Heterogeneity in oligodendrocyte precursor cell proliferation is dynamic and driven by passive bioelectrical properties

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Background: Oligodendrocyte precursor cells (OPCs) are the primary proliferative cells in the adult central nervous system, responsible for generating myelinating oligodendrocytes. However, OPCs are a heterogeneous population, with proliferation and differentiation capacities varying with brain region and age. Myelination and remyelination capabilities decline with age, partly attributed to reduced OPC proliferation potential. The passive bioelectrical properties of cell membranes, particularly inward potassium (K+) conductance mediated by inwardly rectifying K+ (Kir) channels, are known to regulate how neurons sense and respond to signals and are a distinct feature of some adult gray matter OPCs. However, the function of Kir channels in OPCs, especially their relationship with the cell cycle, remains unclear. This heterogeneity may represent dynamic cell states rather than irreversible cellular subtypes.

Objective: To test whether local neuronal density/activity modulate OPC passive bioelectrical properties; to determine whether cortical OPCs generate spontaneous long inward currents (SLICs) in response to neuronal activity; and to define the ionic mechanism and its relationship to intrinsic OPC properties.

Results: Under 0-Mg^{2+} aCSF to elevate network excitability, simultaneous recordings revealed that field-potential bursts accompanied by rises in extracellular potassium ($[K^+]_e$) were associated with spontaneous long inward currents (SLICs) in nearby OPCs. SLICs were abolished by TTX, and they were strongly suppressed by Kir-channel blockade (Ba^{2+}, nortriptyline, VU+ML) without diminishing neuronal large synaptic events or the oscillatory $[K^+]_e$ signal; correspondingly, Kir inhibition markedly reduced OPC inward conductance. Across cells, SLIC amplitude did not correlate with the magnitude of the $[K^+]_e$ increase but correlated negatively with membrane resistance, indicating that low-Rm/high-conductance OPCs exhibit larger SLICs. Consistent with a microenvironmental influence, SLICs were detected preferentially in regions with higher neuronal density and in OPCs with intrinsically higher inward conductance.

Conclusion: Cortical OPCs sense local network activity via Kir-mediated SLICs; synchronous neuronal firing elevates extracellular K^+, which drives these inward currents. Thus, the microenvironment—neuronal density and activity—shapes the passive bioelectrical state of OPCs, providing a mechanistic link to regional heterogeneity in OPC proliferation.