Editorial: Stressors in animals and humans : Practical issues and limitations

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Editorial: Stressors in animals and humans - Practical issues and limitations

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Stress – the physiological response to an environmental challenge - is now a fundamental scientific, clinical and societal concept, which serves as testimony to the importance of its initial description by Hans Selye some 80 years ago (Fink, 2016; Selye, 1936). Whilst the stress response (and related states such as emotionality and arousal) is typically the focus of attention, in the present special issue of *Neurobiology of Stress* emphasis is placed on the environmental stimuli – the so-called stressors – that induce stress, emotionality and arousal. Stressors can be neurogenic (e.g. painful stimuli) or psychogenic (e.g. social stimuli) or a combination of the two; this issue comprises contributions that focus on psychogenic stressors.

Stressors can already impact on mammals at the prenatal stage of development, and the first paper (M. Weinstock: Prenatal stressors in rodents: effects on behavior) presents a review of recent studies of maternal-gestational stressors and their long-term effects on offspring brain and behavior in mice and rats. Postnatally, environmental stressors can impact on the lactating mother who in turn acts as a stressor on her dependent offspring. One major maternal stressor is atypical maternal care and H. J. Krugers, J. M. Arp, H. Xiong, S. Kanatsou, S. L. Lesuis, A. Korosi, M. Joels and P. J. Lucassen review the evidence for this (Early life adversity: lasting consequences for emotional learning). They describe some of various manipulations of maternal care that have been applied in controlled experiments in rodents, as well as the descriptive evidence for correlates of postnatal stress in humans, with emotional learning being the major dependent variable of interest across species. Another, complementary approach to the study of postnatal stressors is to increase levels of maternal corticosteroids (corticosterone in rodents). In his contribution, S. Macri (Neonatal corticosterone administration in rodents as a tool to investigate the maternal programming of emotional and immune domains) proposes that “this mother-offspring transfer mechanism can be leveraged to devise experimental protocols based on the exogenous administration of corticosterone during lactation”. He describes studies of neonatal corticosterone administration in rats and mice that have demonstrated programming of phenotypes with respect to emotionality and immune status. Of course, as emphasized by Selye, the organism’s own hypothalamic-pituitary-adrenal (HPA) system is one of the major components of its stress response, and the final developmental contribution considers the major stressors that are used to investigate HPA stress responses and their consequences in adolescence and at puberty in rats. This topic is discussed in the contribution “Translational relevance of rodent models of hypothalamic-pituitary-adrenal function and stressors in adolescence” by C. M. McCormick, M.R. Green and J. J. Simone.

Two contributions focus on intrinsic factors that shape the stress responses of individuals. In their article, “How age, sex and genotype shape the stress response”, A. Novais, S. Monteiro, S. Roque, M. Correia-Neves and N. Sousa, emphasize that the response to any stressor is heterogeneous dependent on factors intrinsic to individuals, such as age, sex and genetics. They review the evidence for this in rodents, as obtained using various experimental stressors and physiological and behavioral readouts. C.E. Koch, B. Leinweber, B.C. Drengberg, C. Blaum and H. Oster (Interaction between

circadian rhythms and stress) bring to the fore the essential role of the circadian clock in mediating between the environmental stressor and the individual's stress response. The master pacemaker located in the suprachiasmatic nucleus of the hypothalamus impacts on both the HPA axis and the autonomic nervous system, such that both of these stress response systems receive strong circadian input. Accordingly, environmental stressor-circadian state interactions are extensive and have physiological and pathophysiological consequences.

The remaining five contributions focus on stressors experienced in adulthood. Chronic mild stress (CMS) in rat is the experimental stressor that has been applied for the longest period of time and in the most studies to-date, with CMS-induced decreased gustatory reward sensitivity being the most common model. Paul Willner established this model and it is very fitting that he contributes two papers to this issue: Firstly, in "Reliability of the chronic mild stress model of depression: A user survey", Willner presents the outcome of a questionnaire survey of laboratories that have published CMS studies. This is extremely useful in demonstrating the extent of the reliability of the procedure and also that there is indeed a minority of laboratories in which the characteristics effects of CMS could not be reproduced reliably. Second, in "The chronic mild stress (CMS) model of depression: History, evaluation and uses", Willner provides an update on the validity and reliability of CMS and reviews recent data on the neurobiological bases of CMS effects on reward sensitivity and the mechanisms of antidepressant action. Whilst CMS comprises a combination of primarily physical stressors presented on an unpredictable schedule, social stressors are also of high translational relevance, and in our own contribution we review and compare chronic psychosocial stressors (CPS) in three different species (C.R Pryce and E. Fuchs: Chronic psychosocial stressors in adulthood: studies in mice, rats and tree shrews). The CPS paradigms are based on resident-intruder confrontations and are typified by brief proximate interactions and attacks by and otherwise continuous distal exposure to the social stressor. J.M. Koolhaas, S. de Boer, B. Buwalda and P. Meerlo (Social stress models in rodents: towards enhanced validity) expand on the theme of CPS, and emphasize the importance of the individual's appraisal of the stressor in determining its stress response. Outcome expectancy and feedback from own actions during the social stress, are suggested to be important factors in determining the stress response and development of stress-related diseases. Such concepts are directly at the translational interface between animal and human studies, and the final contribution addresses the experimental study of stress in humans directly. The Trier social stress test (TSST) represents the gold standard with respect to the empirical study of stressor effects in humans. A. P. Allen, P. J. Kennedy, S. Dockray, J. F. Cryan, T. G. Dinan and G. Clarke (The Trier social stress test: Principles and practice) review the evidence that the TSST has yielded in terms of understanding effects of variables such as sex and age on the human acute stress response, and how it is now also being applied to study factors such as the epigenome and microbiome in terms of their effects on stress reactivity and the etio-pathophysiology of stress-related disorders and their treatment.

Understanding the processing of environmental stimuli, including stressors, is essential to understanding the contribution of the environment during development and adulthood. As such, it is essential to focus as much on the nature of the environmental stimuli and their processing, as it is to focus on the effects, including stress responses, of these stimuli. We anticipate that the present special issue will serve to stimulate further high-quality research into the study and understanding of stressors in animals and humans.

References

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