Apelin: new treatment for postoperative cognitives dysfunction?

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Introduction : Postoperative cognitive dysfunction (POCD) is a common complication after surgery, especially amongst elderly patients. They are associated with increased dependence, postoperative morbidity and mortality. To date, there is no preventive treatment. The main physiopathological hypothesis is based on the occurrence of postoperative neuroinflammation. Because apelin is an adipokine with anti-inflammatory and neuroprotective proprieties, we want to investigate the effect of postoperative apelin treatment to prevent POCD.

POCD model : Fear Conditionning

Test : During 4 minutes, mice was observed. We were hoping for fearful behavior : freezing
During test period, if mice didn't have memory problems, freezing was observed

Freezing ?

Yes
=
No POCD

No
=
POCD

Surgery induce POCD on mice

Result : After surgery, mice had a significantly reduced freezing rate compared to control mice (35% vs 57%, $p < 0.05$). After anesthesia alone, mice had the same freezing rate compared to control mice.

Apelin prevent POCD on mice

Apelin treatment
0,5 $\mu\text{mol/kg/day}$

First injection : 1 hour before surgery

Result : Apelin warned POCD, level of freezing was similar after surgery in mouse with apelin treatment. Freezing rate was similar on control mice and surgery apelin mice (57% vs 65%, NS). Apelin did not improve memory capacities, freezing was similar in control mice without or with apelin treatment (57% vs 62%, NS).

Apelin prevent postoperative inflammation

Hematoma - Apelin reduce expression of inflammatory cytokine : IL6 and $\text{TNF}\alpha$

Blood - Apelin reduce plasma level of inflammatory cytokine : IL6

Brain - Apelin reduce expression of inflammatory cytokine : IL6 and $\text{TNF}\alpha$

3h PBS 6h PBS 24h PBS
3h apeline 6h apeline 24h apeline

Conclusions - Perspectives

- In mice, perioperative treatment with **apeline reduced postoperative cerebral inflammation and prevent the POCD development**. Apeline appears to be a promising treatment of POCD.
- In future, we need to understand the actions pathways of apelin, and identify targets cells population.
- Investigation are needed to transpose results in the human.