Neuroaxonal de- and regeneration in early multiple sclerosis and traumatic brain injury

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Apart from the characteristic inflammatory demyelinated lesions, the brain of multiple sclerosis (MS) patients is characterized by axonal and neuronal loss. Both may contribute to the observed insidious clinical progression that is observed in later disease stages. However, little is known about the extent and microscopic correlate of neuroaxonal regeneration in MS. In the present study, we compared the extent and pattern of neuronal and axonal damage as well as neuroaxonal repair in early MS and traumatic brain injury (TBI) lesions. We applied markers for phosphorylated (SMI31) and non-phosphorylated (SMI32) neurofilaments as well as GAP43 and synaptophysin as markers for regenerative attempts.

Comparing MS with TBI lesions, we could demonstrate that neuronal damage as evidenced by the density of SMI31-positive neurons in the cortex was more pronounced in TBI lesions. However, GAP43 and synaptophysin-positive neurons occurred at approximately the same densities. This was also true for the density of APP-positive axonal spheroids and SMI32 positive axons reflecting acute axonal transport disturbances in the subcortical white matter. However, in MS lesions more GAP43 and synaptophysin-positive axonal profiles were observed. Also, the ratios of GAP43 to APP-positive and synaptophysin to APP-positive axons were higher in MS compared to TBI. Densities of GAP43 and APP-positive spheroids correlated with macrophage density in TBI. Of interest, GAP43-positive axon spheroids were more abundant in TBI patients with longer survival times. Evidence for axonal sprouting and formation of new synapses, indicated by double-labelling of synaptophysin-positive structures with GAP43, was evident in MS and TBI.

In summary, our data show a more pronounced regenerative response in early MS compared with TBI lesions. Furthermore, a correlation between GAP43-positive spheroids with the density of macrophages and also with survival time was noted. Thus, our data may provide circumstantial evidence that adaptive as well as innate inflammation contributes to neuroaxonal repair. These findings may underline the Janus face of inflammation in TBI.

Reference:

Schirmer L, Merkler D, König FB, Brück W, Stadelmann C. Neuroaxonal regeneration is more pronounced in early multiple sclerosis than in traumatic brain injury lesions. Brain Pathol. 2013 Jan;23(1):2-12.