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Which physiological systems are most strongly affected by stress? Does chronic stress cause brain damage?

Throughout phylogenetic history, our organism has developed different physiological systems to successfully adapt to environmental demands. These systems communicate closely within a stress response network. This network consists of numerous areas of the brain and peripheral organs. However, there are three major players in the orchestra of the stress response:

First, there are ergotropic systems, which synchronize the stress response network when we need to actively cope with a stressor. Under such circumstances, noradrenergic nerve fibres originating from the Locus caeruleus in the brain stem enhance wakefulness, attention and cognitive performance. At the same time, the brain activates the sympathetic nervous system to allow optimal peripheral organ function to enhance physical performance. Previously, ergotropic systems allowed us to survice fight and flight situations. Today, they are still activated in daily life, particularly in situations, which demand high psychological and/or physical performance.
Secondly, there are trophotropic systems, mainly represented by serotonergic nerve fibres originating in the Raphe nuclei of the brainstem and the parasympathetic nervous system in the periphery. These systems facilitate recovery and regeneration, relaxation, sleep, and resilience.
Thirdly, there are glandotropic systems, namely the hypothalamus-pituitary adrenal axis. CRF neurons in the brain can be considered the conductor of the orchestra of the stress response. They facilitate cognitive and emotional processes, which preferably help us to cope with an anticipated stressful event. In addition, CRF neurons indirectly stimulate the release of cortisol from adrenal glands. Cortisol supports the energy supply of the brain and adaptional processes of the cardiovascular and immune systems under stressful conditions. Adaptation to stress works if all three systems can be activated in a balanced mode. However, deleterious effects of stress may occur once the balance cannot be maintained.

To what extent are depression and anxiety stress-related disorders?

Both depression and anxiety adopt brain processes, which largely overlap with those of the stress response network. CRF-neurons play a key role in depression as noradrenergic

neurons do in anxiety disorders. However, many other additional brain areas contribute to the specific pathology in a given patient. These processes vary considerably among patients, resulting in a broad heterogeneity, even if patients share the same diagnosis. Thus, both diagnostic and therapeutic treatments need to be personalized to improve therapeutic efficacy.

Why do people react to stress differently?

People are genetically different. Some gene variants are stress protective, while others enhance stress vulnerability. Our preliminary data clearly suggest that most of the patients with stress pathology have a history of pre- and postnatal stress. It seems that maternal stress mainly affects the glandotropic system in the fetus, while adversity in childhood enhances noradrenergic responsivity in later life. Probably such alterations are epigenetically programmed. In other words, the readability of specific genes is altered in a way that improves adaptation to a foreseeable adverse future. Such genetic and epigenetic dispositions may persist over one‘s lifespan. However, a permanent hyperactivity of the stress response network may put people at risk for stress pathology, once they are exposed to chronic or traumatic stress.

What led you to develop the stress diagnostic tool Neuropattern and what is its function?

Neuropattern™ is a new translational tool to detect and treat stress pathology. The term „translation“ refers to a transfer of knowledge from basic research to the bedside. Currently, translational research is most prominently represented by the search for biomarkers and pre-clinical research. Aside from generating such new measures and methodologies, translational research also refers to the translation of integrated knowledge. This strategy involves synthesis, exchange, and dissemination of available knowledge, with the goal of improving health services and health care systems. For stress-related disorders, such as depression and anxiety disorders, this strategy meets numerous challenges, as the great majority of these patients are treated by family physicians. Thus, we developed Neuropattern™, a diagnostic tool, which allows bedside translation of psychobiological knowledge, especially with respect to depression and anxiety disorders.

Neuropatterns are conceptualized ergotropic, trophotropic, and glandotropic endophenotypes of the activity and reactivity status of neurobiological interfaces, which participate in the crosstalk between the brain and peripheral organs under stressful conditions. Most of the respective biological, psychological, and symptom measures are taken by the patient at home. Neuropattern™ can be easily implemented in routine clinical work, and helps the physician to individualize those therapeutic interventions that are already available. In the first of our randomized clinical studies, we already observed a significant increase of treatment success in inpatients, as verified by a symptom check list. In the future, Neuropattern™ may well serve as a convenient carrier for new biomarkers, thus combining both translational approaches.

Could you tell us about some of the latest developments in the field of stress medicine?

Let me comment on your question from a clinical viewpoint. Basic research on mental, psychological, or behavioral stress is flourishing with an average of about 150 publications per week. At the bedside, however, the repertoire of pharmacological treatments has not changed much in the past decades. Rather, it seems that the development of new psychotherapeutic interventions is more successful. One reason is that psychological methods such as schema therapy can already account for the profound impact of pre- and postnatal adversity. On the other hand, pharmacological manipulations targeting genetic and epigenetic mechanisms need far more time. However, there is hope that clinically valid biomarkers may, in the near future, help to identify and individually treat persons with stress related disorders. Other important developments include neuroimaging studies on functions within the stress response network. Alterations in specific areas of depressed patients, for example, have been detected and may soon offer new neurological therapeutic options in treatment-resistant depression.