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**Public Summary:**

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Oligodendrocytes are the primary source of myelin in the adult central nervous system (CNS), and their dysfunction or loss underlies several diseases of both children and adults. Dysmyelinating and demyelinating diseases are thus attractive targets for cell-based strategies since replacement of a single presumably homogeneous cell type has the potential to restore functional levels of myelin. To understand the obstacles that cell-replacement therapy might face, we review oligodendrocyte biology and emphasize aspects of oligodendrocyte development that will need to be recapitulated by exogenously transplanted cells, including migration from the site of transplantation, axon recognition, terminal differentiation, axon wrapping, and myelin production and maintenance. We summarize studies in which different types of myelin-forming cells have been transplanted into the CNS and highlight the continuing challenges regarding the use of cell-based therapies for human white matter disorders.

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