results show that 4-OH PCB 52 is more toxic than PCB 52 to N27 cells - a dopaminergic cell line. Our work intends to understand how PCB 52 and its metabolites modulate the dopaminergic system. This includes analyzing dopamine metabolism in cell culture and rat brain tissue. We have also performed preliminary studies on detecting reactive oxygen species. Furthermore, we will analyze changes in gene expression to explore alterations in dopamine cell trafficking. PCB 52 and 4-OH PCB 52 have previously shown toxicity in neuronal cell lines. However, not much is known about how these compounds alter and modulate the dopaminergic system. Future studies will employ neuroprotective strategies.

1345 Dietary Strategies Affect Marine Algal Toxin Levels in Subsistence Harvested Alaskan Pinnipeds

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Domoic acid (DA) and saxitoxin (STX) are marine algal-produced toxins that elicit acute neurotoxic symptoms in mammals following ingestion. Trophic transfer of both toxins allows for their spread through marine food webs. Cases of acute DA and STX toxicity are termed Amnesiac Shellfish Poisoning and Paralytic Shellfish Poisoning respectively, as the primary vector of human exposure is contaminated shellfish. Knowledge of these toxicoses has led to the implementation and enforcement of seafood safety regulatory limits for both DA and STX in shellfish (20 and 0.8 ppm, respectively). However, human exposure to algal toxins can occur through additional vectors. Native communities in Alaska conduct annual subsistence harvests of marine mammals that are a part of complex marine food webs. As DA and STX prevalence in Alaskan arctic food webs has not been extensively quantified, such harvests are of interest both with regard to potential human toxin exposure and to marine mammal health. We tested 856 samples collected from the gastrointestinal tracts of pinnipeds subsistence harvested in Alaska between 2007 and 2016. Samples were analyzed for DA and STX presence using commercially available Enzyme-linked Immunosorbent Assay (ELISA) kits. Toxin prevalence was found to be highest in bearded seals and walruses and lowest in ribbon seals. Maximum DA and STX concentrations followed similar trends. Additionally, few samples were found to have toxin concentrations above the seafood safety limits for acute toxicity. Dietary strategy is suggested as one explanation for interspecies variations in toxin level, though the clarity of this relationship is complicated by features of the opportunistic dataset as well as oceanographic, seasonal, and physiological factors.

1346 Behavioral and Histological Evidence of a Neuroimmune Basis for Gulf War Illness

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Chronic exposure to the glucocorticoid, corticosterone (CORT), at levels associated with high physiological stress, has been shown to prime the neuroimmune response to neurotoxic exposures and systemic inflammation, significantly increasing the expression of proinflammatory cytokines/chemokines following exposure. Gulf War Illness (GWI) is a multi-symptom, neuroimmune-based disorder that presents with features characteristic of persistent sickness behavior. Using a preclinical mouse model of GWI, we have found that chronic exposure to the stress hormone corticosterone (CORT; 200-400 mg/L) in the drinking water for 7 days exacerbated the initial neuroinflammatory response to the sarin surrogate diisopropylfluorophosphate (DFP; 4 mg/kg, i.p.). A more recent study using this exposure protocol has found that CORT+DFP exposed animals exhibit cognitive impairment in the Novel Object Recognition Test with decreased discrimination of the novel versus familiar object. However, this acute exposure model is more representative of the veterans' time in theater, and those suffering with GWI are nearly 30 years removed from their tours of duty. Thus, a more extended duration animal model is necessary. Our model of GWI at 5 weeks after the initial CORT+DFP event, constituting periodic administration of CORT for 7 days every other week and a subsequent systemic immune challenge with the bacterial mimic lipopolysaccharide (LPS; 0.25-0.50 mg/kg, s.c.) mimics the long-term illness and 'flare up' of symptoms as is reported in GWI. This longer CORT regimen produced signs of decreased cognition in the Novel Object Location Test, signified by CORT+DFP+LPS animals less able to distinguish the displaced versus familiar object. This paradigm reveals a further exacerbation of neuroinflammatory markers and emergence of activated microglia in key brain areas including hippocampus and cortex that affects behavior for at least 12 days after the last LPS dose. Together, these data provide additional support that GWI is a chronic, stressor-primed, neuroinflammatory condition with adverse long-term neurobiological and behavioral outcomes. *Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.*

1347 Comparison of Acute Effects of Neurotoxic Compounds on Network Activity in Human and Rodent Neural Cultures

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Assessment of neuroactive effects of chemicals in cell-based assays remains challenging as complex functional tissue is required for biologically relevant readouts. Recent *in vitro* models using rodent primary neural cultures grown on multielectrode arrays (MEAs) allow quantitative measurements of neural network activity and have been demonstrated to be suitable for neurotoxicity screening. However, robust systems for testing effects on network function in human neural networks are still lacking. The increasing number of differentiation protocols for generating neurons from induced pluripotent stem cells (iPSCs) holds great potential to overcome the unavailability of human primary tissue and expedite human cell-based assays. Yet, the variability in neuronal activity, prolonged ontogeny and rather immature stage of most neuronal cells derived by standard differentiation techniques greatly limit their utility for screening neurotoxic effects on neuronal networks. Here, we used excitatory and inhibitory neurons that were separately generated by direct conversion from human iPSCs together with primary human astroglial cells to establish highly functional neural cultures (ratio=3:1 neurons/glia). Such neuron/glia co-cultures showed pronounced neuronal activity and robust formation of synchronized network activity on MEAs, albeit with noticeable delay vs primary rat cortical cultures. We further investigated the effects of neurotoxic test compounds, including 4 $GABA_A$ receptor antagonists, an organotin, and 4 pyrethroid insecticides, as well as 3 negative control compounds on network activity in these human neuron/glia co-cultures. Importantly, we observed largely corresponding dose-dependent alterations in firing, burst and synchrony metrics of neuronal network activity in iPSC-derived human neuron/glia and rat primary cortical cultures. These results demonstrate the utility of this direct-differentiated human model for neurotoxicity screening using MEAs.

1348 Validation of High-Throughput 3D microBrain Model to Predict Drug-Induced Neurotoxicity across a Diverse Set of Pharmaceuticals

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Drug-induced central nervous system (CNS) toxicity is a top three cause of safety-related attrition across the pharmaceutical industry. Undesired side-effect on CNS in human account for 10% of all drugs withdrawn from sale during the periods 1960-1999. A main reason for the high failure rate is that the concordance rate is low between human adverse drug reaction (ADR) and identification in preclinical toxicity studies. The development of predictive CNS toxicity assays is needed to help pharmaceutical companies design and optimize safer therapies. Over a dozen different iPS-derived microBrain and miniBrain models have been published in recent years, but their ability to predict CNS toxicity in patients is as of yet unproven. To evaluate the predictive capabilities of one of these models, we validated an iPS-derived microBrain model using 84 structurally diverse pharmaceuticals, a combination of US FDA-approved drugs and clinical drug candidates with varying levels of seizurogenic and neurodegenerative liability. Seven endpoints were analyzed using Ca oscillations and cellular ATP levels after a single and repeated exposure treatment, respectively. The microBrain *in vitro* IC_{50}s for each endpoint were rooted into clinical used therapeutic exposure (fCmax) as classifiers (fCmax/IC_{50}s) to predict clinical drug-induced seizures and neurodegeneration. We used logistic regression with clinical reported CNS toxicity as binary response variable and combined each endpoint as independent variables [fCmax/IC_{50}s] to calculate probability for CNS toxicity. After refining these endpoint cutoffs on separate training and test sets, we find that in total

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