Feinstein Institute for Medical Research

Noninvasive Neurograms for Determining Etiology and Severity of Infectious Illness

Research since the turn of the millennium has revealed, in increasing detail, numerous facets of interaction between the immune and nervous systems. Once thought mutually independent, it is now evident that communication and reciprocal influence between these two systems are critical in maintaining homeostasis. Importantly, this dynamic relationship is prone to disruption by intrinsic or environmental stimuli, forming a heuristic window into disease pathogenesis. For example, it has been demonstrated that in various environments including the gut and respiratory mucosae, lymph nodes, spleen and peritoneum, immune cells and nerve terminals exist in close juxtaposition. Furthermore, numerous 'canonical' receptors of innate immunity, including the pathogen recognition receptors toll-like receptors 3, 4, 7 and 9, formylated peptide receptors, and C-type lectins are expressed on sensory nerve terminals and glial cells, whereas numerous 'canonical' receptors of the nervous system including nicotinic and muscarinic acetylcholine receptors, serotonergic receptors, and neurotrophic growth factor receptors are expressed on immune cells. The significance of these findings has been elevated by recent reports of specific pathogen detection by nociceptors in cutaneous infections with *Staphylococcus aureus* and gastrointestinal infections with *Salmonella typhimurium*, the report of neural control of lymphatic antigen flow, and the description of distinct relay of cytokine presence to the CNS via the vagus nerve in intraperitoneal challenge experiments. Our proposal aims to take advantage of these findings to develop a noninvasive tool, detecting and interpreting neural activity, to shed light on the location, severity, and specific nature of illness of infectious etiology. Specifically, we aim to use noninvasive neurography to distinguish between viral and bacterial infections in a biospecimen-free, point-of-care manner, thus subverting the use of empiric antibiotics in patients with viral illness. In addition, we aim to localize bacterial infections to pave the way for anatomically targeted delivery of antibiotics, limiting the area of exposure to drug. Finally, we aim to decipher pathogen-specific neurogram patterns to direct the optimal selection of antibiotic class where indicated. Altogether, our strategy will limit the use of antibiotics to maximize individual patient outcomes while minimizing public health concerns regarding the emergence of highly virulent, drug-resistant organisms.