EDITORIAL

Recent developments in stress and anxiety research

Urs M. Nater^{1,2}

Accepted: 13 August 2021 / Published online: 1 September 2021 © The Author(s), under exclusive licence to Springer-Verlag GmbH Austria, part of Springer Nature 2021

Stress and anxiety are virtually omnipresent in today's society, pervading almost all aspects of our daily lives. While each and every one of us experiences "stress" and/or "anxiety" at least to some extent at times, the phenomena themselves are far from being completely understood. In stress research, scientists are particularly grappling with the conceptual issue of how to define stress, also with regard to delimiting stress from anxiety or negative affectivity in general. Interestingly, there is no unified theory of stress, despite many attempts at defining stress and its characteristics. Consequently, the available literature relies on a variety of different theoretical approaches, though the theories of Lazarus and Folkman (1984) or McEwen (1998) are relatively pervasive in the literature. One key issue in conceptualizing stress is that research has not always differentiated between the perception of a stimulus or a situation as a stressor and the subsequent biobehavioral response (often called the "stress response"). This is important, since, for example, psychological factors such as uncontrollability and social evaluation, i.e. factors that may influence how an individual perceives a potentially stressful stimulus or situation, have been identified as characteristics that elicit particularly powerful physiological stressful responses (Dickerson and Kemeny 2004). At the core of the physiological stress response is a complex physiological system, which is located in both the central nervous system (CNS) and the body's periphery. The complexity of this system necessitates a multi-dimensional assessment approach involving variables that adequately reflect all relevant components. It is also important to consider that the experience of stress and its psychobiological correlates do not occur in a vacuum, but are being shaped by numerous contextual factors (e.g. societal and cultural

Urs M. Nater urs.nater@univie.ac.at



The goal of the World Association for Stress Related and Anxiety Disorders (WASAD) is to promote and make available basic and clinical research on stress-related and anxiety disorders. Coinciding with WASAD's 3rd International Congress held in September 2021 in Vienna, Austria, this journal publishes a Special Issue encompassing stateof-the art research in the field of stress and anxiety. This special issue collects answers to a number of important questions that need to be addressed in current and future research. Among the most relevant issues are (1) the multidimensional assessment that arises as a consequence of a multi-faceted consideration of stress and anxiety, with a particular focus on doing so under ecologically valid conditions. Skoluda et al. 2021 (in this issue) argue that hair as an important source of the stress hormone cortisol should not only be taken as a complementary stress biomarker by research staff, but that lay persons could be also trained to collect hair at the study participants' homes, thus increasing the ecological validity of studies incorporating this important measure; (2) the incongruence between psychological and biological facets of stress and anxiety that has been observed both in laboratory and field research (Campbell and Ehlert 2012). Interestingly, there are behavioral constructs that do show relatively high congruence. As shown in the paper of Vatheuer et al. (2021), gaze behavior while exposed to an acute social stressor correlates with salivary cortisol, thus indicating common underlying mechanisms; (3) the complex dynamics of stress-related measures that may extend over shorter (seconds to minutes), medium (hours and diurnal/circadian fluctuations), and longer (months, seasonal) time periods. In particular, momentary assessment studies are highly qualified to examine short to



¹ Department of Clinical and Health Psychology, Faculty of Psychology, University of Vienna, Vienna, Austria

² University Research Platform 'The Stress of Life – Processes and Mechanisms Underlying Everyday Life Stress', University of Vienna, Vienna, Austria

medium term fluctuations and interactions. In their study employing such a design, Stoffel and colleagues (Stoffel et al. 2021) show ecologically valid evidence for direct attenuating effects of social interactions on psychobiological stress. Using an experimental approach, on the other hand, Denk et al. (2021) examined the phenomenon of physiological synchrony between study participants; they found both cortisol and alpha-amylase physiological synchrony in participants who were in the same group while being exposed to a stressor. Importantly, these processes also unfold over time in relation to other biological systems; al'Absi and colleagues showed in their study (al'Absi et al. 2021) the critical role of the endogenous opioid system and its relation to stress-related analgesia; (4) the influence of contextual and dispositional factors on the biological stress response in various target samples (e.g., humans, animals, minorities, children, employees, etc.) both under controlled laboratory conditions and in everyday life environments. In this issue, Sattler and colleagues show evidence that contextual information may only matter to a certain extent, as in their study (Sattler et al. 2021), the biological response to a gay-specific social stressor was equally pronounced as the one to a general social stressor in gay men. Genetic information is probably the most widely researched dispositional factor; Kuhn et al. show in their paper (Kuhn et al. 2021) that the low expression variant of the serotonin transporter gene serves as a risk factor for increased stress reactivity, thus clearly indicating the important role of dispositional factors in stress processing. An interesting factor combining both aspects of dispositional and contextual information is maternal care; Bentele et al. (2021) in their study are able to show that there was an effect of maternal care on the amylase stress response, while no such effect was observed for cortisol. In a similar vein, Keijser et al. (2021) showed in their geneenvironment interaction study that the effects of FKBP5, a gene very closely related to HPA axis regulation, and early life stress on depressive symptoms among young adults was moderated by a positive parenting style; and (5) the role of stress and anxiety as transdiagnostic factors in mental disorders, be it as an etiological factor, a variable contributing to symptom maintenance, or as a consequence of the condition itself. Stress, e.g., as a common denominator for a broad variety of psychiatric diagnoses has been extensively discussed, and stress as an etiological factor holds specific significance in the context of transdiagnostic approaches to the conceptualization and treatment of mental disorders (Wilamowska et al. 2010). The HPA axis, specifically, is widely known to be dysregulated in various conditions. Fischer et al. (2021) discuss in their comprehensive review the role of this important stress system in the context of patients with post-traumatic disorder. Specifically focusing on the cortisol awakening response, Rausch and colleagues provide evidence for HPA axis dysregulation in patients diagnosed with borderline personality disorder (Rausch et al. 2021). As part of a longitudinal project on ADHD, Szep et al. (2021) investigated the possible impact of child and maternal ADHD symptoms on mothers' perceived chronic stress and hair cortisol concentration; although there was no direct association, the findings underline the importance of taking stress-related assessments into consideration in ADHD studies. As the HPA axis is closely interacting with the immune system, Rhein et al. (2021) examined in their study the predicting role of the cytokine IL-6 on psychotherapy outcome in patients with PTSD, indicating that high reactivity of IL-6 to a stressor at the beginning of the therapy was associated with a negative therapy outcome. The review of Kyunghee Kim et al. (2021) also demonstrated the critical role of immune pathways in the molecular changes due to antidepressant treatment. As for the therapy, the important role of cognitive-behavioral therapy with its key elements to address both stress and anxiety reduction have been shown in two studies in this special issue, evidencing its successful application in obsessive-compulsive disorder (Ivarsson et al. 2021; Hollmann et al. 2021). Thus, both stress and anxiety are crucial transdiagnostic factors in various mental disorders, and future research needs elaborate further on their role in etiology, maintenance, and treatment.

In conclusion, a number of important questions are being asked in stress and anxiety research, as has become evident above. The Special Issue on "Recent developments in stress and anxiety research" attempts to answer at least some of the raised questions, and I want to invite you to inspect the individual papers briefly introduced above in more detail.

References

- al'Absi M, Nakajima M, Bruehl S (2021) Stress and pain: modalityspecific opioid mediation of stress-induced analgesia. J Neural Transm. https://doi.org/10.1007/s00702-021-02401-4
- Bentele UU, Meier M, Benz ABE, Denk BF, Dimitroff SJ, Pruessner JC, Unternaehrer E (2021) The impact of maternal care and blood glucose availability on the cortisol stress response in fasted women. J Neural Transm (Vienna). https://doi.org/10.1007/ s00702-021-02350-y
- Campbell J, Ehlert U (2012) Acute psychosocial stress: does the emotional stress response correspond with physiological responses? Psychoneuroendocrinology 37(8):1111–1134. https://doi.org/10. 1016/j.psyneuen.2011.12.010
- Denk B, Dimitroff SJ, Meier M, Benz ABE, Bentele UU, Unternaehrer E, Popovic NF, Gaissmaier W, Pruessner JC (2021) Influence of stress on physiological synchrony in a stressful versus non-stressful group setting. J Neural Transm (Vienna). https://doi.org/10. 1007/s00702-021-02384-2
- Dickerson SS, Kemeny ME (2004) Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol Bull 130(3):355–391
- Fischer S, Schumacher T, Knaevelsrud C, Ehlert U, Schumacher S (2021) Genes and hormones of the hypothalamic-pituitary-adrenal

axis in post-traumatic stress disorder. What is their role in symptom expression and treatment response? J Neural Transm (vienna). https://doi.org/10.1007/s00702-021-02330-2

- Hollmann K, Allgaier K, Hohnecker CS, Lautenbacher H, Bizu V, Nickola M, Wewetzer G, Wewetzer C, Ivarsson T, Skokauskas N, Wolters LH, Skarphedinsson G, Weidle B, de Haan E, Torp NC, Compton SN, Calvo R, Lera-Miguel S, Haigis A, Renner TJ, Conzelmann A (2021) Internet-based cognitive behavioral therapy in children and adolescents with obsessive compulsive disorder: a feasibility study. J Neural Transm. https://doi.org/10. 1007/s00702-021-02409-w
- Ivarsson T, Melin K, Carlsson A, Ljungberg M, Forssell-Aronsson E, Starck G, Skarphedinsson G (2021) Neurochemical properties measured by ¹H magnetic resonance spectroscopy may predict cognitive behaviour therapy outcome in paediatric OCD: a pilot study. J Neural Transm. https://doi.org/10.1007/ s00702-021-02407-y
- Keijser R, Olofsdotter S, Nilsson WK, Åslund C (2021) Three-way interaction effects of early life stress, positive parenting and FKBP5 in the development of depressive symptoms in a general population. J Neural Transm. https://doi.org/10.1007/ s00702-021-02405-0
- Kuhn L, Noack H, Skoluda N, Wagels L, Rohr AK, Schulte C, Eisenkolb S, Nieratschker V, Derntl B, Habel U (2021) The association of the 5-HTTLPR polymorphism and the response to different stressors in healthy males. J Neural Transm (Vienna). https://doi. org/10.1007/s00702-021-02390-4
- Kyunghee Kim H, Zai G, Hennings J, Müller DJ, Kloiber S (2021) Changes in RNA expression levels during antidepressant treatment: a systematic review. J Neural Transm. https://doi.org/10. 1007/s00702-021-02394-0
- Lazarus RS, Folkman S (1984) Stress, appraisal, and coping. Springer Publisher Company Inc, New York
- McEwen BS (1998) Protective and damaging effects of stress mediators. N Engl J Med 338(3):171–179
- Nater UM (2018) The multidimensionality of stress and its assessment. Brain Behav Immun 73:159–160. https://doi.org/10.1016/j. bbi.2018.07.018
- Rausch J, Flach E, Panizza A, Brunner R, Herpertz SC, Kaess M, Bertsch K (2021) Associations between age and cortisol

awakening response in patients with borderline personality disorder. J Neural Transm. https://doi.org/10.1007/s00702-021-02402-3

- Rhein C, Hepp T, Kraus O, von Majewski K, Lieb M, Rohleder N, Erim Y (2021) Interleukin-6 secretion upon acute psychosocial stress as a potential predictor of psychotherapy outcome in posttraumatic stress disorder. J Neural Transm (Vienna). https://doi.org/10.1007/ s00702-021-02346-8
- Sattler FA, Nater UM, Mewes R (2021) Gay men's stress response to a general and a specific social stressor. J Neural Transm (Vienna). https://doi.org/10.1007/s00702-021-02380-6
- Skoluda N, Piroth I, Gao W, Nater UM (2021) HOME vs. LAB hair samples for the determination of long-term steroid concentrations: a comparison between hair samples collected by laypersons and trained research staff. J Neural Transm (Vienna). https://doi.org/ 10.1007/s00702-021-02367-3
- Stoffel M, Abbruzzese E, Rahn S, Bossmann U, Moessner M, Ditzen B (2021) Covariation of psychobiological stress regulation with valence and quantity of social interactions in everyday life: disentangling intra- and interindividual sources of variation. J Neural Transm (Vienna). https://doi.org/10.1007/s00702-021-02359-3
- Szep A, Skoluda N, Schloss S, Becker K, Pauli-Pott U, Nater UM (2021) The impact of preschool child and maternal attention-deficit/hyperactivity disorder (ADHD) symptoms on mothers' perceived chronic stress and hair cortisol. J Neural Transm (Vienna). https://doi.org/10.1007/s00702-021-02377-1
- Vatheuer CC, Vehlen A, von Dawans B, Domes G (2021) Gaze behavior is associated with the cortisol response to acute psychosocial stress in the virtual TSST. J Neural Transm (Vienna). https://doi. org/10.1007/s00702-021-02344-w
- Wilamowska ZA, Thompson-Hollands J, Fairholme CP, Ellard KK, Farchione TJ, Barlow DH (2010) Conceptual background, development, and preliminary data from the unified protocol for transdiagnostic treatment of emotional disorders. Depress Anxiety 27(10):882–890. https://doi.org/10.1002/da.20735

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.