Atomic force microscopy (AFM) is not only an advanced imaging tool, but can also be used for exploring the mechanical properties of tissues. We are using AFM to investigate the stiffness of acute rat brain slices in demyelination, a condition causing severe functional impairment and disability.

The most common demyelinating disease is multiple sclerosis. Due to an inflammatory reaction axons lose their protective insulating layer, the myelin sheath, which in the central nervous system is formed by oligodendrocytes. To remyelinate axons and restore full functionality, recruitment and maturation of oligodendrocyte precursors cells (OPCs) is essential. As OPC function has been shown to depend on the mechanical environment [1], we are studying the tissue stiffness in remyelination.

Lesions were created by injecting ethidium bromide into the caudal cerebellar peduncle of rats and the tissue was harvested 7 and 21 days post lesion in accordance with regulations issued by the Home Office of the United Kingdom under the Animals (Scientific Procedures) Act of 1986. The resulting lesions were measured as acute slices with a JPK Nanowizard III by nano-indentation, data were analyzed using the Hertz model following a routine developed by Christ et al. [2]. AFM measurements show that at 7 days demyelinated areas of tissue are consistently more compliant than their surroundings, healthy white matter has an elastic modulus of $210 \pm 150$ Pa, lesion tissue of $148 \pm 115$ Pa. At 21 days the inner areas of the lesion are still soft at $163 \pm 106$ Pa, whilst the outer areas of the lesion begin to stiffen to $202 \pm 105$ Pa, approaching healthy tissue stiffness at $238 \pm 125$Pa. The differences in stiffness between the two values of each healthy and lesion tissue are not statistically significant, the differences between healthy tissue and lesion tissue however are significant (Kruskal-Wallis test, $p < 0.01$). The migration speed of OPCs that has been reported for such lesions [3] matches the speeds observed in OPC cultures on hydrogels [1] with the same stiffness as we report for the lesion, suggesting an explanation for the perceived mismatch between OPC behaviour in lesion and OPC behaviour in culture as an effect created by the different mechanical properties of the cells’ environment.

In summary, our results show that in demyelination the mechanical properties of brain tissue change and that changes in mechanics are indicative of underlying changes in biology. Further work will concentrate on harnessing these novel insights for improved therapeutic approaches to treat these devastating neurological disorders.


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