

Francesca Patacchioli

## IATROGENIC SIDE EFFECTS INDUCED BY HPA AXIS DERANGEMENT

**Abstract**

Functional disorders are characterized by combinations of symptoms which can be associated with virtually any body system and what's more, symptom-based drug therapies have proven to have only limited success.

This presentation outlines the interferences of the most widely used drugs with hypothalamo-pituitary adrenal (HPA) axis function. In fact, many neurotransmitter-modulating drugs interfere with basal HPA activity. The effects of these compounds depend on the dose administered, the length of treatment and the underlying disorder. Moreover it should be taken into account patients' behavioral habit, such as smoking. In fact, cigarette smoking appears to be associated with increases in cortisol levels, whereas a cortisol decline is observed upon ceasing to smoke. Further, an excess of alcohol intake is a well-known cause of clinical and/or biochemical pseudo-Cushing.

Hypo-secretion of cortisol is known as adrenal insufficiency and HPA axis suppression results when there is an inadequate level of glucocorticoids to regulate normal body functions. Iatrogenic HPA axis suppression might appear secondary to steroid drug withdrawal. Moreover, some pharmacokinetic / pharmacodynamic risk factors for HPA axis suppression are well recognized such as steroid biological potency and half-life, in addition to affinity of the steroid for the glucocorticoid receptor.

Benzodiazepines are among the most commonly drug used for symptomatic treatment of insomnia and anxiety: human and animal studies suggested that benzodiazepines suppressed the HPA axis activity. A case report (Müssig et al. Secondary adrenal failure due to long-term treatment with flunitrazepam *Clinical Endocrinology* 2006 65:549-550) will be discussed, about a 66-year-old man with persistent feelings of physical exhaustion. The patient's past medical history revealed a long lasting treatment with flunitrazepam 1 mg once daily; the patient has taken this medication continuously over the last 35 years without interruption or changes in the dosage. Routine haematological and biochemical findings were normal, while basal concentrations of plasma ACTH and serum cortisol as well as mean 24-h urinary free cortisol excretion were significantly decreased. During and after reduction of the benzodiazepine treatment, were observed marked and stable increase of the serum and urinary concentrations of cortisol and its urinary metabolites and plasma levels of ACTH. Therefore, the patient suffered from a chronic benzodiazepine treatment-induced side effect and at the end of the tapering period he reported a clear improvement in asthenia symptoms.

Functional disorder symptoms can be changeable, affecting different bodily systems and overlapping between one type of disorder and another. Therapies need to be

specifically oriented to the single patient, based on a positive diagnosis of the functional disorder. Stress and lifestyle undoubtedly play a role in these problems making the management of the disorders frequently complex.

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Francesca Patacchioli

Dpt Physiology and Pharmacology – 2nd Medical School - Sapienza University of Rome - Italy

Francesca.Patacchioli@uniroma1.it

#### *Curriculum vitae*

#### *PATACCHIOLI FRANCESCA ROMANA, MD Biologist*

She was born in Rome on December 29th 1950

Prof Patacchioli started almost 35 years ago studies on hypothalamus-pituitary-adrenal (HPA) axis activity and its modulation by central neurotransmitters. In the last 10 years she extended previous research on rodents to human being by measuring adrenocortical hormones in saliva, so avoiding the stress of venipuncture. She is interested on answering the question whether steroid hormones induced neurodegeneration and/or neuroprotection. Moreover, she is involved in the studies on HPA activity in different physiopathological conditions: aging, menopause, irritable bowel syndrome, amyotrophic lateral sclerosis, acute and chronic stress.

Her professional experience started in 1980 as Assistant Professor Researcher. Since 2005 she is Associate Professor of Pharmacology in Department of Physiology & Pharmacology of Sapienza University, S. Andrea Medical School.

Since April 12th 2007, she was elected for function of Honorary Associate Professor of Pharmacology in the “Gr.T.Popa” University of Medicine and Pharmacy, Iasi, Romania.

She is member of

Italian Society of Pharmacology

Italian Society of Neuropharmacology

EMAS (European Menopause & Andropause Society)

EBPS (European Behavioural Pharmacology Society)

She is principal investigator of presently funded national and international research projects on “Stress and woman physio-pathological condition”. Moreover, she is the Italian coordinator of Executive Scientific and Technology Program of collaboration between Italy and Egypt, entitled “The use of blocked mutant and co-metabolism fermentation techniques in the production of new antineoplastic anthracycline antibiotics”.

She participate to international activities as Promoter of Bilateral Agreement and Teaching Staff Mobility of Socrates Program, coordinating the cultural and scientific collaboration between Sapienza University of Rome and “Gr.T.Popa” University of Iasi.

Main scientific publications are:

Original Articles, Reviews and Editorials: 76

Abstracts and Short Communications: 70