FIRST INTERNATIONAL CONGRESS
of the
POLISH NEUROSCIENCE SOCIETY

ABSTRACTS

Warsaw, 21-23 September 1992
A Congress in the Decade of the Brain

Part 1

(Part 2, the symposial papers, will be supplemented to Vol. 53, No 1)
THE DECADE OF THE BRAIN: AN INTERNATIONAL FOCUS ON NEUROSCIENCE RESEARCH

M. Goldstein, Bethesda

Plenary lectures

L1

THE DECADE OF THE BRAIN: AN INTERNATIONAL FOCUS ON NEUROSCIENCE RESEARCH

M. Goldstein, Bethesda

Monday, Plenary lectures ...

L2

History of Neuroscience with Special Reference to Polish Contributions

K. Karbowksi, Berne, Switzerland

About 400 B.C. Hippocrate believed that the site of the disorder in epilepsy was in the brain. Besides "major attacks" he described several other neurological diseases. Galen (129-200 A.D.) studied the anatomy and pathophysiology of spinal cord. In the Renaissance period scientific anatomy was developed by Leonardo da Vinci and Vesalius. In the "Cerebri anatome" of Willis, edited 1664, the word "Neurology" was used for the first time. The neuroanatomic and neuroclinical knowledge was developed in the 16th Century by Soemmering, Morgagni, Haller, Tissot and others. In 1768 Galvani discovered electrical properties of excised tissue. In the 19th Century the anatomic studies of Rolando, the pathophysiological experiments of Hitzig, Fritsch, Ferrier and the clinical observations of Jackson formed the topical diagnostics of the brain. The neurological semiology was developed by Semmberg, Charcot, Duchoene, Dejerine, Gowars, Babinski and others. 1875 Caton investigated the electrical activity of the brain in rabbits. Polish physiologists Beck and Cybulski explored this activity 1891 - 1914 in more details. Clinical neurology in Poland was founded at the end of 19th Century by Eduard Flatay. International neurological reputation was also obtained by many other Polish doctors, for example by Brudzinski, Fajersztajn, Goldfian and Rose.

Symposium (S1) - Alzheimer’s disease

S1.1

EPIDEMIOLOGY AND CLINICAL ASPECTS OF ALZHEIMER’S DISEASE (AD)

Anaducci L., Lippi A.

Department of Neurological and Psychiatric Sciences, University of Florence, Florence, Italy

AD was described by Alzheimer (1907) as characterized, from a pathological point of view, by the presence in the brain of "typical" lesions such as neurofibrillary tangles and senile plaques. No close correlation between the clinical picture and the pathological findings has been demonstrated, and "new pathological findings" (i.e. Lewy bodies) have been described in clinically diagnosed AD. The epidemiology of clinically diagnosed AD also underlined the heterogeneity of the disorder. Prevalence rates of AD are estimated to range from 0.6 to 10.3 cases per 100 (65). Prevalence and incidence rates of AD exponentially raise with age and are higher in females. Case-control studies highlighted risk factors related to a genetic hypothesis, such as dementia in first-degree relatives and late-maternal age. The meta-analysis of case-control studies conducted to date confirmed the association of AD with genetic factors and a true difference in relative risks for late-onset AD between those who have an affected sibling and those who have an affected parent was turned out. Moreover, the risk of AD was significant different for those with two or more first-degree relatives with dementia as compared to those with one. Among environmental factors, the role of a previous head trauma as a risk factor is suggested by a number of studies. In summary, the analytic studies seem to suggest that the most important risk factor in AD is the advanced age, suggesting that the problem of the definition of AD have to be reconsidered on the basis of data on the aging process.

NEUROPATHOLOGY OF ALZHEIMER DISEASE - CURRENT CONCEPTS OF LESION DEVELOPMENT H.M. Wisniewski and J. Wegiel. NYS Institute for Basic Research in Dev. Dis., 1050 Forest Hill Road, Staten Island, NY 10314, USA

Plaques, intraneuronal accumulations of paired helical filaments (PHF) in the form of neurofibrillary tangles, and neuronal loss are the basis for neuropathological diagnosis of Alzheimer disease (AD). Our studies show that s-amyloid fibril deposition in the neuropil initiates plaque formation. This process is associated with secondary neuronal and astrocytic changes. Synapses and nutritive processes degenerate, usually with PHF accumulation. Proliferating astrocytic processes penetrate the amyloid deposits and cause fragmentation and dispersal of amyloid aggregates, with gradual degradation of amyloid fibrils. Amyloid deposition in the wall of the vessel causes degeneration of endothelial cells and reduction or obliteration of the lumen of vessels, with local ischemic degeneration of the neurons.

Our studies of the routes of migration of microglial cells in AD, aging, and scrapie brain suggest that perivascular cells derived from a bone-marrow precursor enter the CNS and produce amyloid fibrils in the vascular wall. When these cells migrate into the neuropil they initiate the formation of the primitive, classical and diffuse plaques. The identification of these cells as a place where s-amyloid fibrils are made is as important as Glenner and Wong’s findings concerning the sequence of vascular amyloid from AD brains. Glenner’s studies led to the discovery of a novel protein - the amyloid precursor protein (APP) gene and the chromosome on which the APP gene is located. We expect that the discovery of the cells making amyloid fibrils will lead to their isolation and to the identification of the genetic and/or biochemical defect(s) responsible for failure of these cells to properly make or process the APP, with tragic consequences to the AD victim. It provides also a new approach to developing therapy for AD.
1.3 MOLECULAR PATHOLOGY OF ALZHEIMER NEUROFIBRILLARY DEGENERATION, Khalid Iqbal and Inge Grundke-Iqbal, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY 10314, USA.


1.4 HIPPOCAMPAL ATROPHY IN ALZHEIMER DISEASE - MRI STUDIES.

Olgerd Narkiewicz1 and Mony J. De Leon2/3/; Y Department of Anatomy, Medical School, Gdansk, Poland 1/Aging and Dementia Research Ctr., New York University Medical Ctr., New York, NY, USA.

The pathology of the hippocampal formation in AD is so severe that it has been characterized by some authors as a hippocampal dementia. The hippocampal atrophy seen in CT and MR images correlates with the presence and severity of AD. In cross-sectional and longitudinal radiological studies of AD it has been demonstrated that the hippocampal atrophy is of diagnostic and predictive value.

MRI offers a high-resolution non-invasive method for quantifying volumetric changes of the hippocampal formation and parahippocampal gyrus. In most cases the shape of the hippocampal formation seen in MRI alters. It is due to the different degree of atrophy of various hippocampal areas. CA1 area, subiculum, entorhinal cortex and parahippocampal isocortex belong to the most affected.

The ventricular and sulcal dilatation in normal aging overlap considerably with the changes seen in AD. However, it has been found that the transverse fissure of the brain reflects well the hippocampal atrophy in AD and may serve as an indicator of the progress of the disease.

1.5 The Epidemiology of Presenile Dementia in Scotland 1974-1988

Authors L.J.Whalley, G.McGonigle, C.McQuade, B.Thomas

Geographical and temporal variations in incidence of presenile dementia in Scotland 1974-1988 were studied using hospital records, Registrar General death returns, Department of Neurology and Neuropathology diagnostic indices, and information provided by voluntary agencies. The information services division of Scottish Office Home and Health Department identified 6.81 1 discharges or deaths in Scottish mental hospitals where a diagnostic statement had been made that was suggestive of dementia in patients aged less than 73 years. Trained observers scrutinised all case records to which standard diagnostic criteria were applied. Clinical data from neuropathologically validated cases of presenile dementia were entered into a discriminant function analysis and improved clinical criteria that better separated sub-types of presenile dementia were applied to “uncertain” cases. Sub-types of dementia were then examined by cause of death, symptomatic onset, place of birth, residential stability, occupational exposure to putative environmental toxins, parental age at birth and family history of dementia.

An analysis of geographical and temporal variations of Alzheimer presenile dementia in Scotland will be presented. These will be related to variations in the quality of the public water supply, local exposure to environmental toxins, and a positive family history of presenile dementia or Down’s syndrome. Variations in the local provision of health services that may account for some findings will also be addressed.

AGING OF THE BRAIN CHOLINERGIC SYSTEM; PHARMACOLOGICAL INTERVENTIONS

G.Pepeu, F.Casametti and M.G.Vannucchi; Department of Pharmacology, University of Florence, Florence, Italy.

A hypofunction of brain cholinergic mechanisms has been shown in normal aging in man and animals; and is particularly severe in age-related degenerative diseases such as Alzheimer’s dementia. In old rats a decrease in the size of the cholinergic neurons in the rat is little or no change occurs in choline acetyltransferase activity. There have been conflicting reports of reversible age-related changes in the number of muscarinic receptors in aged rats. Reversible age-related changes in the molecular structure of M1 receptors have been observed in monkeys. In aging animals, two types of pharmacological interventions have been investigated: 1) administration of cholinomimetic, and nootropic drugs for correcting behavioral deficits presumably resulting from cholinergic hypofunction; 2) treatments with nerve growth factor, serine phospholipids, calcium antagonists for reducing cholinergic hypofunction. The results obtained in several laboratories, including our, suggest that aging of the cholinergic neurons in the rat is temporarily reversible. To what extent these findings can be transferred to man requires investigation.
S2.1 ON SPINAL MECHANISMS OF MUSCLE COORDINATION DURING LOCOMOTION.
E. Jankowska. Department of Physiology, University of Göteborg, Sweden.

Two main problems are usually discussed with respect to the organization of locomotion: the mechanisms of the rhythmicity of locomotory movements and of patterns of muscle activation during locomotion. I'll restrict myself to the 2nd problem and summarize observations on interneurones which are used to excite and inhibit motoneurones during locomotion (as last order excitatory and inhibitory interneurones) and on interneurones which may assist in the selection of the various patterns of locomotion.

S2.2 NEURONAL NETWORK UNDERLYING LOCOMOTION IN A VERTEBRATE - CIRCUITRY, TRANSMITTERS AND MODELLING
STEN GRILLNER
Nobel Institute for Neurophysiology, Karolinska Institutet, Stockholm, Sweden

The brain consists of interacting neural networks that generate different aspects of our behavioral repertoire. To understand the brain, we must therefore understand its circuits. To account for how circuits operate, the role of the component nerve cells and the individual characteristics of the cell must be understood.

Vertebrate locomotion is produced by a family of control systems generating (1) propulsion (2) equilibrium control during ongoing movements (3) steering control and (4) compensation for predicted and unpredicted perturbations. I will focus on the network providing propulsion, and discuss that in relation to the lamprey CNS used as an experimental model. The neuronal network consists of a reticulo-spinal system used for initiating of activity, a spinal network generating the pattern on both the segmental and intersegmental level, and a sensory feedback system acting directly on the pattern generating circuitry, but also feeding back information to supraspinal structures. The backbone of the network consists of L-glutamate and glycine neurones. L-glutamate provides the excitatory synaptic transmission in all components, whereas glycine is used for reciprocal postsynaptic inhibition. In addition the network has two major modulatory systems using 5-HT acting on Ca²⁺ dependent K⁺ channels and GABA, and GABA, acting on HVA and LVA Ca²⁺ currents gating synaptic transmission by an action on both the presynaptic and the postsynaptic levels. The details of operation of the network is now understood and extensive computer simulations have been used in the analyses.

S2.3 CHANGES IN THE FORE- AND HINDLIMB COORDINATION AFTER PARTIAL SPINAL LESIONS IN THE CAT.
T. Górska, T. Bem, H. Majczyński.
Nencki Institute of Experimental Biology and Institute of Biocybernetics and Biomedical Engineering, Pol. Acad. Sci., Warsaw, Poland.

The effects of incomplete low thoracic spinal lesions on the fore- and hindlimb coordination was investigated in freely moving cats walking at speeds of 0.4 to 1.0 m/s. The locomotion was tested 5-6 months postoperatively. Three types of impairment were found: 1. in steps with the same rhythms of the fore- and hindlimb movements a sequence of limb movements typical for walking was preserved, but different cycle elements were found to be independent on the step cycle duration in intact and operated animals; 2. the occurrence of episodes with different rhythms of the fore- and hindlimbs, composed of four forelimb and three hindlimb steps. The dissociation of the fore- and hindlimb rhythms began with synchronization of homolateral limbs (as in pacing), followed by synchronization of diagonal limbs (as in trot) and then a reappearance of sequence of limb movements typical for walking was preserved, but different cycle elements were found to be independent on the step cycle duration in intact and operated animals; 3. permanent dissociation of rhythms of the fore- and hindlimb movements, with hindlimb steps being about 200 ms longer than in the forelimbs. The latter kind of impairment was found in cats in which both the ventral and, to a large extent, the dorsolateral funiculi of the spinal cord were destroyed.

S2.4 ORGANIZATION OF CEREBELLO-THALAMIC AND CEREBELO-RUBRAL INTERCONNECTIONS IN THE CAT
R. Tarnecki and P. Kalużyń
Nencki Institute of Experimental Biology
02-093 Warsaw, POLAND

The purpose of these experiments is to clarify the organization of the intercellular connections between nucleus interpositus (IP) and the ventro-lateral thalamic nucleus (VL) and the red nucleus (RN) cells.

The brain consists of interacting neural networks that generate different aspects of our behavioral repertoire. To understand the brain, we must therefore understand its circuits. To account for how circuits operate, the role of the component nerve cells and the individual characteristics of the cell must be understood.

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S2.5 Intracortical Mechanisms for the Recruitment of Motor Cortex Neurons.
Peter Zarzecki, MRC Group in Sensory-Motor Physiology, Department of Physiology, Queen's University, Kingston, Ontario, Canada

Motor cortex neurons discharge during motor tasks to encode movement parameters and in response to sensory feedback. Neurons project out of motor cortex to the spinal cord and to many other targets. Not all projection neurons recruit during behaviour like corticospinal tract neurons, but instead recruitment patterns depend on the projection target of the neurons. The problem is to understand how neurons projecting to different targets are selectively recruited. We have investigated this issue in anesthetized cats. Motor cortex neurons projecting to six targets were identified antidromically. Corticocortical, callosal and thalamocortical pathways were stimulated electrically to determine if neurons projecting to different targets have selective input connectivity from extrinsic sources. Intracortical connections to identified output neurons was evaluated by spike-triggered averaging and cross-correlation. Output neurons in different layers along single electrode tracks usually had different inputs. Neurons in clusters were more likely to share the same inputs, especially if they projected axons to the same target. Our results support the conclusion that combinations of inputs to motor cortex neurons could selectively recruit efferent neurons from separate cortical layers or from within clusters of nearby neurons, according to the target of their axonal projections.

Supported by the Medical Research Council of Canada.

Symposium (S3) - Physiology and pharmacology of neurotransmitters and their receptors

S3.1 SEROTONIN (5-HT) SYSTEMS MEDIATE DOPAMINE (DA) RECEPTOR SUPERSENSITIVITY
R.M. Kostrzewa, L. Gong and R. Brus
Department of Pharmacology, East Tennessee State Univ., Johnson City, TN 37614, U.S.A. and Department of Pharmacology, Silesian Academy of Medicine, 41-808 Zabrze, Poland

To study interactions between DA and 5-HT systems in the D, supersensitized induction of oral activity in neonatal 6-hydroxydopamine (6-OHDA) lesioned rats, the following studies were done. A series of agonists with affinity to 5-HT1A, 5-HT1B, 5-HT2C, 5-HT3 and 5-HT, receptors was first administered to rats. Only m-chlorophenylpiperazine (m-CPP), which acts at 5-HT1C and 5-HT3 receptors, had enhanced effects, thereby indicating that 5-HT receptors are co-sensitized with D, receptors. In a series of antagonists with affinity for the different 5-HT receptor subtypes, only mianserin (1 mg/kg) attenuated the effect of m-CPP. The D, receptor antagonist, SCH 23390 (0.3 mg/kg) did not attenuate the m-CPP effect, but mianserin did attenuate the effect of the D, agonist, SKF 38393 (1.0 mg/kg). It is felt that 5-HT1C receptors become sensitized when D, receptors are supersensitized. D, receptor supersensitivity was eliminated by the 5,7-dihydroxytryptamine (5,7-DHT; 75 μg) destruction of 5-HT fibers. These studies demonstrate that 5-HT systems play an important role in mediating DA D, receptor supersensitivity. (Supported by a Fogarty grant, the Scottish Rite Schizophrenia Research Program, U.S.A. and by NS 29505 from the National Institute of Neurological Disorders and Stroke)

S3.2 EXCITATORY AMINO ACIDS: PHYSIOLOGICAL AND PHARMACOLOGICAL PROBES FOR NEUROSCIENCE RESEARCH
H. SHINOZAKI, THE TOKYO METRO. INST. OF MED. SCI. TOKYO 113, JAPAN.

Acromelic acid is a new potent kainate derivative, and its systemic administration to the rat causes marked tonic extension of the hindlimbs which is ultimately replaced by persistent spastic paraplegia causing neuron damage preferentially in the lower spinal cord. NBOX depressed depolarizing responses to acromelic acid and AMPA more effectively than those to kainate. 4-(2-Methoxyphenyl)-2-carboxy-3-pyrrolidineacetic acid (MFPA) is so far the most powerful excitatory amino acid, which is more potent than acromelic acid in the newborn rat spinal motoneuron. MFPA, acromelate and kainate caused a depolarization of dorsal root fibers of immature rats, however, AMPA and quisqualate were much less active than kainate.

MFPA, acromelate and kainate induced marked desensitization of kainate receptors on the fibers, which is useful for pharmacological classification of non-NMDA receptors.

2-(Carboxycyclopropyl)glycine (CCG) is a conformationally restricted analog of glutamate, that provides useful information about the interaction between the conformation of glutamate molecules and activation of receptor subtypes. 2S,3S,4S-CCG (L-CCG-I) is a potent metabotropic glutamate receptor agonist, and 2S,3R,4S-CCG (L-CCG-IV) is an NMDA-type agonist, being about 5 times more potent than NMDA in causing depolarization in the newborn rat spinal motoneuron. In cultured rat hippocampal neuron, L-CCG-IV caused significant increase in intracellular Ca2+ concentration. L-CCG-I stimulated PI formation in the rat brain and caused oscillatory responses in Xenopus oocytes. L-CCG-I depressed monosynaptic excitation of motoneurons in the newborn rat spinal cord in extremely low concentrations well below those causing postsynaptic depolarization. These new excitatory amino acids would provide useful probes for neuroscience research.
Non-cholinergic, non-adrenergic(NANC) nerve stimulation results in excitation(e.j.p., rebound depolarization, contractions) or inhibition(i.j.p., relaxation) of the gut. NANC neuronal mechanisms participate in the maintenance of the basal tone and spontaneous activity of the gut. There are however species differences, i.e. both NANC excitation and inhibition are present in the guinea pig and only NANC inhibition in the rat intestine. Substance P-like neuropeptide/s are suggested to be mediators released from excitatory NANC and sensory nerves. The latter are activated by histamine and degenerated by capsicin. There is evidence in favour of a nitric oxide-like substance and against of ATP, dopamin, GABA and neuropeptides (e.g. VIP, PHI/PHM) being the inhibitory NANC mediator in the gut. TTX, high Mg²⁺—low Ca²⁺ media, 3,4-diaminopyridine, dipryridamol and adenosine deaminase modulate NANC excitation and inhibition. While NANC excitation is sensitive, the NANC inhibition is resistant to the action of catecholamines, reserpine, 6-hydroxydopamine, chymotrypsin, prednisolon, bacitracin, opioids, free oxygen species or low concentration of local anesthetics. In contrast NANC inhibition is attenuated and NANC excitation augmented by the action of TEA and apamin. The rebound excitation was found to be due to an indomethacin independent mechanism.
Workshop (W1) - Motor control and locomotion: behavioural and electrophysiological aspects

W1.1 PHYSIOLOGICAL MECHANISMS OF OPERANTLY CONDITIONED SPINAL REFLEX PLASTICITY
Jonathan R. Wolpaw
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New York State Dept. of Health and State Univ. of New York
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Spinal cord reflex pathways operate under the control of descending pathways from supraspinal structures. This control is both acute, in that it can quickly change reflexes, and chronic, in that it can gradually produce lasting reflex changes. Until recently, the impact of chronic control was evident mainly in abnormal circumstances, such as after complete or partial spinal cord transection. However, recent studies from several laboratories demonstrate that chronic non-pathologic changes in descending control can also change spinal cord reflexes (reviewed in Wolpaw and Carp, Trends Neurosci., 13:37-142, 1990). Primates, human or non-human, can gradually increase or decrease the size of the monosynaptic stretch reflex (i.e., the tendon jerk) when reward depends on change. Effects of this chronic operant conditioning are still present after all descending control is removed. Thus, the conditioning actually changes the spinal cord itself.

Current intracellular physiologic and anatomic studies are defining the location and nature of this spinal cord plasticity. Attention focuses on the most likely sites of change, the Ia afferent synapse on the alpha motoneuron and the motoneuron itself. Results to date indicate that changes occur at several sites in the spinal cord.

Comparable spinal reflex plasticity probably occurs during the learning of a variety of motor skills. Furthermore, it may provide a basis for new therapeutic approaches to spasticity and other forms of abnormal spinal reflex function that result from damage to supraspinal structures.

W1.2 LOCALIZATION OF SYNAPTIC TRANSMISSION ASSOCIATED WITH LOCOMOTION WITHIN THE MESENCEPHALIC LOCOMOTOR REGION (MLR)
Stefan M. Brudzynski, Michael Wu and Gordon J. Mogenson
Department of Physiology, University of Western Ontario, London, Ontario, N6A 5A5 Canada.

One of the major output pathways from the limbic structures to the motor system is the projection from the nucleus accumbens to the ventral pallidum and to the mesencephalic locomotor region (MLR). It has been shown that the MLR plays a crucial role in locomotion initiated from the nucleus accumbens or from the ventral pallidum. There are, however, conflicting data whether or not the accumbens-ventral pallidal projection mediating locomotion terminates on MLR neurons. The purpose of the study was to clarify this question by demonstrating synaptic transmission associated with locomotion within different regions of the MLR. Locomotion was induced by injecting dopamine into the nucleus accumbens or picrotoxin into the ventral pallidum in freely behaving rats. Synaptic transmission in the MLR was eliminated by excitotoxic lesions or was reversibly interrupted by injecting cobaltous chloride, a calcium channel blocker. Excitotoxic lesions or injections of cobalt significantly decreased, although did not block completely, locomotion. The most effective sites for cobalt and excitotoxic lesions markedly overlapped but were not identical. The results indicate that synaptic transmission within the MLR contributes to centrally-triggered locomotion.

Supported by the NRC and NSERC of Canada.

W1.3 CHANGES OF THE MUSCLE CONTROL AFTER PARTIAL SPINAL LESIONS IN THE CAT
W. Zmyslowski, T. Bem, T. Goska, H. Majczyński
Institute of Biocybernetics and Biomedical Engineering and 1Nencki Institute of Experimental Biology, Warsaw, Poland

Foot contact signals and the electrical activity of m.m. gastrocnemius lateralis (GL), tibialis anterior (TA), vastus lateralis (VL) and semitendinosus (ST) were recorded simultaneously during unrestrained locomotion in intact cats and cats with lesions of the dorsolateral quadrants of the spinal cord. The results showed that: lesions remodeled the spinal generator (SG) in such a way that the activity and timing of the GL, VL and ST led to strong relationship between the swing phase and the step cycle duration. The activity of TA was strongly impaired resembling disturbances observed in hemiplegic patients and could be, to some degree, restored by means of n. peroneus electrostimulation. The obtained results support also the view that the SG is a two level hierarchical system in which the higher level is mainly engaged in determining the structure of the cycle while the lower one forms the muscle control signals.

W1.4 ACTIVITY OF THE ELBOW FLEXOR AND EXERTOR MUSCLES DURING PLACING REACTIONS TO TACTILE STIMULATION OF VARIOUS ASPECTS OF THE PAW.
J. Czarkowska-Bauch, T. Bem*, H. Majczyński
The activity of the biceps brachii (Bi) and lateral head of the triceps brachii (LaT) muscles were studied during contact placing (CP) reactions elicited by stimulation of either lateral or medial side of the fore paw in the cat to verify whether common strategy of movement is used in CP reactions to stimulation of various aspects of the paw. Patterns of activation of Bi and LaT during medial CP were similar to those described earlier for the dorsal CP reactions, i.e., the latencies of Bi were very short (10-18 ms) and its activity occurred first 60% of the reaction time. The LaT was activated either with long or with short latencies. Both timing and patterns of activation of Bi and LaT during lateral CP were different than during medial and dorsal CP reactions: latencies and duration of Bi activation were longer and latencies of LaT were much more variable. The coactivation of Bi and LaT was observed in all reactions but it was distributed in different way during lateral, medial and dorsal CP reactions. It indicates that the elbow flexion movement started in different phases of CP reaction depending on stimulated side of the paw. It is suggested that different movement strategy has been used during CP reactions elicited by tactile stimulaton of various sides of the paw.
W1.5 THE INFLUENCE OF CEREBELLAR LESIONS ON SEP STUDIED BY MEANS OF A WAVELET ANALYSIS

K.J. Blinowska, P.J. Durka, A. Kołodziejak*, R. Tarnecki*
Warsaw University and * Nencki Institute
Warsaw, Poland

The mechanism of interaction between cerebellum and motor cortex, important for motor control, was studied by means of ablations combined with electrophysiological techniques. Cortical sensory evoked potentials were registered by means of silver ball electrodes positioned over pericrucial cortex of anaesthetized cat. Recordings were performed before and after removal of the right cerebellar paravermal cortex.

A novel method of wavelet analysis was applied. The multiresolution decomposition of the single SEP and EEG signals was performed, then the wavelet components which distinguished in the best way SEP from EEG were found by means of the discriminant analysis. Single evoked potentials were reconstructed. Multivariate techniques were used to compare the evoked potentials in the same cortex sites before and after the lesion. The method made possible the extraction of SEP components of latency longer than 50 ms, not identified by other methods. The interpretation of their origin was attempted.

W1.6 MOTOR CONTROL IN EPILEPTIC PATIENTS BEFORE AND AFTER FRONTAL LOBECTOMY

Bidziński J. Dimitrijević M.R. Chęciński S. Bacia T.

In 10 epileptic patients we investigated motor activity using BMCA method before and after frontal lobectomy. The BMCA was described in previous paper. The size of resection was different in every patient and we will show it for peculiar patient separately. Before surgery in patients was motor deficit in form of slight hemiparesis contralaterally to localization of epileptic focus. After surgery the present deficits were not increasing, but BMCA investigations showed increased motor activity generally, loss of inhibition or presence of co activation of muscle contralateral to the cortical resection when the "unaffected side" is voluntarily activated and loss of agonist/antagonist reciprocation. These changes were more pronounced in patients with motor deficit before surgical intervention. There were some modification of tonic stretch reflex induced by vibration too. Our investigation showed partial removal of frontal lobe induced distinct changes in motor performance not visible by simple neurological and psychological investigations.

W1.7 BMCA AFTER TEMPORAL LOBECTOMY IN EPILEPTIC PATIENTS

Bacia T. Bidziński J. Dimitrijević M.R. McKay E.W. Chęciński S.

To determined role of different cortical structures in motor control in men we performed BMCA in epileptic patients before and after temporal lobectomy. Polyelectromyographic (PENM) recording of bioelectric activity of muscles lower and upper extremities during functional test were done before, 10 days, 1 month, and 1 year after surgery. 30 patients were investigated, 13 with left and 17 with right lobectomy. The size of resection was from 3cm to 4.5cm in left hemisphere and from 4cm to 9cm in right one. BMCA made before surgery didn’t show any gross abnormality, some abnormalities-slowing up of motor acts appear in short lasting follow-up investigations. In long lasting follow-up (1 year or more) in part of patients we noticed mild abnormalities or changes in performance of some of the motor test applied. The results of analysis of 120 BMCA recordings in epileptic patients before and after temporal lobectomy showed that temporal lobes have the indirect influences on motor activity of men only.
W2.1 ANIMAL MODELS OF BRAIN AMYLOIDOSIS
Jerzy Wegiel, Henryk M. Wisniewski, Janusz Morys, Maciej Bobinski, Zenon Soczyski
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Our light microscopic and ultrastructural studies of human biopsies from brains of aged patients and patients with Alzheimer disease, brains of aged monkeys, dogs and wolves, brains of scrapie-infected mice; organs of mice with experimental systemic amyloidosis; and hamsters with spontaneous amyloidosis showed similar similarities of the cellular apparatus involved in amyloid formation and deposition. Our morphometric studies show that the extent of brain amyloidosis in aged dogs is much greater than previously reported and that the number of amyloid deposits in brains of dogs and wolves is comparable to the number of plaques in the brains of people with AD. Amyloid deposits initiate the neurupathi pathy. Senile plaque formation is a two-step process with (1) amyloid deposition and (2) neuronal degenerative changes. Studies of the cells involved in amyloid fibril formation along the injection channel of the scrapie agent revealed that as in Alzheimer disease and aging, the same populations of cells - the perivascular cells - and their progeny - the perivascular and neuropil microglia - are engaged in amyloid plaque formation. Amyloid is formed in the posttraumatic scar, which consists of many vessels, perivascular cells, and perivascular microglia but no neuronal elements. In scrapie, the perivascular cells and the cells derived from them are both producer and processor of the amyloid protein. Brain cells behave like Kupffer cells in the liver or the cells of the RES in the spleen and kidneys in systemic amyloidosis, which all produce amyloid fibrils from SAA or light-chain gamma globulins. Isolation of amyloid-making cells in different animal models will provide in vitro models for the study of the cellular and environmental conditions needed for the formation of amyloid fibrils.

(Supported by funds from the New York State Office of Mental Retardation and Developmental Disabilities and a grant from the National Institutes of Health, National Institute of Aging, Grant No. P01-AGO-42220)

W2.2 TRANSMISSIBLE AND NON-TRANSMISSIBLE CEREBRAL AMYLOIDOSIS
Paweł P. Liberski
EM Lab. Dept. Oncol. Med. Acad. Łódź, Poland

I report here the decade-long neuropathological studies of transmissible and non-transmissible cerebral amyloidoses. The central pathogenetic event in both types of amyloidosis is a synthesis and processing of amyloid precursor followed by accumulation of a final deposit, while PrPsc and APP serve as amyloid precursors and PrPsc and beta-A4 as final deposits in transmissible and non-transmissible amyloidoses, respectively, the basic building blocks of neuropathology remain virtually the same. The amyloid plaque composed of different proportions of amyloid deposit, dystrophic neurites and glial cells is the crucial neuropathological entity. The role of microglial cell as amyloid producer/processor cell seems to be analogous in both types of cerebral amyloidoses. The impairment of slow axoplasmic transport which leads to the accumulation of neurofilament triplet proteins in transmissible and tau protein for non-transmissible cerebral amyloidosis is responsible for development of dystrophic neurites and neuropil threads. The other elements of neuropathology may be only secondary phenomena as clearly demonstrated for spongiform changes and PrP-c mutation expressed in transgenic mice. Finally, the role of tubulovesicular structures in transmissible cerebral amyloidoses is discussed.

Gene Therapy in Animal Models of Alzheimer's Disease
La Jolla, CA. U.S.A. 92093

Genetic modification of cells offers a potential means of delivering substances to the brain in a localized, high-dose, safe and chronic manner. Cells may be modified to produce such substances as neurotrophic factors, neurotransmitters or other molecules. In Alzheimer's disease (A.D.), deficiencies in cholinergic function probably contribute to cognitive decline. Previous studies have shown that nerve growth factor (NGF) can prevent both lesion-induced and age-related cholinergic neuronal degeneration, improve mnemonic function, and promote cholinergic fiber growth. Thus, we genetically modified primary rat and monkey fibroblasts to produce and secrete NGF to determine whether these cells could prevent cholinergic degeneration and promote neurite sprouting in animal models. A retroviral vector containing the cDNA for the active, B fragment of human NGF together with a selectable gene for neomycin resistance was constructed and used to infect primary fibroblasts. Control fibroblasts were infected with the gene for B-galactosidase (B-gal) rather than NGF. In vitro, NGF-producing cells secreted up to 990 ng NGF/ul/day into the culture medium. NGF-secreting or control (B-gal) cells were then grafted to the brains of adult rats and monkeys after fornix lesions; fornix lesions normally result in cholinergic neuronal degeneration. NGF-secreting cells but not control cells prevented neuronal loss in the rat; evaluation in the primate is underway. In both rat and primate brains, NGF-secreting grafts but not control grafts promoted growth of cholinergic fibers as seen in the cortex. Thus, genetically modified cells genetically modified to produce and secrete NGF promote cholinergic neuronal survival and sprouting in the adult brain. This may be a potential means of rescuing cholinergic neuronal populations in A.D. Studies are in progress utilizing the gene for choline acetyltransferase, a biosynthetic enzyme for acetylcholine (ACh), in an attempt to augment brain levels of ACh and ameliorate cholinergic dysfunction.

W2.3 MICROGLIA WITHIN BRAINS WITH DIFFERENT FORMS OF CEREBRAL AMYLOIDOSIS
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The role of microglial cell within amyloid deposits is still a matter of discussion. The aim of our study was to compare microglial reaction in different forms (non- and transmissible) of cerebral amyloidosis (Beta-peptide, PrP, or A4 and PrP). Material consisted of representative slides from brains with: Alzheimer's (AD)-10 cases, Creutzfeldt-Jacob (CJD)-7 diseases, Gerstmann-Sträussler syndrome (GSS-2) and Parkinson's (PD-10), paroxysmal progressiva (PSP-2) cases and 6 "normal aged" brains. All specimens after routine staining were examined immunohistochemically. Following antibodies were used: anti A4, and anti PrP, for concomitant neurofibrillary (NFT) changes anti tau and anti ubiquitin antibodies. For microglial cell anti-ferritin and RCA 1 and GFAP as a marker for astroglia. A 4 deposits were observed in AD, six PD and in one CJD cases. PrP plaques were presented in two GSS and one CJD brains. In ten AD, two PD and two PSP cases NFT were labeled. Microglial cells located always in the center, no matter PrP or A4 plaque were observed in all cases within approximately 50% of focal amyloid deposits. Diffuse microglial reaction limited to the cortex was visible in 3 CJD and 2 PSP cases. However, the microglial cells are more often encountered within plaque with NFT, and in regions free of amyloid in AD and PSP cases suggested may be their involvement in NFT phagocytosis as well.
MAPPING OF EEG AND CORTICAL EVOKED POTENTIALS IN DEMENTIAS OF ALZHEIMER TYPE (DAT)

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The new form of an information exploration of functional state of central nervous system within dementia of Alzheimer type patients demonstrating the structural damages in computerized tomography (CT) scans is now possible by mean of the quantified EEG and evoked potentials tests, which were performed using the imaging of brain bioelectrical activity by the mapping method.

The 16 channel EEG and EP recordings were performed with 21-channel SIEMENS-ELEMA MINICORD connected to specially design computer system based on IBM AT PC with analog-digital converter and original software (NEUROSCAN).

The evoked potentials were tested also by mean of the DANTEC CONCERTO digital electroencephalograph. The analysis by mean of the mapping method in time and frequency domains was performed.

The EEG mapping has showed no differences in the localization of bioelectrical changes compared to the ones concerned in CT scans, but it has revealed a larger spatial transmission of them, what can confirm a higher sensitivity of the method, and it can suggest a possibility of an earlier detection of the functional disturbances in a zone, where structural changes are not yet visible in CT scans.

It is worthy to be underlined, that the detection of changes by the mapping performed in the frequency domain (spectral analysis) reveals more information in these cases, when compared to the mapping in the time domain. This relates predominantly to the problem of depth of the changes, and not to their extensiveness and topolocation.

ALZHEIMER'S DISEASE-IMMUNOLOGICAL ASPECTS

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Alzheimer’s Disease (A.D.) is a multifarious, complex syndrome, which probably comprises different etiopathogenetic subunits. Works by some authors focused on immunological disturbances underline the importance of immunological imbalance in explanation of the disease stiopathogenesis and progress at least of some forms of A.D. (ca 25%) (Fudenberg et al.1984, 1987, Gottfried 1988, 1991). An early diagnosis of an A.D. form is very important because changes in the CNS respond well to immunomodulatory treatment in the early course of disease (Leszek et al.1999). This justifies a search for diagnostic methods permitting an early diagnosis and consequently an early start of treatment. According to literature on our own observations, immunococontrol (immunomodulatory treatment) in the early stage of disease is beneficial to patients with A.D., both in their psychoneurological and immunological functions.

Workshop (W3) - Neurotransmitters and their receptors

STUDIES ON EXPRESSION AND REGULATION OF NICOTINIC ACETYLCHOLINE RECEPTOR SUBTYPES IN CLINICAL CELL LINES

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For many years, it has been known that nicotinic acetylcholine receptors (nAChR) in muscle, in autonomic neurons, and in the central nervous system are pharmacologically diverse. More recent studies have identified over a dozen genes that code for different nAChR subunits, which combine in unique ways to constitute specific members of the nAChR family. We have used clonal cell lines related to muscle or nerve cells and that naturally express different nAChR subtypes to establish (i) the subunit make-up of those nAChR, (ii) profiles of drugs acting at radioligand binding and functional sites of different nAChR subtypes, (iii) effects of nicotinic ligands, second messenger modulation, and transcriptional modifiers on nAChR numbers and function, and (iv) whether effects of those agents are mediated transcriptionally or at the post-translational level. Our most recent studies indicate (i) that the ganglionic nAChR subtype that dominates functional responses to nicotinic agonists is composed of at least two subunits whereas ganglionic and central nicotinic alpha-bungarotoxin binding sites, like muscle nAChR, are composed of four subunits, (ii) that cytisine, nicotine, mecamylamine, and donepezil can be used to distinguish nAChR subtypes, and (iii) that there is upregulation of nAChR numbers induced by chronic nicotinic agonist treatment, those effects are accompanied by a loss of nAChR function and are not due to transcriptional activation, whereas (iv) exposure to drugs such as sodium butyrate, cyclic AMP analogues, or protein kinase C-directed phorbol esters changes in nAChR numbers via transcriptional mechanisms.

ADAPTIVE PROCESSES OF MUSCARINIC RECEPTOR AND POST-RECEPTOR MECHANISMS IN THE CENTRAL AND AUTONOMIC NERVOUS SYSTEM OF YOUNG AND AGED RATS

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Potential age-related differences in the response of the cerebral cortex and ileum strip to a repeated treatment with an anticholinesterase compound DFP were evaluated in 3-and 24-month Sprague Dawley rats. The response was measured in terms of total muscarinic receptors (mAChR-QNB binding) and in the case of ileum its in vitro contractility upon stimulation by cholinergic agonists. In untreated rats there was an age-related decrease of both cortical and ileal ACHE (about 30%); there were no age-related differences in the Bmax of cortical mAChR but there was a 45% deficit of ileal mAChRs. At the end of 2-week DFP treatment (causing 75% inhibition of brain ACHE and 30% inhibition of ileal ACHE, independently of age) the adaptive down-regulation of brain mAChR was more pronounced in aged than in young rats (50 and 25%, respectively), while that of ileal mAChR was greater in young than in aged rats (50 and 35%). There was only a little age-related decrease in sensitivity of the contractility of the isolated ileum to carbachol. In some additional experiments the responsiveness of phosphatidylinositol system (measured as accumulation of inositol phosphate-IP) after stimulation with carbachol in ileal slices was evaluated in young and aged untreated rats. The accumulation of IP at most carbachol concentrations was higher in the latter than in the former, similarly to the brain. The overall data indicate that age- or treatment-induced changes of mAChR mechanisms in the ileum strip differ considerably from those in the brain. However, the increased efficiency of post-receptors mechanisms is their common feature and may be regarded as a compensatory mechanism.
MODULATION OF MAST CELL IONIC CHANNELS BY NEUROPEPTIDES

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Mast cells (MC) are responsible for immediate hypersensitivity diseases that include allergy, asthma and anaphylaxis. The clinical symptoms are mediated by compounds released from degranulating MC including histamine, serotonin, prostaglandins and interleukins. An increasing number of reports demonstrate the existence of a neural component in MC-dependent pathological reactions in numerous tissues of different species, pointing at nerve/MC interaction as a key element in the burgeoning field of neuroimmunology.

We discuss the role of ionic channels as targets of neuropeptide action in MC activation. Current evidence shows that membrane permeabilities for calcium, chloride, sodium and potassium have a significant role in MC activation and can be modulated by neuropeptides. Moreover, ionic mechanisms of MC activation are specific for different MC types.

We propose that neuropeptides acting at physiological concentrations may not necessarily lead to complete MC activation (degranulation), but still change cellular physiology. This "priming" may lower the activation threshold for a subsequent immunological stimulus. The molecular understanding of the phenomenon of neuromodulation contributes to the treatment of the pathological symptoms for which MC are responsible. Supported by M.R.C. of Canada.

ORGANOPHOSPHATE POISONS TARGETING TO THE NICOTINORECEPTOR

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Organophosphate poisons are powerful inhibitors of cholinesterases. However the nicotinoreceptor might be another target of the poisons in the cholinergic system. Membrane-bound nicotinoreceptor from the electric organ of Torpediniforms (mammalian timilei) was used in the radioactive receptor binding assay, where \textsuperscript{125}I-a-toxin or \textsuperscript{3}H-PtP were used as ligands. At concentration of 1 mmol/L, VX inhibited about 30% of the binding of a-toxin to nicotinoreceptor, whereas soman and sarin did not at all. VX, soman, sarin and tabun obviously inhibited the binding of \textsuperscript{3}H-PtP to nicotinoreceptor at concentrations ranging from 0.05-1 mmol/L. One mmol/L VX completely blocked the binding.

THE EFFECT OF p-CHLOROAMPHETAMINE AND p-CHLOOROPHENYLALANINE ON THE LEVEL OF THYROTROPIN-RELEASING HORMONE (TRH) AND ITS RECEPTORS IN THE CENTRAL NERVOUS SYSTEM OF THE RAT

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The concentration of TRH and the density and affinity of TRH receptors were examined in the ventral (VLSC) and dorsal (DLSC) lumbar spinal cord, nucleus accumbens (NA) and striatum (ST) of rats with the 5-hydroxytryptamine (5-HT) nerve terminals destroyed with p-chloroamphetamine (PCA) or in animals treated with the inhibitor of 5-HT synthesis p-chlorophenylalanine (PCPA). PCA (2x10 mg/kg ip 9 and 8 days before killing) and PCPA (3x300 mg/kg ip 72, 48 and 24 h before killing) - either of them dramatically diminished the 5-HT and 5-HIAA concentrations in all the examined structures - reduced the TRH level and increased the density of TRH receptors in the VLSC. PCPA also reduced the TRH content in the NA. The PCA-induced reduction in the TRH level and increase in the density of TRH receptors in the VLSC were significantly attenuated by citalopram (2x20 mg/kg ip 30 min before PCA), a selective inhibitor of 5-HT uptake. Our results constitute further proof that coexistence of TRH and 5-HT takes place in the VLSC and then indicate that other form(s) of relationship between 5-HT and TRH may exist in some parts of the central nervous system. They also suggest that up-regulation of TRH receptors occurs in the spinal cord as a result of TRH depletion.

CAUDATE AND ACCUMBENS DOPAMINE RESPONSE TO STIMULANTS

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Microdialysis techniques in behaving animals were used to characterize the dopaminergic response profiles in caudate-putamen and nucleus accumbens to a variety of amphetamine-like stimulants. These studies have revealed both similar and contrasting region- and stimulant-specific response profiles. First, the increase in extracellular DA in both caudate and accumbens is markedly greater in response to amphetamine compared to behaviorally comparable doses of uptake blockers like cocaine, nomifensine, and fenfluramine. Second, over a wide range of doses, whereas amphetamine promotes quantitatively and qualitatively similar DA responses in both caudate and accumbens, the uptake blockers produce a significantly greater accumbens DA response. All three drugs promoted dose-dependent increases in dialysate 3-methoxytyramine which, although temporally delayed, generally paralleled the increases in dopamine. However, following the administration of uptake blockers, the ratio of dialysate 3-methoxytyramine to dopamine was greater in caudate than in accumbens. In addition, the acid metabolite patterns were the same in the two regions after amphetamine, but were qualitatively different after the uptake blockers. These results, along with the results of our characterization of the dopaminergic response in the presence of monoamine oxidase or catechol-O-methyltransferase inhibition are consistent with our hypothesis that regional differences in the degree of metabolism of released dopamine to 3-methoxytyramine in caudate and accumbens may contribute to the regional differences in dopamine response to uptake blockers.
Effect Of Injury On α₁-Adrenoreceptors In Rat Brain in vivo

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A widespread decrease of cortical glucose utilization occurs in the lesioned hemisphere following focal freezing lesions in rats. This is interpreted as a reflection of depression of cortical activity. Both serotonergic and noradrenergic neurotransmitter systems were implicated in functional alterations associated with injury. In case of the latter, norepinephrine (NE) level decreased and that of its metabolite MHPG-SO₄ increased bilaterally in the cortex while prazosin, a specific NE antagonist at α₁-adrenergic receptors, prevented the development of mainly unilateral cortical dysfunction as reflected in decreased glucose utilization.

In normal rat brain specific bi-affinity binding of [³²P]HEAT, another selective α₁-adrenoreceptor ligand, was demonstrated in vivo at two sites similar to α₁A and α₁B adrenergic receptor subtypes. In the present studies specific binding of [³²P]HEAT in rat brain in vivo was determined 3 days after a freezing lesion, when cortical glucose use is at its lowest suggesting the greatest degree of functional depression.

The data show that Bmax of the high-affinity site was bilaterally decreased 3 days after a lesion at the time when NE metabolism is bilaterally activated. In sharp contrast, Bmax of the low affinity site was increased but only in cortical areas of the injured hemisphere where major decrease in glucose utilization occurs. These results suggest that changes in low-affinity α₁-adrenoreceptors are of functional importance in injured brain.

STEROID REGULATION OF GABA A RECEPTOR: THE BRAIN AND BODY DIALOGUE
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Some endogenous steroids regulate function of the brain GABA A receptor. Tetrahydroprogesterone (THP) and tetrahydrodeoxycorticosterone (THDOC) behave as allosteric agonists of the GABA A receptor, while pregnenolone sulfate (PS) and dehydroepiandrosterone sulfate (DHEAS) act as antagonists. THP and THDOC increase binding of [³H]GABA and [³H]flunitrazepam, allosterically inhibit binding of the convulsant TBPS, stimulate chloride (Cl⁻) transport in synaptoneurosomes and neurones. In vivo, these steroids behave as anxiolytics/hypnotics in animals and humans. The neurosteroid, PS, behaves as a GABA receptor antagonist similar to the convulsants, picrotoxin or TBPS. PS competitively inhibits binding of TBPS and blocks GABA-activated Cl⁻ transport in synaptoneurosomes and neurones. In vivo, PS reduces barbiturate-induced sleep-time. The neurosteroid DHEAS also acts as an allosteric GABA A receptor antagonist.

Due to their GABA-modulatory actions, PS and DHEAS increase neuronal excitability and CNS arousal, whereas THP and THDOC inhibit these functions. Neurophysiological aspects of the regulation by steroids of the brain GABA A receptor will be discussed, such as: stress, the estrous/ menstrual cycle, pregnancy, development and aging (Majewska, Prog. Neurobiol., 38:379-395, 1992).

DOPAMINE MEDIATED LOCOMOTOR ACTIVITY IN RATS IS INFLUENCED BY HIPPOCAMPAL INPUT TO NUCLEUS ACCUMBENS.
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Experiments examined the effects of hippocampus - n. accumbens pathway section in Sprague-Dawley rats on the locomotor activity induced by systemic administration of the direct dopamine agonist amphetamine (AMPH) and the direct dopamine agonist morphine (AP0).

It has been shown that injection of amphetamine (0.2 mg/kg, s.c.) or morphine (1 and 10 mg/kg, i.p.), resulted in 2-3 fold increasing of general locomotor activity, as well as the changing in scale scoring of stereotypy (Greeene, Verseen 1975) from 0 to 3 points for ventral subicular pathway sectioned rats, tested in shuttle-box experiments. No significant changes have been observed in operated, as well as sham-operated and intact rats treated by appropriate doses of saline.

The data obtained support suggestion, that hippocampus - n. accumbens pathway may be as a link modulating dopamine dependent behaviour (Mogensen, 1987), and demonstrate that lesion (sectioning) of this pathway, made a month before testing, was accompanied by increasing in DA-receptors supersensitivity rather than the elevation of DA-level in n. accumbens.

Research was funded by the Royal Society Exch. Program at the Dept. of Exp. Psychol. of Oxford University, U.K. (prof. L. Weiskrantz).

Ay CHANGES IN LOCOMOTION AFTER DORSAL SPINAL LESIONS IN CATS.
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In freely moving cats walking at moderate speed (0.4-1.0 m/s) bilateral lesions of the dorsolateral funiculi of the spinal cord, performed at low thoracic level, produced the following changes in locomotion: 1. a decrease in locomotor speed; the upper limit of speed in operated animals was about 0.2 m/s lower than before surgery; 2. changes in the duration of the swing and stance phases; in the hindlimbs the durations of these phases were increased, while in the forelimbs decreased comparing to intact animals walking at the same speed; 3. changes in the relationships between the hindlimb stance and swing duration and the step cycle: the slopes of swing regression lines became significantly greater after the surgery, while those of the stance became smaller. In the forelimbs the slopes of regression lines were similar pre- and postoperatively. 4. changes in the stride length; in the hindlimbs the stride length was increased, while in the forelimbs it was decreased. All these changes led to different step cycle durations in the fore- and hindlimbs. The results suggest that in the cat the dorsolateral funiculi of the spinal cord play a major role in ensuring the coordination between the locomotor movements of fore- and hindlimbs.
P1.3 UNRESTRAINED LOCOMOTION IN NORMAL AND CEREBELLECTOMIZED CATS


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It is generally accepted that cerebellar cortico-nuclear system plays an important role in the control of movements. It remains unsettled, however, whether the spino-cerebellar sensory feedback is important for normal locomotion. In this study the support patterns and some locomotor parameters were analyzed in cats with various cerebellar lesions and in intact ones. Lesions did not disturb the general picture of locomotion: cats were able to walk with 8 element support pattern and the structure of the step was not remarkably changed. However, some measures of interlab coordination and durations of particular support phases were changed. Removal of right hemisphere resulted in abnormal increase of duration of support phases on homolateral limbs (up to 23% of the step cycle duration in comparison with 12% in intact cats) and their high variability. Strong linear relationships between homolateral and diagonal support phases durations as well as between lateral and diagonal time shifts were observed. Lesions damaging representations of the hindlimbs as well as partial cerebelloctomies sparing cerebellar nuclei did not resulted in such distinct changes. However, lesions of the second type led to some reduction of lateral or diagonal support phase durations. These data suggest that information processed in cerebellum may be of importance for fore- and hindlimb coordination.

P1.4 EFFECT OF ACUTE HEMICEREBELLECTOMY ON EVOKED POTENTIALS RECORDED FROM PERICRUCIATE CORTEX OF THE CAT

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There is both anatomical and electrophysiological evidence that the cerebellar paravermal cortex-interpositus nucleus system has bilateral projection to sensorimotor cortex. But the influence of this projection on cortical neurons responsible for generation of cortical activity is yet unclear. Using 12 cats, immobilized by gallamine under chloralose anesthesia, brain potentials (BR), recorded from pericruciate cortex of both hemispheres, to electrical stimulation of limb nerves were compared before and after acute hemicerebelleclectomy. There were no significant differences for latency or for amplitude of the averaged evoked components recorded from either side before lesion. The preliminary analysis revealed that after cerebellecctomy the first two BP components differed between normal and "cerebellectomized" side. At the "operated" side their amplitude was slightly reduced (in 3-5%), while in "normal" side there was a significant increase in amplitude (30-45%) of these components as compared to preenuerectomy, whereas, the ipsilateral BP appeared about the same at pericruciate cortex of both hemispheres. This finding may point to the possibility that thalamocortical sensory input responsible for activation of BP generators is reciprocally regulated through pathways from corticonuclear systems of both cerebellar hemispheres.

P1.5 STABILITY OF MONOSYNAPTIC HOFFMANN-REFLEX IN FREELY MOVING RATS

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Stability of monosynaptic Hoffmann (H) reflex (an analog of spinal stretch reflex) has been studied in awake rats. The H-reflex of the soleus muscle was elicited by direct electrical stimulation of 3a fibers of the tibial nerve with chronically implanted, bipolar cuff electrode (a square-wave current pulses of 200us duration and .2 Hz). H-reflex was recorded with the bipolar electrode implanted chronically into the muscle.

It was found that at least two factors determine the amplitude of H-reflex (stimulus intensity being unchanged) in freely moving animal: (i) the amplitude of the EMG activity before the stimulus application (a background EMG), (ii) the animal's behavior. The optimal range of background EMG activity has been found which allows to elicit H-reflex with high probability. Within that optimal range the H-reflex amplitude changed as a function of an intensity of the stimulus as described in the literature. The best behavioral state to elicit stable H-reflexes appeared while the animal was awake and quietly sitting whereas some rhythmical behaviors (e.g. a grooming) seemed to inhibit H-reflex even if the background EMG activity was within the optimal range. The results allow to proceed with our further studies on influences exerted by exteroceptive stimuli on the Mns.

P1.6 PERCEPTION AND MATCHING OF THE ANKLE ANGLE DURING QUIET STANCE IN YOUNG AND ELDERLY SUBJECTS

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Ability to detect a magnitude of passive angular displacement in the ankle joint and its static position as well as ability to match the perturbed joint angle to a reference position from the second limb during quiet stance were studied in 12 elderly and 12 young subjects. Subjects were standing barefoot one limb on the stationary surface with the second leg placed on the tilt platform. In response to initial displacement of the tilt platform within + 4 deg range/step 1 deg./subject returned level of their support surface using handhold switches based upon all sensory inputs from the contralateral leg but without direct visual control. Whereas the mean error of the matching in the young group was 0.12 ± 0.25 the respective value for the elderly ranged 0.94 ± 0.21. There was no statistically significant differences between limbs on the 5% level. Detection and matching of the small ankle angles were more impaired in the elderly but for greater angular perturbations both groups performed similarly. The results document an age related reorganization of the postural control within a single joint.
Changes in tension and action potentials of motor units during fatigue test.

Jan Selichowski, Kazimierz Grottel, Alicja Nowak: Department of Neurobiology, AWF Poznań

The studies were performed on medial gastrocnemius motor units of the rat. Changes in tension and amplitude, duration and latency of motor unit action potentials were monitored in the course of fatigue test in three types of motor units: FF, FR and S. In majority of the motor units amplitude of action potential decreased. The most pronounced decrease took place in FF units, less pronounced one in FR units while in S type motor units the decrease was insignificant. In a part of investigated motor units the amplitude of their action potential increased at the beginning of the fatigue test and, then, decreased or was maintained at the same level till the end of the fatigue test. In a few motor units, particularly the slow ones, no changes in action potential amplitude was observed. Changes in action potential duration were much more marked than changes in their amplitude. The changes in action potential of fast motor units were less pronounced than changes in their tetanic tension while in the slow motor units they resembled each other in intensity. Comparison of motor unit action potential changes with changes in their tetanic tension in the course of fatigue test demonstrated no clear-cut relationship between the two phenomena.

Electrographical responses to cortical application of antibiotics on different levels of the nervous system in cats.


Developing previous studies on experimental epilepsy (Huber, Z & al. Neurol. Neurochir. Pol. 1974; 3: 307-321) various antibiotics have been locally applied on the motor neocortex and a series of bioelectrical discharges from the cortical level and their propagation to the spinal cord, nerve trunks as well as from the muscles have been registered. The analysis of responses has shown that neuroexcitatory results were recorded after penicilline derivatives, polymixin, etc., whereas after some aminoglucosides, lincomycines neurodepressive influence has been confirmed. Our experimental effort has proven itself as an useful model in epilepsy research as well as it provides further experience about adverse side effects of antibiotics in clinical practice - either hyperekstatory & paralyzing.
Posters (P2) - Theoretical neuroscience and brain modelling

P2.1 A DYNAMIC MODEL OF THE PRESYNAPTIC TERMINAL OF THE ADRENERGIC SYNAPSE
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A hypothetical, conceptual model of mechanisms involved in the release of norepinephrine in the adrenergic synapse is presented. An illustrative, mathematical equivalent of the model was constructed allowing computer simulation of considered processes in varying conditions. The mathematical model has the form of a set of equations that allow to compute the state of the system at the moment $t+\Delta t$ on the basis of the state at the moment $t$. The computer implementation of the mathematical model makes it possible to observe changes of various parameters during the release of norepinephrine and as well as to monitor activity of enzymes concentration of metabolites etc.

P2.2 SPIKE MODEL BASED ON CONFORMATION DYNAMICS OF IONIC CHANNELS
Stanislaw J. PANECI and Andrzej WR6BEL. Department of Neurophysiology, Nencki Institute of Experimental Biology, 3 Pasteur St., 02-093 Warsaw, Poland.

The Hodgkin-Huxley equations of the spike model (1) use the experimental parameters which can be think of as reflecting the transition between conformational states of voltage dependent channels (2). These parameters were substituted with the first order approximation of the function which correlates states’ energies and membrane potential, for both sodium and potassium ionic channels. It appears that simulation of the classic spike mechanism (1) requires introduction of two related inactivated states. The minimalization procedure for six states of channel conformation yielded a good fit of membrane potential course to experimental Hodgkin-Huxley data obtained for different voltage stimuli.

From the resulting fit we could find the evolution of relative energies and barriers between different states as well as conductance changes during the spike. From these data we could estimate also the protein charge engaged in the chain of conformational transitions for about 4-5 e, which corresponds to the value measured previously (2).


P2.3 ON THE DETERMINISTIC FEATURES OF SERIES OF NEURONAL ACTION POTENTIALS
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Nencki Institute, Department of Neurophysiology 02-093 Warsaw, Poland.

The temporal structure of trains of neuronal action potentials was studied to evaluate the possibility that dynamics of these signals results from a low dimensional deterministic mechanisms. Spike trains were treated as a state-variable trajectories of a dynamical system and examined with the method of recurrence plots (Eckmann et al, 1987, Europhys. Lett., 4, 973). Spontaneous activity of single neurons was recorded extracellularly from cerebellar cortex, red nucleus, and ventro-lateral nucleus of thalamus in anesthetized with chloralose and paralyzed cats.

It was found that series of interspike intervals in some part of apparently random spike trains exhibited increased number of recurring similar sequences of 3-10 consecutive interspike intervals, compared to randomized interval sequences. This observation confirms the existence of certain degree of stochastic dependencies in spike trains but do not support the evidence of low dimensional chaos. The rate of sequence repetition is often, but not always, greater at higher firing frequencies. Qualitative changes of similarity structure of spike trains were observed, resulting mainly from modulation of rate and regularity of firing. Repeating segments of "homologous" firing structure, comprising 50-100 spikes, are often detected in data. This suggest occasional emergence of quasi-stable, repeatable modes of operation of spike train generating mechanism.

P2.4 MODELING OF BURSTS IN NEURAL NETWORKS
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The synaptic organization of neural networks and the principles underlying their operation remain important questions in neurobiology and computational neuroscience. Investigation of network synchronization manifested by bursting activity is of special significance in explaining dynamics of epileptic seizure. Bursts recorded from dissociated mouse spinal cord neurons in tissue culture after applying of tetanus toxin are a good experimental model (Macdonald et al., 1977 and Bergey et al., 1983, 1987).

Our efforts go towards explaining experimental observations in a mathematical model of 'small' neural network. We use neuron equations of Hodgkin-Huxley type and generate random connection patterns. We observe influence of different physiological parameters on generation of specific activity patterns. Phase plane analysis methods yields to better understanding of network dynamics. Our preliminary results show that burst activity can be obtained by varying the number of active connections, ratio of inhibitory to excitatory neurons and synaptic weights. Varying these parameters imitates changes in synaptic activity induced by tetanus toxin. Final aim of the research is to tune the model to reproduce network dynamics both in cultured neurons and in brain during epileptic seizure.
P2.5 RECEPTIVE FIELD NONLINEARITY RESULTING FROM LATERAL INHIBITION

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Two spots presented simultaneously on the same flank of the receptive field of lateral geniculate principal cell weaken the surround inhibition elicited from this site (1). This phenomenon can be mimicked in the simple model of single-layer network of 1,000 cells with built-in lateral inhibitory connections of recurrent type. We have evaluated the possible extent and contribution of such nonlinearity for summation processes within the given receptive field. The deviation from the simple linear model of summation which results only from considering the closest neighbor inhibitory connections can reach up to 20 % of the amplitude of the maximal center response. In general this value is determined by the distance between the two stimuli, spatial resolution and strength of inhibition assumed for particular calculation.


P2.6 "QUANTUM" NEURAL NETS - A NEW TOOL IN NEURAL NETWORK MODELLING

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We propose a new method of neural network modelling, based on two-state neurons that can be either "excited" or "de-excited. Transitions from excited to de-excited states are associated with emission of spikes. The basic quantities used for the description of these phenomenological models are correlation functions that characterize statistics of successive spike emission acts. The models are especially suited for description of attractors in neural network, and in particular dynamic attractors with low firing rates. Such behavior has been recently observed in many neurophysiological experiments of Miyashita, Koch, Fuster and others.

P2.7 THE NEURON-LIKE NETWORK FOR IBM PC

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The new neural network model including 1024 neuron-like cells with 256 synaps each has developed in Biocybernetics Department of Medical Academy in Cracow.

Presented network enables separate selecting of refraction-waveform and other parameters, like axions delay and threshold, for each neuron, separate selecting of weight for each synaps - before and during the simulation. The event-driven network is implemented in Turbo Pascal 6.0. The each separate simulation process can run fast or in the step-by-step mode, can be stopped and revived at any moment. The behavior of the neuron-like cells is based upon the knowledge of cellular mechanisms of the natural neurons. So, it is too sophisticated to technical applications; the implementers intend simulate the biological phenomenous.

P2.8 MODELING OF NEURONAL NETWORKS AS EVALUATED BY DRAWING TECHNIQUE

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On the basis of the neurocbernetic model of image processing it is hypothesized that when the examined persons are given names of complex situations they will first produce the images of component elements of a situation presented. The components taken together form the complex image. The aim of the study is to test this hypothesis in aphasic persons and in healthy people. An evaluation of drawings designating complex situations obtained from 50 persons with various types of non-severe aphasia and 50 healthy subjects matched for age nad sex will be presented. The significance of the findings for neuropsychology will be discussed.
P2.11 SELECTED PROBLEMS CONCERNING THE ACQUISITION OF ANALOG BIOMEDICAL SIGNALS - A COMPUTER PROGRAM

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Julian Myrcha - University of Technology, Warsaw, Poland.

This paper meets anybody who wishes to use the small computer based acquisition systems (IBM compatible computer and analog to digital (a/c) board) in the laboratory of physiology.

The digital acquisition of analog data by the computer system is now the leading method for biological data recordings. It combines the advantages of the paper chart recorder and of various possibilities of data analysis that gives a computer system. There are however some relevant conditions to be satisfied concerning the signal, hardware and software.

1. Sampling frequency - In various applications the well known Nyquist principle is far insufficient. We suggest oversampling that enables the reconstruction of the full shape and not only the frequency of the signal.

2. The length of convertor word. At least 12 bits resolution is suggested but the optimal adjustment of the signal voltage is required to take a full advantage of that resolution.

3. Data transfer rate. Most computer systems based on IBM compatible machines are much slower than the speed of the a/c converter and limits the system.

4. Memory storage. Use of RAM memory on IBM computers produces known problems to the programms. In a real time systems it makes a real problem. RAM is always treated as a temporary storage during sampling, then the data are copied to a hard disk. The amount of RAM limits recording length.

Some systems can transfer data directly onto a hard disk, using RAM as a buffer only. The recording length is limited by a disk empty space. The rate of sampling is generally lower in comparison to the RAM storage.

The above remarks brought us to the idea of building out our own acquisition system. A fully interactive, user friendly multichannel analog data collecting system JULADC is presented. The system is provided in an on-line display and off-line presentation program as well. Oscilloscope like system gives a great opportunity to monitor the data before and during the data acquisition.

The data presentation system is provided in a Command Processor that enables the data parameterization and the interface to the statistics. The parameters that can be measured are the amplitudes, Integrals, latencies, frequencies.
Posters (P3) - Alzheimer's disease and other types of dementia

P3.1 HIPPOCAMPAL PATHOLOGY IN ALZHEIMER DISEASE - 3-D RECONSTRUCTION AND MORPHOMETRIC STUDY
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The hippocampal formation from five control brains and eight brains of patients at the end stage of Alzheimer disease was reconstructed, employing coronal serial sections. This study reveals significant topographical differences in the number of plaques, tangles and neurons. The numerical density of senile plaques in the hippocampal formation is greatest in the head, lower in the body and lowest in the tail. The pyramidal layers of the hippocampus and subiculum complex, the deep layers of the entorhinal cortex, and the molecular layer of the dentate gyrus are mainly affected. Distribution of NFT reveals the biggest topographical differences. Neurofibrillary pathology develops in 20% of neurons in the pyramidal layer in the cornu Ammonis, in 14% in the entorhinal cortex, in 5% in the subiculum complex and only in 4% of neurons in the granular layer of the dentate gyrus. Neuronal loss is highest in the cornu Ammonis (27%) and the entorhinal cortex (17%) and is lower in the dentate gyrus (10%) and the subicular complex (1%). The significant differences in atrophy among the cornu Ammonis (almost 40%), the entorhinal cortex (20%), the subiculum complex (over 18%) and the dentate gyrus (12%) lead to changes in the shape of the hippocampal formation.

(Supported by funds from the New York State Office of Mental Retardation and Developmental Disabilities and a grant from National Institutes of Health, National Institute of Aging, Grant No. P01-AGO-4220)

P3.2 PATHOLOGY OF THE CLAUSTRO-CORTICAL LOOP IN ALZHEIMER DISEASE
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The human claustrum is located medially to the orbital and insular cortices and laterally to the putamen and the amygdaloid body. The claustrum is divided into the dorsal and ventral parts. In the ventral part we distinguish three parts: temporal, orbital and periamygdalar. Whereas the dorsal and temporal parts of the claustrum are connected with the neocortex, the periamygdalar and orbital parts are connected with the limbic lobe - especially with the entorhinal cortex. Our study of five control brains and eight brains of patients with Alzheimer disease reveals significant topographical differences in the volume of the parts of the claustrum and in the number of plaques, tangles and neurons. The numerical density of the senile plaques is the greatest in the periamygdalar part (20/mm²) and much lower in the other parts of the claustrum (ranging from 7/mm² in the orbital to 9/mm² in the temporal part). The numerical density of the tangles varies from 15/mm² in the periamygdalar to 1/mm² in the temporal part. The tangential constituent about 7% of the total number of neurons in the periamygdalar part, 4% in the orbital, and less than 1% in the temporal part. Significant neuronal loss is noticed in the orbital (greater than 37%) and periamygdalar parts (greater than 45%), which corresponds to the decrease in the volume of these parts. The intensity of atrophy, neuronal loss, and numerical density of the senile plaques generally decreases as follows: periamygdalar > orbital > dorsal > temporal part.

The great neuronal loss in the periamygdalar and orbital parts of the claustrum correlates with extensive pathological changes in the entorhinal cortex. The implication of this finding is that among the claustra-cortical connections, periamygdalo-entorhinal and orbito-entorhinal loops are the most affected.

(Supported by funds from the New York State Office of Mental Retardation and Developmental Disabilities and a grant from National Institutes of Health, National Institute of Aging, Grant No. P01-AGO-4220)

P3.3 Contribution to differential diagnosis of Alzheimer dementia versus multi-infarct dementia
Marko N. Gołębiowski, Maria Barcickowska, Anna Pfeffer-Baczuk, E. Luczywak
Alzheimer's Disease:Measuring the atrophic hippocampus with CT imaging.
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The purpose of this study was to establish the role of computerized tomography in diagnosis of Alzheimer's (AD) with special emphasis on atrophic hippocampal changes. We tried to show correlation between the hippocampal atrophy and early clinical evidence for memory impairment and it's role as the predictive marker of the progressive dementia of AD.

We examined 100 patients using a medical and neuropsychological protocol. 54 individuals had mild to severe AD, 21 had minimal memory changes, 25 were control subjects. The CT findings were rated for dilatation of the hippocampal fissure.

Hippocampal atrophy was typically bilateral and was more prevalent in the groups with memory dysfunction. 25% of the controls, 41% of the group with minimal memory changes and 92% of the moderate to severely impaired had hippocampal atrophy. An age effect was discernible only in the controls such that after 80 years of age the diagnostic value of hippocampal atrophy was adversely affected.

The longitudinal study of the cases with minimal memory impairment is in progress. First follow-up ratings show that most patients who deteriorated had hippocampal atrophy at the baseline.

P3.4 PATHOLOGY OF THE CLAUSTRO-CORTICAL LOOP IN ALZHEIMER DISEASE
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The diagnostic criteria of probable and possible senile dementia of Alzheimer type are internationally accepted based on report of the NINCDS-ADRDAD Work Group. In epidemiological screening studies the differential diagnosis of Alzheimer dementia /DAT/ against multi-infarct dementia /MID/ is often possible by general, neurological and psychological examinations including isoelectric scale questionnaire after Hachinski et al. /1975/.

EEG scan may often help in positive diagnosis of MID. Evoked potentials evaluation /visual and acoustic/ is of limited value only. According to our opinion the significant contribution to differential diagnosis of DAT against MID prings the brain mapping. In many cases of DAT quantification of EEG shows some slow down of basic rhythm with increase of low alpha waves /7.5-8.5 Hz/ and with presence of trace account of 9.0-12.5 Hz waves only. In patients with MID focal changes with theta or even delta waves were observed.
P3.5  NIGHT SLEEP OF ALZHEIMER DISEASE PATIENTS
Sh.I.Sibilishvili

It is known that patients with different clinical forms of progressive dementia reveal disturbances of night sleep of this or that degree. We investigated polygraphically the night sleep of 18 patients with Alzheimer disease. Their age ranged within 53-65 years. All the patients underwent EEG, CT and MRI checks. The majority of patients during an EEG check in awakenings showed a marked slowing and disorganization of alpha rhythm, the presence of generalized asynchronous slow waves as well as bursts of high amplitude sharp waves of theta range in frontotemporal areas. 12 examined patients had a prolonged latency of sleep, 9 revealed a marked decrease in the percentage of REM sleep stage and 6 in stage of slow wave sleep (SWS). All the patients had marked increase in stage 2 of SWS (P < 0.001). The given disturbances in the sleep structure are the sharper the more marked dementia is. 11 patients out of 18 in stages 2 and 3 of SWS showed bilateral synchronous bursts of spike-wave complex with frequency of 2.5-3.5 Hz. The bursts also had paroxysmal rhythmic waves (14-16 Hz). Some patients showed focal epileptic discharges in frontotemporal areas, mainly on the left. The obtained data and the fact that serotonergic mediation is essential in initiation and maintenance of night sleep, let us prove functional deficiency in Alzheimer disease not only of cholinergic but also serotonergic system of the brain.

P3.6  THE EFFECT OF ALZHEIMER'S DISEASE ON THE COURSE OF HIGHER MENTAL PROCESSES
E.Luczywek, M.Barciikowska, E.Fersten, A.Pfeffer

In the study a specially devised series of tests was used to assess higher mental processes in elderly people. Subjects in the study were 18 persons without any specific damage to the CNS and 11 patients diagnosed as suffering probably from Alzheimer's disease. Statistical analysis of obtained results indicated a significant impairment of linguistic performance, visuo-spatial functions, learning process and of verbal memory in the later group.

P3.7  A COMPARISON OF COGNITIVE IMPAIRMENT IN DEMENTIA OF THE ALZHEIMER'S TYPE (DAT) AND MULTI-INFARCT DEMENTIA (MID)
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We studied 75 inpatients with dementia or complaints of progressive memory loss. The diagnosis of dementia was based in all cases on clinical examination and a neuropsychological test battery according to the criteria outlines in the DSM-III-R for primary degenerative dementia or vascular dementia.

The aim of this study was the evaluation of the differences in the levels of cognitive functions between MID and DAT and also a detailed analysis of intellectual functions in cerebrovascular disease in cases with only slight cognitive impairment in MMSE.

25 patients fulfilled the clinical criteria for DAT and 25 those for MID. Twenty five of the remaining patients scored 24 or more on MMSE, had multiple vascular lesions on CT or MRI and were placed into a third group - MID.

Patients in the MID group had much higher IQ scores on the Wechsler-Bellevue Scale than MID patients, but other subtest results were much below the mean and did not differ from those in the MID group. Patients in the DAT group were more demented than the MID group. DAT patients were unaware of their failing capacity. Attention and orientation were similar in the groups. Almost all patients showed severe disturbances of these functions.
Verbal memory was assessed in 38 subjects aged over 60, divided into three groups:

a) those without any discernible damage to the CNS (N=18);

b) patients suffering probably from Alzheimer’s disease (N=11);

c) those with Parkinson’s disease (N=9).

The process of learning new verbal material and remembering it after an interference, as well as the ability to retrieve information acquired much earlier were assessed under 4 experimental conditions.

Statistical analysis of obtained data indicated a similar performance level in patients with Parkinson’s disease and in healthy subjects as regards both memorization and retrieval of new and old verbal material, while significantly inferior performance was found in patients suffering from Alzheimer’s disease in respect of all the verbal memory dimensions under study.

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Anticardiolipin antibodies as a risk factor in patients with Multi Infarct Dementia.

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Anticardiolipin antibodies together with Lupus anticoagulant belong to the group of Antiphospholipid antibodies. Present studies draw attention to these antibodies as a risk factor cerebrovascular events(CVE). ACPLA, having a particular relation to phospholipid antigene, cause hemostatic disturbances probably through binding with antigens present in platelet, endothelial membranes or by interfering with different clotting factors. MID is caused by frequent CVE. The role of ACPLA as a risk factor for this type of dementia has not yet been determined.

42 patients with MID were examined for the prevalence of quantitative and qualitative ACPLA present in sera. ACPLA were investigated using a solid phase enzyme immunoabsorbent assay (ELISA). An increased titer of ACPLA was detected in the sera of 17 patients (40,5%). 5 patients had IgM antibodies, 10 had IgG and two had antibodies belonging to both classes.

From this we can conclude that although the pathogenic role of ACPLA in MID is still not completely clear, they merit further investigation, particularly their potential influence on thrombotic events.

Immunological alterations in the MPTP induced model of Parkinson’s disease in mice.

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Discovery of 1-nethyl-4-phenyl-1,2,3,5-tetrahydropiridine (MPTP), neurotoxin which produces extensive, relatively selective destruction of nigrostriatal dopaminergic neurons, prompted development of an animal model of Parkinson’s disease. In our experiments we examined the influence of central catecholamine depletion in MPTP treated mice. C57Bl/6 mice weighting 30-35g were treated i.p. with 4 injections of MPTP at one hour intervals. This schedule induced about 90% dopamine depletion in the striatum 7 days post-treatment, as verified by HPLC.

IgM antibody production of splenocytes to SRBC was reduced in MPTP treated animals. Proliferation of spleen cells in response to wide range of mitogen concentrations (PHA, ConA, LPS) was also significantly diminished in MPTP treated animals. Testing for MIF revealed differences only in low mitogen concentration. Observed modifications of immune responses related to destruction of dopaminergic system suggest its possible role in immune regulation.
Contemporary epidemiological situation of tuberculosis is characterized by tendency to increase of tuberculosis illness including tuberculous meningitis. As a rule early revealing of tuberculous meningitis is difficult because clinical signs of meningitis are reduced and atypical and the course of illness is short. Characteristic symptoms are: headache, vomiting, weakness, whereas meningeal syndrome may be attenuated.

Our scheme of investigations makes possible directed immunological examination, including nosological form of the disease and in some cases reduces terms of analyses and their volume. Immunodiagnostic includes the following complex of methods: functional activity and quantitative characteristic of B-lymphocytes populations and subpopulations, quantitative characteristic and function of T-lymphocytes, of microbe and tissue sensitivity, level of autoimmune processes, functional state of phagocyting cells.

P3.

Scalp recordings were within normal limits in 79% cases. The common abnormality was the lack of cortical waves in the damaged area (mostly frontal region) or the absence of SEP in the whole hemisphere when control region was involved. Comparison of scalp and cortical responses showed similar polarization and latency when present and its were absent in both types of recordings (scalp, cortical).

Our investigations showed, the SEP are directly influenced by organic brain lesion, functional changes (epileptic foci) had no effect on its.
MAGNETIC STIMULATION OF THE LUMBOSACRAL ROOTS


Magnetic stimulation of the nervous tissue has become a valuable research and clinical tool since it was first introduced in 1985. Its advantage over electrical stimulation include the ability to stimulate deep-located nerve tissue without pain component. Thus, the magnetic stimulation appears a promising technique for the noninvasive evaluation of the function of the lumbosacral roots with great potential as a simply painless procedure for diagnosis of lumbosacral radiculopathy. Applying the magnetic stimulation an experiment were undertaken to evaluate lumbosacral root innervation by study response from 4 selected pairs of homologous leg muscles in 10 healthy subjects. A 10 cm round magnetic coil were positioned at L1-S2 spinal segments in plane parallel to the axis of lumbosacral spine with handle pointed towards the feet. Compound muscle action potential /CMAP/ were collected simultaneously by means of EMG surface electrodes placed over vastus lateralis, tibialis anterior soleus and extensor digitorum brevis. The responses were reproducible on repeated stimulation while the coil was kept in the same location. Collected CMAPs from homologous muscles exhibited high temporal symmetry whereas their amplitudes differed significantly due to stimulation asymmetry immanent in the magnetic stimulation.

LUMBO-SACRAL DERMATOMAL SOMATOSENSORY EVOKED POTENTIALS /DSEPs/-METHODOLOGICAL STUDY

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The conventional electrophysiological methods such as EMG, F wave, H reflex and somatosensory evoked potentials assess mainly motor or mixed nerves supplied by more than one spinal root. Scalp recorded evoked potentials following stimulation of L5 and S1 dermatomes have been established by Sedgwick/1985/ and Aminoff/1985/ as a useful method for evaluating of the functional status of single spinal root in patients with chronic back pain and prolapsed disk. The normal value of DSEPs from L3 and L4 roots are not work out till now. We used this method to study 37 healthy volunteers aged 16-56y /mean 36.4/ in order to obtain normative values for L3 and L4 roots, and verify the values of DSEPs from L5 and S1 roots, published so far. The signature areas of L3, L4, L5, S1 in both legs were stimulated with bipolar surface electrodes. Two sequential runs of 512 sweeps were averaged and recorded from the scalp /Cz- Fpz/. The latency of initial deflection /N33/ and latency and amplitude of subsequent peaks were measured. Our control values obtained from L5 and S1 DSEPs are comparable with the data provided by Sedgwick/1986/. The values obtained from L3 and L4 DSEPs are reproducible and faithful in the similar extent as L5 and S1 results, and can be used for diagnosis in patients with chronic lumbosacral pain. The detailed data will be presented.

SPINAL OPIATES FOR CHRONIC PAIN: AN UPDATE

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For more than 10 years spinal (epidural (EO) and intrathecal (IO)) opiates have been one of the palliative treatments for intractable pain. We analysed the success of treatment in 1201 and 363 patients who received EO and IO, respectively. The success rates of EO and IO treatment is lower than generally believed. Excellent analgesia was only achieved in about 30 % of the patients. The failure rate of the method was about 30-40 %. Duration of treatment was about 3 (EO) and 6 months (IO). It seems likely, that the longer the duration of treatment, the higher the incidence of side-effects and complications (will be). The success of treatment is dependent on the criteria for the selection of patients. Main criteria include plate-sensitive pain, intractable pain, ineffective conventional analgesic treatment and adequate patient status. There are different systems available to administer EO and IO: Percutaneous or subcutaneous catheters, port systems, externally portable or implantable infusion devices. Before a dosing device is implanted, it has to be assured that the method provides sufficient pain relief. Morphine is the most suitable opiate for spinal use because far lower spinal than systemic morphine doses are necessary. It is doubtful wheather EO or IO should be injected when spinal and systemic opiate dose requirements are equal. Because of the risk of respiratory depression, careful observation is necessary for patients under EO or IO treatment. Side-effects and complications may result in treatment failure. If tolerance develops, sufficient analgesia may be achieved by spinal DADD, met-enkephalin, clonidine, labetalol, lysin-acetyl-salicylate, calcitonin, somatostatin or octreotide.

Frequency analysis of eeg in patients after head trauma

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In 103 patients, i.e. 54 persons after 6-28 days and 49 persons after 6-12 months after cerebrocranal trauma frequency analysis of eeg using Neuroscan system, routine eeg and CT of the head were carried out. Basing on neurological examination and CT in 54 patients cerebral concussion and in 52 patients contusion of the brain was diagnosed. Relative power theta/beta indicator was evaluated from the: C3-P3, O1-P1, C4-P4, P04, P7-P3, T3-T5, F8-T4 AND T4-T6. In the early period after the head trauma theta/beta indicator was elevated in 14,3% of patients with cerebral concussion and in 35,7% of patients with brain contusion, who had normal routine eeg.

During the second half of the year after the accident in patients with cerebral concussion the theta/beta indicator was evaluated in 11,1% and in patients with brain contusion in 20,0%.

Frequency analysis of eeg detects the pathology in cases where routine eeg is normal and allows to monitor the recession of pathologic changes.
P4.11 The deep rapid-rate magnetic stimulation of the brain - a new psychiatric therapy?
Tomasz Zyss, M.D.; Chair and Clinic of Psychiatry, Medical Academy in Cracow

The biophysical processes during electroconvulsive therapy (ECT) were investigated. An important question regards the influence of the path of the current on the efficiency of the ECT. The tissues offer a rather complex network of resistance to impede the electrical stimulus. The high resistance of the scalp and the skull causes a shunting and spreading of the major portions of the current through extracranial tissues. The final effect is that only a small percentage of the injected current passes into the brain. The most important problem is therefore the stimulus transmission into the neurochemical disturbed mesencephalic regions.

The stimulation of the brain with a time-variing magnetic field makes this problem possible. Barker et al. (1985) described a non-invasive and painless method of transcranial brain stimulation involving the use of brief magnetic field pulses. The rapidly changing magnetic field serves to energy transfer process. Magnetic field passes through all head structures with no attenuation and hence can stimulate the brain without discomfort. Our calculations of stimulus strength for various distances below the magnetic coil have assumed that this inductive method is able to evoke the same therapeutical effects as ECT, but in more safe mode (without motor seizure).

P4.13 Dysplaxia in hydrocephalus
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Department of Neurosurgery
Medical Academy in Lublin

Dysfunction of the higher cortical functions is one of the major symptoms of hydrocephalus. Remission of cortical dysfunction is an important factor of therapeutic result of the shunt. One of the common signs of cortical dysfunction is dysplaxia and dysgraphia.

25 patients with hydrocephalus of various grades and etiology were evaluated by graphic neuropsychological tests before and after shunt surgery.

The obtained neuropsychological results were graded into three categories of dysfunction: dysfunction - 10, dysfunction - 12 and euphoria - 3 patients. Control assessment after shunt surgery demonstrated improvement of graphic abilities in 17 cases.

Improvement or no improvement in graphic tests were correlated with interventricular pressure and ventricular size.

P4.12 Seasonal and meteorological changes as risk factor of cerebro-vascular disease
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The attempt to clarify the risk factors of cerebro-vascular disease is a key problem in epidemiology of cerebral stroke and carries high practical value. Solution of the problem, even if partial, might promote prophylaxis against acute vascular disease of the brain.

In our epidemiological studies performed in province of Poznañ, the highest percentage of cerebro-vascular diseases was observed in January and in the first quarter of the year, with a negative correlation between temperature and the number of cases. Fibrinogen concentration higher in elderly during cold weather months may be responsible for the excess frequency of stroke in winter among this population.

It seems justified to recommend for persons with high risk of stroke /arterial hypertension, diabetes/ in the winter months, as well as in days of sharp atmospheric variations the antiaggregating agents as the prophylactic measure.

P4.14 Concentration of some aminoacids in blood in depression
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Serum concentration of some aminoacids /AAs/ were studied in 32 patients who fulfilled the DSM-III-R criteria for major depression: bipolar affective illness /13/ and unipolar affective illness /19/. All patients were hospitalized throughout the study. Blood samples were taken during the depressive episode /after two weeks of pharmacological washout/ on 15th day of therapy and in the remission. The chromatographic procedure on Multichrom-Beckman automatic amine analyzer for analysis of AAs was used. Patients were treated with amitryptiline. Clinical status was assessed with HAMD, HAMA, CIG at baseline, at day 15th and at remission of depressive symptoms. Dynamic changes in the concentration of 15 AAs in blood serum were observed. Glycine, phenylalanine, arginine and valine showed significant correlation with the intensity of psychopathological symptoms. In patients with more pronounced depression the concentration of these AAs were lower.
The testing of motor activity in hyperactive boys means visual-manual recording.

Tomasz Zysy, M.D.; Chair and Clinic of Psychiatry, Medical Academy in Cracow

Hyperactivity is a childhood behaviour disorder with cardinal feature of overactivity. Measuring habitual physical activity in man is extremely difficult. All previous employing methods for the measurement of hyperkinesis (rating scales, observation codes, mechanical devices) estimate the individual activity level either incompletely or in a very subjective manner. We have used a motoscopy-motometrical method (the visual-manual recording) as one of the most objective instruments for assessing hyperkinesis. Matched pairs of hyperactive and normally active boys were observed in 4 test situations. The art and the number of specific behaviours were continuously recorded. 4 standardized situations were: sitting, standing, lying and reading. The whole motion behaviour was divided into 4 movement groups (according to the main body parts); head, trunk, upper and lower extremities. In all observed settings displayed the hyperactive children significantly more activity as the boys from control group. The best method for discrimination between the two groups was the recording of lower limb movements in sitting. We present the normal and pathological values for motor activity. Results were discussed in terms of their implications for motor control and locomotion.

Posters (P5) - Neurotransmitters and their receptors

P5.1 Differences in adrenergic regulation of cyclic AMP formation in cerebral cortex of the spiny mouse and the rat

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The responsiveness of adrenergic cyclic AMP generating system in the cerebral cortical slices from two species: Acomys cahirinus and rat, after exposure to adrenoceptor agonists and antagonists, was investigated. Density and affinity of adrenoceptors in cortical membranes and the influence of chronically administered imipramine on cyclic AMP was also compared. The results suggest that two subpopulations of beta adrenergic receptors exist in the cerebral cortex of both examined species. The first subpopulation is able to stimulate cyclic AMP generating system without interaction with alpha adrenoceptors and is down-regulated after chronically administered imipramine. The second subpopulation forms cyclic AMP only when interacts with alpha adrenoceptors and is not down-regulated by imipramine. The first hypothethical subpopulation of beta adrenergic receptors plays a more important role in the cerebral cortex of the rat while the second one functionally dominates in the cerebral cortex of Acomys cahirinus.

IN VITRO EFFECTS OF ANTIDEPRESSANTS ON NORADRENA- LINE-DEPENDENT SECOND MESSENGER SYSTEMS
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The activation of a1-adrenergic receptor leads to phosphatidylinositol breakdown followed by the generation of inositol phosphates (IP) and an kinase C (PKC) activator, diacylglycerol. The B-adrenoceptor is linked with the cyclic AMP (cAMP) generating system. We have examined how antidepressants: imipramine (IMI), mianserin (MIA) and citalopram (CIT), affected noradrenaline (NA)-induced IP accumulation (a1-response) and NA- and ISO-induced cyclic AMP accumulation (B-response) in rat cerebral cortical slices, in the absence and presence of a PKC activator, a phorbol ester (TPA). IMI and MIA (1-100 μM) significantly inhibited NA-stimulated IP accumulation, but 0.1 μM IMI enhanced it. IP accumulation was saturated by high concentration of CIT (100 μM). TPA decreased NA-induced IP accumulation (by 40%) and that action was abolished with low concentrations of IMI (0.1 and 1 μM) and MIA (0.1 μM). CIT at all concentrations except 100 μM partially counteracted this inhibition. ISO-induced cAMP accumulation was unaffected by antidepressants, while cAMP response to NA was significantly inhibited only by the highest concentrations of drugs. TPA potentiated NA- and ISO-induced cAMP accumulation (60% and 130% resp.). The action of TPA on cAMP response to NA was attenuated by IMI>MIA>CIT. The TPA-potentiation of the response to ISO was attenuated by MIA more than by IMI, but remained unaffected by CIT. The acute effects of antidepressant drugs on second messenger systems seems to be paralleled by their antagonistic actions at the adrenergic receptors: IMI is an α1-antagonist, MIA - α2,α1-antagonist, while CIT inhibits the serotonin uptake only. Some antidepressants may act on the PKC-related cross-talk between receptors.

Neurological and psychical aspects of noxious food effects.
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Food allergy is considered as a first clinical symptom of atopic disease in child. If allergic reactions resulting from harmful food consumption by a hypersensitive person and concerning the symptoms coming from the digestive tract, respiratory system or the skin are better known the allergic symptoms from the central nervous system or vegetative one are poorly recognized. To define these symptoms we examined 67 children with food allergy. The diagnosis procedure for this group included Goldman-lynghyken criteria and some chosen laboratory test. Special attention was given to those examined children who demonstrated neurological or psychical symptoms occurring after noxious food consumption (speech disorders, tic events, subdural hygroma, muscular hypotonia or hypertonia, seizures, hyperactivity headaches). We concluded that when there is no organic cause damaging the nervous system, the existing neurological or psychical symptoms may be connected with hypersensitivity to certain food. Elimination of that food results in complete regression or alleviation of symptoms from the central or autonomic nervous system. Undivided attention should be paid to the neurologic reactions caused by food intolerance.
P5.3 CHANGES OF EMOTIONAL BEHAVIOR IN DSP4 TREATED RATS
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Central NE neurons are considered to exert an inhibitory control over affective aggression (Mogilnicka et al.83, Paculowski et al.86,87). Physiological findings suggest however, that NE is involved in modulation of the reactivity to stressful stimuli rather than in transmission of specific information (Foote et al.83, Rasmussen et al.86).

The aim of this study was to investigate the effect of selective noradrenergic neurotoxin DSP4 on social behavior and responsiveness to stressful stimuli in rats. It is known that DSP4 injected i.p. in the dose used, produce prominent depletion of NE in neocortex, hippocampus, amygdala and hypothalamus (Dooley et al.83). Concentration of NE, DA, SHT and their metabolites will be HPLC measured after completion of the experiment.

Intruder-Resident paradigm and ethological analysis were used to evaluate the occurrence of offensive and defensive/submissive behaviors in both partners. DSP4 (60mg/kg) preceded by Zimelidine to prevent SHT depletion, was injected to intruders only. DSP4 treatment increased the occurrence of offensive postures in previously submissive rats in comparison with pretreatment period (p<0.05) as well as in comparison with residents (p<0.05). Consequently the occurrence of defensive postures diminished in DSP4 treated rats, increased in residents (p<0.05). Photophbic forced open field (illuminated in the center with 200W bulb) was used as a test for stress reactivity. Ambulation and the total time spent in the center were recorded during 6 min. The exploratory activity and the time spent in the center were significantly augmented in DSP4 treated rats in comparison with normal controls (p<0.01, p<0.01).

It is suggested that the role shift during the intruder - resident encounter might reflect inadequate responsiveness to the environmental stimuli rather than increase of aggression per se. This is in agreement with our previous results on cats (Kubiak & Zagrodzka 92).

P5.5 Effect of adrenaline on the activity of the cockroach nervous system.
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Octopamine, the substance release in stress conditions in insects is a analog of adrenaline (A) in vertebrates. It has an excitatory effects on the escape system in the cockroach. Function of the cockroach nervous system is a widely accepted model for neurobiological research. Do it have the possibility to answer to A ? If so, cockroach nervous system would be also a good model for experiments with adrenergic stimulation.

Action potentials frequency was recorded before and after wind stimulation of cerci in control animals and after applied A. Recordings were performed immediately, 0.5h, 2 and 24 h after amine application.

Spontaneous activity and response to mechanostimulation increase significant after A. The most effect appeared 2 h after A injection. 24h later decrease was observed. Response delay and excitation time did not change after amine application.

P5.6 DEVELOPMENTAL CHANGES OF GLUTAMATE RECEPTORS IN MOUSE BARREL CORTEX
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Two different forms of plastic changes can be distinguished in the barrel cortex - the developmental plasticity of barrel morphology, occurring during the first 4 days of life and a later expressed phenomenon of purely functional plasticity. We studied changes in sensitivity and distributions of NMDA, MK 801, AMPA and glutamate metabotropic binding sites in development of mouse barrel cortex using quantitative in vitro autoradiography. The density of labeling of NMDA and MK 801 binding sites increased during the first month of life, reaching a plateau at the end of third week. In adults NMDA receptor-channel complex labeling was denser in layers II, III and IV than in lower cortical layers. Laminar distribution of NMDA receptor-channel complex changed during development. The density of labeling of AMPA binding sites increased during the first two weeks and later decreased until postnatal day 70 without gross interlaminar changes. In contrast quisqualate metabotropic receptors showed a decrease of binding during postnatal life. Thus the metabotropic receptor is the only glutamate receptor with high binding values during the time of morphogenesis of the barrel field. Other receptors reach adult binding values at the time when functional plasticity develops.

P5.4 THE EFFECT OF INCREASED SENSORY STIMULATION UPON NMDA AND GABAA RECEPTORS IN THE BARREL FIELD OF ADULT MICE.
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The pattern of distribution of NMDA channels and GABAA receptor sites was examined using [3H]MK-801 and [3H]muscimol and in vitro quantitative autoradiography in the barrel field of SI cortex of mice following increased sensory stimulation of mystacial whiskers. For this purpose mice (n=6) had the row B on one side of the muzzle stimulated with paint brush with frequency of 3 stimuli per 10 s. Overall duration of the session was 10 min, and it was repeated during 4 succeeding days. The unstimulated side served as a control. In control barrel field (3H) MK-801 and (3H)muscimol labeling showed characteristic barrel-like pattern corresponding to anatomically defined barrel-field, and no differences were found in the intensity of labeling between rows of barreis both for (3H)MK-801 and (3H)muscimol. On the stimulated side in row B (3H)MK-801 binding decreased by about 15% in comparison to neighbouring rows in each mouse examined. However, (3H)muscimol binding in row B remained unchanged. The results suggest the differential involvement of NMDA and GABAA receptor sites in functional plasticity of the barrel cortex.
Various calcium ionophores have been identified in hippocampal neurons, but it is not clear what their participation in pathological conditions is. Enhanced stimulation of glutamate receptors is one of the reasons of neuronal death in ischemia. Our previous studies suggest that calcium channels coupled to the glutamate, NMDA sensitive receptors may play a key role in ischemic calcium redistribution in the hippocampus. Present study was aimed to investigate the possibility of opening different calcium ionophores by glutamate receptor agonists in the hippocampus and to characterize the mechanism of this effect.

To measure changes in $[Ca^{2+}]_i$ in the hippocampus of anesthetized, freely moving rabbits, and to apply active substances locally to the hippocampus, a microdialysis technique was adapted. Application of NMDA resulted in dose-dependent fall of $[Ca^{2+}]_i$ (by 60% at 5 mM NMDA), which was inhibited by competitive and noncompetitive antagonists of NMDA receptors, potentiated by glycin and D-serine and inhibited by 7-Cl-kynurenate. N Sidipine and amiloride only slightly reduced this effect, ethanol retarded but not altered the max. fall. Application of 5 mM kainate evoked 30% decrease in $[Ca^{2+}]_i$, completely inhibited by DNQX, partially by nismopidine and was insensitive to NMDA antagonist – APV. 5-(N,N-dimethyl)amiloride shortened the $[Ca^{2+}]_i$ decrease, but amiloride only slightly. These data indicate that glutamate receptor stimulation evokes opening of different calcium ionophores. Although NMDA receptor-operated calcium channels probably play the main role in Ca$^{2+}$ redistribution in ischemia, also reversed Na$^+$/Ca$^{2+}$ exchange and secondary activation of the voltage operated channel might play an additional role.

**P5.7** CHARACTERIZATION AND MODULATION OF CALCIUM IONOPHORES ACTIVATED BY NMDA AND NON-NMDA-RECEPTOR STIMULATION

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**P5.8** CHOLINERGICALLY-INDUCED THETA RHYTHM IN THE CAT HIPPOCAMPAL FORMATION

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The present investigation was undertaken to assess the role of the cholinergics in the production of theta rhythm in the cat hippocampal formation. Intrahippocampal injections of carbachol, muscarine and eserine produced a well synchronized high-frequency cholinergic theta-like activity (HFT) in a range of 5-12 Hz. Subsequent intrahippocampal injection of muscarinic agonist, atropine sulphate, completely blocked this cholinergically-induced EEG pattern. Nicotinic antagonist, hexamethonium, was without any effect on cholinergically-induced high-frequency rhythmical waves. We suggest that HFT may result from activation of the oscillatory mechanism intrinsic to the cat hippocampal formation.

**P5.9** ROLE OF VASOACTIVE INTESTINAL POLYPEPTIDE (VIP) AND ATROPINE IN THE REGULATION OF THYROID GROWTH PROCESSES IN THE RAT

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The goal of present study has been to examine effects of VIP and atropine on 3H-thymidine incorporation into DNA of rat thyroid lobes in vitro. In Experiment I, we incubated thyroid lobes for 4 hrs in RPMI 1640 medium + 15% FCS, with 3H-thymidine and with the following substances: TSH (20 mIU/ml), VIP (10^{-6}-10^{-7}M), VIP together with TSH, VIP-antagonist ([4Cl-D-Phex, Leu^1]VIP) (10^{-6}-10^{-7}M) and VIP together with VIP-antagonist. In Experiment II, direct intrathyroidal injections of the same substances as in Experiment I, were performed, except of atropine (1 mg), which was applied intraperitoneally – in groups which received VIP and VIP-antagonist directly into the thyroid. After 24 hrs, thyroid lobes collected from all the animals, were incubated with RPMI 1640 medium + 15% FCS and 3H-thymidine.

**Results:** VIP decreased 3H-thymidine incorporation into DNA of rat thyroid lobes in vitro and suppressed the stimulatory effect of TSH. Intrathyroidal injection of VIP did not alter significantly 3H-thymidine uptake. Pretreatment with atropine decreased the effect of VIP, but not of VIP antagonist. In both experiments, VIP-antagonist, when used alone, had no effect on 3H-thymidine incorporation.

**P5.10** MODIFICATION OF ACETYL-CoA AND ACH METABOLISM IN NERVE TERMINALS BY DICHLOROACETATE

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Dichloroacetate (DCA), is known activator of pyruvate dehydrogenase in peripheral tissues. However, in rat brain synaptosomes incubated with 30 mM K+ and with no Ca$^{2+}$ added, neither 0.05 mM DCA nor 1 mM (-)hydroxycitrate (HC) affected pyruvate utilization, acetyl-CoA content and ACh synthesis. The addition of 1 mM Ca$^{2+}$ reduced pyruvate utilization, citrate accumulation and level of acetyl-CoA in synaptosomal mitochondria but simultaneously markedly stimulated release and synthesis (100%) of ACh at unchanged level of synaptosomal acetyl-CoA. Under these conditions HC increased citrate accumulation and suppressed synaptosomal acetyl-CoA and ACh synthesis by one third. DCA partially reversed inhibitory effects of Ca$^{2+}$ on pyruvate/citrate metabolism and prevented suppression of ACh synthesis and synaptosomal acetyl-CoA by HC. It is concluded that in K+/Ca$^{2+}$-activated nerve terminals the DCA might markedly improve provision of synaptosomal acetyl-CoA by ATP-citrate lyase independent pathways.
**P5.11** SHT and Reward: The Effects of Selective SHT3, Antagonist and Mixed SHT1/SHT3, Ago-Antagonist on the Establishment of Morphine-Induced Place Conditioning in Rats.

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Serotonin (5HT) containing brain neurons have been linked to reward function in self-administration and conditioned place preference experiments. The purpose of the present research was to study the role of SHT1 and SHT3 receptors in development of motivational properties of morphine. We investigated the influence of the selective SHT3 antagonist ondansetron (GR 38032F) and mixed SHT1/SHT3, ago-antagonist BIMU 8 on the rewarding properties of morphine. The unbiased procedure in two-compartment place-conditioning paradigm was used. Both drugs failed to affect the spontaneous unconditioned preference of the animals. Pacing of morphine (2 mg/kg sc) with one of the compartments induced significant preference for that compartment. When injected systemically before conditioning, ondansetron blocked acquisition of morphine-induced place preference in dose-dependent manner. On the contrary BIMU 8 potentiated morphine-induced place preference in the dose 0.001 mg/kg ip.

This findings indicate that SHT by means of SHT3 and SHT1 receptors plays the diverse role in rewarding properties of morphine.

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**P5.13** THE DISTRIBUTION OF 5-HT1 RECEPTOR SITES IN THE VISUAL STRUCTURES OF KITTEN’S BRAIN

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The distribution of 5-HT1 receptor sites was examined using quantitative in vitro autoradiography in the visual structures of 5 weeks old kittens 1) with normal binocular vision, and 2) monococularly deprived during the last 3 days of life. Distinct regional, areal and laminar differences in [3H]S-HT labeling were observed. The primary visual cortex (area 17) had high density of binding and tri-laminar pattern of 5-HT1 sites corresponding to cortical layers II-III, IVc and VI. This features distinguished area 17 from other cortical area investigated. We registered very high labeling in the superficial-visual layers of superior colliculus, but LGN showed rather weak labeling. Neither density nor pattern of 5-HT1 sites were affected by 3 days of monocular deprivation. High density of labeling and the distinct pattern of 5-HT1 receptor sites in the primary visual cortex suggest the important role of serotonergic transmission in the modulation of visual afferent input activity.

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**P5.12** Bulbospinal Serotonergic Override of the Withdrawal Reflex

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As indicated by the work of other investigators, there exists a system of serotonin (5-HT)-containing neurons which originates in the nucleus raphe and terminates in the dorsal and ventral horns of the spinal cord. This pathway has opposite effects on motor output and sensory input. Electrical stimulation of the raphe increases motoneuronal activity, and iontophoric application of 5-HT decreases the threshold of motoneuronal cell bodies. Using pharmacological manipulation with 5-HT antagonists, precursors and reuptake inhibitors, our laboratory has demonstrated that this pathway has a nonspecific excitatory effect on both alpha and gamma motoneurons innervating both flexor and extensor muscles. Behavioral effects include catalepsy and tonic immobility. The 5-HT pathway, therefore, provides a nonspecific gain or volume control for the level of activity of the motoneurons. Sensory input, on the other hand, is inhibited by the 5-HT pathway. Using similar techniques, it has been demonstrated that the 5-HT pathway blocks nociceptive information coming from flexor reflex afferents in the dorsal horn, and is part of the mechanism by which narcotics alleviate pain. In summary, the descending 5-HT pathway has the ability to hold a limb rigid and reduce nociception at the same time. It is suggested here that this dual effect of the bulbospinal serotonergic system provides an ideal mechanism for the motivational overriding of the withdrawal or flexor reflex by supraspinal centers.
P5.15 THE EFFECTS OF ACUTE AND SUBCHRONIC GAMMA-VINYL-GABA ADMINISTRATION ON THE NON-EPILEPTIC RATS PERFORMANCE IN 5-CHOICE SERIAL REACTION TIME TASK

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The present study investigated whether pharmacological administration of GABA-ergic system affect attention. The effects of vigabatrin, a novel antiepileptic drug which increases the GABA levels in brain through inhibiting GABAaminotransferase on the performance of rats in 5-choice serial reaction time task assessing selective attention were studied. The effects of acute (doses 100 mg/kg, 300 mg/kg, 500 mg/kg and 1000 mg/kg), and subchronic (doses 50 mg/kg, 100 mg/kg, 200 mg/kg and 300 mg/kg) administration of vigabatrin were investigated. Previous studies have shown that at the doses 100-500 mg/kg acute administration and 50-200 mg/kg subchronic administration vigabatrin has anticonvulsant activity. At the doses 100 mg/kg, 300 mg/kg acute administration and 50 mg/kg, 100 mg/kg, 200 mg/kg subchronic administration vigabatrin has no effect on selective attention. At the dose 500 mg/kg acute administration vigabatrin slightly decreased behavioural activity. At the doses 100 mg/kg, 200 mg/kg and 300 mg/kg acute administration and 50 mg/kg acute administration vigabatrin has no effect on selective attention. The highest doses used produced an overall behavioural deficit with no marked depletion of any particular function. The present results showed that administration of vigabatrin at the antiepileptic doses produced a slight impairment in attentional function possibly due to decrease behavioural activity.

P5.16 MODULATORY EFFECT OF ARACHIDONIC ACID ON BRAIN CORTEX GABA<sub>A</sub>-CI<sup>-</sup> RECEPTOR COMPLEX FUNCTION

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Our previous studies indicated that arachidonic acid (AA) is actively released by the action of phospholipases and lipases from brain membrane lipids in the Ca<sup>2+</sup>-dependent, independent and receptor coupled manner. In this study the effect of AA at 100 nmol/mg protein on the agonist binding to the GABA<sub>A</sub> receptors and on the chloride current in brain cortex synaptic plasma membranes was investigated. It was observed that AA increases of high and low affinity [3H]muscimol binding, enhancing B<sub>max</sub> by 60% and K<sub>B</sub> by 30%, respectively. Simultaneously, AA inhibits uptake of chloride ions through the GABA-operated chloride channel by about 25%. Our results indicate differential regulatory action of AA on GABA<sub>A</sub> and chloride channel receptor function in the brain.

P5.17 CONTRALATERAL ROTATIONS INDUCED BY INTRA-STRIATAL INJECTIONS OF AGONISTS OF EXCITATORY AMINO ACID RECEPTORS

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Glutamate is an excitatory amino acid which acts on different (NMDA, kainate, AMPA and metabotropic) receptors. It has been postulated that strionigral neurons receive a glutamatergic input from the sensorimotor cortex. It is believed that unilateral stimulation of a strionigral GABAergic pathway leads to contralateral rotations. In the present study we examined the influence of agonists of excitatory amino acid receptors, injected into the region wherefrom the strionigral pathway originates, upon the rotational behavior of rats.

We found that N-methyl-D-aspartate (NMDA) (100, 250 and 500 mg/0.5 μl), kainic acid (100 ng/0.5 μl) and AMPA (500 ng and 1 μg/0.5 μl), injected unilaterally into the ventrolateral part of the caudate-putamen of cats, induced a contralateral turning. It is concluded that: (1) NMDA, kainate and AMPA receptors are present on strionigral neurons, and (2) the contralateral behavior induced by agonists of excitatory amino acid receptors may be a relevant model to study functions of these receptors in the striatum.

P5.18 POSSIBILITY OF DOPAMINERGIC REGULATION OF NEUROPEPTIDE Y IN THE LOCUS COERULEUS. IMMUNOHISTOCHEMICAL STUDIES

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It was found previously that in the locus coeruleus (LC) neurons neuropeptide Y (NPY) is present in a small amount, which increases after reserpine, a monoamine-depleting agent. Therefore we tried to find out whether other monoamine-counteracting compounds influence NPY-immunoreactivity (−ir) in the LC neurons of the rat brain. After about 24 h of the drug administration brains were taken out for NPY immunohistochemistry by the PAP method.

An increase in NPY-ir in LC neurons was found after monoamine depletion by reserpine, as well as after blockade of dopaminergic receptors by haloperidol. No such effect was observed after impairment of serotonergic transmission (p-chlorophenylalanine), after specific blockade of D<sub>1</sub>- or D<sub>2</sub>-(SCH-23390, sulpiride), alpha-adrenergic (phenoxybenzamine) and beta-adrenergic (propranolol) receptors or after benzodiazepine receptor stimulation (diazepam).

The obtained results suggest that the content of NPY-ir material in the LC neurons is inhibitorily controlled by dopaminergic mechanisms, and extensive impairment of the function of both D<sub>1</sub> and D<sub>2</sub> receptors is needed for an increase in the NPY-ir level.
A BIZARRE DOPAMINE RECEPTOR REGULATING MELATONIN BIOSYNTHESIS IN CHICK RETINA

Jolanta B. Zawilska and Jerzy Z. Nowak

Vertebrate retina produces melatonin in a circadian rhythm, primarily in photoreceptors. The act. of serotoninin N-acetyltransferase (NAT), a key regulatory enzyme in melatonin synthesis, is low and high during light and dark phase, resp., of a natural or imposed light/dark illumination cycle. The nocturnal NAT act. is decreased by acute light exposure of animals. It is suggested that dopamine (DA) mediates the inhibitory effect of light on retinal NAT act. In this work we tried to characterize pharmacologically the DA effect on NAT act. of chick retina. DA agonists: receptor-nonselective apomorphine (APo; 0.1-10 mg/kg), D-2 receptor selective bromocriptine (BRC; 4 mg/kg), and D-2/D-3 receptor selective quinpirole (QNP; 0.003-0.3 mg/kg), given ip potently and dose-dependently decreased the nighttime NAT act. of chick retina. QNP and BRC were the most and least potent drug, resp. The inhibitory effect of APO on NAT act. was blocked by spiperon (a selective D-2 antagonist), but not by SCH 23390 (a selective D-1 antagonist). Interestingly, of the tested DA receptors blockers, members of different chemical groups, only spiperon, sulpiride, and clozapine antagonized the QNP-evoked decline of the nocturnal NAT act. of chick retina. Moreover, the potency of stereoisomeric forms of sulpiride, i.e. "S", "R" and "S/R" in abolishing the suppressive effects of QNP were similar. It is suggested that the DA receptor (localized to photoreceptor membrane) that mediates the depressive effects of DA agonists on the nighttime NAT act. in chick retina does not represent any of the known DA receptor subtypes (D-1, D-2, or D-3). Supp. by KBN grant 4 1054 91 01.

DEVELOPMENT OF NMDA RECEPTORS AND NMDA GENE EXPRESSION IN MOUSE BRAIN

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In vitro binding autoradiography and in situ hybridization technique were used to compare distribution of NMDA receptor associated channels and NMDA-receptor related mRNA in mouse brain during development. The experiments were performed on 10 µm cryostat slices taken from 3,7,14,21,28 and 60-day-old mice. NMDA receptor associated channels were labelled with [3H]MK 801. The oligonucleotide complementary to residues 268-327 of NMDA receptor's CDNA clone (Masu et al.,1991) was synthesized and served as a probe for in situ hybridization. The pattern of [3H]MK 801 binding was not similar to this obtained by in situ hybridization at any tested ages. Beginning with postnatal day 21 [3H]MK 801 label was confined mostly to supragranular cortex, nucleus caudatus, hippocampus and dorsal thalamus whereas with in situ hybridization to frontal cortex, nucleus caudatus and cerebellum. At postnatal day 28 we observed distinct pattern of labeling by in situ hybridisation in cerebellum confined to gray matter. With [3H]MK 801 binding we never observed any labeling of cerebellum. These discrepancies may prove that there is more than one type of NMDA-receptor related mRNA in the brain.

PRELIMINARY PHARMACOLOGICAL STUDY ON "REFLEX IMMOBILITY" IN RATS

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P6.1 HETEROGENEOUS STRUCTURE OF DIRECTIONAL RECEPTIVE FIELDS IN THE SUPERIOR COLLICULUS OF THE CAT

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With the aim to study a substructure of the visual receptive fields of the superior colliculus cells, the extracellular responses of single units to moving light stimuli were examined. The receptive fields of 45 neurons were tested with a spot moved 0.5° up to 5° in both directions around different points along the receptive field axis. The intensity of responses and the direction sensitivity factors varied in different locations within the receptive field. In some of the tested domains the direction preference of such range limited movement could be opposite to the direction preference for the movement throughout a whole receptive field. The results suggest that receptive fields of collicular units are composed of heterogeneously responding domains which interact to form a global response of collicular cells.

P6.2 VISUAL RESPONSES OF THE SUPERIOR COLLICULAR NEURONS AFTER LESION IN THE CONTRALATERAL COLLICULUS IN CATS

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The responses of 80 single units in the superficial layers of the superior colliculus were examined in 10 cats with pretrigeminal transection and a lesion in the contralateral colliculus. Single neuron activity was studied using extracellular recordings. The collicular units were tested with a moving light spot and diffuse flash. The number of cells sensitive to visual stimuli was not changed. The number of direction selective cells was reduced and a response to diffuse flash was increased as compared to nonlesioned cats. The results indicate the functional significance of projection from the contralateral superior colliculus and presumably from the other structures of the contralateral hemisphere.

P6.3 COORDINATION OF CORTICO-THALAMIC ACTIVITY DURING VISUAL ATTENTION

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Four cats were trained to differentiate visual or acoustic stimuli during the same experiment. The continuous recordings of EEG activity from aligned sites of lateral geniculate nucleus (LGN) and visual cortex were analyzed off-line using Fourier transform and directed coherence. The directed coherence method reveals in frequency domain, the direction of information flow between the relevant sites of simultaneous recordings. The amplitudes of the power spectra in beta frequency range obtained at the visual cortex were significantly higher during visual- than acoustic-attentive task. The directed coherence spectra calculated between the visual cortex and LGN activities tend to be also larger during the visual differentiation task. These coherence spectra oscillate in time and incidentally, reach significant values in both directions.

P6.4 COMPENSATION OF TIME DELAYS FOLLOWING STIMULATION WITH MOVING LIGHT BARS IN CAT VISUAL CORTEX

KOCHEH, J. AND DINSHE, H. INST. F. NEUROINFORMATIK D-4430 BOCHUM

For the localization of moving objects the time delays in the neuronal networks must be compensated. This study assesses the suitability of area 17/18 neurons for compensation. We recorded single neurons in cat visual cortex with an array of eight microelectrodes. The distance between the electrodes varied between 1 and 2 mm. The receptive fields (rf) were stimulated with bars at various speeds forward (f) and backward (b) along the trajectory to stimulate each rf. The activity of the simultaneously recorded neurons was analyzed on the basis of paths. The latency (L) and so-called apparent velocity (vapp) for the spread of activity were determined off-line.

About 30% of the neurons showed a slope ≤ -1 on L vs. bar velocity (log) diagram and therefore did not produce any time delay. Compared to the positions plotted before stimulation some neurons did even even earlier than expected. When vapp was calculated for pairs of neurons motion typically either preceded or lagged behind the stimulating bar. Dependent on the stimulus velocity and background 30 to 70% of the vapp exceeded the speed of the bar. Systematic influences of On/Off latencies were excluded. In general, the activity was shifted towards the stimulus direction both for f and b motion. In conclusion, area 17/18 neurons are obviously suited for compensation of time delays in motion processing probably by fascilitation of activity during a sweep across the cortex.
P6.5 RETICULAR FACILITATION OF CAT VISUAL CORTICAL RESPONSES IS MEDIATED BY NICOTINIC- AND MUSCARINIC- LIKE CHOLINERGIC MECHANISMS.

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Stimulation of the mesencephalic reticular formation (MRF) in the cat facilitates the electrically evoked visual cortical responses. Some authors stated that this effect is mediated muscarinically however the other indicating that this effect is mediated nicotinically. This conflicting reports stimulate us to re-examined the question which kind of cholinergic receptors are involved in the mechanism of reticular facilitation of the cortical responses.

In the present study, separately administration of cholinergic blocking agents atropine (muscarinic blocker) or mecamylamine (nicotinic blocker) did not significantly alter the facilitation of optic radiation (OR) response. However, simultaneous intravenous atropine and mecamylamine administration reliably reduced this effect. We conclude from this findings that facilitatory effect of MRF stimulation is blocked reliably only if both muscarinic and nicotinic transmission is interfered with.

P6.6 SLOW DEVELOPMENT OF FUNCTIONAL CHANGES OF CORTICAL MAPS IN YOUNG BARREL CORTEX

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By functional changes of cortical maps we mean plastic changes occurring after sensory deprivation of vibrissae, without no damage to hair follicles or nerve endings takes place. Prolonged sensory deprivation (whisker trimming) can produce an enlargement of spared vibrissae representation (Hand, 1982). We investigated, by 2DG autoradiography, the development of plastic changes in a single vibrissal column in the rat when all the surrounding vibrissae were trimmed close to the skin daily 1) from the day of birth and 2) in young adult animals. 2DG experiments were done 3, 7, 10, 14, 21, 28 days after the beginning of deprivation. During the 2DG experiment the spared C3 whisker on one side of the anesthetized and control C3 whisker on the intact side were stimulated with a rotating stimulator. Sensory deprivation, started both early and later in life produced changes in the appearance of the cortical column. The columns driven by the spared vibrissae were larger than normally. The changes took longer to develop in neonatal than in young adult animals. Deprivation started on the first day of life produced enlargement of the vibrissal column of the spared whisker in the third week of life. Deprivation started in the sixth week of life was effective already after one week.

P6.7 Localization of front limb representation in SI and SII of mice with normal and locally anesthetized snout - a 2DG study

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2DG uptake was examined in the somatosensory cortex following stimulation of front limbs in restrained, unanesthetized mice. Before stimulation the mystacial vibrissae were clipped close to the skin and on one side local anesthetic (Xylocaine) was injected to the mystacial pad, to examine the possibility of rapid respecification of cortical maps during a short-lasting functional silencing of a major input. 20 min after application of the local anesthetic a 2DG dose was injected and both front limbs (hands and arms) were stroked with a fine brush. The autoradiograms revealed labeling of SI above the barrel field and in SII below the SII vibrissae representation. The labeling had similar intensity in layers II/III, IV and V. In the infragranular layers the labeling, both in SI and SII was more diffuse and occupied a larger area than in layer IV, suggesting larger receptive fields of neurons in these layers. Local anesthesia of the mystacial pad did not affect localization of labeling in SI or SII, except that in the infragranular layers contralateral to the anesthetized mystacial pad the diffuse labeling extended more towards the SII vibrissae representation.

P6.8 INHIBITORY RESPONSES OF SINGLE RENAL POSTGANGLIONIC NEURONS TO LIMINAL STIMULATION OF C-FIBRES IN THE AORTIC NERVE

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Multifibre recordings from the renal nerve were employed to determine the inhibition of the tonic sympathetic discharge to prolonged repetitive stimulation of C-fibres in the aortic nerve. To assess the pattern of inhibitory response (IR) to liminal stimulation of non-myelinated aortic afferents we recorded the discharge of single renal postganglionic neurons in anaesthetized and vagotomized rabbits. C-fibres were selectively activated by single shocks or short trains (2-5 shocks at 10 Hz) and the responses were accumulated to produce per-stimulus time histograms. IR was observed in 6 out of 10 fibres. In 5 fibres it was elicited by 1 shock and in 1 fibre by 2 shocks. The mean duration of IR to 1 shock was 195.6 ± 22.2 ms (X ± S.E.) and its latency was 316.2 ± 17.5 ms. The increase in the number of shocks greatly increased the duration of the IR and after 5 shocks it amounted to 323.7 ± 19.5 ms. Its effect on the latency of IR was probably related to the appearance of the preceding excitatory component. In 4 fibres in which the excitatory component was observed, the latency of IR was longer than in fibres responding to shocks in the aortic nerve by a pure IR.
Influence of Cerebral Ventricles Perfusion with Hexa Substance P and Naloxon on the Reflexes Evoked by Tooth Pulp or Infraorbital Nerve Stimulation in Rats.

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Experiments were performed on male rats in chloralose anaesthesia, in which perfusion between lateral cerebral ventricles and cerebellomedullary cistern was carried out. Firstly Naloxon in 50 nmol/ml concentration and later Hexa Substance P (Polyscience) in 50 nmol/ml concentration were perfused 10 min. each and the amplitude of tongue retractive movements evoked by tooth pulp or infraorbital nerve stimulation was recorded. Perfusion with Naloxon induced a significant increase of tongue movements amplitude evoked by tooth pulp and infraorbital nerve stimulation by 26% and 46%, respectively. Perfusion with Hexa SP induced a significant increase of the amplitude of tongue movements evoked by tooth pulp and infraorbital nerve stimulation by 20% and 45%, respectively. Perfusion with Hexa SP, which was not preceded with Naloxon, increased significantly the reflex evoked by infraorbital nerve stimulation without alteration of the reflex amplitude evoked by tooth pulp stimulation. These results suggest that opioid receptors are more effective in suppression of the reflex evoked by tooth pulp stimulation.

PERIPHERAL ANTIINOCICEPTIVE EFFECT OF MU AND KAPPA OPIOID RECEPTOR AGONISTS IN NORMOTENSIVE WISTAR (NR), WISTAR KYOTO (WKY) AND SPONTANEOUSLY HYPERTENSIVE RATS (SHR).

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Several lines of evidence suggest the participation of exogenous opioids in the antinociceptive effects outside the CNS through the activation of the peripheral opioid receptors in inflamed tissues.

The antinociceptive effects of intraplantar and subcutaneous injections of mu and kappa opioid receptor agonists in unilateral hindpaw inflammation were studied in normotensive (NR and WKY) and hypertensive (SHR) rats. Morphine U-50,488H markedly enhanced the increase of paw pressure thresholds in the inflamed hindpaws as compared to those of non-inflamed paws in all strains. This effect was more pronounced in SHR and WKY rats compared to NR rats. The antinociceptive activity of both opioid agonists was dose dependent and antagonized by local and systemic injections of naloxone.

THE CONTRIBUTION OF THE HYPERTENSIVE STATE TO THE EXPERIMENTAL MODEL OF CHRONIC PAIN

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To address the contribution of the hypertensive state to the inflammation in the arthritic model of chronic pain we examined the effect of Freund's adjuvant inoculation in normotensive Wistar (NR) and Wistar Kyoto rats (WKY) compared to spontaneously hypertensive (SHR) and renal hypertensive rats (RHR).

Body weight (indirect index of feeding behaviour) has been used to quantify the chronic pain state. Inflammation scores of the radiocarpal and tibiotalar joints of the hindpaws were used as the clinical parameters of the illness.

The present studies have shown an increase of body weight gain in acute and post acute stage in WKY group compared to NR, SHR and RHR groups of rats. RHR rats showed lack of body weight gain only during the first preclinical stage. Analysis of inflammatory changes in the hindpaws joints revealed the highest score for NR and SHR groups during acute stage contrary to the WKY group. It seems that hypertension does not influence the course of the inflammation; the differences are due to strain distinctions or changes in the activity of renin-angiotensin system.
LATE EFFECTS OF ACTIVATION OF NON-MYELINATED CUTANEOUS AFFERENTS ON SYMPATHETIC POSTGANGLIONIC DISCHARGE

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Inhibition of the tonic sympathetic discharge evoked by conditioning stimulation of somatic afferents is followed by changes in the excitability of the neuronal systems generating this activity. We tried to find out whether these alterations are reflected in the pattern of tonic sympathetic discharge. Postganglionic background firing was recorded from single fibres of the renal nerve in anaesthetized rabbits. Interspike-interval histograms were compiled in control conditions and then after conditioning stimulation of cutaneous (sural or nerve) and superficial peroneal nerves. Stimulation at intensity which excited non-myelinated afferents had frequency of 2 Hz and lasted 2-10 min. 10-17 min. after stimulation of the sural nerve (n = 9) the interval was shortened to 44.7% of the control. The shortest and longest intervals decreased to 75.5% and 88.7%. The mean discharge rate increased to 144%. Similar effects were observed after stimulation of the superficial peroneal nerve. Different reductions of 3 analysed parameters of the interval histograms suggest the late changes in the pattern of postganglionic sympathetic discharge after conditioning stimulation of cutaneous afferents.

BACKGROUND FIRING OF RENAL SYMPATHETIC POSTGANGLIONIC FIBRES IN THE RABBIT


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The study of the distribution of interspike intervals of ongoing sympathetic discharge seems to be an adequate method for detecting its slight modulations, as for example, the late effects of conditioning stimulation of somatic afferents. As a starting point for this type of experiments we performed the time-series analysis to determine the pattern of background firing of sympathetic postganglionic fibres. In adult rabbits anaesthetized with urethane and chloralose, irregular spike trains were recorded from single fibres of the renal nerve. After converting into standard pulses they were used to measure the rate of discharge and to compile interspike-interval histograms. Only discharges showing stable repetition rate were taken into consideration. The mean rate was 1.77 ± 0.15 impulses/s (X ± S.E.; n = 9). Out of 9 studied histograms, 4 were unimodal, 4 unimodal and 1 bimodal. The histograms were broad as evidenced by the values of the shortest (131 ± 31) and longest (6460 ± 1440 ms) intervals. The mean preferred interspike interval amounted to 1662 ± 709 ms and was located closer to shorter intervals. This resulted in low mean coefficient of symmetry of the histograms which was 0.24.

THE METHOD OF ELECTROPHYSIOLOGICAL EVALUATION OF SMALL SENSORY FIBERS

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Routine clinical electrophysiological methods assess function in the large diameter, motor and sensory nerve fibres but not in the smaller diameter ones subserving pain, thermal sensation and autonomic function. Several authors have developed a technique for the objective measurement of thermal threshold to warming and cooling. The method has proved to be a useful, complementary test in diagnosis of different types of neuropathy. Tender/alcohol dependent subjects without clinical symptoms of neuropathy and 4 subjects with alcoholic neuropathy were tested. The thermal thresholds from the hand and foot were determined bilaterally by means of a commercial version of the Thermal Threshold Tester - TTT /Medelec Ltd./. The sensory nerve potentials in both median and peroneal nerves were examined simultaneously and the preferred latency intervals were found with the similar frequency as impaired sensory action potentials in routine methods. The results indicate that in alcohol dependent subjects all types of sensory fibres are affected to the same extend, especially in the lower limbs. The method of quantitative thermal thresholds measurement is easily performed and clinically useful.

EXCITATORY COMPONENT OF SYMPATHETIC POSTGANGLIONIC NERVE RESPONSE TO STIMULATION OF AORTIC C-FIBRES

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Recordings from single sympathetic postganglionic fibres of the renal nerve showed that inhibitory responses to liminal activation of C-fibres in the aortic nerve are in some units accompanied by the excitatory component (EC). It consisted in transitory increase in the rate of the tonic discharge. In anaesthetized and vagotomized rabbits single shocks or short trains (at 10 Hz) were used to activate nonmyelinated afferents of the aortic nerve. EC was observed in responses of 4 out of 10 fibres. The excitatory and inhibitory components had similar thresholds, i.e. they were elicited by 1 or 2 shocks. EC always preceded the inhibitory response and was separated from it by a short period of tonic discharge. When evoked by single shocks it appeared after the mean latency of 221.3 ± 7.9 ms (X ± S.E.) and had duration of 91.2 ± 12.3 ms. The gradual increase in the number of shocks reduced the latency and prolonged duration of EC and after 5 shocks they amounted to 197.4 ± 3.3 and 132 ± 14.8 ms. The occurrence of EC as a part of excitatory-inhibitory sequences suggests that it differs from that evoked by stimulation of myelinated somatic afferents which in some units may appear as a pure excitatory effect.