profitant du fait que les neurones matures sont les cellules qui possèdent la plus haute concentration cytoplasmique d'acide ribonucléique, nous avons employé le colorant fluorochromique acridine-orange pour montrer les neurones dans les coupes congelées ou incluses en paraffine du côlon terminal de 21 nouveau-nés et nourrissons soupçonnés de souffrir de la maladie de Hirschsprung. Sous la lumière ultraviolette, dans les segments qui comprennaient des cellules ganglionnaires, on pouvait clairement distinguer les neurones les plus petits par leur cytoplasme orange lumineux, en contraste avec la couleur verte pâle du muscle lisse et du tissu conjonctif dans l'arrière-plan. Ces tels neurones étaient absents d'autres segments, cependant on trouvait quelques ganglions vides qui manquaient des neurones malgré une structure bien préservée du tissu appuyant. Puisque la technique de l'acridine-orange est tellement facile et rapide, elle peut servir de méthode supplémentaire pour le diagnostic de mégacôlon aganglionnaire.

. — 0002

68.

Classification of rapidly adapting cutaneous mechanoreceptors in the hairy skin of cats.

S. S. LECLERC, R. W. DYKES (Montreal, Quebec)

Over the last decade an elaborate classification scheme for cutaneous mechanoreceptors has evolved. There is general agreement upon the two categories of slowly adapting (SA) mechanoreceptors. Type I is recognized by a visible dome on the skin and type II is very sensitive to lateral stretching of the skin. In contrast, of the eight categories of rapidly adapting (RA) receptors only the Pacinian corpuscle has a distinctive functional signature. The other classes are not generally recognizable by routine tests. Functional differences between the classes are not statistically reliable nor does each have an anatomical correlate.

A total of 104 RA fibers from cats were sampled using standard electrophysiological procedures for peripheral nerve recordings. Vibration entrainment thresholds were obtained at a range of frequencies in 88 of these. The remainder were sufficiently insensitive that they could not be activated by the stimulator. When the thresholds for each fiber were joined to form a tuning curve, three distinct groups were observed. One had positive slopes, a second had relatively horizontal slopes and required large stimulus amplitudes. The third group also had horizontal slopes but was much more sensitive than the second group. Although there was some evidence for a fourth group, it was not possible to recognize eight categories of RA fibers. By analogy to the wide range of response characteristics displayed by the type I SA and type II SA fibers, we suggest that the large differences in sensitivity shown by individual RA fibers led to the creation of artificial divisions when actually only a few RA classes exist each having a wide range of response properties.

(Supported by the Medical Research Council of Canada)

. — 0003

69.

Étude fluorochromique d'ARN de neurons en développement normal et dans la dysgénésie cérébrale

H. B. SARNAT (Calgary, Alberta)

On a employé le fluorochrome acridine-orange comme coloration histochimique pour étudier l'acide ribonucléique (ARN) cytoplasmique dans les neurones des cerveaux normaux de 15 enfants nouveau-nés à terme et prématurés, à l'autopsie, ainsi que de 13 autres cerveaux dysplasiques. On n'entrevoie pas la couleur orange lumineux d'ARN dans les neurones immatures chez l'enfant prématuré dans la zone germinative sous-épendymaire ni pendant leurs migrations vers le cortex cérébral non plus, jusqu'à leur arrivée au lieu définitif. La probable raison de ce manque d'ARN pendant la migration, c'est parce que des neurones immatures ne montrent pas encore la croissance en taille ni la biosynthèse de neurotransmetteurs. Chez les enfants atteints de la dysgénésie cérébrale, les hétérotopies comprennent des neurones qui sont parvenus à leurs foyers définitifs et qui montrent beaucoup d'ARN cytoplasmique par cette technique, peu importe que le lieu dans le cerveau soit anormal, tandis que les cellules nerveuses qui sont encore en train de migrer en montrent très peu. Cette formule est également vraie à l'égard des malformations cérébelleuses et cérébrales. Grâce à l'application de la méthode d'acridine-orange au tissu inclus en paraffine après la fixation à formaldéhyde ainsi qu'à des coupes congélées sans fixation, la technique donc est utile pour l'étude de cerveaux à l'autopsie. On peut faire digérer l'ARN par ribonucléase comme contrôle technique. L'acridine-orange est un bon marqueur pour distinguer à l'intérieur des hétérotopies lesquels des neurones sont déjà arrivés à leurs foyers définitifs et lesquels sont encore en migration.

. — 0004

70.

Spontaneous Remission In CNS Lymphoma

M. RUBIN, M. L. BRISSON, M. GOLDENBERG and I. LIBMAN (Montreal, Quebec)

Primary lymphoma of the CNS is a rare disease, representing less than 2% of all extranodal lymphomas[1]. It is a highly malignant neoplasm, with an average survival of 3.3 months with supportive care alone, and thirty three months following excision and radiation therapy[2]. Recent reports however, suggest variability in the prognosis, possibly corresponding to diverse responses to therapy[3]. Case reports document both steroid-induced remission[4,5] and spontaneous, though incomplete, regression[6].

We report a case of complete, spontaneous remission of primary CNS lymphoma that occurred within twenty seven weeks of onset and which, by CT and clinical data, lasted approximately one year before relapse. To our knowledge, this is the first such reported case in the literature and it lends further support to the notion that CNS lymphoma is a heterogeneous disorder. At the very least, it is clearly capricious in its natural history.

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. — 0005

71.

Management of Head Injuries in Bellevue Hospital, New York.

A. MEDHKOUR (Québec, Québec)

One of the most important factors in the ultimate outcome of the severely injured patient is the early prehospital and Emergency Room (E.R.) management. A well trained Emergency Medical Service (E.M.S.) will certainly provide a better care to the patient on the scene and during transportation.

Bellevue Hospital, one of the largest trauma centers in the city of New York, has a very active E.R., equipped with a trauma "slot" unit where minor surgical procedures are undertaken (i.e.: burr holes, ICP monitoring placement, abdominal taps, etc. . . .).

The E.M.S. is highly qualified and contributed a great deal to the improvement of the physiological condition of the patient in the field, thus reducing the systemic insults, aiming toward a better outcome. The trauma team, composed of a general surgery, orthopedic, neurology, neurosurgery and anesthesia resident (etc.) cooperates together to provide in a rapid and stereotyped manner the life saving procedures to the severely injured patient. When faced with a rapidly deteriorating condition, the neurosurgery resident performs a burr hole prior to CT Scan.

Corticosteroids are still used in certain cases. ICP monitoring is used when there is a suspicion of intracranial hypertension. Raise in ICP is treated with hyperventilation, mannitol and Lasix. Barbiturate Coma has been used and abandoned.

Measurement of creatine phosphokinase (CK-BB) was performed for a certain period of time in order to predict the ultimate outcome. But the best tool at this time seems to be the multiple evoqued potentials.

The outcome of the severely injured patient depends on a rapid response of the E.M.S., a trauma team able to make accurate diagnosis and perform life saving procedures in a short period of time.

. — 0006

72.

The Face In Progressive Supranuclear Palsy

A. COSTANTINO, C. F. BOLTON (London, Ontario)

The appearance of the face may be a striking feature of progressive supranuclear palsy. Termed spastic facies, it is unlike true spasticity, prompting us to study 3 patients in some detail. Movies were taken of 2 patients. In repose, all facial muscles were in tonic contraction, making skin creases unusually accentuated. During talking or laughing, facial movements were slow in developing and relaxing, causing a symmetrical "dystonic" posturing of the face which might last a matter of minutes. The facial movements were characteristic of dystonia, and were in keeping with similar movements in other parts of the body, particularly the neck and trunk muscles, as observed in our patients and originally described by Steele, Richardson and Olszewski. Autopsy examination of the third patient disclosed a distribution of cerebral lesions consistent with progressive supranuclear palsy, but failed to reveal involvement of either cortical bulbar or cortical spinal tracts, as noted previously in the literature. We, therefore, propose that the distinctive facial appearance in progressive supranuclear palsy be called "dystonic facies" rather than "spastic facies".

. — 0007

73.

Recurrent Loss of Consciousness While Eating: Swallow Syncope or Eating Epilepsy?

A. GUBERMAN, (Ottawa, Ontario)

Two women aged 62 and 40 presented several syncopal episodes (with clonic movements in case 2) when eating. No cardiac, EEG or structural esophageal/para-esophageal abnormalities were found. Both had excessively high pressures on esophageal manometry and inflation of an esophageal balloon produced second-degree heart block in case 1. Pre-prandial propantheline bromide markedly reduced attacks in case 1 over the next 3 years. The third case, a 62-year-old man, had 3 episodes of swallow syncope related to digoxin toxicity and no further episodes after discontinuing digoxin.

A 42-year-old woman had a 3-year history of seizures almost always provoked by eating. A complex-partial seizure arising from the right temporal area and a secondarily generalized tonic-clonic seizure were

recorded by EEG telemetry and video monitoring during eating. Graded stimuli related to food were introduced but only swallowing of food produced seizures.

Swallow syncope is due to enhanced vagal tone during deglutition with or without an underlying cardiac abnormality. Reflex eating epilepsy is distinguished on the basis of additional seizures apart from eating, more fully-developed seizure phenomena and epileptiform (usually temporal) EEG abnormalities. EEG/EKG/video monitoring during eating may help establish the diagnosis.

. — 0008

74.

Baclofen Treatment For Dystonia and Torticollis

O. S. KOFMAN, (Toronto, Ontario)

Baclofen (B-parachlorphenyl gammabutyric acid) is an analogue of gamma-aminobutyric acid (GABA) which has been successfully used in the treatment of spasticity and flexor spasms. Some of the side affects of baclofen such as sedation and ataxia suggest a more rostral site in the C.N.S. The question is whether baclofen produces these effects by suppression of the excitatory-transmitter release, a direct post-synaptic action, or by both mechanisms.

Torsion dystonia or dystonia musculorum deformans of the primary variety is a rare, sometimes familial involuntary movement disorder of unknown etiology which involves the caudate nucleus and putamen. Despite various medical and surgical attempts, there is no known consistent treatment available. Similarly, spasmodic torticollis and other forms of focal dystonia have not been responsive to medical therapy.

Our primary purpose in presenting this paper is to report upon a new and revealing therapeutic success with baclofen in a patient with dystonia musculorum deformans with adequate placebo control. In addition we will report upon our experiences during the past three years in patients with secondary dystonia, spasmodic torticollis and writer's cramp. At times these problems have responded satisfactorily although the pattern has been variable and inconsistent. Previous observations have referred to limited improvement of morning dystonia and foot dystonia in Parkinson patients. There have also been some recent observations relative to involvement of blepharospasm and oromandibular dystonia with baclofen.

Although the response to baclofen in dystonia and focal dystonia is not constant or predictable some of the beneficial responses have been encouraging. As a result of some of these positive observations, further long term controlled assessments including placebo trials are currently in process and additional confirmatory studies by others are indicated and have already been encouraged.

. — 0009

75.

Adrenaline Induced Potentiation of Electrogenic Sodium Pumping in Sympathetic Ganglia

P. A. SMITH (Edmonton, Alberta)

The potassium activated hyperpolarization (K_H) and the adrenaline induced hyperpolarization (Ad_H) of neurones in bullfrog sympathetic ganglia were examined by means of the sucrose gap technique. The K_H was elicited by briefly introducing normal Ringer's solution to ganglia which had been stored in a K-free medium for >3 hours. This response was blocked by 1 μm ouabain and was attributed to activation of the electrogenic Na^+ pump. 0.1 μN adrenaline (in the presence of 0.5 μM desipramine) increased the amplitude of the K_H to 121.5±7.5% of control (n=7). This potentiation was blocked by both yohimbine (50 nM) and prazosin (1 μM) but not by propranolol (1 μM). Clonidine (10 nM) potentiated the K_H to 113.5±3.4% of control (n=5) whereas methoxamine (0.1 μM) was ineffective. Na^+ pump stimulation does not contribute to the electrogenesis of the Ad_H because i) the Ad_H was sometimes completely unaffected when the K_H was blocked by ouabain and ii) the Ad_H was eliminated by Ba^{2+} (2 mM) even though this substance potentiated the K_H. These results imply that adrenergic stimulation of Na^+ pumping is not involved in the short term electrophysiological effects of catecholamines. Despite this, it is possible that the homeostasis of Na^+ and K^+ in nerve may be regulated by α-adrenergic mechanisms. Such mechanisms may become important in pathophysiological situations where sympathetic outflow is greatly increased.

Supported by MRC, AMHAC and AHFMR.

. — 0011

76.

Axotomy Attenuates Ca^{2+} Sensitive Potassium Conductance (g_K) in Amphibian Sympathetic Neurones.

M.E.M. KELLY, J. SHAPIRO, P.A. SMITH and T. GORDON (Edmonton, Alberta)

A 40% reduction in the amplitude and a 70% reduction in the duration of the action potential after hyperpolarization (AHP) of bullfrog sympathetic neurones occurred within 2 weeks of sectioning the post ganglionic nerves 2-8 mm from the ganglia. We used standard intracellular recording techniques to investigate the ionic basis for this change.

The Ca^{2+} channel blocker, Cd^{2+} (0.2 mM) reduced the AHP duration in normal neurones and also increased the rate of firing in response to depolarizing currents (1-5 x rheobase). In axotomized cells, where the AHP duration was already reduced and the firing rate in response to depolarizing current was substantially increased, 0.2 mM Cd^{2+} failed to promote further shortening of the AHP or further increase in the firing rate. This data indicated that axotomy attenuates Ca^{2+} sensitive g_K in these neurones.

To investigate whether this effect is due to loss of Ca^{2+} channels, we recorded responses to depolarizing currents in the presence of 2 μM TTX and 10 mM TEA to block Na^+ and K^+ channels, respectively. Regenerative Cd^{2+} sensitive responses were recorded in both axotomized and control cells, showing that Ca^{2+} channels were still present after axotomy.

Our data therefore suggests that the attentuation of the Ca^{2+} sensitive g_K in amphibian sympathetic neurones after axotomy, is due to a change in the intracellular sequestration of Ca^{2+} or an alteration in the Ca^{2+} sensitive K^+ channels.

Supported by MRC and AHFMR. Travel for M.E.M.K. from the Wellcome Foundation.

. — 0012

77.

An *In Vitro* Mammalian Preparation to Study Supraspinal Control of Segmental Reflex Activity in the Spinal Cord

M. E. M. KELLY, J. BAGUST (Edmonton, Alberta) (Southampton, England)

Analysis of synaptic activity in the CNS has been greatly aided by the development of *in vitro* preparations, such as brain slices and hemi-spinal cord. These isolated preparations afford the experimenter a more flexible control over the experimental situation and have facilitated the study of the underlying ionic events involved in various electrophysiological phenomena.

As an extension of the *in vitro* mammalian hemi-spinal cord preparation, we have developed an *in vitro* hemi-brainstem spinal cord system from fully developed golden hamsters, 3-5 weeks old. This preparation preserves the integrity of the circuitry so as to allow both long and short reflex loops to be studied in an isolated system. The preparation was viable for up to 10 hours and conditioning stimuli applied in the bulbar reticular areas were found to alter reflex activity recorded from the lumbar spinal ventral roots. The predominant effect of brainstem stimulation was inhibition of the spinal monosynaptic reflex and depression of motoneurone discharges. Effects recorded with a microelectrode on spinal interneurones were more variable. The efficacy of the descending effects could be altered by varying the intensity and frequency of the conditioning stimulus to the brainstem and the test stimulus to the dorsal roots. Conditioning-delay times were optimum between 25-50 ms. The results obtained from the *in vitro* preparation were found to

compare favourably with data reported previously *in vivo* (Shapovalov, Rev. Physiol. Biochem. & Pharmacol., 72, 2, 1972) and indicate that it is possible to use isolated preparations as models for studying supraspinal control of segmental mechanisms.

Supported by SERC and travel for M.E.M.K. from Wellcome.

. — 0013

78.

Pediatric Patients with Achondroplasia at Risk for Cervico-Medullary Cord Compression

C. S. REID, B. L. MARIA, R. W. McPHERSON, J. WINFIELD, M. WANG, R. E. PYERITZ and O. MURKO (Baltimore, Maryland)

Compression of the caudal medulla and upper cervical cord has been demonstrated in post-mortem studies of patients with achondroplasia who have had normal neurologic examinations but abnormal respiratory function. To identify patients at risk for cervico-medullary compression, we prospectively evaluated 26 children (13 males, 13 females, ages 4 months to 6 years) with extensive cardio-respiratory and neurologic studies. Patients with normal neurologic examination were assigned to *group I* and patients with paresis, hyperreflexia or asymmetric reflexes were assigned to *group II*. Results are summarized in the table below:

	CCJC (CT)	ASAS (CT-MPR)	ASEP	Respiratory Abnormality	Surgery	Neurological Function Post-Op
Group I						
(14 pts)	6	1	1	1	1	Improved
Group II						
(12 pts)	10	8	8	11	8	3 Normal, 4 Improved 1 Dead

Of 16 patients with constricted cranio-cervical junctions (CCJC) by CT scan, 9 (1 group I and 8 group II patients) also had absent subarachnoid space (ASAS) posterior to the cord at the foramen magnum by multiplanar reconstruction CT scan (CT-MPR) and abnormal somatosensory evoked potentials (ASEP). These 9 had confirmed cervico-medullary cord compression at surgery. One patient died post-operatively; in follow-up (1 month to 2 years) of 7 patients with abnormal examinations preoperatively, 3 now have normal examinations and 4 have shown improvement in neurologic function.

We conclude that neurologic examination is important in following pediatric patients with achondroplasia but cord compression may also occur without neurologic findings (1 of 14). Abnormal neurologic examination should mandate a prompt evaluation with CT-MPR and somatosensory evoked potentials since compression is likely and most operated patients are better following surgery. Pediatric patients with achondroplasia and unexplained respiratory symptoms should also have thorough cardio-respiratory and neurologic evaluations.

. — 0015

79.

Treatment of Recurrent Choroid Plexus Papilloma with Combination Chemotherapy

B. L. MARIA, M. L. GRAHAM and L. C. STRAUSS (Baltimore, Maryland)

Choroid Plexus tumors account for less than one percent of all primary intracranial tumors in children. Although most of these are benign papillomas (CPP) with histology mimicking the architecture of normal choroid plexus, malignant variants (carcinoma) may occur, making complete removal and cure difficult. To date, options of therapy have included surgery alone, surgery plus radiotherapy at diagnosis and surgery followed by radiotherapy at recurrence. The effectiveness of radiotherapy is not clear.

An 8-year-old girl presented with symptoms and signs of increased cranial pressure. Computed tomography (CT) of the head showed a large irregular enhancing tumor close to the trigone of the left lateral ventricle. She underwent biopsy and subtotal removal of a CPP. Follow-up CT 4 months later showed enlarging tumor; surgical debulking was performed prior to her receiving radiation therapy in a total dose of 5040 rads (4500 rads to the brain and 540 rads to a tumor cone down). One year from completion of radiotherapy, serial CT scans showed a rapidly enlarging mass in the same location. Combination chemotherapy of cis-platinum, bleomycin and vinblastine (CBV) was given. The regimen was well tolerated and marked reduction in tumor size was observed. There is no evidence of disease 6 months after completion of 10 weeks of chemotherapy.

Until now, chemotherapeutic trials for aggressive variants of choroid plexus tumors have not been successful. We recommend that CBV therapy be considered for future trials with choroid plexus tumors in which recurrence has occurred following surgery and radiotherapy. Chemotherapy might also be a therapeutic option at diagnosis in infants in whom radiation therapy might pose a risk of unacceptable long-term toxicity.

. — 0016

80.

Two Primary Brain Tumors in One Child:

B. L. MARIA, L. C. STRAUSS and M. D. WHARAM (Baltimore, Maryland)

The simultaneous occurrence of two different primary brain tumors has not been reported in a pediatric patient in the absence of specific genetic predisposition. Accurate detection of multiple tumors with potentially different sensitivities has important therapeutic implications.

A 4-year-old patient presented with symptoms and signs of a posterior fossa tumor. Computed Tomography (CT) of the head, however, showed one mass lesion surrounding the fourth ventricle and a second mass adjacent to the frontal horn of the left lateral ventricle. A diagnosis of choroid plexus papilloma (CPP) was made following posterior fossa exploration. Although the tumor lacked histopathological criteria for carcinoma, the presence of brain stem invasion suggested a higher degree of malignancy with probable metastatic dissemination to the lateral ventricle. Radiotherapy was administered with a total of 4190 rads to the cranium, 5400 rads to the frontal lobe, 5220 rads to the posterior fossa and 3040 rads to the spine. Follow-up CT showed no change in the infratentorial CPP but further enlargement of the frontal mass was noted. A specimen obtained from the frontal mass at a second craniotomy revealed sub-ependymal giant-cell astrocytoma.

To our knowledge, this is the first report of two simultaneous occurring malignant central nervous system tumors in a child. This case emphasizes that, even in the absence of special genetic predisposition to central nervous system tumors, two separate intracranial masses may not represent cerebrospinal fluid metastasis of a single primary tumor. We therefore recommend biopsy (stereotactic or open) on any coexistent intracranial mass in a child prior to initiation of therapy for the first brain tumor.

. — 0017

81.

Carbamazepine-Induced Complex Tics

M. BRILL-EDWARDS and D. L. MacGREGOR (Toronto, Ontario)

The development of movement disorders in association with anticonvulsant therapy is considered to be unusual. We report the case of a 5 year old boy, who following a history of simple febrile seizures, developed a partial complex seizure disorder at the age of 2 years. His neurological examination was normal and the family history was negative. Due to inadequate seizure control and mild hyperactivity on initial phenobarbital therapy, this medication was discontinued and carbamazepine (CBZ) was introduced gradually attaining a total dose of 15 mg/kgm/day over a one month period. Within a week, the patient developed multiple frequent facial tics consisting of eye blinking with greater frequency on the left, grimacing and chewing movements. CBZ plasma levels were within the therapeutic range. On simultaneous video-EEG recording, the facial movements were independent of electrical seizure activity. The CBZ was discontinued and the facial move-

ments diminished moderately, but were still present 4 months later. Adequate seizure control was subsequently obtained with valproic acid.

Neglia et. al. (Pediatrics 1984; 73: 841-844) report 3 cases of children who developed complex tics associated with CBZ treatment for partial complex seizures. One child presented with de novo tics and a second experienced worsening of facial tics after introduction of CBZ. The third reported case is confounded by methylphenidate therapy.

The tricyclic ring structure of CBZ is common to one group of tic associated drugs including imipramine, chlorpromazine and cyproheptadine. The known central anti-serotonin properties of these tricyclic agents implicates alteration of serotonin mediated neurotransmission, with possible concomitant alteration of other neurotransmitters such as dopamine, in the pathogenesis of complex tics.

The prognosis following the development of facial tics in association with CBZ therapy, even with prompt discontinuation, appears to be poor and we would therefore suggest that in any patient developing complex tics during CBZ therapy, that there be an immediate stoppage of the medication.

. — 0018

82.

Immunohistochemical Mapping of Adenosine Deaminase-Containing Neural Systems in the Rat CNS

J. I. NAGY, E. SENBA and P. E. DADDONA (Winnipeg, Manitoba) (Ann Arbor, Michigan)

Standard immunohistochemical techniques were used to examine the distribution of adenosine deaminase (ADA) in the rat CNS. ADA-immunoreactivity was detected only in neurons of several discrete brain and spinal cord regions which included hypothalamus, superior colliculus, septal nuclei, striatal-pallidal interface, parafascicular nucleus of the thalamus, some pre-ganglionic parasympathetic nuclei, substantia gelatinosa of the dorsal horn and dorsal root ganglia. In contrast, axons immunoreactive for ADA were observed throughout the brain and, invariably, these were most heavily concentrated in suspected projection areas of central structures harboring ADA-positive cell bodies. Of particular interest was the posterior basal hypothalamus where ADA-containing neurons gave rise to massive bundles of immunostained axons which could be followed to many and diverse brain regions including forebrain, anterior hypothalamus, thalamus, midbrain and medulla. It is concluded that ADA may be a convenient marker for neuroanatomical studies of this recently discovered hypothalamic projection system. In addition, if ADA participates in the regulation of the putative neuromodulatory actions of adenosine, then this enzyme may represent a marker for adenosinergic systems.

. — 0020

83.

The Effect of Lidocaine on Focal Cerebral Ischemia in Cats

M. T. SHOKUNBI, A. W. GELB and S. J. PEERLESS (London, Ontario)

The effect of lidocaine on the histological changes in the cerebral cortex during acute focal ischemia was evaluated in twenty cats in which the left middle cerebral artery (MCA) was clip-occluded (for six hours in 13, and four hours in seven cats). Eleven cats received lidocaine hydrochloride intravenously beginning half an hour before vessel occlusion and infused at a rate titrated to maintain burst suppression or isoelectric EEG. The remaining nine cats served as controls. The extent and severity of cerebral cortical ischemia was histologically assessed in a blinded manner from coronal sections obtained at the level of the optic chiasm.

In the lidocaine-treated animals, the EEG showed either burst suppression or became isoelectric over both hemispheres. There was no seizure activity. In the control group, voltage reduction and/or delta activity were recorded over the ischemic hemisphere. There was no statistically significant difference in the mean percentage area of cerebral cortical infarction between the treated (40 ± 17%) and control (38 ± 12%) groups (p value 0.8). This study, which has demonstrated that lidocaine does not reduce the size of cerebral infarcts following MCA occlusion in cats, does not support claims based on biochemical studies that lidocaine may be protective in acute focal cerebral ischemia.

Supported by Ontario Heart Foundation Grant No. 3-20.

. — 0022

84.

Prolonged PML Without Immunosuppression

D. ZOCHODNE and J. C. E. KAUFMANN (London, Ontario)

A previously healthy 70 year old female developed an atypical slowly advancing form of progressive multifocal leukoencephalopathy (PML). Her neurologic disease was heralded by frequent falls due to unsteadiness of gait. Over the ensuing months she developed dysarthria, dementia, "global" weakness and contractures. CT scan disclosed cerebral atrophy. Bilateral slowing was recorded on EEG. Her course culminated in inanition and death due to broncho-pneumonia 43 months after the onset of illness. A premortem diagnosis was not established. General autopsy did not reveal an underlying source of immunosuppression. The brain was atrophic and contained multiple punctate foci of demyelination that were asymmetric, sometimes confluent and often microscopic. The lesions involved deep cerebral white matter bilaterally but spared cerebellum and brainstem. Crops of enlarged bizarre gemistocytic astrocytes and swollen oligodendrocytes bearing intranuclear inclusions accompanied foci of demyelination. EM identified papova virus particles within these inclusions. Perivascular mononuclear cuffing of adjacent white matter arterioles was an additional finding.

The clinical presentation, prolonged course, and lack of apparent immunocompromise are unusual features of PML. This case lends credence to previous suggestions that relentless and opportunistic progression is not invariable in this disease.

. — 0023

85.

Opposite Directions of Circling Produced by Lesions of the Medial and Lateral Substantia Nigra Pars Compacta or Pars Reticulata in the Rat.

K. B. J. FRANKLIN and J. WOLFE (Montreal, Québec)

It has been shown in stimulation and lesion experiments that cells in the medial substantia nigra pars compacta (SN_C) appear to stimulate the animal to move away from the stimulated side (contraversive circling) while laterally placed cells drive ipsiversive circling. The present study examined the relationship between the lesion site and the direction of circling in more detail using glyoxilic acid histofluorescence to visualize dopamine cells. After 6-hydroxydopamine lesions (2-6μg in .5-1μl) in the medial SN_C and ventral tegmental area amphetamine (.8 or 2.0 mg/kg) caused rats to circle ipsiversive to the lesion while after lesions restricted to the lateral SN_C animals circled contraversively. When cell destruction extended towards the middle of the SN_C or deeper into the SN_R the direction of circling was inconsistent. In rats given 0.05% ascorbate control injections the direction of circling depended on the location of the 30g canula track. Tracks which passed through the lateral SN_R or to the cerebral peduncle produced ipsiversive circling while medial SN_R damage led to contraversive circling. Thus both medial and lateral SN pars compacta lesions and pars reticulata lesions produced circling in opposite directions. This four way division of the SN is consistent with emerging models of nigro-striato-nigral connections.

. — 0024

86.

Prevalence of Multiple Sclerosis in British Columbia: Final Report

A. D. SADOVNICK, V. P. SWEENEY, V. BRANDEJS, J. SPINELLI and R. H. WARD (Vancouver, B.C.)

A province-wide prevalence study of multiple sclerosis (MS) was conducted in British Columbia (B.C.). The major portion of this study was a review of all the files of neurologists practicing in B.C. as this was judged to be the most accurate source of identifying MS patients. 239,412 neurologists' files were hand-searched by one researcher using modified Schumacher criteria for classification. Other sources used during this study for identifying MS patients were the MS Clinic, general practitioners, urologists, ophthalmologists, specialized facilities such as rehabilitation centers and long term care facilities, and patient self-referrals.

The prevalence rates per 100,000 population for MS in B.C. are as follows:

	Clinically definite/ Probable MS	Clinically definite/ Probable/Possible MS	Clinically definite/ Probable/Possible MS/ Probable/Possible MS/ *Optic Neuritis*
MALES	N = 827	N = 1,040	N = 1,134
Prevalence	59.8	75.2	81.9
FEMALES	N = 1,769	N = 2,300	N = 2,498
Prevalence	126.4	164.3	178.4
TOTAL	N = 2,596	N = 3,340	N = 3,632
Prevalence	93.3	120.4	130.5
Standardized Prevalence	91.0	117.2	127.6

These prevalence rates for MS are among the highest reported in Canada or elsewhere.

. — 0026

87.

Relationships between Intracranial Pressure Measurements and Cognitive Test Results in Normal Pressure Hydrocephalus

B. DIBKIN, D. ROWED, G. SNOW and I. ALTMAN (Toronto, Ontario) (Victoria, B.C.)

One unresolved issue in the study of NPH is the role which increased pressure plays in the development of the syndrome. Thus, while intracranial pressure (ICP) is said to be normal, one of the cardinal neuroradiologic features is increased ventricular size. Furthermore, the surgical approach to this condition is to place a shunt into either of the ventricles or lumbar subarachnoid space as a means of providing an alternative route for drainage of cerebrospinal fluid, and hence presumably for reduction of ICP.

This retrospective study investigated the relationship between intracranial pressure and measures of intellectual and memory functioning in a group of 20 patients with a diagnosis of normal pressure hydrocephalus (NPH). No significant correlations (Pearson rs) were found between the two classes of measures (i.e., pressure and neuropsychological functioning). These findings call into question the role of increases in pressure in the etiology of NPH. The methodological problems (including issues such as smallness of sample size and the restricted range of pressure readings obtainable in (NPH) associated with this area of investigation are discussed.

. — 0027

88.

Causes of Death in Multiple Sclerosis

A. D. SADOVNICK, G. C. EBERS, D. W. PATY, K. EISEN, S. A. HASHIMOTO and J. HOOGE (Vancouver, B.C.) (London, Ontario) (Vancouver, B.C.)

Cause of death was examined for 81 multiple sclerosis (MS) patients who died among 1,826 attending the Multiple Sclerosis Clinics in London, Ontario (N = 976) or Vancouver, British Columbia (N = 850). All patients were diagnosed as clinically definite, probable, or possible MS. 71 deaths occurred among London's Clinic population during the years 1972-1984 and 10 deaths were from Vancouver's Clinic population during the period 1980-1984.

Autopsy reports were available for most cases. Cause of death was looked at in association with the sex of the patient, age of onset and duration of the MS, and Kurtzke disability score prior to death. 39.6% of the deaths were the result of suicide. 41.5% of the deaths were apparently unrelated to MS; the majority of these deaths were due to either carcinomas or myocardial infarcts. The remainder of the deaths (18.9%) were related to progressive MS.

The results from this study indicate that suicidal tendencies among MS patients should be taken seriously and patients should be given appropriate therapy. It is also important to remember that MS patients can develop other illnesses. Pain and discomfort reported by patients must be thoroughly investigated before being attributed to MS.

. — 0028

89.

Vein of Galen Malformation (VGM): A Reversible Cause of Progressive Cerebral Calcification and Mental Retardation?

S. J. PHILLIPS, J. M. DOOLEY and P. R. CAMFIELD (Halifax, Nova Scotia)

Progressive intracranial calcification and mental retardation have not been previously emphasised as predominant manifestations of vein of Galen malformations (VGM). We report 2 such cases with striking C.T. scan appearances.

Case 1 is a 17 month old boy with marked neurodevelopmental deterioration. He was neurologically normal when first seen at 6 months of age because of seizures. C.T. scans showed progressive calcification affecting both cerebral hemispheres. A VGM was documented at angiography.

Case 2 is a 12 year old boy with psychomotor retardation and seizures. He was initially seen at 6 months of age because of macrocephaly. His C.T. scan closely resembled those in case 1. Angiography showed a VGM.

The underlying pathophysiology is discussed. As the mechanisms involved may be reversed by early surgery it is important to consider VGM in the differential diagnosis of children with suspected neurodegenerative disease, especially if there is intracranial calcification.

. — 0030

90.

Immunodeficience Acquise et Toxoplasmose

E. BERGER, C. AUGER and L. PELLETIER (Montréal, Quebec)

Onze malades avec un syndrome d'immunodéficience acquise furent traité dans notre Centre Hospitalier depuis 1982. Parmi ce groupe on distingue sept hommes (donc cinq d'origine haitienne) et quatre femmes (toutes d'origine haitienne). Les hommes étaient âgés de 16 à 36 ans (âge moyen des Haitiens 30.4 ans) et les femmes de 31 à 48 ans (age moyen 35.5). Deux hommes de race blanche étaient âgés de 31 et 42 ans respectivement. Ces deux derniers patients étaient des homosexuels. Tous les Haitiens ont nié l'emploi de drogues tandis qu'un patient de race blanche utilisait de diverses drogues, mais pas par voie intraveineuse. Cinq patients souffraient d'une pneumonie à pneumocystis carinii (PCP) un d'Escheria coli, six de candida albicans, trois de monilia, trois d'herpes, un d'hémophilus infl., et deux d'un sarcome de Kaposi.

Neuf patients avec symptomatologie impliquant le système nerveux central ont subi des tomodensitométries, et chez cinq patients des granulomes multiples arrondis au niveau des hémisphères cérébraux ou cérébelleux furent démontrés. Trois malades ont eu des biopsies positives pour toxoplasmose. Chez un patient, l'exérèse d'un granulome du lobe frontal droit par crâniotomie a permis un diagnostic histologique positif pour toxoplasmose. Le traitement avec pyrimethamine et sulfisoxazole est efficace temporairement tel que témoigné par des

tomodensitométries subséquentes. Cependant la toxoplasmose cérébrale récidive dans l'espace de deux à trois semaines après l'arrêt de ces médicaments. La forte dose de pyriméthamine requise pour le traitement de la toxoplasmose peut provoquer une leucopénie, une anémie mégaloblastique, une thrombocytopénie et pancytopénie.

D'autres pathogènes que la toxoplasmose peuvent donner des images tomodensitométriques semblables à celles causées par la toxoplasmose. Une biopsie positive de chaque lésion vue à la tomodensitométrie pourrait permettre une thérapie plus complète mais est difficilement réalisable techniquement surtout en tenant compte de la condition clinique précaire de ces patients.

. — 0031

91.

Increase in Intracranial Pressure may Result in a Selective Increase of Spinal Cord Grey Blood Flow

E. ARBIT, A. RUBINSTEIN and S. BREM (Montreal, Quebec) (Israel) (Montreal, Quebec)

The fact that elevation of intracranial pressure (ICP) may result in increase spinal blood flow has previously been described. We have shown that a cerebrovasodilatation can result from electrical stimulation of the DMRF — the anatomical substrate of the Cushing response. We studied the effects of increase in ICP to the point of the Cushing response, on spinal cord white and grey matter blood flows.

The experiments were carried out in adult Sprague-Dawley rats. The rats were anaesthetized with chloralose, paralyzed and artificially ventilated. Arterial pressure, heart rate and body temperature were continuously monitored: pCO_2, $p0_2$, and pH were maintained within the physiological range. SCBF was measured using ^{14}C-iodoantipyrine as an indicator, simultaneously with the hydrogen clearance method. The Cushing response was elicited by a graded intracranial pressure increase with a Fogarty balloon catheter. Blood pressure elevations were maintained within the range of autoregulation.

In control animals (N = 63) white SCBF was 20 ± 4 ml/min/100g and grey SCBF was 41 ± 2 ml/min/100 g. Associated with the Cushing pressor response (N = 56) SCBF — white matter remained essentially unchanged, whereas SCBF — grey matter increased to 55 ± 7 ml/min/100 g i.e. a 35% increase (p0.001).

We concluded that in the rat a) spinal grey blood flow is approximately twofold greater than spinal white blood flow, b) a selective increase in spinal grey blood flow can be obtained with increase in ICP, c) there may exist a suprasegmental center for SCBF modulation, perhaps common to spinal and cerebral blood flows.

. — 0032

92.

The Transpedicular Approach to Spinal Metastatic Cord Compression

E. ARBIT, S. BREM and A. RUBINSTEIN (Montreal, Quebec) (Montreal, Quebec) (Israel)

Currently, the recommended initial treatment of spinal cord compression from metastatic cancer is with radiation and steroids. Several recent studies have recommended the anterior, transthoracic approach to decompress the cord, the rationale being that in most instances the tumor involves the vertebral body and cord compression arises ventrally. The results of these procedures are more favourable than obtained by radiation and steroids and far superior to those obtained with laminectomy. In order to avoid thoractomy as an approach to the thoracic spine, we have adopted the transpendicular operation introduced by Patterson and Arbit for thoracic disc herniation, to decompress the cord and fuse the spine with acrylic, simultaneously. In this pilot study, we included nine patients that had a follow-up of at least five months. Two additional patients died within three months of surgery. Five patients had failed prior radiation, one was progressing despite radiation. Three had metastatic cord compression of unknown primary. We have obtained 65% good relief of pain, 40% converted from non ambulatory to ambulatory and 40% regained urinary continence and control. There was no neurological deterioration and no peri-operative mortality. Our results are comparable to other non surgical and surgical studies. Although our series is small, these preliminary results are encouraging and indicate that the transpedicular decompression and fusion may be of benefit for patients with metastatic cord compression.

. — 0033

93.

Résultat de la Stimulation Epidurale Utilisée Comme Traitement de la Douleur Chronique dans les Traumatismes des Nerfs Périphériques

S. N. MARTINEZ, P. MOLINA-NEGRO and M. SEGUIN (Montréal, Québec)

Depuis mai '79, 112 patients référés pour douleur chronique ont bénéficié de stimulation épidurale. De ce nombre, 18 patients présentaient un traumatisme des nerfs périphériques avec un tableau correspondant à une causalgie mineure:

- 13 patients avec différentes pathologies au niveau des membres supérieurs
- 5 patients avec différentes pathologies au niveau des membres inférieurs

Ces patients avaient subi antérieurement diverses interventions directes telles que: libération d'un névrome et neurolyse, greffe nerveuse, phénolisation, débridement allant quelquefois à l'amputation, bloc sympathique et sympathectomie et ce, sans avoir obtenu de résultat positif.

La stimulation épidurale s'est avérée efficace chez 14 de ces patients qui estiment être soulagés de 50 à 75%. Toutefois, 4 autres patients n'ont obtenu aucun effet bénéfique.

D'après notre expérience, nous considérons que la stimulation épidurale est, présentement, un traitement adéquat pour la causalgie mineure puisque les méthodes conventionnelles se sont révélées inefficaces.

. — 0036

94.

Changes in Saccadic Accuracy, Velocity and Latency with Advancing Age

D. H. ZACKON and J. A. SHARPE (Ottawa, Ontario) (Toronto, Ontario)

Effects of aging on saccades were investigated in 34 normal young, middle aged, and elderly subjects. Horizontal saccades were recorded by infrared oculography and digitized at 200 samples/sec for computer analysis. Three target paradigms were employed: 1) predictable 20° targets at 2 second intervals, 2) unpredictable amplitude targets, and 3) unpredictably timed target steps.

Saccadic peak velocities were significantly reduced in the elderly only when timing was predictable. Saccadic durations were not significantly different, suggesting that brainstem burst unit frequency is more affected than burst duration in senescence. Latencies were significantly prolonged in the elderly under all tasks. Delay to regularly timed targets was longer than delay to randomly timed targets. This indicated impaired target prediction in senescence. In the middle-aged peak velocities, latencies and durations were degraded compared to the young, but differences were not significant. Saccadic accuracy was significantly decreased in elderly subjects; they had more frequent hypometric saccades and reduced amplitudes of primary saccades. However, intervals between hypometric saccades were normal (mean 154 ms) indicating integrity of internal and retinal feedback loops that generate corrective saccades. The results indicate that saccadic dysfunction in disease must be qualified by the age of the patient and by the target task. Saccades may be used to quantify the aging process.

Supported by the MRC and CNIB, Canada.

. — 0037

95.

Diagnostic Value of EEG in Early Stroke

M. GUTTMAN, W. GOLDSTEIN, F. TYNDEL and R. GIAMMARCO (Toronto, Ontario)

In acute cerebral infarction, internal capsule lacunes may be clinically difficult to distinguish from cortical lesions. CT is currently the best means of differentiating the lesion sites. Since CT may be negative in the first few days after the event, the electroencephalogram may be useful in discriminating between cortical and capsular lesions.

To determine the diagnostic value of EEG in the early differentiaton of cortical from capsular infarction, thirty two patients were assessed prospectively. All met the following criteria: 1. Clinical stroke syndrome compatible with a capsular lacune or a cortical infarct. 2. EEG within 48 hours of onset. 3. CT scan compatible with a capsule lacune or cortical infarct. If initial CT scan was negative, it was repeated after 6 days. Exclusion criteria were: 1. Previous stroke or neurological illness. 2. Resolution of neurological deficit within 24 hours 3. Negative CT scan.

Twenty-five out of twenty-six patients with cortical infarction had an abnormal EEG on the side of the lesion. Six out of six patients with capsular lacunes had a normal EEG. The positive predictive value of a focally abnormal EEG was 100% to predict cortical infarction. The positive prediction value of a normal EEG was 86% to predict internal capsule lacunar infarction.

We suggest that the EEG is a clinically useful means of distinguishing cortical from capsular lesions.

. — 0039

96.

Lead Poisoning Through Gasoline Sniffing

P. J. COOPER and M. A. MOSS (Halifax, Nova Scotia)

The prevalence of gasoline sniffing (GS) has probably been underestimated; it is endemic in certain communities in the Canadian North. It has been most frequently reported amongst Indian and non-Indian rural adolescents from lower socioeconomic backgrounds. This entity is also prevalent in rural and urban Nova Scotia, but is probably much more common than recognized by the medical community. The neurological manifestations of GS are quite varied, and their aetiology may not be apparent unless the physician obtains a thorough history and makes the association.

In this paper, a 19 year old chronic gasoline sniffer is described who presented with myoglobinuria, and subsequently with acute lead encephalopathy. This was attributed to his "recreational" use of gasoline. The clinical presentation of GS with myoglobinuria is rare. This case touches upon two very important current medico-social issues, namely the problem of solvent abuse in general, and the problem of lead poisoning. This paper will discuss the various sequelae of GS, with emphasis upon the varied neurological presentations. The role of chelating agents in the treatment of lead encephalopathy is discussed, and the importance of drug rehabilitation programs stressed.

. — 0040

97.

Ethmoidal Sphenoidal Mucocele Presenting With Visual Loss and Pseudo Sixth Nerve Palsy

R. A. PURDY, V. BAHN and F. CHAN (Halifax, Nova Scotia)

Sphenoidal sinus mucoceles are rare clinical entities. Only 82 cases are reported in the modern literature since 1970.

A 66 year old woman is presented who developed sudden visual loss and pseudo sixth nerve palsy due to an ethmoidal sphenoidal mucocele. Forty-five years before she had surgery on her ethmoidal sinus for persistent nasal drip.

The pertinent literature is reviewed and the clinical pathological correlation with emphasis on the dramatic CT findings in this case is presented.

. — 0041

98.

Multiple Sclerosis Presenting as Cerebral Neoplasms

D. MacDONALD, S. MacDOUGALL, R. A. PURDY and V. SANGALANG (Halifax, Nova Scotia)

Five cases of multiple sclerosis, four pathologically confirmed, which mimicked cerebral neoplasms clinically and on computerized tomography are presented. The literature regarding this problem is reviewed and the difficulties in managing such cases are discussed.

. — 0042

99.

Electro-Micturition in Paraplegia: Rationale, Techniques and Obstacles

A. TALALLA, J. W. BLOOM and M. V. KAMATH (Hamilton, Ontario)

Electrical stimulation techniques for the neuropathic bladder have centred on three approaches — direct bladder wall stimulation; stimulation of bladder centres in the conus medullaris, and; most recently, selective sacral nerve stimulation. The authors review the merits of each of these techniques and in detail describe the electrophysiological manipulations necessary for stimulation induced urinary voiding. They present their experiences in a clinical feasibility study of sacral nerve stimulation including modest success with this technique and discuss prospects for the future.

. — 0043

100.

Effects of Chronic Cerebellar Stimulation (CCS) Setting on the Gait and Speech of a Spastic Cerebral Palsy Adult

C. HERSHLER and A. R. M. UPTON (Vancouver, B.C.) (Hamilton, Ontario)

Quantitative gait analyses were done on a patient (D.A.) who is a spastic cerebral palsy adult. This patient had continued to experience CCS for 9 years without any change in his stimulator settings. Comparisons were made with identical gait analyses done on the same patient 7 years ago. Both studies show on-off effects on gait which related to both acute and chronic cerebellar stimulation.

The patient (D.A.) was also assessed at six different stimulator settings by a neurologist, a speech therapist, quantitative gait and speech analyses as well as somatosensory evoked potentials (SSEP's). Alteration in stimulator settings occurred one week apart to allow for stabilization and all assessments were completed in the same sequence each day. None of the individual stimulator settings were known to any of the assessors or to the patient.

The results showed consistently that the patient's gait and speech were poorest when the stimulator was switched off completely. Switching on the stimulator caused improved function according to all assessments. There was consistent improvement in gait and speech when the rate of cerebellar stimuli was high (irrespective of the amplitude of the stimuli). Changing the amplitude (voltage) of the stimuli (with the rate constant) did not appear to have as much effect.

. — 0044

101.

Atypical Neuroleptics Facilitate Amphetamine-induced Stereotypy but not Apomorphine-induced Stereotypy

A. ROBERTSON, C. McDONALD (Montréal, Quebec)

We previously reported that the atypical neuroleptics clozapine (5-10 mg/kg SC), thioridazine (5-10 mg/kg SC) and sulpiride (5-20 mg/kg SC) may be differentiated from classical neuroleptics by their ability to facilitate rather than antagonize stereotyped behaviors produced by amphetamine (1,2). The effects of neuroleptics on amphetamine-induced stereotypy have been reported to be highly correlated with their effects on apomorphine-induced stereotypy (3). Therefore in the present experiment we tested the effects of the same three atypical neuroleptics on behaviors produced by apomorphine (0.1-1.0 mg/kg SC). None were effective in enhancing apomorphine-induced stereotypy. In fact, all three were weakly antagonistic. We also tested two classical neuroleptics, haloperidol (0.05 mg/kg SC) and metoclopramide (2 mg/kg SC). As expected, both were potent antagonists of apomorphine-induced stereotypy.

The differential effects of atypical neuroleptics on amphetamine vs. apomorphine-induced stereotypy suggest that these behaviors are generated by different neural systems. Indeed stereotypies produced by amphetamine and apomorphine are qualitatively different — apomorphine characterized by sniffing down, licking and gnawing, and amphetamine by repetitive head movements and some sniffing down.

Hypomotility produced by a low dose (0.1 mg/kg) of apomorphine, an effect thought to be mediated by presynaptic dopamine receptors (4), was blocked by sulpiride but not by any of the other drugs tested. This suggests that sulpiride preferentially blocks presynaptic dopamine receptors, and would explain sulpiride's facilitation of amphetamine-induced stereotypy and its lack of effect on apomorphine-induced stereotypy.

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. — 0045

102.

The Treatment of Restless Legs with Clonazepam

D. BOGHEN, L. LAMOTHE, R. ELIE, J. MONTPLAISIR and R. GODBOUT (Montréal, Quebec)

Encouraged by recent favorable reports we have undertaken to study the effect of clonazepam on the restless legs syndrome (RLS) in a prospective double-blind controlled fashion. 13 patients with an average duration of the disease of 16.5 years, were studied. Following a 4-week drug-free period the patients were randomly assigned to either a clonazepam (0.5 mg tablets) — first group (G_1 = 8 patients), or an identical looking placebo — first group (G_2 = 5 patients), for a four-week period. Upon the termination of this period they took the alternate drug for another four weeks. The initial dosage of 1 tablet daily was gradually increased to 4 tablets daily in the last week. The patients rated the severity of their symptoms daily using a scale in which 0 = none and 4 = very severe. Patients were also assessed as being either "improved" or "not improved" on the basis of a weekly clinical evaluation. Statistical analysis in 9 patients for whom data was available showed no difference between the intensity scores in the two treatment periods (F = 2.0, NS) and the two possible treatments (F = 1.55, NS). 4 out of 13 patients improved with clonazepam alone but not with placebo alone. This difference was not statistically significant. Clonazepam did not prove to be significantly more effective than placebo in relieving the bothersome symptoms of RLS.

. — 0047

103.

Increased Lactate and Glucose Levels in Rat CSF Following Probenecid Administration

V. H. MacMILLAN (Toronto, Ontario)

Probenecid is a well documented competitive inhibitor of the transport of the monoamine acidic metabolites 5-HIAA and HVA from brain and CSF to blood. Measurements of brain uptake of radio-labelled substances have suggested that short chain monocarboxylic acid transport into brain may also be inhibited by Probenecid. In the present study male rats were prepared with a permanent cannula in the cisterna magna which allowed for repeated sampling of CSF in the unanesthetized animal. After an initial CSF sampling, Probenecid (200 mg/Kg) or equivalent amounts of drug dilutent were given intra-peritoneally and followed by CSF sampling at 1, 2, 3, 4, 5 and 6 h. CSF lactate and glucose contents were determined by fluorometric enzymatic assay. In Probenecid treated animals CSF lactate and glucose levels increased to 130 - 170% and 130 - 200% control ($P<0.05$), respectively at the 1 - 2 h samplings. The results are in agreement with a recent suggestion that lactate, 5-HIAA and HVA efflux from brain may share a common carrier. The results suggest that this carrier may also be involved in glucose transport.

. — 0048

104.

Effects of Hyperglycemia on Regional Indoleamine Levels of Ischemic and Post-Ischemic Brain

V. H. MacMILLAN (Toronto, Ontario)

Administration of glucose to animals prior to the induction of cerebral ischemia results in an accentuation of metabolic and histological evidence for ischemic tissue damage. In the present study normoglycemic (blood glucose 10 mM/L) and hyperglycemic (blood glucose >20 mM/L) rats were exposed to global cerebral ischemia for 0.5 h with subsequent recirculation for 0, 1, 6 or 24 h and measurement of cerebral cortical, striatal, thalamic and brain stem contents of serotonin (5-HT) and 5-Hydroxyindoleacetic acid (5-HIAA) by HPLC — electrochemical detection methods. The main abnormality in the normoglycemic — ischemic group was a transient increase of striatal 5-HT to about 200% control at 1 h recirculation, followed by a complete normalization of all metabolites by 24 h. In hyperglycemic-ischemic animals, although a similar pattern was observed for striatal 5-HT at 1 h (increased) and 6 h (normalized) the 24 h sampling revealed secondary massive increases of 5-HT content (300% control). The possible mechanisms of these effects are discussed in light of current concepts of ischemic tissue damage.

. — 0050

105.

Repetitive Pseudoseizures Incorrectly Managed as Status Epilepticus

M. LEVITAN, J. BRUNI and M. FREEDMAN (Toronto, Ontario)

In suspected epilepsy pseudoseizures can present diagnostic and therapeutic difficulties. Ten patients aged 12 to 73 presenting with unrecognized, frequent pseudoseizures were treated for incorrectly diagnosed status epilepticus. Eight were females. Four had a prior history of epilepsy. Pseudoseizures presented as atypical, often bizarre, limb, trunk, head, and pelvic movements lasting up to 3 hours and occurred up to 30 times in 20 hours. Alertness during pseudoseizures was noted in 3 patients and between pseudoseizures in 2 patients. Treatment included intravenous phenytoin, diazepam, phenobarbital, and paraldehyde. One patient received lidocaine and another received pancuronium. Iatrogenic respiratory depression occurred in 3 patients, 2 of whom required ventilatory assistance. EEG examination, including a positive provocation test in 6 patients, ultimately confirmed the diagnosis in 9 patients. Psychiatric disorders including conversion

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hysteria and major depression were noted in 8 patients. Three patients demonstrated functional deficits. Recognition of repetitive pseudoseizures may obviate the inappropriate use of potentially harmful anticonvulsants. Clinical features, psychiatric history, and EEG methodology will be discussed regarding strategy for diagnosis.

. — 0051

106.

Familial Oligodendroglial-Astrocytic Gliomas

A. LOZANO, Y. ROBITAILLE and R. LEBLANC (Montréal, Quebec)

We report the first cases of mixed oligodendrocytic and astrocytic gliomas occurring in 2 members of the same family, a father and a son.

A 20 year old white male began having focal motor seizures with secondary generalization five years before his admission to the Montreal Neurological Hospital. Craniotomy revealed a lobulated tumor involving the cortical surface of the pre-central gyrus and extending anteriorly. This was subtotally removed and the patient underwent radiotherapy. Histological examination demonstrated a grade II mixed glioma consisting of haphazardly scattered, well-differentiated, neoplastic stellate and piloid astrocytes, and oligodendrocytes. There was moderate vascular hyperplasia without necrosis and mitotic figures were not seen. The patient received radiotherapy and died seven years later.

His son, a 37 year old white male, presented with rapid onset of hemiparesis and papilledema. Radiological investigations suggested a space-occupying lesion which was verified at surgery to be a cystic tumor with areas of necrosis involving the right parieto-occipital lobe and extending towards the central region. Histological examination revealed a grade II mixed glioma consisting of well-differentiated neoplastic oligodendrocytic cells merging with nests of piloid and stellate neoplastic astrocytes. There was mild vascular hyperplasia without areas of necrosis and mitotic figures were absent. The patient underwent radiotherapy and is alive six months after diagnosis.

The occurrence of familial tumors with common biological and histological characteristics occurring at similar sites and at similar ages supports the concept of genetic determination in some gliomas. The importance of genetic determination in the etiology of some glial tumors will be discussed.

. — 0053

107.

Neurocysticercosis: Combined Surgical and Medical Management with Praziquantel, a New Antihelminthic Agent

R. LeBLANC, K. F. KNOWLES, D. MELANSON and J. D. MacLEAN (Montréal, Quebec)

We report our experience with the combined surgical and medical management of two patients with neurocysticercosis, and contrast their outcome with that of a third treated surgically before the advent of Praziquantel.

Case I, a 54 year old white Bolivian male, presented with obstructive hydrocephalus from aqueductal stenosis and granulomatous meningitis secondary to neurocysticercosis that proved refractory to numerous shunting procedures because of repeated, near fatal obstructions of the tubing with inflammatory debris. Blood and CSF serology were positive for cysticercosis and the patient was treated with a final shunt revision and with Praziquantel. Eighteen months later he is alive and caring for himself. *Case II*, a 28 year old black female from Haiti, presented with headaches, stupor, and ocular muscle palsies. CT scanning demonstrated cysts at the base of the brain and in the mesencephalon producing hydrocephalus. Serology was positive for cysticercosis and a shunting procedure and a course of Praziquantel cured her hydrocephalus and reversed all of her neurological signs. *Case III*, a 35 year black man from Haiti, presented with acute hydrocephalus from meningobasal and cystic neurocysticercosis prior to the advent of Praziquantel. Despite numerous shunt revisions he died of cerebral infestation with poorly controlled intracranial pressure.

These cases illustrate the dramatic recovery that can be expected in patients with this usually fatal presentation of neurocysticercosis with combined surgical control of intracranial hypertension and eradication of the brain infestation with Praziquantel. The indications, contraindications, and precautions to be exercised with the use of Praziquantel, as well as the results expected with treatment will be discussed.

. — 0054

108.

Middle Latency Auditory Evoked Responses in Cortical Deafness

K. J. HO, D. R. McLEAN and P. KILENY (Edmonton, Alberta)

The localization of the cortical generator of the Pa component of the auditory middle latency response (MLR) and the relationship of this response to the central processing of auditory information are still unsolved issues.

We had the opportunity to address these issues in a 67 year old woman who incurred infarction of her right and subsequently her left auditory cortex. Following the second event she developed cortical deafness with no response to pure-tone or speech. She was able to communicate effectively by writing, reading and speaking. Initially, paraphasic errors were frequent. Fifteen days following this second event pure-tone thresholds across frequencies returned to normal. Speech awareness thresholds were measured at 15 dB HL but no measurable discrimination of speech or of nonspeech sounds was obtained. Brainstem auditory evoked responses (BAER's) showed slightly delayed interpeak latencies and the Pa component of the auditory MLR was bilaterally absent. When examined seven months following her second event discrimination of speech and non-speech sounds, had considerably improved. The Pa component of the auditory MLR over the left hemisphere and vertex returned but it remained absent over the right hemisphere. The implications of these findings in relation to cortical localization of the Pa component of the MLR will be discussed.

. — 0055

109.

The Role of Multiple Sclerosis in the Practice of Neurology

V. P. SWEENEY, A. D. SADOVNICK, V. BRANDEJS, R. H. WARD, and J. SPINELLI (Vancouver, British Columbia)

Forty-one of forty-three neurologists practicing in British Columbia agreed to a search of their clinical files as part of a prevalence study of M.S. Confidential guidelines were approved by participants and the Canadian Medical Protective Association. Approximately 240,000 files were reviewed by a single research worker and cases ascertained were classified using modified Schumacher criteria. The patterns of diagnostic classification by neurologists over time were documented and cross reference allowed calculations of multiple consultations.

3,892 cases were identified from neurologists' files, representing 84% of all cases ascertained through all sources including general practice and institutional contact and public advertising. An additional 5% were attending a University M.S. Clinic. Multiple Sclerosis cases accounted for 2% of the case-load of neurologists not specializing in M.S. 83% of patients consulted only 1 neurologist, 14% saw 2 and 3% saw 3 or more. A diagnosis of definite/probable M.S. was made on 65% of patients at first consultation. This proportion rose to 84% and 86% respectively at second and third visits. Optic neuritis accounted for 9% of first consultations. There was little difference in diagnostic classification of patients who consulted multiple neurologists.

Although the prevalence of M.S. in British Columbia is high (120/100,000) the burden of such cases in neurological practice is not large. Considering the complexity of this disease a surprisingly high percentage of patients were diagnosed early and multiple opinions were sought only by 17% of patients or their referring doctors. Most identified patients had seen a neurologist. The excellent co-operation of neurologists made this prevalence study unique in the accurate classification of cases.

. — 0056

110.

Modification of EAE in the SJL/J Mouse with a Synthetic Imunoregulatory Peptide

R. M. ARMSTRONG, R. S. BRAY and D. L. ARMSTRONG (Houston, Texas)

A synthetic peptide, derived from human Ig G Fc, which suppresses the lymphocyte response to antigen presented in vitro, was used to modify experimental allergic encephalomyelitis in SJL/J mice.

Sixty five mice were immunized with subcutaneous injection of mouse spinal cord homogenate and complete Freund's adjuvant. Two injections were given one week apart. Neurologic signs developed in all mice. The onset was usually 12-15 days after the first immunization. Thirty mice were treated with subcutaneous injection of 1 mg of the peptide given three times per week. Treatment was started just before or at the onset of clinical signs. Of the treated group 86% developed only minimal or mild deficits and 14% were graded as moderate or severe. 55% of the untreated group were graded as moderate to severe and 45% were graded as mild and none were graded as minimal.

Pathologically the changes of EAE were much less pronounced in the treated mice which were examined.

The peptide is effective in this model in modifying the severity of the EAE. The basis for this remains to be defined and its effect in severely diseased animals will be examined.

. — 0057

111.

Focal Axonal Swellings in Rat Cerebellar Purkinje Cells during Normal Development

C. GRAVEL, N. LECLERC, A. PLIOPLYS and R. HAWKES (Québec, Québec)

We have used monoclonal antibodies to investigate the postnatal development of the rat cerebellar cortex. MabMIT-23, MabN210 and MabQ113 are three antibodies derived from immunisations with synaptosomal plasma membranes and directed against a neuron-specific mitochondrial polypeptide, the 210KD component of neurofilament and a Purkinje-cell specific polypeptide respectively. Immunocytochemical staining of neonatal rat cerebellar slices with any of these reveals the presence of focal swellings on Purkinje cell axons in the granular layer and white matter tracts, taking the form of prolate ellipsoids from 2 to 8 μm in length. Quantitative data accumulated with MabMIT-23 show that the focal swellings follows a characteristic developmental time-course. Focal swellings first appear at P7, their frequency increases to a maximum at P11 and then subsides. We have not seen focal axonal swellings in normal animals older than 15 days of age. In some instances, we have observed an association between swellings and the emergence point of a Purkinje cell axon collateral. Although they are a feature of normal corticogenesis, Purkinje cell axonal swellings are reminiscent of the focal swellings common in a range of encephalopathies and neuropathies.

Supported by MRC and Fonds de la paralysie cérébrale.

. — 0058

112.

Effect of Storage on the Response of Canine Cerebral Arteries to Biogenic Amines

D. A. COOK and C. A. KRUEGER (Edmonton, Alberta)

It has been shown that in cerebral arteries tyramine is not well antagonised by a pretreatment with reserpine while we have found that the responses to tyramine are actually larger than those to noradrenaline. In peripheral arteries the reverse is true. This has raised the possibility that tyramine acts through its own receptor. We have perfused the entire canine Circle of Willis for up to 5 days with a culture medium containing antibiotics and fetal calf serum. Segments of middle cerebral artery were then removed and examined using standard organ bath techniques. This procedure leads to some degeneration of adrenergic nerves, and we observe that in these tissues the response to noradrenaline in enhanced relative to fresh segments of middle cerebral artery, while the response to tyramine is considerably attenuated. These results would be expected if tyramine had the same action in middle cerebral artery as it does in peripheral vessels, and thus it may be premature to conclude that this agent has its own receptors in the cerebral vasculature.

Supported by the Alberta Heart Foundation.

. — 0059

113.

Histamine H_1 Receptors in Canine Brain

B. BIELKIEWICZ and D. A. COOK (Edmonton, Alberta)

The properties of promethazine-sensitive ^{3}H-mepyramine binding sites in brain suggest that these sites have the expected characteristics of the histamine H_1 receptor. It is also known that species differences exist in the affinity of H_1 antagonists for their binding sites and that, at least in some species, histamine is a poor inhibitor of binding of labelled antagonist. In order to clarify this issue we have examined the binding of ^{3}H-mepyramine to several structures of dog brain. Specific binding was defined as that fraction of the total binding which can be displaced with 2μM promethazine. ^{3}H-mepyramine binds in a saturable fashion with half-maximal binding at about 3nM. Scatchard analysis suggests a small homogenous population of binding sites. Neither the affinity constant nor the binding capacity differed significantly between the different structures of the brain, and in all cases the Hill co-efficient was close to unity. Chlorpheniramine, Promethazine and Mepyramine itself inhibited the binding of ^{3}H-mepyramine with IC_{50} values of 10nM, 6nM and 4nM respectively. Comparison with other data suggests that the H_1 receptor in dog brain is not significantly different from that in monkey brain or in smooth muscle.

Supported by the MRC of Canada.

. — 0060

114

The Incidence and Distribution of Stress GI Bleeding in Neurosurgical Patients

P. J. MULLER, D. JIRSCH, J. D'SOUZA and C. KNAPP (Toronto, Ontario)

The medical records of 268 patients coming to craniotomy at St. Michael's Hospital in 1983 were reviewed with the intent of identifying the incidence of stress (GI) bleeding and assessing the relationship of stress bleeding to the Glasgow Coma Scale (GCS) and to the use of prophylactic anti-ulceration treatment.

There were 168 males and 100 females; their ages ranged from 16 to 95 years (median = 56.5). Fifteen patients underwent craniotomy for spontaneous intracerebral hemorrhage (SICH), 49 for head injury (HI), 53 for treatment of spontaneous SAH, 127 for treatment of brain tumor (BT), and 24 with other diagnoses. For the entire group the mean GCS was 13.3 ± 3.5. Forty (15%) patients had a GCS of 10 or less. In the diagnostic categories of BT, SAH, HI or SICH the proportions with a GCS of 11 were 5/127 (4%), 7/53 (13%), 21/49 (43%) and 3/15 (20%), respectively.

Of the entire group 27 (10%) had a GI bleed. The GI bleed rates for those with a GCS >10 or a GCS 11 were 13/228 (5.7%) and 14/40 (35%), respectively, [$p<0.0005$]. The mean GCS's for patients who had a GI bleed or those that did not have a GI bleed were 10.4 ± 4.6 and 13.6 ± 3.1, respectively, [$p<0.01$].

Seventy-six patients received prophylactic treatment and 11/76 (14%) bled; 192 did not receive prophylactic treatment and 16/192 (8%) bled (x^2 = 1.639, N.S.). Of the 40 patients with an admission GCS of 11, 13 received prophylactic treatment and 5 (38%) bled; 27 did not receive prophylactic treatment and 9 (33%) bled [x^2 = 0.0013, N.S.).

These data show that the risk of GI hemorrhage is greater in those patients with a low GCS; however these data do *not* demonstrate that the present modes of prophylaxis are effective.

. — 0062

115.

The Effect of CCNU-BCNU Combinations on the Toxicity and Tumor Growth Retardation in a Murine Ependymoblastoma

P. J. MULLER and K. CHADA (Toronto, Ontario)

The toxic effect of BCNU, CCNU, and BCNU-CCNU combinations was assessed in male C57B1/6J non-tumor bearing mice in a 4 x 5 factorial design. The LD50 of BCNU and CCNU was 55 and 77 mg/kg, respectively. The LD50 values for CCNU in mice which also received BCNU at doses of 20, 30, 40 or 50 mg/kg were 47, 45, 43 and 26 mg/kg, respectively. The LD50 for BCNU-CCNU combinations (sum of doses of BCNU & CCNU) was 75 mg/kg. Analysis of variance showed the expected highly significant effect of dose escalation but showed only mild interaction between BCNU and CCNU.

The effect of BCNU, CCNU and BCNU-CCNU combinations on survival and tumor growth rate of ependymoblastoma implanted into the right leg of mice was assessed. Three BCNU-CCNU combination dose ranges were used — low (6-8 mg/kg), mid (11.5-16 mg/kg) and optimal (20-30 mg/kg total dose). In the individual experiments no synergistic effects between BCNU and CCNU were identified. The calculated dose values of nitrosourea for a 200% increase in life span for BCNU, CCNU and BCNU-CCNU combinations were 22, 20 and 16 mg/kg respectively; and, the dose values required to prevent a 25% increase in leg tumor diameter for 30 days were 24, 28 and 21 mg/kg, respectively. Although no synergism between BCNU and CCNU was identified the BCNU-CCNU combination therapy had therapeutic indices which were superior to those of BCNU and CCNU alone (TI-regrowth: BCNU = 2.3, CCNU = 2.8, BCNU-CCNU = 3.6; TI-survival: BCNU = 2.5, CCNU = 3.9, BCNU-CCNU = 4.7).

. — 0064

116.

Increase in Post-Traumatic Spinal Cord Blood Flow with a Calcium Channel Blocker.

A. GUHA, C. H. TATOR and I. PIPER (Toronto, Ontario)

Spinal cord trauma causes a decrease in spinal cord blood flow (SCBF) which may result in infarction. Intracellular influx of calcium has been implicated in causing ischemia and neuronal death due to post-subarachnoid hemorrhage vasospasm which shares pathophysiological similarities to post-traumatic ischemia of the spinal cord. Nimodipine, a calcium channel blocker with selective C.N.S. action, has shown promise in the treatment of vasospasm. The present study is the first where its role in modifying SCBF has been investigated.

The first part of this study showed an improvement of SCBF by 41.0 ± 7.5% in the normal rat as measured by the hydrogen clearance technique when Nimodipine was infused at 1.5 μg/kg/min. Higher doses were not as beneficial due to the large drop in systemic blood pressure (mSAP). In the second part, rats were injured with a 53 gm clip for 1 minute at the T1 spinal level and then treated with either saline, whole blood transfusion, Angiotensin or Adrenalin in an attempt to counteract the post-injury hypotension. SCBF was measured before injury and then after injury when one of the above infusions was given. Finally, Nimodipine (1.5 μg/kg/min) was added to all groups. Compared to saline, all the other groups achieved normotension but without improving SCBF. Nimodipine decreased the mSAP in all groups except the animals which also received Adrenalin, in whom there was a 24.7 ± 7.3% improvement in SCBF relative to the post-injury flow with Adrenalin alone. In the third part, rats were assigned to three randomized treatment groups (Saline, Adrenalin, Adrenalin plus Nimodipine), after injury. Normotension was maintained after injury by Adrenalin or Adrenalin plus Nimodipine, but only with the latter treatment was there a significant improvement of SCBF by 59.2 ± 15.3%, compared to the post-injury pretreatment SCBF.

Maintenance of normotension to allow for the local vasodilatory and possible cellular protective action of Nimodipine is crucial, especially in the traumatized cord unable to autoregulate. Research is underway to determine whether this improvement in post-traumatic SCBF improves neurological recovery.

. — 0065

117.

Autosomal Dominant Olivopontocerebellar Degeneration

M. D. NEWMAN, M. D. FAST and A. A. F. SIMA (Winnipeg, Manitoba)

Fourteen members of 4 generations of a family of Ukranian origin have been examined and shown to suffer from a progressive cerebellar ataxia of dominant inheritance pattern. Disability begins between the ages of 10 and 25 and is characterized by dysarthria and incoordination of the limbs but no nystagmus and no loss of proprioceptive sensation. Reflexes are lost in the upper limbs early in the clinical course, but not in the lower. There is no foot deformity. Death due to dysphagia and aspiration has occurred in 7 members of the family between 28 and 78 years and 1 affected member is alive at age 67. Autopsy was performed on 1 member who died at the age of 49 after 26 years of progressive ataxia. Neuropathological examination revealed olivopontocerebellar degeneration. In addition, there was marked degeneration of the dorsal columns and a severe sensory peripheral neuropathy. The striatonigral system was also noticeably involved with moderate loss of neurons in the pars reticularis as well as the pars compacta of the substantia nigra and a mild loss of large neurons in the putamen and globus pallidus.

The hereditary cerebellar ataxia in this family reveals an unusual combination of systems involved which underlies the wide range of variabilities in olivopontocerebellar degeneration.

. — 0066

118.

Substance P and Serotonin-Immunoreactive Nerve Terminals in Spinal Cord of Rodents with Experimental Allergic Encephalomyelitis (EAE)

D. VYAS, D. BIEGER, S. R. WHITE (St. John's, Newfoundland) (Pullman, Washington)

EAE was induced in male Lewis rats and female Hartley guinea pigs by innoculating the animals with spinal cord emulsion in complete Freund's adjuvant containing myobacterium tuberculosis (CFA). Control animals received CFA injections only. Spinal cord vibratome sections taken from control and paraplegic animals 11-17 days after innoculation were stained for serotonin (5HT)- and substance P(SP) -like immunoreactivity using the peroxidase-antiperoxidase method. Paraplegic rats showed marked changes in morphology of 5HT-immunoreactive fibres which increased in a cervico-lumbar direction. Preterminal axons appeared grossly distorted at both cervical and lumbar levels, with terminals surrounding motoneuronal somata exhibiting more and larger varicosities compared with controls. Thus, the total number of varicosities per 1000 μm^2 of lumbar ventral horn increased from 67 ± 12 (S.D.) in controls to 112 ± 16 in EAE. This change was due to an increase in large varicosities (>1.6 μm); controls: 10 ± 6; EAE: 59 ± 7. Small varicosities (dia. .8 μm) were significantly reduced in both cervical and lumbar ventral horns. The latter region again showing the greatest decrease (controls: 36 ± 9; EAE: 18 ± 6). The spinal cords of paraplegic guinea pigs manifested a striking loss of 5HT-immunoreactive axons and terminals, lumbar grey matter appearing almost completely denuded in some cases. In both species, changes in density of SP immunoreactive axon terminals were neither consistent nor marked.

In conclusion, our results suggest that in acute EAE there is extensive damage to bulbospinal 5HT neurons with relative sparing of SP neurons. The severity and extent of neuronal damage is species-dependent. The functional significance of these observations in relation to the pathophysiology of both EAE and human demyelinating disorders requires further study.

Supported by Multiple Sclerosis Society of Canada.

. — 0068

119.

Functional Hemispherectomy

J-G. VILLEMURE and T. RASMUSSEN (Montréal, Quebec)

The serious, late complication of superficial cerebral hemosiderosis which appears after several years in 25-30% of patients who have undergone hemispherectomy, has resulted in recent years in reluctance to carry out this operation despite its effectiveness in certain category of patients with seizures.

Preservation of a small portion of the hemisphere, usually the frontal or occipital pole, has proved to be effective in preventing this late complication, but at the cost of a significant reduction in the effectiveness of the operation in reducing the patient's seizure tendency. Preserving the frontal and occipital poles but disconnecting them from the rest of the brain, resulting in a functional complete but anatomical subtotal hemispherectomy, retains the therapeutic effectiveness of a complete hemispherectomy while still protecting adequately against the serious late complication of cerebral superficial hemosiderosis and its associated neurologic deterioration, hydrocephalus and sometimes death.

Sixteen (16) patients who underwent a functional hemispherectomy are presented. Fourteen (14) patients had a complete functional hemispherectomy and two (2) incomplete, in view of preserving residual visual field. The age ranged from 3 to 38 years old. The most frequent etiological factors were birth trauma, chronic encephalitis and head injury early in life. In all the cases, the occipital or frontal lobes or both were left in situ but disconnected from the brain. There was one early pressure complication of hydrocephalus treated by shunting. Seventy-five (75%) percent of patients are seizure free in follow-up. All the others had major or moderate improvement in their seizure tendency. The follow-up is one to ten years.

Functional hemispherectomy is recommended to prevent the late complication of cerebral superficial hemosiderosis seen with complete hemispherectomy.

. — 0070

120.

Differential Aspects of Sleep Epilepsy in Children

G. B. YOUNG, W. T. BLUME, G. A. WELLS. W. C. MERTENS and S. EDER (London, Ontario) (Saskatoon, Saskatchewan)

Of 265 consecutive children with epilepsy 24 (9%) had seizures exclusively in sleep (ES group) and 18 (6.8%) had seizures predominantly but not exclusively in sleep (PS group). From the remaining children with seizures mainly in wakefulness 23 were randomly chosen (W group).

The following differences were found: (1) seizure types: generalized convulsions predominated in ES and W groups and simple partial seizures predominated in the PS group ($p<.005$); (2) seizure frequency: PS patients had a higher frequency of seizures than ES and W groups ($p<.05$); (3) "Rolandic spikes" on EEG were found in 7/21 ES, 7/18 PS but in only 1/20 W patients.

We conclude that there are 2 distinct subgroups of children with sleep epilepsy, namely ES and PS patients. ES patients are more likely to have generalized convulsions while PS patients more commonly have simple partial seizures. Seizure frequency is higher in the PS patients. We also suggest that "Benign Rolandic epilepsy" is more strongly represented in ES and PS than W patients.

. — 0073

121.

C.N.S. Complications of Bacterial Endocarditis — Role of C.T. Scanning

L. CHAPMAN and J. G. D'ALTON (Ottawa, Ontario)

A retrospective study identified 71 cases of bacterial endocarditis in a University hospital during a 5 year period. C.N.S. complications occurred in 24 (33%) and several had more than one. These were classified as cerebral or retinal infarction due to embolism — 12, intracerebral hemorrhage — 4, diffuse encephalopathy — 11, acute meningitis — 4. No macroscopic brain abcesses were found.

Of those with neurological complications, 12 (50%) had a brain C.T. scan. This helped to differentiate hemorrhage from infarction or suspected brain abcess. There were 5 patients with diffuse encephalopathy who came to autopsy and all had multiple micro-infarcts and/or micro-abcesses. Only two of these had a C.T. scan, in both cases which was normal. Several patients with C.T. scan proven large infarcts, had multiple unsuspected micro-infarcts at autopsy. One patient who died because of an acute intracerebral hemorrhage due to a ruptured mycotic aneurysm, at autopsy had a previous contralateral hemorrhage which might have been diagnosed by earlier C.T., at a time when he was confused, without lateralizing signs.

It is concluded that C.T. scanning is particularly useful in diagnosing large infarcts or hemorrhage but misses many small infarcts or micro-abcesses, in patients with bacterial endocarditis.

. — 0075

122.

Pharmacological Profile of Suspected Presynaptic Dopamine Receptor Agonists

M. N. HASSAN, A. M. CRIDER, J. D. GRIMES and S. FAHN (Ottawa, Ontario) (New York, New York)

It is generally accepted that dopaminergic neurons possess receptor sites at their nerve terminals. The activation of these presynaptic receptors by dopamine or dopamine agonists inhibits tyrosine hydroxylase activity with a consequent decrease in dopamine synthesis. This mechanism explains the inhibition of locomotor activity in rodents and the improvement of schizophrenic symptoms by low doses of apomorphine. Dopamine agonists with selective presynaptic receptor activating properties are being developed. We report our early experience with two such compounds.

Male Sprague Dawley rats (150-200 g) were treated with reserpine (5mg/kg). The animals developed marked hypokinesia and catalepsy as a result of reserpine-induced catecholamine depletion. Groups ($n = 6$) of reserpinised rats were challenged with the experimental dopamine agonists (AMC 32-1 and AMC 33-1) in doses ranging from 10 to 100 mg/kg and assessed for catalepsy, stereotypy and locomotor activity. Neither the experimental compounds induced any stereotypy or produced any significant changes in catalepsy or locomotor activity over reserpinised control rats. The ability of these compounds to induce rotational activity in rats with unilateral 6-hydroxydopamine lesions of the substantia nigra and to inhibit dopamine turnover are currently being investigated. Failure to induce rotational behaviour coupled with an inhibition of dopamine turnover will indicate selective presynaptic receptor properties of these drugs.

If these additional tests confirm our present data, it can be anticipated that these compounds may have potential for the treatment of conditions in which there is hyperactivity of the dopamine system (e.g., tardive dyskinesia, schizophrenia) by a mechanism of action analagous to that of presynaptic alpha adrenergic agonists (e.g., clonidine and alpha methyldopa) in hypertension.

. — 0076

123.

Decreasing Dyskinesias with Long-Term Levodopa-Bromocriptine Therapy

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

A group of advanced Parkinson's disease (PD) patients who benefitted from Sinemet reduction and bromocriptine addition had an initial reduction in dyskinesias and then tolerated a gradual increase in levodopa to the original or higher dose without an increase in dyskinesias.

These 15 patients (PD duration 15.5 years) had taken levodopa for

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10.9 years and bromocriptine from 2 to 7 (mean 4.9) years. Initial average Sinemet daily dosage was 750 mg and this was reduced to 447 mg combined with 30 mg of bromocriptine. Over several years, daily Sinemet was increased to 753 mg and bromocriptine to 37 mg.

Dyskinesias before bromocriptine were scored at a mean of 3.4 (1-4 scale). Early in combination therapy this score reduced to 2.0 and the final mean dyskinesia score after increasing both drugs was only 2.2. Despite dosage increases, 10 of 15 patients had an increase in Parkinsonian disability. Dyskinesia severity and clinical deterioration were not related.

No clear explanation is obvious, for decreased dyskinesias despite increased drug therapy. The natural course of dyskinesias may be gradual reduction over time. Reduced striatal drug access seems an unlikely cause. The long-term use of levodopa-bromocriptine may induce striatal dopamine receptor subsensitivity, as demonstrated in laboratory studies.

. — 0078

124.

Improvement in Advanced Parkinson's Disease with Larger less Frequent Doses of Dopamine Agonists

J. D. GRIMES, M. N. HASSAN, L. W. PAYNE and P. GRAY (Ottawa, Ontario)

In the long-term follow-up of patients with end of dose failure we noted a group of patients who had developed a regime of taking Sinemet 5-8 times daily in combination with 4-7 dopamine agonist doses.

After a 2-week baseline period, 14 patients (Bromocriptine, 11: Pergolide, 3) were entered into a 13-day single-blind placebo controlled trial to assess the effects of less frequent, larger dopamine agonist doses on daily mobility. Total daily agonist doses were unchanged. While keeping Sinemet doses and times the same, the frequency of agonist administration was changed from 4-7 times daily to 2-3 daily doses.

Ten of the 14 patients had a mean 2.6 (range 0.5-5) hour reduction in off time. Dyskinesias increased in 8 patients but were subsequently reduced in 6 patients with a mean 75 mg Sinemet reduction. End of dose dystonia was improved in 6 of 8 patients. These 10 patients have continued on the larger, less frequent dose regime.

The 36% reduction in off time, the transient increase in dyskinesias and the improvement in end of dose dystonia all indicate a more prolonged central dopamine agonist effect, in keeping with the extended duration of action of these drugs in laboratory studies. These results show that the majority of levodopa-dopamine agonist treated patients are best managed with less frequent, larger dopamine agonist doses.

. — 0079

125.

Treatment of De Novo Parkinson's Disease with Bromocriptine: Long-Term Follow-Up

J. D. GRIMES, P. R. BOURQUE and M. N. HASSAN (Ottawa, Ontario)

Late treatment complications impose serious limitations on levodopa therapy. Low dose levodopa reduces the incidence of daily fluctuations and dyskinesias by about 50%. Dopamine agonists have proven useful in the management of fluctuations and dyskinesias in advanced PD and bromocriptine has been suggested as initial therapy for levodopa-naive patients.

Twenty de novo patients were treated with bromocriptine at a mean daily dose of 13.2 (maximum 30) mg. Thirteen patients (65%) were initially improved as demonstrated by a 32% reduction in the combined score for tremor, rigidity and bradykinesia. In long-term follow-up, the number of patients maintained on bromocriptine monotherapy was: 7 at 1 year, 4 at 2 years, 1 at 3 and 4 years. Five patients were changed to Sinemet alone and 6 to a combination of bromocriptine and Sinemet. One patient had a myocardial infarction and stopped all drugs. The reasons for a change in therapy were: loss of effect (7 patients) and adverse effects (5 patients). Overall, 55% of the patients developed gastric upset.

This experience has demonstrated that low dose bromocriptine alone is not an adequate replacement for levodopa in the therapy of de novo patients. The degree of initial improvement is only mild to moderate, the incidence of adverse effects is high and few patients remain on the drug long-term. Future de novo studies should use higher dopamine agonist doses that will compare in potency to levodopa (10 mg bromocriptine = 100 mg Sinemet). The high incidence of gastric upset may be reduced by concomitant use of anti-emetic agents such as domperidone.

. — 0080

126.

Brainstem and Spinal Cord Pathways Involved in the Control of Avian Locomotion

G. N. WEINSTEIN, D. WEBSTER and J. D. STEEVES (Vancouver, B.C.)

Like primates, birds have bipedal modes of locomotion. Recent studies in birds suggest that the spinal cord neural mechanisms for locomotion are only activated via brainstem-spinal projections. There does not appear to be a direct telencephalic-spinal projection, analogous to the mammalian corticospinal tract. We have therefore been interested in using birds as models for assessing the roles of brainstem-spinal motor pathways.

Selective subtotal lesions of the low thoracic spinal cord indicate that spinal cord pathways in the ventral half of the cord are essential for chronic intact hindlimb locomotion and acute decerebrate brainstem stimulated locomotion. The avian ventral cord funiculi contain reticulospinal and vestibulospinal pathways previously implicated in the descending control of mammalian locomotion.

Retrograde fluorescent tracer studies (True blue) identify brainstem neuronal cell bodies with projections to the spinal cord via the ventral funiculi. One prominent area is the gigantocellular field of the reticular formation. These brainstem-spinal neurons are found in areas which when stimulated elicit locomotion in acute decerebrate birds, thereby suggesting a descending motor control function.

The results of these studies indicate strong parallels in the neural control of locomotion between birds and mammals.

. — 0081

127.

Headache: Not Always What It Seems

R. H. WILSON (Scarborough, Ontario)

Headache is one of the commonest problems that confront a neurologist. As a result of universal health insurance patients are seen at a very early stage in the development of their condition. This places an increasing burden on the consultant to identify the potential life-threatening causes which present solely as headache.

It is the purpose of this paper to describe, by case reports, three serious conditions which strongly resemble common innocent causes of headache. These cases illustrate how specific intracranial pain sensitive structures can result in the perception of pain in a region remote from the pathology.

The discussion will consist of the clinical features and the mechanism of referred pain of: a cervical syrinx producing unilateral frontal pain, a vertex headache caused by cerebellar tumor, and marked posterior neck pain with unilateral limitation of lateral neck flexion due to a cerebellar tumor. These patients were referred for neurological assessment with the diagnoses of: sinusitis, muscle tension headache, and cervical disc degeneration respectively.

Despite the fact that most headaches have an innocent cause, it is essential to analyse each headache with care because it may not always be what it seems.

. — 0082

128.

Spinal Myoclonus: A Rare Presentation of a Spinal Cord Tumor

R. H. WILSON (Scarborough, Ontario)

Myoclonus that is symptomatic of a disease is mainly associated with a cerebral disturbance. Spinal myoclonus, regardless of its cause, is a rare condition and is normally described as being rhythmic.

This paper will describe a case of a lipoma at the thoracolumbar junction that presented solely with extreme sporadic arrythmic nocturnal myoclonus. During the day the patient's legs functioned normally and felt normal. Minor physical findings were present which suggested a spinal cord disturbance. A CAT scan and myelogram indicated a spinal cord tumor at the thoracolumbar junction. Despite a laminectomy and partial removal of the lipoma, the myoclonic jerks persisted. Depakane produced a dramatic reduction of the myoclonus.

Spinal myoclonus will be reviewed and its management will be discussed.

. — 0083

129.

Seizures in Cerebral Tumors: A Reappraisal

M. B. M. SUNDARAM and J. VARUGHESE (Saskatoon, Saskatchewan)

347 consecutive cases of supratentorial tumors (primary — 164, metastatic — 183) in patients over 16 years, seen in our hospital over a period of 80 months were analysed for seizures. The diagnosis was based on one or more of the following: CT scan, radionuclide scan, biopsy and autopsy. Overall seizure incidence was 31% (N:112). Mean age for these patients was 56 years (range — 17 to 80). For primary brain tumors, seizure incidence was 42% (N:69); this was 23% for metastatic tumors (N:42).

Seizure was the initial presenting symptom in 61 of 69 patients with primary tumors associated with seizures. In 31 of these, neurologic examination, when first seen for seizures, was normal. CT scan was available in 64 of 69 patients; in 5, initial scan was normal but subsequently became abnormal during the next 6-12 months. 52 patients in this group had EEG when first seen for seizures; of these, 16 (31%) had normal recording initially. In 10, the EEG became abnormal during the next 6-24 months.

In patients with primary tumors, seizure incidence was highest in those with frontal tumors (35 of 68 patients; 51%), closely followed by temporal tumors (22 of 45; 49%). 4 of 14 patients with occipital tumors (28%) and 5 of 22 with parietal tumors (22%) had seizures. Grade I and II astrocytoma were more likely to produce seizures (27 of 36 patients; 75%) than Grade III and IV astrocytoma (32 of 109; 29%). Seizures occurred in 3 of 8 patients with meningioma (37%). All 3 patients with oligodendoglioma suffered seizures.

42 of 183 patients with metastatic supratentorial tumors had seizures (23%); in only 4 of these patients, seizures began prior to the diagnosis of primary cancer.

This study confirms the clinical impression that in adults presenting with seizures, initial normal neurological examination and EEG do not exclude primary brain tumors. CT scan in such patients remains the most useful investigation and may have to be repeated. Seizure incidence is higher in primary brain tumors that metastases. Benign astrocytomas are more often associated with seizures than malignant astrocytomas.

. — 0084

130.

Seizures in Spontaneous Subarachnoid Hemorrhage

M. B. M. SUNDARAM and F. CHOW (Saskatoon, Saskatchewan)

133 consecutive cases of non-traumatic subarachnoid hemorrhage seen in our hospital over 67 months, were retrospectively analysed for seizures; care was taken to exclude those with decerebrate attacks. 33 patients (24.8%) suffered one or more seizures (Aneurysms — 29, others — 4); there were 16 males and 17 females with mean age of 48.8 years. Seizures were generalized in 17 and partial in 16. Motor manifestations of partial seizures were ipsilateral to aneurysm in 6 patients, contralateral in 8, both ipsilateral and contralateral in 1 (in one patient, bleeding source was unknown). Seizures were multiple in 22 and single in 11 patients.

26 patients suffered early seizures (within 2 weeks of hemorrhage) — 18 of these first seizure occurring within 24 hours. 9 died within 2 weeks. Among 15 survivors, only 2 had seizure recurrence beyond 1 month. Delayed seizures (for the first time after 2 weeks) occurred in 5 of 33 patients, and were infrequent during the follow-up period. In 2 patients, chronic recurrent seizures preceded hemorrhage.

Aneurysms at all supratentorial locations were seen among seizure patients. Intracerebral hematoma and infarction were seen more often in the seizure group (42.4% and 24.2%) than the non-seizure group (30% and 15%); mortality rates, however, were similar in both groups.

These findings suggest that i) seizures in spontaneous subarachnoid hemorrhage occur most often within 24 hours of bleeding; ii) type of seizure is of no localizing or lateralizing value as to aneurysm site; iii) routine prophylactic anticonvulsants could be withheld because of low long-term seizure recurrence rate; iv) seizures in spontaneous subarachnoid hemorrhage do not affect mortality rates.

. — 0085

131.

Unilateral Ischemic Optic Neuropathy Following Prolonged Systemic Hypotension

M. B. M. SUNDARAM, D. AVRAM and A. CZIFFER (Saskatoon, Saskatchewan)

Neurological complications of prolonged systemic hypotension are well recognized and include varying degrees of coma, watershed infarcts and seizures. Ischemic optic neuropathy (ION) in this setting is rare but has been known to occur following blood loss (Chisholm, 1969) and cardiac by-pass surgery (Sweeney et al., 1982). We report the occurrence of unilateral ION following cardiopulmonary arrest and prolonged hypotension in a 36 year old female patient. She had a cardiopulmonary arrest while recovering from multiple fractures suffered one month earlier. Cardiac rhythm was restored in ½ minute but systolic BP remained below 80 mm for 20 minutes. On regaining full consciousness, about 48 hours later, she was blind on the right with afferent pupillary defect. Acuity on the left was 20/20. Right optic atrophy became apparent 2 weeks later. An ophthalmologist detected no other ocular disease including glaucoma. CT scan of the orbits and brain was normal. There was no functional improvement on follow-up at 4 months.

Unilateral ION with relative preservation of cerebral function can occur as a result of cardiopulmonary arrest and prolonged hypotension. Prognosis for recovery, based on the reported cases, appears variable. Mechanisms of visual dysfunction (Hayreh, 1974) include a) poor perfusion in posterior ciliary arteries b) occlusion by microemboli.

. — 0086

132.

Thyroxine Induced Petit-Mal Status Epilepticus

M. B. M. SUNDARAM, A. N. HILL and N. LOWRY (Saskatoon, Saskatchewan)

Thyroxine reduces the seizure threshold in experimental animals (Timiras and Woodbury, 1956, Seyfried et al., 1979) and produces high amplitude photic response in healthy volunteers (Wilson et al., 1964). In addition, seizures may occur in thyrotoxicosis (Jabbari and Huott, 1980). We report the occurrence of petit-mal status epilepticus (PSE) in a mentally retarded female shortly after starting on high doses of thyroxine.

The patient was a 17 year old female without previous seizures. She was found to be hypothyroid and started on thyroxine (0.15 mg. b.i.d.).

One week later, she began to have episodes of unresponsiveness, staring, unsteadiness associated with blinking and eyelid twitching (frequently brought on by eye closure) and low amplitude myoclonic movements of the toes. These lasted from 3 to 8½ hours. The EEG during one such episode revealed nearly continuous bisynchronous spike-wave discharges which were prominent in the occipital regions. The clinical seizures and spike-wave discharges were abolished by intravenous Diazepam and subsequently by Valproic acid. Serum thyroxine level at this time was 164 nmol/L (N:54-154). The patient has remained seizure-free since discontinuation of thyroxine.

These observations suggest that thyroxine may reduce seizure threshold in humans and may precipitate PSE. This might have implications in experimental models for epilepsy. Occipitally predominant bisynchronous spike-wave discharges should be included among the various electroencephalographic patterns of PSE.

. — 0087

133.

Cardiogenic Seizures in Congenital Prolonged QT Syndromes

M. B. M. SUNDARAM, S. GULAMHUSSEIN and J. D. McMEEKIN (Saskatoon, Saskatchewan)

Romano-ward syndrome (RWS) and Gervell-Lang-Nielson syndrome (GLN, variant of RWS associated with deafness) are hereditary disorders characterized by congenital prolongation of QT intervel. Clinical features include syncope, cardiogenic seizures and sudden death due to paroxysmal ventricular dysrhythmias. Cardiogenic seizures are sometimes the presenting symptom and hence recognition of these syndromes by neurologists is important for appropriate management. We present indexed patients from two families — one with RWS and the other with GLN.

The patient with RWS, 33 year old female, presented following 3 blackouts characterized by stiffness, jerking of limbs, cyanosis and incontinence. Her 12 year old daughter had had 2 seizures. The patient's 3 brothers also had suffered chronic recurrent blackouts associated with stiffening, tongue biting, cyanosis and incontinence and all died during apparent seizure. Neurologic examination, EEG and CT scan of the patient were normal. Electrocardiogram showed QT interval of 460 msec with regular heart rate of 78/minute (normal corrected QT for this heart rate is 350 msec). Her daughter and mother were also shown to have prolonged QT. The patient remains seizure-free on propranolol.

The patient with GLN is a 17 year old congenitally deaf female with recurrent blackouts characterized by generalized stiffening, cyanosis and at times incontinence. Most of the attacks were precipitated by emotional stress. Neurologic examination was normal. Her QT was prolonged and ranged from 520 to 720 msec. She is being treated with beta blockers.

We emphasize awareness of RWS and GLN when dealing with seizure patients with positive family history of seizures and sudden death; routine ECG monitoring is important in such patients, with special attention to QT; treatment is usually with beta blockers.

. — 0088

134.

Significance of Cerebral Edema on CT Scan in Prediction of Invasion of Brain by Meningiomas

M. DELGADO, B. LACH and G. BELANGER (Ottawa, Ontario)

In order to correlate histological and CT scan features of meningiomas with occurrence of brain edema, 40 supratentorial tumors were reviewed by a radiologist and neuropathologist, and analyzed by an independent observer. The tumor size and shape, location, cellularity, vascularity, mitotic activity, nuclear atypia, presence or absence of necrosis, calcifications, and presence or absence of brain tissue in the specimen were assessed in every case. The sensitivity of the detection of the brain invasion in surgical tissue material was enhanced by use of immunohistochemical method for glial fibrillary acidic protein.

Sixteen patients (40%) showed significant edema on CT scan; 56% of these had proven cerebral invasion, 37.5% did not have brain in the surgical specimen, and only one (6.25%) had brain without histological evidence of infiltration. The edema was present in 82% (9/11) of the cases with proven brain infiltration; all with tumors larger than 4 cm. There was no significant correlation between the histological type, size alone, vascularity or necrosis of tumor and development of edema.

It is concluded that the occurrence of edema around meningiomas has a high degree of sensitivity and specificity in radiological diagnosis of infiltration of the brain, and prediction of potentially malignant behaviour of these tumors.

. — 0089

135.

Wernicke's Encephalopathy Complicating Malignancy — A Report of 2 Cases

M. LEVITAN and J. BRUNI (Toronto, Ontario)

Although the relationship between severe nutritional deficiency and the development of Wernicke's encephalopathy (WE) is well established, antemortem diagnosis of this treatable disorder is easily missed unless clinical suspicion is raised in appropriate clinical circumstances. We report 2 non-alcoholic patients in whom WE developed in association with complications of malignancy. The first patient was a 49 year old female who following AML chemotherapy developed anorexia, sepsis, and multi-organ failure. She became obtunded, dysarthric, and developed pan-directional nystagmus and diffuse tremor. CT scan, CSF, and EEG were non-diagnostic. At autopsy classical features of WE were found. The second patient was a 61 year old female who following a hemicolectomy for adenocarcinoma suffered nausea, vomiting, and renal failure. She developed agitated delirium, bilateral VIth nerve palsies, and horizontal and vertical nystagmus before succumbing after two weeks in coma. CT, EEG, and CSF examinations were non-diagnostic, and autopsy revealed WE. Gross and microscopic neuropathological findings will be presented along with a literature review of WE in the non-alcoholic.

. — 0090

136.

Effects of Taurine Depletion on the Rat Electroretinogram

S. COCKER and N. LAKE (Montreal, Quebec)

Although the function of taurine in the CNS remains unclear, decreased electroretinogram (ERG) responses have been described in several mammalian species when tissue taurine levels are unusually low. In the present experiments ERG responses to flash stimuli were measured using a wide range of intensities in Sprague Dawley rats before and during chronic administration of 1% Guanidinoethyl Sulfonate (GES). GES is a taurine analogue previously shown to decrease retinal taurine *in vivo* by antagonism of its transport into the eye. After 28 days of treatment, the ERG's showed a significant decrease in a and b wave amplitude, and sensitivity, to about 2/3 of the untreated response values, with no change in peak latencies. In order to examine whether this effect involves a light-dependent process, a similar experiment was done rearing rats in total darkness (after the initial recordings). A detailed analysis revealed significant decreases in ERG amplitude in control and treated animals after one week in the dark but changes between the groups remained minimal up to 10 weeks. There was a tendency for treated animals to have smaller a and b wave amplitudes with longer latencies after 8 to 10 weeks. These experiments describe parameters of the ERG which are suitable for obtaining an index of the visual function of chronic animals and indicate that the light regime may be important in modifying the retinal consequences of taurine depletion. Indirectly they suggest that taurine may have a role in protecting against light damage.

. — 0093

137.

Intracranial Mucoceles and Basal-skull Osteomas

M. SEGUIN, G. MOHR, S. N. MARTINEZ and N. B. GAGNON (Montreal, Quebec)

Osteomas of the anterior skull-base may lead to the formation of intracranial mucoceles when the sinus mucosa is pushed intracranially: the sequestrated mucosa keeps on secreting and destroys progressively the dural investment. Two cases are presented in which osteomas were associated with significant intracerebral mucoceles.

The first case manifested itself acutely as a spontaneous rhinorhea followed by a severe headache. The radiological work-up showed an intracranial pneumatocele associated with a frontal sinus osteoma: first, a bifrontal craniotomy allowed removal of an intracerebral mucocele within the frontal pole. Retrospectively, it was concluded that the spontaneous emptying of the mucocele was followed by aspiration of air under pressure leading to an invaginated pneumo-mucocele. The osteoma was removed successfully by fronto-ethmoïdal sinusectomy a few months later.

In the second case, a giant spheno-ethmoïdal osteoma was revealed during work-up for recurrent sinusitis: the CT-Scan showed a totally silent, ring-enhanced right frontal mass. In order to rule out an abscess, a needle biopsy via frontal burr-hole revealed greenish mucus from which culture remained negative. The intracerebral mucocele was removed by right frontal craniotomy and the patient was discharged in good condition after prophylactic antibiotic treatment. He was readmitted 4 weeks later in acute meningitis and left frontal cerebritis which was rapidly controlled by antibiotics: the osteoma was removed 6 weeks later using extensive reconstruction of the anterior base with bone graft and duroplasty without complications.

In both instances, osteomas originating from sinuses were followed by erosion of the dura and intracerebral mucosal sequestration. It is concluded that in presence of significant osteomas of the anterior skull-base, the diagnosis of intracranial mucoceles should be kept in mind even in neurologically asymptomatic patients.

. — 0095

138.

Craniofacial Dysostoses — Effect of Neonatal craniectomies on the re-shaping of the Skull Vault and Base during Growth to Skeletal Maturity

J. E. BLUNDELL (Montreal, Quebec)

In the infant with severe craniofacial dysostoses, early craniectomies of the vault and base allow the growing brain to re-align the whole skull.

Ideally, operation is performed as soon as possible after the neonate has regained his birth weight. At this age, the infant supports the operation remarkably well, and intervention at this early age allows optimal remolding of the skull at the period of most rapid post-natal brain growth.

The steep rise of the floor of the middle and anterior fossae seen in the infant producing a basilar angulation approximating to 180° is replaced by the age of 12-15 years by a normal basilar angle of 140° or less without any second operation.

The change in contour is cosmetically desirable. The change in intracranial volume is essential for normal cerebral development. These changes are amply illustrated in the poster presentation submitted.

. — 0096

139.

Fatal Head Injuries in Children

L. P. IVAN, K. B. MALLYA and H. N. K. BABUR (Ottawa, Ontario)

Fifty-five children suffered fatal head injury from 4,400 children admitted to the Children's Hospital of Eastern Ontario between 1974 and 1984. Of the 55 patients, 15, or 27.3%, were dead on arrival and 40, or 72.7%, were admitted and died in the Intensive Care Unit. The 55 patients represent (D.O.A. included) a 29.7% of mortality of severe head injuries.

Of the 55 fatal injuries, 35 (63.4%) children were struck by a motor vehicle and 7 (12.7%) were hit by a car while riding a bicycle. An additional 8 children were passengers or drivers of a motor vehicle which brings the total of motor vehicle related accidents in our material to 90.9%.

Potentially serious systemic insults to the brain were present in 65% of the patients who were transferred from another hospital and 15% developed systemic insults during transit. In 12.5% of the patients, systemic insults developed in our own emergency facility before neurosurgical consultation.

From this material we conclude:

(i) that motor vehicle accidents are the commonest cause of fatal head injuries in children;
(ii) that systemic factors play a major role in causing fatal outcome; and
(iii) fatal head injuries in children can further be reduced by preventive measures and earlier application of systemic resuscitation and brain oriented life support.

. — 0097

140.

Trigeminal Neuralgia (TN) Secondary to Dental Causes

A. S. GORDON and D. MOCK (Toronto, Ontario)

Trigeminal neuralgia (TN) manifests itself as dental or mouth pain leading to unnecessary dental procedures until the etiology of the pain is elucidated. We would like to report three patients in whom dental trauma, dental disease or dental procedures led to a clinical syndrome indistinguishable from TN.

The first such patient is a 12 year old boy who developed tic like pain in his upper central incisors after suffering trauma to these teeth severe enough to require dental reimplantation and endodontic procedures. He responded dramatically to Tegretol and after a year and a half his pain went away. The second patient is a 30 year old man who bit down hard on a cherry pit and developed severe right lower quadrant mouth pain. He developed trigeminal neuralgia pain on the right side which did not respond to dental treatment including endodontics and which also cleared after one year. The third patient is an 86 year old woman who was asymptomatic in the left lower quadrant of her mouth until a restorative procedure was carried out on the left lower bicuspid. She immediately developed a TN pain which was treated by dental means without improvement and then responded dramatically to Tegretol.

These three previously asymptomatic patients developed a TN syndrome after a dental process. The mechanism of this pain is uncertain but it may represent increased central excitability secondary to dental pulp or nerve injury.

. — 0098

141.

A Previously Unrecognized Papillary Endolymphatic Sac Tumor Presenting as a Cerebellopontine Angle Lesion

A. D. MacDOUGALL, V. E. SANGALANG and S. HUESTIS (Halifax, Nova Scotia)

A 36 year old man presented with symptoms of headache, vertigo and unilateral deafness, and demonstrated radiologic evidence of a left cerebellopontine angle lesion. Posterior fossa craniotomy revealed a vascular epidural mass eroding the petrous portion of the temporal bone and the posterior wall of the internal auditory meatus, thereby compressing cranial nerves VII and VIII. Medially, the mass indented both the brain stem and cranial nerve V. Comparative morphological and immunohistochemical studies of the tumor and normal human endolymphatic sac epithelium established the precise origin of the neoplasm. Similar comparative studies of a papillary thyroid carcinoma and choroid plexus papilloma ruled out a metastatic lesion.

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Furthermore, the lesion was found to be histologically identical to a small papillary adenoma confined to the endolymphatic sac as recently reported by Hassard et al. The significance of considering this tumor in the differential diagnosis of cerebellopontine angle lesions, as well as recognizing it as distinct from middle ear adenomas and papillary meningiomas, is discussed.

. — 0099

142.

Amyotrophic Lateral Sclerosis in Nova Scotia

T. J. MURRAY, J. CAMERON, L. P. HEFFERNAN, D. B. KING, H. N. A. MacDONALD, A. SHEARS, S. BEDWELL, M. SCOTT, J. PATIL and H. MALIK (Halifax, Nova Scotia)

A study of ALS in Nova Scotia between 1975 and 1984 was contrasted with a previous study of 1964-1974. (TJ Murray, S Pride, G Haley. CMAJ 1974. 110:815-817). A retrospective study of ten years was completed and a prospective monthly assessment through 1984 from all available records in hospitals, laboratories, and from all neurologists, neurosurgeons and physiatrists in Nova Scotia.

In the decade 1964-1974 the incidence of ALS was 0.73 cases per one hundred thousand with an increase to 1.92 per one hundred thousand in 1974-1984. The increase appears genuine as there was a progressive increase of 1.2 in 1975 to 2.0 in 1984, with the peak at 2.6 in 1982. The ratio of males to females was consistent at 1.72:1.

Recent epidemiological studies have been carried out in Iceland (0.8); Sardinia (0.6); Mexico City (0.4); Israel (0.75); NW Switzerland (1.4); England and Wales (1.6); and Rochester Minn (1.8). Of the studies that showed an increasing incidence of ALS were Rochester, England and Wales, and Israel.

Nova Scotia has a high and increasing incidence of ALS.

. — 0100

143.

Long Term Treatment of Fatigue in Multiple Sclerosis

T. J. MURRAY (Halifax, Nova Scotia)

We previously reported a controlled study of amantadine hydrochloride in the treatment of excessive fatigue in M.S. In that first study, on 200 mg per day, 31% of the subject patients reported marked improvement; 15.6% moderate; 15.6% mild and 36.5% no improvement. Overall 62.5% improved on amantadine compared to 21.8% mild responses on placebo.

In the present study 95 patients were followed for up to two years (average 8 months). Using a self-grading system monthly, the results long term were 14.7% marked improvement; 18.9% moderate and 20% mild improvement. 7% continued the drug despite no improvement and 29.5% discontinued the drug.

Of those discontinuing amantadine 14 did so because of side effects, six for lack of improvement, and eight for miscellaneous reasons including costs. All patients had some side effects notably insomnia (21%), hyperactivity (7%), dry mouth (17%) and constipation (11.5%).

Also, 54% of the patients continued to have some long term improvement in fatigue with amantadine. All experienced some side effects.

We will discuss the attempt to better define and categorize fatigue in MS and some objective measures that may be employed in the future. A Canadian Cooperative Trial is planned through the MS Research Clinics.

. — 0101

144.

Phosphofructokinase in Alzheimer's Disease

P. H. ST GEORGE-HYSLOP and D. R. CRAPPER-McLACHLAN (Arlington, Massachusetts) (Toronto, Ontario)

Patients with Down's Syndrome (trisomy of q21 - q22 segments of chromosome 21) have a greater than 90% incidence of Alzheimer's Disease (AD) after 40 yrs of age. Relatives of patients with AD have increased incidences of both AD and of Down's. In vivo PET studies show reduced rates of glycolysis in AD cortex. The L-type isoenzyme of Phosphofructokinase (PFK), which is the rate controlling enzyme of glycolysis, is encoded on the q22 segment of chromosome 21. It is possible that acquired or inherited abnormalities in chromosome 21 or its products may underlie AD. We measured PFK activities in temporal cortex from 9 patients with AD and 2 patients with Down's plus AD who were matched to normal and to non-AD dementia controls for 3 parameters known to affect PFK activity in post-mortem cerebral cortex. We found a significant decrease in PFK in AD and in Down's plus AD compared to both control groups ($p < 0.001$). This reduction in PFK in AD and in Down's plus AD was present in all but 1 case of AD, suggesting that reduced glycolysis and PFK activity is not a necessary condition for the occurrence of AD. Michaelis-Menten constants (Km) of PFK for fructose-6-phosphate and for ATP were not different in the various groups, arguing against acquired or inherited modification of the PFK gene and against post-translational modification of the PFK protein. We conclude that the reduction in glycolysis and in PFK activity in AD cortex is a secondary event, most probably reflecting loss of metabolically active neurons or synaptic terminals.

. — 0102

145.

Co-existence of Idiopathic Parkinson's Disease (IPD) and Creutzfeldt-Jakob Disease (CJD): A Case Report

C. EZRIN-WATERS, L. RESCH and A. E. LANG (Toronto, Ontario)

A 68 year old female presented with slowly progressive akinesia, shuffling of gait and resting tremor which responded to Sinemet and Artane. She remained improved for two and a half years but then developed confusion and visual hallucinations. Drug withdrawal aggravated her parkinsonism but failed to improve the psychiatric disturbances. Subsequently she deteriorated rapidly developing cortical blindness, spasticity and startle myoclonus with periodic complexes on EEG. She died six months after the onset of her confusional symptoms.

Autopsy revealed a slightly atrophic brain with a thinned cortical ribbon. Histological examination revealed varying degrees of neuronal loss, spongiosis, and gliosis throughout the cerebral and cerebellar cortex and lenticular nuclei. The substantia nigra and locus ceruleus showed neuronal loss, gliosis, loss of pigment and Lewy body inclusions in some remaining neurons.

To our knowledge, this is the first reported case of associated IPD and CJD. To date there is no evidence that these two disorders are etiologically related. Unlike CJD, transmission studies using brain tissue from IPD patients have not resulted in neurological disease in animal recipients. Although the occurrence of the two separate diseases in our patient is likely no more than coincidence, planned transmission studies may provide further insight into this unusual association.

. — 0103

146.

Spontaneous Dissection of the Cervicocephalic Carotid Artery

P. W. COOPER, R. A. WILLINSKY, M. GAWEL, D. ROWED and E. E. KASSEL (Toronto, Ontario)

Spontaneous dissection of the carotid artery should be considered in the investigation of younger patients presenting with cerebral ischemic symptoms. Three patients under age 50 had cerebral angiography showing dissections of the cervical carotid artery with narrowing. In one case there was an aneurysm of the cervical carotid and in another an aneurysm of the petrous carotid.

In addition to headache which was present in all three cases, presenting symptoms were; in case 1 — expressive dysphasia, right hemiplegia and numbness, in case 2 — visual blurring, expressive and receptive dysphasia and right hand weakness, and in case 3 — visual blurring and slight numbness and weakness of the left forearm. In case 1, symptoms recurred 2 months later and EC-IC bypass was performed after the

carotid was found to be occluded. In case 2, right-sided paralysis and dysphasia recurred 1 month later. In case 3, transient symptoms of indistinct right vision and left hand weakness recurred. Repeat angio in the third case 2 years later showed the narrowing and the petrous aneurysm to be gone. Features suggestive of fibrous dysplasia were seen in one case. In two patients despite easy catheterization, intimal dissections of a carotid and a vertebral artery occurred at the site of the catheter tip following injection at angiography. Comparison of clinical and radiographic findings in these three cases are made with cases described in the literature.

. — 0105

147.

Positron Emission Tomography Scanning in Frontal Lobe Epilepsy

S. J. PURVES, W. AMMANN, J. A. WADA, W. B. WOODHURST, D. LI, W. MARTIN and B. PATE (Vancouver, B.C.)

FDG Positron Emission Tomography (PET) Scans have been used to demonstrate areas of focal metabolic change which correlate with the focal origin of seizures in patients studied as temporal lobectomy candidates. Focal changes with PET have not yet been demonstrated for seizures originating from extra temporal sites.

Three patients with frontal lobe seizures demonstrated with simultaneous video and EEG recordings have had FDG PET Scans before, and eight weeks after anterior corpus callosum bisection. Magnetic Resonance Imaging (MRI) Scanning has also been used to demonstrate the extent of the surgical lesions. All three have had some reduction in seizure frequency and severity post-operatively.

A preliminary visual analysis of these PET Scans has not demonstrated any frontal, focal metabolic change as obvious as those previously reported for temporal lobe seizures. A quantitative analysis of the metabolic PET data is in process, including comparisons of pre- and post-op scans to determine if this powerful technique will provide any localizing information for frontal lobe seizures. Metabolic changes after corpus callosum section are also being studied. The applications and limitations of these imaging methods for frontal lobe epilepsy will be discussed.

. — 0106

148.

Inventaire des Problèmes Vécus par 138 Patients par Rapport à Leur Epilepsie

G. M. REMILLARD, L. LE BOURHIS and C. MURPHY (Montréal, Québec)

On a interrogé 146 épileptiques dont 97 sont suivis dans une clinique générale de neurologie et 49 dans une clinique d'épilepsie, on a pu analyser les données chez 138 candidats. Seulement 12 (9%) n'avaient rencontré aucune difficulté. Les autres ont identifié les problèmes suivants: incompréhension, attitude de rejet, marginalisation (41), solitude, isolement, ennui, inactivité (34), effets indésirables des médicaments (29), surprotection (24), impossibilité de conduire un véhicule (21), recherche d'emploi sans succès (18), difficulté d'adaptation à la médication quotidienne, la privation d'alcool et le régime fixe d'heures de sommeil (13), refus, négation, révolte lors du diagnostic (12), réaction de peur suscitée chez les gens (10), sentiments de dépendance, insécurité (10), troubles financiers (10).

Trente-cinq patients (26%) n'étaient pas fonctionnels même si les crises étaient contrôlées chez 22 d'entre eux. Les mentions de solitude, inactivité, effets indésirables des médicaments, l'impossibilité de conduire, la recherche d'emploi sans succès et les troubles financiers étaient moins fréquentes si les crises étaient contrôlées mais, par ailleurs, l'énumération des problèmes demeurait la même. Les crises en soi ne constituent pas le handicap principal de l'épileptique.

. — 0109

149.

High Plasma Arginine-Vasopressin (AVP) Levels in a Patient with Carbamazepine Induced Hyponatremia

N. DANEAULT, D. BICHET and G. RÉMILLARD (Montréal, Québec)

Carbamazepine has been reported to lower plasma sodium at times sufficient to produce symptomatic water intoxication. Direct stimulation of AVP release has been suggested but a recent report failed to demonstrate this abnormality in a series of manic depressive patients treated with this drug. A 73 year old patient had repeated episodes of hyponatremia upon administration of carbamazepine for trigeminal neuralgia. His renal function, thirst and anterior pituitary function were normal and he was taking no other medication that could have induced an antidiuretic state. His urinary sodium was >40 mEq/l. Plasma sodium after water restriction was 130 mEq/l with a urinary osmolality of 450 mOsm/kg H_2O. His minimal Uosm during a waterload test was 320 mOsm/kg H_2O. During waterload and hypertonic saline infusions (3% saline at 0.1 ml/kg/min) his AVP (radioimmunoassay, B/Bo = 50% for 1.2 pg/ml) randomly varied independently of plasma sodium from 0.5 to 24.7 pg/ml suggesting type I syndrom of inappropriate antidiuretic hormone secretion. During the same procedure, 19 normal volunteers increased their plasma AVP according to the linear relationship: (Pavp = .23 [PNa - 135.6], n = 163, r = 0.54, $p < .001$). We conclude that inappropriate stimulation of AVP release could be associated with carbamazepine therapy and could induce hyponatremia.

. — 0110

150.

Post Vaccinal Poliomyelitis, A Case Report

N. DANEAULT, G. ALBERT, Y. GIROUARD, G. RÉMILLARD and J. FURESZ (Montréal, Québec) (Ottawa, Ontario)

A 25 year old patient complained of fatigue, sore throat and fever followed by headache on July 24, 1984. On examination he had a stiff neck and overwhelming lumbar myalgia and his temperature was 38.5°C. Lumbar puncture was compatible with viral meningitis but 24 hours after admission he experienced weakness in left leg. Progressively within 3 days his paresis involved both upper limbs asymmetrically and mostly proximally. Clinical and laboratory data were compatible with involvement of spinal motor neurones. The patient claimed that he received Salk vaccine during childhood. Forty-six days before onset of symptoms his two month old son has had his first dose of DPT vaccine along with Sabin vaccine.

Electron microscope examination of stools showed Picornavirus particles, and viral culture grew Poliovirus serotype I. Temperature marker test, intratypic (McBride) and neutralization (Van Wezel) tests were performed by the Bureau of Biologics, Health and Welfare Canada in Ottawa. Results of these tests showed that the isolated Poliovirus had Sabin-like characteristics. Viral culture of the CSF was negative. Neutralization tests performed on the sera collected 16, 23 and 87 days after the onset of disease showed no detectable antibodies to type III Poliovirus, no change in antibody titer (1/156) to type II Poliovirus, and a fourfold increase in antibody titer (1/150 in the first serum to 1/600 in the third serum) to type I Poliovirus isolated from the patient.

The clinical, epidemiological and virological data strongly suggest that type I Sabin vaccine was implicated in the development of paralytic poliomyelitis of this household contact case. The incidence of this vaccine complication and the strategy for vaccination of contacts are discussed.

. — 0111

151.

Lymphocytic Thyroiditis: A Major Cause of 'Idiopathic' Vertigo

W. J. VANAST (Edmonton, Alberta)

In the course of an investigation into the association of thyroiditis and chronic benign headaches, serum thyroid antibodies were mea-

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sured in 168 consecutive nonheadache female office patients, of which 25 presented with vertigo. Of the 23 whose vertigo was unexplained, 6 had thyroid microsomal antibodies at 1:1600, 1 at 1:6400 and 2 at 1:25,600. Only one of these had significant changes in T3, T4 or TSH. this thyroiditis incidence of 39% contrasts with that of 6.3% in 143 nonvertigo, nonheadache women. Of the 15 vertigo women under age 45, 7 had thyroiditis (47%) while only 4 of 87 nonheadache, nonvertigo women in this age group had thyroiditis (5%). In the age group 36 - 45, the incidence of thyroiditis in women with unexplained vertigo was 60% (6 of 10 patients).

These results provide evidence that 'idiopathic' vertigo is a neurologic complication of thyroiditis in young women and suggest that thyroid antibodies may attack nonthyroid tissue.

. — 0113

152.

The Role of Autoimmune Thyroid Disease in Chronic Benign Headache

W. J. VANAST (Edmonton, Alberta)

Because of failure of therapy in many patients with chronic headaches, we searched for alternatives to tension theories. In pilot studies, FANA, rheumatoid factor, ESR, IGA, IGE, protein electrophoresis and thyroid antibodies were measured in considerable numbers of headache patients. Only the thyroid microsomal antibody levels were frequently abnormal. A prospective study on 575 consecutive nonvertigo* female office neurology patients showed serum thyroid microsomal antibody at 1:1600 or above in 76 of 432 headache women (17.6%) compared to 9 of 143 nonheadache women (6.2%). Under age 45 this occurred in 60 of 284 headache women (17%) and in 4 of 87 nonheadache women (4.6%). This fourfold increase in thyroiditis (often in the absence of T3, T4, or TSH changes) points to an autoimmune trigger in some forms of chronic benign headache in young women. This may lead to new research and treatment strategies in a disorder that has defied explanation.

*Vertigo patients excluded because they also have a very high incidence of thyroiditis (reported by us elsewhere).

. — 0114

153.

Predicting the Course of Multiple Sclerosis (MS): Factors Which May Be Associated with Disability

S. WARREN, M. PATERSON and I. PATTERSON (Edmonton, Alberta)

Some MS patients experience a benign form of the disease, while others experience a course which results in increasing disability. 48 probable or definite MS patients who were still ambulatory ten years after diagnosis were compared to 45 patients using canes/wheelchairs, on several factors which might influence course. These included pre-onset age infectious disease history, characteristics of initial attack, lifestyle factors/experience from onset onward, and possible susceptibility. There was no difference between non-disabled and disabled patients on mean number of infections experienced pre-onset age; and, although disabled patients tended to report experiencing some typical infections at a later age (mumps, chicken pox), there was no overall trend. As for initial attack, there was no difference between the two groups on season of onset; but two other factors, highly intercorrelated with sex, were associated with a benign course: under 20 onset was more common among women and associated with a benign course; when first symptoms were visual (more common among women), course tended to be benign. No post-onset lifestyle factors/experiences (including diet, vitamin, alcohol and tobacco use, physical activity or emotional stress, urban/rural residence, SES, and other illnesses) were associated with disability. However, non-disabled patients were more likely to be female, and to report a family history of diabetes; again a diabetes family history was protective among women only. A greater proportion of non-disabled than disabled patients reported North European as opposed to British ancestry, but the difference was not quite significant. Finally, disability tended to increase with age.

. — 0115

154.

Acetylcholine Synthesis by Adult Adrenal Chromaffin Cell Cultures

P. BOKSA (Verdun, Quebec)

Adrenal chromaffin cells normally synthesize and release catecholamines. Recently, however, electrophysiological studies have shown that neonatal rat adrenal chromaffin cells can form functional cholinergic synapses with each other in culture[1], suggesting that these cells can synthesize acetylcholine (ACh). In the present study, I have shown that monolayer cultures of adult bovine adrenal chromaffin cells can take up ^{3}H-choline from the extracellular medium and synthesize ^{3}H-ACh. On incubation with 10 μM ^{3}H-choline for 1 h, day 6 cultures synthesized about 4 pmol ^{3}H-ACh/mg protein. The rate of ^{3}H-ACh synthesis was constant in cells maintained in culture from 6 to 15 days and increased from day 19 up to day 28, such that ^{3}H-ACh synthesis in day 28 cultures was 2.4 times that in day 6 cultures. Depolarization of the cells with 60 mM K^+ increased the subsequent synthesis of ^{3}H-ACh. However the ability for K^+ to stimulate ^{3}H-ACh synthesis only developed by day 28 in culture. ^{3}H-choline was taken up by a single mechanism with a K_T of 8-18 μM. Na^+ omission increased (≃2-fold) ^{3}H-choline uptake by day 14 cultures but inhibited (≃50%) ^{3}H-choline uptake in day 29 cultures. ^{3}H-choline uptake was inhibited by hemicholinium-3 with an IC_{50} <10 μM. It is concluded that bovine adrenal chromaffin cells, maintained in culture, are able to exhibit cholinergic properties and this neurotransmitter plasticity is retained even by the mature adult cell. This work was supported by the Medical Research Council of Canada.

[1]Ogawa, M. et al. Nature *307*, 66-68.

. — 0116

155.

Operative Findings in the Cubital Tunnel Syndrome: Confirmation of Focal Nerve Constriction by the Arcuate Ligament

J. N. ST. JOHN (Martinez, California)

Decompression of the cubital tunnel was performed in 214 cases (168 patients) of the cubital tunnel syndrome. In 197 cases (92%), some decrease in the number and/or size of the superficial vessels on the surface of the nerve in the region of constriction was noted. Some yellowish discoloration was noted in the region of decreased vascularity in almost all cases.

In the second ½ of this series full appreciation of the significance of abnormalities on palpation of the nerve has been gained. In all but 1 of the last 90 cases, some degree of indentation and softening of the nerve was detected. The length of the indentation ranged from approximately 5 to 15mm and it was noted to be centered 5 to 10mm distal to the ulnar notch in 80% of cases.

In 12 cases (6%) with severe neuropathy there was evidence of pseudoneuroma formation. There were 21 cases in which anomalous anconeous epitrochlearis muscles was identified and 1 case of an anomalous triceps muscle. Exclusive use of local anesthesia in the 2nd half of this series has allowed for frequent confirmation of the significance of the regions of focal softening and indentation; significant motor and sensory improvement was consistently demonstrable immediately following lysis of the aponeurosis at this level.

. — 0120

156.

Ulnar Entrapment Neuropathy Associated with the Anconeous Epitrochlearis Muscle

J. N. ST. JOHN (Martinez, California)

Analysis of 215 cases of cubital tunnel syndrome revealed 21 cases in which the anconeous epitrochlearis muscle was found at the proximal end of the cubital tunnel. The average age of these patients was 53 and

the average duration of symptoms was 43 months (range: 3 months to 20 years). In 12 of the 19 patients the syndrome was bilateral although the muscle was found to be bilateral in only 2 of the 7 patients who have undergone bilateral decompression.

All patients had weakness of the ulnar intrinsic hand muscles and the flexor digitorum profundus. In 16 cases Tinel's sign was noted and in 9 cases there was evidence of tenderness to palpation in the region of the post condylar grove. Passive flexion of the arm at the elbow for 3 minutes resulted in accentuation or reproduction of symptoms in all cases.

The muscle was noted to be quite small in 3 cases and quite prominent (1cm or more in width) in 8 cases. In 3 cases it was clear that the nerve was not constricted by the muscle and the muscle was therefore not transected. In all other cases the anconeous epitrochlearis muscle was divided and in 4 cases the focal lesion of the nerve was identified immediately deep to the muscle (at the level of the ulnar notch). The presence of the muscle did not significantly alter the prognosis following decompression. Improvement of the ulnar innervated forearm muscle function routinely promptly followed decompression; early improvement in sensation was frequently seen and eventual decrease in pain was common as was seen in patients without anomalous muscles.

. — 0121

157.

Pathogenesis of the Atherosclerotic Plaque: Neovascularization Induced by the Cellular Component of the Atheroma

H. ALPERN-ELRAN, S. BREM, E. ARBIT and N. KALANT (Montreal, Quebec)

Several investigators have noted that new blood vessels, derived from the vasa vasorum, appear in the wall of the atherosclerotic plaque but are absent in the areas adjacent to the plaque. Barger et al recently hypothesized that neovascularization within the plaque itself could account for some of the clinical complications and postulated a role for angiogenic factors.

We report here that the cellular component of atherosclerotic plaques can induce neovascularization by the production of a diffusable endothelial mitogen. This putative factor, Atherosclerotic Neovascular Factor, (ANF) could be important in the progression of the complicated atheromatous plaque.

We tested 58 fragments of plaque, 1mm^2, taken from patients at the time of carotid endarterectomy and transplanted to the rabbit cornea, a standard assay for studies of neovascularization. Blood vessels from the limbus appeared 72 hours after implantation and grew on the avascular cornea towards the plaque.

In a separate study, 26 of these fragments prior to implantation into the cornea, were bisected and preserved for histopathologic study. We found that each of eleven positive fragments were characterized by an abundance of smooth muscle cells. By contrast, 13 of 15 fragments (86%) that failed to elicit neovascularization were composed of the calcific, acellular, necrotic debris.

In summary, we propose that atheromatous plaques contain an angiogenic factor, A.N.F., produced by the cellular component of the plaque. This factor is absent in the acellular, necrotic, calcific zone.

. — 0123

158.

Acromegaly and Lumbar Spinal Stenosis

R. N. GOYAL, N. A. RUSSELL, R. DEL CARPIO and B. G. BENOIT (Ottawa, Ontario)

Acromegaly involves the bones, joints, discs, and ligaments of the spine. Although the plain x-ray changes have been extensively described, computerized tomographic evaluation of these spines has not been previously documented. In this study we have used CT imaging of the spine in an attempt to answer the following: 1. Is lumbar spinal stenosis more common in acromegalic patients? 2. Is the pattern of such stenosis (if identified) different from the more commonly recognized varieties?

18 acromegalic patients were identified of which 2 had been operated upon for spinal stenosis. 7 of the others were assessed clinically and radiologically; the latter by plain films and CT scanning of the lumbar spine. All assessed patients were asymptomatic and neurologically intact. One of these showed radiological evidence of the developmental type of spinal stenosis. Disc hypertrophy in the vertical plane was identified by increase in the intervertebral disc space on plain x-rays and in the anteroposterior plane by foraminal encroachment on CT scan in 1 case. In assessing spinal stenosis, the diameter of the spinal canal was measured on CT scan at the disc level in addition to the standard measurement.

We feel that acromegaly may be associated with spinal stenosis but we have not been able to identify a specific pattern in this small series. Measurement of the spinal canal diameter at the disc level may serve as another parameter for assessment of spinal stenosis in these cases.

. — 0126

159.

Transient Global Amnesia (TGA): Clinical Features and Etiologic Factors

G. ISRAELIAN and A. K. W. BROWNELL (Calgary, Alberta)

We reviewed the clinical records of thirty patients who presented with the syndrome of TGA. Patient ages ranged from 29 to 83 years with seventy-seven percent (77%) of them falling in the 50 to 69 year age group. At the time of presentation, three patients were experiencing their second episode of TGA.

Eight (26%) patients had a history of previous stroke or heart disease, nine (30%) were migrainers and seventeen (56%) had hypertension. Two-thirds of the migraine patients also had hypertension and in addition, one of these patients had atrial fibrillation and one, ischemic heart disease. Twenty-two of these patients have been followed for periods ranging from six to ninety-two months and no further episodes of TGA have occurred. No patients have experienced new transient ischemic attacks or stroke.

Our series confirms the accepted view of the benign nature of the syndrome and its frequent association with hypertension. Although thirty percent (30%) of our patients had migraine, the presence of hypertension in two-thirds of these patients suggests that migraine alone is an infrequent etiologic factor thus casting doubt on the importance of migraine in the pathogenesis of TGA.

. — 0127

160.

Partial Deficiency of Carnitine Palmityl Transferase (CPT): The Proposed Underlying Metabolic Disorder in Patients who Develop Alcoholic Rhabdomyolysis

R. B. BELL, A. K. W. BROWNELL, D. L. SEVERSON and S. SCHORR (Calgary, Alberta)

CPT deficiency in skeletal muscle, first reported in 1973, is probably the commonest recognized metabolic disorder of muscle which causes recurrent myoglobinuria. Fasting, prolonged exercise, infection and exposure to cold are known precipitating factors of rhabdomyolysis in these patients. Most of the reported cases occurred in males and CPT levels in muscle are generally less than twenty-five percent (25%) of normal.

Our patient, a sixty-five year old woman, had experienced three episodes of myoglobinuria (two required renal dialysis) over a fifteen year period. Each episode of myoglobinuria occurred during a period of binge drinking associated with decreased food intake. A normal ischemic exercise test ruled out any underlying disorder of glycogen metabolism. Her muscle CPT level was forty percent (40%) less than control values.

We propose that patients with similar levels of CPT are asymptomatic until exposed to the combination of alcohol and fasting at which time the enzyme deficiency is unmasked and becomes clinically significant. An hypothesis will be advanced to explain the observations.

We recommend that all patients with alcoholic rhabdomyolysis be screened for a partial deficiency of CPT to ascertain the significance of this observation for providing an explanation of the metabolic basis of this syndrome.

. — 0128

161.

Intermittent Torticollis due to Rotatory Atlanto-Axial Dislocation in an Adult

O. SUCHOWERSKY, K. M. HOYTE, C. J. PENNEY and H. A. SWANSON (Calgary, Alberta)

A 25 year old man was seen because of torticollis which came on suddenly while turning his head to the left. On examination, the head was displaced laterally and rotated to the left. This posture was fixed, but a spasmodic component was present in the sternomastoid and trapezius muscles. He had 3 similar previous episodes, the first one following blunt injury to the neck. Each resolved completely following traction. On this occasion, routine Xrays of the cervical spine were initially reported as normal. Special views of the C1-C2 region both on plain Xray and CT Scan showed an abnormal separation between the left lateral mass of the atlas and the odontoid. With neck rotation the odontoid did not move with respect to the axis, confirming a fixed rotatory dislocation. While waiting for atlanto-axial fusion, the patient had a spontaneous correction of the dislocation with no residual torticollis.

In children, fixed torticollis due to rotatory atlanto-axial dislocation is an uncommon though well-recognized disorder. This condition is rare in adults but should be considered when evaluating a patient with torticollis when onset occurs following trauma. It should also be recognized that the rotatory dislocation may be intermittent with spontaneous resolution and recurrence.

. — 0129

162.

Inexcitable Motor Nerves in Guillain-Barre Polyneuropathy

D. W. ZOCHODNE, T. E. FEASBY, W. F. BROWN, J. J. GILBERT, W. J. KOOPMAN and A. F. HAHN (London, Ontario)

Five patients who satisfied the diagnostic criteria for Guillain-Barre Syndrome (GB) were found to have inexcitable motor nerves when first examined neurophysiologically 4-11 days after the onset of symptoms. Despite inability to evoke an M response by nerve stimulation, direct muscle stimulation produced an obvious twitch. Reappearance of the M potentials was slow and incomplete and in one patient they remained absent 14 months after onset. Widespread fibrillations and positive sharp waves were recorded on sequential EMG examinations. In contrast, sensory action potentials of low amplitude but normal latency were recorded early in the disease.

Peak clinical disability was attained in 5-8 days (our average for GB is 11 days, n = 48). Recovery was slow and incomplete. Only 1 of 4 surviving patients walked independently at one year. All patients had significant distal muscle atrophy. One patient died 26 days after onset, prior to significant improvement. Autopsy disclosed extensive Wallerian degeneration involving cranial nerves, ventral roots, dorsal roots and peripheral nerves. Minimal inflammation was seen and there was no evidence of primary demyelination. Thirty-five percent of teased fibers from both the deep and superficial peroneal nerves showed Wallerian degeneration while less than 5 per cent showed demyelination.

Patients with GB who have inexcitable motor nerves appear to have widespread axonal degeneration and have a poor prognosis. They may be biologically different from typical cases of GB.

. — 0131

163.

Complement Depletion Suppresses Lewis Rat Ean

T. E. FEASBY, J. J. GILBERT, A. F. HAHN and M. NEILSON (London, Ontario)

Invading lymphocytes are prominent in Lewis rate experimental allergic neuritis (EAN) but it is uncertain whether there is complement-dependent antibody-mediated demyelination. We studied the effect of complement depletion on EAN. Lewis rats were immunized with bovine myelin and Freund's complete adjuvant to induce EAN. To produce complement depletion, two groups of rats were injected with cobra venom factor (CVF) (250 units/kg), one group (A) at day 9 and one group (B) at days 9 and 12. Following injection with CVF, total hemolytic complement was reduced to less than 20% of control values, returning to normal by day 15 in group A and 18 in group B. Animals were assessed daily by weight and a clinical grading scale.

Neurological signs of EAN began on day 12 in control EAN rats but were delayed to days 14 and 15 in groups A and B whose complement was depleted. Weight loss began in all groups by day 11 but was most severe in control EAN rats. Complement-depleted rats became less ill than control EAN rats.

Cobra venom factor suppresses EAN, probably by means of complement depletion. This suggests that complement-dependent demyelination may occur in EAN.

. — 0132

164.

Entrapment of the Posterior Cutaneous Nerve of the Arm

G. J. V. MAKIN and W. F. BROWN (London, Ontario)

This communication is the first report of an isolated mononeuropathy affecting the posterior cutaneous nerve of the arm (PCNA).

A 21 year old drummer had experienced pain in the posterior aspect of the distal third of the upper arm whenever the "hi-hat" cymbals were struck. This motion requires the right arm to be drawn across the body (i.e., flexed, medially rotated and hyperadducted at the shoulder) followed by forceful extension of the elbow to hit the cymbals which are stationed on the player's left. Throwing a ball was also painful. Examination revealed an area of hypesthesia corresponding to the cutaneous field of the PCNA, without abnormalities of motor or reflex examination. Electromyography was normal. Typical pain was induced during examination by doing pushups, but no additional findings emerged.

The PCNA originates from the radial nerve in the axilla, anterior to the tendons of latissimus dorsi and teres major. It curves around the medial and finally posterior apects of the long head of triceps, then perforates the brachial fascia just below the insertion of deltoid. The long head of triceps differs from the lateral and medial heads in that it inserts on the lateral margin of the scapula, rather than the humerus. The repeated shoulder movement peculiar to this patient (flexion, medial rotation and hyperadduction), followed by triceps contraction, therefore stresses the long head preferentially. We believe that this action was traumatic to the closely related PCNA and the cause of this syndrome.

. — 0133

165.

Brachial Plexus Injury in the Newborn

G. ISRAELIAN and H. Z. DARWISH (Calgary, Alberta)

The outcome of brachial plexus injuries in the newborn has varied in different reported series. The cause is usually presumed to be a combination of traction and rotation of the infant's head at the time of delivery. We reviewed 25 infants with brachial plexus injury seen in the neonatal nursery over a 6 year period. In 60% of the infants, mid-forceps extraction was used. 6/25 infants had evidence of an elevated diaphragm ipsilateral to the paretic limb. Phrenic nerve conduc-

tion time was serially assessed and recovery lagged 2 mths behind the onset of recovery in the upper limb. Even when unilateral paresis of the diaphragm was demonstrated on fluoroscopy, clinical examination was considered normal. We found that for the infants with a phrenic nerve palsy the mean birth weight (2947±400 gms) tended to be less than those without phrenic nerve injury (3980±1362 gms). Forceps marks on the neck were present on the side of the injured plexus in half the infants with phrenic nerve injury but only in one of the other infants. Facial forceps marks were present in equal numbers in both groups. The injury was confined to the upper roots (C4,5,6) in 60%. 30% of the infants had involvement of all the roots and in 10% there was isolated involvement of a particular nerve. Half of the infants showed evidence of encephalopathy in the newborn period, and this varied equally between Grade I and Grade II (mild and moderate). Although 65% of the infants showed some recovery in the 1st week, in many this recovery was not continuous but a plateau was reached after initial improvement. Subsequent improvement was then noted between 3 and 6 mos. 1/3 of infants followed to 6 or more months of age demonstrated some abnormality of the neurodevelopmental exam. There was no relation between the presence of the encephalopathy and the severity of the brachial plexus injury. The residual deficits noted in limb function were related usually to excessive internal rotation of the arm, and decreased abduction at the shoulder. We conclude that mid-forceps application should be abandoned when possible. The presence of phrenic nerve palsy can not be detected by the clinical exam alone, and anoxic encephalopathy is common in these infants. The parents should be prepared for a probable slow recovery after initial rapid improvement.

. — 0135

166.

Effet de la Substance P (SP) sur la Reponse Motrice de la Moelle Lombaire chez le Rat Deafferente et Paralyse

L. E. TREMBLAY et P. J. BEDARD (Québec, Québec)

Chez le rat certains noyaux du raphé projetant vers la moelle épinière ont leurs terminaisons près ou autour des motoneurones. Des études immunohistochimiques récentes ont démontré la coexistence de la sérotonine (5-HT), de la SP et la thyrotropine releasing hormone (TRH). Nous avons démontré (Brain Res., 169 (1979), 393; Neuropharmacol., 20 (1981), 477) l'action excitatrice du précurseur de la sérotonine (5-HTP) et de la TRH sur l'activité motoneuronale lombaire chez le rat déafférenté (5-7DHT) et paralysé (T6) telle que mesurée par l'activité EMG des muscles de la cuisse. En utilisant une méthode similaire on a pu observer que la SP administrée intrathécalement (I.T.) 50μg provoque aussi une augmentation de l'activité EMG des muscles de la cuisse chez le rat déafférenté et spinalisé. Cette excitation est considérablement réduite par l'administration de la cyproheptadine (10mg/kg), un antagoniste sérotoninergique. De plus, si dans une série de 3 injections de 5-HTP ou de TRH étalées sur 2 jours, la SP (IT) est administrée 1 heure avant la deuxième injection de 5-HTP ou de TRH, cet undecapeptide influence les réponses excitatrices subséquentes de 5-HTP et de la TRH. La réponse à la TRH est réduite de 25% lorsque injectée 1 heure après la SP (IT) (50μg), mais le lendemain, la réponse suivant la 3e injection de TRH est revenue au niveau contrôle. La réponse à la 5-HTP est diminuée de 36% une heure après la SP (dose moyenne de 334μg) et demeure diminuée le lendemain. Cependant dans un certain nombre de cas, la SP (IT) ($\bar{X}$ = 112μg) provoque une perte des réflexes nociceptifs des pattes arrières, la réponse à la 5-HTP, 1 heure après la SP est diminuée de 16%, mais est augmentée de 55% le lendemain, suite à la troisième injection de 5-HTP. Les injections successives de 5-HTP et de TRH sont stables sur une période de 2 jours chez les animaux non traités par la SP. Il semble donc que la SP interagit avec la 5-HT et la TRH au niveau de la moelle lombaire. Cette interaction chez le rat déafférenté et spinalisé se produirait au niveau post-synaptique. Ces observations sont probablement reliées à la coexistence de la 5-HT, la SP et la TRH dans les voies bulbo-spinales.

. — 0137

167.

Spontaneous Carotid Artery Dissection: Diagnosis, Evolution and Management

C. ROBERGE, J. LAFLEUR and J.-P. BOUCHARD (Québec, Québec)

We present four cases of spontaneous cervical internal carotid artery dissection. The varied symptoms and signs can be classified in three categories: unilateral head and neck pain, ischemia in carotid artery distribution and "local carotid indicator" signs. Three patients had a prior history of migraine. Angiography in three cases showed the typical "string sign"; in the other a saccular aneurysm was seen on the internal carotid just below its entry in the carotid canal. Computed tomography of the neck and ultrasonography were also used in diagnosis and follow-up respectively. Neither surgery nor anticoagulant therapy were used in our cases. The outcome was good in all four patients; none had serious neurological residua; in two cases, control angiography showed healing of the dissection; in one case, paresis of the tongue recovered well. We stress, however, the possibility of recurrence of symptoms. We discuss possible etiologic factors, among them microtrauma and preexisting local vascular abnormalities.

. — 0138

168.

Central Mechanisms Mediating Emesis in the Dog

M. KONDYSAR, R. K. HARDING, H. HUGENHOLTZ and J. KUCHARCZYK (Ottawa, Ontario)

Many of the clinically used anti-emetics, including metoclopramide and chlorpromazine, are thought to inhibit vomiting by altering brain dopamine metabolism (JAMA 247: 2693, 1983). In our studies in purebred beagles, electrolytic lesions of the area postrema (AP) on the dorsal surface of the fourth ventricle abolished vomiting induced by whole body ionizing radiation (600-800 rad.), and by intravenous (I.V.) and intracerebroventricular (I.C.V.) injections of the dopaminergic (DA) agonist apomorphine (APO) (Neurosci. Lett., in press). We have also found that i.v. pretreatment with the specific DA antagonist sulpiride (Pharmacol. 25: 61, 1982) had a significantly greater anti-emetic effect than i.c.v. sulpiride pretreatment, when dogs were tested with emetic doses of APO. These data suggest that receptors for APO-induced emesis may be located on the blood side of the blood-brain barrier in the AP.

In preliminary experiments in beagles, surgical interruption of venous outflow from the AP abolished i.v. APO-induced emesis for 2-3 weeks, whereas recovery of vomiting to i.c.v. APO has not occurred after 3 months. Although the basis for this finding is not known, one possible explanation is that following venous occlusion in the region of the AP, blood flow is reestablished by collateral vessels. While this could account for the resumption of i.v. APO sensitivity, it does not explain the loss of responsiveness affecting APO receptors accessed via the cerebrospinal fluid.

. — 0139

169.

Functional Mapping of Experimental Partial Complex Status Epilepticus in Rat.

A. HANDFORTH and R. F. ACKERMANN (Los Angeles, California)

Intermittent trains of bipolar pulses delivered to the rat amygdala via a chronically implanted electrode for 20-50 min results in a self-sustained status epilepticus which does not require further current stimulation, prior kindling or drugs for its occurrence. In the model of partial complex status which we have termed ambulatory status, the animal displays increased motor activity with incessant non-habituating exploration, explosive behaviour on attempted handling, and continuous EEG seizure activity, usually lasting at least 4 hours.

Functional mapping entailed 14_C-2-deoxyglucose (2-DG) injection

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via femoral vein at 1-1½ hours after current was discontinued. Markedly increased 2-DG utilization was found in contiguous basolateral structures from olfactory bulb to entorhinal cortex. Ipsilateral to the electrode these included olfactory areas, nucleus accumbens, septal nuclei, hypothalamus, hippocampus, subiculum, amygdala, entorhinal cortex, and restricted areas of prefrontal cortex. The medial dorsal thalamus and substantia nigra were bilaterally increased, and some contralateral propagation of activity occurred in hippocampus, select amygdala nuclei and n. accumbens. This model of experimental partial complex status reveals predominantly unilateral involvement of paleocortical structures and their immediate connections.

. — 0140

170.

Benign Outcome in Progression to Carotid Occlusion

J. W. NORRIS and N. M. BORNSTEIN (Toronto, Ontario)

The two major factors in symptomatic carotid stenosis which indicate surgical intervention are serverity (>50%) and ulceration. Carotid endarterectomy is considered urgent in critical (>90%) stenosis, to prevent occlusion. Total carotid occlusion is regarded as having serious implications for morbidity and mortality, and is invariably inoperable.

During monitoring by Doppler of progression of the arterial lesions, we observed 17 patients evolve to the point of carotid occlusion. Eight remained asymptomatic, seven had ipsilateral carotid and one had vertebrobasilar TIAs just prior to the occlusion and one patient had an ipsilateral carotid infarction. No further cerebral ischemic episodes occurred but two patients died vascular deaths and two had myocardial infarction. All were smokers, with severe (>75%) carotid stenosis, and ten were male, but otherwise their age and other risk factors did not differ from the rest of the study population.

The risk of cerebral ischemic events in carotid stenosis increases with the severity of the stenosis but reduces once the artery occludes.

. — 0141

171.

Subclavian Steal — A Harmless Phenomenon

N. M. BORNSTEIN, L. CHADWICK, S. CORRIGAN and J. W. NORRIS (Toronto, Ontario)

Reversal of flow down the vertebral artery, associated with severe subclavian artery stenosis, is said to 'steal' blood from the brainstem, producing TIAs or infarction.

Using carotid Doppler, we identified 60 patients with severe subclavian stenosis among 500 with asymptomatic cervical bruits. Twenty-three patients (5% of the study population) had subclavian steal (angiographically confirmed in eight), evidenced by reversed or bi-directional vertebral flow and often characterised by a unique waveform. None of these patients were or became symptomatic during 14-36 months of follow-up, nor did they develop symptoms during provocation of reversed vertebral blood flow (using an arm tourniquet and vigorous forearm exercise).

Discovery of subclavian steal is a useful Doppler or angiographic index of severe subclavian stenosis, but is largely, if not entirely, asymptomatic.

. — 0142

172.

Detecting Progression in Carotid Stenosis

N. M. BORNSTEIN and J. W. NORRIS (Toronto, Ontario)

During a continuing clinical and Doppler follow-up of 500 patients in the Toronto Asymptomatic Cervical Bruit Study, we previously noted that some carotid lesions progressed while others appeared to regress. Neurological events were closely related to both the degree and progression of the carotid lesions (*Stroke* 1984; 15:186).

Over two years' follow-up with serial Doppler of 156 carotid arteries, mean overall initial ICA stenosis changed from 31 ± 33% to 43 ± 33% ($p<0.001$). Using raw Doppler data, arterial stenosis progressed in 47%, was unchanged in 42%, and regressed in 11%. To relate changes in arterial calibre to the residual lumen with greater sensitivity than the raw data permits, we developed a 'stenotic index'. Using this index with 46 arteries followed over three years, the lesions had progressed in 52%, remained unchanged in 26%, and regressed in 22%.

Since progression and regression of carotid stenosis reflects underlying arterial pathology, this data may help in planning future treatment strategies.

. — 0143

173.

Value of I.C.P. Monitoring in Head Injuries — A Retrospective Study of 74 Patients

F. B. MAROUN, R. RAHN, D. MORRISON, J. C. JACOB, M. FARIDI and W. O. GITTENS (St. John's, Newfoundland)

Though the severity of the head injured patient correlates well with the Glascow Coma Scale, controversy still exists about the beneficial role of I.C.P. monitoring in those patients. Our data confirms a better outcome in the more severely head injured patients who were treated with an I.C.P. monitor (Gsc ≤ 8) with significant difference in good and impaired recovery but no significant difference in number of deaths. The series compares favorably with other recent series in the number of good and impaired recoveries but less well in the number of deaths, a reflection of delayed treatment due to long referral distance.

. — 0144

174.

Malignant Trigeminal Neuroma

F. B. MAROUN, G. MURRAY, M. SADLER, J. C. JACOB, M. MANGAN, G. MATHIESON and M. FARIDI (St. John's, Newfoundland)

Malignant neuroma of the trigeminal nerve are extremely rare. Review of the literature reveals only five cases. A sixth patient is reported with detailed clinical, radiological and pathological findings. Analysis of previously reported cases is presented.

. — 0145

175.

Hemifacial Spasm in a Chiari Patient

F. B. MAROUN, J. C. JACOB, M. MANGAN and M. FARIDI (St. John's, Newfoundland)

The pathogenesis of hemifacial spasm, a relatively uncommon clinical problem is controversial. Compression of the facial nerve, at its exit from the brain stem has been reported in a large number of patients (Janetta). To our knowledge, the association of hemifacial spasm with Chiari malformation have not been described. The improvement of the spasm following unroofing of the foramen magnum and laminectomy without microvascular decompression of the facial nerve raises the possibility that other pathogenic factors may be involved in the genesis of hemifacial spasm.

. — 0146

176.

Surgical Management of Intracranial Aneurysms Associated with Arteriovenous Malformation

F. B. MAROUN, G. P. MURRAY, M. A. MANGAN, M. FARIDI and J. C. JACOB (St. John's, Newfoundland)

The association of multiple intracranial aneurysms particularly giant ones with A.V. Malformation is extremely rare. The pathogenesis and overall management is still controversial. In this communication, we present the case of a male patient with a large A.V. Malformation and four intracranial aneurysms, two of which are giant. Management of this type of lesion is discussed together with review of the literature of this complicated problem.

. — 0147

177.

Familial Intracranial Aneurysms

F. B. MAROUN, G. P. MURRAY, M. MANGAN, J. C. JACOB and M. FARIDI (St. John's, Newfoundland)

The pedigree of three families with seven members suffering from subarachnoid hemorrhage secondary to rupture of intracranial aneurysm is presented. Review of the literature up to 1983 shows 53 families with a total of 110 members affected. Genetic implications are reviewed.

. — 0148

178.

Cavernous Phlebography — Anatomical Consideration and Hormonal Sampling in Sellar Lesions

M. MANGAN, F. B. MAROUN, J. C. JACOB, C. ROSS, T. CUMMINGS, M. HARDJASUDARMA and E. R. REDDY (St. John's, Newfoundland)

The technique of inferior petrosal venous sinus catheterization is reviewed. Radiographic anatomy of the cavernous sinus, including some normal variations will be illustrated together with abnormal radiographic anatomy caused by intrasellar and parasellar pathologic process.

In addition, to provide additional information about abnormal anatomy obtained by clinical neuroradiologic techniques such as computerized tomographic scanning, intracranial sinus venography also permits sampling of blood from different sites in the venous circulation. A review of hormonal levels from the inferior petrosal sinus, internal jugular and antecubital vein at time of cavernous venography mainly in prolactinoma will be reviewed. The desirability of this mode of investigation in light of new methods such as CT scan will be discussed.

. — 0149

179.

Familial Spino-Cerebello-Cerebral Degeneration with Amyloid Plaques (Gerstmann-Sträussler-Scheinker Syndrome)

J. Y. CHU, A. J. LEWIS (Etobicoke, Ontario) (Toronto, Ontario)

A family with late-onset dominantly-inherited spino-cerebello-cerebral degeneration affecting two generations is described. The pertinent clinical features were nystagmus, hearing loss, progressive dysarthria and dysphagia, cortical-spinal tract signs, cerebellar ataxia, impaired vibration sense, areflexia of the lower limbs and pes cavus. Dementia was not apparent until late in the illness.

Neuropathological examination on post-mortem specimen showed demyelination of the posterior columns and spinocerebellar tracts. Neuronal loss and Lewy bodies were found in the substantia nigra. The cerebellum showed diffuse neuronal loss in the Purkinje cell layer, the molecular layer and the dentate nucleus. Multiple amyloid plaques without neurofibrillary tangles were found in all layers of cerebral cortex, basal ganglia, amygdala and molecular layer of cerebellum.

Gerstmann-Sträussler-Scheinker Syndrome should be considered as a possible diagnosis in cases with familial late-onset spinocerebellar degeneration. Current literature with regards to the etiology of this rare syndrome will be presented.

. — 0150

180.

Paraneoplastic "Optic Neuritis" and Encephalomyelitis

D. BOGHEN, J. MICHAUD and M. SEBAG (Montréal, Québec)

A 63-year-old man presented in June 1984 with signs consistent with a left partial third nerve palsy. Six weeks later the oculomotor disorder had progressed to a paralysis of upward gaze and limitation of levo-and dextroversion in both eyes. CSF yielded 40 lymphocytes /cc, and oligoclonal bands. In October 1984 he complained of decreased vision in the right eye. The visual acuity (VA) in that eye which had previously been normal was now 3/200. The right disc was swollen. Subsequently the VA in the right eye improved to 20/60 and the disc oedema decreased. His ocular motility impairment remained unchanged. He was found to have an oat-cell carcinoma of the lung. He died 9 months after the onset of the disease. Neuropathological examination demonstrated leptomeningeal, optic nerve and mid-brain changes consistent with paraneoplastic involvement. There was no evidence of leptomeningeal or parenchymal tumoral infiltration.

This case indicates that midbrain paraneoplastic encephalomyelitis, a rarely reported entity, ought to be considered in the differential diagnosis of isolated ocular motor palsy. It also allows an appreciation of the clinical course and pathological findings of paraneoplastic optic neuropathy. There is only one previous report of a case of the latter condition for which pathological confirmation was available.

. — 0151

181.

The Incidence and Early Electrophysiological Features of the Polyneuropathy of Critical Illness

N. J. WITT, C. F. BOLTON and W. J. SIBBALD (London, Ontario)

The peripheral neuropathy of critical illness has been characterized clinically, electrophysiologically, and morphologically (Bolton, Gilbert, Hahn, Sibbald. J. Neurol, Neurosurg, and Psychiat 1984; 47:1223-1231). However, the early signs and precise incidence are still in doubt. In a prospective study, patients were entered if they had sepsis and critical illness (failure of at least two major organs). It was possible to perform initial and follow-up studies during a four-month period in 12 of 14 critically ill patients. Clinical signs were often equivocal. However, six of 12 patients had reduced compound muscle and sensory action potential amplitudes, prolonged or absent F response latencies, relatively preserved conduction velocities, and fibrillation potentials and positive waves in various limb muscles. These abnormalities were present initially in four patients, but developed over one month in two others. Tests for a defect in neuromuscular transmission were negative.

Thus, an axonal polyneuropathy was identified in 50% of patients who had critical illness and sepsis, indicating this is likely a major cause of morbidity in these patients. Follow-up has shown improvement in these electrophysiological abnormalities if the patient recovers from the critical illness.

. — 0152

182.

An Unusual Case of Dysarthria and Dysphagia with Hemiatrophy and Hemianaesthesia of the Tongue

M. J. STRONG and J. H. NOSEWORTHY (London, Ontario)

Lesions of the floor of the mouth occasionally present with predomi-

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nantly neurological signs and symptoms. We report a case which clearly illustrates the time-honoured principle that an understanding of regional anatomy coupled with a careful neurological examination are essential for precise localization of neurological lesions in this area.

A 72-year-old woman presented with an 18-month history of throat discomfort and progressive dysphagia for liquids and a 4-month history of dysarthria and loss of taste on one-half of her tongue. The neurological findings were restricted to one-half of the tongue which showed complete anaesthesia together with loss of taste (anterior two-thirds) and hemiatrophy. Sensation was normal on the chin and along the inferior alveolar ridge. Mild induration of the submandibular fossa was initially overlooked despite careful examination of the oropharynx. The recognition that unilateral involvement of the lingual (V), chorda tympani (VII) and hypoglossal (XII) nerves is best explained by a lesion at the base of the tongue led to CT study which revealed changes in the region of the submandibular gland. Subsequent exploration of this area revealed an infiltrating squamous cell carcinoma arising from the submandibular gland.

The neurological anatomy of this region together with the review of the pertinent literature will be presented in this poster.

. — 0153

183.

Nemaline Myopathy — Clinical Features and Management

B. D. HOUSTON and R. C. TERVO (Toronto, Ontario)

Eleven patients, 6 males and 5 females with nemaline myopathy were reviewed to outline their clinical features and management. This represents all the cases known to H.S.C. Ages at diagnosis ranged from 1 month to 4½ years. Three children died between 1½ and 7 months. Seven patients, now aged 4 to 27 years, survived. The current status of one patient is unknown.

8/11 had hypotonia and weakness at birth. 2/11 had respiratory distress. Two affected siblings had arthrogryposis. One girl, aged 14 years, required long-term ventilation since year two. (She currently attends normal school).

Five patients continue to be community ambulators. 4/7 patients have scoliosis or kyphoscoliosis. Of these four, one required surgical correction.

Two pairs of siblings had definite, and one sibling of an index case had probable nemaline myopathy. No parent was clinically affected.

Abnormalities on muscle biopsy could not be related to clinical severity.

6/7 surviving patients live at home and are managed as outpatients. One ventilator-dependent child has required long-term hospitalization. Functional outcomes justify aggressive management except for the severest cases.

. — 0155

184.

Neurophysiological and Neuroradiological Findings in a Biopsy-Proven Case of Alexander's Disease

I. TEIN, L. E. BECKER, P. A. HWANG, S. CHUANG, M. J. TAYLOR and R. C. TERVO (Toronto, Ontario)

We have extensively studied a 6 year old girl with Alexander's disease with histopathology, EEG, nerve conductions, evoked potentials, CT and MRI, the results of which may direct future diagnostic assessments. Our patient presented with developmental delay at 8 months, macrocrania at 15 months, and progressive developmental regression over the subsequent 4 years, exacerbated by seizures. She underwent a right ventriculoperitoneal shunt insertion at 22 months for presumed hydrocephalus. Her neurological exam at 6 years revealed severe global developmental delay, bilateral optic atrophy, bilateral corticobular, corticospinal and extrapyramidal findings and positive primitive reflexes.

A brain biopsy at 34 months was consistent with Alexander's disease. Serial EEG's from 18 months of age have shown a progressive deterioration of background activity followed by an active multifocal epileptiform disturbance. VEP's and ERG to flash stimulus and nerve conduction studies were unremarkable. The ABR's revealed only wave I clearly with markedly delayed latencies and poor reproducibility of waves II, III and V bilaterally. SEP's from median nerve stimulation showed a normal peripheral response at C_7 but absent cortical response. Initial CT head at 16 months showed white matter disease with minimal ventricular enlargement. Follow-up CT's showed further ventricular enlargement with continued patchy areas of enhancement at the grey-white matter junction.

The outlined investigations, particularly the pattern of evoked potentials, warrant further studies as this may facilitate the noninvasive diagnosis of Alexander's disease.

. — 0156

185.

Syndrome of the Superior Cerebellar Artery: Contralateral Saccadic Lateropulsion and Ipsilateral Limb Ataxia

P. J. RANALLI and J. A. SHARPE (Toronto, Ontario)

Distinctive motor defects were recorded in a patient with rostral cerebellar infarction from occlusion of the superior cerebellar artery, identified by angiography, CT and MRI. Directional errors in saccadic accuracy, and postural and intentional tremor of the ipsilateral upper limb comprise this syndrome. Contralateral saccades are hypermetric, ipsilateral saccades are hypometric, and vertical saccades are associated with contralateral saccadic pulses. This saccadic lateropulsion is directed away from the side of rostral cerebellar damage.

High resolution magnetic search coil oculography showed synchronous onset and termination of vertical and contralateral saccades, which generated oblique trajectories in response to vertical retinal errors. The oblique errors were corrected by vertical and ipsilateral saccades. Lateropulsion persisted in darkness. There was no nystagmus or postsaccadic drift. Saccadic velocities were normal. In darkness the eyes drifted smoothly toward the lesion. Smooth pursuit gain was low in all directions. These observations indicate that saccadic lateropulsion does not specify lateral medullary damage. Lateropulsion of saccades away from the side of limb ataxia signifies damage to the rostral cerebellum in the distribution of the superior cerebellar artery.

. — 0158

186.

Nuclear Magnetic Resonance (NMR) Localization of Lesions in Higher Cerebral Function

A. KERTESZ, S. E. BLACK, J. HOWELL and M. POLK (London, Ontario)

Inversion Recovery (IR) images provide superior grey-white matter distinction and anatomical information in any desired plane. Complimenting Spin Echo (SE) pulse sequences allow delineation of CSF spaces and stroke lesions for sophisticated localization.

112 infarcts and 18 hemorrhages with higher cerebral impairment were scanned on a 1.5 Kilogauss resistive magnet imager.

A study of cerebral asymmetries in 20 volunteers' brains show a larger left planum temporale and a sharper opercular demarcation in (R) handers. A composite measure of anterior frontal width, parietal width and opercular demarcation on NMR images predicted handedness with 95% accuracy.

Further correlation with dichotic listening and visual field laterality will be available. NMR provides an in vivo assessment of normal anatomical asymmetries.

The patients were examined in the acute (3-21 days) and chronic stable 6-12 months state, with standardized tests of language and cognition, as well as specialized experiments for individual case studies.

Aphasic syndromes were better localized with respect to the cortical subcortical distinction. The extent of involvement correlated with the severity of cognitive deficit, regardless of the extent of grey matter involvement. The extent of recovery negatively correlated with lesion size. Crossed dextral aphasia, cortical blindness, reduplicative paramnesia,

amnestic syndrome, transcortical motor and sensory aphasia, isolation of language, motor impersistence and hemispatial neglect are correlated with anatomical localization. The complex relationship between anatomical location, lesion size and time from brain damage is studied with NMR optimally.

. — 0160

187.

Adrenoleukodystrophy Presenting as Presenile Dementia

M. MacEACHERN, R. F. NELSON, V. MONTPETIT, D. A. GUZMAN and D. T. STUSS (Ottawa, Ontario)

Adrenoleukodystrophy is a rare genetically determined disease in which very long chain fatty acids are found in the cells of the brain, adrenal cortex and interstitial cells of the testes. The disease usually appears in childhood although some cases have been described in early adult life.

A 47-year-old man presented with a rapidly dementing illness which lead to his death within 18 months of onset. CT scan showed diffuse loss of density of white matter but he had no motor or sensory deficits clinically. At autopsy, the classical features of adrenoleukodystrophy were found in brain, adrenal cortex and testes.

Although siblings shared with him curious and as yet unexplained features of early baldness and cataracts, they do not have dementia or neurological deficits. Studies for long chain fatty acids were carried out on the living siblings and will be reported along with tissue studies in the patient.

Adrenoleukodystrophy must be considered as a rare cause for presenile dementia.

. — 0161

188.

Serum Lipids after Stroke

I. MENDEZ, V. C. HACHINSKI and B. M. WOLFE (London, Ontario)

Determination of a serum lipid profile in stroke patients is important because abnormal lipid patterns represent a risk for coronary heart disease and perhaps recurrent stroke.

Serum total Cholesterol (T CHOL), total triglycerides (T TG), high density (HDL), low density (LDL) and very low density (VLDL) lipoproteins were determined in 11 consecutive stroke and transient ischemic attack (TIA) patients admitted to an investigative stroke unit. All patients studied were male and within the 60-90 age group. Fasting serum lipids were measured serially within 24 hours of admission to hospital, at seven days and at three months after the onset of the acute attack.

A fall in mean serum T CHOL from 196 ± 23 (SEM) mg/dl to 170 ± 18 mg/dl and LDL from 136 ± 22 mg/dl to 117 ± 17 mg/dl was observed only in the cerebral infarct group (n = 6). This was detected at seven days. Fasting T CHOL 227 ± 19 mg/dl and LDL cholesterol 161 ± 16 mg/dl were both significantly higher ($P<0.05$) at three months than on day seven. No significant changes were noted in transient ischemic attack (TIA) patients (n = 5). High density lipoprotein (HDL) rose slightly from the admission day level when measured at seven days and three months later in both the cerebral infarcts and TIA groups, but the changes were not statistically significant.

Serum T TG and VLDL triglycerides showed no significant change between admission and day seven, but they rose significantly at three months from 141 ± 15 mg/dl to 191 ± 16 mg/dl ($P<0.05$) for cerebral infarct patients. No significant changes were found in TIA patients. The results of this study suggest that serum lipoprotein levels may be significantly altered by stroke. The likelihood of detecting an underlying hyperlipidemia is markedly improved by waiting for three months to measure lipids.

Supported by The Heart and Stroke Foundation of Ontario and University Hospital.

. — 0164

189.

Transient Brainstem Auditory Evoked Response Abnormalities Associated with Arnold-Chiari Malformation

J. VAJSAR, P. HUMPHREYS and E. VENTUREYRA (Ottawa, Ontario)

Various abnormalities in brainstem auditory evoked responses (BAER) have been reported in patients with hydrocephalus associated with meningomyelocele and Arnold-Chiari malformation, but it is unclear whether these abnormalities are caused by hydrocephalus, increased intracranial pressure, brainstem anatomical abnormalities or progressive mechanical deformity of the brainstem.

We report a case of a female infant born with a meningomyelocele repaired at age 1 day, followed by placement of a ventriculoperitoneal shunt at age 6 days for hydrocephalus. She remained well until 3½ months of age when she presented with an upper respiratory tract infection, stridor, dysphonia and respiratory failure. Physical examination showed an alert infant with no evidence of increased intracranial pressure, bilateral palatal and vocal cord paralysis and flaccid paraplegia. BAER studies showed a small amplitude delayed wave I with later components being absent. The patient underwent a cervical laminectomy with cervicomedullary decompression following which the lower cranial nerve pareses disappeared. Postoperative BAER studies showed normal waves I-V with normal amplitudes, interpeak latencies and V/I amplitude ratios. The absence of increased intracranial pressure and the reversibility of the BAER abnormalities suggest that these findings were related to progressive deformity of the brainstem associated with a type II Arnold Chiari malformation, rather than to increased intracranial pressure, hydrocephalus or abnormal brainstem anatomy. Our experience with this patient suggests that routine prospective BAER testing in children with Arnold-Chiari malformation may be helpful in the early detection of progressive brainstem compromise.

. — 0165

190.

An Immunological and Genetic Study of Partial Epilepsy

O. EEG-OLOFSSON, K. OSTERLAND, R.D. GUTTMANN, F. ANDERMANN, A. OLIVIER, N.A. JANJUA and E. ANDERMANN (Montréal, Québec)

Modern immunological techniques have made it possible to investigate the immunogenetic basis of epilepsy. This study focuses on serum immunoglobulins and HLA antigens in 24 unselected patients with partial epilepsy of temporal lobe origin, and in 30 of their near relatives. In the patients, the distribution of T-lymphocytes in blood and CSF protein was also investigated. In 12 patients who underwent surgical treatment of their epilepsy, immunological studies on brain tissue were performed. Sixteen of the patients had a previous history of febrile seizures or CNS infections: 7 febrile convulsions; 3 seizures starting with a febrile illness; 5 encephalitis; and 1 meningitis.

The mean serum levels of IgG, IgA and IgM, as well as C3 in patients and relatives did not differ significantly from controls. None of the patients and only one relative possessed the HLA haplotype A1, B8 which is the most common haplotype in the general population. This haplotype has previously been found to be significantly decreased in patients with benign epilepsy of childhood with controtemporal foci (Eeg-Olofsson et al., Epilepsia 23: 27-34, 1982), and increased in patients with primary generalized epilepsy (Fichsel and Kessler, Adv. Epileptol. XI, Raven Press, pp 475-477, 1980; Rivas, Epilepsia 24:115, 1983).

Significant differences were found in the distribution of T-lymphocytes, where the epileptic patients showed a lower T4 ('helper')/T8 ('suppressor') ratio as compared to controls. Immunofluorescence studies were performed on samples of epileptogenic tissue removed at operation. No immune complex-like deposits were observed. In a number of specimens, indirect fluorescent staining suggested the presence of serum antibody directed against neural structures.

These results suggest a relationship between immunodeficiency and partial epilepsy.

. — 0167

191.

BAER Amplitude in Multiple Sclerosis

M. JAVIDAN, D.R. McLEAN and K.G. WARREN (Edmonton, Alberta)

Interpretation of brain stem auditory evoked responses (BAER) relies heavily on latency measurements especially in multiple sclerosis (MS) where central conduction time (CCT) is frequently prolonged. Often CCT cannot be measured as waves I or V are unobtainable. Amplitude analysis using wave I/V ratio faces the same limitation. To overcome this we have utilized combined amplitude (CA) of waves III, IV and V, in assessing BAER in patients with MS. This paper reports the results of CCT compared to CA in regards diagnostic yield in MS patients.

The BAER were analyzed in 219 patients referred from the MS research clinic with hearing thresholds below 25 dB. There were 58 possible, 62 probable, and 98 definite MS patients (Rose 1976). BAER were recorded with a Nicolet 1000 from electrodes attached to the ipsilateral ear reference to the vertex with the contralateral ear masked with 30 dB white noise. 2000 stimuli were delivered by earphone 65 dB above HSL at 11.1/sec. CCT was calculated by subtracting the peak latency of wave I from wave V. An abnormal response was 3SD above mean. Amplitudes of wave III, IV and V were measured from the peak to the aftercoming trough and summated. An abnormal CA was 2 SD below mean. Controls were 30 age matched neurologically normal people. In 116 ears examined in 58 possible MS patients the CCT was *normal* in 111 (CA-Abnormal (A) 9, Normal (N) 102), *abnormal* in 1 (CA-N1), *not measurable* in 4 (CA-A3, N1). In 124 ears in 62 probable MS patients the CCT was normal in 104, (CA-A18, N 86), *abnormal* in 11 (CA-A 4, N 6) and *not measurable* in 9 (CA-A 9). In 194 ears in 98 definite MS patients (2 ears excluded by deafness) the CCT was *normal* in 114 (CA-A 14, N 100), *abnormal* in 22 (CA-A 9, N 13) and *not measurable* in 58 (CA-A 56, N 2).

Using the CA clearly increased the diagnostic yield. The method does have limitations and these will be discussed.

. — 0168

192.

Neonatal Muscle Biopsies — A Clinical, Radiological and Pathological Review

H. RUIZ-FUNES, W. C. HALLIDAY, E. G. MURPHY and L. E. BECKER (Toronto, Ontario)

The pathology, radiology and clinical features of 26 neonates who had muscle biopsies in the first six weeks of life were reviewed. The patients presented at the Hospital for Sick Children between 1970-1984. 24/26 of the children were hypotonic and 2/26 were hypertonic. Fifteen neonates had diagnostic pathology, five had nonspecific changes and six muscle biopsies were normal.

The muscle biopsy in eight children showed neurogenic changes, correlating with the abnormal EMG in 6/8. 2/8 had a positive family history, 2/8 had breech presentations, 1/8 had x-ray changes (thin ribs, "bell-shaped" chest) and 4/8 had contractures. 5/8 are known to have died during the first three months.

Seven muscle biopsies were myopathic (2 central nuclear myopathy, 1 nemaline rod myopathy, 2 congenital myotonic dystrophy, 1 congenital muscular dystrophy, 1 unclassified). The EMG was abnormal in only 1/7 patients. The family history was positive in 4/7, 3/7 children had breech presentation, 5/7 had radiological changes and 6/7 had contractures. 4/7 died in the neonatal period and 3/7 showed some improvement.

The 5 patients in whom biopsies showed nonspecific changes had a variety of clinicial diagnoses. One had a positive family history, one had radiological changes and 3/5 had joint contractures. 4/5 improved during follow up. Of the six children with normal biopsies, 3/6 were breech presentations, 5/6 had cesarean sections and 4/6 died.

In summary, the radiological changes are most common in those patients with myopathies, a normal EMG does not rule out a myopathic condition and, as a group, neonates with neuromuscular disorders have a 33% incidence of breech presentation.

This review highlights the importance of the neonatal muscle biopsy for genetic counselling and for appropriate clinical management decisions.

. — 0169

193.

Physiologic Activity in Rat Retinal Ganglion Cells Regenerating Axons into Peripheral Nerve Grafts

S.A. KEIRSTEAD, M. VIDAL-SANZ, M. LEVESQUE, M. RASMINSKY and A.J. AGUAYO (Montréal, Québec)

As is the case for neurons in many parts of the adult mamalian central nervous system, axotomized rentinal ganglion cells regenerate axons into autologous peripheral nerve grafts inserted into the retina (So & Aguayo, *Brain. Res.*, in press). We have now recorded activity in single axons teased from such grafts 1.5 to 2 cm from the retina and have examined the responses in these regenerated fibres to changes in illumination of the retina.

Many ganglion cells regenerating lengthy axons from the retina into peripheral nerve grafts had a low level of ongoing activity in darkness or ambient light and responded with increases or decreases of firing frequency either to changes in background illumination or to changes in illumination within limited receptive fields. Changes in firing frequency with brief changes in illumination were both tonic and phasic and occured at the beginning and/or at the end of the light stimulus. These responses are similar to those recorded from optic nerve fibres of normal rats (Brown & Rojas, *J. Neurophysiol. 28*: 1073, 1965).

The results of these experiments indicate that some retinal ganglion cells retain responsiveness to light following axotomy and regeneration of their axons into peripheral nerve grafts. Those retinal ganglion cells responding to stimulation within small defined receptive fields must retain or reestablish much of their normal input from the cells making up the local retinal microcircuitry.

. — 0170

194.

PNS Grafts Used as Bridges Between the Rat CNS and Skeletal Muscle

A.J. AGUAYO, M. BENFEY, M. VIDAL-SANZ, M. LEVESQUE, and G.M. BRAY (Monteal, Quebec)

Segments of peripheral nerve inserted into different regions of the adult mammalian brain support the regeneration of axons from injured CNS nerve cells. This experimental strategy has also been used to guide growing axons to regions of the CNS situated several cms away from the sources of central axonal growth. In the present experiments we investigated anatomically the origin and termination of regenerating nerve fibers bridging the brain and a skeletal muscle across an autologous peripheral nerve graft.

Adult Sprague-Dawley rats weighing 200-300 gm were anesthetized and a 3-4 cm segment of one sciatic nerve was removed for transplantation into brain. One end of the graft was inserted into selected areas of the brain. After intervals of 2 months to permit the growth of axons along the grafted segment of nerve, the distal end of the graft was exposed surgically and anastomosed end-to-end to the stump of the nerve to the sternomastoid (SM) approximately 1 cm from the muscle. After 2 to 6 months, the brains, peripheral nerve grafts, and SM muscles were examined. In different groups of animals, it was shown that: 1) the nerve grafts contained myelinated and unmyelinated fibers ensheathed by Schwann cells; 2) there was tissue continuity at the end-to-end anastomoses between the nerve grafts and the distal stumps of the nerve to SM; 3) as visualized light microscopically with a combined silver-cholinesterase stain, motor end-plates in the SM muscle were reinnervated; 4) horseradish peroxidase (HRP) applied to the regenerated nerve to SM reached the end-plate regions of the muscle; and, 5) neurons near the central tip of the graft in the brain were retrogradely labelled by HRP injected into the SM muscle.

Although these findings demonstrate that axons of CNS neurons can grow along nerve grafts to reach skeletal muscle fibers, it remains to be proven that the newly-formed neuromuscular junctions are indeed the result of terminal synapse formation by intrinsic CNS neurons and are not due to reinnervation by neighbouring peripheral nerves.

. — 0171

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195.

Podophyllin Neurotoxicity

H. RUIZ-FUNES, P. A. HWANG, E. G. MURPHY, M. McGUIGAN and D. ARMSTRONG (Toronto, Ontario)

We report a previously healthy 18 month old boy who was accidentally exposed (topical and oral ingestion) to approximately 2500 mg of podophyllin tincture of Benzoin. Two hours later he developed diarrhoea and vomiting. This was followed by obtundation by 4 hours, with progression to coma. Hypotonia, areflexia and hypoventilation were noted on examination. Initial metabolic acidosis, bone marrow suppression, renal and hepatic dysfunction were followed by complete recovery. CSF protein was elevated to 1.5 g/l. Spontaneous respirations returned by 72 hours, with an early improvement of the comatose state. Abnormal dystonic posturing of the limbs was observed. EEG showed diffuse slow wave activity. Initial CT scan showed mild atrophic changes, progressing in 10 days to severe cortical and subcortical atrophy with bilateral hypodensities in the basal ganglia and deep white matter. Motor nerve conduction studies in the upper extremities showed a reduction in MEP with slight decrease in velocities. No MEP was obtained in the lower limbs. Sensory potentials were unobtainable in upper and lower extremities. ABRs and VEPs showed no abnormalities. SEPs were unobtainable.

Spastic quadriparesis, speech loss and global developmental delay were found at 7 months follow up. CT scan showed moderate cortical atrophy and mild ventricular enlargement.

Our case report suggests a more persistent toxic effect on the central than on the peripheral nervous system, which may be related to direct cytotoxic effect.

. — 0175

196.

Selective Decreases of αKetoglutarate Dehydrogenase in Brain in Experimental Wernike's Encephalopathy

R.F. BUTTERWORTH, J.-F. GIGUÈRE and A.-M. BESNARD (Montréal, Québec)

Treatment of adult rats with the central thiamine antagonist pyrithiamine results in neurological signs of thiamine deficiency and ultimately to pathological lesions of pons, midbrain, hypothalamus and medulla oblongata. The nature and distribution of the thiamine-dependent enzymes pyruvate dehydrogenase PDHC, (EC 1.2.4.1.) and α-ketoglutarate dehydrogenase α KGDHC, (EC1.2.4.2.) in 10 brain structures of pyrithiamine-treated rats revealed the following:

(a) No changes in PDHC in any brain structure.

(b) Significantly reduced activities of α KGDHC (most severe of the order of 60-70%) in pons, hypothalamus, midbrain and medulla oblongata. Measurement of enzyme activity in the presence of excess TPP cofactor did not lead to increased enzyme activities in these regions.

Thiamine administration to early symptomatic pyrithiamine-treated rats resulted in reversal of neurological symptoms and in normalization of cerebral α KGDHC abnormalities. These findings suggest that the "biochemical lesion" responsible for the the reversible neurological abnormalities in Wernicke's Encephalopathy may be decreased activity of α KGDHC.

Supported by grants from MRC and FRSQ.

. — 0176

197.

A Trial of Nimodipine in Migraine

A. HAKIM, D. STEWART and A. GELSTON (Montreal, Quebec)

We have evaluated the effectiveness of nimodipine, a calcium channel blocker, in the treatment of migraine headaches by a double-blind radomized placebo controlled trial.

Fifty patients were confirmed by a neurologist to give a history compatible with common or classic migraine and to have a normal clinical exam. To be eligible a minimum of two and a maximum of ten headache episodes per month were necessary. Excluded were pregnant patients and those with significant hypertension, medical or psychiatric diseases. Prophylactic migraine medication was not permitted but use of analgesics for relief of acute migraine attacks was acceptable during the trial. Patients underwent routine blood and urine analysis.

Patients received placebo for one month then were randomly assigned to receive either placebo or nimodipine, 40 mg PO tid, for the following 3 months. Patients kept a diary of the frequency, duration and severity of the headaches and any new or associated symptoms. All medications taken were tabulated and the patients were seen on a monthly basis.

Twenty-four patients completed the trial. Statistical evaluation compared the "headache index" (hours of headache x intensity graded 1-3) for nimodipine and placebo groups by the student t-test. Nimodipine was significantly more effective than placebo in the third and fourth months of the trial ($p < 0.05$). There were no important side effects to the use of the drug.

Supported in part by Miles Laboratories.

. — 0178

198.

Computerized Ambulatory EEG Data Base in Children

P.B. JAYAKAR, E. SHWEDYK, S.S. SESHIA, J. PATRICK and E. BRUSSE (Winnipeg, Manitoba)

Prolonged ambulatory EEGs (AEEGs) are undertaken to aid diagnosis of epilepsy or to assess electrographic seizure frequency. The vast amount of AEEG data produced necessitates the development of automated analysis to assist visual interpretation. An AEEG database, its structure and content, useful for this development is described.

The database is designed to store 30 second 4 channel AEEG segments sampled at 128/second. Each channel is associated with 8 annotation files, 1 consensus file and a profile listing of its contents. Each 1/8th second time duration can be coded into one of a maximum of 99 classes.

At present, the database contains 90 segments, selected from 45 AEEGs recorded on patients aged 1 to 22 years. A classification scheme of 40 classes of background activity, epileptiform and artifactual patterns was designed to account for variations in amplitude and morphology. Each epoch, defined as 3/8th second or more was annotated independently by 2 electroencephalographers into 1 of the 40 classes. The annotated data was stored on either a digital magnetic tape or a hard disc.

Data corresponding to a particular class can be recalled independently for designing EEG signal processing algorithms. The database has been and is being used for evaluation of a hardware realization of a pattern recognition system for automatic analysis of AEEGs.

Funded by: Health & Welfare Canada, CHWRF Inc., NSERC.

. — 0185

199.

Frequency of EEG Changes With Time in Pediatric Epileptic Population

M. DELGADO, D. KEENE and P. HUMPHREYS (Ottawa, Ontario)

It has become the practice in many centres to do serial EEG's in pediatric epileptic patients to help determine the prognosis of outcome and the possibility of development of new foci with brain maturation. The purpose of this study was to determine the frequency of EEG changes with time in this population.

434 EEG's of 100 epileptic patients were retrospectively reviewed. The criteria for inclusion were older than 30 days of age at onset of their seizures; more than 2 documented seizures; no progressive CNS pathology; no infantile spasms, Lennox-Gastaut, or febrile seizures; they had to have at least 3 EEG's over a 3 year period of time. 37% of the patients had partial seizures while 63% were generalized. 33% of the patients had normal initial EEG's; 19% had generalized spike wave; 20% had

right focal spike, 20% had left focal spike and 8% multifocal. 57% of patients showed a change in EEG pattern over the time of study. 27% changed from initial epileptiform abnormality to normal. 8% changed from initial normal recording to epileptiform, 22% showed a change in type or location of epileptiform abnormality. No significant difference in the frequency of EEG change with time was seen between partial and generalized groups.

. — 0187

200.

The Effects of Environmental Complexity on the Numerical Density of Neurons in the Visual Cortex of the Cat.

C. BEAULIEU and M. COLONNIER (Québec, Québec)

Interindividual differences in the numerical density of neurons (Nv) and in the number of neurons under 1 mm^2 of cortical surface (Nc) have been demonstrated in the visual cortex of the cat. Such differences may be due to age, breed or environmental factors.

Sex paired littermates were raised from the time of weaning in two different environments: an impoverished condition (IC) in which kittens were isolated in separate cages and an enriched condition (EC) in which they lived in a colony. All the animals were sacrificed at 8 months of age.

Using stereological methods, we have estimated the Nv of neurons in area 17 is about 57,000/mm^3 in IC and 47,000/mm^3 in EC cats. This 21% difference is highly significant at a $p < 0.001$ (2-way ANOVA). Moreover, the Nc of neurons is 18% significantly higher ($p < 0.05$) in IC than EC cats (97,000 and 82,000 neurons under 1 mm^2 of cortical surface respectively). The lower neuronal Nv in EC cats signifies that cell bodies are more widely separated from each other and that there is more intervening neuropil. This suggests that the number of synapses per neuron may be increased in an enriched environment. The lower Nc of neurons in EC cats may signify that there are fewer neurons in area 17 or that the visual cortex has actually increased in size. If the latter is true, the number or width of dominance columns should be increased, presumably the latter.

Supported by MRC grant MT-3735 and by a training grant to C.B. from FRSQ.

. — 0188

201.

The Contribution of Biceps/Brachialis to Brachioradialis Strength Testing

A. J. WILBOURN and P. J. SWEENEY (Cleveland, Ohio)

Physicians are taught that flexing the forearm against resistance can be used to test both biceps/brachialis and brachioradialis strength, by varying forearm position: supination evaluates biceps/brachialis, while neutral position (thumb superior) evaluates brachioradialis strength.

We have performed EMG examinations on several patients whose peripheral nerve lesions were mislocalized by clinicians following this dictum. In fact, this test procedure is primarily evaluating the biceps/brachialis muscles, regardless of forearm position, because of their much larger mass. Two examples will be discussed. (1) Lateral cord/brachial plexus tumor causing biceps wasting/weakness and sensory loss in the thumb and index fingers, clinically considered a C6 radiculopathy because of "weak" brachioradialis (normal on EMG examination). (2) Radial nerve lesion at spiral groove causing wrist drop, clinically considered a posterior interosseseous mononeuropathy because of "normal" brachioradialis (paralyzed on EMG examination). Thus, the brachioradialis muscle, even if normal, can appear weak when biceps/brachialis are weak, and conversely, even if paralyzed, can appear of normal strength when biceps/brachialis are normal.

Conclusion: Brachioradialis muscle integrity should be evaluated by palpation of muscle bulk and tendon during contraction, because strength testing is unreliable.

. — 0189

202.

Ulnar Neuropathy with Co-Existing Median to Ulnar Nerve Forearm Communication

P. J. SWEENEY, A. J. WILBOURN and M. J. MOSS (Cleveland, Ohio)

Forearm communications between median and ulnar nerves (Martin-Gruber anastamoses; M-U crossovers) are common anomalies, detectible on nerve conduction studies (NCS) in 30% of people. The crossing fibres originate from median and pass to ulnar, are typically solely motor, and ultimately supply ulnar-innervated hand muscles to varying degrees.

We recently studied an 18 year old male with complete ulnar nerve severance whose surgical treatment was appreciably delayed because of a co-existing, prominent M-U crossover. A puncture wound proximal to the right medial epicondyle was sustained while playing football (2° to sharp rock). Ulnar sensation was lost, and 5th finger abduction was weak, but the first dorsal interosseous (1DI) was normal. No recovery occurred over the next year. Subsequently, EMG examination revealed unelicitable ulnar sensory NCS's (recording both fifth finger and hand dorsum), total denervation of ulnar-innervated forearm muscles, partial denervation of hypothenar muscles, and normal 1DI. NCS demonstrated that 40% of hypothenar and 100% of 1DI innervation was from median nerve at elbow, but ulnar at wrist, via a M-U crossover. Surgery revealed total interruption of the ulnar nerve at lesion site.

Conclusion: M-U crossovers should always be considered when unexpected clinical findings occur with proximal median/ulnar neuropathies.

. — 0190

203.

Cervical Lipomatosis, Hyperuricemia and Multisystem Neurological Degeneration

M. MAHARAJ, M. RUBIN, C. MELMED and L. PINSKY (Montreal, Quebec)

A 55 year old male presented with gradually progressive dysarthria, muscle weakness and gait disorder dating from early adult life. Family history was negative. Examination revealed a huge concentric cervical fat pad as well as gouty tophi over extensor surfaces of joints. Neurological examination disclosed optic atrophy, neurosensory hearing loss, facial diplegia and dysarthria, anterior neck weakness and marked scapulo-humeral and pelvi-femoral weakness and atrophy. Mild corticospinal signs were present as well as limb and gait ataxia. Routine laboratory findings included hyperglycemia, hypertriglyceridemia and hyperuricemia, with normal adrenal cortical function. Skin and sural nerve biopsies were normal. Muscle biopsy revealed chronic neurogenic atrophy with giant fibres and central nuclei. Electrodiagnostic tests were compatible with an anterior horn cell disorder.

The aggregation of the neurological and metabolic features in this patient closely resembles that described in other cases, some familial, under the eponyms Lanois-Bensaude or Madelung's disease. The coexistence of metabolic and neurological findings suggests a common (? genetic) pathogenesis. Investigations including erythrocyte hypoxanthine-guanine phosphoribosyl and adenine-guanine phosphoribosyl transferase assays were normal, excluding an adult form of Lesch-Nyhan syndrome. Hexosaminidase assays and search for dolichols were normal.

Speculation of a neurogenic pathogenesis for patients with focal adiposity will be presented.

. — 0191

204.

Suppression of Kindled Seizures by Cysteamine: Dependence on Injection-to-Kindled Seizure Interval

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

Hippocampal kindled rats were injected with cysteamine (ß-mercaptoethylamine — 200 mg/kg, IP) 4 hrs before or 2, 4 or 6 hrs after a kindled seizure. On the 24 hr kindling test, none of the rats in the 4 hr pre-injection group exhibited a stage 5 seizure. This suppression of kindled seizures lasted for 4 to 10 days in individual rats. In contrast, none of the rats in the 6 hr-post group, exhibited suppression; i.e., they all had a stage 5 seizure on the 24 and 48 hr test. The effect of injection 2 or 4 hrs-post was intermediate. In the 2 hr-post group, 2 out of 5 rats did not have a stage 5 seizure on the 24 hr test (the other 3 had stage 5 seizures). All these rats had a stage 5 seizure on the 48 hr test. In the 4 hr-post group, 3 out of 4 rats had stage 5 seizures on the 24 hr test, 4 out of 4 on the 48 hr test. Thus, the percentage of rats exhibiting suppression and the duration of the suppression is dependent on the administration-to-kindled seizure interval. We therefore conclude that the suppression of kindled seizures following cysteamine administration is not due to the cysteamine per se, but must be due to an interaction of the cysteamine with the kindling process.

. — 0192

205.

Evoked Potentials Studies in the Leudodystrophies

M. J. TAYLOR, L. J. DeMEIRLEIR and W. J. LOGAN (Toronto, Ontario)

The leukodystrophies are a group of inherited diseases, characterized by white matter degeneration, with variable clinical presentations and age of onset. Diagnosis can be made in some by enzymatic assays; others are confirmed only by brain biopsy or autopsy. Evoked potentials (EPs) are useful in revealing early diffuse demyelinating process, indicating lesions in the central (and/or peripheral) sensory pathways.

We studied EPs in 12 patients (4 mos. - 13 yrs), 6 metachromatic (m.l.d.), 2 Pelizeus-Merzbacher (P.M.), 2 Krabbes, one adrenal leukodystrophy (a.l.d.) and one Alexander's disease. ABRs were done in 11/12, SEPs in 5/12 and VEPs and ERGs in 6/12. The ABRs were abnormal in all patients, but the abnormalities varied with the leukodystrophy. Those with early onset leudodystrophy (P.M., Krabbes) had markedly abnormal ABRs with a loss of all waves except waves I and II, even though they were clinically diagnosed and studied as young as 4 mos. The m.l.d. and a.l.d. patients had prolonged interpeak latencies, particularly between waves I-III. The abnormalities appear to increase with clinical severity. Two patients (1.5 and 3 yrs) who had no clinical signs, but were positively diagnosed as m.l.d., also had abnormal ABRs, suggesting that it is useful as an early diagnostic test. The cortical SEPs were absent in all patients tested (except the a.l.d., who was clinically mild); all had cervical spinal SEPs within normal range, except the Krabbes patient studied. The ERGs were normal in all patients. The VEPs were normal in 2, had increased latencies in 2 and were absent in one; they did not seem to covary with clinical severity.

ABRs are the most valuable EPs in these disorders, in both differentiation and diagnosis. SEP and VEP abnormalities were not sufficiently characteristic to be helpful in classifying the leukodystrophies, but may be useful in documenting CNS degeneration.

. — 0194

206.

Positron Emission Tomography with ^{11}C-Choline in Human Subjects

S. GAUTHIER, M. DIKSIC, L. YAMAMOTO, J. TYLER and W. FEINDEL (Montreal, Quebec)

Biochemical parameters of cholinergic activity are severely altered in the cerebral cortex of patients suffering from Alzheimer's Disease. There is a great practical interest in developing an *in vivo* scanning technique that could quantitate the density of cerebral cholinergic innervation in man. Choline, the natural precursor of acetylcholine, crosses the blood-brain barrier when administered systemically and reaches the cholinergic synapses through a high-affinity uptake system. We have thus synthesized ^{11}C-choline and tested this tracer in three human subjects who volunteered and gave informed consent. One suffered from Huntington's Disease and had shown striatal hypometabolism on the ^{18}F-2-deoxyglucose PET scan; one suffered from moderately advanced Alzheimer's Disease with mild parietal and temporal hypometabolism on his ^{18}F-2-deoxyglucose scan; the last one was the spouse of an Alzheimer victim. Doses of up to 20mCi of ^{11}C-choline were administered intravenously in an awake resting state. In all three subjects a marked uptake of the tracer was visible in the cranium. Unfortunately kinetic studies from the time-radioactivity data indicated that there was no specific pharmokinetic pattern in the cerebral parenchyma as compared to the vascular compartment. These results suggest that ^{11}C-choline penetrates the brain in amounts proportional to the cerebral blood flow but that no significant incorporation of the tracer occurs in the parenchyma. This is possibly due to the small amount of labeled choline injected as compared to the cerebral precursor pool and the large amount of labeled choline absorbed in extracerebral tissues.

Supported by M.R.C. of Canada.

. — 0196

207.

Clinical and Laboratory Studies of a 15 Year Old Girl with Mild Sialidosis Type 2: A 15 Year Assessment

G. V. WATTERS, L. PINSKY, L. WOLFE and S. CARPENTER (Montreal, Quebec)

Sialidosis Type 1, normosomatic, (cherry red spot myoclonus syndrome) and sialidosis Type 2, a dysmorphic group have been identified in patients with decreased neuraminidase activity.

Our patient presented at age 5 months with opisthotonus, hepatosplenomegaly and mildly spastic legs. At age 8 months beta-galactosidase activity in white cells and skin fibroblasts was depressed to 10% of controls but was 2 to 10 times greater than GM gangliosidosis type 2 strains. An appendicial biopsy showed intraneuronal cytoplasmic bodies. At age 8 years, urine oligosaccharides showed a non-specific pattern consistent with a sialidosis. Neuraminidase activity in fibroblasts showed depressed activity at α 2-3 and α 2-6 linkages.

She talked and walked by 16 months. Motor performance has been normal since with no deterioration. Hepatosplenomegaly resolved around age 3. Over the past 10 years, intelligence has remained stable in the educable retarded range. She has good social skills.

Height and head circumference were at the 10th percentile until age 9 and then fell below the third percentile. A somatomedin level was low. Menarche was at age 14. Bone changes include a thoracic kyphosis. A cardiac murmer occurred at age 10 and has become more prominent though asymmetric. Echograms show thickened aortic and mitral valves. Her facies is difficult to assess due to her background.

She has not shown eye abnormalities, neural hearing deficits, epilepsy, myoclonus, or ataxia while her CT-Scans, EEG, nerve conduction studies, auditory brainstem responses have all remained normal.

This patient has shown a relatively benign clinical course with mild intellectual, growth, and cardiac deficits. Her biochemical studies indicate she has a variety of sialidosis type 2. Her clinical course compels cautious prognostication in this group of disorders.

. — 0198

208.

Roles of the Noradrenergic, Dopaminergic and Serotoninergic Systems in the Modulation of the ACTH Response to Stress by the Amygdaloid Central Nucleus

S. BEAULIEU, T. Di PAOLO and N. BARDEN (Ste Foy, Québec)

We have previously shown that the amygdaloid central nucleus (ACE) is involved in the control of the ACTH response to stress. This study was designed in order to assess the activity of the noradrenergic

(NE), dopaminergic (DA) and serotoninergic (5-HT) systems in various brain structures of normal or ACE-lesioned rats submitted to immobilization for a period of one hour. Brains from control or stressed animals were rapidly removed and frozen at −70°C until microdissected. The concentration of norepinephrine, dopamine, serotonin and their metabolites was measured by HPLC coupled with electrochemical detection and turnover rates determined. In intact animals, stress increased the NE activity and decreased the DA activity in the ACE while the 5-HT activity was not modified in any of the structures studied. In stressed animals, lesion of the ACE reduced the activity of the NE system in the bed nucleus of the stria terminalis, the paraventricular and arcuate nuclei of the hypothalamus and in the anterior and lateral hypothalamic areas. These latter two areas also exhibited decreased DA activity which may indicate the existence of a mechanism to compensate for the decreased noradrenergic activity in these structures. Lesion of the ACE increased the activity of the 5-HT system in the medial, basolateral and cortical amygdaloid nuclei of control or stressed animals. The same phenomenon occured in the hypothalamic dorsomedial, ventromedial and paraventricular nuclei as well as in the anterior hypothalamic area, but was partially reversed by stress. These results support the hypothesis that the NE and DA systems act, respectively, as stimulator and inhibitor of ACTH secretion, particularly in the ACE and in the anterior and lateral hypothalmic areas. The 5-HT system may also play an important role within particular amygdaloid nuclei well known for their high concentration of glucocorticoid receptors.

Supported by the MRC.

. — 0199

209.

Rapid Propagation of Seizure Activity in Epileptic Patients

J. GOTMAN (Montreal, Quebec)

Seizure activity, recorded by extracerebral or intracerebral EEG electrodes, often appears simultaneously in several locations. This may be either from the very onset or only after a focal onset and spread to several recording contacts. Although the rhythmic discharge seems then synchronous in several locations, small time differences of 5 to 50 msec can often be measured, indicating a lead of one location over others. We have developed the method of coherence and phase for this measurement and report on its use in analysing seizures recorded from 7 patients with intracerebral electrodes and 1 patient with subdural electrodes.

When seizures have clear focal onsets, the focus leads the discharge just after it has become widespread. In most instances this lead does not persist throughout the seizure. Either some other region takes over from the original focus and drives the discharge, or activity in various regions becomes asynchronous, indicating that they are probably discharging without direct influence on each other.

These observations indicate that regions outside the focus of onset do not simply respond passively to excessive discharge from the focus. Although these regions may not be capable of triggering seizures, they appear capable of sustaining seizure discharges independently of direct influence from the focus.

. — 0201

210.

Electrophysiological Demonstration of a Projection from Lamina I of the Medullary Dorsal Horn to the Medial Thalamus of the Cat

J. O. DOSTROVSKY and J. G. BROTON (Toronto, Ontario)

A recent anatomical study (Craig and Burton, J. Neurophysiol., 45, 443-466, 1981) has described the existence of a specific projection from lamina I of the spinal and medullary dorsal horns to nucleus submedius (SM) in the medical thalamus. We have investigated this pathway using antidromic stimulation techniques in 6 chloralose anesthetized cats. A tungsten stimulating microelectrode was stereotaxically placed in or adjacent to SM. Thalamic stimulation antidromically excited 45 neurons located in or close to lamina I of the medullary dorsal horn (trigeminal subnucleus caudalis). The mean latency of antidromic activation was 5.2 ms (range of 2.0 to 14.5 ms) corresponding to a mean conduction velocity of approximately 4 m/s and the threshold stimulation currents ranged from 3 to 120 μA (mean 37μA). All stimulation sites and some recording sites were verified histologically. This study has confirmed, using electrophysiological techniques, the existence of a direct pathway from the superficial medullary dorsal horn to the region of SM and indicates that it is composed of slowly conducting axons which are probably small diameter myelinated fibers.

Supported by the U.S.N.I.D.R.: JGB is an NIH postdoctoral research fellow.

. — 0202

211.

Specificity of the Serotoninergic Reuptake Mechanism in the Control of Cataplexy

R. GODBOUT and J. MONTPLAISIR (Montreal, Quebec)

Narcolepsy is a neurological syndrome characterized by two major symptoms: excessive daytime sleepiness (EDS) and cataplexy. Biochemical and pharmacological data suggest that different mechanisms are involved in the two symptoms. EDS implies most likely dopaminergic neurons whereas cataplexy could be related to 5-HT and/or ACh neuronal systems. In the present study we measured the effect of a selective 5-HT reuptake blocker, zimelidine, on diurnal and nocturnal symptoms of narcolepsy.

Method: Eleven narcoleptic patients were studied. Polysomnographic recordings (including anterior tibialis EMG) were preformed for three consecutive nights and five naps before and one month after treatment with zimelidine. All had sleep onset REM periods and no sleep apneas. Blood concentration of 5-HT was determined by HPLC. Cataplexy and anticholinergic side effects were evaluated by questionnaires.

Results: 1. Mean blood concentration of 5-HT was 127.8 ng/ml before and 25.6 ng/ml during treatment;
2. Cataplexy improved in all subjects and no anticholinergic effect was reported;
3. No effect on EDS was noted;
4. Nocturnal sleep was disrupted but remained unchanged after treatment;
5. Four patients presented periodic movements in sleep (PMS) before zimelidine. Two of these patients were free of PMS after treatment.

Conclusion: These results suggest that a single monoaminergic system, namely serotoninergic, is possibly involved in the control of human cataplexy.

. — 0204

212.

Akinetic Mutism and Parkinsonism: A Case with Two Distinct Dopaminergic-Deficient States

L. BERGER, S. GAUTHIER and R. LeBLANC (Montreal, Quebec)

We report a 21 year old patient with acquired aqueductal stenosis and hydrocephalus treated by ventriculo-atrial shunt. She developed several distinct episodes of akinetic mutism, each preceded by shunt malfunction and hydrocephalus, successfully treated by shunt revision. In addition, our patient developed parkinsonian features resistant to shunt revision but responsive to antiparkinsonian medications. The occurrence of the two distinct dopaminergically deficient states in the same patient illustrates well the clinical relevance of the separate dopaminergic pathways projecting to the cingulate cortex and to the striatum.

. — 0208

213.

Selective Posterior Rhizotomy in the Treatment of Spasticity

G. E. OUAKNINE (Montreal, Quebec)

Selective Posterior Rhizotomy (S.P.R.), was performed in 110 cases of spasticity (C.P.: 45; M.S.: 33; trauma: 25; degenerative diseases:6).

Age at operation ranged from 5 to 67 and the follow-up from 1 to 16 years. The S.P.R. consists of the microsurgical partial resection of each rootlet from L-1 to S-1 with preservation of the minute radicular arteries. The selective resection (from 1/2 to 2/3 of the "spastic rootlets") depends on the muscular testing and preoperative electrophysiological stimulation. The reduction of the nociceptive afferents reduces the spasticity in the corresponding muscular territory and also, unexpectedly, in the suprasegmental level.

A spectacular reduction of the spasticity of the lower limbs was observed in every case and painful spasms disappeared in 90% of the cases. Movements became more free allowing improvement of the sitting position, standing position and gait. Improvement of a neurogenic bladder was obtained in 22 cases. In patients observed up to 16 years, these results have persisted in 80% of the cases. Improvement of spasticity at the level of the upper limbs was noticed in 28 cases permitting improvement both in writing and feeding. Speech improved in 15 cases. This paradoxical improvement at the suprasegmental level has permitted a better social reinsertion and raises an interesting neurophysiological problem.

The S.P.R. is a benign operation without mortality or motor complications. Hypoesthesia, reversible in a few weeks, is sometimes noticed. Only 5 patients with extensive rhizotomy were left with persistent hypoesthesia. There are no sphincter disturbances if the rhizotomy does not extend beyond S-1. Bladder incontinence was observed in 6 cases. Contra-indications are bad general condition, severe mental retardation and abnormal movements.

. — 0209

214.

Synaptogenesis in the Mouse Cerebral Cortex Studied with Monoclonal Antibody mabQ155

A. V. PLIOPLYS and R. HAWKES (Quebec, Quebec)

As witnessed in abnormalities of dendritic spine morphology and number, such as in Down's syndrome, aberrations of synaptogenesis may underlie a number of human neuropathological conditions. MabQ155 selectively recognizes synaptic vesicles and thus is a useful probe of synaptogenesis in the developing mammalian nervous system. We have mapped the development of mabQ155-immunoreactivity in ventral frontal (area 13), anterior cingulate (area 24), motor (area 6), sensory (area 3), visual (areas 17 and 18a) and piriform cortical areas of C57 mice from birth through adulthood. This was done as a prelude to investigating cortical synaptogenesis in mouse mutant strains, as well as serving as a basis for comparative studies of human and other species material. At birth the intermediate zone is densely labeled by mabQ155 with slight labeling of the marginal zone and almost no labeling of the cortical plate. Already at birth there is a regional cortical variation such that the marginal zone of the piriform cortex is thicker and more deeply stained. At postnatal days P2 and P3 there is rapid spread of immunoreactivity into the cortical plate of the rostral neocortical areas such that by P4 and P5 the density of mabQ155-immunoreactivity is uniform, a pattern maintained through adulthood. Similar spreading takes place in visual cortical areas but is delayed, starting on days P3 and P4 and becoming uniform by P6. Another regional cortical variation appears during development of the marginal zone (subsequently layer 1) in area 24. Here layer 1 becomes thicker than in other cortical areas, a pattern maintained through adulthood, but unlike the piriform cortex is not more intensely labeled.

. — 0210

215.

Selective Staining of a Subset of Purkinje Cells in the Human Cerebellum with Monoclonal Antibody mabQ113

A. V. PLIOPLYS, J. THIBAULT and R. HAWKES (Québec, Québec)

MabQ113 is a monoclonal antibody raised against rat cerebellum which selectively stains Purkinje cells. Likewise, in mabQ113-immunoperoxidase stained sections of human cerebellum, deposits of reaction product are found only in Purkinje cells. The dendritic arborizations, cell body, and axonal processes are immunoreactive. In rat, mabQ113 reveals a series of parasagittal bands which run throughout the cerebellar cortex. The staining distribution in human cerebellar cortex likewise reveals heterogeneous staining but the pattern is a complex one and seems to be unlike the parasagittal banding found in the rat. In a number of human diseases Purkinje cell degeneration is not uniform throughout the vermis and cerebellar hemispheres. This is intriguing because it is possible that mabQ113+ and mabQ113− subsets of Purkinje cells may respond differentially to various pathological conditions, such as cerebellar dysgenesis, toxin exposure, and heredofamilial cerebellar atrophies.

. — 0211

216.

TRH Intrathecally Increases Arterial Pressure and Heart Rate in the Rat

K. YASHPAL, V. V. ROMITA, S. GAUTHIER and J. L. HENRY (Montreal, Quebec)

On the basis of anatomical and electrophysiological evidence thyrotropin releasing hormone (TRH) has been suggested as a possible chemical mediator of synaptic transmission onto spinal sympathetic neurones. The present study examined the effects of intrathecal administration of TRH on arterial pressure in the Sprague-Dawley rat anaesthetized with urethane. The intrathecal catheter was inserted to either the second or ninth thoracic spinal segment (T2 and T9, respectively). Arterial pressure and heart rate were monitored via another catheter in the left common carotid artery. TRH (6.5 nmoles in 10 μl of artificial CSF) increased arterial pressure and heart rate when it was given at either the T2 or the T9 level. At T2, TRH increased systolic and diastolic pressures by about 12 and 15mm Hg, respectively, the effect appearing about 2 min after administration, peaking at about 5 min and falling off slowly over the next 15-25 min. At T9, the increases were about 15 and 18 mm Hg respectively, and the time course was similar to that at T2. Heart rate increases were about 20 bpm at T2 and 25 bpm at T9; the maximum increase also occurred at about 5 min, but recovery was slower than that of the arterial pressure response. Our results support the suggestion that TRH may be a chemical mediator of synaptic transmission onto spinal sympathetic neurones and furthermore provide physiological evidence that its role may be excitatory.

Supported by the Quebec Heart Foundation.

. — 0212

217.

Insulin Resistance and Insulin Receptors in Friedreich's Ataxia (FA)

I. G. FANTUS, R. J. KHAN, B. I. POSNER, M. H. SENI and E. ANDERMANN (Montréal, Québec)

FA is an autosomal recessively inherited neurological disorder associated with a high prevalence of impaired glucose tolerance. To assess the role of insulin (I) secretion and I resistance (IR), we have compared glucose (G) and I responses to oral G in 11 subjects with FA and 9 age-matched controls (C). While basal levels were not different, both G and I responses were significantly higher in FA from 1 to 3 hours. The mean corrected I responses calculated from the OGTT were not different (0.71 ± 0.24 vs 0.51 ± 0.08, FA vs C) while peripheral I activity was significantly decreased in FA (0.77 ± 0.16 vs 1.38 ± 0.22, FA vs C, $p < 0.025$), indicating the presence of IR. A significant correlation between the degree of IR in subjects with FA and the duration of neurological symptoms was found ($r = 0.65$, $p < 0.025$).

To assess the role of receptors, insulin binding (IB) to dextran gradient fractionated and unfractionated red blood cells (RBC) (% specific binding/3×10^9 cell/ml) and to monocytes (M) (% specific binding/10^7 cells/ml) was determined. The youngest RBC fraction had the highest binding (9.72 ± 0.94 vs 12.6 ± 1.95, C vs FA), but no differences in IB between C and FA RBC were found. However, IB to M was significantly decreased in FA (4.51 ± 0.39 vs 6.29 ± 0.78, FA vs C, $p < 0.05$) associated with a decrease in receptor affinity.

We conclude that 1) the impaired glucose tolerance associated with FA is due to IR; 2) the IR correlates with the duration of neurological

impairment; 3) IB to M suggests that the IR may be partially explained by a receptor defect; and 4) IB to RBC and M do not always correlate even in the youngest RBC.

. — 0215

218.

Evidence of a Localized Diminution in Inhibitory Neuromodulation in Human Cerebral Cortex Underlying Epileptic Spike Foci

A. L. SHERWIN, E. MATTHEW and M. BLAIN (Montreal, Quebec)

A reduction of inhibitory control mechanisms in cortical areas likely contributes to the emergence of the characteristic high frequency spike discharge of the epileptic focus. The catecholamines play an important role in modulating cortical excitability and norepinephrine inhibits experimental foci. We studied brain tissue excised from over 200 patients with focal epilepsy and compared regions of spontaneous focal spiking and peripheral nonspiking areas. To date the following evidence of diminished inhibitory neuromodulation in the focus has emerged: A significant reduction in the number of alpha-1 postsynaptic adrenergic receptor sites (14/18 patients, $p < 0.01$, mean -20%). This defect could be the basis of a decrease in inhibitory noradrenergic efficiency. We also found a significant compensatory increase in the activity of tyrosine hydroxylase (14/14, $p < 0.001$, mean $+ 52\%$). This enzyme, which is responsible for catecholamine synthesis, is stimulated by presynaptic activation. A related decrease in the activity of $Na^+ K^+$ ATPase, a catecholamine dependent enzyme important in univalent cation transport, has previously been reported by Rapport. Regulation of these altered synaptic mechanisms by appropriate adrenergic agonists may offer a novel approach to future therapy.

. — 0217

219.

Hemispherectomy for Treatment of Epilepsy: Current Approaches

P. TINUPER, F. ANDERMANN, J. G. VILLEMURE, T. RASMUSSEN, L. F. QUESNEY and M. AVOLI (Montreal, Quebec)

In hemiparetic patients with no useful finger movement and incoercible seizures, hemispherectomy remains the surgical treatment of choice. Improved behaviour and cognitive function often follow, and may be related to reduction of interference from the often diffuse epileptic discharge.

Complete hemispherectomy is usually followed by loculation and increased pressure due to superficial pial hemosiderosis. In order to prevent this complication, partial but functionally complete hemispherectomy was devised (T. Rasmussen), leaving the frontal and/or occipital poles in place, disconnected but with vascular supply intact. This procedure was carried out in 16 patients.

Patients with a more normal contralateral hemisphere benefited most from the procedure. Severe mental retardation is the cardinal sign of malfunction of the "good" hemisphere.

Epileptogenic discharge may be more abundant and regular over the contralateral hemisphere. This is usually due to secondary generalization and is not a contraindication to the procedure.

The isolated cortical slabs retain the ability to produce striking epileptic discharges which have of course no clinical manifestation.

The concept of hemispherectomy continues to surprise beginners in the field, but the procedure greatly enhances the quality of life of both the patient and the family.

. — 0219

220.

Paroxysmal Alternating Hemiplegia in Infancy: Treatment With Calcium Channel Blockers

M-H. ST-HILAIRE, F. ANDERMANN, K. SILVER, A. HAKIM and N. MORRIS (Montréal, Québec) (Hamilton, Ontario)

This syndrome first described by Verret and Steele has emerged as a clinical entity which is still often diagnosed as epilepsy. Twenty-two cases have been described, and we present five additional patients. Characteristic features include onset before 18 months, and frequent attacks of alternating hemiplegia preceded by irritability and crying as if in pain. Transient ocular palsies, nystagmus and monocular nystagmus, dystonia, choreo-athetosis, tonic stiffening, autonomic dysfunction (respiratory embarrassment, tachycardia, mydriasis, diaphoresis) are also part of the attacks, which last from several minutes up to three weeks.

The patients deteriorate mentally and often develop fixed neurological signs or epilepsy. Follow up is up to 20 years. The relationship of this disorder to migraine is suggested by some of the clinical signs and the family history, but continues to be debated.

Vigorous treatment with propranolol and pizotyline seems to modify the intensity and freqency of the attacks. Nimodipine also modifies the clinical pattern, but does not stop the attacks. Flunarizine, also a calcium channel blocker, has been reported to control attacks almost completely, and a Canadian cooperative trial of this drug is underway.

. — 0220

221.

Secondary Paroxysmal Choreoathetosis

M. RUBIN, S. BERKOVIC, F. ANDERMANN and S. GAUTHIER (Montréal, Québec)

Paroxysmal kinesigenic choreoathetosis (PKC) is a well known genetic disorder that responds well to anticonvulsants. Only rare patients have been described who developed secondary PKC in association with their fixed neurological deficit. We present three patients with secondary paroxysmal choreoathetosis, two of whom had attacks induced by movement. The first patient had mild choreoathetosis and from the age of 9 months, developed attacks of violent choreoathetosis and dystonic posturing. She was treated unsuccessfully with a variety of medications.

The second patient had a longstanding ataxic disorder related to birth injury. At the age of 31 years, he began experiencing attacks of slurred speech, left hemibody weakness, stiffness and increased unsteadiness. These were unresponsive to medication as well.

The third patient had chronic encephalitis of the Rasmussen type with seizures and hemiplegia. She underwent hemispherectomy and after a seizure-free interval of 5 years, developed attacks of right upper and lower extremity dystonia, oculogyric crises and eyelid fluttering. These were readily precipitated by neck retroflexion.

All three patients were initially diagnosed to have epilepsy. However, these attacks can be distinguished from seizures induced by movement by the absence of frank clinical and electrographic epileptic manifestations. In all our patients, the attack did not respond to a wide range of medications, which produced abundant side effects.

. — 0221

222.

Postictal Serum Prolactin: Value in the Diagnosis of Seizures and Pseudoseizures

S. F. BERKOVIC, P. F. BLADIN and F. J. E. VAJDA (Montréal, Québec) (Melbourne, Australia)

The diagnosis of pseudoseizures remains a major problem in the management of patients with epilepsy. A lack of rise of postictal serum prolactin has been found to be characteristic of pseudoseizures. In comparison, postictal prolactin levels are elevated after most major epileptic seizures.

Prolactin levels do not rise after all epileptic seizures. Levels were not elevated after absences, myoclonic seizures and simple partial seizures, but these are rarely confused with pseudoseizures. Of greater importance is the failure of prolactin levels to rise after certain tonic-clonic and complex partial seizures.

Postictal prolactin levels were markedly elevated after isolated tonic-clonic seizures (baseline 5.6 ng/ml, peak 67 ± 5.1 ng/ml, n = 16). Following clusters of seizures, the peak prolactin level was significantly lower

(35 ± 4.6 ng/ml, p=0.001), and even lower levels were found during status epilepticus (9.0 ng/ml).

Prolactin levels were elevated following 40 out of 50 complex partial seizures (peak 42 ± 4.2 ng/ml). The level of rise of serum prolactin was not related to the length of the seizure, but rather to the extent of the electrical spread.

Measurement of serum prolactin is a simple way of clarifying the diagnosis of pseudoseizures in the setting of single attacks mimicking tonic-clonic seizures. The method is helpful, but less definitive, in the case of differentiating pseudoseizures from complex partial seizures, and in the setting of multiple seizures.

. — 0223

223.

Plasma Amino Acid and Genetic Studies in Epilepsy

N.A. JANJUA, E. ANDERMANN, O. EEG-OLOFSSON, K. METRAKOS, R. PALMOUR, B. LEMIEUX and R. GIGUÈRE (Montréal, Québec) (Sherbrooke, Québec)

The role of amino acids in epilepsy has become the focus of considerable interest in recent years. Investigations on epileptogenic brain tissue from experimental animals and humans have provided evidence for an altered amino acid metabolism in various forms of seizure disorders. Glutamic acid and taurine have most frequently been implicated. Altered amino acid levels have also been observed in blood, CSF, and urine of epileptic patients. Results of these investigations, however, have been variable. In the study of 3/sec spike-wave epilepsy, increased plasma levels of glutamic acid and decreased levels of aspartic acid and of taurine were found in both patients and their relatives (van Gelder et al., Neurochem. Res. 5 (6):659-671, 1980).

Recently, a study of plasma amino acids in epileptic patients and their families has been undertaken at the Montreal Neurological Institute. The main objective of this project is to determine plasma amino acids in well defined groups of epileptic patients and in their relatives. To date, amino acid analyses have been completed in 57 individuals: 14 probands with primary generalized corticoreticular epilepsy (A); 15 of their first degree relatives (B); 11 probands with partial epilepsy (C); and 17 of their first degree relatives (D) have been investigated. Of the 22 amino acids determined, only the mean plasma levels of glutamic acid and/or taurine were found to be significantly altered in the studied groups, as compared to controls (glutamic acid increased and taurine decreased: $p < 0.05$). The ratio of taurine/glutamic acid was significantly decreased in all groups investigated ($P < 0.001$ for groups A, C, and D; $p < 0.05$ for group B).

These preliminary results confirm the findings of van Gelder et al. with respect to glutamic acid and taurine, and suggest a genetically determined role for these amino acids in the etiology of both generalized and partial epilepsy.

. — 0224

224.

Evidence for Improvement of Intellectual Function Following Anterior Temporal Lobectomy

A. OLIVIER (Montréal, Québec)

Out of a personal series of 390 patients submitted to temporal lobectomy for intractable seizures, fifty (50) patients with speech representation in the left hemisphere were chosen, in whom both the pre- and the post-operative (one year) neuropsychological data were available.

The average pre-operative full scale I.Q. (FSIQ) for this group of fifty patients (both right and left-sided resections) was 96.5. When studied one year later, the FSIQ in the same group had increased to 105.6 — a gain of 9.1 ($P < 0.01$).

Thirty (30) patients had right-sided resections. Their pre-operative FSIQ of 97.7 reached 106.7 one year or more after surgery, a gain of 9.0 ($P < 0.10$). Twenty patients had resections on the left side; their FSIQ as a group was 94.7 pre-operatively and 104.0 after one year — a gain of 9.3 ($P < 0.05$).

In patients with right-sided resections, the pre-operative performance IQ tended to be lower (96.6) than the verbal one (98.8). After surgery, there was a gain in both quotients — but it was more striking in the performance (10.7 points) than in the verbal test (6.0). In patients with left-sided resections, the verbal IQ (93.4) was lower than the performance IQ of 96.5; both improved following surgery — with a gain in the performance quotient (9.5) being also greater than the verbal one (7.9).

Data will also be given concerning the memory scores. When correlated with the results on the seizure tendency and the levels of anticonvulsant medication, these figures provide additional evidence that the resection of an actively discharging epileptic focus decreases its nociceptive effects on other areas of the brain.

. — 0225

225.

Case Study of Cyproheptadine/Periactin as an Antispastic Agent

H. BARBEAU, M. WAINBERG and S. GAUTHIER (Montreal, Quebec)

Preliminary observations suggest that the serontonin antagonist, Cyproheptadine/Periactin® is beneficial in patients suffering from spasticity due to spinal cord trauma (Barbeau, H., Richards, C. and Bédard, P., J. Neurol. Neurosurg. and Psychiat. (1982) 45: 923-926). A marked decrease in the number of spasms and clonic episodes was noted and improved locomotor function was subjectively reported. The present investigation examines the effect of Cyproheptadine on spasticity and spastic paraparetic gait.

While taking Cyproheptadine, a spastic paraparetic patient was able to walk on a treadmill with 20 and 40% of body weight supported externally (EWS). Selective proximal movements such as hip flexion were 'unmasked' and certain functional activities (dressing, transfers) were facilitated during Cyproheptadine therapy. An increase in appetite was subjectively reported. Following termination of Cyrpoheptadine therapy, spontaneous sustained clonus was noted and nocturnal spasms worsened to interfere with sleep. Locomotor performance deteriorated and was impossible at FWB, while at 20 and 40% EWS the number of steps per trial was reduced (20-25 to 6-10) and the effort required was greatly increased as evidenced by a precipitious rise in heart rate.

This case forms part of a larger trial currently in progress studying the effects of Cyproheptadine on spasticity and spastic paraparetic gait.

. — 0227

226.

Parasagittal Bands in Rat Cerebellar Cortex Produced by Selective Repression of Antigen Expression

N. LECLERC, C. GRAVEL, A. PLIOPLYS and R. HAWKES (Québec, Québec)

We have produced a library of monoclonal antibodies against the P15 rat cerebellum. One of these, mabQ113, recognizes a polypeptide antigen which is confined exclusively to the Purkinje cells. In the adult cerebellum not all Purkinje cells contain the Q113 antigen. Bands of $Q113^+$ cells run rostracaudually through the cerebellar cortex interposed by similar $Q113^-$ zones. The arrangement of bands is symmetrical about the midline with a central band and three others laterally in the vermis and a more complex, but highly reproducible, display of bands in the hemispheres.

MabQ113 has been used to investigate Purkinje cell maturation and the development of longitudinal zonation in the rat cerebellar cortex. We first observe mabQ113 immunostaining at postnatal day 7 (P7) in a posterior vermis as a weak coloration of the Purkinje cell soma and developing dendritic tree. At P9, some Purkinje cells express the Q113 antigen in the anterior and posterior vermis. In the next days, all Purkinje cells become $Q113^+$ in the vermis and in the cerebellar hemispheres. The first signs of differential staining start to emerge at P12, with the Purkinje cells destined to become the vermal $Q113^+$ triplet of bands staining more intensely than their neighbours. The

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distinction between Q113$^+$ and Q113$^-$ zones is clearly visible in the vermis by P15 although in the hemispheres the great majority of Purkinje cells are still Q113$^+$. The ectopic Q113 expression gradually disappears during the third and fourth weeks and the mature pattern of bands is established by P30.

It is not known if differential expression of antigen Q113 is an intrinsic property of Purkinje cells or a secondary response to cell position or connectivity.

Supported by M.R.C., F.C.A.C. and Fonds Paralysie Cérébrale.

. — 0230

227.

Non-uniform Distribution of the Spontaneous Release at the Frog Neuromuscular Junction

R. ROBITAILLE, J.P. TREMBLAY and G. GRENON (Québec, Québec)

A new method is described in order to study the distribution of spontaneous release along the frog neuromuscular junction (nmj). Up to now, the investigators used extracellular recording to analyse the distribution of quantal release at the frog nmj. However, the spatial decay method presented here to study the spontaneous release used simultaneous recording with two intracellular electrodes. The electrodes were positioned at the distal ends of the nmj using Nomarski optic and the MEPP amplitudes (A_1 and A_2) were recorded simultaneously in electrode 1 and in electrode 2. The amplitude A_1 is different of the amplitude A_2 and the amplitude ratio (A_1/A_2) varies from one MEPP to the following. The method is based on the assumptions that the MEPP is due to the release of neurotransmitter at one active zone and that the MEPP amplitude decays exponentially along the muscle fiber. With these assumptions, it is possible to evaluate the space constant λ for a given muscle fibre. The closer the release occurs from elect. 1, the higher will be the ratio A_1/A_2. At the limit, the highest ratio for 2000 MEPPs can be considered to occur at or very close to electrode 1. Therefore, the space constant λ can be evaluated using the distance D between the two electrodes and the highest amplitude ratio: $\lambda = D/\ln(A_1/A_2)$. Using λ, it is then possible to calculate for any MEPP the distance (X) between elect. 1 and the release site: $X = (D - \lambda \ln (A_1/A_2))/2$. The distance X was calculated for 2000 MEPPs in each preparation and a freqency distribution of the release site distances was made. This shows that the occurrence of spontaneous release is not uniformally distributed along the nmj, i.e. it is less frequent at the distal end and it is polymodally distributed along the nerve terminal.

. — 0231

228.

Elevation du Taux des Catécholamines et Anomalies de la Contraction Ventriculaire Chez Les Patients Porteurs de Dystrophie Musculaire de Duchenne

M. VANASSE, A. PASTERNAC and J. de CHAMPLAIN (Montréal, Québec)

La dystrophie musculaire de Duchenne (DMD) est caractérisée par un défaut génétique régional affectant le métabolisme et la perfusion myocardique de la paroi postérieure du ventricule gauche. Pour tester la relation entre cette anomalie et la fonction adrénergique nous avons mesuré le taux des catécholamines (CA) plasmatiques (norépinéphrine, épinéphrine et dopamine (DA)) chez 12 garçons âgé de 8.0±0.3 ans et quantifié la dynamique ventriculaire par échocardiographie.

Conclusion: 1) le taux des CA plasmatiques est élevé dans DMD; 2) la fonction ventriculaire est déprimée; 3) il existe une corrélation entre les paramètres du mouvement de la paroi postérieure et le taux de DA en position couchée. Ces données suggèrent que les CA pourraient jouer un rôle dans la pathogénèse des cardiomyopathies de DMD.

. — 0232

229.

Plasma Catecholamines in Obligate Heterozygotes of Friedreich's Ataxia (FA)

A. PASTERNAC, E. ANDERMANN, H.M. SENI, S. MELANÇON, G. GEOFFROY, J. de CHAMPLAIN and A. BARBEAU (Montréal, Québec)

In a previous study, significantly increased levels of total plasma catecholamines, in particular norepinephrine (NE) and epinephrine (E) were found in 23 patients with classical FA, as compared to controls, both in the supine and standing positions (Pasternac et al., Can. J. Neurol. Sci. 9(2): 195-203, 1982). These findings were positively correlated to the degree of neuromotor impairment, as well as to the presence of cardiomyopathy, as evaluated by echocardiography.

In view of the previous evidence for an increased frequency of ECG abnormalities in asymptomatic parents and siblings of FA patients (Andermann et al., Can. J. Neurol. Sci., 3(4):287-298, 1976), and the autosomal recessive nature of the disorder, we have decided to carry out plasma catecholamine determinations in relatively young parents of FA patients, in order to determine whether obligate heterozygotes would also show these abnormalities.

A preliminary study on 8 parents (4M, 4F) with mean age 48.6 years was carried out. The systolic blood pressure ± SEM was significantly elevated in these parents in both the supine and standing positions ($p < 0.01$), as was the heart rate ($p < 0.02$), but there was no change in diastolic pressure.

The free catecholamine levels were significantly elevated, as follows: NE supine: mean ± SEM in parents: 235.88 ± 27.96 vs 169.1 ± 12.0 pg/ml in controls ($p < 0.05$); Dopamine standing: 43.5 ± 14.95 pg/ml vs 25 ± 5.0 pg/ml ($p < 0.05$). No significant differences were found in the E levels.

In view of the above findings, further studies would seem to be indicated to rule out a genetically determined abnormality of catecholamines in carriers of the Friedreich's ataxia gene. Abnormalities in glucose tolerance in FA heterozygotes have previously been described (Tolis et al., Can. J. Neurol. Sci., 7(4):397-400, 1980).

These studies have important implications from the point of view of genetic counselling, carrier detection, prevention and treatment.

. — 0233

230.

Hydrocephalus: VEP and Cranial Ultrasound Measures

S. G. COUPLAND and D. D. COCHRANE (Calgary, Alberta)

Previously we have reported visual evoked potential (VEP) alterations with increasing intracranial pressure (ICP) in hydrocephalic infants with shunt obstruction. In a group of 23 infants, VEPs were found to undergo partial or complete normalization following surgical intervention. This investigation attempted to assess the relationship between the VEP measures and ventricular size in hydrocephalic patients.

Electrophysiological studies were performed on 30 hydrocephalic patients (aged 1 day - 26 months, mean = 7½ months) within 24 hours of cranial ultrasound examination. Monocular flash VEPs were recorded over left and right hemispheres and a 7-point scale of normality-abnormality was derived. In addition, a 4-point scale of clinical assessment of ICP was also obtained. Using cranial ultrasounds, the coronal and parasagittal views of the lateral ventricles were digitized and ventricular widths, lengths, perimeters and areas were measured. Lateral ventricular volumes were then computed from these measures and correlated with both the flash VEP and clinical parameters obtained.

The results of this study confirmed our previous investigations in demonstrating a highly significant correlation between flash VEP scores and the clinical grading of ICP. Both computed volume and area measures of the lateral ventricles taken in the coronal and parasagittal planes were not found to be significantly related to VEP scores or to the clinical assessment of ICP. The only specific ultrasound measure which significantly correlated with VEP score and clinical grade was the lateral ventricle perimetry taken in the parasagittal plane.

. — 0234

231.

Conditioned Odour-Aversion Learning Following Total and Selective Amygdaloid Lesions in Rats

N. BEAULIEU and M. PETRIDES (Montreal, Quebec)

The present study investigated the contribution of the amygdala, and its main subdivisions, to the acquisition of a conditioned odour aversion. Rats with large lesions of the amygdala, or selective lesions of the basolateral or corticomedial amygdaloid nuclei, were tested for their capacity to develop an aversion to an odour (isoamyl acetate) that was paired with Lithium Chloride (LiCl) toxicosis. The animals were water-deprived and exposed to three odour-LiCl pairings on three different drinking sessions; the acquired aversion was measured as a suppression of water-drinking in the presence of the odour. Large lesions of the amygdala caused a severe deficit, which appeared after the second pairing session. Damage to the basolateral amygdaloid nuclei also resulted in a clear attenuation of the odour aversion, whilst damage to the corticomedial nuclei did not significantly alter the animals' performance. The observed deficit was interpreted as a disorder in the ability to form associations between neutral stimuli and aversive consequences following lesions of the amygdala, and more specifically its basolateral subdivision.

. — 0236

232.

Prolapsus Mitral: Récidive D'Embolie Cérébrale Sous Héparine

D. SIMARD (Québec, Québec)

La survenue d'embolies cérébrales chez les malades porteurs d'un prolapsus de la valve mitrale est actuellement bien connue. Il est par ailleurs habituellement accepté, lorsque l'on est en phase aigue d'un ramollissement non hémorragique prouvé d'origine embolique, de placer ces malades sous héparine et même de les anticoaguler à plus ou moins long terme.

Nous avons observé récemment dans notre milieu au cours de la même hospitalisation une récidive d'embolie cérébrale chez deux jeunes patients âgés de 19 et 26 ans, porteurs de prolapsus mitral alors que ces malades étaient sous héparine. Ces récidives d'embolies cérébrales ont été prouvées par une deuxième angiographie cérébrale ou le nouvel embolus est démontré et qui de plus démontre dans un cas la recanalisation de l'artère préalablement obstruée par le premier embolus.

Cette récidive d'embolies cérébrales originant d'un prolapsul mitral, prouvé cliniquement et échographiquement, est rare et le fait que ceci soit survenu chez des patients héparinés nous améne à revoir la physiopathologie et surtout le traitement en phase aigue de ces embolies.

Ceci sera dicuté et les documents seront présentés.

. — 0237

233.

Retrograde Effects of Chronic Axotomy on Neurons and Axons of the Rat Sural Nerve

L. F. CHARRON, J. M. PEYRONNARD, J. LAVOIE, J. P. MESSIER and F. X. BERGOUIGNAN (Montréal, Québec)

In an attempt to solve ambiguous evidence on the ultimate fate of adult primary neurons permanently axotomized, the HRP served as a cell marker to label the motor, sensory and postganglionic sympathetic neurons of the rat sural nerve which had been sectioned at the ankle and prevented to regenerate for periods up to 80 weeks. Contrasting with an absence of effect on sympathetic neurons, axotomy resulted 4 weeks later in a sudden reduction in the number of labeled sensory and motor cells which persisted unchanged to the end of the study. In this missing neuronal population amounting to 41 and 46% respectively of the normal sensory and motor contingent, the vast majority of large afferent and efferent neurons were included. However, examination of sural nerves at thigh level away from the neuroma revealed marked axonal atrophy but no change in the number of myelinated and unmyelinated fibers up to 52 weeks after axotomy. Prolonged survival of the peripheral process indicates that axotomized neurons can live through long term detachment from their end organ and that HRP unlabeling of certain sensory and motor neurons does not imply their degeneration but most likely expresses one of many retrograde dysfunctions triggered by axonal lesions.

. — 0238

234.

Our Experience in the Use of Acetylcholine Receptor Antibody Assay to Diagnose Myasthenia Gravis

J. OGER, R. KAUFMAN and D. W. PATY (Vancouver, B.C.)

We have been measuring acetylcholine receptor antibody (AchR-Ab) levels by a technique derived from J. Lindstrom. Briefly, acetylcholine receptor extracted from human muscle is incubated with I^{125} alpha bungarotoxin, 10µl of serum to be tested is then added. After overnight incubation at 4°C, complexes are precipitated by staphylococcus A. Pellet is then washed and counted in a gamma counter.

In each experiment counts precipitated in the presence of sera to be tested are compared to those obtained with sera from normal healthy individuals. Sera are considered negative (−) if they do not precipitate more than the mean plus two SD of the control sera in parallel (95% confidence). Samples are then considered borderline (±) if they precipitate more than the mean of the healthy control population plus one SD but less than the mean plus two SD. Sera giving negative and borderline results are systematically reassayed on a second preparation. Our experience for the first 9 months of use of this assay stands as follows:

	+	±	−
generalized MG (21)	20	0	1
remission (4)	0	0	4
ocular MG (6)	4	0	2
other neurological diseases (16)	0	1	15
healthy controls (40)	0	0	40

To summarize: On repeated testing, 95% of generalized MG show increased levels of AchR Ab when only 1/56 (2%) non MG samples showed borderline elevation. As these numbers are comparable to published results, we have recently made this assay available for clinical purposes across Canada.

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Enhanced Release of Acetylcholine by Diaminopyridine from Quinolinate-Lesioned Striatum

R. J. BOEGMAN, K. JHAMANDAS, R. J. BENINGER and L. SHIPTON (Kingston, Ontario)

The endogenous tryptophan metabolite, quinolinic acid (Quin) causes neuronal lesions following injection into discrete areas of the brain. Since a role for Quin in the cholinergic hypofunction associated with Alzheimer's Disease has been postulated, we were interested in the effect of drugs on the release of acetylcholine (ACh) from Quin-lesioned tissue. A unilateral partial lesion of the right striatum was made in adult rats by infusing Quin. This resulted in a 30% reduction in striatal cholineacetyltransferase activity. The release of ACh from striatal slices was studies using ^{3}H-choline and a superfusion chamber. K^+-evoked release of ^{3}H was 35-40% lower in slices prepared from Quin-lesioned striata. In contrast, diaminopyridine (DAP)-evoked release of ^{3}H was the same in both lesioned and non-lesioned striata. This finding suggests that DAP may be useful in enhancing release of ACh from the brain under conditions of cholinergic hypofunction.

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