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The annual meeting Experimental Biology ’99 (previously known as FASEB) took place in the Washington Convention Center, Washington, DC, from April 17 through April 21, 1999. Twenty-six professional research organizations participated, including six principle societies: the American Physiological Society (APS), American Society for Pharmacology and Experimental Therapeutics (ASPET), American Society for Experimental Pathology (ASEP), American Society for Nutritional Sciences (ASNS), the American Association of Immunologists(AAI), and American Association of Anatomists (AAA). Approximately 12,000 scientists and guests attended the meeting. The meeting consisted of 863 sessions, including lectures, slide presentations, and poster sessions. This report covers only those sessions and/or presentations that were attended by the author and are of possible interest for the development of drugs affecting central nervous system.

In the ASPET symposium on the molecular basis of cytokine action in neuronal injury and disease, M. P. Mattson (Univ. of Kentucky, Lexington, KY) discussed the role NFκB in the TNFα signalling in the nervous system. TNFα has neuroprotective effect, it protects primarily hippocampal neurons. The protective effect of TNFα is mediated by MnSOD and activation of NFκB is required to obtain protection. NFκB stabilizes calcium homeostasis. The activation of NFκB can be antagonized by PAR-Y, a proapoptotic 36-KD protein (its gene was discovered at the Univ. of KY). Oxidative stress, increases calcium influx, and overexpression of PAR-Y increases vulnerability to apoptosis. Increased intracellular calcium leads to glutamate release and activation of caspases. In the same symposium, Y. Sun (Harvard Univ. Med. School, Boston, MA) spoke about molecular pathways of cytokines in glial cells. He emphasized the role of ciliary neurotrophic factor (CNTF) in astrocyte maturation and neuroprotection. CNTF induces differentiation of cortical precursor cells and stimulates gliagenesis. Sun described the structure of the CNTF receptor and various second messengers involved in the transmission and modulation of CNTF signalling.

In the poster session on learning and memory, J. A. Harvey et al. (MCP Hahnemann Univ., Philadelphia, PA) reported that mianserin (0.1 to 10 μmol/kg s.c.) antagonized acquisition of conditioned response (rabbit’s nictitating membrane reflex). This effect was blocked by d-bromolysergic acid diethylamide, a 5-HT2 receptor antagonist. The authors attributed mianserin effect to an inverse agonism at 5-HT2 receptors. J. J. Buccafusco and A. V. Terry (Medical College of Georgia, Augusta, GA) studied effects of mecamylamine, a well known ganglionic-blocking drug, on memory-related tasks in rats and Rhesus monkeys. At 1 mg/kg i.p., mecamylamine initially improved spatial learning in rats (Morris water maze) but inhibited learning subsequently. In eight aging monkeys, meca-
mylamine (0.13 mg/kg i.p.) improved accuracy in delayed matching-to-sample test. It appears that mecamylamine at small doses acts as a nicotinic agonist, while at higher doses or following repeated administration it acts as an antagonist or desensitizes nicotinic receptors.

In the poster session on aging and Alzheimer’s disease, R. L. Bowen et al. (RLB Med-Search, Naples, FL) found that gonadotropins (LSH and LH) were elevated in the blood of 40 male patients with Alzheimer’s disease compared to 30 age-matched controls. The authors speculated that gonadotropins may play a role in the etiology of Alzheimer’s disease by increasing deposition of abnormal proteins in neurons. C. Basset et al. (Vanderbilt Univ., Nashville, TN) found that cerebrospinal fluid (CSF) from patients with Alzheimer’s disease is more vulnerable to oxidative damage than the CSF from normal individuals and that lipoproteins (apoE and apoA1) from patients with Alzheimer’s disease are more susceptible to covalent modification. C.-I. Sze et al. (Univ. of Colorado, Denver, CO) reported that hippocampal levels of synaptic proteins (synaptobrevin, synaptotagmin, syntaxin, and Rab3a) were lower in patients with Alzheimer’s disease (postmortem) than in age-matched controls.

P. Grammas et al. (Univ. of Oklahoma, Oklahoma City, OK) discovered the presence of a neurotoxic factor in the brain microvessels of patients with Alzheimer’s disease. Coculture of microvessels from patients with Alzheimer’s disease leads to the death of neurons. Microvessels from age-matched controls are much less toxic, whereas vessels from younger individuals are not neurotoxic. The neurotoxic factor is present in the medium in which microvessels were incubated. The factor is neurospecific, killing primarily cortical neurons; it appears to be a heat-labile and trypsin-sensitive protein.

A. D. Snow et al. (Univ. of Washington, Seattle, WA; ProteoTech, Inc., Redmond, WA; and Rexall Sundown Inc., Boca Raton, FL) claimed to have discovered a dietary supplement (PTI 00703; NEUROSHARP) that prevents and disrupts amyloid deposits. The composition of PTI 00703 was not revealed. Experiments were performed in vitro or by sustained intrahippocampal infusion to rats. J. L. Giacchino et al. (The Scripps Research Inst., La Jolla, CA) demonstrated attenuated hippocampal synaptic transmission in transgenic Alzheimer mice. These mice express a mutant human amyloid precursor protein (hAPP) and age-dependent Alzheimer neuropathology (first described by Games et al. in 1995). The investigators recorded evoked-field potentials from CA1 and dentate gyrus areas of anesthetized mice. In transgenic mice, CA1 population spikes were significantly decreased in amplitude and increased in latency; long-term potentiation (LTP) was also decreased. Experiments in young mice suggested that changes in synaptic transmission in hippocampus are correlated with the β-amyloid deposition. E. T. Sutton et al. (Univ. of South Florida, Tampa, FL) demonstrated that β-amyloid can cause endothelial dysfunction and structural disruption in rat aorta; this effect is enhanced with the age of the animals. $K_{\text{ATP}}^+$ and $K_{\text{Ca}}^+$-channel openers (diazoxide and NS1619) protected rats from β-amyloid-induced vascular pathology. The authors suggested that β-amyloid disrupts potassium channels in endothelial cells, creating an imbalance of NO and superoxide radicals, and that K-channel openers may conceivably be useful in the treatment of Alzheimer’s disease. S. E. Montoya et al. (Univ. of Pittsburgh, Pa) generated bleomycin hydrolase (BH) free mice. The levels of this enzyme were previously found to be genetically associated with an increased risk for Alzheimer’s disease. Montoya et al. found that amyloid precursor protein (APP) levels in the hippocampus and cortex of BH-free mice were higher than in control animals.
Huntsville, AL) found that tacrine and quinacrine protect PC-12 cells from β-amyloid toxicity in vitro.

In the session on opioids, S. C. Lee and B. C. Yoburn (St. John’s Univ. Queens, New York, NY) reported that nimodipine (by osmotic minipump at 100 mg/kg/d for 7 d) increased the potency of morphine by 50%. Naltrexone also increased morphine’s potency, its effect was additive to that of nimodipine.

The Otto Krayer award lecture, entitled “Studies on Membrane Opioid Receptors,” was delivered by H. H. Loh (Univ. of Minnesota, Minneapolis, MN). There are three major types of opioid receptors: delta (δ, now called OP₁), kappa (κ, now called OP₂) and mu (μ, now called OP₃). Delta and mu receptors have two subtypes each. Kappa receptors have four subtypes. There is some evidence for the existence of epsilon as well as zeta receptors. All opioid receptors have seven transmembrane domains and are G-protein coupled. Opioid receptor gene expression is under transcriptional control. There is a high homology between delta and mu receptors, but delta receptors are shorter than mu receptors. Ligands induce receptor internalization. Endogenous ligands for delta receptors, kappa receptors, and mu receptors are enkephalins, dynorphins, and endomorphins, respectively. In addition to analgesia, opioid receptors have been implicated in gastrointestinal motility, mood, behavior, cardiovascular regulation, diuresis, feeding, thermoregulation, neuroendocrine secretion, and immune functions.

In the session on ion channels K. L. Whiteaker et al. (Abbott Laboratories, Abbott Park, IL) reported molecular and pharmacological differences between K<sub>ATP</sub> channels in the A10 cell line and rat ventricular myocytes. One of the isoforms of sulfonylurea receptors (SUR2A) was not detected, and the potency of activators was higher in A10 cell line.

In the cannabinoid pharmacology session, E. S. Onaivi and B. E. Akinshola (Vanderbilt Univ., Nashville, TN) reported that SR 141716A, a selective antagonist of cannabinoid receptor CB₁ [N-(piperidine-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide hydrochloride], has anxiolytic activity. They also presented evidence that anandamide inhibits kainate-activated currents in oocytes and this effect is potentiated by forskolin.

In the same session, E. Z. Dajani et al. (International Drug Development Consultants Corp., Long Grove, IL; Drug Res. Labs., Inc, Buckingham, PA; Univ. of Utah and Western...
Inst. for Biomedical Res., Salt Lake City, UT) described analgesic properties of CT-3 [1′1′-dimethyl-heptyl-δ-8HTC-11-oic acid], a new cannabinoid developed by Atlantic Pharmaceuticals, Inc., Raleigh, NC. It has sustained analgesic activity in rats at 5 mg/kg, either i.p. or i.g. (intragastric). In mice its potency was similar to that of morphine, but its duration of action was longer. It was well tolerated and produced no intestinal ulceration.

The Burroughs-Wellcome Fund Lecture entitled “The Nicotinic Acetylcholine Receptor and Synaptic Plasticity” was delivered by J-P. Changeux (Pasteur Institute, Paris, France). The nicotinic acetylcholine receptor (nAChR) is an allosteric protein with the molecular weight of ~300,000, five subunits (2 α, β, δ, and γ), four segments (M1-4), a neurotransmitter binding site at the M1 segment, and phosphorylation sites between M3 and M4 segments. There are at least eight subtypes of the α subunit and four subtypes of the β subunit. There are bungarotoxin-sensitive and -insensitive nAChRs. Mutations convert ion selectivity from cationic to anionic. An aminoacid in position 251 determines ion selectivity. Knockout mice without the β2 subtype were produced; their learning ability rapidly declines with age. Mutations in the β2 subtype alter avoidance learning. The high-affinity nicotine binding site is suppressed in β2 mutant mice. The antinociceptive action of nicotine is reduced in α4-knockout mice. Mutations in the α4 subtype appear to be responsible for some forms of epilepsy (frontal lobe?), mutations in the α7 subtype were associated with schizophrenia. Parkinson’s disease and Tourette’s syndrome may also involve mutations in the subtypes of nAChRs. In Alzheimer’s disease, the availability of nAChRs is reduced.

The symposium “Herbal Medicine: Pharmacotherapy and Research” was organized and chaired by C. N. Gillis (Yale Univ., New Haven, CT). Gillis reviewed the pharmacology and clinical experience with Ginseng. Y. C. Cheng (Yale Univ., New Haven, CT) spoke about Chinese medicine in the XXIst century. Chinese herbal medicines are usually mixtures. There is one key herb, while other serve to enhance or promote the activity or improve the formulation of the major herb. The Chinese herbal medicines will probably be better accepted in the Western countries in the next century since the popularity and the acceptance of drug combinations are increasing. The source of herbal medicine should be consistent, and the means to assess its quality should be available. J. M. Cott (NIMH, NIH, Bethesda, MD) discussed the properties of Ginkgo biloba and Kava (Piper methysticum). It is claimed that Ginkgo biloba has antioxidant properties, stabilizes capillary membranes, enhances microcirculation, and inhibits lipid peroxidase. A large-scale, NIH-supported clinical study, will test Ginkgo biloba in the prevention of Alzheimer’s disease. Kava is claimed to have anxiolytic, muscle relaxant, anticonvulsant, and analgesic properties and is widely used in South Pacific in spiritual ceremonies. Its use in the United States is rapidly increasing. Ginkgo biloba contains Kava pyrones, its likely active ingredients. Some psychiatric disorders appear to respond to the treatment with essential fatty acids present in fish oil. ω-3 was used in the therapy of bipolar disorders. It was claimed to inhibit sodium and calcium channels as well as COX-2.