Small-Volume yFFP® Therapeutic Plasma Exchange for Neurodegeneration

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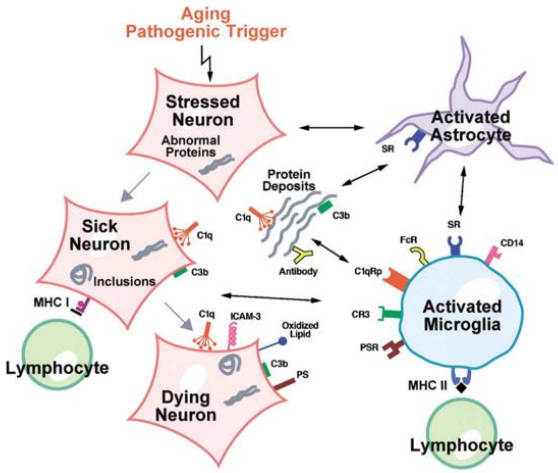
Neurodegenerative disorders are generally characterized by a contiuous loss of selectively vulnerable populations of neurons, causing devastating clinical symptoms. While they are typically defined by specific protein accumulations, "neurodegenerative diseases share many fundamental processes associated with progressive neuronal dysfunction and death, such as proteotoxic stress and its attendant abnormalities in ubiquitin–proteasomal, and autophagosomal/lysosomal systems, oxidative stress, programmed cell death, and neuroinflammation". [1]

Inflammation in neurodegenerative disorders is believed to result from a number of causes. While studies are still searching, it seems that protein aggregates, accumulation of other abnormally modified cellular components, molecules released post neuronal, or synapse damage and loss of regulation or balance of inflammatory control mechanisms have become the main culprits. "Most neurodegenerative disorders are associated with the accumulation of abnormal protein assemblies that create cellular and oxidative stress leading to chronic neuroinflammation. This chronic inflammation appears to be maintained by cellular distress signals sent from neurons that survive for prolonged periods of time despite the abnormal accumulation of proteins and their ongoing injury." [2]



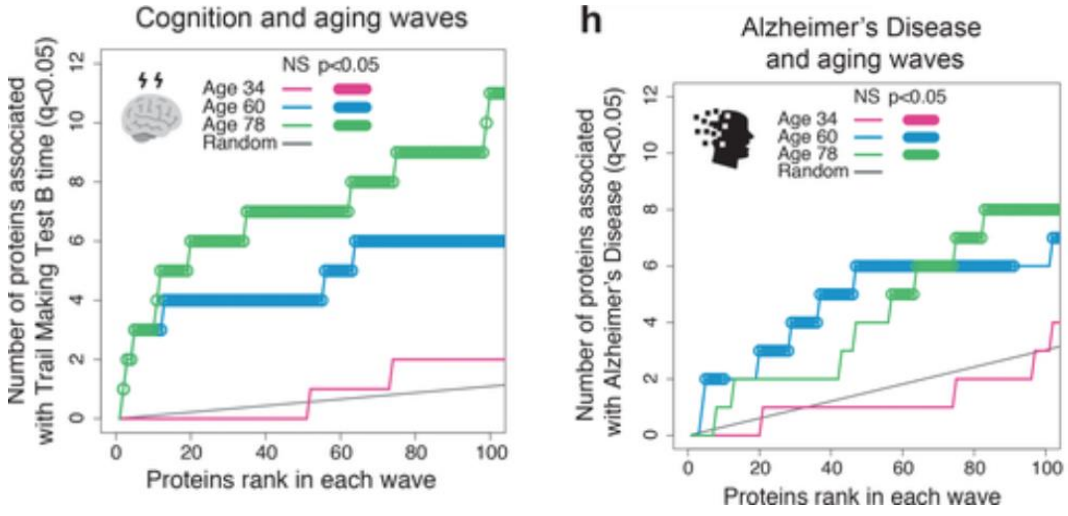
Definitive agents causing neurodegeneration have yet to be identified, however, recent data has pointed to the inflammatory process as being closely linked with the degeneration of multiple neuronal pathways. These pro-inflammatory cytokines appear to be an important contributor in the developmental pathophysiology of depression and dementia. Pro-inflammatory agents, which are a large part of causative effects of neuroinflammation, occur widely, particularly in the elderly. These data suggest that the role of reversing neuroinflammation in neurodegeneration must be a large part of the treatment process. [3] Therapeutic plasma exchange has been shown to remove pathologic inflammatory markers [4] and treat a multitude of diseases, including those with an autoimmune and neurological basis. [5, 6]

Berkley's Conboy lab recently published a plasma exchange study illustrating that "dilution of old blood plasma yields an increase in the determinants of brain maintenance and repair in mice, and in people." They quoted…" rapid cognitive improvements of old mice in this study are thought to arise from abrogating (through NBE-Neutral blood exchange) the otherwise age-increased extent of neuroinflammation." [7]

While these studies show some promise, exchanging 3 liters of blood volume in a human is not without significant risks [8] requiring at times placement of a central line in the jugular vein [9] to complete the procedure, or large expenses. Total plasma exchange also assumes that old and damaged tissues 'when cleaned up' can be rejuvenated to youthful state producing all the youthful growth factors. This theory does not, however, take into consideration the aging hormones, microbiome and tissue damage that cannot be repaired by simply removing the inflammatory load.

Mini-Therapeutic Plasma Exchange - The Optimal Approach

Combining an approach of removing 1 liter of plasma and then replacing the same amount with young Fresh Frozen plasma (yFFP) combines two therapies with maximal effect and minimal risk profile. The use of a small peripheral line to complete the removal of only 1,000 ml of plasma enables the procedure to be done in any office just as more than 150,000 plasma donations are done safely every day. [10] Removal of 1,000 ml of plasma will take out a significant amount inflammatory cells while creating an upregulation of repair in the body. At the completion of the removal, 1,000 ml of young fresh frozen plasma, complete with its young proteome [11] is infused. It is evident below that as we age the proteins that control our cognitive functioning become more and more important. Simple removing senescent cells and inflammatory cells is not sufficient.



It is the additional replacement of the young factors and proteins that completes the healing process.

"On the pathway level, young blood invokes novel gene sets in addition to reversing established ageing patterns, with the global rescue of genes encoding electron transport chain subunits pinpointing a prominent role of mitochondrial function in parabiosis-mediated

rejuvenation. Intriguingly, we observed an almost universal loss of gene expression with age that is largely mimicked by parabiosis: aged blood reduces global gene expression, and young blood restores it. Altogether, these data lay the groundwork for a systemic understanding of the interplay between blood-borne factors and cellular integrity." [12]

This combination procedure can be personalized to each patient in both volume and frequency depending upon clinical and laboratory response. It provides the best of safety and treatment in any setting.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5495060/

[2] https://core.ac.uk/reader/82808734?utm_source=linkout

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4805095/

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4588244/

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7415086/

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7984263

[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8050203/

[8] https://onlinelibrary.wiley.com/doi/10.1002/jca.21703

[9] https://pubmed.ncbi.nlm.nih.gov/11746539/

[10]https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Fatalities-Reported-to-FDA-Following-Blood-Collection-and-Transfusion--Annual-Summary-for-FY2016.pdf

[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7062043/

[12] https://www.nature.com/articles/s41586-022-04461-2

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