Degenerative cervical myelopathy and alterations in functional cerebral connectivity

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Does spinal cord injury ever lead to synaptic plasticity and reorganisation of brain circuitry? Which parts of the brain are involved in such an effort to preserve function? Does this mean a higher chance of recovery?

Such a concept is not new and was postulated even decades ago.[1] A complete traumatic spinal cord injury is still considered an irreversible insult in humans; and while regeneration after spinal cord injury is arguably the holy grail of modern translational neuroscience research, evidence exists from more chronic spinal cord injury patterns that supports the notion of supraspinal reorganisation. Encouraging results come from studies on the chronic condition of degenerative cervical myelopathy, the leading cause of adult spinal cord dysfunction worldwide.[2] In an exciting piece of work, Wang et al.[3] provide evidence that alterations in functional cerebral connectivity take place throughout the stages of DCM pathophysiological progression, building on previous work that suggested that this process is occurring in those regions responsible for the perception and integration of sensory information, motor regulation, and pain modulation.[4]

A few years ago it was shown that there were electrophysiological abnormalities even very early after symptom onset in DCM, despite minimal disability.[5] And that abnormal corticospinal MEP changes correlated with fMRI increased brain activation. This supported the hypothesis that brain reorganisation does happen, with positive neuronal plasticity, but it did not help identify at which point surgical intervention might be optimal.

Wang et al. provide further evidence that reorganisation of brain architectonic circuitry continues to take place not only in early DCM but throughout the stages of its severity. And that such connectivity changes can happen in a predictable pattern as patients progress from asymptomatic spinal cord compression through to severe myelopathy.[3] Furthermore, they demonstrate that the brainstem and cerebellum are both involved in the optimisation of sensorimotor function during symptomatic deterioration. How did they do that? They used resting state functional MRI (fMRI) in both symptomatic and control patients. The symptomatic group included patients throughout the spectrum of severity of DCM, from asymptomatic to severe. Information was correlated between clinical assessment, mJOA scores, and radiology. The functional brain connectivity, as exhibited at each stage of DCM, was assessed and compared between the different symptomatic stages of severity of myelopathy, and any strengthening or weakening of the connections observed.

An interesting part of the study is that it established a link prediction model. This model can help estimate the changes in the circuitry (i.e., the strength between the connections) as a patient deteriorates through the stages of myelopathy. One of the implications is predictive modelling, whereby the connectivity differences can theoretically assist in the monitoring of DCM severity. It is thereby suggested that an increasing severity of myelopathy is associated with an increased effort for compensatory plasticity, with adaptable input from subcortical regions such as the brainstem and cerebellum.

Can we postulate that such modelling can go further than the monitoring of disease progression and potentially predict surgical outcomes? Or guide the optimal timing of surgical intervention? This remains to be seen, as models based on artificial intelligence can sound and look impressive but are always subject to limitations.

Yet data involving surgery for DCM and its effect on synaptic reorganisation do exist too. Hrabálek et al. had, in fact, proceeded to compare and correlate electrophysiological and fMRI changes both before and after decompressive surgery for early DCM (within 6 months of symptoms). Brain hyperactivation was evident in the cerebellum preoperatively; it also persisted up to 12 months postop in the contralateral sensorimotor cortices.[5] Wang et al., in another elegant study, also have assessed the effect of decompressive surgery for DCM; there was upstream recovery of microstructural integrity along the corticospinal tract and other sensorimotor pathways; and supraspinal reorganisation of connectivity within sensory and motor-related regions, associated with neurological improvement.[6]

One of the points of interest that remains unanswered is the possibility of differences in compensatory connectivity and neuroplasticity when the myelopathy is due to anterior compression (affecting the efferent

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pathways of the anterior columns and anterior horns) or due to posterior compression (affecting the sensory afferent pathways of the posterior columns and posterior horns), or indeed due to circumferential compression.[7]

The work by Wang et al.[4] does provide hope that cerebral connectivity can be further studied via a multimodal methodology that can bring together information from a variety of angles-neurophysiology, radiology (both structural and functional MRI), clinical score assessment, machine learning and artificial intelligence-in order to build a more complex understanding of the different stages of myelopathy, before and after treatment.[8,9] This may lead to different classifications, prognostication, and indications for targeted intervention.

Declaration of interests

None.

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