aid in identifying responses falling within the normal range. Our pathway research with receptor-mediated signaling (PPAR and AhR) and with DNA-damage shows the application of these tools in practice.

S 696 Is Neuroimmune Crosstalk Important to Neurotoxicology? Critical Insight from Animal and Human Studies

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Convincing evidence of bidirectional communication between the immune system and the nervous system has led to a paradigm shift in our understanding of neuroimmune interactions. Emerging evidence establishes a role for immune signaling in key neurodevelopmental events. Additional evidence suggests immune system contribution to neuronal responses in the form of neuroprotection and repair of tissue injury, as well as in the pathogenesis of neurodevelopmental and neurodegenerative disease. Simultaneously, neurons may actively participate in immune responses in the nervous system by signaling to resident and infiltrating immune cells. The net result of the neuroimmune crosstalk depends on the balance between protective and destructive signaling pathways. There is increasing consensus that exposure to neurotoxicants may tip this balance towards a more disruptive outcome and augment the risk and/or severity of disease. How the immune system can act as a mediator/modulator of neurotoxicity remains elusive. Understanding gained by investigation into neuroimmune interactions will guide improvement of disease diagnosis, prevention, and treatment. This session will present evidence of neuroimmune perturbations in human studies and animal models of neurotoxicant exposure. Evidence from human studies will focus on immune alterations following developmental neurotoxicant exposure in children with documented neurological deficits and in a pediatric population with autism spectrum disorders. Supporting data from animal models will focus on peripheral immune alterations and neuroinflammation following developmental or adult nervous system insult.

S 697 Neuroimmune Interactions in CNS Development, Repair, and Damage: An Overview

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It is becoming increasingly clear that the nervous system and the immune system can no longer be considered as separate entities. Evidence suggests that molecules traditionally thought to be exclusive members of either the immune or the nervous system have a dual role in both systems and can regulate CNS function and central innate immune responses, not only in disease but also during normal physiological processes (development, aging, pregnancy, chronic stress). Such molecules include complement and major histocompatibility complex proteins, cytokines, chemokines and neurotrophins. Expression patterns of these molecules are altered in Parkinson's, Alzheimer's and multiple sclerosis and mutations in some of the corresponding genes have been linked to neurodevelopmental disorders (Autism Spectrum Disorders, schizophrenia). Neurons, astrocytes and microglia express a wide variety of these molecules, which in turn function to mediate cell-cell interactions including neuronal control of microglial activation and conversely microglial regulation of neurodevelopmental events such as synaptic pruning. Depending on the timing and context of the neuroimmune interaction, such crosstalk may mediate normal neurodevelopment or, in the case of CNS insult, may result in disease or repair. The net effect depends on the balance of neuroprotective and destructive pathways activated. Exposure of the CNS to neurotoxic chemicals could tip this balance towards a detrimental outcome and evidence of immune alterations in the CNS following exposure to environmental factors such as manganese, air pollution and pesticides, provide a compelling reason for further investigation. However, our understanding of the regulatory switches that determine neuroimmune interactions, and of the implications of their perturbation is still in its infancy. This talk will provide an overview of the cell types and molecules that mediate this bidirectional communication in the CNS, assess experimental evidence of their alteration by neurotoxicants, and highlight knowledge gaps in this rapidly growing field.

S 698 Effect of Polybrominated Diphenyl Ethers (PBDEs) on Immune Function and Cellular Signaling in Children with Autism

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Elucidating the impact of environmental toxicants on the pediatric population, specifically children with autism spectrum disorders (ASD), is of critical importance. Previous studies implicate gene-by-environmental interactions in the etiology of autism, a disorder characterized by abnormal neurodevelopment and immunological dysfunction. PBDEs have been shown to influence development of both the nervous and immune systems. Research in the field lacks investigation in humans, especially sensitive populations, such as children with neurodevelopmental disorders. For this study, we sought to examine the impact of a potent congener, BDE-49, on the immune function in peripheral blood mononuclear cells (PBMCs) isolated from children ages 2-5 years old with neurodevelopmental diagnoses, such as ASD, developmental delayed (DD) and aged-matched typically developing (TD) subjects. Isolated PBMCs were exposed ex vivo for 4 hours to BDE-49 (0, 50nM, 250nM) prior to challenge with bacterial lipopolysaccharide (LPS), an innate immune cell activator, or the T cell mitogen, phytohemagglutin A (PHA). Cytokine and chemokine levels from cell supernatants were analyzed via a 21-multiplex bead-based assay. Ex vivo exposure of peripheral immune cells from a pediatric population to BDE-49 had global effects on the production of certain cytokines and chemokines, regardless of diagnosis. When diagnosis was taken into account, ex vivo exposure of PBMCs to BDE-49 at 50nM resulted in a differential inflammatory immune response in children with ASD compared to TD. We found that in each population, female subjects were more immune-sensitive to BDE-49 compared to male subjects, with a down regulation of cytokine and chemokine expression. This novel human study may aid in a better understanding of the interplay between immunological and neurotoxicants and the combined role in the etiology of autism.

S 699 The Immune and Neurological Impacts of Developmental BPA Exposure

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Environmental exposure to exogenous agents during critical time points of development may be associated with the onset of deleterious effects, including autoimmune and neurological disorders. Numerous studies have shown that bisphenol A (BPA) exposure can disrupt myriad biological systems. This presentation will focus on the immune and neurological impacts of a "double hit" of developmental exposure to BPA and an acute exposure to lipopolysaccharide (LPS) in an in vivo C57BL/6 mouse model. LPS exposure given around the time of learning has been shown to "unmask" developmental deficits in learning and memory. We hypothesize that postnatal exposure to LPS will unmask BPA-induced developmental impacts to hippocampal-dependent learning and memory of C57BL/6 offspring. Behavioral changes will be correlated with markers of immune dysfunction to determine the relationship between immunological alterations and behavioral changes. C57BL/6 female mice were given 0, 0.4, or 50 mg/kg of BPA in a corn oil vehicle by gavage, beginning at pairing with males and ending at weaning of pups. Offspring were assessed on a Barnes maze at postnatal day 60 (PND60), 24 hours after challenge with LPS. Splenic lymphocyte immunophenotype, total serum immunoglobulins, and inflammatory cytokines were evaluated after behavioral testing. Our findings suggest that developmental immunotoxicity induced by BPA exposure, in the absence of a postnatal trigger, is insufficient to induce changes in learning and memory.

S 700 Exploring the Relationship between Neuroinflammation and Neurotoxicity

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The enhanced expression of proinflammatory cytokines and chemokines accompanies brain injury induced by neurotrauma, disease or neurotoxicity as well as systemic infection. Elevations in proinflammatory mediators may serve as modulators or mediators of astroglial and microglial activation, cellular responses associated with all types of brain injury and collectively referred to as neuroinflammation. The "acute phase" response to systemic inflammation also leads to upregulation of proinflammatory cytokines/chemokines in the brain in the absence of underling neural damage, responses thought to be mediated largely by microglia and that serve as the basis of "sickness behavior". Activated glia may have neuroprotective roles or may exacerbate neural damage. Exposure to the known dopaminergic

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