

Endocrine Entropy

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Abstract

This communication defines and describes the novel concept of endocrine entropy. The authors share insights regarding the various facets of entropy in endocrine epidemiology, physiology, clinical presentation and management. The discussion opens up a new way of approaching endocrinology. Recent advances in artificial intelligence, assessment and addressal of entropy may become integral part of endocrine diagnostics and therapeutics.

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Entropy

Coined by Rudolf Clausius in 1865, the word entropy has been used in various disciplines. For the physicist, entropy is a thermodynamic phenomenon which quantifies the degree of disorder or randomness in a system. High entropy suggests a lack of order or predictability. In information theory, entropy is a logarithmic measure of the rate of transfer of information in a particular language or message. Entropy represents the spontaneous change that occurs in many everyday phenomena, and also describes the energy in a system that is unavailable for doing useful work.¹

In endocrinology, approximate entropy algorithms have been used to quantify hormone pulsatility. While various models have been explored, the concept of entropy has not found success in endocrine assay interpretation.² In this communication, we define and discuss the concept of endocrine entropy. We explore this phenomenon and suggest various interpretations of the multifaceted construct.

Epidemiology

Endocrine and metabolic diseases are increasing rapidly in

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incidence as well as prevalence. While multiple factors have been put forward to explain this epidemiological trend, no single etiology can account for the sudden rise in endocrine diseases. Due to advances in diagnostics, there is also an increase in the variety of presentation of endocrine disorders. This occurrence may be termed as endocrine entropy, or epidemiological entropy in endocrinology. These terms are especially apt for disorders associated with exposure to endocrine disruptor chemicals, as a clear cause-and-effect relationship can usually not be demonstrated.³

Development

It is well known that pre-conception and peri-conception health of both parents, as well as post-conception health of the antenatal mother, contribute to the endocrine and metabolic health, of unborn offspring. This phenomenon has been termed as transgenerational karma.⁴ However, there are more unanswered questions than definite facts in this field of science. Endocrine entropy, therefore, is a fit descriptor for the milieu of the embryo and foetus in the mother's womb.

Endocrine entropy can also be used to describe the perception of changes that occur before and during puberty. 'The Ugly Duckling', immortalized in the eponymous book by Hans Christian Anderson,⁵ is an example of self-limited endocrine entropy which has a happy ending. Children and adolescents who pass through the awkward stages of puberty may connect with the use of endocrine (and psychosocial) entropy to describe their state of mind and body.

Transgender Health

Another situation where endocrine entropy seems appropriate is in transgender health. A transgender person passes through various phases before understanding his/her/their gender identity. The process of this self-discovery may be termed as 'neural entropy', or colloquially, as endocrine entropy. Neuroendocrine entropy may be a more accurate term to explain the confusion faced by some transgender persons as they come to terms with their gender identify incongruence. A specific situation where this term resonates is gender fluidity, which is characterized by changes in an individual's gender identity.⁶

Specific Endocrine Disorders

While environmental and genetic causes have been identified for many endocrine disorders, many such conditions continue to be labelled as idiopathic.⁷ Endocrine entropy is a plausible explanation for the development of diseases such as precocious puberty, endocrine incidentalomas, autonomously functioning nodules in endocrine glands, endocrine-dependent malignancies, and cyclic pheochromocytoma.

It may also be used to characterise seemingly paradoxical findings, such as differential resistance at various insulin receptors in persons with diabetes or polycystic ovary syndrome.

Clinico-Biochemical and Geno-Phenotypic Discordance

There are many endocrine conditions where concordance between clinical features and biochemical or hormonal values is limited. Though an exhaustive list is difficult to prepare, it includes pseudopseudohypoparathyroidism, androgen insensitivity syndrome, pseudohypoglycaemia, and various states of hormone resistance. Another example is thyroid eye disease, where ophthalmic signs and thyroid function tests may not correlate with each other.

Similarly, the correlation between genotype and phenotype is not necessarily absolute, even in genetic endocrine syndromes.⁸ These observations suggest a degree of endocrine entropy in the presentation, and identification of endocrine disorders.

Cyclic changes in laboratory values, such as those of adrenal steroids, plasma rennin activity, and pituitary hormones are another facet of endocrine entropy.

Diabetes

One clinical picture where the term endocrine entropy or glycaemic entropy fits perfectly is that of glycaemic variability.⁹ This condition is characterised by unpredictable changes in glycaemia over time, at an inter-individual as well as intra-individual levels. Glucose, in chemistry, is a molecule with low entropy. In diabetes practice, however, glucose exhibits extremely high randomness. It is this disorganized or unpredictable behaviour which makes glucose management challenging. Artificial intelligence tools, such as those in modern insulin pumps, help in predicting glycaemic trends, and assist in preventing glycaemic entropy as well.

Obesity

Obesity is a multidimensional syndrome, with multifactorial etiopathology and multifaceted clinical presentations.¹⁰ For persons living with obesity, and for their care providers, it is a “multiplexing” condition as well. It is not possible to quantify weight change as a function of relative energy intake and expenditure alone. Multiple other factors, including endocrine metabolic, behavioural and environmental, contribute to weight homeostasis. This challenging landscape, or ‘baroscape’, can be taken as an example of endocrine entropy or disorder.

Therapeutic Entropy

The management of certain diseases too, can be described as a state of disorder, chaos or randomness. Though evidence-based, effective interventions are available for the vast majority of endocrine and metabolic diseases, the management of certain illnesses still eludes us. There is a certain amount of therapeutic entropy, or uncertainty, in the treatment of some endocrine syndromes. Multiple options are available, and the choice is based upon individual factors, rather than standardized algorithms. This situation, described earlier as lack of equipoise, can also be termed therapeutic entropy.

Summary

The concept of endocrine entropy is an interesting one. The communication shares insights which may help advance endocrine diagnosis and treatment.

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