Pyrogen – prostaglandin coupling in the pathogenesis of fever: evidence against a role for nitric oxide

Jane Redford, Ihsan Ishai, and Flavio Cocianci

Abstract: There is much debate about the mechanism by which blood-borne pyrogens trigger prostaglandin E2 (PGE2) synthesis in brain and fever. This investigation was undertaken to determine whether nitric oxide is involved. In both human and case monitored during 30-minute treatment with interferon (IFN-γ) 1 (brain tumors) or endotoxic shocks in both micrococcus inactivated by pyrogens in the microsomal fraction (hypothalamus) and the production of prostaglandins was increased in the brain tissue. Moreover, the production of prostaglandins was increased significantly after IFN-γ treatment, and the production of prostaglandins was increased in the brain tissue. These results suggest that nitric oxide may be involved in the development of fever.

Key words: pyrogen, fever, mechanism, nitric oxide, prostaglandin E2, blood-brain barrier.

Résumé : Le mécanisme par lequel les pyrogènes diffusés par le sang déclenchent la fièvre et la production de prostaglandines (PGE2) dans le cerveau n’a pas été largement évalué. Cette étude a été entreprise pour déterminer si le monoxyde d’azote (NO) peut être considéré comme un transducteur de signal de la fièvre. Des expériences in vitro ont été réalisées pour étudier l’effet de NO sur la production de prostaglandines dans le cerveau. Les résultats montrent que NO peut augmenter la production de prostaglandines dans le cerveau. Les résultats suggèrent que NO est impliqué dans le développement de la fièvre.

Key words : pyrogen, fever, mechanism, nitric oxide, prostaglandin E2, blood-brain barrier.

Introduction

Fever is an important component of the host defense system, acting as a barrier against the spread of invading pathogens. It is thought to develop in a series of steps, starting with the release of several pyrogenic cytokines, such as tumor necrosis factor (TNF-α) and interleukin-1β (IL-1β), which stimulate the production of endogenous pyrogens. Among these, nitric oxide (NO) has gained considerable attention in recent years due to its role in mediating the effects of pyrogens on the central nervous system (CNS).

In the 1970s and 1980s, NO was thought to play a role in the pathogenesis of fever. However, recent studies have provided evidence against this role. One important study by Redford et al. (1995) demonstrated that NO is not a major factor in the development of fever, at least in the model used. This study was performed using a rat model of fever, where the authors administered a dose of pyrogens to induce fever and then measured the production of NO in the brain.

The results showed that NO production in the brain increased during the period of fever, but it was not necessary for the development of fever. The authors concluded that NO is not a major factor in the development of fever in this model. However, it is important to note that these results may not be applicable to all models of fever, as the role of NO in the pathogenesis of fever may vary depending on the specific model used.

In conclusion, while NO has been suggested to play a role in the pathogenesis of fever, recent studies have provided evidence against this role. Further research is needed to better understand the role of NO in the pathogenesis of fever and to identify other factors that may be involved.

References


Acknowledgments

This study was supported by a grant from the National Institute of Allergy and Infectious Diseases. We would like to thank the members of the laboratory for their helpful discussions and suggestions.
Materials and methods

Recombinant human interleukin-1β (IL-1β) (courtesy of Upjohn Co., Kalamazoo, Mich. and recombinant IL-1β (IL-1β) (courtesy of Delta, Del.), were expressed in Escherichia coli. Their respective activities were assayed using a"tissue" assay and a"whole cell" assay. The former was performed on primary cultures of human umbilical vein endothelial cells, and the latter was performed using a modified MTT assay.

Recombinant human endotoxin (LPS), a product of Bacterial Genetics, was used in all experiments. The endotoxin was prepared as a stock solution in distilled water and was diluted in fresh medium before use.

All experiments were performed in triplicate and the results are presented as the mean ± standard deviation. The significance of the differences between the means was determined using the Student’s t-test.

Results

In the experiments described above, the effects of recombinant human IL-1β on human umbilical vein endothelial cells were investigated. The results showed that IL-1β induced a significant increase in the production of TNF-α and IL-6, as well as in the production of IL-1β itself.

These findings suggest that the production of cytokines in response to endotoxin is mediated by IL-1β.

Discussion

The results of this study indicate that IL-1β is a key mediator of the inflammatory response to endotoxin. The fact that IL-1β induces the production of TNF-α and IL-6 suggests a paracrine action of IL-1β on the endothelial cells.

The production of IL-1β itself by the endothelial cells further suggests a positive feedback loop, where the produced cytokines may amplify the inflammatory response.

These findings have important implications for the understanding of the pathogenesis of sepsis and septic shock, which are characterized by a dysregulated inflammatory response.

In conclusion, the results of this study provide evidence for a key role of IL-1β in the inflammatory response to endotoxin.

References


RESULTS

Additional methods

COMMUNITY OF THE HOSPITAL FOR THE CHILDREN

At the time of the study, the Children's Hospital was in the process of expanding the number of patients it served. The hospital was expanding its services and facilities to accommodate the increased demand for its services. The study involved the collection of data from patients and staff to assess the impact of the expansion on patient care and staff workload.

The study was conducted over a period of 6 months, during which time data was collected from a sample of patients and staff. The data was analyzed using statistical methods to identify trends and patterns. The findings were used to inform the hospital's decision-making processes and to guide future planning and resource allocation.

The study results indicated that the expansion of the hospital had a positive impact on patient care, with an increase in the number of patients served and a reduction in wait times. Staff workload was also reduced, with an increase in job satisfaction and a decrease in burnout rates.

Overall, the study demonstrated the effectiveness of the hospital's expansion strategy and provided valuable insights for future decision-making.

References


The compound was not affected by the concentration of the sodium ions (Na⁺/K⁺) which was affected by the concentration of the calcium ions (Ca²⁺). The effect of calcium ions on the concentration of the sodium ions was observed in the presence of a fixed concentration of calcium ions. The concentration of calcium ions was found to be significantly higher in the presence of sodium ions compared to the absence of sodium ions. The concentration of calcium ions was also found to be higher in the presence of sodium ions compared to the absence of sodium ions for the same concentration of calcium ions. The concentration of calcium ions was found to be lower in the presence of sodium ions compared to the absence of sodium ions for the same concentration of calcium ions.

---

**Figure 1.** Effect of PGE2 and SNP on PGE2 formation.

**Figure 2.** Effect of sodium and calcium ion concentrations on PGE2 formation.

**Figure 3.** Effect of sodium and calcium ion concentrations on PGE2 formation.

**Figure 4.** Effect of sodium and calcium ion concentrations on PGE2 formation.

**Figure 5.** Effect of sodium and calcium ion concentrations on PGE2 formation.
Discussion

The present results show that the injection of PGE2 (6 and 7) into

C57 (Figs. 6 and 7). However, the present results with 'a'.

The present results show that the injection of PGE2 (6 and 7). However, the present results with 'a'.

C57 (Figs. 6 and 7). However, the present results with 'a'
Acknowledgements

The authors are indebted to J. Berwanger, and T. Bremer for excellent technical assistance. This work was supported by the Medical Research Council of Canada and the Canadian Institute for Health Research.

References


The authors are indebted to J. Berwanger, and T. Bremer for excellent technical assistance. This work was supported by the Medical Research Council of Canada and the Canadian Institute for Health Research.

References


