Transient hypothyroidism favors oligodendrocyte generation providing functional remyelination in the adult mouse brain

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In the adult brain, both neurons and oligodendrocytes can be generated from neural stem cells located within the Sub-Ventricular Zone (SVZ). Physiological signals regulating neuronal versus glial fate are largely unknown. Here we report that a thyroid hormone (T3)-free window, with or without a demyelinating insult, provides a favorable environment for SVZ-derived oligodendrocyte progenitor generation. After demyelination, oligodendrocytes derived from these newly-formed progenitors provide functional remyelination, restoring normal conduction. The cellular basis for neuronal versus glial determination in progenitors involves asymmetric partitioning of EGFR and TR?1, expression of which favor glio-and neuro-genesis, respectively. Moreover, EGFR+ oligodendrocyte progenitors, but not neuroblasts, express high levels of a T3-inactivating deiodinase, Dio3. Thus, TR? absence with high levels of Dio3 provides double-pronged blockage of T3 action during glial lineage commitment. These findings not only transform our understanding of how T3 orchestrates adult

brain lineage decisions, but also provide potential insight into demyelinating disorder.