The role of Hypoxia in periventricular white matter degeneration

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The deep and periventricular white matter is preferentially affected in several neurological disorders, including cerebral small vessel disease (SVD) and multiple sclerosis (MS), suggesting that common pathogenic mechanisms may be involved in this injury. Here we consider the potential pathogenic role of tissue hypoxia in lesion development, arising partly from the vascular anatomy of the affected white matter. Specifically, these regions are supplied by a sparse vasculature fed by long, narrow end arteries/arterioles that are vulnerable to oxygen desaturation if perfusion is reduced (as in SVD, MS and diabetes) or if the surrounding tissue is hypoxic (as in MS, at least). The oxygen crisis is exacerbated by a local preponderance of veins, as these can become highly desaturated 'sinks' for oxygen that deplete it from surrounding tissues. Additional hemodynamic deficiencies, including sluggish flow and impaired vasomotor reactivity and vessel compliance, further exacerbate oxygen insufficiency. The cells most vulnerable to hypoxic damage, including oligodendrocytes, die first, resulting in demyelination. Indeed, in preclinical models, demyelination is prevented if adequate oxygenation is maintained by raising inspired oxygen concentrations. In agreement with this interpretation, there is a predilection of lesions for the anterior and occipital horns of the lateral ventricles, namely regions located at arterial watersheds, or border zones, known to be especially susceptible to hypoperfusion and hypoxia. Finally, mitochondrial dysfunction due to genetic causes, as occurs in leukodystrophies or due to free radical damage, as occurs in MS, will compound any energy insufficiency resulting from hypoxia. Viewing lesion formation from the standpoint of tissue oxygenation not only reveals that lesion distribution is partly predictable but may also inform new therapeutic strategies.

Speaker Biography

Santiago Martinez Sosa is a medical student at University College London, from where he also received his bachelor's in Neuroscience (Hons). His interests include hippocampal physiology, neuroinflammation, and neurodegenerative disease. He is the UCL Medical Society coordinator for the Neurology society, which serves to facilitate student involvement in all branches of the specialty. This is his first publication.

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