Lipoplysaccharide preconditioning prevents acceleration of kindling epileptogenesis induced by traumatic brain injury

Mansoureh Eslami, Mohammad Sayyah, Mansoureh Soleimani, Leila Alizadeh, Mahmoudreza Hadjighassem

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ABSTRACT

10–20% of symptomatic epilepsies are post-traumatic. We examined effect of LPS preconditioning on epileptogenesis after controlled cortical impact (CCI). LPS (0.01, 0.1 and 0.5 mg/kg) was injected i.p. to rats 5 days before induction of CCI to parieto-temporal cortex. Kindling started 24 h after CCI by i.p. injection of 30 mg/kg of pentylenetetrazole every other day until manifestation of 3 consecutive generalized seizures. CCI injury accelerated the rate of kindled seizures acquisition. LPS (0.1 and 0.5 mg/kg) prevented the acceleration of kindling. LPS preconditioning significantly decreased IL-1β and TNF-α over-expression and the number of damaged neurons in the hippocampus of traumatic rats.

1. Introduction

Epilepsy is one of the most common neurologic disorders with the global incidence of 1%. Five percent of all epilepsy cases are attributed to trauma, and 10–20% of those cases that are of known cause, are post-traumatic (Pitkänen et al., 2014). Mechanisms linking traumatic brain injury (TBI) to post-traumatic epilepsy (PTE) are not known and no measure for prevention of PTE is yet available (Pitkänen et al., 2014). TBI is caused by the acceleration force of a primary shockwave, blast wave or the force of a direct contact. Following the primary injury, secondary injury is caused by activation of the immune response due to blast wave or the force of a direct contact. Following the primary injury, secondary injury is caused by activation of the immune response due to inflammation of neuro-inflammatory cells, increased production of inflammatory cytokines, and edema (Hunt et al., 2013).

Lipopolysaccharide (LPS) is a stimulator of macrophage and microglia leading to release of proinflammatory and/or cytotoxic factors such as TNF-α, IL-1β, nitric oxide, and prostaglandin E2 (Marsh et al., 2009). LPS modulates the immune system through activation of Toll-like receptor (TLR) 4 (Marsh et al., 2009). LPS preconditioning is a phenomenon in which pretreatment of the cells or experimental animals with low-dose LPS blunts harmful response to subsequent destructive damage such as stroke (Bordet et al., 2000; Furuya et al., 2005; Lin et al., 2009; Marsh et al., 2009; Rosenzweig et al., 2004 and 2007; Tasaki et al., 1997), epilepsy (Dmowska et al., 2010; Mirrione et al., 2010; Sayyah et al., 2003; Ahmadi et al., 2013), spinal cord injury (Hayakawa et al., 2014), acute excitotoxicity (Larochelle et al., 2015), and TBI (Longhi et al., 2011). In this regard, it has been shown that mice receiving LPS 5 days before TBI, illustrate reduced lesion magnitude and restoration of neuro-motor function and cognitive performance (Longhi et al., 2011). We recently reported that induction of trauma to parieto-temporal cortex of rats accelerates the rate of acquisition of electrical and chemical kindled seizures (Eslami et al., 2015). In the present study we assessed if LPS preconditioning is able to prevent facilitating the effect of TBI on the kindling epileptogenesis. Due to the consequential role of the hippocampus in epileptogenesis, the effect of LPS preconditioning on the number of dark neurons as a depiction of damaged neurons, and on the expression of classical inflammatory cytokines IL-1β and TNF-α in the different hippocampal regions were determined in traumatic rats.