KAPPA3 OPIOID ANALGESIA

Grazyna Ciszewska, Gavril W. Pasternak
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Novel opioid drugs have provided major tools in understanding opiate actions. Since the first suggestion of the kappa receptors by Martin, many groups have searched for kappa binding sites. We synthesized NalBzoH (6-desoxy-6-benzoylhydrazino-N-allyl-14-hydroxydihydronormorphinon) which is a novel opiate with potent action at both mu and kappa receptors. In binding studies 3H-NalBzoH labels mu receptors quite potently as well as a discrete population of sites with a unique binding profile termed kappa3. The density of kappa3 receptors in rat, mouse and calf brain are 2-fold higher than mu and delta receptors. In vivo, NalBzoH potently reverses morphine actions, consistent with antagonist activity at mu receptors. However, given alone NalBzoH is a potent analgesic acting through supraspinal mechanisms. This analgesia is resistant to selective antagonists against mu (δ-funaltrexamine), delta (naltrindole) and kappa (nor-binaltorphimine) receptors. Furthermore, NalBzoH analgesia was not cross tolerant to mu or kappa3 analgesics. On the other hand NalBzoH and nalorphine analgesia were cross tolerant, implying that kappa3 receptors represent the nalorphine, or "N", receptors first proposed by Martin over 25 years ago.

Plenary lectures

L3 K+ CHANNELS: STRUCTURE, REGULATION, MOLECULAR PHARMACOLOGY AND INVOLVEMENT IN DISEASE STATES
M. Lazdunski, Sophia Antipolis

See page 196

Salt-appetite, its neuroendocrine basis
Eliot Stellar
University of Pennsylvania

Based on the early work of Richter (1936), showing that the adrenalectomized rat kept alive by drinking hypertonic NaCl solutions, Epstein & Stellar (1955) demonstrated that salt appetite was not dependent on learning. A series of papers by Epstein and his students made clear that in addition to the adrenal steroid, aldosterone, salt appetite depended upon the action of angiotensin II in the brain. Blocking either hormone in the brain reduced depletion induced salt appetite in half; blocking both eliminated it. Two or three salt depletions enhanced salt appetite by nearly a factor of two, even when the rats never had a chance to drink salt in the first depletion. With multiple depletions, need-free salt intake also increased when the rats were replete, producing an elevated chronic salt appetite. Strikingly, female rats drink almost twice as much as males and become more enhanced. The neural circuitry involved in the synergy of angiotensin and aldosterone is becoming clearer with lesions of the amygdala that reduce aldosterone’s effects and lesions of the anterior wall of the third ventricle that reduce angiotensin effects. The significance of salt appetite in nature, in body fluid homeostasis, and in blood pressure is discussed.
S4.3 EFFECT OF A SELECTIVE METABOTROPIC EXCITATORY AMINO ACID RECEPTOR AGONIST ON cAMP ACCUMULATION.

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Excitatory amino acids (EAA) stimulate both ionotropic and metabotropic receptors. There are several data that metabotropic receptors are coupled to cAMP accumulation. In this study we describe the effect of a selective metabotropic receptor trans-1-amino-cyclopentane-1,3,5-dicarboxylic acid (trans-ACPD) on noradrenaline or forskolin stimulated cAMP accumulation in slices from rat cerebral cortex. Trans-ACPD produced a small increase in basal cAMP accumulation and greatly (4 fold), in a dose dependent manner enhanced the cAMP response to noradrenaline. This enhancement was dose-dependently inhibited by the metabotropic EAA receptor antagonists L-2-amino-3-phosphonopropionic acid (L-AP3) and L-2-amino-4-phosphonobutyric acid (L-AP4). The third effect of trans-ACPD was a dose dependent inhibition of forskolin-stimulated cAMP accumulation. The results indicate, that multiple metabotropic receptors for EAAs coupled to adenylate cyclase may exist.

S4.4 BEHAVIOURAL EXPRESSION OF GLUTAMATERGIC FUNCTION - FOCUS ON BASAL GANGLIA

W. J. Schmidt, Univ. Tübingen, Neuropharmacology Div. Mohlstr. 54/1 D-7400 Tübingen.

Glutamate is a main transmitter in the cortico-striato-thalamo-cortical-loops. The behavioural effects of glutamate (mediated via NMDA receptors) in the striatum is opposite to that of dopamine (mediated via D2 receptors). The blockade of the glutamatergic transmission, either by lesions or by NMDA-antagonists, induces psychomotor stimulation (in the rat, locomotion and continuous sniffing). In dopamine deficiency states, behaviourally expressed as akinesia and rigidity (catalepsy), there is a relative overactivity of the glutamatergic system (in the striatum, the subthalamic nucleus and its efferent connections) which can be effectively counteracted by NMDA-antagonists. Antagonists at the different binding sites of the NMDA receptor show different behavioural and biochemical profiles. Antagonists at the NMDA receptor, such as MK-801, are useful for the treatment of glutamate-associated neurological disorders, particularly under conditions where high levels of the amino acid would render competitive antagonists relatively ineffective.
GLUTAMATE, LONG-TERM POTENTIATION AND MEMORY
Klaus G. Reymann
Institute of Neurobiology, PSF 1860, O-3010 Magdeburg, Germany.

Long-term potentiation (LTP) of synaptic responses is a model used for the investigation of cellular mechanisms of memory formation. According to our three-stage hypothesis of LTP, the Ca^2+ /calmodulin-dependent induction is followed by protein kinase C (PKC)-dependent intermediate and late protein synthesis-dependent stages. Here we investigated with extracellular techniques in the CA1 region of hippocampal slices the involvement of different glutamate receptors in the induction and maintenance of LTP. NMDA receptor activation during tetanization is an essential condition for all 3 stages of LTP. Our data suggests that in contrast to NMDA-receptors metabotropic Gq receptors and the subsequent activation of protein kinase C are involved in mechanisms enabling only the late stages of LTP.

The sensitivity of potentiated neurons to test pulses of the iontophoretically-applied quisqualate receptor ligand _lamin-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) slowly increases after tetanization. This delayed increase in agonist sensitivity is prevented by both the NMDA-antagonist APV and the protein kinase inhibitor K-252b. This data suggests that LTP is maintained initially (0-30 min) by a presynaptic mechanism and then by a postsynaptic mechanism or by both pre- and postsynaptic mechanisms. The increased postsynaptic sensitivity of ionotropic glutamate (AMPA) receptors might be due to a posttranslational transformation of the receptor-ionophor complex or expression of new AMPA-receptors.

The possible involvement of such mechanisms in memory processes will be discussed.

SYNAPTOSOMAL TRANSPORT AND METABOLISM OF GLUTAMATE PRECURSORS IN HYPERAMMONEMIA.
J. Albrecht, L. Faff-Michalak, W. Hilgier and U. Rafalowska,
Departments of Neuropathology and *Neurochemistry,
Medical Research Centre, Polish Academy of Sciences,
Warsaw, Poland.

Moderate hyperammonemia (HA) was induced in rats by 3 i.p. administrations at 24h intervals of a hepatotoxin - thioacetamide (model A), or ammonium acetate (model B). HA in model A inhibited the uptake to cerebral synaptosomes of glutamine, which is a major metabolic precursor of glutamate (GLU). Of the precursors playing a minor role, HA inhibited the uptake of ornithine, but stimulated that of 2-oxoglutarate (2-OG) and arginine (ARG). HA enhanced the synaptosomal activity of enzymes involved in ARG metabolism to GLU: arginase and ornithine aminotransferase. HA in models A and B, but also in vitro treatment with ammonium chloride, inhibited the malate-aspartate shuttle enzymes: malate dehydrogenase and aspartate aminotransferase, as well as the glutamate dehydrogenase activity in the direction 2-OG towards GLU, and the inhibitory effects involved the synaptic but not the nonsynaptic mitochondria. Pyruvate carboxylase, the astrocytic mitochondrial enzyme thought to furnish 2-OG for the synaptic synthesis of GLU, was markedly inhibited in the nonsynaptic mitochondrial fraction. The results taken together point to the decrease of the synaptic glutamate formation as a cause of failure of excitatory neurotransmission during HA.

THE ROLE OF CALCIUM IN GLUTAMATE-MEDIATED TOXICITY
Jerzy W. Lazarewics
Medical Research Centre, Pol. Acad. Sci., Warsaw, Poland

The physiological importance of calcium in glutamatergic signal transduction and its pathogenic role in glutamate neurotoxicity is well documented and generally accepted. Glutamate and calcium may be involved in several brain disorders, leading in ischemia to neuronal damage in susceptible regions such as the hippocampal CA1. Evidence from studies of animal models of global cerebral ischemia indicate that calcium ionophores induced by the NMDA-sensitive glutamate receptors represent the major pathway of calcium influx into hippocampal neurons during ischemia, whereas the L subtype of voltage-sensitive calcium channels seem to be less important in this phenomenon. In vivo studies have revealed that the maximal capacity of calcium ionophores induced by glutamate receptor agonists greatly exceeds the maximal calcium influx throughout the voltage-gated L channels in the hippocampus. Although the bulk of Ca\(^{2+}\) influx evoked by glutamatergic stimulation reflects activation of the NMDA channels, the L channels and Na\(^+\)/Ca\(^{2+}\) exchange are secondarily involved in this phenomenon. Several calcium-related processes have been suggested to play the role of effector mechanisms cooperatively participating in the excitotoxic and ischemic neuronal injury. In this context the NMDA receptor-induced, Ca\(^{2+}\)-and phospholipase A\(_2\)-mediated arachidonic acid (AA) release deserves consideration. Recent involvement of AA in the mechanism of long term potentiation of glutamatergic fast excitatory neurotransmission in the hippocampus, and AA-evoked protein kinase C activation in the brain were shown. This suggests that AA and/or its metabolites may induce pathogenic amplification of cell signalling mechanisms in neurons, thus mediating their injury.
S5.1 Accumulation of Beta-Amyloid Protein (bAP) and its Precursor (bAPP) in Vacuolated Muscle Fibres of Inclusion-Body Myositis; Similarities to Alzheimer's Disease Brain

V. Askanas, W. K. Engel, R.B. Alvarez, Los Angeles

Not received

S5.3 Molecular Mechanisms of Treatment of Dysimmune and Viral Neuromuscular Diseases

W. King Engel
USC Neuromuscular Center, University of Southern California School of Medicine, Los Angeles, CA.

I. Anti-Dysimmune. A. Circulating Malignant Body - 1. Stop antigenic stimuli: a) remove antigen (e.g. virus, toxin or gene abnormality that "foreigned" the cell) b) hit presenting macrophages. 2. Stop antibody production: i) Hit upregulated a) antibody-producing B-cells, b) T-helpers/their receptors, c) facilitating cytokines; ii) Help d) T-suppressors, e) inhibitory cytokines. 3. Address circulating malignant body: a) remove, b) give antidiotype antibody. 4. Block action on target cell (e.g. with IVIG): a) specific receptor (Fab), b) non-specific receptors (e.g. Fac). B. Cytotoxic T-cells - 1. as A-1. 2. Stop mal-T-cell production: a) Hit upregulated cytotoxic T-cells/their receptors, b-c) as in A2. 3. Address T-cell cytotoxic products: a) block release, b) block receptor site. 4. Block action on target cell: a) specific receptors, b) non-specific receptors. C. Mast cells/products - block proliferation, release of products. D. Drugs discussed include - prednisone, cyclophosphamide, 2-chlorodeoxyadenosine, cyclosporin, cromolyn, α-interferon, thalidomide, monoclonal antibodies, cytokines.

II. Anti-Viral. I. Attack the virus: a) kill, b) stop proliferation (e.g. anti-reverse transcriptase). 2. Stop effect on infected cell: a) level of viral or cell a) DNA/RNA, b) protein. 3. Stop effect on organism: a) dysimmune reaction (e.g. in HTLV-1 myelopathy), b) others.

S5.2 Viral Diseases of Neuromuscular System

L. P. Weiner, Los Angeles

Not received

S5.4 Possible Consequence of Disruptions of Neuromuscular Contact in Early Development

Professor Gerta Vrbova, Department of Anatomy and Developmental Biology, University College London.

Shortly after birth motoneurones and muscles are critically dependent upon continued contact with each other. If interaction between the 2 cell populations is temporarily disrupted motoneurones die, and muscle development is permanently impaired. The possible cause of motoneurone death in this situation will be discussed. Evidence will be presented to support the hypothesis that interaction with the target muscle is necessary for the motoneurones to become competent to survive the increase of afferent excitatory inputs that occurs during the development of the CNS. Strategies that could prevent or counteract motoneurone loss after target deprivation will be suggested.

The dependence of skeletal muscle fibres on continued contact with motoneurones persists even longer after birth. In rats at 5 - 6 days old motoneurones no longer require contact with the muscle for their survival, but muscle fibres still depend on motoneurones. At this stage muscle fibres have several inputs. With development this polynemural innervation gives way to the adult situation where each muscle fibre is contacted by only 1 axon. Evidence will be presented to show that the initial excessive input that is polynemural innervation is essential for normal muscle development.
S5.5 MECHANISM OF CLINICAL MANIFESTATION OF MOTOR UNIT DESINTEGRATION IN MOTOR NEURAL DISEASES
B. M. Gecht, Moscow

Not received

S5.6 INTERRELATIONSHIP BETWEEN GENE, ITS PRODUCT AND PHENOTYPE IN DMD/BMD
I. Hausmanowa-Petrusewicz, J. Zaremba, A. Fidziańska
J. Zimowski, B. Badurska, E. Fidziańska, A. Łusakowska,
J. Borkowska
Neuromuscular Unit Medical Research Center Pol.Ac.Sci;
Department of Genetics, Institute Psych. Neurol.;
Department of Neurology Medical Academy, Warsaw, Poland

Analysis of DNA was performed in 84 families affected with muscular dystrophy Duchenne type (DMD) or Becker type (BMD). Deletions were detected in 49 families (58%). In the same families the test for dystrophin was carried out. In the analysis of material extent of deletion, amount of dystrophin and clinical status were considered of 10 cases of BMD deletions were detected in 9 cases, usually involving exons 45-52. A marked variability regarding the amount of dystrophin was involved in cases of BMD. Attention is drown to female case with DM0 and X-autosomal translocation; one family with detected deletion and apparently normal dystrophin; one family with abnormal dystrophin and deletion but close to normal level of CK. The diagnostic importance of those findings is discussed.

Symposium (S6) - Sensory networks: anatomy, physiology, modelling

S6.1 SPECIFICITY OF NEURONAL CONNECTIONS IN THE VISUAL THALAMUS OF THE CAT
A. Wróbel, S. Lindström and M. Bekisz
1Nencki Institute, Warsaw, Poland and 2University of Gothenburg, Sweden.

A typical principal cell (PC) of the dorsal lateral geniculate nucleus receive monosynaptic excitation from 1-3 retinal ganglion cells of one eye, the same center type (on or off) and belonging to either the X or Y system. It receives also the inhibitory connections from several feed-forward intrageniculate interneurones with the same specific pattern, and via recurrent perigeniculate neurons of corresponding X/Y categories, but binocular and of on/off type. The deviations from this typical connection scheme were checked intracellularly in a sample of 500 PCs. Four (0.8%) PCs received binocular, and one (0.2%) mixed excitation from on- and off-center ganglion cells; all five were Y neurons. Two percent of the X PCs received additional EPSPs from Y retinal fibers, while 20% of Y cells - small EPSPs from X fibers. The atypical excitation was quantitatively small and did not affect significantly the firing of the cells. With no exceptions the on- or off-center PCs were inhibited by type specific (on or off) feed-forward interneurones and only 1% of the X PCs received a small IPSP from Y pathway (no IPSPs originated from X pathway were found in Y PCs). In our experiments the recurrent inhibitory system was found to be also specific, although in the extracellularly recorded sample of 90 perigeniculate cells 14% had mixed X/Y input. The specificity of connections in the visual thalamus is striking. The rare atypical inputs seem not to change the output characteristic of the visual thalamic cells.

S6.2 POSITIVE FEED-BACK CIRCUITS AND EPILEPTIC SEIZURE IN THE CAT'S VISUAL CORTEX
S. Lindström, A. Hedström, E. Taubol and A. Wróbel,
Department of Physiology,
University of Göteborg, Göteborg, Sweden.

It is an old notion that focal epileptic seizure develop as an oscillation of neuronal activity in closed excitatory neuronal chains within the cortex and between the cortex and subcortical structures. We have identified several such chains in the early visual system of the cat. The role of different elements in these circuits for seizure initiation and maintenance will be reviewed together with examples of mechanisms of action of some antiepileptic drugs.
The organization of the visual system in primates: an evaluation of theories and the use of the comparative method

Jon H. Kaas, Psychology Department
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Over the last 20 years considerable progress has been made in understanding the organization of the visual system in primates. Current proposals from a number of laboratories portray visual cortex as an extensive sheet of tissue that is subdivided into as many as 20-30 visual areas, each connected with several others to form a complex processing array. While there are many features of agreement across proposals, there are also notable differences. Comparative studies across primate and even non-primate taxa can help resolve these differences. Since all mammals evolved from a common ancestor, all brains are modifications of a common plan, and can be understood, in principle, as modifications of the common plan along branching lines of descent. Therefore, any theory of organization proposed for any specific taxonomic group can be evaluated, not only by the evidence for that group, but also by the degree of compatibility with evidence from other taxa, especially sister groups. Such a comparative approach suggests that current proposals of visual cortex organization contain errors and misinterpretations. The differences in theories indicate regions of cortex of uncertain organization and of the need for further investigation.

DIFERENT FORMS OF PLASTICITY IN THE BARREL CORTEX

MALGORZATA KOSZUT
Department of Neurophysiology, Nencki Institute, 02-093 Warsaw, Poland

Besides changes in morphology of the barrels following neonatal destruction of vibrissal follicles (Van der Loos and Woolsey, 73), several manifestations of plasticity can be demonstrated in the barrel cortex. Changes of spatial pattern and intensity of functional activity can be found in the cortex after both neonatal and adult denervation of rows of barrels. Sensory deprivation without damage to nerve endings (by cutting off the whiskers) also alters functional activity of cortical vibrissal columns. Barrel cortex in the adult rat can be invaded by afferents from non-vibrissal receptors - after removal of vibrissae stimulation of the common fur of the mystacial pad can activate the barrel field. This last process takes much longer to develop than the intra-barrel field plasticity. Stimulation of a row of whiskers during a sensory conditioning training can increase the cortical representation of this row already after 30 min of stimulation. Different mechanisms are suggested for processes occurring within the barrel field and as a result of interactions of the barrel field and neighboring cortical regions.

Conversion of Temporal Correlations Between Stimuli to Spatial Correlations Between Attractors

Daniel J. Amit, INFN, Sezione di Roma, Istituto di Fisica Universita di Roma, La Sapienza, P.le Aldo Moro, Roma
(On leave of absent from Racah Institute of Physics)

Single electrode recordings in performing monkeys by Miyashita et al, show that the internal representations of uncorrelated images memorized in associative cortex reproduce in their activity distribution the temporal correlations present in the training sequence. The internal representations exhibit correlations up to the fifth neighbor in the training sequence. These experiments are described in detail. A simple modification of synaptic structures (of the Hopfield type) constructed to produce auto-associative attractors, produces neural networks whose attractors are correlated with several (learned) uncorrelated patterns used in the construction of the matrix. The modification stores in the matrix a fixed sequence of uncorrelated patterns, introducing couplings between patterns which are nearest neighbors in the sequence. The network then has correlated attractors, provoked by uncorrelated stimuli. The attractors are correlated up to the fifth neighbor. Thus, the network converts the temporal order (or temporal correlation) expressed by the sequence of patterns, into spatial correlations expressed in the distributions of neural activities in attractors. This number 5 is universal in a range of parameters, and requires essentially no tuning. We then discuss learning scenarios which could lead to this synaptic structure as well as experimental predictions following from it. Finally, we speculate on the cognitive utility of such an arrangement, emphasizing in particular their potential role in priming effects.

Neurochemical characterization of projections in the cat visual system. Leo M. Chalupa, Center for Neurobiology, University of California, Davis CA 95616 U.S.A.

The availability of antibodies directed at putative neurotransmitters and neuromodulators has made it feasible to relate the morphological and functional properties of selective populations of cells in the mammalian visual system to their neurochemical content. Evidence will be provided that two major classes of cat retinal ganglion cells (alpha and gamma) can be differentiated on the basis of their content of different neuropeptides (somatostatin and neuropeptide Y, respectively). Interestingly, not all alpha cells are immunoreactive for somatostatin (SRIF). Rather, the SRIF-immunoreactive alpha cells are preferentially localized in the inferior retina. Collectively, the available immunohistochemical results indicate that the functional diversity of retinal ganglion cells in the mammalian visual system may be greater than suspected on the basis of previous anatomical and electrophysiological findings. (This work was supported by Research Grants from the National Institute of Health.)
MEMANTINE - SAFE AND THERAPEUTICALLY EFFECTIVE MODULATOR OF GLUTAMATE RECEPTORS.

Memantine was tested as an antagonist of N-methyl-D-aspartate (NMDA) receptors in cultured superior colliculus and hippocampus cells using the patch clamp technique in the whole cell mode. Memantine (2 to 16μM) selectively and concentration-dependently antagonized responses to NMDA 100μM with an IC50 of 2.58±0.16 μM. In contrast, current responses to (S)-α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (L-AMPA) and gamma-aminobutyric acid (GABA) were unaffected by Memantine 8μM. Memantine 8 μM caused a non-parallel shift of the NMDA dose-response curve to the right indicative of a non- or uncompetitive mechanism of action. However, the antagonistic effects of Memantine were not reversed by increasing concentrations of glycine (1-100μM) ruling out the possibility of an interaction of Memantine with the strychnine-insensitive glycine site associated with the NMDA receptor-channel complex. Previous studies have demonstrated that NMDA antagonists displace the binding of the prototypic NMDA channel blocker MK-801. As the effects of Memantine seen in this study were both use- and voltage dependent it seems likely that Memantine, like MK-801, exerts its antagonistic effects through an open channel block of the NMDA receptor-channel complex. However, the use-dependency of this uncompetitive antagonism showed much faster kinetics than reported by others for MK-801. Furthermore, unlike MK-801, Memantine actually potentiates synaptic transmission in the CA1 region of hippocampal slices. The precise mechanism of action for this effect is unclear but may be related a, to modulation of AMPA receptors following an increase in PI turnover, possibly via activation of metabotropic glutamate receptors and b, to the faster kinetics of the NMDA blockade. It therefore seems likely that many of the positive effects of Memantine seen in the treatment of dementia can be explained by its properties as a modulator of glutamatergic transmission.

Excitatory amino acid antagonists and the therapy of epilepsy. Astrid G. Chapman, Department of Neurology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF.

Excitatory amino acid antagonist acting at different sites of the NMDA receptor, as well as at the non-NMDA receptors, exhibit potent anticonvulsant activity in a number of animal seizure models. Thus, NMDA- and non-NMDA (e.g. NBQX or GYK 52466) antagonists provide potent protection against reflex-induced seizures in rodents (sound-induced seizures in DBA/2 mice or GePFF rats) or primates (photically-induced seizures in Papio papio), against a range of chemically- or electrically induced seizures, or against development of seizures by kindling. Selective, competitive NMDA antagonists (e.g D-CPPene, CGP 37849 or CGP 39551) provide prolonged anticonvulsant protection following their acute administration to rodents or primates, with more favorable therapeutic ratios observed than those seen for the non-competitive NMDA antagonists acting at the channel site (e.g MK 801 or dextromethorphan). The anticonvulsant potencies of the competitive NMDA antagonists, AP7 or CPPene, do not appear to be diminished following their chronic administration. Most of the currently available strychnine-insensitive glycine antagonists acting at the NMDA receptor have poor CNS uptake and a short time-course of action. However, following their acute, icv administration this group of antagonists offer promising anticonvulsant protection in several animal seizure models.

Therapeutic prospects of excitatory amino acid antagonists in neuronal degeneration. Brian Meldrum, Department of Neurology, Institute of Psychiatry, London, SE5 8AF, U.K.

Excitotoxic mechanisms contribute to selective neuronal damage occurring after cerebral ischemia, cerebral and spinal trauma and status epilepticus. They may also contribute to cell loss in various chronic neurodegenerative disorders. In animal models of focal ischemia NMDA antagonists (such as D-CPPene and dizocilpine) administered within 60-90 min of the occlusion decrease the volume of cortex showing infarction. Similar effects are also seen with the non-NMDA antagonists, NBQX and GYK 52466. The latter compounds are also protective in models of transient complete global ischemia. Behavioural outcome is also improved in models of spinal or cerebral percussion injury. Limbic system pathology is reduced by NMDA antagonists given during status epilepticus. Stroke and trauma appear the most promising immediate therapeutic targets for excitatory amino acid antagonists but the design and conduct of appropriate clinical trials remains a formidable task.
Tuesday, Workshop: ... hemispheric asymmetry ...

Workshop (W5) - Functional hemispheric asymmetry: neuropsychological and electrophysiological aspects

W5.1 INTERHEMISPHERIC TRANSMISSION TIME AND FUNCTIONAL ASYMMETRY OF THE HUMAN BRAIN.

NOWICKA A', FERSTEN E", GRABOWSKA A'.
"Nencki Institute of Experimental Biology, Dept. of Neurophysiology, Warsaw, Poland; "Medical Research Institute, Warsaw, Poland

Several reaction time studies suggest that interhemispheric transfer of information plays an important role in the formation of functional brain asymmetry. One could hypothesize that, depending on which hemisphere is dominant for a given function, the transfer of information from one hemisphere to the other is not equally effective. The present study aimed at verifying this hypothesis by an electrophysiological (VEPs) method. Specifically, we tested whether the interhemispheric transmission time (ITT), (measured as a difference between latencies of VEPs registered in the hemisphere ipsilateral to the stimulated hemifield and those registered in the contralateral hemisphere) depends on the type of the processed material (verbal vs nonverbal). Twenty two right handed subjects participated in two experimental sessions. In one session VEPs were recorded in response to 12 different 3-letter words, randomly appearing in the left and right visual field for 20 ms. In the other session 12 square-wave laterally presented gratings of various spatial frequencies were used as stimuli. Electrodes were located over the left and right occipital lobes at O1 and O2 according to the 10/20 system and referenced to linked ear lobes. The latencies of three VEPs components (P100, N170, P300) in the left and right hemisphere were compared. As expected the latencies of VEPs registered in the hemisphere contralateral to the stimulated hemifield were shorter than the latencies of VEPs recorded in the ipsilateral hemisphere. This difference was evident in two earlier (P100 and N170) components for both types of material. ITT depended on the type of material: for words ITT was shorter when the information was transferred from the right hemisphere to the left one, while for gratings, it was shorter when the information was transferred in the opposite direction. The results support the view that interhemispheric transfer is an important factor influencing the functional brain lateralization.

Generalization of Induced Interhemispheric Interference: A Chronometric Approach to One-brain Vs Two-brains Models of The Hemispheres' Cooperation

Piotr Wolski
Jagiellonian University, Cracow, Institute of Psychology

A reaction time study with normal subjects was conducted to obtain some support for one or the other model of interhemispheric relations - referred to as the "one-system" and the "two-systems" hypotheses. 12 subjects were extensively trained in a complex reaction time task consisting of a "priming sub-task" which introduced interhemispheric interference and two different "test sub-tasks" measuring the generalization of interference.

The interference priming produced visible slowing of RT's on the following trials. Interestingly, the deterioration of the two test sub-tasks was alike, despite the marked difference in the amount of the interhemispheric communication they required. This result is more in line with the one-system hypothesis, as the two-systems hypothesis predicts deterioration proportional to the amount of the required interhemispheric communication.

W5.3 HEMISPHERIC DIFFERENCES IN NONVERBAL VISUAL MATERIAL PROCESSING.

Jerzy Mroziak
Faculty of Psychology, University of Warsaw, Poland

Research findings indicate a more consistent pattern of hemispheric asymmetry for the auditory rather than visual modality, and within the latter - for verbal rather than nonverbal material. The effect of nonverbal visual material codability (susceptibility to verbalization), on functional hemispheric asymmetry was studied using pairs of figures of either easy or difficult codability (as assessed by the author in his earlier research). Four groups of 20 healthy subjects each were run: of righthanders, male (RM) or female (RF), and lefthanders (LM,LF). No interhemispheric differences were obtained for easy figures, while for difficult material the right hemisphere superiority, i.e. shorter RTs was found, but only in righthanders of either sex. The results suggest that uncontrolled codability of nonverbal visual material may lead to discrepancies reported in the literature.

CEREBRAL LATERALIZATION AND SEVERITY OF STUTTERING IN CHILDREN.

E.Szelag1, D.Garwarska-Kolek2, A.Herman1.
1 Nencki Institute of Experimental Biology, Dept. of Neurophysiology, Warsaw, Poland; 2 Monument Hospital of the Child's Health Centre, Warsaw, Poland

This experiment was designed in order to test the effect of different severity of stuttering on hemispheric asymmetry in visual perception of verbal material.

We tested 9 severe stuttering, 11 mild stuttering and 48 fluent speakers aged 13-15 years. Severity of stuttering was assessed by Iowa 7-point scale. The subjects were asked to identify 3-letter words presented on the screen in the left or right visual field for 20 ms. The children answered by pointing to the exposed word on the response card. The number of errors showed that while the performance of the normal speakers was consistent with literature on hemispheric specialization, the asymmetry was reversed only in severe stuttering. In mild stuttering the pattern of asymmetry was similar to that found in normal speakers. Our results show the different cerebral lateralization and the engagement of the right hemisphere in processing verbal material only in severe stuttering children.
W5.5 Hemi-neglect in left- and right-brain-damaged patients
Ania Herzyk, Lucja Spiewa
Maria Curie-Sklodowska University
A great amount of clinical data confirms spatial deficits limited to one half of the space. It is still not determined if neglect symptoms form an isolated syndrome or they contribute to the global non-specific spatial impairment after right-hemisphere lesions. The main question of the present study is: do the manifestations of neglect correlate with the lateralization of brain lesion. The following tasks were used to evaluate neglect: line crossing, line bisection, drawing, detail adding. The method of directed interview was used to assess anosognosia. The difference between right- and left-brain-damaged patients' performance are analysed. Some methodological questions are discussed.

Functional hemispheric asymmetry: neuropsychological and electrophysiological aspects.

W5.6 Title: Discourse functions and hemispheric asymmetry. Author: Emilia Osiejuk M.A. Faculty of Psychology, University of Warsaw.
This presentation will review the main results of an application of discourse analysis in aphasics with left hemisphere damaged (LHD) and right hemisphere damaged patients (RHD). The cognitive processes connected with micro- and macrostructure of discourse will be defined. The differences and similarities of processing at these structures of discourse in LHD and RHD patients will be presented on the base of current researches. The results of experiment on knowledge of scripts and plans as the most cognitive representation connected with discourse will be also considered.
Obtained data indicate that aphasics have marked deficits on the level of microstructure, especially cohesion of discourse, whereas the coherence and superstructure of their texts are relatively well preserved. RHD patients show difficulties at the microstructure of discourse but not so marked as in aphasic patients. The language impairments of RHD patients’ discourse can be observed at the levels of text coherence and superstructure. The both populations have also preserved cognitive representation concerned with scripts and plans. Abilities to abstract thinking are affected in aphasics as well as in RHD patients. These results indicate that the correct processes in both hemispheres are necessary for normal discourse processes.

Workshop: Functional asymmetry: neuropsychological and electrophysiological aspects.

W5.7 THE SIGNIFICANCE OF STUDIES IN COGNITIVE BRAIN MECHANISMS FOR CULTURAL ANTHROPOLOGY
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The research of neuropsychologists on cognitive brain mechanisms and certain models implied by it, have become indispensable for the analysis of human symbolic activity and its evolutionary development. This especially concerns the relation between language and signs of a different morphology, associated with different functional brain structures (e.g. icons, music, gestures). At the communication level, the emergence of human society is characterized by a combination of two processes. First, the development of symbolic systems, and second, their capacity for modelling interpersonal relations. A successful combination of these two processes enabled the transition from general cooperation mechanisms among non-related group members (Axelrod and Hamilton’s model) to specifically human forms of cooperation. These transformations were accompanied by changes within the functional architecture of the cognitive apparatus and included the formation of a collective community memory, the symbolization of human forms of ownership and kinship, as well as the appearance of mythology and deities responsible for exchange, acceptance and treatment of aliens. Modular models form a sound theoretical basis for the description of such transformations.

W5.8 ALPHAN DIFFERENCES IN RELATIVE HEMISPHERIC ASYMMETRY
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Left (L) and right (R) hemisphere-specific mechanisms of reaction to persuasion were studied in 32 males. Each subject was presented with 4 attitude objects, of which 2 were unimportant and 2 important. Of each pair, 1 object was presented verbally and 1 visually. Following each presentation, the subject was exposed to a counterattitudinal message from a purported expert source. EGG was recorded from the left and right parietal areas, sampled 100 times/sec and filtered through a 3-13 Hz band-pass filter, yielding a relative LH to RH activity alpha abundance index. Hemisphericity was assessed on the basis of mean EGG index from initial and final resting epochs. Changes in objects positivity and importance were measured on standard dimensional scales and with a manipulospatial task devised to tackle responses produced by RH activity. Subjects also listed and assessed evaluativeness of thoughts generated in the course of experiment. Results showed that (a) LH subjects yielded more than RH subjects; (b) LH subjects differentiated their responses more to objects presented verbally, whereas RH subjects - to those presented visually; (c) changes in positivity were pronounced more on dimensional measure whereas in importance - on manipulospatial measure; and (d) no support was found to the claim that RH mediates attitudinal changes through increased evaluativeness of thought. These results are discussed in terms of LH and RH specialization.
MU Firing Characteristics in Human Dystrophic Muscle

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During isometric contractions of constant force surface EMG as well as intramuscular MU potentials from extensor digitorum communis and biceps brachii muscles were recorded on magnetic tape for further offline analysis. Surface EMG power spectra were computed and transformed so as to reveal low-frequency peaks which might correspond to MU firing rates. From intramuscular recordings, single MU action potentials were identified with an aid of semi-automatic recognition program. For each single MU action potential train (MUAPT) statistical parameters of interspike intervals (ISIs) such as mean value, standard deviation, skewness, kurtosis and serial correlation coefficient were determined and related to the measured muscle force level. 64 MUAPTs from 8 patients and 55 MUAPTs from 3 normals were analysed so far.

The low-frequency part of surface EMG power spectrum from dystrophic muscle contains much more rate-related peaks than that from normal muscle. This means probably that in diseased muscle the MU firing rates are more widely dispersed.

From the parameters of MUAPTs, only firing rates and standard deviations of ISIs have shown significant differences between normal and dystrophic muscle. The MU firing rates were higher in muscular dystrophy and this difference was more pronounced for higher levels of muscle force. The tendency towards mean MU firing rate increase is stronger for the patients with more advanced disease.

The typical dependency of standard deviation of ISIs on their mean value may be approximated by two lines of different slope. There were reported experimental data indicating that the breaking point of this dependency may be an estimate of AHP duration in motoneurones. Our results for dystrophic muscle showed a shift of this breaking point towards shorter ISIs, as compared to normals. This suggests that in muscular dystrophy also motoneurones may be altered, either by the disease itself or as a compensation for changes in muscular part of a MU.