TIME COURSE OF BRAIN PGE_2 LEVEL AND SYNTHESIS PATHWAY IN LPS-FEVERED RATS

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Brain prostanoids levels and in particular PGE_2 are linked to body temperature changes and direct injection of PGE_2 into specific brain areas causes body temperature rise (1). The purported sequence of the events that lead to PGE_2 level increase in the brain is the following: bacterial cell wall >LPS>IL-1β>COX-2>mPGES-1> PGE2> body temperature increase (2).
Aim of the present study is the characterization of brain PGE_2 level time course and synthesis pathway in LPS-fevered rats. Animals were treated with LPS (50µg/kg i.p.) or saline and sacrificed at different times from injection to collect brain samples. Wistar adult males (200-225g) were used. Experiments were performed starting at 9:30 AM (time 0) to take account of circadian variation and were carried out in a room at 24°C±2. Body temperature was measured by a thermistor rectal probe and temperature at time 0 was used to assemble homogeneous groups. PGE_2 brain levels were measured by EIA assay. Specific mRNA levels were assessed by Real Time PCR. Body temperature measurement just before sacrifice revealed differences in LPS-treated rats compared to saline starting from 3h post-injection and lasting up to 7 h. Analysis of brain content showed that control animals are characterized by a PGE_2 basal level of about 6ng/g brain, that was increased by LPS treatment already 1 hr following injection. PCR analysis of brain from saline injected animals confirmed constitutive expression of the specific mRNAs coding for main enzymes involved in the PGE_2 pathway synthesis (COX-1, COX-2, cPGES, mPGES-1, mPGES-2). On the other hand, brains from LPS-treated rats showed overexpression of mPGES-1 specific mRNA with a peak at 5 hr post-injection.
Obtained data support the fact that, following LPS administration, PGE_2 levels increase before brain mPGES-1 overexpression, suggesting the existence of an independent mechanism to regulate the quick onset of febrile response. At present investigations at protein level are in progress to explain the mechanism underlying the early PGE_2 increase.

(1) Milton AS and Wendlandt S (1971) J Physiol. 218(2):325-36
(2) Blatteis CM, Li S, Li Z, Feleder C and Perlik V (2005) Prostaglandins & other Lipid Mediators 76: 1–18.