Editorial

Neurology - Research & Surgery

Bacterial Lipopolysaccharides and Neuron Toxicity in Neurodegenerative Diseases

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Received: 09 June 2018; **Accepted:** 05 July 2018

Citation: Ian James Martins. Bacterial Lipopolysaccharides and Neuron Toxicity in Neurodegenerative Diseases. Neurol Res Surg. 2018; 1(1): 1-3.

Keywords
Neuron death, Bacterial lipopolysaccharides, Sirtuin 1, Protein aggregation, Mitophagy.

Editorial
Research into the role of bacterial lipopolysaccharides (LPS) has escalated with the improved understanding of the LPS effects on astrocytes and neurons with relevance to brain neuroinflammation [1,2] that is now of major concern in neurodegenerative diseases. LPS activates the toll-like receptor 4 (TLR-4) in mouse and human astrocytes with TLR-4 linked to neuroinflammation and neuron death [3-6]. LPS related toxicity may influence neuron membrane cholesterol by binding to cell membranes that promote amyloid beta (Aβ) aggregation and fibril formation [7] to mediate accelerated neuron death. LPS are endotoxins and essential components of the outer membrane of gram negative bacteria and consist of covalently linked segments, surface carbohydrate polymer, core oligosaccharide and acylated glycolipid that can bind to cell membranes to alter membrane interactions [8,9]. LPS regulate plasma acute phase proteins (gelsolin, serum amyloid protein A, serum amyloid protein, C-reactive protein, clusterin, transthyretin) [7] and various other acute phase proteins (APP) involved in Aβ aggregation (transferrin, albumin, phospholipid transfer protein, LPS binding protein (LBP), albumin).

The cluster of differentiation 14 (CD14) receptor is referred to as the LPS receptor and involved with brain Aβ metabolism [7]. The CD14 receptor assists in the co-ordination of the microglia that promotes Aβ mediated and oxidative neuron death [10]. In the developing world increased plasma LPS levels have raised major concern with relevance to CD14 regulation of TLR-4 mediated accelerated neuron death [11,12]. Detailed studies now indicate that LPS now repress the nuclear receptor Sirtuin 1 (Sirt 1) with its toxic effects related to interference with Sirt 1's role in the regulation of transcription factors [13] related to neuron proliferation and induction of Type 3 diabetes. Sirt 1 is now closely linked to the immune system [14], insulin resistance and metabolic activity [7]. Sirt 1's role in neuron death is now connected to cellular proteins (Figure 1) such as heat shock protein (HSP), cellular prion protein (PrPc), alpha-synuclein and tau that are connected to Aβ aggregation [15-23] and accelerated neuron death. LPS represses Sirt 1 [13] with HSP involved in the regulation of PrPc and Aβ aggregation relevant to mitochondrial apoptosis and neuron death [24-39]. The nuclear receptor Sirt 1's role on neuron survival/apoptosis via LPS is primary with effects of LPS secondary on CD14 regulation of TLR-4 mediated neuron apoptosis [7,10-12].

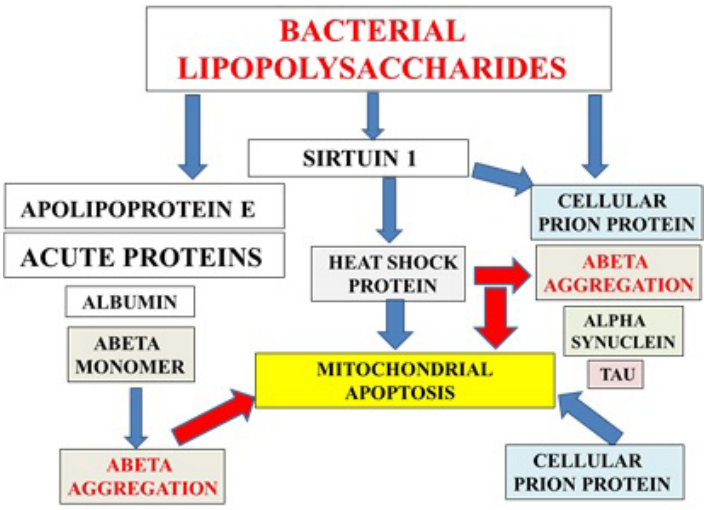

Figure 1: LPS neutralize apolipoprotein E and repress the nuclear receptor Sirt 1 relevant to protein aggregation and mitochondrial apoptosis. The effects of LPS on mitophagy may be mediated by acute phase proteins, albumin, cellular prion protein or amyloid beta aggregation. Under core body temperature disturbances heat shock proteins induce amyloid beta/ cellular prion protein aggregation and induce neuronal mitophagy with relevance to neurodegenerative disease and epilepsy induced stroke.

LPS and its involvement with Sirt 1 in protein aggregation is linked to magnesium deficiency [40] with induction of mitochondrial apoptosis associated with epilepsy induced stroke [41-44]. Other Sirt 1 inhibitors such as palmitic acid, suramin, sirtinol, alcohol and fructose should be carefully controlled to prevent mitochondrial apoptosis [45] and neuron death. Excessive consumption of arginine, patulin, xenobiotics and butyric acid should be avoided to prevent Sirt 1 downregulation. Excessive caffeine consumption should be avoided with relevance to magnesium deficiency [45] and nuclear receptor Sirt 1 disturbances associated with Type 3 diabetes [45]. The effects of core body temperature inactivate Sirt 1 with HSP and PrPc connected to protein aggregation [15,46-49] and mitophagy in neurodegenerative diseases and epilepsy induced stroke [42].

Conclusion

Toxic protein aggregation and neuron death has become of major concern to neurological stroke, cerebrovascular diseases, neurological disorders and functional/epilepsy Res Surgery. Plasma LPS should be monitored early in life to prevent mitochondrial apoptosis in neurodegenerative diseases. Dietary and pharmacological inhibition of neuron nuclear receptors will determine neuron proliferation and remodeling with excessive nuclear receptor inhibitor consumption related to protein aggregation in neurological diseases. Core body temperature malfunction will lead to uncontrolled aggregation of proteins with neuronal mitophagy associated with neurological stroke.

Acknowledgments

This work was supported by grants from Edith Cowan University, the McCusker Alzheimer's Research Foundation and the National Health and Medical Research Council.

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