The Noradrenergic System and Environmental Health Science

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Brainstem noradrenergic neurons comprise a small population of cells that project to virtually all areas of the central nervous system. Through the release of norepinephrine, these neurons modulate functions as diverse as attention, emotion, appetite, memory, and response to stress. Consistent with this functional diversity, norepinephrine signaling is disrupted in a spectrum of neurodegenerative and neurodevelopmental disorders and following exposure to a number of environmental toxicants and stressors. Interestingly, it has been observed that subpopulations of noradrenergic neurons are differentially vulnerable to disease-related cell death and environmental insult. Given these observations, we suspect that the key to understanding noradrenergic system dysfunction will not be found by focusing on the noradrenergic system as a whole. Rather, this phenotypic complexity will only be understood by uncovering the developmental and genetic factors that define unique functional subtypes of noradrenergic neurons.

The long-term goal of our research is to understand the mechanistic relationship between perturbation of distinct noradrenergic neuron subtypes during development and increased susceptibility to emotional and cognitive deficits in adulthood. In pursuit of this goal, we use the mouse as a model system to: 1) define subtypes of noradrenergic neurons based on differences in developmental gene expression; 2) determine their circuitry and function in the adult brain; and 3) perturb their function during development to uncover critical windows of susceptibility and the long-term effect of these perturbations on adult behavior. Results from our studies promise insight into the basic biological mechanisms underlying noradrenergic neuron subtype function and their differential response to disease and environmental insult. Together, these studies are in line with Themes One and Three of the NIEHS Strategic Plan. Theme One: Advancing Environmental Health Sciences (EHS) through basic biological research designed to, understand the pathways that are disrupted by environmental exposures, and to assess the impact of developmental exposures on the risk of disease later in life. Theme Three: Enhancing EHS through Stewardship and Support by training of the next generation environmental health scientists, and the implementation of cutting-edge, collaborative research.