New Research Examines Connection Between Inflammatory Stimulus and Parkinson’s Disease

University of Texas Health Science Center study suggests inflammation’s role in the development of the disease

BOSTON—Parkinson’s disease (PD) is a progressive degenerative disease affecting a person’s ability to coordinate and control their muscle movement. What starts out as a tremor in a finger will eventually lead to difficulty in writing and speaking, and ultimately the inability to walk without assistance. Since the 1950s research has shown that people with Parkinson’s have decreased levels of the chemical dopamine in their brains, which is involved in sending messages to the part of the brain that controls coordination and movement. Subsequent research has found that dopamine-generating cells, known as dopaminergic neurons, are also absent in a specific area of the brain in those with PD.

The precise cause or causes of PD is unknown, but there is a consensus that an inflammatory event or episode is involved in the initiation of neurodegeneration, and that chronic neuroinflammation is a sustaining and exacerbating reason for the loss of the dopaminergic neurons. A new study conducted by a team of Texas researchers brings the understanding of inflammation’s role a step further. They have found that a single, high-dose exposure of an experimental inflammatory agent in an animal model causes changes in brain tissue that are similar to those associated with the development of the disease.

The study was conducted by Roger Bick and his colleagues Marie-Francoise Doursout, Michael S. Schurdell, Lauren M. Young, Uzondu Osuagwu, Diana M. Hook, Brian J. Poindexter, Mya C. Schiess, and Diane L. M. Bick, all at The University of Texas Health Science Center at Houston (UTHealth), Houston, Tex. Dr. Schiess will discuss the team’s findings at the Experimental Biology 2013 meeting, being held April 20-24, 2013 at the Boston Convention and Exhibition Center, Boston, Mass.
The poster presentation is entitled, “Inflammatory cells and cytokines in the olfactory bulb of a rat model of neuroinflammation; Insights into neurodegeneration?” and is sponsored by the American Society for Investigative Pathology (ASIP), a co-sponsor of the meeting. The full study will appear in an upcoming edition of the Journal of Interferon & Cytokine Research.

Methodology
In the study, the researchers examined inflammatory cell and cytokine production in brain tissue from a lipopolysaccharide (LPS)-treated rat model that mimics many of the neuropathologic changes associated with PD. Concurrently, they monitored the appearance of glial cell line-derived neurotrophic factor (GDNF), a neuronal protective agent, and circulating nitric oxide (NO) levels. They also examined the immune system associated cells in the olfactory bulb of the brain. It is known that Parkinson’s starts with this mechanism.

Twelve male Sprague-Dawley rats were treated with intravenous LPS in saline, 12 control rats were treated with saline, and all were maintained for up to 48 hours before euthanasia and brain removal. Brains were removed from both groups at defined times, blood and other tests were conducted, and images of various sections of the brain, including the olfactory bulb, cortex and cerebellum, were taken using fluorescent microscopy.

Results and Conclusions
In general, the researchers found that a single injection of LPS elicited a systemic inflammatory response in the rats, as indicated by an elevation in certain circulatory cytokines. Tissue taken from the olfactory bulb showed the presence of immune associated cells. Individual cytokines within the olfactory bulb showed an increase in certain types of cytokines. Taken together, the complete analysis indicated that the single dose of LPS stimulated an inflammatory response that closely resembled the hallmarks of the development of the disease.

The results suggest an involvement of both the peripheral and the central nervous system immune components in response to inflammation and inflammatory episodes. As a result, the researchers suggest: (1) inflammation initiates an immune response; (2) the presence of continuing and increasing pro-inflammatory mechanisms results in a process whereby cellular protective mechanisms are overcome and the more susceptible cells, such as the dopaminergic neurons, enter into cell death pathways; and (3) this leads to a series of events that are a key part of the progression of PD.

Next Steps
Neuroinflammation is a significant problem for those with PD, and it persists throughout the course of this debilitating illness. Understanding of the essential processes behind it is the best pathway to finding therapeutic approaches to address it. This study highlights an opportunity to better understand the role inflammation plays in the process.

About Experimental Biology 2013
Six scientific societies will hold their joint scientific sessions and annual meetings, known as Experimental Biology, from April 20-24, 2013, in Boston. This meeting brings together the
leading researchers from a broad array of life science disciplines. The societies include the American Association of Anatomists (AAA), American Physiological Society (APS), American Society for Biochemistry and Molecular Biology (ASBMB), American Society for Investigative Pathology (ASIP), American Society for Nutrition (ASN), and American Society for Pharmacology and Experimental Therapeutics (ASPET). Additional information about the meeting is online at http://bit.ly/ymb7ay.

About the American Society for Investigative Pathology (ASIP)
The American Society for Investigative Pathology (ASIP) is a society of biomedical scientists who investigate mechanisms of disease. Investigative pathology is an integrative discipline that links the presentation of disease in the whole organism to its fundamental cellular and molecular mechanisms. It uses a variety of structural, functional, and genetic techniques and ultimately applies research findings to the diagnosis and treatment of diseases. ASIP advocates for the practice of investigative pathology and fosters the professional career development and education of its members. This year marks its centennial celebration.

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NOTE TO EDITORS: To receive a copy of the abstract or schedule an interview with Dr. Schiess, please contact Donna Krupa at DKrupa@the-aps.org, 301.634.7209 (office) or 703.967.2751 (cell) or @Phyziochick on Twitter.