Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Stress research during the COVID-19 pandemic and beyond

Lena Sophie Pfeifer [a,*], Katrin Heyers [b,c], Sebastian Ocklenburg [b,1], Oliver T. Wolf [a,1]

[a] *Cognitive Psychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Bochum, Germany*
[b] *Biopsychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Bochum, Germany*
[c] *General Psychology II and Biological Psychology, Institute of Psychology, School of Human Sciences, Osnabrück University, Osnabrück, Germany*

A B S T R A C T

The COVID-19 pandemic confronts stress researchers in psychology and neuroscience with unique challenges. Widely used experimental paradigms such as the Trier Social Stress Test feature physical social encounters to induce stress by means of social-evaluative threat. As lockdowns and contact restrictions currently prevent in-person meetings, established stress induction paradigms are often difficult to use. Despite these challenges, stress research is of pivotal importance as the pandemic will likely increase the prevalence of stress-related mental disorders. Therefore, we review recent research trends like virtual reality, pre-recordings and online adaptations regarding their usefulness for established stress induction paradigms. Such approaches are not only crucial for stress research during COVID-19 but will likely stimulate the field far beyond the pandemic. They may facilitate research in new contexts and in homebound or movement-restricted participant groups. Moreover, they allow for new experimental variations that may advance procedures as well as the conceptualization of stress itself. While posing challenges for stress researchers undeniably, the COVID-19 pandemic may evolve into a driving force for progress eventually.

1. Introduction

Feeling stressed is familiar to all of us as in our everyday life we encounter numerous situations that may be perceived as stressful (e.g., having to give an oral presentation at work, acting under time pressure, or facing the next exam). Stress is often defined as a state in which external demands exceed internal resources, causing the organism to initiate a neuroendocrine stress response (Lazarus, 1993). First, this leads to activation of the sympathetic nervous system (SNS) which causes catecholamines such as adrenaline and noradrenaline to be secreted by the adrenal medulla and physiological parameters such as heart rate, blood pressure, or sweating to increase (Goldstein, 1987; Joëls and Baram, 2009; Mason, 1968). Second, the hypothalamus-pituitary-adrenal cortex (HPA) axis is activated (Aguilera, 2011). This initiates a hormonal cascade which terminates in the release of glucocorticoids such as cortisol that target cells across the whole body (de Kloet et al., 2005). Glucocorticoids have been shown to affect various cognitive processes like decision-making (Shields et al., 2016; Starcke and Brand, 2016), memory (Wolf, 2009), or extinction learning and its relapse (Meir Drexler et al., 2019). The induced changes

are assumed to help the organism to meet current environmental demands. The acute stress response is hence considered an adaptive coping mechanism. However, when stress is experienced too strongly or too frequently, it is likely to harm the organism (Epel et al., 2018; McEwen, 1998). While substantial progress has been made during the last decades, the exact mechanisms and the complex interactions between genetic and environmental risk factors across the life span are still insufficiently understood (Ehlert et al., 2001; Zänkert et al., 2019).

The ongoing COVID-19 pandemic can be characterized as a universal and chronic stressor affecting people worldwide and across all sections of society. Hence, it has the potential to cause a public mental health crisis of unprecedented dimensions (Pfefferbaum and North, 2020). Taking into account the ongoing increase in the prevalence of mental health problems (Baxter et al., 2014; Cohen and Janicki-Deverts, 2012; DeVries and Wilkerson, 2003), this review article (1) outlines the urgent need to conduct experimental stress research using standardized stressors during the current COVID-19 pandemic; (2) discusses conceptual as well as methodological challenges the discipline is confronted with in this peculiar situation; and (3) reviews trends, perspectives, and technological advances in order to solve the conflict between the urgent

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* Corresponding author at: Lena Sophie Pfeifer (Cognitive Psychology, Ruhr University Bochum, Universitätsstraße 150, Room: IB 6/77, 44780, Bochum, Germany).
E-mail address: lena.pfeifer@rub.de (L.S. Pfeifer).
[1] Shared senior-authorship.

need and the procedural challenges for stress research during the COVID-19 pandemic and beyond.

2. The need for stress research during the current COVID-19 pandemic

In recent years, the prevalence of stress-related mental disorders has been following an upward trend (Baxter et al., 2014; Cohen and Janicki-Deverts, 2012; DeVries and Wilkerson, 2003), causing both individual burden and financial and social problems for society as a whole (Hassard et al., 2018; Trautmann et al., 2016). In general, stress has been discussed as a crucial factor in etiological diathesis-stress models of mental disorders (Cohen et al., 2016; Cohen et al., 2007; Ottenweller et al., 1989) such as posttraumatic stress disorder (PTSD; Yehuda, 2002) and anxiety disorders (Sandín and Chorot, 1993; Shin and Liberzon, 2010), depression (Colodro-Conde et al., 2018; Musliner et al., 2015), or neurodevelopmental (Gunnar and Quevedo, 2007; Huizink et al., 2003) and psychotic disorders (Thompson et al., 2007).

Assuming that stress is of crucial relevance in the development of these mental disorders, it must be emphasized that the COVID-19 pandemic may function as an additional stressor. This hypothesis is based on the fact that the pandemic is novel, unpredictable, and uncontrollable (three key features of stressors) (Mason, 1968). Moreover, the political measures imposed to prevent the virus from further spreading may also be perceived as stressful. The latter has been confirmed by public surveys (Groarke et al., 2020; Kowal et al., 2020; Qiu et al., 2020). In particular, many individuals express concerns about COVID-19 infections, altered everyday life routines, and great uncertainty regarding future developments (Amirkhan, 2021; Hagger et al., 2020; Mahmud et al., 2021). Among others, health care workers (Bohlken et al., 2020; Chew et al., 2020; Spoorthy et al., 2020) and individuals who have lost their jobs or face financial problems due to the pandemic report increased levels of stress (Achdut and Refaeli, 2020; Blustein et al., 2020). Similarly, people who experience loneliness on account of strict contact restrictions (Brooks et al., 2020; Groarke et al., 2020) as well as parents struggling with childcare with schools and kindergartens being closed (Brown et al., 2020) were revealed to be under extreme stress. Therefore, the COVID-19 pandemic, due to being chronic and universal, must be considered a unique stressor that will have severe implications for health and wellbeing.

2.1. Epidemiological and clinical stress research

Recent studies have revealed heightened levels of anxiety and depression during the ongoing pandemic, with specific factors such as social or lower economic resources influencing stress perception (Bueno-Notivol et al., 2021; Ettman et al., 2020; Kowal et al., 2020). Holman et al. (2020), at an early but critical phase of the unfolding pandemic in the U.S., used a probability-based approach in a nationally representative sample to predict the progression of mental disorders. The authors reported that (1) individuals with pre-existing health problems, (2) individuals exposed to secondary stressors, and (3) individuals with increased exposure to COVID-19 related media coverage are particularly at risk for adverse mental health outcomes. Along these lines, Boyraz and Legros (2020) and Bridgland et al. (2021) highlight that the pandemic may even constitute a traumatic experience which could increase the prevalence of PTSD.

In the past, events such as 9/11 (Laugharne et al., 2007; Lowell et al., 2018; Neria et al., 2011; Yehuda, 2002), school shootings (Rossin-Slater et al., 2020), or natural disasters such as earthquakes (Garfin et al., 2014) or hurricanes (Ironson et al., 1997) have caused surges in mental health problems. The Great Recession in 2007–2009 led to an increase in mental health issues (Margerison-Zilko et al., 2016). For pandemics, data on previous epidemics such as the Middle East Respiratory Syndrome (MERS; e.g., Jeong et al., 2016) or the Severe Acute Respiratory Syndrome (SARS; e.g., Chan et al., 2006) reveal an increase in mental

health problems. Based on these findings, one can conclude that the COVID-19 pandemic as a universal and long-lasting stressor will have comparably devastating consequences. Kickbusch et al. (2020) even call it "[….] the biggest threat in living memory to health and wellbeing, social welfare, and the global economy", implying that it is of greater destructive power than every former crisis of the more recent past. To illustrate the implications of the COVID-19 pandemic on society and research, Fig. 1 provides a schematic diagram of stressors encountered in laboratory contexts and in everyday life, along with their relevance for basic, clinical, and epidemiological stress research.

Other approaches, however, reverse the causality and suggest that stress, or more specifically stress overload, serves to explain an unsolved variance in the actual spread of COVID-19. Given that infections were distributed unequally over different countries and social classes, Amirkhan (2021), for example, hypothesized stress to increase the individual susceptibility for COVID-19 infection. In line with this, evidence has been accumulating on chronic stress impairing immune function thereby increasing the risk for and the severity and duration of infectious diseases or other illness episodes (Glaser and Kiecolt-Glaser, 2005).

To conclude, various lines of research confirm a relation between stress and adverse health outcomes under conditions of COVID-19, highlighting the urgent need to consider the pandemic a public health priority (Ettman et al., 2020; Pfefferbaum and North, 2020). This also entails high societal relevance of stress research under these extraordinary circumstances. On the one hand, epidemiological and clinical perspectives are needed to understand the impact of the COVID-19 pandemic (Daly and Robinson, 2021; Ettman et al., 2020; Khan et al., 2020). On the other hand, basic stress research is of special relevance in the current pandemic, as will be outlined below.

2.2. Basic stress research

In addition to epidemiological and clinical stress research during the pandemic, we argue that basic stress research can provide fundamental insights that are crucial for clinical applications. In this context, basic research already yielded studies on acute laboratory stress that had direct or indirect consequences for clinical practice. For example, Pruessner et al. (1997) and Kirschbaum et al. (1995) provided first evidence that cortisol response kinetics characterized by lacking habituation towards repeated stress exposure might represent a marker for health. Buske-Kirschbaum et al. (2003) and Buske-Kirschbaum et al. (2010) supported this idea by showing blunted cortisol responsiveness in atopic diseases. Finally, such findings can be integrated in theoretical considerations on allostatic load introduced by McEwen (1998).

Along these lines, clinical approaches to stress during COVID-19 should be paralleled by basic research integrating relevant information into a general consent on fundamental mechanisms. Clinical conditions typically manifest progressively, often starting with rather subtle symptoms (Myin-Germeys et al., 2009; van Os et al., 2009). Considering psychopathological outcomes related to COVID-19 to be an extreme on a wider continuum, it would be simplistic to only focus on people with manifest clinical symptoms. Instead, it seems conceivable that even individuals not meeting diagnostic criteria may have undergone subclinical and latent changes (Khan et al., 2020). These may be caused by stress-related changes in brain function and brain structure. In this context, previous works has suggested associations between chronic stress and reduced volume in prefrontal and limbic regions (Ansell et al., 2012; Berretz et al., 2021) and altered functional connectivity within frontoparietal brain circuits (Liston et al., 2009).

Salomon et al. (2020) investigated stress-related brain plasticity at an early stage of the pandemic in Israel using magnet resonance imaging (MRI). The authors scanned healthy participants before and after the outbreak of the pandemic and analyzed volumetric alterations in the brain relative to control participants scanned twice under pre-pandemic conditions. Salomon et al. (2020) found volumetric increases in brain regions implicated in the neural circuits of stress and anxiety.
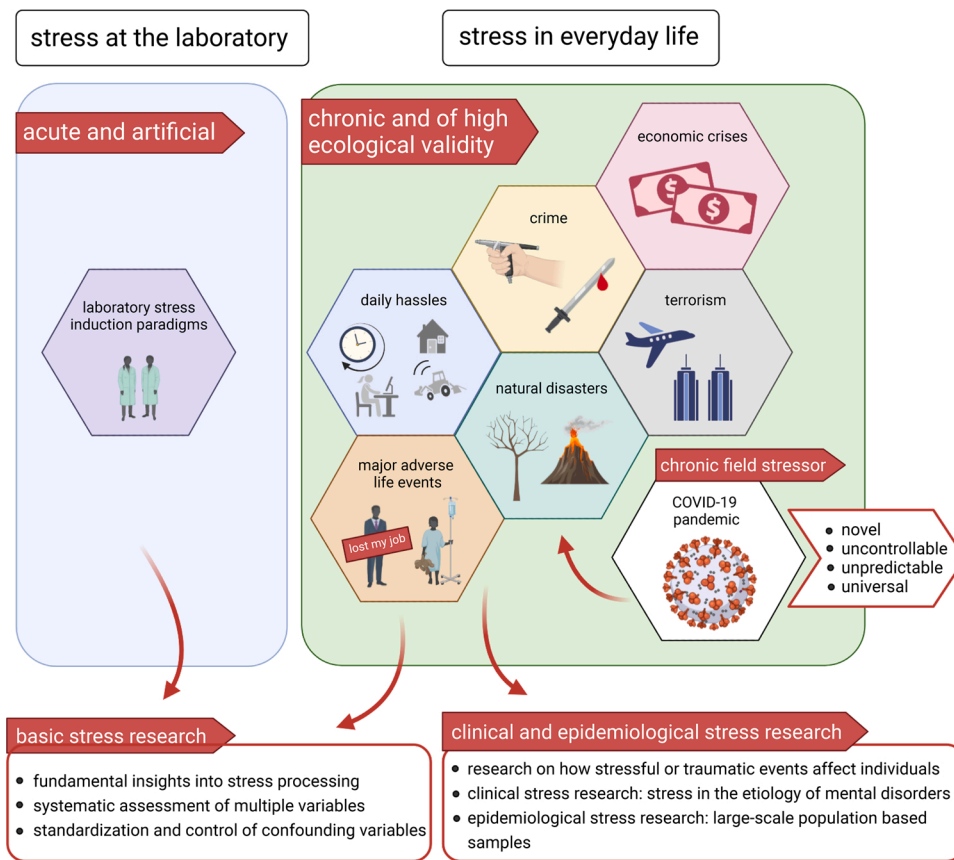
Fig. 1. Schematic illustration of how stress can be induced in the laboratory or experienced in everyday life, and of their relevance for basic and clinical or epidemiological stress research. In the laboratory, researchers make use of standardized stress induction paradigms that are acute and well-controlled, but also rather artificial. In everyday life, we are confronted with various stressors that are rather chronic and of interest for basic as well as clinical and epidemiological stress research. Basic stress research acknowledges field stressors because of their high ecological validity. Therefore, some events of stressful or traumatic nature have already been subject of stress research. The COVID-19 pandemic can be considered a chronic field stressor that bears a potential for clinical and epidemiological as well as for basic stress research. Created with BioRender.com.

Importantly, these findings confirm that the COVID-19 pandemic is capable of inducing changes on a neural level not only for those who were actually infected with the virus (Crunfli et al., 2020; Lu et al., 2020).

Pandemic-related changes might also manifest as slight changes of habits on a behavioral level. For instance, alcohol consumption has been shown to have increased in some countries (Calina et al., 2021; Ingram et al., 2020). Such maladaptive ways of coping with stress can themselves adversely affect individual health and increase the risk for contracting COVID-19 and/or developing other physical or mental illnesses (Gouin, 2011).

By trying to unravel subtle as well as severe alterations caused by adverse conditions during the COVID-19 pandemic, basic stress research can complement epidemiological or clinical approaches. Assuming that stress is a significant factor in the ontogenesis of mental disorders, its effects are likely mediated by physiological or endocrine processes of the HPA axis or the SNS (Ehlert et al., 2001; Zänkert et al., 2019). Specific pathways, however, are rarely assessed in large-scale population studies as it is costly and laborious to collect physiological markers such as saliva samples from larger cohorts (Adam and Kumari, 2009; Friedman et al., 1988). Basic stress research can close this gap because it can assess multiple physiological and neural stress markers. A combination of comprehensive assessment of the stress response and the fundamental strengths of laboratory research (e.g., control of confounding variables, standardization of experimental procedures) has been successful in identifying sources of intra- and interindividual variability (Ehlert et al., 2001; Zänkert et al., 2019). Taking these factors into account may clarify how and why individuals differ in their vulnerability to stress-related health problems (Epel et al., 2018; McEwen, 1998).

With regard to how COVID-19 related basic stress research may enrichen our general understanding of human stress processing, it is still debated whether chronic levels of increased stress affect acute stress

processing (Kudielka and Wüst, 2010; Lam et al., 2019; Matthews et al., 2001). A growing body of literature indicates that chronic or cumulative stress leads to insensitivity towards acute stressors as reflected in a dampened stress response (Fries et al., 2005; Lam et al., 2019; Matthews et al., 2001; Sandner et al., 2020). However, systematic studies on this matter are as yet sparse, as it is ethically not justified to expose participants to chronic stress and thereby put them at risk for poor mental health outcomes for research purposes only.

The issue of chronic stress was extensively discussed by McEwen (1998). In the laboratory, he found evidence for four scenarios in which the allostatic response that is adaptive under normal conditions is initiated (1) too often, (2) too long, (3) not at all, or (4) lacks environmental adaptation. Assuming that the COVID-19 pandemic may force the organism to show one or more of these maladaptive response patterns, it can be considered a unique opportunity to advance our general knowledge of chronic stress.

Similarly, everyday life typically confronts us with stressors that persist over longer periods of time and lack a clear beginning or ending (Epel et al., 2018). Therefore, naturalistic stressors resemble those conditions leading to allostatic load as suggested by McEwen (1998). Investigating chronic stress is thus of higher ecological validity than solely focusing on its acute counterpart. Such ecological validity would further be enhanced by the fact that COVID-19 constitutes a real-world field stressor that is personally relevant for the designated individual (Rohleder et al., 2007). As under normal conditions, basic stress researchers are restricted to experimental stress induction that is rather artificial in nature, it has often been questioned to what extent laboratory findings expand to real world scenarios (Johnston et al., 2008; Rohleder et al., 2007; Turner et al., 1990; van Doornen and van Blokland, 1992). Taken together, the COVID-19 pandemic can be considered an excellent opportunity to assess stress in a field context.

Some researchers have already recognized this potential and

operationalized the COVID-19 pandemic as an independent variable in ongoing experiments. For example, Somma et al. (2021) had collected data from a range of behavioral tests assessing asymmetry of visual-spatial attention in a larger sample right before COVID-19 quarantine in Italy. They repeated their measurement in a subsample several months later and demonstrated that quarantine further lateralized their participants' performance outcomes. This shows that the COVID-19 pandemic had a significant influence on visual-spatial information processing. Further studies could clarify in how far it also affected other cognitive and behavioral domains and how putative alterations could relate to mental health and wellbeing in general.

Despite its high ecological validity, the COVID-pandemic may not meet all quality criteria for experimental research. In particular, the pandemic as well as other field stressors do not represent uniformly standardized stressors and thus bear many confounding variables (Amirkhan, 2021; Bueno-Notivol et al., 2021; Kowal et al., 2020). Therefore, stress researchers are still reliant on laboratory stress induction. Decades of well-controlled laboratory research have led to the development of highly reliable experimental paradigms for stress induction, such as the Trier Social Stress Test (TSST; Allen et al., 2017; Dickerson and Kemeny, 2004; Goodman et al., 2017; Kirschbaum et al., 1993). Unfortunately, it is these well-established protocols that cause stress researchers to face huge challenges during the COVID-19 pandemic.

3. Challenges for stress research during the current COVID-19 pandemic

Most laboratory stress research paradigms designed for human participants rely on exposing them to situations containing elements of social-evaluative threat. In comparison to other features of a stressor, the social-evaluative component is considered particularly crucial

(Dickerson and Kemeny, 2004). Its importance is explained by the *Social Self Preservation Theory* (Dickerson et al., 2004; Kemeny et al., 2004). According to this theory, humans (as well as primates and other animals) do not only strive to preserve their physical wellbeing but also their social self and their social status. Any threat to one's social integrity is registered by the so-called *social self-preservation system* which provokes specific biological responses to combat the threat. These biological responses are suggested to be supported by the HPA axis (Dickerson et al., 2004; Dickerson and Kemeny, 2004; Kemeny et al., 2004). Given that in our everyday life, stress is mostly experienced in social contexts (von Dawans et al., 2021), social-evaluative threat accounts for a substantial portion of the ecological validity of laboratory stress induction paradigms.

For this reason, most commonly used stress induction paradigms include some sort of social-evaluative threat, which is per definition most effectively produced in human interactions such as in-person social encounters. For example, in the TSST, participants must perform a mock job interview and solve challenging arithmetic tasks while being judged by a panel of reviewers who do not provide any feedback (Kirschbaum et al., 1993). As the TSST has been shown to reliably produce significant release of cortisol (Kirschbaum et al., 1993), this paradigm demonstrates the effectiveness of explicit social-evaluative components for successful stress induction. Other paradigms which include social evaluation are the Socially Evaluated Cold-Pressor Test (SECPT; Schwabe et al., 2008), the Simple Singing Stress Procedure (SSSP; Le et al., 2020), and the Maastricht Acute Stress Test (MAST; Smeets et al., 2012). Since these common stress induction paradigms depend on the social-evaluative element, it is difficult to use them during COVID-19 due to contact restrictions and stay-at-home practices (Table 1).

Of note, stress induction paradigms such as the TSST may still be applied in research laboratories during the pandemic, with adaptations made due to COVID-19 (Table 1). For example, it seems feasible to

Table 1
Most commonly used stress induction paradigms in their feasibility under circumstances of the COVID-19 pandemic as assessed by the following three criteria: (1) Apart from any contact with the experimenter, do they include a social interaction for stress inductive purposes that requires a physical social encounter? (2) Are facial expressions of the source of the social-evaluative threat important for the paradigm's stress inductive potential so that face masks may restrict their success? (3) Do they require the participant to come to the laboratory? In (4), we evaluate if the paradigms are feasible with unchanged stress inductive potential under conditions of the COVID-19 pandemic.

Stress induction paradigm	(1) Physical social encounter for stress inductive purposes?	(2) Importance of facial expressions?	(3) Presence at the laboratory?	(4) Result: COVID-19 compatible?
TSST (original)	✓	✓	✓	X
TSST (with adaptations)*	✓	?	✓	✓
CPT	X	X	✓	X
SECPT	✓	✓	✓	X
SSSP	X	X**	✓	X
PASAT-C	X	X	✓	X
MMST	X	X	✓	X
MAST	X	✓	✓	X
MIST	X	X	✓	X
SET	X	X	✓	X
ScanSTRESS	X	✓	✓	X
MISTiC	X	✓	✓	X
IMPRESS	X	✓***	✓	X

Abbreviations: TSST = Trier Social Stress Test; CPT = Cold-Pressor Test; SEPCT = Socially Evaluated Cold-Pressor Test; SSSP = Simple Singing Stress Procedure; PASAT-C = Paced Auditory Serial Addition Task – Computer Version; MMST = Mannheim Multicomponent Stress Test; MAST = Maastricht Acute Stress Test; MIST = Montreal Imaging Stress Test; SET = Social-Evaluative Threat Paradigm; MISTiC = Minnesota Imaging Stress Test in Children; IMPRESS = Imaging Paradigm for Evaluative Social Stress.

*Note that the TSST might still be conducted during the COVID-19 pandemic with adaptations made to the procedures. These may include that all people involved (experimenter, panel members, participants) wear face masks or keep an adequate distance (using shields, different rooms, windows and intercom systems). For such adaptations, however, future research needs to clarify in how far they alter the effectivity of the TSST.

**Note that even though facial expressions are not crucial for stress induction in the SSSP as the participant is not confronted with a panel and the experimenter is standing behind the participant during the singing procedure, face masks may severely impair participants while singing.

***Note that in the IMPRESS paradigm, participants are confronted with a panel that may convey social-evaluative threat via facial expressions but that the panel is pre-recorded. Therefore, under conditions of the COVID-19 pandemic, it may be possible to show a video that was recorded under pre-pandemic conditions in which panel members were not required to wear masks.

conduct a TSST setting an adequate distance between participant and panel by using shields, different rooms, windows or intercom systems and by ensuring that all people involved wear face masks. To the best of our knowledge, several laboratories opted to adapt TSST-procedures in such a way implementing shields and face wearing for people involved including panel members (Heinrichs, 2021, pers communication; Pützer and Wolf, 2021, pers communication; Rohleder, 2021, pers communication). Even though such adaptations may probably not render the TSST ineffective, it is conceivable that they alter the paradigm's impact. In particular, wearing of face masks might not be an ideal solution. For example, it has been shown that they impair social communication (Calbi et al., 2021; for a review on masks affecting face reading, see Pavlova and Sokolov, 2021). Hence, it is reasonable to assume that masks covering facial expressions may also alter social-evaluative components in stress induction procedures.

As far as we can conclude from the literature, this hypothesis has yet not been experimentally tested. However, there is evidence in children supporting this assumption. For example, Guarnera et al. (2015) report that neutral expressions were better discriminated when the mouth region of a face was shown. In the TSST, the panel is instructed to maintain a neutral expression in order to not provide any feedback (Kirschbaum et al., 1993). Therefore, the mouth region – that is covered by face masks – may be of great importance to effectively convey this attitude. On the contrary, one may argue that face masks may even help panel members to not show any feedback and to keep their neutral attitude. Along these lines, one may, however, still doubt whether face masks may be considered neutral themselves as for many people they may represent the epitome of the COVID-19 pandemic and hence be associated with negative emotions and unpleasant memories. Future research should empirically test in how far TSST-procedures adapted for mask wearing may alter the effectiveness of the paradigm.

Of course, there are stress induction paradigms without an explicit social-evaluative component such as the Paced Auditory Serial Addition Task - Computer Version (PASAT-C; Lejuez et al., 2003), the Mannheim Multicomponent Stress Test (MMST; Reinhardt et al., 2012) or the Cold-Pressor Test (CPT; first described by Hines and Brown (1932)). In turn, these paradigms are also less powerful in activating HPA-related parameters of the stress response. However, these paradigms, among all others, also require a presence at the laboratory and are thus still difficult to apply at the time of a pandemic (Table 1).

As a result, the COVID-19 pandemic has challenged stress researchers to re-evaluate their methodological repertoire regarding the need for presence at the laboratory (Kirschbaum, 2021). As Table 1 illustrates, stress researchers can either choose between paradigms that feature a social-evaluative component in form of an in-person social encounter (TSST, SECPT, SSSP, MAST) or paradigms that lack social-evaluative elements (CPT, PASAT-C, MMST).

While the significance of psychosocial components for stress induction is undisputed, this does not necessarily imply that in-person encounters are needed to implement social-evaluative threat. Along these lines, alternative approaches for laboratory stress induction are needed during COVID-19. Once established, such approaches may also stimulate the field beyond the pandemic.

4. Perspectives for stress research during the current COVID-19 pandemic

As outlined above, it is their social-evaluative component that mainly impedes the use of established stress induction paradigms under conditions of the COVID-19 pandemic. Even though we mentioned experimental approaches that lack this component, it is generally regarded a key to valid and ecological stress induction. Therefore, it is worth asking whether stress researchers are forced to decide between (a) conducting (less efficient) stress induction without social-evaluative threat, (b) suspending their studies until the end of the pandemic, or (c) whether there are some promising alternatives to the induction of psychosocial stress.

Recent work indicates that it is possible to deviate from in-person social encounters of participants and panel in order to create social-evaluative threat. For example, Andrews et al. (2007) demonstrated that stress reactivity can be achieved by means of an invisible TSST panel. Düsing et al. (2016), amongst others, triggered significant elevations in cortisol levels by replacing the panel by a video camera. Of note, Düsing et al. (2016) considered their application a milder version of the TSST and accordingly expected a less pronounced increase in cortisol levels. This is in line with Dickerson and Kemeny (2004) who provided meta-analytic evidence that stronger social evaluation produces larger effects sizes. This suggests that it is not sufficient to consider differences in mean cortisol release as these do not take into account the strength of cortisol reactivity. In sum, one may conclude that HPA axis reactivity may be a function of the intensity of the social-evaluative component which one can manipulate according to individual research proposes (Andrews et al., 2007). For basic stress research, it may be desirable to implement significant social-evaluative threat (feasible under the given circumstances) in order to achieve substantial cortisol reactivity.

Labuschagne et al. (2019) concluded that due to the short methodological description of the TSST in the original publication, the paradigm likely varies with respect to its actual administration in different laboratories. Although this may account for differences observed in participants' stress responses between different laboratories and different studies, the general effectiveness of the TSST seems highly conserved. Therefore, future research should clarify which procedural components are truly central to the validity of the paradigm and which ones are rather optional or may serve as target for further adaptations. Narvaez Linares et al. (2020), for example, provided a recent systematic overview over methodological variations of TSST applications over different laboratories and reveal several factors (e.g., number of panel members, number from which serial subtraction is started) that may impede reliability and replicability for this paradigm.

4.1. Stress research in the MRI scanner

Importantly, research contexts in which in-person encounters of participants and panel are not feasible already exist. The MRI setting - which harbors great potential to advance our knowledge about the neural mechanisms of stress processing – renders it impossible to produce social-evaluative threat by means of direct social confrontation (Noack et al., 2019). However, several different solutions for neuroimaging stress induction in the scanner have been suggested (Berretz et al., 2021).

For example, in the Social-Evaluative Threat Paradigm (SET; e.g., Eisenbarth et al., 2016), participants are instructed to prepare for a speech that will be recorded and evaluated by others that are not actually present. In the Montreal Imaging Stress Task (MIST; Dedovic et al., 2005), participants are asked to solve challenging arithmetic tasks under extreme time pressure while feedback on their average performance relative to the performance of alleged other participants is given. Furthermore, in the ScanSTRESS paradigm (Streit et al., 2014), a panel is physically present but seated in the control room of the scanner. The panel is shown on the participant's screen via a live video feed in order to provide individual (disapproving) feedback on the participant's performance in arithmetic tasks. For adolescents a similar approach is implemented in the Minnesota Imaging Stress Test in Children (MISTiC; Herzberg et al., 2020). Highly consistent with the original TSST, after a 5 min. preparation period, participants have to give a speech introducing themselves to a jury panel shown via live video feed while lying in the scanner. Afterwards, participants have to perform a multiple-choice arithmetic task. Whereas imaging is possible during the arithmetic task of this paradigm, the speech task cannot be accompanied by scanning due to interference of scanner noise with the task. Moreover, speaking-associated movements would negatively affect scanning

quality due to motion artefacts. Similarly, the recently developed Imaging Paradigm for Evaluative Social Stress (IMPRESS; Fehlner et al., 2020) requires participants to prepare and give a speech in front of a pre-recorded panel.

These adaptations to contextual challenges clearly suggest options for how established stress induction paradigms can be adjusted to new settings. Since the MRI setting and the current pandemic situation have in common that in-person encounters inducing social-evaluative threat are not feasible, researchers currently conducting laboratory stress research may find inspiration in the progress made in MRI-based stress research.

Importantly, for the MRI setting itself, different neuroimaging stress induction paradigms lead to overlapping but also distinct activations (Berretz et al., 2021). Therefore, further research in this field should define which paradigm is suited best for the individual study purposes. To this end, it is crucial to clarify whether there is a certain stereotypic neural stress response, and if so, how discrepancies produced by different stress induction paradigms can be explained (Berretz et al., 2021). In general, one can conclude that approaches to social-evaluative stress induction in the MRI context are promising and may help to advance basic laboratory stress research when it comes to remote stress induction.

4.2. Stress induction with virtual reality and pre-recordings

Regarding the TSST and its application in traditional laboratory settings, several adaptations of the procedure that aimed to render it independent of a physical panel had been published well before the onset of the COVID-19 pandemic (Helminen et al., 2019; Jönsson et al., 2010; Zimmer et al., 2019). These protocols can be classified into two broader categories: virtual reality and pre-recorded applications. In both cases, social-evaluative threat is realized without any in-person social encounter. In the virtual reality TSST (TSST-VR), participants are confronted with avatars in contrast to a real panel (Fallon et al., 2016; Helminen et al., 2019; Standard et al., 2020). In the context of the COVID-19 pandemic, such procedures reduce the number of people that meet at the laboratory and thereby reduce the risk for infection. However, this is still not completely without risks. For example, experimenters need to clean and disinfect VR devices which may be contaminated. In pre-recorded applications of the TSST, participants are exposed to a real panel, but this is neither presented in person nor in real-time, but in pre-recorded videos (DeJoseph et al., 2019; Hawn et al., 2015; Smith et al., 2020). More details on procedural aspects of TSST-VR and pre-recorded versions will be provided below, along with information on effect sizes.

Adapting both experimental paradigms and therapeutic interventions for virtual reality has been a key objective in a number of other research fields (Emmelkamp, 2005; Lohse et al., 2014; Slater, 2009). Virtual reality relies on computer-generated sensory input that resembles physical experience sufficiently enough to create the illusion of operating within real world scenarios (Fallon et al., 2016). On a neuronal level, such simulations suffice to activate a system that encodes imaginations of real-world scenarios in terms of schemas so that minimal computer-generated information is needed to trigger comprehensive concepts of social-evaluative threat (Fallon et al., 2016) or fear (Diemer et al., 2014; Parsons and Rizzo, 2008). Along these lines, even the confrontation with a virtual panel should evoke social conventions (Zimmer et al., 2019).

A recent meta-analysis by Helminen et al. (2019) on 13 studies using different versions of the TSST-VR providing a total sample size of n = 266 participants concluded that this procedure generally serves to successfully induce stress as indicated by a significant cortisol response. With ESsg = 0.65 (interpreted similar to effect sizes of Cohen's d according to Helminen et al. (2019)), the average size of this effect was moderate, suggesting that, albeit significant, the cortisol response elicited by TSST-VR seems to be smaller. In comparison, cortisol responses

in the standard TSST typically reach large effect sizes. For example, it has been approximated by d = 0.925 by Allen et al. (2014) or d = 0.93 by Goodman et al. (2017). Zimmer et al. (2019) as well as Shiban et al. (2016) who directly compared applications of the TSST in virtual reality and in vivo corroborate this. However, as the general patterns of cortisol reactivity largely resemble each other for the virtual and original versions of the TSST, these authors concluded that the TSST-VR has a similar power to the original TSST.

However, success in triggering the desired stress response might depend on technology providing the resolution needed to ensure a realistic feeling of being present in that virtual environment (Jönsson et al., 2010; Montero-López et al., 2016). Hence, one would assume that the more input is derived from the virtual reality (i.e., the more immersive the paradigm is), the stronger emerges the feeling of being involved and spatially present within this virtual world (Slater, 2009). This was also shown by Helminen et al. (2019) as effect sizes of individual studies using the TSST-VR seemed to be affected (amongst other factors) by the immersivity of the virtual environment. Specifically, these authors compared two groups of studies relying on high and low immersive environments and found greater mean effect sizes for studies using more immersive virtual realities. As a consequence, it seems desirable to opt for more immersive Computer Automatic Virtual Environment (CAVE) systems or head-mounted displays (Helminen et al., 2019).

Besides low immersivity, it is detrimental when participants take the position of an "observer" to the scene and cannot interact with the panel. Even though this aspect was not examined in its influence on effect sizes of individual studies in the meta-analysis by Helminen et al. (2019), low interactivity may severely diminish the experience of social-evaluative threat (Fallon et al., 2016; Jönsson et al., 2010). To prevent this in the TSST-VR, avatars representing the panel are programmed to show subtle gestures. These movements as well as other interactive features are typically activated by an experimenter who remains invisible for the participant. Doing so allows matching the behavior of the avatars with the performance of the participant in order to account for some sort of interaction (Fallon et al., 2016; Fich et al., 2014; Jönsson et al., 2010; Liu and Zhang, 2020). Some protocols do not only feature this situational flexibility for the panel's non-verbal appearance but make further use of pre-recorded audiotapes in order to give a voice to their panel (Jönsson et al., 2010; Santl et al., 2019; Shiban et al., 2016).

In contrast, Standard et al. (2020) addressed the idea of minimal interaction in a non-peer reviewed conference contribution by introducing a TSST-VR that runs independently of any experimenter. However, to the best of our knowledge, this procedure was not yet empirically tested so that it remains unclear whether it may suffice to trigger a substantial stress response.

TSST variants using pre-recorded panels are an alternative (or even add-on) to VR-based approaches. In this context, it was acknowledged that a TSST-VR might benefit from a pre-recorded panel as it resembles a real panel more than computer-generated avatars (Kelly et al., 2007). However, in-vivo application of the TSST still led to higher increases in cortisol levels (90 %) than the procedure introduced by Kelly et al. (2007) (30 %).

Other studies such as Hawn et al. (2015) or Smith et al. (2020) use pre-recorded panels in non-avatar 2D environments (not considered immersive by Helminen et al. (2019)). In comparison to a neutral condition, Hawn et al. (2015) reported their procedure to produce significant cortisol reactivity with an effect size of $\eta_p^2 = 0.11$ corresponding to a medium effect of d = 0.70. However, a traditional TSST procedure triggered greater cortisol levels compared to the pre-recorded version with $\eta_p^2 = 0.18$ (Hawn et al., 2015) corresponding to a large effect of d = 0.94. Smith et al. (2020), adapting the procedure to a TSST-C (Buske--Kirschbaum et al., 1997) for application amongst children, produced responder rates comparable to the original version of the TSST-C (Smith et al., 2020). Indeed, for adolescent participants, such TSST-variants are not new in that Westenberg et al. (2009), for example, used the so-called

Leiden Social Stress Test requiring adolescent participants to deliver a speech in front of a pre-recorded classroom of peers just a decade earlier. For their study it may be worth mentioning that participants were informed about the nature of the task in advance in order to prepare their speech at home. The delivery itself, however, was still performed at the laboratory. Interestingly, DeJoseph et al. (2019) chose the same video-based approach but conducted their study comprehensively at the children's homes, thereby introducing a home-based procedure of the TSST (TSST-H). While traveling is typically demanded from participants when they are invited to a laboratory, this study was quite unusual in that it sent researchers to their participants' local facilities. However, under pandemic conditions, both types of travels should be avoided. In the following, we therefore review approaches that do not involve traveling for either party.

4.3. Stress induction with online applications

Recently, online applications have further advanced the TSST protocol (Eagle et al., 2021; Gunnar et al., 2020; Harvie et al., 2021; Kirschbaum, 2021). As outlined in Section 4.2, one critical aspect that may reduce the success of stress induction in virtual reality or video-based applications of the TSST lies in restricted opportunities to interact with avatars or a pre-recorded panel. This issue is resolved in a recently developed online version of the TSST (TSST-OL), which implements the original protocol in a video communication software (Gunnar et al., 2020). In such online adaptations of the TSST, the panel still consists of real people who convene in real time.

In detail, in the TSST-OL, the investigator arranges an online meeting that participant as well as experimenter can participate in from home. Within this meeting, Gunnar et al. (2020) conserved the original administration of the TSST-C and demonstrated that their online version was able to elicit a significant cortisol response in adolescents. However, as yet, no study has directly compared the TSST-OL with the original in-person TSST administration. Therefore, it remains unknown whether an online application is similarly effective in triggering stress reactivity. Of note, Gunnar et al. (2020) provided an effect size of $d_z = 0.57$ for the peak in cortisol release. This is comparable with the most recent meta-analysis on the TSST-C (in the traditional application), approaching the mean effect size for cortisol reactivity with $d' = 0.47$. (Seddon et al., 2020). As Gunnar et al. (2020) further provide a detailed study protocol, they enable other laboratories to perform a direct comparison between online and in-person administration of the TSST. Kirschbaum (2021) – the developer of the original protocol – stated that modifications of the TSST to online settings are needed under conditions of the current COVID-19 pandemic, thereby encouraging such approaches.

Other publications are echoing the trend for online adaptations of the TSST (Eagle et al., 2021; Harvie et al., 2021). Both similarly applied the original TSST protocol in video conference software but referred to it as an internet-delivered TSST (iTSST) instead of the TSST-OL. While Gunnar et al. (2020) exclusively included adolescents in their study, Eagle et al. (2021) and Harvie et al. (2021) further established a highly similar procedure for adult participants. However, similar to the study by Gunnar et al. (2020), Eagle et al. (2021) lack a control condition. In contrast, Harvie et al. (2021) chose to expose all their participants to a stress as well as a control condition which was represented by an online adaptation of the placebo TSST (Het et al., 2009). Even though these three studies applied different methods of statistical hypotheses testing, they do come to the shared conclusion that online adaptations of the TSST serve well to trigger a stress response. This conclusion was based on self-reports of stress or stress questionnaires (Eagle et al., 2021; Gunnar et al., 2020; Harvie et al., 2021), sympathetic (Gunnar et al., 2020) and parasympathetic activation (Eagle et al., 2021; Harvie et al., 2021) as well as cortisol release (Gunnar et al., 2020).

The range of parameters used by different studies to validate the TSST-OL, however, is countered by the fact that individual studies often miss important dimensions of the stress response. For example, Harvie et al. (2021) as well as Eagle et al. (2021) did not measure HPA axis related variables. This may prevent a direct comparison to previous work with the standard TSST. To address this issue, we will discuss the comprehensive assessment of stress markers in Section 4.5. In general, for true validation of the TSST-OL, studies should strive for a multilevel assessment of the stress response including measures of self-reported stress as well as biomarkers shedding light on the overall activation under stress (Epel et al., 2018).

4.4. Stress induction with smartphones

In addition to online applications using computers, smartphones have a high potential to complete the methodological repertoire used in psychological (stress) research (Miller, 2012). In this context, several applications have been designed for usage among patient groups. For example, Wisniewski et al. (2019) designed a platform including a whole battery of simplified neuropsychological tests that appear in form of "games". More specifically, Lam et al. (2021) used smartphones to monitor cognitive functioning in multiple sclerosis (MS) patients by means of an app-based version of the Symbol Digit Modalities Test (SDMT; Smith, 1982, 1968). Since in both studies, the apps were compatible with common smartphone software, it seems conceivable to also apply them in healthy samples in order to address non-clinical research questions. Broader application was already intended for the *iDichotic* app (Bless et al., 2013), a smartphone-based implementation of the dichotic listening task. This app has been used successfully in a number of studies on language lateralization in participants from all over the world (Beste et al., 2018; Ocklenburg et al., 2016; Schmitz et al., 2018).

Stress induction via smartphone seems feasible in principle, given that it should be reasonably easy to run a TSST-OL in video communication software on smartphones. Compared to online adaptations, added value may lie in the increased portability of smartphones relative to laptop computers. However, small screen size might be problematic. For instance, Gunnar et al. (2020) only included participants if their devices had at least a 13-inch screen.

Nevertheless, smartphone applications allow data collection in larger samples than online versions (Bless et al., 2013). Moreover, smartphone-based research can be done without the supervision of any experimenter. This perspective was also emphasized by Torous et al. (2020), with a focus on the COVID-19 pandemic. These authors state that the current crisis requires asynchronous telehealth provided by app-based tools. For researchers, such a development may be considered beneficial as it strongly increases accessibility and scalability of data (Torous et al., 2020).

However, stress researchers might not benefit from unlimited scalability as studies typically depend on a more in-depth assessment of variables whose quality might suffer. In line with that, it is widely accepted that stress should not solely be measured by behavioral or self-reported parameters (Dickerson and Kemeny, 2004; Epel et al., 2018). Therefore, in the next paragraph, we will review techniques to ensure reliable assessment of stress markers in advanced versions of established stress induction protocols.

4.5. Beyond stress induction: assessment of the stress response

A factor that should not be omitted when evaluating new approaches to stress induction is the reliable assessment of stress markers (Harvie et al., 2021). The subjective psychological dimension of the stress response is typically assessed by means of questionnaires or other self-reports (Epel et al., 2018) which can easily be adapted to procedures such as the TSST-OL. Online survey software enables collection of self-reported data by means of a shared link and can be used to obtain subjective measures of stress during a video call on any device with stable internet connection.

Portable devices like smartphones further harbor the potential for

more advanced self-report techniques, like ecological momentary assessment (EMA). EMA refers to a whole battery of methods and can be classified as an approach to collect data in real-time in an individual's ecological context (Shiffman et al., 2008). With regard to stress research, EMA is capable of registering random fluctuations in individual stress levels at (random or fixed) time intervals (Kudielka et al., 2012; Schlotz, 2011; Shiffman et al., 2008). Sicorello et al. (2020), for example, asked their participants over several days to complete stress-related questionnaires on their smartphones. They further monitored circumstances associated with observed variations. Sicorello et al. (2020) were able to show that the participants' susceptibility to external events was shaped by variation in the serotonin transporter gene. Vice versa, EMA allows stress researchers to systematically track fluctuations in individual stress levels along a specific stressful event (event-based monitoring) (Shiffman et al., 2008). In the context of the COVID-19 pandemic, a smartphone-based longitudinal EMA approach was used by Huckins et al. (2020) in a student sample to reveal a COVID-19 related increase in symptoms of anxiety and depression.

The assessment of physiological stress markers might come along with such approaches. As EMA ranges from written self-reports over telephone interviews to physiological assessments by means of sensors (Harari et al., 2016; Shiffman et al., 2008; Wang et al., 2014), other stress markers like heart rate or blood pressure can be recorded, too, possibly in parallel with saliva samples (Anjum et al., 2011; Foody et al., 2014; Steptoe et al., 2007). Beyond EMA-related measurement, in order to assess sympathetic parameters, Eagle et al. (2021) opted to mail ambulatory cardiac hardware to their participants' homes and have it sent back to them. However, since this procedure may not be feasible in larger samples, other researchers opted to use wrist-worn Polar watches (e.g., Jentsch and Wolf, 2020) or Apple watches (e.g., Hernando et al., 2018), sometimes in combination with heart rate chest straps which can track a number of activity parameters (Wang et al., 2017).

Importantly, such approaches depend on additional sensors or even invasive devices (Ciman and Wac, 2016). As these are typically portable or even wearable, they allow usage outside the laboratory, but must be purchased and transported, nevertheless. Therefore, to enable broad usage, devices need to function computer- or smartphone-based. This opportunity was already acknowledged in a TSST-OL variant by Harvie et al. (2021) who assessed heart rate variability on top of self-reported stress by means of suitable smartphone software. A growing body of literature is debating the use of smartphone's built-in software or sensors, given that most devices are already equipped with technology capable of collecting a wealth of information on people's behavioral lifestyle patterns (Can et al., 2019; Garcia-Ceja et al., 2016; Harari et al., 2016; Miller, 2012). Therefore, data collected by onboard smartphone sensors may provide a proxy for individual behavior, allowing for so-called digital phenotyping (Wisniewski et al., 2019).

Measurement of HPA axis-related endocrine parameters seems practicable as well. Typically, stress researchers ask participants for saliva samples to extract cortisol. It appears to be a straight-forward approach to mail collection material to participants when using online stress paradigms. For example, Gunnar et al. (2020) opted to mail all material needed for saliva collection to their participants' homes and let them return the material after study completion. And this was not a novel idea. Friedman et al. (1988), for example, already used it decades ago in the so-called CARDIA (Coronary Artery Risk Development in Young Adults) study. It has been shown that cortisol is relatively stable in non-frozen mailed samples (Clements and Richard, 1998) or can at least be assumed to survive a regular postal delivery taking a few days at room temperature (Garde and Hansen, 2005). However, it does seem critical to instruct participants well on how to properly take saliva samples in order to ensure data quality (Adam and Kumari, 2009; Lucas et al., 2019).

Saliva also allows for the extraction of alpha amylase which is considered an indirect marker for sympathetic activation (Nater and Rohleder, 2009). Indeed, Gunnar et al. (2020), assessed both alpha amylase and cortisol from samples taken at home and mailed back to the laboratory. It is important to note that studies systematically verifying stability in non-frozen samples or under thermal constraints for alpha amylase are as yet lacking. Still, there is initial evidence for salivary alpha amylase to remain stable when stored at room temperature for at least five consecutive days (O'Donnell et al., 2009).

In conclusion, the collection of saliva samples for the assessment of stress hormones seems feasible in contexts outside the laboratory. Therefore, online or smartphone-based procedures for stress induction do not eliminate the possibility to assess all central stress markers in order to ascertain the success of a given stress exposure.

4.6. Beyond stress induction: assessment of stress affecting other cognitive processes

Having reviewed tools and techniques for stress induction and measurement of the stress response in times of the COVID-19 pandemic, it is crucial to mention that most studies in basic stress research focus on stress induction or the stress response in isolation. In contrast, some experiments explore how stress, or rather alterations in endocrine or other physiological parameters initiated in response to stress, affect cognitive functions (Shields, 2020; Shields et al., 2016). Therefore, when developing new paradigms to experimentally induce stress, these must ideally allow to investigate other cognitive functions or behavioral patterns as well. Additional tasks that are occasionally conducted before or after stress exposure must ideally be similarly applicable in an online context. Creating new technologies to do so would not only enrichen stress research but psychological research as a whole (Grootswagers, 2020) as the COVID-19 pandemic challenges the entire discipline with respect to conducting experiments outside of laboratory premises. Different platforms and software already allow online collection of behavioral data within psychological experiments. For a recent methodological comparison of current options in different internet browsers regarding their feasibility for specific task demands, see Bridges et al. (2020) and Anwyl-Irvine et al. (2020).

For the matter at hand, it appears feasible to first stress participants in an online context and to subsequently ask them complete other (cognitive) tasks online in the aftermath of stress exposure.

5. Perspectives for stress research beyond the current COVID-19 pandemic

The technologies reviewed in Sections 4.2–4.4 will be crucial for stress researchers during the ongoing pandemic. However, they are also likely to stimulate the field far beyond COVID-19 and will set trends for future stress research (Fig. 2).

5.1. New contexts

While settings such as the MRI can inspire basic stress research (Lederbogen et al., 2011; Streit et al., 2014), this effect may not be unidirectional. New procedures to induce stress approaching the social-evaluative component without in-person contact may in return influence neuroimaging research. Exchange of new considerations may then lead to a theoretical consensus on key features of stress induction as well as their standardized implementation.

Moreover, novel approaches may allow the exploration of new contexts. The procedures reviewed in Sections 4.2–4.4 increase accessibility and may pave the way for research in field contexts. For example, it would be possible to investigate athletes participating in sports competitions. Such a sample was already tested by Rohleder et al. (2007) who studied professional ball room dancers. Exams are omnipresent stressors that are encountered in educational institutions around the globe. However, Merz et al. (2019) were the first ones to show that stress impairs memory retrieval in the aftermath of an oral presentation held in a naturalistic university context. Even though many people fear the
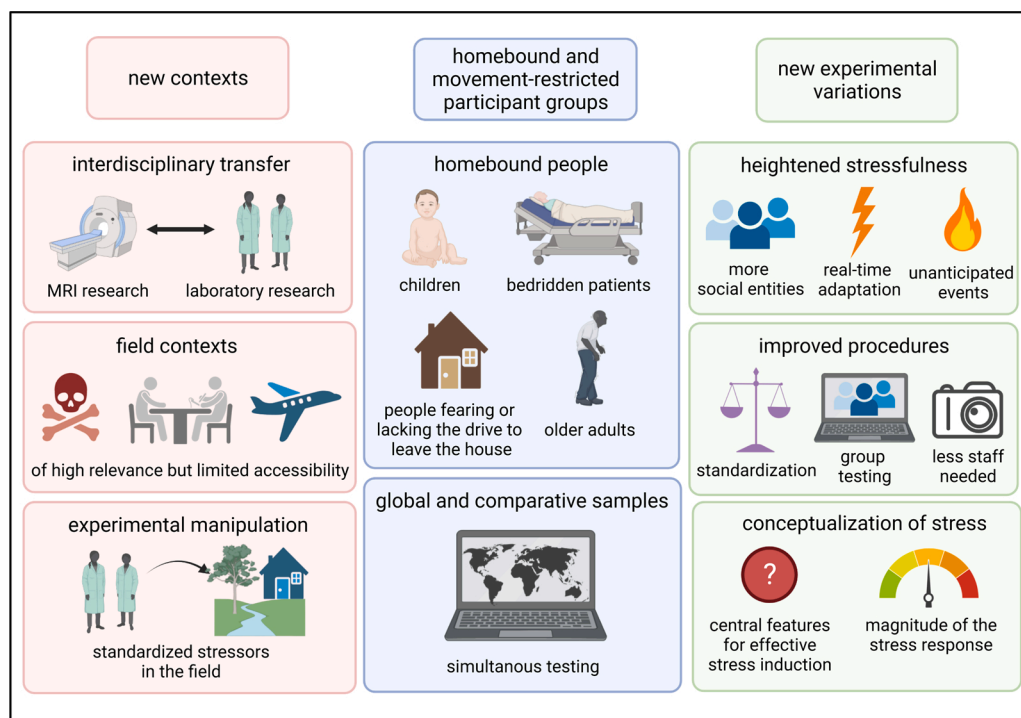
Fig. 2. Schematic representation of opportunities of advanced stress induction procedures to advance the field beyond the COVID-19 pandemic. Adaptations of established paradigms may open (1) new contexts, (2) special samples, and (3) new experimental variations. (1) Interdisciplinary transfer may open up new avenues for psychological stress research. (2) Access to special samples such as homebound people, children, (neurological) patients, or people fearing or lacking the drive to leave their house as well as older people may be facilitated. Beyond that, global and comparative samples are accessible for simultaneous testing. (3) New experimental variations may allow manipulation of the stressfulness of established stress induction paradigms, e.g., by exposing participants to more social entities, unanticipated events, or procedures that are adjusted to individual responsiveness in real time. New technology can improve standardization and resource efficiency. The systematic manipulation of experimental variables may ultimately help advance the conceptualization of stress by identifying features that are central for stress induction and features that mediate the magnitude of the stress response. Created with BioRender.com.

confrontation with a prospective employer, stress effects in the context of job interviews or assessment centers have not been investigated in all aspects (Feeney et al., 2015). Interestingly, Rockawin (2012) acknowledged that the modern technology can help applicants overcome anxiety in job interviews. In line with that, virtual reality is frequently used to simulate job interviews for candidates (Kwon et al., 2013).

Previous research has been exploring other occupational applications for real world simulators and virtual reality features (Kluge et al., 2014). For example, Kluge et al. (2019) found an adverse effect of social stress on monitoring processes in a simulated control task requiring multiple operating procedures. Such findings may be translated to field applications like cockpits in aviation (Sieberichs and Kluge, 2018). Interestingly, mobile devices have already proven useful when it comes to guiding workers through multi-stage processes (Kluge and Termer, 2017). Other workplaces setting people at risk for adverse effects on wellbeing are the health care sector (Demerouti et al., 2000; Embriaco et al., 2007; McVicar, 2003; Wisetborisut et al., 2014) and the educational system (Hall-Kenyon et al., 2014; Kelly and Berthelsen, 1995) as well as the stock market (Blair-Loy, 2009) or the seafaring industry (Agterberg and Passchier, 1998; Iversen, 2012; Oldenburg et al., 2013, 2009). Likewise, we see opportunities to use the TSST-OL to investigate individuals in war-affected or military regions in which the prevalence for mental disorders is higher than in other areas (Husain et al., 2011; Njenga et al., 2006; Priebe et al., 2010; Summerfield, 2000) but which are rather inaccessible to researchers. Similarly, districts with high crime rates (Dustmann and Fasani, 2016; Stafford et al., 2007) or poverty (Belle, 1990; Das et al., 2007; Lund et al., 2011) are characterized by increased prevalence of mental health problems. Of note in this regard, the study by DeJoseph et al. (2019) that validated the TSST-H was integrated into the Family Life Project (FLP) initiated to approach families living in geographical regions of extreme poverty in the U.S.

With respect to clinical perspectives, participants could be tested in disorder-relevant, real-world fear-inducing settings such as airplanes or in elevated locations. Virtual reality or computer-based exposure therapy are already well-established (Baños et al., 2002; Botella et al., 2004; Coelho et al., 2009; Krijn et al., 2004; Mühlberger et al., 2001; Tortella-Feliu et al., 2011). With novel approaches of stress assessment, one may query participants sitting in a doctor's or dentist's waiting room pre- and post-treatment to document stress and anxiety levels (Appukuttan, 2016; Ramirez et al., 2017) or investigate techniques to reduce phobic anxiety (Wang et al., 2017).

Of course, researchers have already found ways to investigate participants in special situations. However, when an experimental manipulation was desired, stress research in the field has as yet relied exclusively on real-life stressors (Michaud et al., 2008). Importantly, this can impede robust conclusions since - as already discussed in Section 2.2- naturalistic settings yield many confounding variables (Epel et al., 2018). Therefore, experimental paradigms discussed in this review may be considered an opportunity to advance stress research in field contexts in two ways:

procedures evaluated in Sections 4.2–4.4 may encourage future studies to implement an experimental manipulation in terms of stress induction. (2) This kind of stress induction can be conducted in field contexts but still features all aspects of a standardized experimental manipulation (Fallon et al., 2016; Gunnar et al., 2020). This might help identify features of field settings that are crucial to drive stress or anxiety (Epel et al., 2018).

It is well-known that field stressors typically activate individuals more strongly than laboratory ones, possibly due to increased personal relevance and a higher intensity (Dickerson et al., 2004; Dickerson and Kemeny, 2004; Epel et al., 2018; Michaud et al., 2008). Along these lines, the nature of the stressor rather than situational variables may be responsible for stronger stress responses in the field than the laboratory. Even though it might sound paradoxical, procedures that lack true personal relevance but are still feasible in field settings might shed light on such processes. By applying standardized stress induction paradigms such as the TSST-OL in naturalistic environments, researcher may be

able to assess the weight that individual relevance gives to a stressor (Dickerson et al., 2004; Dickerson and Kemeny, 2004).

Ultimately, such approaches may help us clarify why specific real-life stressors such as the COVID-19 pandemic affect individuals differently and may lead to mental health problems for some but not others (Ehlert et al., 2001; Kudielka et al., 2009; Zänkert et al., 2019).

However, it is crucial to bear in mind that alike traditional stress induction, also online formats may cause burden and negative side effects for participants. Stress induction can lead to severe emotional responses and heightened arousal (e.g., Vors et al., 2018). Hence, ethical considerations should always be concerned in calculations on costs and benefits of new studies which might hold particularly true for above-mentioned examples of use in highly vulnerable individuals such as patient groups. Along these lines, we emphasize the importance for evaluation of online stress induction projects through local ethic committees as ethical votes are not lapsed due to increased practicability and applicability of online protocols. On top of that, comprehensive debriefing of participants in the aftermath of the procedure as well as opportunities for contact and communication beyond study completion are crucial to expand acceptable stress research to online settings (Labuschagne et al., 2019).

5.2. Homebound and movement-restricted participant groups

Stress induction paradigms that are not bound to the laboratory setting have another advantage. They allow to access samples that cannot come to local research facilities or that are difficult to test with standard stress induction procedures. First and foremost, online applications would allow the assessment of older adults with limited movement space (Jeon and Dunkle, 2009; Osmanovic-Thunström et al., 2015), bedridden, or homebound people (Churproong et al., 2016; Ornstein et al., 2015; Qiu et al., 2010), provided they are easy to use and do not require extensive experience with digital technology. Moreover, home-based stress research also enables access to specific patient groups such as patients with neurodegenerative diseases likes MS for which a dysfunction of stress systems has been discussed as an important factor in pathogenesis as well as disease progression (Gold et al., 2005). Interestingly, for such patients, previous research has established online tools or automatic internet-based programs for therapeutic purposes (Fischer et al., 2015). The COVID-19 pandemic has further boosted online applications in this context. Moccia et al. (2020), for example, reviewed different tools contributing to so-called tele-neurology which is focused on neurological examination of patients suffering from MS by means of video-based or digital technology in general.

Studies conducted at home might also be helpful when recruiting participants who fear or lack the drive to leave their homes due to severe forms of depression or anxiety disorders (Cox et al., 2003; Hallam and Hafner, 1978; Kim et al., 2019; Loken et al., 2014; Ravesloot et al., 2016). Importantly, the latter aspect is especially relevant in the COVID-19 pandemic as stay-at-home practices seem to affect prevalence of anxiety and depression disorders (Benke et al., 2020; Kumari and Mahla, 2021; Tang et al., 2020).

Stress research in children is particularly challenging as minors depend on parents or other family members to accompany them to the laboratory. As a result, study participation of children often fails due to logistic difficulties – a problem DeJoseph et al. (2019) combatted by visiting families at their homes. Tolep and Dougherty (2014) considered traveling to the laboratory itself a stressor, thereby questioning if testing in the laboratory actually accounts for a valid baseline of stress markers in general. The protocols reviewed in the Sections 4.2–4.4 may resolve such issues.

Likewise, online applications set new standards for stress research engaging in comparative cultural research because samples from all over the world are more accessible as long as they have access to a certain device with internet connection. To date, few studies have compared Scottish and Australian (Pithers and Soden, 1998) or Turkish and

Macedonian teachers (Eres and Atanasoska, 2011) with respect to their stress levels and their coping abilities. Berry et al. (1987) reviewed publications on acculturative stress resulting from cultural changes confronting migrants, refugees, or ethnic minorities in Canada. However, these early studies solely assessed stress by means of questionnaire methods. In contrast, modern technology as well as experimental stress procedures reviewed in Section 4 allow for a more in-depth assessment. For example, different people from all over the world could meet in an online meeting and undergo a TSST-OL. Dufau et al. (2011) concluded that new technologies are capable of revolutionizing cognitive science in that suitable devices may help collect data from participants all over the world. Thereby, sampling biases originating from (1) the requirement to come to the designated research facilities, and (2) the natural homogeneity of study participants may be overcome.

Another opportunity may lie in new standards for specialized screening of desired samples. In general, many questions are as yet unanswered concerning individual differences in stress responsiveness. Online stress experiments would enable researchers to gather initial data from large samples first, and then to selectively invite only a subset of individuals to the laboratory for further testing who fulfill specific predefined criteria (Parker et al., 2020). This may enable systematic and precise investigation of individuals showing a blunted or an elevated cortisol response to stress (Kudielka et al., 2009; Kudielka and Wüst, 2010), for example.

5.3. New experimental variations

In addition to enabling stress research during the current COVID-19 pandemic, virtual reality and pre-recorded or online applications of stress induction paradigms also allow new experimental variations. From a methodological perspective, the TSST-VR or pre-recorded variations foster standardization and resource efficiency (Fallon et al., 2016; Zimmer et al., 2019). From a conceptual point of view, TSST-VR and TSST-OL allow new directions in stress research in that key stress components can be implemented in ways that were not possible before. Such approaches may satisfy two objectives. On the one hand, the stressfulness of the actual stress inductive procedure could be modified. On the other hand, they would allow systematic manipulation in order to clarify which factors are central to stress induction and which variables determine the magnitude of the triggered stress response.

For example, in virtual reality it is not only possible to confront the participant with a panel consisting of two or three reviewers but with a whole audience (Kothgassner et al., 2016; Owens and Beidel, 2015; Slater et al., 2006). This approach could determine if a participant's stress experience might be increased with an increasing number of social entities (Kothgassner et al., 2016; Montero-López et al., 2016). Such an approach is also possible for the TSST-OL in that a greater number of panel members might join the online meeting. Such an approach is also possible for the TSST-OL in that a greater number of panel members might join the online meeting. This would allow panel sizes of, e.g., 20 or more panel members, which would be unrealistic in the real-life TSST.

Moreover, it would be feasible to test more than one participant if they join the same online conference. This would resemble the group version of the TSST (TSST-G) which is established for laboratory stress research (von Dawans et al., 2011).

It has been acknowledged that virtual reality systems may enable the assessment of physiological activation for a real-time adaptation of the virtual situation. Fallon et al. (2016) suggested adapting the intensity or the type of the social-evaluative threat in response to the autonomic activity of the participant (e.g., heart rate). The motivation would be to increase task difficulty or intensity of social-evaluative threat individually for each participant (Fallon et al., 2016). However, one must bear in mind that such adjustments would also diminish the comparability and standardization of the procedure.

6. Conclusion

In conclusion, epidemiological, clinical, and basic stress research are needed to elucidate the effects of the current COVID-19 pandemic on wellbeing and the rising prevalence of mental disorders for a whole generation. With respect to experimental manipulations, the COVID-19 pandemic is a driving force to reconsider social-evaluative components and their implementation in established stress induction paradigms. We conclude that different adaptations can be made for experimental protocols such as the TSST, based on multiple available tools and technologies. Studies on stress will benefit from new approaches far beyond the COVID-19 pandemic. These will facilitate research in new contexts and with homebound and movement-restricted participant groups. Last but not least, they hold new perspectives for experimental variations in terms of flexibility to optimize protocols and experimental manipulations for individual research objectives.

Funding

Declaration of Competing Interest

The authors report no declarations of interest.

Acknowledgements

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