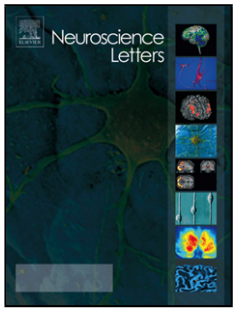

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PII: S0304-3940(15)30051-3
DOI: http://dx.doi.org/doi:10.1016/j.neulet.2015.07.031
Reference: NSL 31454

To appear in: *Neuroscience Letters*

Received date: 28-3-2015
Revised date: 17-7-2015
Accepted date: 24-7-2015

Please cite this article as: Edward Boumil, Rishel Vohnoutka, Sangmook Lee, Thomas B.Shea, Early expression of the high molecular weight neurofilament subunit attenuates axonal neurite outgrowth, Neuroscience Letters http://dx.doi.org/10.1016/j.neulet.2015.07.031

Early expression of the high molecular weight neurofilament subunit attenuates axonal neurite outgrowth

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Running title: NF-H supports axonal outgrowth

Highlights

•High molecular weight neurofilament (NF-H) expression is developmentally delayed.

•We hypothesized that delayed expression of NF-H is essential for axonal elongation.

•Early overexpression of NF-H inhibited axonal elongation and increased axon caliber.

•NF-H lacking the C-terminal sidearm did not inhibit elongation or increase caliber.

•Developmental delay in NF-H expression is essential for axonal elongation.

Abstract 249 words
Text 1762 words

ABSTRACT

Phospho-dependent interactions of the C-terminal region of the high molecular weight NF subunit (NF-H) with each other and with other cytoskeletal elements stabilize the axonal cytoskeleton and contribute to an increase in axonal caliber. The same kinase cascades that mediate axonal pathfinding via growth cone dynamics are those that foster NF-mediated axonal stabilization, yet there is a developmental delay in the accumulation of NF C-terminal phosphorylation. Moreover, the phospho-mediated C-terminal NF-H interactions that stabilize the axonal cytoskeleton also inhibit axonal elongation. We hypothesized that a delay in expression and/or accumulation of NF-H within developing axons is essential to allow axonal elongation and pathfinding.

We tested this hypothesis in differentiating NB2a/d1 cells. The first 3 days of differentiation of NB2a/d1 cells is normally accompanied by rapid elongation of axonal neurites. This period is