

Special Article

Allostasis and Surgical Operations

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Abstract

A surgical operation triggers systemic homeostatic responses in a way that varies but rarely takes place out of range. When it does, an allostatic process is defining the route to survival. When a major operation takes place, with long duration or/and severe violation of organs physiology, brain, liver and adrenals react with scientifically documented patterns described by the theories of organ axes.

According to the classic terminology, allostasis is described mostly as a cumulative phenomenon and not as a sudden shock, so it is more close to this terminology that surgical operations might play a crucial role in allostatic chronic conditions or major post operation disabilities.

Surgical diseases that could represent allostatic phenomena are the inflammatory bowel diseases, morbid obesity and before and after bariatric operation, post injury conditions (multi-trauma cases), patients before and after transplantation, and patients with stomas or long standing artificial enteral nutrition.

In aged-people, concomitant diseases consist the crucial pathways for developing fast allostatic changes which can be documented with stress -related biochemical testing. Common preoperative tests are planned under the limitations for low cost health services. Thus, patients who undergo major operations are in greater danger for allostatic changes, due to the combination of ageing, concomitant diseases and hidden risks (not diagnosed with common tests). For ageing, with or without dementia, the preparation for a surgical operation is a very sensitive and less studied issue, except patients who already have been diagnosed for dementia and have been under specialized therapy and follow up programs.

The special role of the pre-anesthetic examinations could be more extensive in cases where an endocrinologist plays an important role, such as in morbidly obese patients, and where a gastroenterologist is important, as in Inflammatory Bowel Disease cases.

Key Words: Allostasis, Preoperative Diagnostic Tests, Dementia

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Introduction

Socioeconomic status is an unchanged risk factor and bad prognostic criterion for almost every kind of disease arising in conditions of chronic stress. This had been the background for the birth of the term *allostasis*¹, which in turn was described again and again, altered in a sophisticated way- but not inaccurate - as it extends from the society and leads to the cells as well as the DNA of humans and mammals.

While allostasis has been described with clinical and not sociological scope, its appeal among clinical doctors remained vague for some years. Brain imaging contributed in the apprehension of allostatic irreversibility² but the real revolution took place when modern biochemical markers of stress were linked to genes, and thus the term *inherited allostatic load*³ represented the missing documentation for the non- sociological aspect of allostasis and completed this interesting theory.

Aim of the study – Methods

With the purpose to examine if surgical diseases are included in the group of allostasis related conditions, respecting the definition of 1998, and the rest of scientific work related to this theory, the present article recalls known facts of surgery and determines the allostatic load caused by surgery.

A number of 18 articles were chosen for review, with the use of the term words allostasis, surgery, preoperative diagnostic tests, dementia, and aging.

Results

The term allostasis is related to 653 articles in Pubmed database. Under the limitation “allostasis and surgery” a sub-group of 19 articles is produced. Among them, only one article refers to the possibility of having better surgical results if we use the theory of allostasis in our way of planning anesthesia and analgesia. At the moment, there is not any article describing the use of allostatic load as consequence of any operational technique.

Surgery has not been connected with allostasis, except from one article only, coming from Dr Chong V at al⁴, who combined socioeconomic status and operative risk, and for this reason health outcomes were studied in correlation with education, income and occupation. In clinical practice, the socioeconomic status of patients is never reported in the personal history of surgical patients, and does not play a role in Apache Score, used by anesthesiologists to describe their patients' physical condition.⁵ On the other hand, chronic stress has been related to surgical diseases, as inflammatory bowel syndromes, morbid obesity, multiple trauma, transplantation procedures and surgical artificial openings (defecation stomas and feeding stomas).

Coleman LS⁶, in his article titled “*30 years lost in anesthesia theory*” suggests that allostasis is a component of operative stress and limits its power in cognitive function. Coleman makes the conclusion that anesthesia, analgesia and allostasis are three factors that may lead to a good or bad surgical outcome. He uses the theory of “Stress Repair Mechanism” for describing three synergistic pathways: the spinal pathway, the cognitive pathway and the tissue pathway. Allostasis is connected to the cognitive pathway, which is modulated by emotional mechanisms. Anesthesia inhibits the cognitive pathway. Analgesia

inhibits the spinal pathway. The synergistic combination of anesthesia and analgesia are prohibiting the hyperactivity of the Stress Repair Mechanism.⁶

Traumatic early and late neuroendocrine response⁷ might be categorized in allostatic changes, related to surgery. As survival is the main direction for every one of those changes, as well as allostatic theory supports, neuroendocrine defects and dysfunctions, can be studied as post trauma allostatic phenomena, early and late. It is very important that, so far, we never refer to early allostatic changes and late allostatic changes, because allostasis is described as a cumulative and irreversible damage, which worsens only.¹

Allostasis has not been studied as a neuroendocrine phenomenon, but is crucially related to neuroendocrine hormones. Aging is related with allostasis due to the accumulative character given in allostasis definition, and also hormonal degradation is related with aging. In clinical death, hormonal therapy is administered to maintain vitality for the organs to be received for transplantation until the legal procedures are completed and the consent of the family of the donor is received.⁸

Cancer is also connected with aging. Cancer has not been connected with allostasis, but has been related to kynurenine, which is the "*fingerprint of allostasis*"!⁹ Hormonal therapy is an option for some types of cancer. It would be interesting if hormonal therapy could be given to reduce the allostatic load. We already know that glutamine reduces the production of kynurenine¹⁰, and because glutamine is an amino-acid, it is probable that the suitable hormones would be neuroendocrine hormones or neurotransmitters. Recently this knowledge has been expanded because 19 amino acids were found to help towards reductions of kynurenine levels, in experimental studies.¹¹

The positive action of 5-hydroxytryptamine (5-HTP) in inflammatory bowel diseases (IBD) is documented.¹² Allostasis of IBD is clear.¹³ If anti-depressive therapy could help in allostatic load it is not clear, as according to the definition of allostasis, damage is irreversible, and gene faults found in several allostatic conditions³ support the definition of 1998. However, according to Dr Natalie Castanon¹⁴, inflammation and mood disorders are linked via the activation of the kynurenine pathway, and expands her results to obesity and related comorbidity, too.

The difficulty to recover after an admission in ICU is greater in old people. Early worsening heart failure has been reported when anesthetic drugs are stopped. If neuropsychiatric medication replaced a part of the custom sedation protocol administered to ICU patients, then stress might be alleviated and awakening might be facilitated without the morbidity and mortality of present rhythms. Neuroleptics, like sulpiride, have been recognized as helpful drugs for patients with response to inhibit kynurenine metabolism.¹⁵

The ICU administration of adrenaline helps in the pressure abnormalities but does not help with stress. Adrenaline raises stress and provokes a “neuroendocrine storm”. On the other hand, in “rescue therapies”, hydrocortisone offers a *hormonal lifting* to the patients but may predispose to infections.

Discussion

Minimal invasive surgery is very important because lessens pain and succeeds in full recovery and return to work much faster. Robotic surgery has even less loss of blood and mainly minor tissue injuries thanks to the supremacy in surgical dissection.

The operative stress is not yet determined in minimal invasive surgery and robotic surgery.

Operative stress and Allostasis

The correlation of operative stress and allostasis, may be expressed in the long term, if a serious complication changes the quality of life. For example, if a disability occurs early after an operation, the allostatic load that is produced is not yet possible to calculated, because the recovery period changes the conditions that we call “irreversible”.

Timing for Operation

The pre-operative preparation of the patient is very important for the success of the operation and the avoidance of complications. For example, major urgent operations have tremendously higher mortality and morbidity.¹⁶ For aged people, the numbers are worse.¹⁷ Because we cannot always avoid the operation on elderly, kynurenine levels might help us to prepare the patient for a major operation with all available means.

Choice of the Operational Technique

All patients are not suitable for every operational technique. Geriatric surgery has been developed and shows us that minimal invasive surgery is the best way to reduce postoperative morbidity and mortality. Patients with a higher allostatic load, should be treated differently. Kynurenine levels may become a new pre-operative criterion for anesthesiologists and surgeons as well as intensivists.

On the other hand, allostasis maintains life in patients with severe but not lethal complications. This “physical resistance to death” could be resembled to the numerous changes of bacterial flora in complicated and prolonged infectious diseases. It is already prevalent that anological

response has a correlation with allostasis. Because trauma for example has been related to a special nosological response. Up to now, a correlation of kynurenine and immune-mediated inflammation has been reported.¹⁸

Conclusions

A wise pre-operative preparation is one of the best ways to prohibit a raised morbidity and mortality in patients with recognized allostatic load- or not recognized!. The introduction of new pre-operative markers, as kynurenine, as well as the use of novel pharmaceutical stress-relieving drugs, targeting to kynurenine pathway, is a future target for improving surgery results for aged patients, cancer cases, chronic inflammatory gastrointestinal diseases as well as morbid obesity.

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