Ecstasy) and 3.4-methylenedioxyamphetamine (MDA) appears necessary to produce their serotonergic neurotoxicity, and thioether metabolites of α-methyldopamine (α-MeDA), a known metabolite of MDA and MDMA, may play a role in this toxicity. To assess mechanisms by which these metabolites gain access to the brain, we developed *in vitro* cultures of immortalised human cerebrovascular endothelial cells (IHCEC) as a model of the blood-brain barrier. Of five different extracellular matrices examined (collagen, fibronectin, gelatin, laminin, and Matrigelfi), gelatin gave the highest trans-endothelial cell electrical resistance (TEER; Ωcm2) and was used to coat filter inserts placed into larger wells for transport studies. The lumenal to basolateral transport of 5-(glutathion-*S*-yl)-α-MeDA (5-[GSyl]-α-MeDA; 100 μM) was monitored for 60 min, ~5% of 5-(GSyl)-α-MeDA was recovered intact in the basolateral compartment, whereas 78% of the substrate remained intact in the lumenal compartment. The residual 17% is likely metabolized by γ-glutamyl transpeptidase and dipeptidases since evidence of 5-(cystein-*S*-yl)-α-MeDA in both the lumenal and basolateral compartments was obtained by HPLC-coulometric electrode array analysis of the media. The barrier function of the IHCEC monolayers remains intact (no change in TEER) for the duration of the transport studies indicating maintenance of tight junctions. Transport of intact 5-(GSyl)-α-MeDA across the IHCEC monolayer is most likely due to the activity of an intact GSH transporter (DA 10832; Drug Metabolism, Merck & Co).

1376 THE CELLULAR NEUROTOXICITY TEST BATTERY USED IN THE ERGATT/CFN INTEGRATED TOXICITY TEST SCHEME (ECITTS).

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Sponsor: B Ekwall.

Neurotoxicity risk assessment is routinely based on animal studies. The availability of specific cellular test systems has made it possible to study the mechanisms of neurotoxic effects *in vitro*. This also offers economical and ethical advantages over large-scale *in vivo* studies. In the present study, the neurotoxicity of acrylamide, caffeine, diazepam, lindane, parathion and phenytoin was assessed in an *in vitro* test battery. The general cytotoxicity and neurite degeneration, as well as effects on intracellular Ca2+ homeostasis, protein synthesis, Ca2+ channel (VOCC) and acetylcholine receptor function, were investigated in human neuroblastoma (SH-SY5Y) cells after 72 hours exposure with the compounds. The most sensitive parameters were; neurite degeneration for acrylamide and parathion, VOCC function for caffeine, diazepam and lindane, and protein synthesis for phenytoin. The critical cellular neurotoxic concentration for each compound (i.e. lowest EC20 value) was integrated in a biokinetic model and the lowest effective *in vivo* doses (LOEDs) were estimated. The estimated LOEDs for acrylamide, caffeine and lindane correlated well with literature derived experimental LOEDs, implicating that the selected *in vitro* tests were appropriate for these compounds. However, the estimated LOEDs for diazepam, parathion and phenytoin were more than half a magnitude higher than the experimental LOEDs, possibly because no tests for benzodiazepine receptor function and choline esterase activity were included in the test battery. This result illustrates the importance of designing *in vitro* test batteries, in which endpoints, relevant for each class of compounds, are included.

1377 NOISE-INDUCED HEARING LOSS IN DIFFERENT CARBON MONOXIDE ENVIRONMENTS.

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Intense noise, especially its high frequency components, may cause hearing loss (HL). The noise-induced-HL (NIHL) can be enhanced by simultaneous carbon monoxide (CO) exposure. Carbon monoxide exists in many environments. For example, pure cigarette smoking may cause an alveolar CO level of about 300 ppm. Therefore, it is important to know the lowest CO-level at which the CO interacts with intense noise and makes the noise-induced auditory impairment worse. In the present study, high-frequency octave-band noise (9.6-19.2 kHz, 100 dB_{Ln}) and CO-levels of 1200 ppm, 700 ppm, 500 ppm, 300 ppm and 0 ppm were applied. The hearing loss was determined by recording of CAP (compound action potential) from the round window, 4 weeks after exposure. The octave-band noise alone (0-ppm-CO) induced an approximate 30-dB permanent hearing loss in rats at frequencies higher than 10 kHz. CO alone did not induce any hearing losses, even at 30 minutes following the exposure. The combined exposure of the noise and 1200-ppm-CO, however, caused a much greater permanent hearing loss, especially in high frequency region. The HL-enhancement phenomenon by CO was obvious. The enhancement of the noise-induced hearing loss lessened gradually with CO-level. The hearing loss to the combined exposure with 300-ppm-CO was similar to that to the noise alone (0-ppm-CO). The lowest CO-level, which shows interaction with intense noise, must be between 300 ppm and 500 ppm. In human subjects the lowest CO-level, showing interaction with intense noise, might be lower than the data obtained in the rats. (Supported in part by NIOSH grant #03481 and NIH grant ES08082.)

1378 ACUTE DISRUPTION OF COCHLEAR POTENTIALS BY POTASSIUM CYANIDE.

W Tawackoli, and L D Fechter. *University of Oklahoma Health Science Center, Oklahoma City, OK.*

Cyanide is present in various environmental settings and is also an occupational hazard for firefighters. Effects and mechanisms of cyanide (CN) toxicity are unclear in hearing loss. In this study, adult male Long Evans hooded rats were used to examine the effects of potassium cyanide (KCN). Interactions with noise on cochlear potentials, namely, compound action potential (CAP) and cochlear microphonic (CM) were studied. Subjects were injected with KCN (7mg/kg, ip) and compared with controls (saline, ip). CAP sensitivity is dependent upon the function of inner hair cells and spiral ganglion cells. The CM is generated predominantly from outer hair cells. CAP and CM were recorded pre and post administration of KCN. Hearing levels at three frequencies (2 kHz, 12 kHz and 40 kHz) were tested. Blood cyanide levels were measured following KCN administration for a period of 30 min. A temporary threshold shift in both CAP and CM was observed for a period of 5 to 15 min. following KCN administration. Concurrent exposure to KCN and noise (110 dB, broad band) for 2 hours demonstrated no threshold shift in either CAP or CM. (Supported in part by NIOSH grant OH 03481 and NIEHS grant ES 08082.)

1379 EFFECTS OF EXPOSURE DURATION ON POTENTIATION OF NOISE INDUCED HEARING LOSS BY CARBON MONOXIDE.

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Noise induced hearing loss (NIHL) is still the most common occupational disease in the U.S. Concurrent noise exposures with chemical asphyxiants such as carbon monoxide (CO) is common in work environments of firefighters, automobile mechanics and tunnel-toll booth workers. Potentiation of NIHL following acute exposure to noise (102-103 dB, broad band) and CO (1500 ppm) has been demonstrated previously. It is well known that noise exposure of varying duration is related to exposure intensities. The equal energy principle states that an increase in exposure intensity is compensated for by a corresponding decrease (halving) in exposure duration. This study investigates whether or not the NIHL resulting from combined exposures complies with the equal energy principle. Adult male Long Evans hooded rats were acutely exposed to noise alone (100dB_{Ln}, 9.6-19.2 kHz), CO alone (1500 ppm), noise & CO, and air (controls). Duration of exposure varied between 2 and 8 hours. Auditory sensitivity was measured four weeks post-exposure. End points measured were electrophysiological, namely, compound action potential (CAP) and cochlear microphonic (CM). CAP is a measure of cochlear output generated at the inner hair cell-type I spiral ganglion synapse, and, CM is generated largely by the outer hair cell. These potentials were recorded in response to pure tones between 2 and 40 kHz. NIHL was found to comply with the principle of equal energy. However, hearing loss resulting from combined exposure did not follow a similar pattern. (This study is supported in part by NIOSH grant #03481 and NIEHS grant ES 08082.)

1380 SUBCHRONIC TOXICITY OF PILOCARPINE IN RATS.

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Pilocarpine, a cholinergic parasympathetic agent with predominantly muscarinic action, is indicated as a treatment for symptoms of xerostomia in Sjogren's syndrome or head and neck cancer patients following radiation. A 90-day range-finding study was done to assess the toxicity, define an esti-

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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 38th Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.

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

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