β-CIT SPECT showed a bilateral striatal presynaptic damage resembling idiopathic Parkinson's disease. L-DOPA treatment improved the resting tremor.

We performed a systematic review of the literature by means of multivariate statistical techniques (Multiple Correspondence Analysis, Logistic Regression). 223 out of 255 cases of KD, selected from 51 papers published within the period 1968-1996, were considered for analysis. No associations between KD and IPD were reported, even if the comorbility of motoneuron diseases and extrapyramidal disorders is considered a non-casual event.

The differences among symptoms at the onset, clinical progression and outcome allowed us to define some phenotypical sub-groups of the disease. The complete clinical picture was observed only in 20% of the cases; the neurological symptoms were always present, while the signs of androgen insensitivity (gynecomastia, impotence, testicular atrophy) occurred in 30% of the whole sample. The muscular atrophy showed a proximal distribution in 86% of cases. Tremor was usually of postural type, sometimes with a kinetic component. Resting tremor was anedoctally described (1%), without other symptoms and signs of extrapyramidal disorders. Phenotypical differences and clinical severity of the disease appeared to be influenced by the race: in the yellow race the neurological symptoms and the disease progression were more severe. The endocrinological pattern was more pronounced in the white race. No reports were recorded on KD in the black race.

1-02-11 Spinal muscular atrophy: Etiology and pathogenesis

Suzie Lefebvre, Deborah Bartholdi [1], Pierre Miniou [1], Arnold Munnich, Judith Melki [1]. *INSERM, Unit 393, Hôpital des Enfants Malades, Paris, France,* [1] *Institut de Génétique et de Biologie Moléculaire et Cellulaire, INSERM, CNRS, U.L.P, C.U. de Strasbourg, France*

Spinal muscular atrophy (SMA) is a common fatal autosomal recessive disorder characterized by degeneration of lower motor neurons. The survival of motor neuron (SMN) gene has been identified as the determining gene of SMA. SMN encodes a protein located within a novel nuclear structure and interacting with RNA binding proteins. These results suggested that SMN might have a role in nuclear post-transcriptional mechanism of RNA metabolism.

The SMN protein analysis showed a strong correlation of the amount of the SMN protein encoded by the homologous gene copy (SMNc) with the clinical severity of the disease in a large cohort of patients (n = 52), independent of the deletion of the neighbouring genes NAIP or p44. Thus, these results provided the first molecular basis of a severe (type I) or a mild form of the disease (type III). Since the different phenotypes of SMA strongly correlate with the SMNc protein level, the SMNc gene can be considered as a modifying gene in SMA. Therefore, the hyperexpression of the SMNc gene should represent an attractive strategy for therapy in SMA.

No mouse models whose disease locus would map to the 5q13 syntenic region are available. The creation of animal models for this disorder by SMN gene targeting should allow the understanding of the biological bases of motor neuron degeneration which characterizes this devastating and frequent disorder and should assist in the development of therapy.

1-02-12 Measurement of colonic transit time in patients with amyotrophic lateral sclerosis

M. Toepfer, M. Schroeder, H. Lochmüller, A. Klauser, R. Riepl, M. Schlosshauer, S. Werner, W. Müller-Felber, D. Pongratz. *Friedrich-Baur-Institut, Ludwig-Maximilians-University, 80336 Munich, Germany*

Background: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder, characterized by progressive loss of motor neurons. However, ALS has been recognized to involve subclinically several non-motor systems. Cardial and sudomotor autonomic involvement in ALS has been described. Delayed gastric emptying of solids as a gastrointestinal autonomic involvement was reported recently. Measurement of colonic transit time using radio-opaque markers has been proved as a noninvasive and reliable test.

Methodes: We have investigated 10 patients with ALS and 12 healthy age-matched volunteers. None of the patients has had diabetes or other disorders combined with autonomic dysfunction, none had known gastrointestinal disorders. The patients swallowed a gelatine capsule which contained 20 radio-opaque pellets on each of 6 consecutive days at the same time. On day seven a single abdominal x-ray was obtained. Segmental and colonic transit times were calculated from the number of retained pellets.

Results: 9 of 10 patients with ALS showed markedly delayed colonic transit times whereas healthy controls all had normal colonic transit times. Colonic transit was delayed in all colonic segments of ALS patients.

Interpretation: Delayed colonic transit times in patients with ALS encourage the theory of possible gastrointestinal autonomic involvement in ALS.

1-02-13 Inhibition by excitatory sulfur amino acids of glutamate transporter in rat brain cortical synaptosomes

Y. Yoshino [1], K. Kuroda [1], H. Homareda [2]. [1] *The First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan,* [2] *The First Department of Biochemistry, Kyorin University School of Medicine, Tokyo, Japan*

The elevation of taurine in neural tissue of amyotrophic lateral sclerosis (ALS) suggests that excitatory sulfur amino acids (ESAAs), the intermediates of the metabolic pathway toward taurine could also be increased. Since the reduction of glutamate transporter has been reported in ALS, we studied effects of ESAAs on the transport of glutamate in synaptosomes obtained from rat cerebral cortices. Synaptosome fractions were prepared by discontinuous density-gradient centrifugation, and were incubated at 35°C with varying concentrations of L-[^{3}H] glutamate in the absence or presence of ESAAs; cysteine sulfinic acid (CSA), cysteic acid (CA), homocysteine sulfinic acid (HCSA), homocysteic acid (HCA) and S-sulfocysteine (SC). Kinetic characterization of uptake confirmed the high-affinity nature of the transport system, the Michaelis constant (Km) for glutamate uptake being 10 μM. The inhibition pattern was found to be competitive. Among the 5 ESAAs used, CSA and CA showed potent inhibition of transport, while HCSA showed substantially weaker inhibitory effects, and HCA and SC almost no effects. Possible involvement of ESAAs in the pathogenesis of ALS will be a subject in future study.

1-02-14 Excitatory amino acids abnormalities in motor neuron disease: Clinico-neurochemical study

I. Zavalishin, K. Airapetian, S. Nikitin, V. Barchatova, N. Savitskaya. *Department of Neuroinfections, Institute of Neurology, Moscow, Russia*

Degenerative motor neuron disease (MND) is definitely characterized by neurochemical changes. Till now in many studies the conflicting results were published about the role of different neuroactive substances and significance of changes of their concentrations in MND. In 51 patients with amyotrophic lateral sclerosis (ALS); male – 30; female – 21, age – 51.8 ± 11.2; according to the predominance of the clinical signs at the beginning of the disease they were classified: 12 – bulbar disturbances; 29 – cervico-thoracal; 10 – lumbo-sacral symptoms). In all patients the concentrations of glutamate (GLU) and glycin (GL) were detected in cerebrospinal fluid (CSF) and compared with control (20 diagnostic patients without neurological disease, age 34–71). There were no correlation between the changed concentrations of GLU, GL and the duration of the disease, sex, and age of ALS patients. In all patients the level of GLU was increased to 0.71 ± 0.11 in comparison with the control of 0.45 ± 0.04 mmol/l ($p < 0.05$); the concentration of GL was increased to 5.8 ± 1.3 mmol/l in comparison with the control level of 4.2 ± 0.5 mmol/l ($p < 0.05$). At the same time there it was observed that increased GLU concentration in patients with generalized and mostly pronounced neurological symptoms, maximal EMG changes of the motor units parameters, slight central motor conduction time elongation and increased excitatory threshold of the cortical motor neurons tested by transcranial magnetic stimulation. The GLU concentration in these patients was 0.75 ± 0.06 mmol/1; in all the rest patients with ALS – 0.62 ± 0.03 mmol/l. Despite the fact that CSF concentration of analyzed substances does not reflect the concentration in the central nervous system, the revealed changes of CLU (which is an excitatory neurotransmitter) levels in MND confirm its contribution to neuronal death in MND.

04 Bacterial, Fungal & Viral Infections of the Nervous System

1-04-01 Tuberculous meningitis: Review of 200 patients

S. Baig. *Department of Medicine, The Aga Khan University Hospital, Karachi, Pakistan*

Tuberculous meningitis (TBM) is a commonly encountered infection of central nervous system (CNS) in developing countries. A review of 200 cases (120 females) is presented. The diagnosis of TBM was based on clinical manifestations, cerebrospinal fluid (CSF), and CT scan findings. Their age ranged between 15–70 years (mean 27 years). Ninety percent of the patients had fever of variable duration 5–120 days (mean 20 days). The cranial nerve palsies were other most common associated neurological findings. 70% of the patients presented in stage 2, 20% in stage 1, and 10% in stage 3, according to