were rendered in 3-D for computation of MPOC volumes. None of the compounds altered MPOC volume in female offspring at the dose levels employed. However, in male offspring, moderate doses of NON, GEN, or EE each reduced the volume of the MPOC. There were no effects of VIN on MPOC size in either males or females. To facilitate comparisons between the several estrogenic compounds, the doses of each compound were initially expressed upon the same log-scale. Then a series of linear transformations of the dose of each compound was computed in order to adjust for differences in their molecular weights, estrogen receptor binding, and uterotrophic potency. Following adjustment for variations in uterotrophic potency, it was observed that a similar dose range of each compound (the equivalent of about 1 to 10 ppm of 17-beta-estradiol) was associated with decreases in MPOC volume. This finding suggests that a common property of these endocrine disrupters may underlie their effects on both uterine and hypothalamic growth.

1768 PROPYLTHIOURACIL (PTU)-INDUCED HYPOTHYROIDISM: EFFECTS ON SYNAPTIC TRANSMISSION AND LTP IN CA1 OF HIPPOCAMPAL SLICES.

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Concern has been raised over endocrine effects of some classes of environmental chemicals. Severe hypothyroidism during critical periods of brain developmental leads to alterations in hippocampal structure and learning deficits, yet neurophysiological properties of the hippocampus resulting from such treatment have not been well characterized. The present study examined field potentials evoked in area CA1 of hippocampal slices derived from animals rendered hypothyroid from birth to weaning. Pregnant rats were administered 0 or 15 ppm propylthiouracil (PTU) in the drinking water from gestational day 18 until postnatal day (PND) 21. Hippocampal slices were prepared from adult male offspring between PND 200-340. Field potentials were evoked in CA1 pyramidal cell layer and the dendritic field in stratum radiatum by stimulation of stratum radiatum. Excitatory synaptic transmission was assessed by collecting input/output (I/O) functions at intensities ranging from 20-150μA. Paired pulse facilitation was assessed at intervals ranging from 20-1000ms at half maximal stimulus intensities. Finally, long-term potentiation (LTP) was induced by delivering a series of 15 5-pulse 100-Hz train bursts at 200ms intervals. No differences were observed between groups in population spike (PS) or EPSP slope amplitude in baseline I/O recordings. By constrast, slight increases in peak dendritic amplitudes were observed in slices from PTU-treated animals relative to controls. Paired pulse facilitation of the EPSP was reduced in PTU-exposed animals at all but the longest IPI. No change in PS facilitation was observed. Surprizingly, PS LTP was increased in slices from PTU-exposed animals relative to controls, whereas no differences in EPSP slope LTP were evident. These data indicate that developmental hypothyroidism produces persistent alterations in hippocampal synaptic plasticity in this brain region and demonstrate a pattern of effects distinct from that observed in dentate gyrus *in vivo. This abstract does not necessarily reflect USEPA policy.*

1769 SUPRAPHYSIOLOGICAL LEVELS OF CORTICOSTERONE AND KAINIC ACID: FAILURE TO FIND INCREASED HIPPOCAMPAL NEUROTOXICITY IN THE KAINATE RESISTANT C57BL/6J MOUSE.

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Chronic stress mediated through glucocorticoids has been shown to exacerbate neurotoxicity in susceptible populations. To evaluate the role of glucocorticoids in the effects of chronic stress on neurotoxicity, as well as the role of strain in toxicant susceptibility, supraphysiological dosages of corticosterone (CORT)(200 mg/90d release pellet, s.c. implant) and its interactions with kainic acid (KA) neurotoxicity were examined in non-susceptible C57Bl/6J mice. Dose-response comparisons between the KA susceptible strain FVB/N and C57Bl/6J mice revealed a 25mg/kg (i.p.) dosage caused differential patterns of seizures in the two strains with FVB mice averaging 4 (Racine scale of 1 - 6) while C57 mice averaged 1. KA produced substantial CA1 cell loss in FVB/N mice accompanied by elevations in the injury related marker of astrocytic hypertrophy, GFAP (673% over control, seven day survival), while C57Bl/6J mice displayed no observable cell loss and only minor elevations in GFAP (44% over control, seven day survival). CORT exposure for four weeks prior to KA caused marked decreases in thymic and spleen, but not body weights. No overt cell loss was observed in CORT exposed mice, but GFAP was down-regulated in hippocampus as assessed by ELISA and diminished immunohistochemical signal. CORT pretreatment did not alter the GFAP response observed after KA treatment, or produce identifiable hippocampal cell loss. Our data confirm that CORT down-regulates GFAP in mouse brain and that there are differences in the susceptibility of mouse strains to KA-induced hippocampal damage. These results suggest that stress will not increase the neurotoxic effects of KA, other excitotoxicants, or potentially, other hippocampal insults in the resistant C57Bl/6J mouse. It is likely that individuals genetically susceptible to a given toxicant may be more prone to stress-induced exacerbation of toxicity.

1770 ALTERED SYNAPTIC VESICLE DYNAMICS IN 2,4-DITHIOBIURET-TREATED MICE.

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Neuromuscular weakness caused by 2,4-dithiobiuret (DTB) is associated with a reduced vesicle pool size resulting from altered synaptic vesicle trafficking. FM1-43 imaging fluorescent techniques were used on *Triangularis sternii* muscle preparations of mice treated with DTB for 5-6 days (20mg/kg/day, ip) to examine mechanisms of altered vesicle mobility in the presence of okadaic acid, staurosporine,cytochalasin D and colchicine. In DTB-treated mice, characteristic discrete fluorescent spots or clusters freely moved within nerve terminals and spontaneously destained with time. Fluorescence dimmed progressively, without moving or changing shape, during nerve stimulation in untreated mice. In DTB-treated mice, nerve activity caused no dye destaining, but caused dye movement within the terminals. Some bright regions grew dimmer and some dim regions grew brighter during nerve activity, but the average intensity of fluorescence in the entire nerve terminal was unchanged during 60 min of nerve stimulation. When stained untreated and DTB-treated terminals were incubated with 4 μM okadaic acid for 1 h, fluorescence became blurred and was not uniformly distributed in either preparation. Some areas accumulated large amounts of dye and others appeared depleted of dye; the overall intensity in the nerve terminal was unchanged. 20 μM staurosporine blocked dye movement induced by DTB after incubation for 2 h, but neither cytochalasin D (10μM) nor colchicine (10 - 60μM) blocked dye movement in DTB-treated nerve terminals. The results suggest that staurosporine could act by immobilizing synaptic vesicles in DTB-treated mice, while an increased level of protein phosphorylation, actin polymerization and depolymerization and microtubules apparently were not involved in the increased mobility of synaptic vesicles in the nerve terminals treated with DTB. An effect of staurosporine on the cytoskeleton has been proposed, suggesting that interactions with the cytoskeleton may contribute to altered dynamics of vesicle trafficking by DTB. Supported by NIH Grant R01NS20683.

1771 CHANGES IN RAT CORTICAL NEURONS AND GLIA INDUCED BY EXPOSURE TO THE CHOLINERGIC AGONIST PILOCARPINE.

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Pilocarpine induced neuropathological changes due to the ensuing seizures have been well characterized in the rat model. Damage is initially mediated *via* the mACh receptor and then secondarily through the NMDA receptor as an excitotoxic response. The purpose of this study was to 1) determine the pattern of neuronal degeneration using Fluoro-Jade B (FJB), 2)determine if there were myelin changes using Black-Gold (BG), 3) examine astroglial effects using GFAP immunohistochemistry, and 4) examine microglia in the affected areas using ED1/isolectin immunohistochemistry. Adult male Sprague-Dawley rats (360-600g) were pretreated with methylscopolamine (1 mg/kg, s.c) followed 30 min later by i.p. injection of pilocarpine HCl (400 mg/kg). In most animals, behavioral changes were characterized by salivation, rearing, and clonic movements that developed into status epilepticus (SE) after approximately 20-30 min. Rats were sacrificed at 5, 8 and 24 hrs post-injection. FJB staining in cortex was characterized by neuronal necrosis in all layers, and was particularly severe in layers II and III. Myelin changes in the cortex, detected with BG, consisted of varicosities and fragmentation throughout all layers. Examination of astrocytes with GFAP initially (5 hr) showed an increase in glial cells in all cortical layers. At 8 hr, GFAP staining was further increased and occasional "degenerating" astrocytes were evident in layers III-IV in some regions. By 24 hr, the astrocytic "degeneration" was prominent in cortical layers III-IV throughout the cortex. Activated macrophage, detected with ED1 and isolectin, were visible in the meninges 5 hr after pilocarpine injection; by 8 hr, activated macrophage had infiltrated the superficial cortical layers; and, by 24 hr, the macrophage had infiltrated throughout all of the cortical layers. In summary, pilocarpine induced SE results in massive cortical degeneration including neuronal and glial cells exacerbated by breakdown of the blood-brain barrier and macrophage invasion. Supported by FDA #7013.1 and ORISE.

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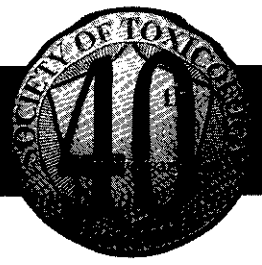

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 40th Annual Meeting of the Society of Toxicology, held at the Moscone Convention Center, San Francisco, California, March 25–29, 2001.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 451.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 479.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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