Neuroproteomics and Environmental Chemical-induced Adverse Effects

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Technological advances in science have aided the field of neuroproteomics with refined tools for the study of the expression, interaction, and function of proteins in the nervous system. With the aid of bioinformatics, neuroproteomics can reveal the organization of dynamic, functional protein networks and macromolecular structures that are the basis for behavioral, anatomical, and functional processes. Neuroproteomics promotes understanding of post-translational modifications where proteins are chemically modified or regulated after synthesis, including protein 3-D conformation which can determine function. The most common techniques used in proteomics are two-dimension differential gel electrophoresis (2-DIGE) and protein arrays, which are powerful tools to separate complex protein mixtures and analyze proteomes. Mass spectrometry in conjunction with multiple databases and computer programs is used in protein identification. This approach can be used to identify all proteins in a particular sample, elucidate components of biochemical pathways, and analyze post-translational modifications in a small or large scale. Neuroproteomics has already demonstrated its value by identifying early biomarkers following neuronal damage in drug addiction or brain injury, and in monitoring nerve growth. In regards to chemically-induced adverse effects on the nervous system, proteomics can aid in understanding mode of action in an efficient way as well as identify biomarkers for the toxic effects. The identification of biomarkers based on mode of action can aid in the development of *in vitro* models to screen and prioritize chemicals for further neurotoxicity testing. Studies on two neurotoxicants well established in both humans and animal models (Aroclor 1254, a commercial polychlorinated biphenyl mixture; DE-71, a commercial polybrominated diphenyl ether mixture) using 2-DIGE have revealed that proteins related to energy metabolism in mitochondria (ATP synthase, sub unit β (ATP5β), creatine kinase and malate dehydrogenase), calcium signaling (endoplasmic reticulum ATPase, voltage-dependent anion-selective channel protein 1 (VDAC1) and Ryanodine receptor type II) and growth of the nervous system (valosine-containing protein (VCP), collapsin response mediator protein 3 (CRMP-3)) may be involved in the developmental neurotoxicity of these persistent chemicals. Studies are underway on other neurotoxic chemicals to identify common protein signatures and pathways. (*This presentation does not necessarily reflect USEPA policy*).