INCREASED BLOOD–BRAIN BARRIER PERMEABILITY IN MICE TREATED WITH REPEATED ADMINISTRATION OF LIPOPOLYSACCHARIDE


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Introduction: Dysfunction of the blood-brain barrier (BBB) is strictly associated with the pathophysiology of numerous neurologic disorders. In this context, experimental studies have been developed in an attempt to provide better understandings on how the BBB works and how it allows for the entrance of certain substances into the brain. In this study, we investigated the potential occurrence of changes in BBB permeability induced by intraperitoneal lipopolysaccharide (LPS) administration in mice. We aimed to standardize an experimental protocol to induced disruption of BBB integrity. Methods: The integrity of BBB, evaluated by the central measurement of fluorescein (previously injected systemically), was measured after three injections of LPS (3, 5 and 7 mg/kg), given in intervals of 48 hours (days 1st, 3rd and 5th). At days 1st, 3rd, 5th, 7th, 10th, 14th, and 21st after the first LPS administration, the mice were anesthetized and fluorescein 4% (4 mL/kg) was injected by intraperitoneal via. After thirty minutes, mice were submitted to cardiac perfusion with saline 0.9%, the brain was removed and the striatum and cerebral cortex were homogenized for fluorimetric determination of fluorescein levels. Results: After one day of exposition to LPS, there was a significant (p<0.001) increase on the levels of fluorescein in the cortex and in the striatum. The same occurred on days 5 and 7 (p<0.01), now after three LPS injections. However, at day 10th there was an increase on fluorescein levels only in the striatum (p<0.05). Further, no significant differences were observed at the 14th and 21st days in the two encephalic structures analyzed. Conclusion: The sub-acute systemic LPS exposure transiently increases the CNS penetration of fluorescein (mainly at the first seven days after the beginning of the exposition), but the BBB selective ability is recovered.

Keywords: Blood-brain barrier, lipopolysaccharide.

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