Neuron
Article

Oligodendrocyte Dynamics in the Healthy Adult CNS: Evidence for Myelin Remodeling

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[1] [illegible]
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[3] [illegible] 7000, [illegible]
[4] [illegible]
[5] [illegible] 020- 505, [illegible]
[6] [illegible] 35 [illegible] 20 2, [illegible]
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[illegible] /10.1016/[illegible].2013.01.006

SUMMARY

Oligodendrocyte precursors (OPs) continue to proliferate and generate myelinating oligodendrocytes (OLs) well into adulthood. It is not known whether adult-born OLs ensheath previously unmyelinated axons or remodel existing myelin. We quantified OP division and OL production in different regions of the adult mouse CNS including the 4-month-old optic nerve, in which practically all axons are already myelinated. Even there, all OPs were dividing and generating new OLs and myelin at a rate higher than can be explained by first-time myelination of naked axons. We conclude that adult-born OLs in the optic nerve are engaged in myelin remodeling, either replacing OLs that die in service or intercalating among existing myelin sheaths. The latter would predict that average internode length should decrease with age. Consistent with that, we found that adult-born OLs elaborated much shorter but many more internodes than OLs generated during early postnatal life.

INTRODUCTION

[illegible] 4 [illegible] ., 200 [illegible] ., 200 [illegible] ., 200 [illegible] ., 2010 [illegible] ., 2011 [illegible] ., 2011). [illegible]

[illegible] ., 200 [illegible] ., 2011 [illegible] (70%) [illegible] 1 0 [illegible]

(., 200), GF 100%),

W

(2 2)

(2 2).

21 60,

(2 2).

(1). 60, T_C

~10 ~15

~20 (1). T_C

60 (~36)

(~27).

(1).

OPs Generate Differentiated OLs throughout the Adult CNS

W *Pdgfra-CreER*^{T2}*: R26R-YFP*

60.

(3 3),

(3 3), (3)

( )

( )

1,

+, 1+

(.,

7 , 60+7),

60+320 (3).

1

60+42, 61%

3% +

41% 3% 1+.

61% 5% + 34% 6% 1+.

45 (., 200). 240 (

., 200),

+, 1+

(3). ~65% +

1+ 60+320 (6 % 4% 64% 2%

).

(

(., 200).

( )

2005), *Pdgfra-CreER*^{T2} *Tau-mGFP*

(2005). *Tau-mGFP*

, 1) *Rosa-*

YFP *Tau*

7).

45 (3) 60 *Pdgfra-*

CreER^{T2}*: Tau-mGFP* (4). 60+37,

(4).

4).

(., 2007

., 2010)

2010 ., 2011).

4). (4)

(4 4)

2^{+}, 2^{+} (

, 1 7), .3030 (2)-241(

Figure 4. Adult-Born Myelinating OLs in Spinal Cord and Optic Nerve

( ) ...), ... ( ) ... 60+37 *Pdgfra-CreER*^{T2}*: Tau-mGFP* ... ( ) ... 1 ( ) ... 1^{+} ... ( ).

... 120 (~6.5% ...) ... (~1%) (... ., 1 77, ..., 1 6).

Late-Born OLs Generate Many More, Shorter Internodes Than Early-Born OLs

W ... *Tau-mGFP* ... 30 ... 60 (30+30) ... 120 ... 1 5 (120+65) (... 6). ... 30+30 (... 6) ... 120+65 (... 6 ... 6) *Pdgfra-CreER*^{T2}*: Tau-mGFP* ... (... 6) ... 30 ... 60 ... 21 ... 7 ...

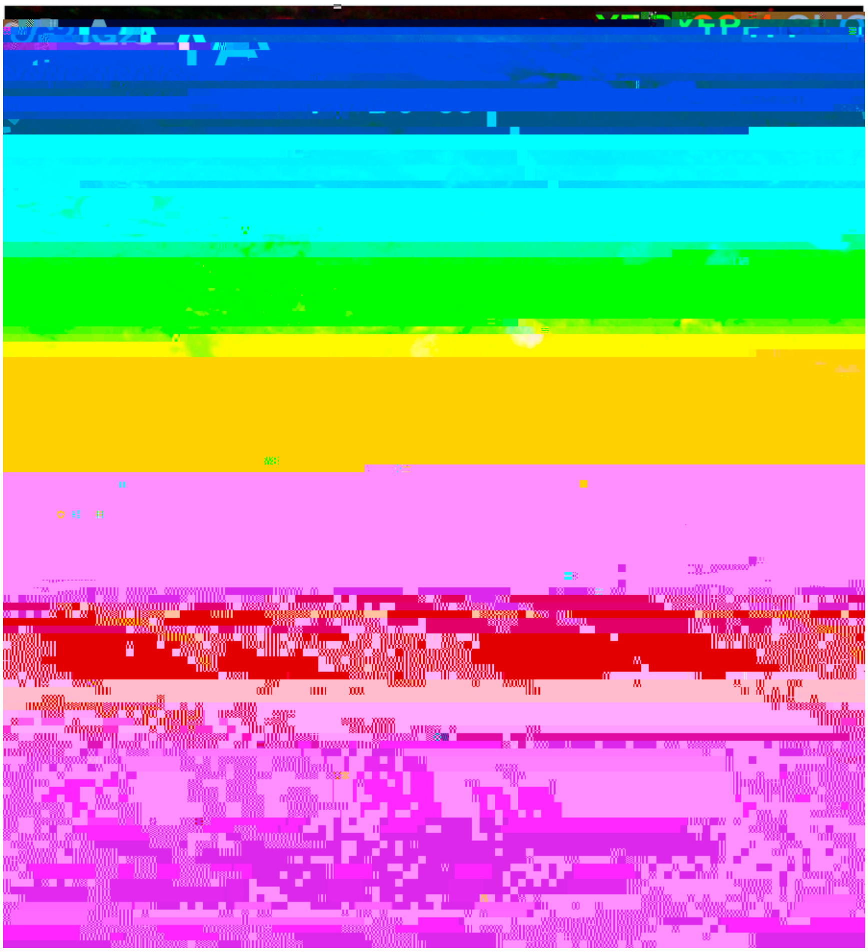

Figure 5. Differentiated OLs Are Generated in the Optic Nerve after Four Months of Age

( ) 120+65 *Pdgfra-CreER*^{T2}*: R26R-YFP*

30+30 (~76 μm) 120+65 (~22 μm) 5

W 5

(2). ,

( ),

($GF \approx 100\%$),

(.,

2012,).

Age-Dependent Rate of Division

GF 2-f ,

T_C … 60 … ~36 … ~37 … 2- … 3- … (… ., 2011) … T_C … 540 (… ., 200). … T_C … (… ., 200). … T_C … (1). … (… ., 200).

… (1 3). … (… ., 2000). … (… ., 2002).

Control of OP Proliferation by Axons?

… 60 … (T_C ≈ 27 …) … (T_C ≈ 15 …). 60 … (T_C ≈ 20 …) … (T_C ≈ 15 …) … (T_C ≈ 10 …) (1). … (T_C ≈ 36 27 …) … (T_C ≈ 10 …) … (T_C ≈ 20 …)

A Significant Fraction of Adult-Born OLs Survive Long-Term

… ~

60

21 60 (1), 77%

60+42 *Pdgfra-CreER^{T2}: R26R-YFP* 1^{+} (

). ~50% 1^{+} (3), ~30%

(70%

, 1 0).

2005)

153,
276 2 2.

(2011).
138, 4443 4450.