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Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuenEditorial for the Special Issue *Festschrift for Dirk Hellhammer*

Dirk Hellhammer was a pioneer in human psychoneuroendocrine stress research and the founder of the *Trier School of Psychoneuroendocrinology*. During decades of enthusiastic and tireless empirical as well as theoretical work, several methodological innovations were generated by him and his group that subsequently impacted on the entire research field. A first milestone was the implementation of the salivary cortisol methodology, serving as a non-invasive marker of stress. Soon, the Trier Social Stress Test (TSST), a highly standardized laboratory stress induction paradigm, was developed and validated. Also the cortisol awakening response (CAR) became an important tool in human stress research. Both paradigms, the TSST and the CAR, are nowadays used by researchers all over the globe and have contributed substantially to a better understanding of human neuroendocrine acute and chronic stress regulation.

While Dirk's work was strongly dedicated to experimental laboratory research, he saw basic research always through the eyes of a clinician. Thus, the motto "from bench to bedside (and back)" was a central theme of his thinking. At a conceptual level, the phenomenon of hypocortisolism and its relationship to (psycho)somatic disorders was of major interest to him, especially with its relevance for chronic pain, burnout, and autoimmune diseases. Especially during the last years, his conceptual work culminated in the development of conceptual endophenotypes and the diagnosis and treatment system termed *Neuropattern*TM (see for example the recent paper in this journal by Hellhammer, Meinlschmidt & Pruessner, 2018).

In honor of Dirk's seminal work and in dedication of his exceptional qualities as research group leader, the "offspring" of the *Trier School of Psychoneuroendocrinology* compiled this Special Issue. It primarily contains review papers but also a number of original empirical studies, which illustrate main themes of the topics, methods, and concepts stimulated by and build upon the work of Dirk Hellhammer.

The special issue starts with a personal introduction by Bruce McEwen from Rockefeller University (NY, USA), describing Dirk's contribution to the development of modern psychoneuroendocrinology, entitled "From Serendipity to Clinical Relevance: How Clinical Psychology and Neuroscience Converged to Illuminate Psychoendocrinology - A Tribute to Dirk Hellhammer".

A following first block of review papers illustrates main topics of Dirk's long-lasting research endeavor, namely HPA axis stress reactivity in laboratory and field settings as well as respective methodological progress. In this section, Kudielka, Wüst and colleagues give an up-to-date summary of sources of inter and intra-individual differences in HPA axis responses to stress in order to facilitate the study of links between stress and disease. Next, Schlotz presents the current state of the art on associations between momentary stress and cortisol in daily

life in psychoneuroendocrine stress research. These empirical findings are based on new developments stemming from methodological frameworks such as ecological momentary assessment. Heim, Buss & Entringer then take a new translational perspective on the early programming of health and disease, a research question grounded in their initial studies conducted in Trier. With respect to methodological advancement, Miller & Kirschbaum present a meta-analysis on the Trier Social Stress Test focusing for the first time on evidence for cultural differences and how this may relate to mental disorders.

The next section of review papers addresses cognitive and affective consequences of stress. First, Wolf illustrates how the TSST can be used to modulate memories but also to test memories of the paradigm itself. Wingenfeld & Otte follow to take a closer look at the mineralocorticoid receptor and its impact on health and disease with a special focus on its relevance for cognition. Engert and coworkers describe the empathic response to psychological stress, thereby addressing cognitive and affective processes. Then, Yim & Kofman place the spot on an often-ignored topic: intimate partner violence and the stress associated with it.

Next, Rohleder combines psychoneuroendocrinology with psychoneuroimmunology in his review on acute, repeated, and chronic stress effects on inflammation, focusing in particular on the transitional phase between acute and chronic stress.

In the following part, Ehlert and her group take on a developmental neuroendocrinological perspective in describing steroid secretion patterns in healthy aging. Gaab takes a new look at the placebo effect applying a psychoneuroendocrine perspective. The last review by Meinlschmidt et al. addresses an area with growing relevance for future societies: automated driving systems.

Finally, in the last block, empirical papers cover HPA axis activity and reactivity issues, ranging from basic research in healthy populations to clinical populations, and finally presenting empirical research applying Dirk's *Neuropattern*TM approach as well as newly-developed interventional methodology. In more detail, Jens Pruessner and colleagues broaden the temporal view on the cortisol awakening response (CAR) by investigating a longer time window for measurement, while Wirtz et al. present mechanistic data on the role of the alpha-adrenergic receptor on the prothrombotic effect of acute stress. Deinzer and her group report the impact of a medical simulation paradigm on human stress systems. Focusing on a clinical perspective, Buske-Kirschbaum et al. raises the intriguing question whether altered HPA axis activity might be the reason for the comorbidity of atopic diseases and ADHD and Marita Pruessner and colleagues present evidence for an altered response to the TSST in patients with first episode schizophrenia. With respect to Dirk's *Neuropattern*TM approach, Bergemann et al. report on first experiences with a practice-based pilot trial in patients suffering

from major depression, while Kumsta and coworkers explore the relationship between a variation of the MR gene and the conceptual endophenotype of CRF hypo-responsivity. Last but not least, the group by Domes & Heinrichs test the effectivity of an internet-based stress management training.

We feel that this set of reviews and research papers reflect quite accurately the breadth and depth of Dirk Hellhammer's academic work

and its impact on human psychoneuroendocrine research. Over the course of 45 years of hard work, he has influenced and shaped the field in a unique and enduring manner. Being proud scholars of the *Trier School of Psychoneuroendocrinology*, we wish to express our sincere gratitude to Dirk and salute him.

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