

FOCUS ON RESEARCH

DEFINING CHANGES IN HIPPOCAMPAL AND CORTICAL EXPRESSION OF SURVIVAL - AND DEATH - RELATED GENES IN HUMAN POST-MORTEM TISSUE FOLLOWING CARDIAC ARREST AND STROKE

Researchers

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Aim

Substantial experimental evidence from our group and others using cell culture and animal models of brain injury suggests an important role for mineralocorticoid receptor (MR) - a receptor which responds to circulating steroids - as an intrinsic mechanism to help brain cells survive after injury. Here, we have studied the regulation of MR in patients with cardiac arrest who survived the original injury only to die in the following days and weeks.

Project Outline/Methodology

Case-control study. Identification of archived paraffin embedded post-mortem brain from patients with cardiac arrest with delayed fatality and matching controls. Measurement of expression of MR in hippocampus.

Key Results

MR expression was increased following cardiac arrest.

Conclusions

Increased MR expression may represent an intrinsic protective response of endangered neurons in human disease as it is in animal models.

What does this study add to the field?

We have previously shown an important role for MR in both cell culture and animal models of the injury caused by not enough blood getting to the brain; in parallel with this project we have shown that mice over-expressing human MR have reduced damage following cerebral ischaemia.

Importantly, this study shows that, as in animal models, MR is regulated in human brain following restricted blood supply. This suggests that interventions which increase MR expression may be

effective in conditions caused by restricted brain blood supply.

Implications for Practice or Policy

This identifies interventions which increase MR as candidate treatments for conditions characterised by cerebral ischaemia including cardiac arrest, stroke and head injury and as pre-treatments for patients undergoing interventions such as cardiac surgery or carotid revascularisation. Conversely, drugs which block MR signalling (spironolactone, eplerenone) may worsen outcome in these patients.

Where to next?

- Systematic review and meta-analysis of the risk and severity of stroke in patients receiving drugs which block MR.
- Further characterisation of drugs upregulating MR in neuronal cell culture.
- Identification of gene targets of MR in both animal models and in human post-mortem brain

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