IMMUNE PROCESSES ARE NOT BENEFICIAL IN NEURODEGENERATIVE DISEASES

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Neurodegeneration is a pathological process characterised by progressive neuron, myelin, or tissue breakdown within the nervous system (1). The release of degraded products evokes a vigorous process of phagocytosis and cellular gliosis. Neurodegeneration also exposes immune-privileged sites of nervous system to innate and adaptive systemic immune responses. Breakdown of blood-brain barrier in response to metabolic or ischaemic injury allows systemic elements of immune response to gain access into the privileged compartment of the central nervous system, leading to the emergence of immune activation within the nervous tissue. Once immune system is sensitised to neural antigens, the immune privileged status of the brain and spinal cord is no longer maintained even if such responses are suppressed (2). Recruitment of systemic immune response to areas of neurodegeneration sets in motion the cascade of immune-inflammatory process that leads to tissue damage and injury that becomes progressive and irreversible, resulting in clinical symptoms of cumulative disability.

Inflammatory and neurodegenerative changes often occur side by side and at the same time in viral and or bacterial infections of the central nervous system. The site of tissue degeneration is usually localised to the area of inflammatory response in microbial infection that could be suppressed by pharmacological therapy. Early treatment with acyclovir in herpes simplex encephalitis or a combination of dexamethasone and antibiotic in pneumococcal meningitis may limit damage to hippocampal neurons. In cerebrovascular ischaemia, the extent of neuronal injury is determined by inflammatory changes in ischaemic penumbra. In multiple sclerosis, neurodegeneration in grey matter and axonal loss in normal appearing white matter occur from an early stage and extend beyond the area of acute inflammatory lesion (demyelinating plaque). Biological therapies in relapsing-remitting multiple sclerosis are often offered to patients in the hope to slow the progression of disability from neurodegeneration associated with inflammatory demyelination. Inflammatory changes to misfolded β-amyloid protein are believed to result in neuronal loss in Alzheimer's disease, laying the concept that anti-inflammatory approaches could be therapeutically protective in this condition.

The perception that immune response in neurodegenerative disease is simply concerned with "clearing away the debris" or is neuroprotective is over-simplistic. On balance, immune response is more likely to contribute to progressive tissue damage by microglial activation, release of pro-inflammatory cytokines and recruitment of systemic immune response. The neuroprotective role of inflammation is primarily attributed to the release of neurotrophic factors and growth factors. However, repair of damaged tissue also depends on the availability of neural progenitor cells and the microenvironment of the injured tissue; experience in traumatic spinal cord injury, stroke and multiple sclerosis suggests that it is the microenvironment that is the key determinant of reparability. Therapeutic strategies that block entry of inflammatory cells into the injured microenvironment of nervous system, inhibit the release or activation of pro-inflammatory cytokines, block excitotoxic neurotransmitters and intracellular calcium ion accumulation could potentially be beneficial by preventing or limiting inflammation (3) associated with immune process activation in neurodegenerative disorders.

Reference

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