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Alzheimer Disease: The Neurodegenerative Triad and the Role Of Microtubule Dynamics

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Mini-Review

The current model of the neurodegenerative processes involving Alzheimer disease (AD); the amyloid cascade hypothesis, maintains that it is oligomeric (consists of a few monomers) soluble Aβ that is the key driver of the pathogenic changes found in AD and those neurodegenerative changes are facilitated (at least to a certain degree) by the changes in tau protein [1-5]. In a recent review by Roland Brandt and Lidia Bakota, Department of Neurobiology, University of Osnabruck, Osnabruck, Germany, it was illustrated that microtubules are directly and indirectly involved in the three pathways of the neurodegenerative triad: synaptic impairment, dendritic simplification (loss of dendritic spines on the dendrite), and neuron cell death [6]. These three hidden connections will be briefly reviewed.

Synaptic Impairment

Synaptic impairment associated with the loss of dendritic spines, which is correlated with impairment in long-term potentiation, appears to be amid the initial events in the AD neurodegenerative cascade [6]. Two studies; one using microtubule tip-tracking protein EB3 and the second using stable isotope labeling to measure the turnover of tubulin, support that abnormal functioning in microtubules may directly lead to a loss of dendritic spines [7,8]. Dendritic spines are found on many cortical neurons and form excitatory synapses. Thus the loss of dendritic spines would be associated with a decrease in synaptic strength.

Dendritic Simplification

Microtubule stability may be coupled with the progression of dendritic simplification. This is supported by a seminal study involving cerebellar Purkinje cells [9]. Subsequent research demonstrates two main themes to further support the involvement of microtubule stability to the progression of dendritic simplification. First, the up-regulation of MAP1A and MAP2 are potentially involved in the stability of dendritic microtubules resulting in more stabilized branches [10,11]. Secondly, the deletion of MAP1A and MAP2 disrupts microtubule spacing which results in decreased dendritic arbor complexity (or dendritic branching) [12,13]. Hence, decreases in dendritic complexity result in less potential excitatory synaptic connections.

Cell Death

Cell death that is caused by the disturbance of axonal transport may be due, in part, to microtubule disruption. This possibility is supported by experimental evidence, using line imaging of fluorescent protein-tagged organelles, that demonstrates Aβ oligomers interrupt axonal transport [14] and that abnormal axonal transport is correlated to microtubule destabilization; which may be caused by mitochondrial dysfunction and deficiencies in the carriage of brain-derived neurotrophic factor [15,16]. Thus defective transport results in the products that are vital to the survival of the neuron to not be delivered. This ultimately results in cell death and is considered an early pathologic event in AD [14].

Conclusion

Microtubule dynamics are important in AD, as they are involved during the early pathological stages seen in AD and also during the process of cell death; as they play pivotal roles in axon transport, the structural integrity of the neurons, and neuronal plasticity. In the review by Brandt and Lidia Bakota [6], it is apparent that researchers should not underestimate the role that microtubule dynamics may play in AD as it is evident, now, that they are involved in various degrees in the three pathways of the neurodegenerative triad.

References

1. Fath T, Eidenmuller J, Brandt R (2002) Tau-mediated cytotoxicity in a pseudo hyper phosphorylation model of Alzheimer's disease. J Neurosci 22(22): 9733-9741.
2. Rapoport M, Dawson HN, Binder LI, Vitek MP, Ferreira A (2002) Tau is essential to beta -amyloid-induced neurotoxicity. Proc Natl Acad Sci USA 90(16): 6364-6369.
3. Roberson ED, Scearce-Levie K, Palop JJ, Yan F, Cheng IH, et al. (2007) Reducing endogenous tau ameliorates amyloid beta-induced deficits in an Alzheimer's disease mouse model. Science 316(5825): 750-754.
4. Shankar GM, Bloodgood BL, Townsend M, Walsh DM, Selkoe DJ, et al. (2007) Natural oligomers of the Alzheimer amyloid-beta protein

induce reversible synapse loss by modulating an NMDA-type glutamate receptor-dependent signaling pathway. J Neurosci 27(11): 2866-2875.

5. Tackenberg C, Brandt R (2009) Divergent pathways mediate spine alterations and cell death induced by amyloid-beta, wild-type tau,and R406W tau. J Neurosci 29(46): 14439-14450.
6. Brandt R, Bokota L (2017) Microtubule dynamics and the neurodegenerative triad of Alzheimer's disease: The hidden connection. J Neurochemistry 143(4): 409-417.
7. Jaworski J, Kapitein LC, Gouveia SM, Dortland BR, Wulf PS, et al. (2009) Dynamic microtubules regulate dendritic spine morphology and synaptic plasticity. Neuron 61(5): 85-100.
8. Fanara P, Husted KH, Selle K, Wong PY, Banerjee J, et al. (2010) Changes in microtubule turnover accompany synaptic plasticity and memory formation inresponse to contextual fear conditioning in mice. Neuroscience 168(1): 167-178.
9. Faivre C, Legrand C, Rabie A (1985) Themicrotubular apparatus of cerebellar purkinje cell dendrites during postnatal development of the rat: the density and cold-stability of microtubules increase with age and are sensitive to thyroid hormone deficiency. Int J Dev Neurosci 3(5): 559-565.
10. Vaillant AR, Zanassi P, Walsh GS, Aumont A, Alonso A (2002) Signaling mechanisms underlying reversible, activity-dependent dendrite formation. Neuron 34(6): 985-998.
11. Szebenyi G, Bollati F, Bisbal M, Sheridan S, Faas L, et al. (2005) Activity-driven dendritic remodeling requires microtubule-associated protein 1A. Curr Biol 15(20): 1820-1826.
12. Teng J, Takei Y, Harada A, Nakata T, Chen J, et al. (2001) Synergistic effects of MAP2 and MAP1B knockout in neuronal migration, dendritic outgrowth, and microtubule organization. J Cell Biol 155(1): 65-76.
13. Harada A, Teng J, Takei Y, Oguchi K, Hirokawa N (2002) MAP2 is required for dendrite elongation, PKA anchoring in dendrites, and proper PKA signal transduction. J Cell Biol 158(3): 541-549.
14. Decker H, Lo KY, Unger SM, Ferreira ST, Silverman MA (2010) Amyloid-beta peptide oligomers disrupt axonal transport through an NMDA receptor-dependent mechanism that is mediated by glycogen synthase kinase 3beta in primary cultured hippocampal neurons. J Neurosci 30(2): 9166-9171.
15. Ramser EM, Gan KJ, Decker H, Fan EY, Suzuki MM, et al. (2013) Amyloid-β oligomers induce tau-independent disruption of BDNF axonal transport viacalcineurin activation in cultured hippocampal neurons. Mol Biol Cell 24(16): 2495-2505.
16. Seifert B, Eckenstaler R, Rönicke R, Leschik J, Lutz B, et al. (2016) Amyloid-Beta induced changes in vesicular transport of BDNF in hippocampal neurons. Neural Plast.

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