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Can we measure surgical resilience?

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ABSTRACT

Surgical resilience describes psychological resilience within a surgical setting. Within a surgical setting, psychologically resilient patients have improved recovery and wound-healing. The search for biological correlates in resilient patients has led to the hypothesis that certain endogenous biomarkers (namely neuropeptide Y (NPY), testosterone, and dehydroepiandrosterone (DHEA)) are altered in resilient patients. The concept of surgical resilience raises the question of whether enhanced recovery following surgery can be demonstrated in patients with high titres of resilience biomarkers as compared to patients with low titres of resilience biomarkers. To determine the prognostic value of resilience biomarkers in surgical recovery, a cohort of patients undergoing major surgery should initially be psychometrically tested for their resilience levels before and after surgery so that biomarker levels of NPY, testosterone and DHEA can be compared to a validated psychometric test of resilience. The primary outcome would be length of hospital stay with and without an enhanced recovery program. Secondary outcome measures such as complications, time in rehabilitation and readmission could also be included. If the hypothesis is upheld, resilience biomarkers could be used to support more individualised perioperative management and lead to more efficient and effective allocation of healthcare resources.

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Introduction

Resilience is characterised by the ability to accept circumstances that cannot be changed, and to adapt to significant changes in the environment [1]. Several authors have raised the question of whether there are biomarkers associated with and individual's resilience, and whether such measures can be used in the clinical setting [2]. To be sure, resilience is ostensibly a psychological concept [1], for which there are at least 15 psychometric measures [3]. If resilience is an ability to adapt to change and cope with stress, then there is good reason to believe that there are physiological associations with psychological resilience. The stress-response mechanism is mediated by the hypothalamus–pituitary–adrenal (HPA) axis, the activity of which is diminished in resilient individuals [2]. This suggests a physiological underpinning for the current hypothesis that certain endogenous biological molecules can be used as biomarkers for resilience. However, this hypothesis has yet to be studied within the surgical context.

A possible link between resilience biomarker literature and the surgical recovery literature has previously been suggested [4]. Resilient patients tend to recover better from surgery than less resilient patients, and therefore may also express higher titres of certain biomarkers than less resilient patients. With a substantial amount of evidence to support both observations in isolation, this raises the question of whether resilience biomarkers can be used for the prognosis of surgical recovery. The relationship between psychological resilience, stress, and state anxiety is important for linking the two bodies of literature [4]:

1. Resilient individuals have diminished stress reactivity and better emotional recovery than individuals who are less resilient. It is therefore hypothesised that resilience has physiological effects associated with HPA activation; this relationship is key for the resilience biomarker literature.
2. Resilience is protective against state and trait anxiety and anxiety disorders, allowing resilient individuals to experience less anxiety than less resilient individuals; this relationship is key for the surgical recovery literature.

The literature supports a psychological mediation of postoperative recovery [5,6]. It is reasonable to assume the contextual stimulus for a given operation is consistent. Yet there is a high degree of variability in the individual response to that stimulus – some patients exhibit a diminished response to the psychological stress of surgery and are more "resilient" than other patients. Their

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anxiety levels are lower than other patients, which increases their likelihood of a better recovery [6]. These patients exhibit what has been coined "surgical resilience" [4].

It is difficult to identify the "ideal" resilience biomarker to measure surgical resilience. Resilience biomarkers are not specific for a surgical context and their sensitivity and predictive qualities within that context are yet to be established.

Hypothesis

We propose an adaptation of the resilience biomarker hypothesis that would allow biomarkers for resilience to be used as prognostic markers of likely patient outcomes following surgery. This new hypothesis is illustrated in Fig. 1. While it is not yet clear how resilience affects the HPA axis, animal models suggest that neuropeptide Y (NPY) in particular may directly modify the corticotropin releasing hormone (CRH)-ergic or the GABA-ergic neurons of the hypothalamus, the noradrenergic neurons of the locus coeruleus, or via glutaminergic neurons projecting from the basolateral amygdala into the hypothalamus [7].

Evaluating the hypothesis

We propose the following null hypothesis for surgical resilience biomarkers

H_0. There is no significant difference in recovery trajectories in surgical patients with high resilience biomarker titres compared with surgical patients with low resilience biomarker titres.

As yet there have been no clinical trials exploring the use of resilience biomarkers to measure surgical resilience [4]. The ideal trial should be a cohort study of patients undergoing elective major surgery at a major tertiary hospital offering a range of surgical services. Patients should be assessed for their level of psychological resilience prior to surgery and followed until discharge from hospital and rehabilitation (if applicable). Resilience biomarker levels should be measured according to biomarker assays and compared to a psychometric test for resilience with good psychometric properties such as the Resilience Scale for Adults, the Connor–Davidson Resilience Scale or the Brief Resilience Scale [3]. Such a test should be chosen for the trial based on its validity, internal consistency, reproducibility, interpretability, and its utility in a surgical context.

The primary outcome data could be time spent in hospital, which is a commonly used proxy for quality of care [8]. Secondary outcomes could include: time in surgery; complications encountered during surgery; postoperative complications; time in rehabilitation following discharge; readmission rate; emergency admissions; overall morbidity; and mortality. Trial outcome data should be analysed for any association with biomarker levels and psychometric test results. A small pilot study could investigate outcomes for all surgical specialties, whereas a large trial could examine outcomes for each surgical specialty. Studies focusing on an individual surgical specialty could also be conducted to gain analytical depth.

Empirical data

While no such trial exists, there is a substantial body of evidence to support our hypothesis. Laboratory-based measurements of resilience derive from the fact that the stress-response mechanism is a stereotypical activation of the HPA axis [2]. The neurobiology underlying individual variation lends itself to the identification of biomarkers for resilience, in particular NPY, testosterone and DHEA:

1. NPY: Recent literature suggests that NPY is a neuroprotective and anxiolytic agent [7]. High levels of NPY released in response to a stimulus are prognostic of better psychological outcomes, while reduced levels of NPY are strongly associated with increased anxiety levels [2].
2. Testosterone: Testosterone has a limited neuroprotective role and is involved in neuroplasticity and the modulation of the HPA axis. High levels of testosterone promote social connectedness and positive mood, both of which are associated with resilience. Testosterone levels decrease following acute stress and low levels are associated with posttraumatic stress disorder (PTSD) and depression [2].
3. DHEA: DHEA is released following stimulation of the HPA axis, though no clear role of DHEA in the stress response has been established. High levels of DHEA are associated with improved outcomes from survival training [2].

It is difficult to determine the interactions between the resilience biomarkers and patient anxiety, and moreover their utility within a surgical context [4]. Nevertheless, these interactions could be exploited for pre-surgical therapies if the clinical relevance of resilience can be firmly established within a surgical pathway.

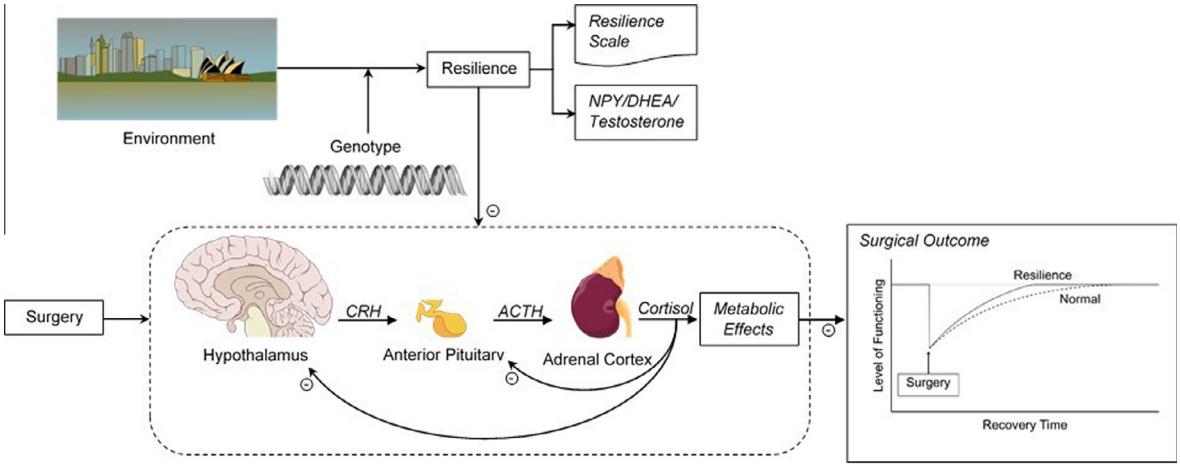

Fig. 1. Biomarkers and surgical resilience. Items indicated in italics are measurable either pre-operatively, peri-operatively or post-operatively. NPY = neuropeptide Y; DHEA = dehydroepiandrosterone; CRH = corticotropin releasing hormone; ACTH = adreocorticotropic hormone.

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