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# HYPOTHALAMUS-PITUITARY-ADRENAL AXIS, HAIR CORTISOL AND THE METABOLIC SYNDROME

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***SUMMARY***

*In this paper we discuss the possibility of using Hair Cortisol in Clinical Practice to monitor HPA status in patents at risk of developing the Metabolic Syndrome, and also its possible use to assess effectiveness of the effectiveness of treatment in patients with the Metabolic Syndrome.*

***Key words:*** *HPA Axis (Hypothalamus Pituitary Adrenal Axis) - ACTH (Adrenocorticotropic Hormone) - CRH (Corticotropic Releasing Hormone) - Hair Cortisol - Metabolic Syndrome (MetS) - OSA (Obstructive Sleep Apnoea) - SWS (Slow Wave Sleep) - ELS (Early Life Stress)*

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Over the past 60 years, there has been an exponential expansion in the field of neuroendocrinology. The HPA Axis (Hypothalamus Pituitary Adrenal Axis) is affected by both internal physiological stressors (cytokines, hypoxia, macromolecules, etc), and by external stressors (source of anxiety, fear, etc), which threaten the organism's homeostasis.

The HPA Axis is affected by both internal physiological stressors (cytokines, hypoxia, macromolecules, etc) and by Neurogenic Stress (fear, etc), which threaten the organism's homeostasis. Researchers are investigating the gene-environment-interaction. The HPA Axis presents a "common Pathway". There seems to be a gap between the individual experiencing trauma/other severe stressors, and the emergence of clinical symptoms. Between the activation of the HPA Axis, and the onset of psychopathology. This provides "a window of opportunity" for early detection of dysregulation, assessment and early intervention.

Cortisol binds to cortisol receptors throughout the body. The hormone receptor complex is to be found in the nucleus of the cells, where it binds to DNA (docking).

The consequences of this bond vary considerably. In some cells cortisol can induce some genes and repress others. In cases where the HPA Axis is overactive the amount of cortisol in the nucleus of the cells may increase by approximately tenfold.

Some researchers (Nemeroff 1999, Jokimen 2007, Coryell 2007, Nova 2006), have suggested that the assessment of the HPA Axis activity may be a useful tool in clinical practice.

Prof. Nemeroff (1999), has emphasised the opportunity of "early intervention in at risk individuals". Prof. Nemeroff suggests that individuals who have been exposed to untoward early life stress, can be considered an "at risk population".

There is emerging evidence showing the usefulness of Hair Cortisol analysis as an indicator of sub-acute and chronic stress (S Van Uum).

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## Could Hair Cortisol levels help to assess the HPA Axis Status, to monitor progress over time, to assess effectiveness of interventions?

Stan Van Uum et al. (2011), mention that Hair Cortisol levels are being increasingly used in a variety of pathological situations, because it can provide a long term measure of systemic cortisol exposure. Dettenborn et al. (2010), used Hair Cortisol analysis to rate levels of psychological stress. Individuals who had been unemployed for at least a year, were compared with currently employed control subjects. Cortisol concentrations were significantly higher in the unemployed group.

The Metabolic Syndrome involves a cluster of cardiometabolic abnormalities, including hypertension, abdominal obesity, hyperglycemia and dyslipidemia. It has been suggested that increased activity of the HPA Axis, with increased levels of glucocorticoid hormones may contribute to the development of MetS (Friedman 1996). Also, normal physiological differences in long term cortisol secretion, assessed through Hair Cortisol levels, shows a relevant relationship with MetS (Stalder2013). New evidence has emerged on early life stress induced metabolic derangements (eg. hyperinsulinemia and altered insulin sensitivity on exposure to a high energy diet later on in life).

Early- life stress can alter the expression of genes in peripheral tissues, such as the glucocorticoid receptor and 11-beta hydroxysteroid dehydrogenase. Margaret J. Morris et al. (2014) propose that interactions between altered HPA axis activity and liver 11-beta hydroxysteroid dehydrogenase modulates both tissue and circulating glucocorticoid availability, with adverse metabolic consequences.

At times of Stress, amygdala glucocorticoid receptors (GRs) may be preferentially activated, increasing CRH. Elevated CRH increases EEG (Electroencephalogram) frequency, decreasing Slow Wave Sleep (SWS), increasing light sleep and wakefulness.

On the other hand, sleep disturbances (insomnia, sleep apnoea), can aggravate HPA Axis dysfunction.

Patients with mental disorder who are on psychotropic medication (eg. Clozapine, Olanzapine, etc), can put on weight, and develop dyslipidemias. The increased weight may contribute to hypertension, insulin resistance, and sleep apnoea. Vogelzangs et al. (2007), suggested that there was a synergistic relationship between depression, cortisol and Metabolic Syndrome.

Atypical antipsychotic drugs like Quetiapine have sleep improvement properties. Low dose of Quetiapine (25mg-100 mg per day), has improved quality of sleep in healthy volunteers (Cohrs et al. 2006). Quetiapine was found to down regulate the activity of the HPA Axis in healthy male volunteers (Cohrs 2006). When the person is able to achieve Slow Wave Sleep (SWS), the HPA Axis is suppressed.

The HPA Axis is fundamentally a dynamic system (Rachel Yehuda). Longitudinal studies are needed to clarify how the HPA Axis evolves in time. Hair Cortisol allows us to look at cortisol levels over a period of months. Could we use Hair Cortisol levels as a biomarker of Chronic stress In Clinical Practice?

Thus we suggest that we could use Cortisol levels in "at risk individuals", due to genetic loading/ELS, other, to facilitate early intervention. Furthermore we suggest that it be used to monitor individuals at risk of Metabolic Syndrome, and it could be used to monitor response to treatment in patients with Metabolic Syndrome.

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