Neuron – Microglial Interactions in TBI, CNS Autoimmunity, and Neurodegeneration

The key pivot in common in all head injury, CNS autoimmune, and neurodegeneration patients.

Cogence Clinical Pearl

In this Cogence clinical pearl, we look at the pivot that connects the immune system and the central nervous system. Learning to address this central mechanism is crucial to your success in working with patients with CNS disorders.

What the research says…

The paper below, from *Frontiers in Psychiatry*, reviews the evidence that **a single key neuro-immunological feature is at the center** of head injury, brain autoimmune processes like MS, PANDAS, etc., and neurodegenerative diseases like Alzheimer's. The signaling interactions between neurons and microglial cells determine whether a person with one of these illnesses will lose more neurons, and therefore have a downward course of disease. **These signaling interactions can be modified clinically, in ways reviewed in the paper.**

Application…

Neurons signal microglial cells. **The signals they send determine if the microglial cell will protect the neuron or eliminate it by phagocytosis.** Signal errors push the microglial cells to phagocytize neurons they should be protecting, resulting in excessive neuronal loss. A host of clinically modifiable factors influence this process, many of which are familiar to functional medicine clinicians, like systemic inflammation, dysglycemia, redox problems, dysbiosis, and others. **Understanding how these factors connect with the underlying immunology can be crucial to optimize your clinical outcomes with patients who have neurodegenerative diseases, CNS autoimmunity, chronic infections, PANS/PANDAS, or TBI.**

The Research…

Microglial Phagocytosis of Neurons: Diminishing Neuronal Loss in Traumatic, Infectious, Inflammatory, and Autoimmune CNS Disorders.
Yanuck SF. Front. Psychiatry 10:712, 2019. doi:10.3389/fpsyt.2019.00712

(Color and bold added.)

Abstract
Errors in neuron-microglial interaction are known to lead to **microglial phagocytosis of live neurons and excessive neuronal loss,** potentially yielding poorer clinical outcomes. Factors that

affect neuron-microglial interaction have the potential to influence the error rate. Clinical comorbidities that unfavorably impact neuron-microglial interaction may promote a higher rate of neuronal loss, to the detriment of patient outcome. This paper proposes that **many common, clinically modifiable comorbidities have a common thread, in that they all influence neuron-microglial interactions.** Comorbidities like traumatic brain injury, infection, stress, neuroinflammation, loss of neuronal metabolic integrity, poor growth factor status, and other factors, all have the potential to alter communication between neurons and microglia. **When this occurs, microglial phagocytosis of live neurons can increase.** In addition, **microglia can shift into a morphological form in which they express major histocompatibility complex II (MHC-II), allowing them to function as antigen presenting cells that present neuronal debris as antigen to invading T cells.** This can increase risk for the development of CNS autoimmunity, or can exacerbate existing CNS autoimmunity. The detrimental influence of these comorbidities has the potential to contribute to the mosaic of factors that determine patient outcome in some CNS pathologies that have neuropsychiatric involvement, including TBI and CNS disorders with autoimmune components, where excessive neuronal loss can yield poorer clinical outcomes. Recognition of the impact of these comorbidities may contribute to an understanding of the common clinical observation that many seemingly disparate factors contribute to the overall picture of case management and clinical outcome in these complex disorders. **In a clinical setting, knowing how these comorbidities can influence neuron-microglial interaction can help focus surveillance and care on a broader group of potential therapeutic targets.** Accordingly, an interest in the mechanisms underlying the influence of these factors on neuron-microglial interactions is appropriate. Neuron microglial interaction is reviewed, and the various mechanisms by which these potential comorbidities influence neuro-microglial interaction are described.