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Salão UFRGS 2019 – Conhecimento, Formação, Inovação

21. 25. OUTUBRO • CAMPUS DO VALE

PERIPHERAL BLOOD MONONUCLEAR CELLS DRIVE ASTROCYTE ENERGETIC FAILURE IN ACUTE SEPSIS

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Introduction

• Sepsis is characterized by a severe and disseminated inflammation;

In the central nervous system it promotes neuronal dysfunction and permanent cognitive impairment

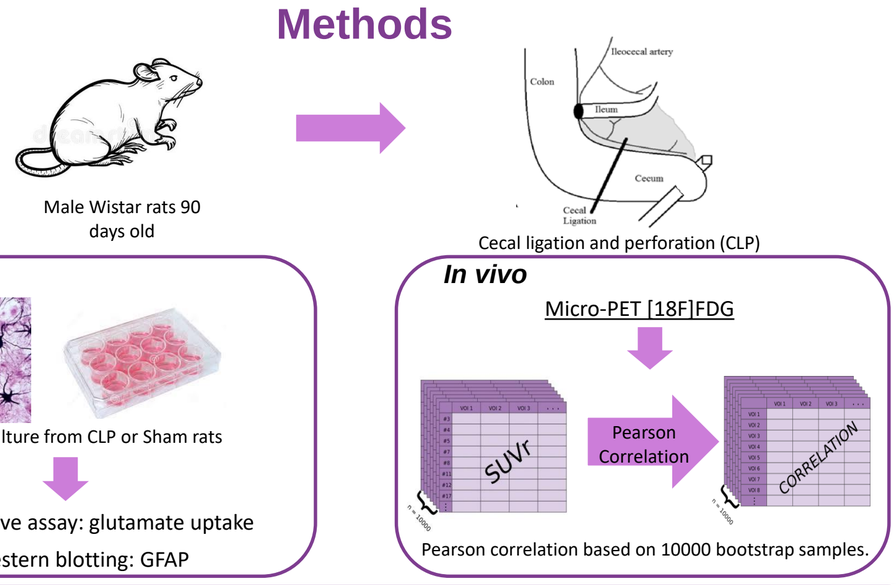
•Astrocytes are specialized immune-competent cells involved in brain surveillance that have been gaining considerable attention in this context;

• However, the communication between peripheral immune system and astrocytes during acute sepsis still remains unclear.

Objective

To investigate the involvement of peripheral blood mononuclear cells (PBMCs) in eliciting astrocyte reactivity in acute sepsis.

Methods



Results

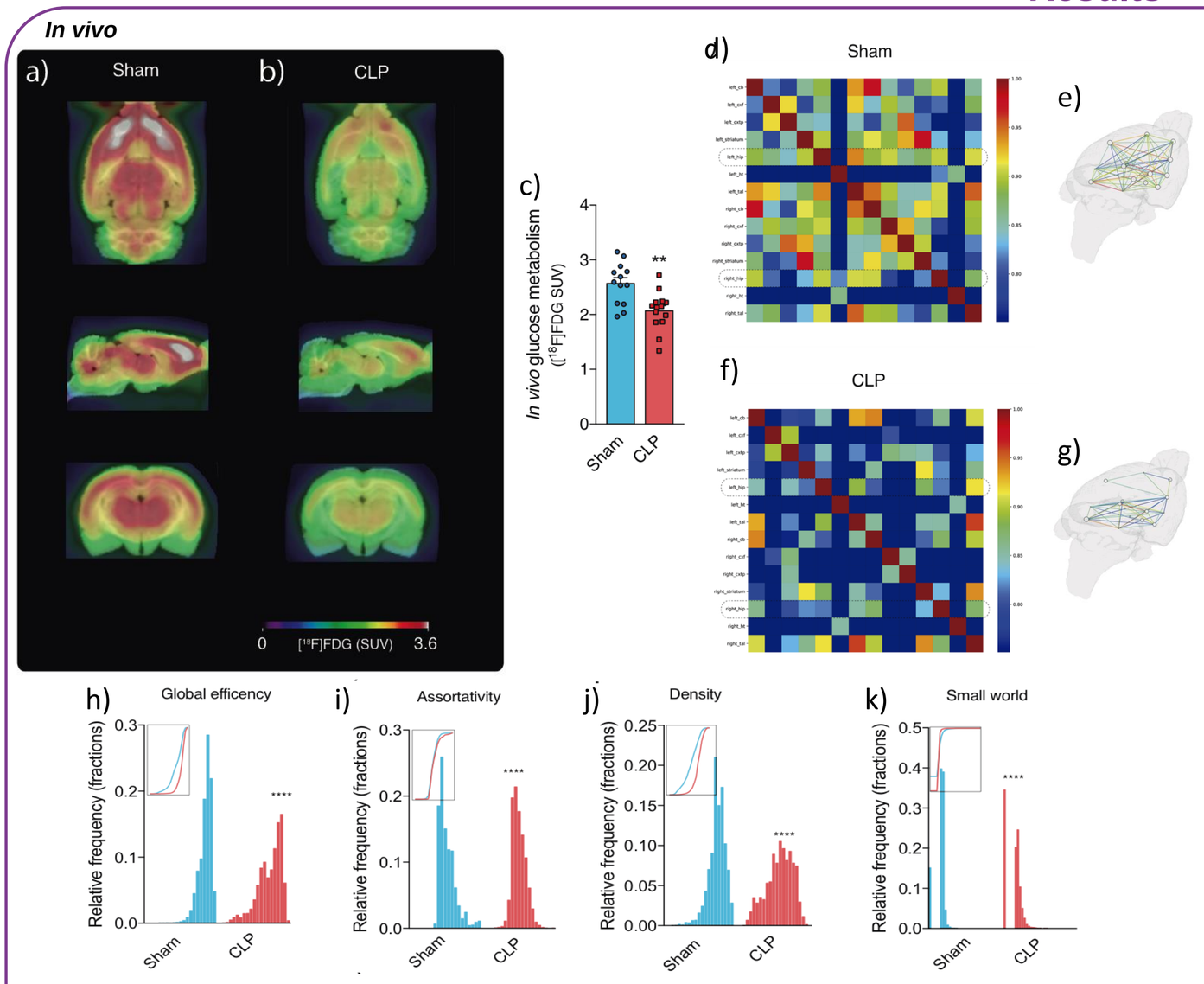


Figure 1. Whole-brain SUV of sham (a) and CLP (b) animals. Whole brain [18F]FDG uptake (c). Cross-correlation matrices: intersubject cross-correlation maps displaying region-to-region associations in sham (d) and CLP (f) rats. Metabolic networks: 3D brain surfaces displaying large-scale metabolic cross-correlation maps in sham (e) and in CLP (g) animals. Metabolic network graph measures of global efficiency (h), assortativity (i), density (j) and small world (k). Cumulative frequencies are depicted in the upper left of graph measures (h-k). *n* = 14 rats per group. *P < 0.05, **P < 0.01, ***P < 0.001 (t test). Data are presented as mean values ± s.d. and individual scatter plots or as correlation values with FDR-corrected (P < 0.005) thresholds for brain networks.

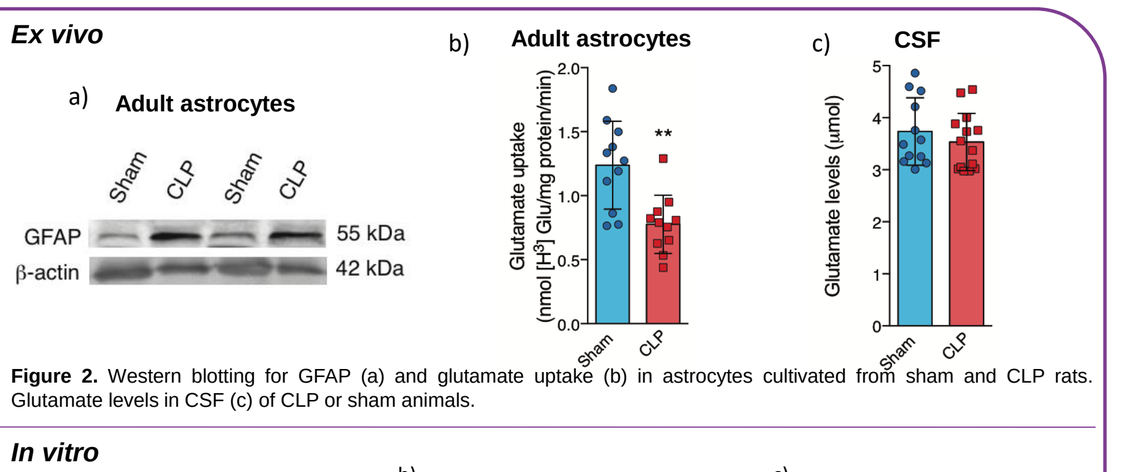


Figure 2. Western blotting for GFAP (a) and glutamate uptake (b) in astrocytes cultivated from sham and CLP rats. Glutamate levels in CSF (c) of CLP or sham animals.

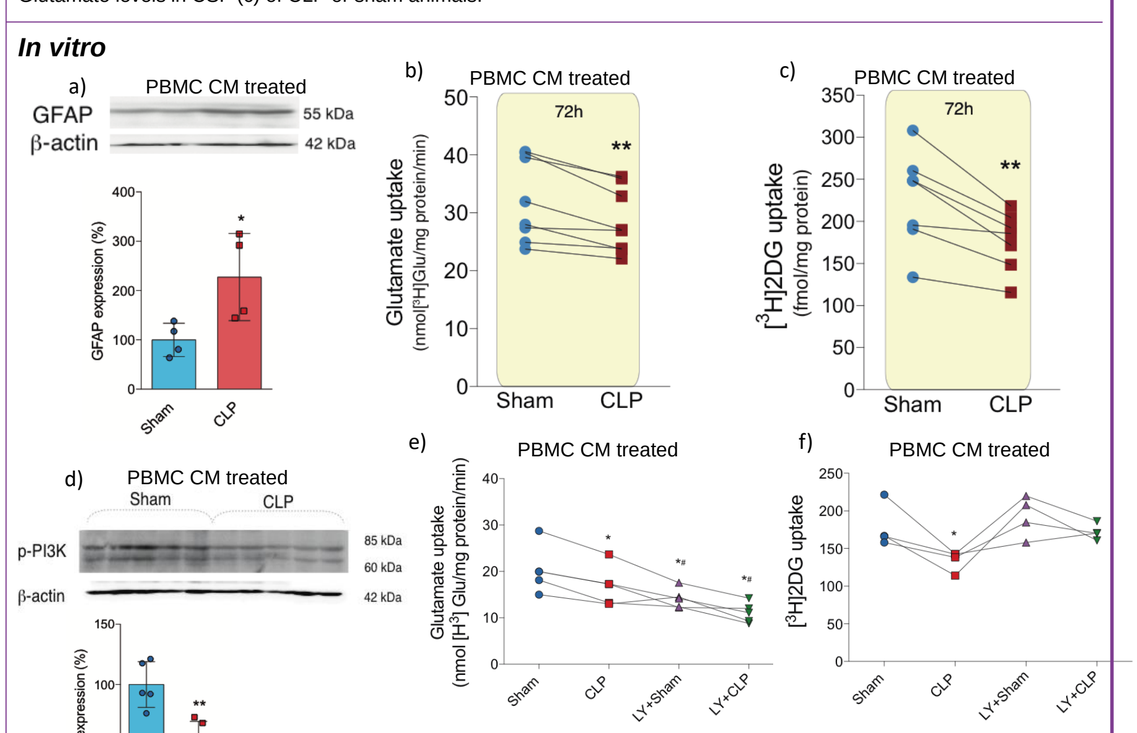


Figure 3. Western blotting for GFAP (a), glutamate (b) and glucose uptake (c) of astrocytes treated with 10% PBMC CM from sham/CLP animals for 72 h. Western blotting for p-PI3K of astrocytes treated with 10% PBMC CM from sham/CLP animals for 72 h (d). Glutamate (e) and glucose uptake (f) by astrocytes pre-treated with 10% PBMC CM from sham/CLP rats and/or 10 µM LY 294002. *n* = 4-6 per group. *P < 0.05, **P < 0.01 (t test). Data are presented as mean values ± s.d. and individual scatter plots.

Conclusions

Together, these results suggest that PBMCs are capable of directly mediating astrocyte reactivity and contribute to the brain energetic failure observed in acute sepsis. Moreover, the evidence of PI3K participation in this process indicates a potential target for therapeutic modulation.

Acknowledgements:
ZIMMER LAB
UFRGS Universidade Federal do Rio Grande do Sul
CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico
CAPES
FAPERGS