EuroSTRESS

https://www.neurodegenerationresearch.eu/survey/eurostress/

Title of project or programme

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- United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

646788.48

Start date of award

01-05-2008

Total duration of award in months

48

The project/programme is most relevant to

- Alzheimer's disease and other dementias

Keywords
Research abstract in English

A fundamental question in stress research is why some individuals become vulnerable to affective disease, while others are resilient and gain strength from stressful experiences. In this multidisciplinary program we focus in a translational approach on the role of the stress mediators, notably the glucocorticoid stress hormone endproduct of the hypothalamic-pituitary-adrenal (HPA) axis. Secreted glucocorticoids target the limbic brain, where their actions on emotional arousal, cognition and motivation are mediated by mineralocorticoid and glucocorticoid receptors (MR and GR). Recent evidence from our laboratories suggests that these receptors operate in concert with the other stress mediators, in all phases of the stress response from the onset to the recovery and from

appraisal to memory storage/retrieval processes and affective responses. We test the hypothesis that imbalance in MR:GR mediated processes threatens affective health as may become manifest from the outcome of inadequate, excessive or prolonged HPA axis responses. Our objective is to understand how glucocorticoids, which are essential for adaptation and mental health, can become harmful. We have the following specific aims:

1) to generate animal models with altered MR:GR balance via transgenic and lentiviral approaches.

2) to induce enduring MR:GR changes in response to maternal care and perinatal challenges.

3) to examine the behavioural and neuroendocrine phenotype of these MR:GR modulated models.

4) in humans, to associate genetic variation in MR:GR we identified with emotional and traumatic memories as well as vulnerability to and symptoms of PTSD.

5) to study HPA axis activity and Alzheimer's Disease and chronic burnout patients and to study MR:GR gene polymorphisms cognition as prospective marker for affective health. In order to achieve these goals we combine the efforts of four pioneering groups in stress-HPA axis biology to rigorously test the MR:GR balance hypothesis in affective health.

Lay Summary