NM> Vol.3 No.4, December 2012

OPEN ACCESS

Early Exposure to Environmental Toxin Contributes to Neuronal Vulnerability and Axonal Pathology in a Model of Familial ALS

PDF (Size:2628KB) PP. 404-417 DOI: 10.4236/nm.2012.34050

Author(s)

Grace Lee, Christopher A. Shaw

ABSTRACT

Adult onset amyotrophic lateral sclerosis (ALS) arises due to progressive and irreversible functional deficits to the central nervous system, specifically the loss of motor neurons. Sporadic ALS causality is not well understood, but is almost certainly of multifactorial origin involving a combination of genetic and environmental factors. The discovery of endemic ALS in the native Chamorro population of Guam during the 1950s and the co-occurrence of Parkinsonism and dementia in some patients led to searches for environmental toxins that could be responsible. In the present paper, we report that an environmental neurotoxin enhances mutant superoxide dismutase (SOD)-induced spinal motor neuron death and pathology and induces motor axon abnormalities. These results cumulatively confirm earlier findings that exposure to an environmental toxin is sufficient to produce the disease phenotype and indicate a role for gene-environment interaction in some forms of the disease.

KEYWORDS

SOD1; ALS; Neurotoxin; Axonopathy; NMJ; Gliosis; Toxicity

Cite this paper

G. Lee and C. Shaw, "Early Exposure to Environmental Toxin Contributes to Neuronal Vulnerability and Axonal Pathology in a Model of Familial ALS," *Neuroscience & Medicine*, Vol. 3 No. 4, 2012, pp. 404-417. doi: 10.4236/nm.2012.34050.

References

[1] D. R. Rosen, T. Siddique, D. Patterson, D. A. Figlewicz, P. Sapp, A. Hentati, et al., "Mutations in Cu/Zn Superoxide-Dismutase Gene are Associated with Familial Amyotrophic-Lateral-Sclerosis," Nature, Vol. 362, No. 6415, 1993, pp. 59-62. doi:10.1038/362059a0

[2] L. R. Fischer, D. G. Culver, P. Tennant, A. A. Davis, M. Wang, A. Castellano-Sanchez, et al., "Amyotrophic Lateral Sclerosis is a Distal Axonopathy: Evidence in Mice and Man," Experimental Neurology, Vol. 185, No. 2, 2004, pp. 232-240. doi:10.1016/j.expneurol.2003.10.004

[3] D. Frey, C. Schneider, L. Xu, J. Borg, W. Spooren and P. Caroni, "Early and Selective Loss of Neuromuscular Synapse Subtypes with Low Sprouting Competence in Motoneuron Diseases," The Journal of Neuroscience, Vol. 20, No. 7, 2000, pp. 2534-2542.

[4] S. Pun, A. F. Santos, S. Saxena, L. Xu and P. Caroni, "Selective Vulnerability and Pruning of Phasic Motoneuron Axons in Motoneuron Disease Alleviated by CNTF," Nature Neuroscience, Vol. 9, No. 3, 2006, pp. 408-419. doi:10.1038/nn1653

[5] P. N. Leigh, "Amyotrophic lateral sclerosis," In: A. Eisen and P. J. Shaw, Eds., Handbook of Clinical Neurology, Elsevier, Amsterdam, 2007, pp. 249-278.

[6] C. E. Shaw, V. Arechavala-Gomeza and A. Al-Chalabi, "Familial Amyotrophic Lateral Sclerosis," In: A. Eisen and P. J. Shaw, Eds., Handbook of Clinical Neurology, Elsevier, Amsterdam, 2007, pp. 279-300.

[7] L. K. Kwong, M. Neumann, D. M. Sampathu, V. M. -. Lee and J. Q. Trojanowski, "TDP-43 Proteinopathy: The Neuropathology Underlying Major Forms of Sporadic and Familial Frontotemporal

NM Subscription
Most popular papers in NM
About NM News
Frequently Asked Questions
Recommend to Peers
Recommend to Library
Contact Us

Lobar Degeneration and Motor Neuron Disease," Acta Neuropathologica, Vol. 114, No. 1, 2007, pp. 63-70. doi:10.1007/s00401-007-0226-5

[8] I. R. A. Mackenzie, E. H. Bigio, P. G. Ince, F. Geser, M. Neumann, N. J. Cairns, et al., "Pathological TDP-43 Distinguishes Sporadic Amyotrophic Lateral Sclerosis from Amyotrophic Lateral Sclerosis with SOD1 Mutations," Annals of Neurology, Vol. 61, No. 5, 2007, pp. 427-434. doi:10.1002/ana.21147

[9] J. Robertson, T. Sanelli, S. Xiao, W. Yang, P. Horne, R. Hammond, et al., "Lack of TDP-43 Abnormalities in Mutant SOD1 Transgenic Mice shows Disparity with ALS," Neuroscience Letters, Vol. 420, No. 2, 2007, pp. 128-132. doi:10.1016/j.neulet.2007.03.066

[10] C. A. Shaw and G. U. Hoglinger, "Neurodegenerative Diseases: Neurotoxins as Sufficient Etiologic Agents?" NeuroMolecular Medicine, Vol. 10, No. 1, 2008, pp. 1-9. doi:10.1007/s12017-007-8016-8

[11] D. R. Koerner, "Amyotrophic Lateral Sclerosis on Guam: A Clinical Study and Review of the Literature," Annals of Internal Medicine, Vol. 37, No. 6, 1952, pp. 1204.

[12] L. T. Kurland and D. W. Mulder, "Epidemiologic Investigations of Amyotrophic Lateral Sclerosis. 1. Preliminary Report on Geographic Distribution, with Special Reference to the Mariana Islands, Including Clinical and Paologic Observations," Neurology, Vol. 4, No. 5, 1954, pp. 355-378. doi:10.1212/WNL.4.5.355

[13] D. W. Mulder and L. T. Kurland, "Amyotropnic Lateral Sclerosis in Micronesia," Mayo Clinic Proceedings, Vol. 29, No. 26, 1954, pp. 666-670.

[14] J. A. Brody, J. M. Stanhope and L. T. Kurland, "Patterns of Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia on Guam," Contemporary Neurology Series, Vol. 12, 1975, pp. 45-70.

[15] J. M. Stanhope, J. A. Brody and C. E. Morris, "Epidemiologic Features of Amyotropic Lateral Sclerosis and Parkinsonism-Dementia in Guam, Mariana Islands," International Journal of Epidemiology, Vol. 1, No. 3, 1972, pp. 199-210. doi:10.1093/ije/1.3.199

[16] A. Hirano, N. Malamud, T. S. Elizan and L. T. Kurland, "Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia Complex on Guam: Further Pathologic Studies," Archives of Neurology, Vol. 15, No. 1, 1966, p. 35. doi:10.1001/archneur.1966.00470130039004

[17] M. G. Whiting, "Toxicity of Cycads," Economic Botany, Vol. 17, No. 4, 1963, pp. 270-302. doi:10.1007/BF02860136

[18] I. Khabazian, J. S. Bains, D. E. Williams, J. Cheung, J. M. Wilson, B. A. Pasqualotto, et al., "Isolation of various Forms of Sterol Beta-D-Glucoside from the Seed of Cycas Circinalis: Neurotoxicity and Implications for ALS-Parkinsonism Dementia Complex," Journal of Neurochemistry, Vol. 82, No. 3, 2002, pp. 516-528. doi:10.1046/j.1471-4159.2002.00976.x

[19] C. A. Shaw, J. M. B. Wilson, R. Cruz-Aguado, S. Singh, E. L. Hawkes, V. Lee, et al., "Cycad-Induced Neurodegeneration in a Mouse Model of ALS-PDC: Is the Culprit Really BMAA or Is a Novel Toxin to Blame," Botanical Review, Vol. 33, No. 9, 2006, pp. 857-862.

[20] P. T. T. Ly, S. Singh and C. A. Shaw, "Novel Environmental Toxins: Steryl Glycosides as a Potential Etiological Factor for Age-Related Neurodegenerative Diseases," Journal of Neuroscience Research, Vol. 85, No. 2, 2007, pp. 231-237. doi:10.1002/jnr.21147

[21] R. C. Tabata, J. M. B. Wilson, P. Ly, P. Zwiegers, D. Kwok, J. M. Van Kampen, et al., "Chronic Exposure to Dietary Sterol Glucosides is Neurotoxic to Motor Neurons and Induces an ALS-PDC Phenotype," Neuromolecular Medicine, Vol. 10, No. 1, 2008, pp. 24-39. doi:10.1007/s12017-007-8020-z

[22] J. M. Wilson and C. A. Shaw, "Evidence for an Excitotoxicity in Murine Model of ALS-PDC," Journal of Neurochemistry, Vol. 96, 2006, pp. 87-87.

[23] J. M. Wilson, I. Khabazian, M. C. Wong, A. Seyedalikhani, J. S. Bains, B. A. Pasqualotto, et al., "Behavioral and Neurological Correlates of ALS-Parkinsonism Dementia Complex in Adult Mice Fed Washed Cycad Flour," NeuroMolecular Medicine, Vol. 1, No. 3, 2002, pp. 207-221. doi:10.1385/NMM:1:3:207

[24] J. M. B. Wilson, M. S. Petrik, S. C. Grant, S. J. Blackband, J. Lai, and C. A. Shaw, "Quantitative Measurement of Neurodegeneration in an ALS-PDC Model using MR Microscopy," Neuroimage, Vol. 23, No. 1, 2004, pp. 336-343. doi:10.1016/j.neuroimage.2004.05.026

[25] M. S. Petrik, J. M. Wilson, S. C. Grant, S. J. Blackband, R. C. Tabata, X. Shan, et al., "Magnetic

Resonance Microscopy and Immunohistochemistry of the CNS of the Mutant SOD Murine Model of ALS Reveals Widespread Neural Deficits," NeuroMolecular Medicine, Vol. 9, No. 3, 2007, pp. 216-229.

[26] H. Kang, L. Tian and W. Thompson, "Terminal Schwann Cells Guide the Reinnervation of Muscle after Nerve Injury," Journal of Neurocytology, Vol. 32, No. 5-8, 2003, pp. 975-985. doi:10.1023/B:NEUR.0000020636.27222.2d

[27] Y. J. Son and W. J. Thompson, "Schwann-Cell Processes Guide Regeneration of Peripheral Axons," Neuron, Vol. 14, No. 1, 1995, pp. 125-132. doi:10.1016/0896-6273(95)90246-5

[28] F. Love, Y. Son and W. Thompson, "Activity Alters Muscle Reinnervation and Terminal Sprouting by Reducing the Number of Schwann Cell Pathways that Grow to Link Synaptic Sites," Journal of Neurobiology, Vol. 54, No. 4, 2003, pp. 566-576. doi:10.1002/neu.10191

[29] A. Eisen and M. Weber, "The Motor Cortex and Amyotrophic Lateral Sclerosis," Muscle Nerve, Vol. 24, No. 4, 2001, pp. 564-573. doi:10.1002/mus.1042

[30] G. Lee, T. Chu and C. A. Shaw, "The Primary Locus of Motor Neuron Death in an ALS-PDC Mouse Model," Neuroreport, Vol. 20, No. 14, 2009, pp. 1284-1289. doi:10.1097/WNR.0b013e32833037ae

[31] F. Coppede, M. Mancuso, G. Siciliano, L. Migliore and L. Murri, "Genes and the Environment in Neurodegeneration," Bioscience Reports, Vol. 26, No. 5, 2006, pp. 341-367. doi:10.1007/s10540-006-9028-6

[32] C. E. McOmish and A. J. Hannan, "Environments: Exploring Gene-Environment Interactions to Identify Therapeutic Targets for Brain Disorders," Expert Opinion on Therapeutic Targets, Vol. 11, No. 7, 2007, pp. 899-913. doi:10.1517/14728222.11.7.899

[33] P. C. Wong, C. A. Pardo, D. R. Borchelt, M. K. Lee, N. G. Copeland, N. A. Jenkins, et al., "An Adverse Property of a Familial Als-Linked Sod1 Mutation Causes Motor-Neuron Disease Characterized by Vacuolar Degeneration of Mitochondria," Neuron, Vol. 14, No. 6, 1995, pp. 1105-1116. doi:10.1016/0896-6273(95)90259-7

[34] J. M. B. Wilson, I. Khabazian, D. V. Pow, U. K. Craig and C. A. Shaw, "Decrease in Glial Glutamate Transporter Variants and Excitatory Amino Acid Receptor Downegulation in a Murine Model of ALS-PDC," Neuromocular Medicine, Vol. 3, No. 2, 2003, pp. 105-117. doi:10.1385/NMM:3:2:105

[35] M. Urushitani, S. Abou Ezzi and J. Julien, "Therapeutic Effects of Immunization with Mutant Superoxide Dismutase in Mice Models of Amyotrophic Lateral Sclerosis," Proceedings of the National Academy of Sciences of the USA, Vol. 104, No. 7, 2007, pp. 2495-2500. doi:10.1073/pnas.0606201104

[36] C. Haenggeli, J. Julien, R. L. Mosley, N. Perez, A. Dhar, H. E. Gendelman, et al., "Therapeutic Immunization with a Glatiramer Acetate Derivative Does Not Alter Survival in G93A and G37R SOD1 Mouse Models of Familial ALS," Neurobiology of Disease, Vol. 26, No. 1, 2007, pp. 146-152. doi:10.1016/j.nbd.2006.12.013

[37] J. Hegedus, T. Putman and T. Gordon, "Progressive Motor Unit Loss in the G93A Mouse Model of Amyotrophic Lateral Sclerosis is Unaffected by Gender," Muscle Nerve, Vol. 39, No. 3, 2009, pp. 318-327. doi:10.1002/mus.21160

[38] A. Schaefer, J. Sanes and J. Lichtman, "A Compensatory Subpopulation of Motor Neurons in a Mouse Model of Amyotrophic Lateral Sclerosis," Journal of Comparative Neurology, Vol. 490, No. 3, 2005, pp. 209-219. doi:10.1002/cne.20620

[39] D. J. Graber, W. F. Hickey and B. T. Harris, "Progressive Changes in Microglia and Macrophages in Spinal Cord and Peripheral Nerve in the Transgenic Rat Model of Amyotrophic Lateral Sclerosis," Journal of Neuroinflammation, Vol. 7, 2010, p. 8. doi:10.1186/1742-2094-7-8

[40] J. Kriz, M. Nguyen and J. Julien, "Minocycline Slows Disease Progression in a Mouse Model of Arnyotrophic Lateral Sclerosis," Neurobiology of Disease, Vol. 10, No. 3, 2002, pp. 268-278. doi:10.1006/nbdi.2002.0487

[41] S. Abou Ezzi, R. Lariviere, M. Urushitani and J. Julien, "Neuronal Over-Expression of Chromogranin A Accelerates Disease Onset in a Mouse Model of ALS," Journal of Neurochemistry, Vol. 115, No. 5, 2010, pp. 1102-1111. doi:10.1111/j.1471-4159.2010.06979.x

[42] J. D. Atkin, R. L. Scott, J. M. West, E. Lopes, A. K. J. Quah and S. S. Cheema, "Properties of Slow-and Fast-Twitch Muscle Fibres in a Mouse Model of Amyotrophic Lateral Sclerosis," Neuromuscular Disorders, Vol. 15, No. 5, 2005, pp. 377-388. doi:10.1016/j.nmd.2005.02.005

[43] J. Zhang, G. Zhang, B. Morrison, S. Mori and K. A. Sheikh, "Magnetic Resonance Imaging of Mouse Skeletal Muscle to Measure Denervation Atrophy," Experimental Neurology, Vol. 212, No. 2, 2008, pp. 448-457. doi:10.1016/j.expneurol.2008.04.033

[44] B. Stephens, R. J. Guiloff, R. Navarrete, P. Newman, N. Nikhar and P. Lewis, "Widespread Loss of Neuronal Populations in the Spinal Ventral Horn in Sporadic Motor Neuron Disease. A Morphometric Study," Journal of the Neurological Sciences, Vol. 244, No. 1-2, 2006, pp. 41-58. doi:10.1016/j.jns.2005.12.003

[45] C. A. Farah, M. D. Nguyen, J. P. Julien and N. Leclerc, "Altered Levels and Distribution of Microtubule-Associated Proteins before Disease Onset in a Mouse Model of Amyotrophic Lateral Sclerosis," Journal of Neurochemistry, Vol. 84, No. 1, 2003, pp. 77-86. doi:10.1046/j.1471-4159.2003.01505.x

[46] P. K. Thomas, R. H. M. King and A. K. Sharma, "Age-Changes in the Peripheral-Nerves of the Rat," Gerontology, Vol. 27, No. 1-2, 1981, pp. 116-117.