Researchers observe three types of hormone response to surgical disruption in cardiac patients

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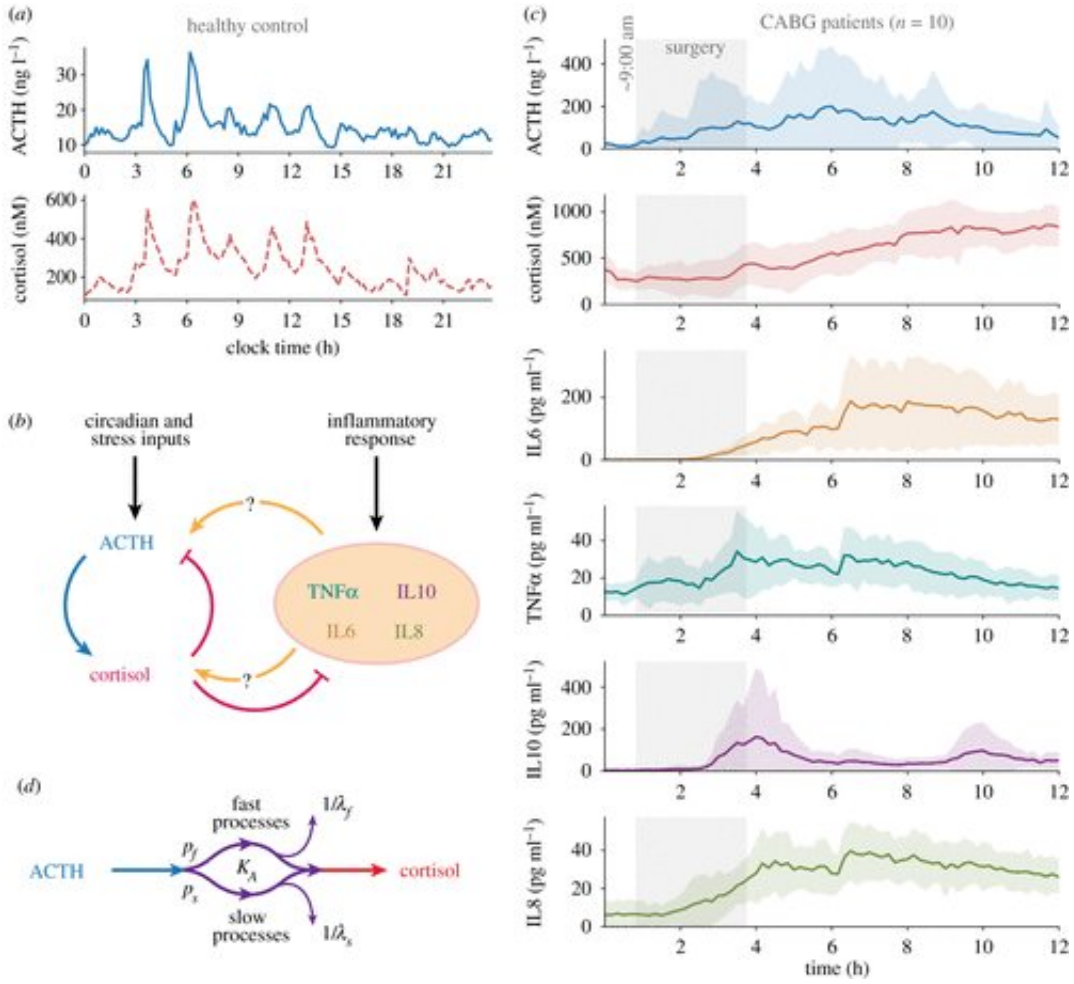

Dynamic stress and inflammatory responses following CABG. (a) Twenty-four hour ACTH and cortisol dynamic profile in a healthy control [4]. (b) Systems-level interactions between the HPA axis and inflammatory mediators. (c) Twelve hour dynamic profile (μ ± σ, n = 10) of ACTH, cortisol and inflammatory

mediators IL6, TNFα, IL10 and IL8 during and after CABG (IL2, IL4 and IL1α were assayed but inconsistently detected across patients). Gray-shaded areas indicate the mean time span of CABG surgery. Detailed individual profiles are shown in electronic supplementary material, figure S2. (d) Schematic illustrating the mathematical model. Eleven hours of ACTH data were used as input into fast and slow cortisol activity compartments. The model was calibrated to healthy controls, and its predictions compared against patient data. Credit: *Journal of The Royal Society Interface* (2022). DOI: 10.1098/rsif.2021.0925

Cardiac surgery patients may experience different levels of disruption to their body producing life-saving hormones during their operations, a new study reveals.

Major surgery and critical illness produce a potentially life-threatening systemic inflammatory response, which is counterbalanced by changes in adrenocorticotrophic hormone (ACTH) and cortisol.

The body's stress response system, known as the hypothalamic-pituitary-adrenal (HPA) axis, controls the production of these hormones as a vital part of patients' response to surgery, but researchers have found that there is no simple graded HPA response to cardiac surgery.

Research by experts at the Universities of Birmingham and Bristol, published today in *Journal of The Royal Society Interface*, shows cardiac surgery causes major dynamic changes in concentration of ACTH and cortisol, as well as their pattern of secretion.

Using novel mathematical techniques, researchers developed a model of HPA axis activity that predicts the physiological mechanisms responsible for different patterns of cortisol secretion.

They found that the HPA axis response can be classified into one of

three dynamic phenotypes: single-pulse, two-pulse and multiple-pulse dynamics.

Co-author Eder Zavala, from the Center for Systems Modeling and Quantitative Biomedicine (SMQB) at the University of Birmingham, said: "We've found that cardiac surgery patients experience one of three different patterns of HPA axis responses following surgery, which may reflect individual differences in how people respond to this type of stressor.

"These patterns may reflect underlying physiological differences in each person's HPA axis, but inflammation caused by surgery also appears to be contributing to changes in at least one of these patterns, the single pulse phenotype, suggesting that patients showing this dynamic could be experiencing the greatest inflammatory response to cardiac surgery."

Researchers discovered that the different patterns of HPA axis response could reflect different underlying physiological changes in adrenal sensitivity, cortisol production and turnover.

Co-author Daniel Galvis, center fellow at SMQB, said: "We now need further studies to investigate whether and how these patterns are correlated with clinical outcomes. This will be critical in establishing whether we can use the patterns to identify and classify post-surgical risk.

"Our research also shows the existing model used for diagnosis and prognosis after major surgery and critical illness may not be giving us the full picture. Improved diagnostics based on individual responses could lead to a better, personalized diagnosis and targeted interventions."

Under normal physiological conditions, ACTH and cortisol are in a state of dynamic equilibration which is disrupted by stressors such as surgery

and critical illness.

Dr. Ben Gibbison, Consultant Senior Lecturer in Cardiac Anesthesia and Intensive Care at the University of Bristol commented: "What is really interesting about this study is that for many years, we have thought that the rise in the anti-inflammatory hormone cortisol was triggered by the inflammation itself—our work shows that this is only true in certain cases and individuals. What's fascinating is that we can see who these people are by the pattern of cortisol that they produce."

Researchers addressed the question of how the inflammatory and HPA axis responses interact by sampling blood from a number of patients during and after coronary artery bypass grafting (CABG) surgery to generate profiles of ACTH, cortisol and inflammatory mediators.

The profiles were analyzed through repurposed computer algorithms originally developed for facial recognition, while the mechanisms underpinning different dynamic phenotypes were investigated through a mathematical model of HPA axis activity.

More information: Daniel Galvis et al, Modelling the dynamic interaction of systemic inflammation and the hypothalamic–pituitary–adrenal (HPA) axis during and after cardiac surgery, *Journal of The Royal Society Interface* (2022). DOI: 10.1098/rsif.2021.0925

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