Dis Model Mech. 2010 May-Jun; 3(5-6): 366–376. PMCID: PMC4068633
Published online 2010 Jan 18. doi: 10.1242/dmm.003442

Neuroligin-deficient mutants of *C. elegans* have sensory processing deficits and are hypersensitive to oxidative stress and mercury toxicity

Jerrod W. Hunter,[1,2,*] Gregory P. Mullen,[1,*] John R. McManus,[1] Jessica M. Heatherly,[1,3] Angie Duke,[1] and James B. Rand[1,2,3,‡]

[1]Genetic Models of Disease Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK 73104, USA
[2]Department of Cell Biology and
[3]Oklahoma Center for Neuroscience, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA
[*]These authors contributed equally to this work
[‡]Author for correspondence (Email: James-Rand@omrf.org)

Received 2009 Apr 8; Accepted 2009 Sep 14.

SUMMARY

Neuroligins are postsynaptic cell adhesion proteins that bind specifically to presynaptic membrane proteins called neurexins. Mutations in human neuroligin genes are associated with autism spectrum disorders in some families. The nematode *Caenorhabditis elegans* has a single neuroligin gene (*nlg-1*), and approximately a sixth of *C. elegans* neurons, including some sensory neurons, interneurons and a subset of cholinergic motor neurons, express a neuroligin transcriptional reporter. Neuroligin-deficient mutants of *C. elegans* are viable, and they do not appear deficient in any major motor functions. However, neuroligin mutants are defective in a subset of sensory behaviors and sensory processing, and are hypersensitive to oxidative stress and mercury compounds; the behavioral deficits are strikingly similar to traits frequently associated with autism spectrum disorders. Our results suggest a possible link between genetic defects in synapse formation or function, and sensitivity to environmental factors in the development of autism spectrum disorders.

INTRODUCTION

Neuroligins are a family of postsynaptic cell adhesion proteins that were originally isolated on the basis of their binding to presynaptic proteins called neurexins (Ichtchenko et al., 1995; Ichtchenko et al., 1996; Boucard et al., 2005; Chih et al., 2006). Although early studies demonstrated that, under certain conditions, the interaction between neuroligin and neurexin was capable of inducing synaptogenesis (Scheiffele et al., 2000; Dean et al., 2003; Graf et al., 2004), recent studies suggest that neuroligins function primarily in the maturation, stability and/or maintenance of synapses, rather than synaptogenesis per se (Varoqueaux et al., 2006; Südhof, 2008).

There are four neuroligin genes in mammals, and several important studies have shown that mutations in