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Neurological Diseases' Function in Relation to Endogenous Lipopolysaccharides

Vinciane Kappos*

Department of Clinical Neurosciences, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Description

The presence of lipopolysaccharide (LPS) reflects the biochemical characterization of the outer cell wall of predominantly Gram-negative bacterial species, such as E. coli, Yersinia pestis, Klebsiella pneumonia, Pseudomonas aeruginosa, Porphyromonas gingivalis, bifidobacterial species Chlamydia trachomatis and Francisella tularensis, etc., but it is absent in Gram-positive bacteria. LPS is primarily composed of glycolipids and serves as an important membrane barrier between the bacteria's cytosolic contents and the external environment. To reflect an asymmetric bilayer membrane LPS is positioned towards the external environment, i.e., the outer leaflet of the bacterial membrane, whereas phospholipids constitute the inner leaflet, i.e., towards the cytosolic contents. Gram-negative bacteria's susceptibility to antibiotics and bile The concentration of salts rises when the LPS layer is disrupted by phospholipid foray or loss of synthesis/transport. LPS is classified as a large oligosaccharide polymer due to its higher molecular mass (>100 KDa). Bacteriophages and the human immune system use LPS glycolipid as an antigen identification marker. LPS binding proteins (LBPs) are known to detach LPS from bacterial membranes and speed up its binding to the pattern recognition receptor CD14, which is found on the surfaces of macrophages, monocytes, and dendrites, as well as toll-like receptors (TLRs), resulting in the activation of an inflammatory response [1].

LPS, a cell-wall immunostimulatory component of Gram-negative bacteria, varies in its ability to act as a neurotoxin based primarily on its lipid A composition. When compared to LPS derived from R. sphaeroides, LPS derived from E. Coli causes severe inflammation. LPS was initially identified as a Toll-like receptor 4 (TLR-4) ligand. LPS interacts with pattern recognition receptors Toll-like receptors (TLRs) and nucleotide-binding oligomerization domain-containing protein (NOD)-like receptors (PRRs). LPS binding to TLR4 is facilitated by LPS binding protein (LBP), resulting in the formation of the TLR4-MD2 complex via the MyD88-dependent pathway. This complex promotes the activation of nuclear factor-kappa B (NF-B), a redox sensitive critical transcription factor for the Many pro-inflammatory cytokines and chemokines are produced. Furthermore, LPS induces MyD88-independent NF-B-mediated interferon-1 release. Microglia are the resident macrophages in the brain and play an important role in neuroinflammation by up-regulating immune responses [2].

TLR-4 is mostly found on microglia. LPS also damages the BBB, causes neuronal cell apoptosis, and causes cognitive impairment and neuroinflammation by activating microglia via the NF-B signalling pathway. LPS-induced chronic or prolonged polarisation (or activation) of microglia results in neuronal death and an increase in proinflammatory cytokines such as tumour necrosis factor (TNF)-, interleukin (IL)-1, prostaglandin E2 (PGE2), and nitric oxide (NO), particularly in the hippocampus. These cytokines and toxic compounds have been identified as key players in neuroinflammation and neuronal damage. TLR-4 activation caused by LPS causes extensive neuronal cell death. Extremely high levels of LPS in the blood causes hyperactivation of microglia and astrocytes, resulting in neuroinflammation and impairment of neurons, synapses, and cognitive functions. Several animal studies have demonstrated that LPS administration causes cognitive impairment as well as a wide range of complex psychological behaviours such as anorexia, decreased locomotion, exploratory behaviour, weight loss, aggravated anxiety, somnolence, and general depression [3].

In addition to playing a role in a variety of neurological disorders, previous research has shown that LPS exposure increases ROS and RNS accumulation, resulting in increased production of pro-inflammatory mediators. LPS administration causes neuroinflammation, which is known to have negative effects on brain function, such as memory impairment and neuroinflammation via TLR4/NF-B signalling with increased expression of inflammation-related genes and/or molecules, including various proinflammatory cytokines/chemokines. A study using both in vitro and in vivo models found that LPS exposure causes neuroinflammation and neurodegeneration by activating microglia, NF-B, and the p38/c-Jun N-terminal Kinase (JNK) pathway. Furthermore, LPS activated phosphorylated-JNK (p-JNK, a stress activated protein kinase pathway), which is frequently associated with the Bax- and mitochondria-dependent cell death pathways. in neuroinflammation and neurodegeneration. A recent study found that systemic LPS administration increased the accumulation and production of ROS/RNS and oxidative/nitrative stress with decreased glutathione levels in the adult mouse brain, resulting in neuroinflammation, synaptic loss, neurodegeneration, and memory impairment. In comparison to saline-treated animals, LPS administration increased activated p-JNK levels in the dentate gyrus (hilum and granular cells) and Cornu Ammonis 3 (CA3) (molecular layer and pyramidal cells) regions of the hippocampus [4].

LPS promotes apoptotic neurodegeneration in adult mice by activating mitochondrial apoptotic and neuroinflammatory pathways through the upregulation of several apoptotic markers such as Bax, cytochrome C release, caspase-9, and caspase-3 cleavage. Increased protein levels of cytochrome C, cleaved caspase-9, caspase-3, apoptotic protease activating factor 1, and poly (ADP-ribose) polymerase-1 were found in hippocampi extracts, indicating LPS-mediated neural damage in adult mice. LPS-treated rodents had an increased number of damaged, shrunken, and degenerative neuronal cells in the cortex as well as the CA1, CA3, and dentate gyrus regions of the hippocampus, according to fluoro-jade B and Nissl staining results. Through the downregulation of pre-synaptic proteins synaptosomal-associated protein 23 (SNAP-23) and synaptophysin, LPS administration caused significant synaptic dysfunctions and memory impairment. PSD-95, phospho-glutamate receptor (p-GluR1), and phospho-cAMP response element-binding protein (p-CREB) have been found in the hippocampus of adult mouse brains. Another study found that a single systemic LPS injection could impair or reduce long-term potentiation, spatial memory, and neurogenesis in the hippocampus.

Alzheimer's disease (AD) is a chronic NDD characterised by increased amyloid-beta (A) plaque deposition and intracellular tangles of misfolded phosphorylated tau-proteins. According to reports, neuroinflammation exacerbates AD pathology. LPS causes neuronal inflammation in mice by impairing BBB integrity. The inflammatory response in Alzheimer's disease

***Address for Correspondence:** Vinciane Kappos, Department of Clinical Neurosciences, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, E-mail: vinciane@hotmail.com*

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starts with microglial cells binding to pre-existing amyloid-beta fibrils and soluble amyloid-beta oligomers via cell surface proteins like CD36, CD47, and TLRs. Microglial cells that have been activated produce proinflammatory cytokines such as IL1, IL6, IL12, IL18, and TNF. These cytokines, in turn, suppress the genes responsible for A clearance, resulting in impaired autophagy and increased A accumulation. A study found that injecting LPS increased TLR4 protein expression while decreasing TREM2 protein expression in 3X-treated mice. APPswe/PS1 Alzheimer's disease transgenic mice. Other researchers discovered microglial hyperactivation and hippocampal neuron apoptosis in LPS-exposed mice.

In another study, intranasal LPS administration increased the number of long noncoding RNAs (lncRNA) in the hippocampus, demonstrating its proinflammatory role in Alzheimer's disease. After intravenous injection of LPS, Agostini et al. discovered sex-dependent effects on metabolism that resulted in hippocampal neuronal death. Female mice had significantly higher levels of pro-inflammatory markers than male mice, but the mechanism underlying this difference in sex-dependent vulnerability remains unknown. Some studies with APP-transgenic mice (such as APPswe/PS1 Tg mice and 4- or 12-month old 3xTg-AD mice) revealed that systemic LPS injection activates microglia, resulting in neuroinflammation, A accumulation, and/or dementia. Tau pathology, synaptic loss, and neurodegeneration are associated with learning and memory deficits, as well as cognitive decline. According to other reports, a disruption in synaptic function is an important primary feature of Alzheimer's disease, along with memory impairments and cognitive dysfunction, with or without the induction of neurodegeneration [5].

Conclusion

These findings undoubtedly highlight LPS's important pathogenic role in mediating systemic and neuroinflammatory processes in a variety of NDDs. New therapeutics targeting LPS reduction and/or LPS-mediated inflammation should be actively investigated in the future as promising neuroprotective candidates for the treatment of NDDs. More mechanistic research is needed to fully comprehend the interactions between LBP and LPS, inflammation, and oxidative stress in neurodegeneration.

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Conflict of Interest

None.

References

1. Matsuura, Motohiro. Structural modifications of bacterial lipopolysaccharide that facilitate gram-negative bacteria evasion of host innate immunity. *Front Immunol* 4 (2013): 109.
2. Vidale, Simone, Arturo Consoli, Marco Arnaboldi and Domenico Consoli. Postischemic inflammation in acute stroke. *J Clin Neurol* 13 (2017): 1-9.
3. Stanley, Dragana, Robert J. Moore and Connie HY Wong. An insight into intestinal mucosal microbiota disruption after stroke. *Sci Rep* 8 (2018): 1-12.
4. Kuriakose, Diji and Zhicheng Xiao. Pathophysiology and treatment of stroke: Present status and future perspectives. *Int J Mol Sci* 21 (2020): 7609.
5. Masrori, Pegah and Philip Van Damme. Amyotrophic lateral sclerosis: A clinical review. *Eur J Neurol* 27 (2020): 1918-1929.

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