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Investigating the temporal dynamic and psychoneuroendocrine impact of the COVID-19 pandemic on mental health

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Vorgelegt von Matthias Haucke, M.Sc. Psychologie

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Erstgutachter (first supervisor):

Prof. Dr. rer. nat. Stephan Heinzel

Zweitgutachterin (second supervisor)

Prof. Dr. phil. Christine Knaevelsrud

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Dedicated to Susanne Haucke-Zumstrull

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"Although the human race is made up of many different people, and despite the diversity of age, sex, culture, language and religious beliefs, there are fundamental similarities. One of the similarities is our yearning for love, acceptance, and understanding, and conversely, our hedonistic nature and aversion to such painful experiences as loneliness."

(Rokach, 1989, p. 382)

1 Summary

1.1 English summary

The COVID-19 pandemic is one of the most severe health crises of the century, with unprecedented public health measures to hinder the virus spreading. As a result, there has been an increase of mental health problems in the general population. The goals of this dissertation project are to understand how a pandemic affects mental health and to find effective mental health intervention targets. In addition, the results can help to understand the effect of involuntary social isolation on mental health. Specifically, I investigated how a lockdown stage changes the temporal dynamics between loneliness, stress-related behaviors and cognitions. Moreover, I investigated whether and how a lockdown impacts hypothalamic–pituitary–adrenal (HPA) axis functioning. Finally, I investigated whether COVID-19-related stressors and mood inertia (i.e., an indicator of mood regulation) persist to impact mental health beyond a lockdown stage. The dissertation project involves smartphone-based ecological momentary assessment (EMA), wrist-worn motion tracking and cortisol sampling in a German population, covering a no-lockdown and a lockdown stage amid the COVID-19 pandemic. Specifically, the following research questions were examined:

1. Do COVID-19 related stressors and mood inertia persist during a no-lockdown stage?
2. How does a lockdown, in comparison to a no-lockdown period, impact the temporal dynamics and network centrality of COVID-19 related stressors, physical activity, social contacts, stress and loneliness?
3. Is there a change of HPA axis activity during a lockdown compared to a no-lockdown? And how does a lockdown affect the association between loneliness, COVID-19-related stressors and HPA axis activity?

Firstly, I found that COVID-19-related worries, perceived restriction, loneliness and mood inertia continued to affect mental health beyond a lockdown stage. Secondly, I found that a lockdown stage, compared to a no-lockdown stage, increases the impact of loneliness on subsequent stress-related cognitions and behaviors. In addition, a lockdown increases the centrality of loneliness (i.e., an index to identify variables that have a strong influence on other variables). Thirdly, I found higher salivary cortisol levels during lockdown than during a no-lockdown stage. Moreover, a lockdown stage moderates the association between loneliness and salivary cortisol. During a no-lockdown stage loneliness is associated with decreased levels of salivary cortisol, whereas during a lockdown stage loneliness is associated

with increased levels of salivary cortisol. The main interpretation of the findings are: Firstly, a majority of pandemic-related stressors outlasts lockdown measures, which indicates the need for mental health interventions beyond a lockdown stage. Secondly, one reason for the mental health decline during a lockdown stage is the temporal and neuroendocrine impact of loneliness. Therefore, loneliness should be a priority for mental health intervention during a lockdown period. To explain the different temporal and neuroendocrine impact of loneliness during a lockdown, I develop the “contextual and cognitive model of loneliness”.

1.2 German summary (Deutsche Zusammenfassung)

Die COVID-19-Pandemie ist eine der schwersten Gesundheitskrisen des Jahrhunderts und es wurden noch nie dagewesene Maßnahmen ergriffen, um die Ausbreitung des Virus zu verhindern. Infolgedessen haben psychischen Probleme in der Bevölkerung zugenommen. Das Ziel dieses Dissertationsprojektes ist es zu untersuchen, wie sich eine Pandemie auf die psychische Gesundheit der Menschen auswirkt, um daraus wirksame Interventionsziele abzuleiten. Darüber hinaus tragen die Ergebnisse dazu bei, Erkenntnisse über die Auswirkungen unfreiwilliger sozialer Isolation auf die psychische Gesundheit zu gewinnen. Zu diesem Zweck untersuchte ich, wie eine Lockdownphase die zeitliche Dynamik zwischen Einsamkeit, stressbedingten Verhaltensweisen und Kognitionen verändert. Außerdem untersuchte ich, ob und wie sich ein Lockdown auf Funktion der Hypothalamus-Hypophysen-Nebennieren-Achse (HPA) auswirkt. Schließlich untersuchte ich, ob sich COVID-19 Stressoren auch nach Beendigung einer Lockdown-Phase noch auf die psychische Gesundheit auswirken und ob die Stimmungsregulierung eingeschränkt bleibt. Das Dissertationsprojekt wurde während der COVID-19 Pandemie ausgeführt und besteht aus Smartphone-basierten Ecological Momentary Assessment (EMA), Bewegungserfassung via Aktigraphie-Geräten und Cortisol-Probeentnahmen während einer „Nicht-Lockdown“ und einer „Lockdown“ Phase. Im Einzelnen wurden folgende Forschungsfragen untersucht:

1. Bestehen COVID-19-bedingte Stressoren und Stimmungsträgheit während einer Phase ohne Lockdown fort?

2. Wie wirkt sich ein Lockdown im Vergleich zu einer Phase ohne Lockdown auf die zeitliche Dynamik und die Netzwerkzentralität von COVID-19-bezogenen Stressoren, körperlicher Aktivität, sozialen Kontakten, Stress und Einsamkeit aus?

3. Verändert sich die Aktivität der HPA-Achse während eines Lockdowns im Vergleich zu einem Nicht-Lockdown? Und wie verändert ein Lockdown den Zusammenhang zwischen COVID-19-bezogenen Stressoren und der Aktivität der HPA-Achse?

Erstens stelle ich fest, dass COVID-19-bezogene Sorgen, wahrgenommene Einschränkungen, Einsamkeit und Stimmungsträgheit die psychische Gesundheit nach einer Lockdownphase weiter beeinflussen können. Zweitens stellte ich fest, dass eine Lockdownphase, im Vergleich zu einer Nicht-Lockdownphase, die Auswirkungen von Einsamkeit auf nachfolgende stressbezogene Kognitionen und Verhaltensweisen verstärkt. Darüber hinaus kann ein Lockdown die Zentralität der Einsamkeit erhöhen (Zentralität ist ein Index zur Identifizierung von Variablen, die sich stark auf andere Variablen auswirken). Drittens kann ein höherer Cortisolspiegel im Speichel der Probanden während des Lockdowns im Vergleich zum Nicht-Lockdown festgestellt werden. Ich stelle fest, dass die Lockdownphase den Zusammenhang zwischen Einsamkeit und Speichelcortisol moderiert. Einsamkeit in der Lockdownphase führt zu erhöhten Speichelcortisolwerten, während Einsamkeit in der Nicht-Lockdownphase zu niedrigeren Speichelcortisolwerten führt. Die oben skizzierten Erkenntnisse legen folgende Interpretationen nahe: Die meisten pandemiebedingten Stressoren überdauern die Lockdownphase, was die Notwendigkeit von Maßnahmen zum Schutz der psychischen Gesundheit nach Beendigung des Lockdowns unterstreicht. Außerdem ist ein Grund für den negative Einfluss der Pandemie auf psychische Gesundheit, dass ein Lockdown die zeitliche und neuroendokrine Wirkung von Einsamkeit verändert. Daher sollte Einsamkeit während eines Lockdowns ein vorrangiges Ziel für Interventionen im Bereich der psychischen Gesundheit sein. Um zu erklären, warum Einsamkeit während eines Lockdowns zu mehr stressbedingten Kognitionen und Verhaltensweisen sowie zu einer erhöhten neuroendokrinen Stressreaktion führt, entwickele ich das "kontextuelle und kognitive Modell der Einsamkeit".

2 The COVID-19 pandemic

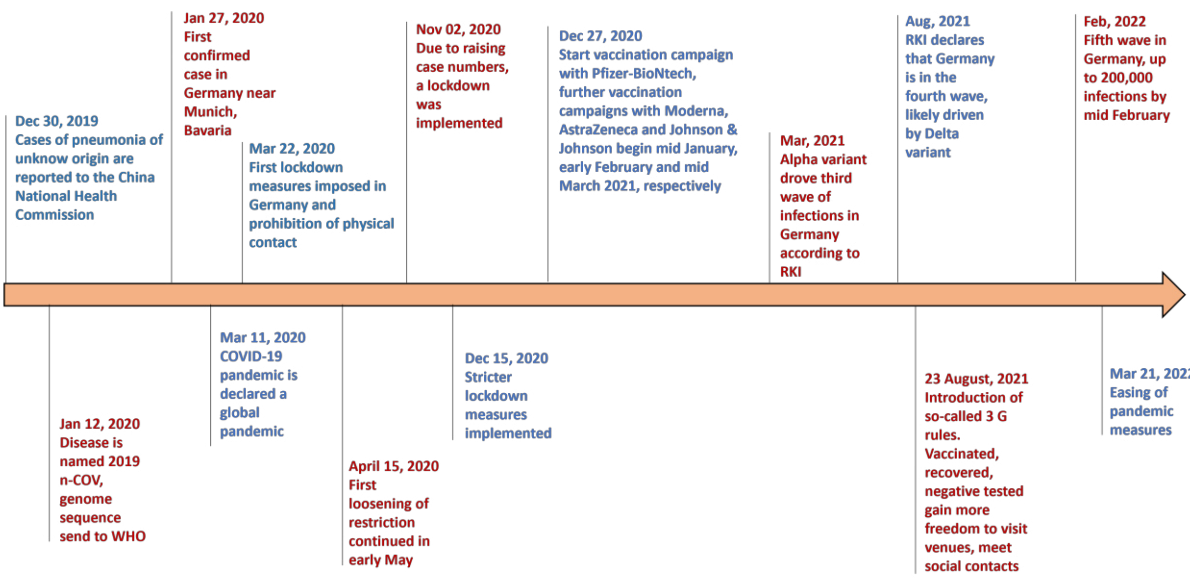
The current COVID-19 pandemic is one of the largest health challenges in the past century and the amount of people affected by the associated public health measures is unprecedented (Yan, 2020). As of August 2022, there are more than 596,873,121 million confirmed cases, and 6,459,684 SARS-CoV-2-associated deaths (WHO, 2022). To counter the rapid virus spread, governments worldwide implemented public health measures which severely disrupted people's daily life. Yet, there is conflicting evidence on the magnitude of the pandemic impact on mental health (Beutel et al., 2021; Liu et al., 2021; Luchetti et al., 2020; Robinson, Sutin, Daly, & Jones, 2022). Multiple factors (e.g., timing of the pandemic, implemented public health measures, individual reaction towards the pandemic) make it difficult to assess if and how the pandemic impacts mental health. To further understand the pandemic impact on mental health, I will compare the temporal dynamics of mental health, as well as the neuroendocrine stress response between a lockdown and no-lockdown period. In addition, to assess the need for mental health interventions beyond times of lockdown, I will investigate whether impaired mood homeostasis (i.e., the regulation of mood via mood-modifying activities) and COVID-19-related stressors persist during a no-lockdown stage. Ultimately, this dissertation project can help to find effective targets for mental health interventions during a pandemic and advance our understanding of the impact of forced social isolation on the temporal dynamics of mental health and the neuroendocrine system. In the following sections, I will give an overview of the medical, historical and political context of the COVID-19 pandemic with a focus on Germany. In a second step, I will describe if the COVID-19 pandemic affects mental health. Finally, I will give an overview of the methodology and aims of this dissertation project.

2.1 The COVID-19 pandemic context and public health responses

The SARS-CoV-2 coronavirus was discovered for the first time in 2019 and causes a respiratory disease, called corona virus disease 2019 (COVID-19; Yuki, Fujiogi, & Koutsogiannaki, 2020). The virus likely originated in bats and was transmitted to humans, by an intermediate animal host, in Wuhan, China, for the first time in December 2019 (WHO, 2021a). Since then, the virus has spread rapidly, until on March 11, 2020, the World Health Organization declared the COVID-19 outbreak a global pandemic. Reasons for this rapid spread are the virus' ability to transmit via inhalation of infected droplets, and its transmission before symptom onset (Lai et al., 2020). The currently dominant variant has an incubation time of 2 to 14 days and includes symptoms such as fever, cough, sore throat, fatigue, breathlessness, loss of smell (anosmia) and taste (ageusia). Symptom severity can range from asymptomatic to pneumonia, acute respiratory distress syndrome and multi organ dysfunction (Singhal, 2020). To counter the virus spreading, most countries enforced prevention and control strategies, including social restrictions, travel bans, stay-at-home orders, and business shutdowns. These measures differed across countries, ranging from less restrictive interventions in Sweden to mandatory stay-at home orders in France (Besançon, Meyerowitz-Katz, & Flahault, 2021). In total over 100 countries instituted a partial or full lockdown at one point during the pandemic (BBC, 2020). In the following section, I will focus on the development of the COVID-19 pandemic in Germany and the associated German public health response.

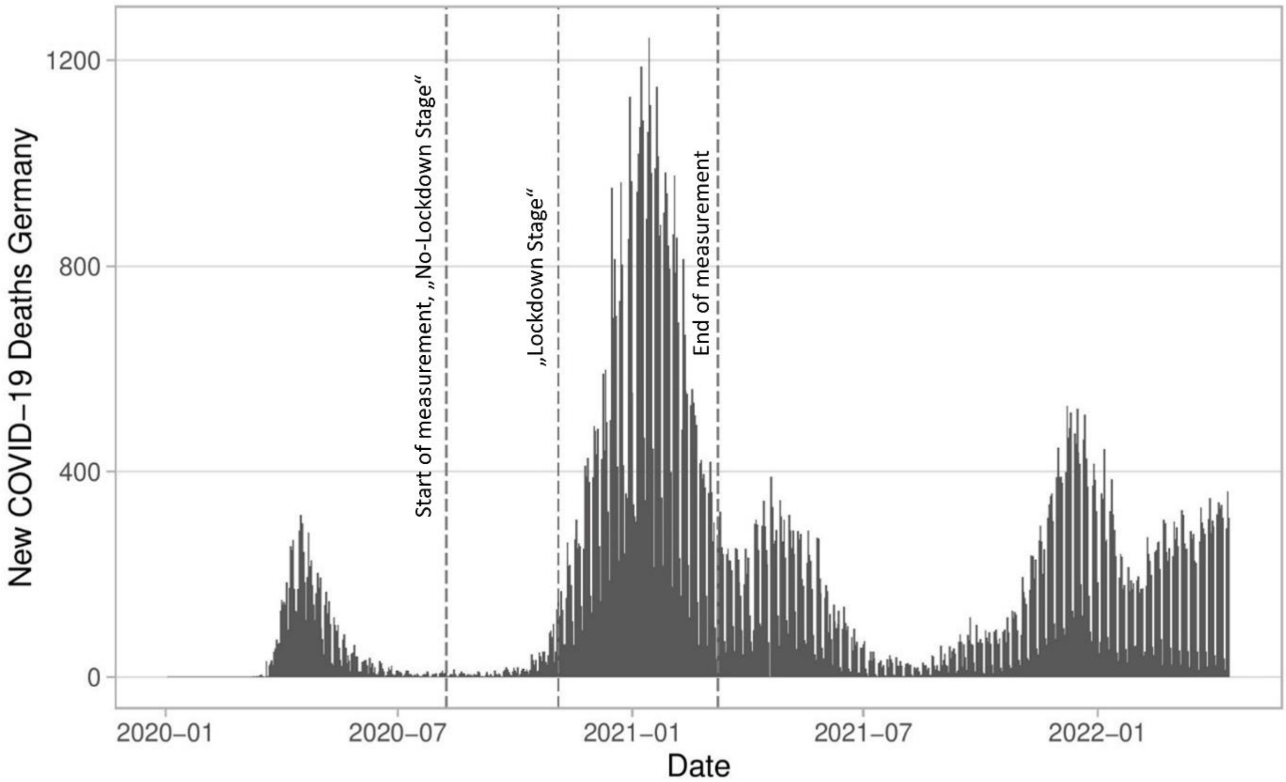
Germany has 32,422,084 accumulated cases, and 148,217 SARS-CoV-2-associated accumulated deaths, as of September 2022 (Robert Koch Institut, 2022). The first confirmed case in Germany occurred on January 27, 2020, near Munich in Bavaria (Gortana et al., 2021). Since then, there have been five waves, partly driven by new variants (e.g., Delta, Alpha, Omicron), during which the infection rates peaked (Deutsche Welle, 2022b). The timeline of the COVID-19 pandemic, including lockdown measures, start of the vaccination campaign and infections waves can be seen in **Figure 1**.

Figure 1. Timeline of COVID-19 pandemic with focus on Germany, starting from the outbreak December 2019 until April 2022. RKI = Robert Koch Institute.



This dissertation research project was conducted in Germany, from August 8, 2020, to March 9, 2021. In total, the project covers 213 days during the pandemic, between a period in which almost all curfew measures from the first wave have been eased (8 August – 1 November 2020) and a lockdown period including, so far, the highest number of COVID-19 related deaths (2 November 2020 – 9 March 2021; see **Figure 2**).

Figure 2. New COVID-19 death in Germany accumulated over a 7-day period. Ref: WHO COVID-19 Dashboard. Geneva: World Health Organization, 2022. Available online: https://covid19.who.int/

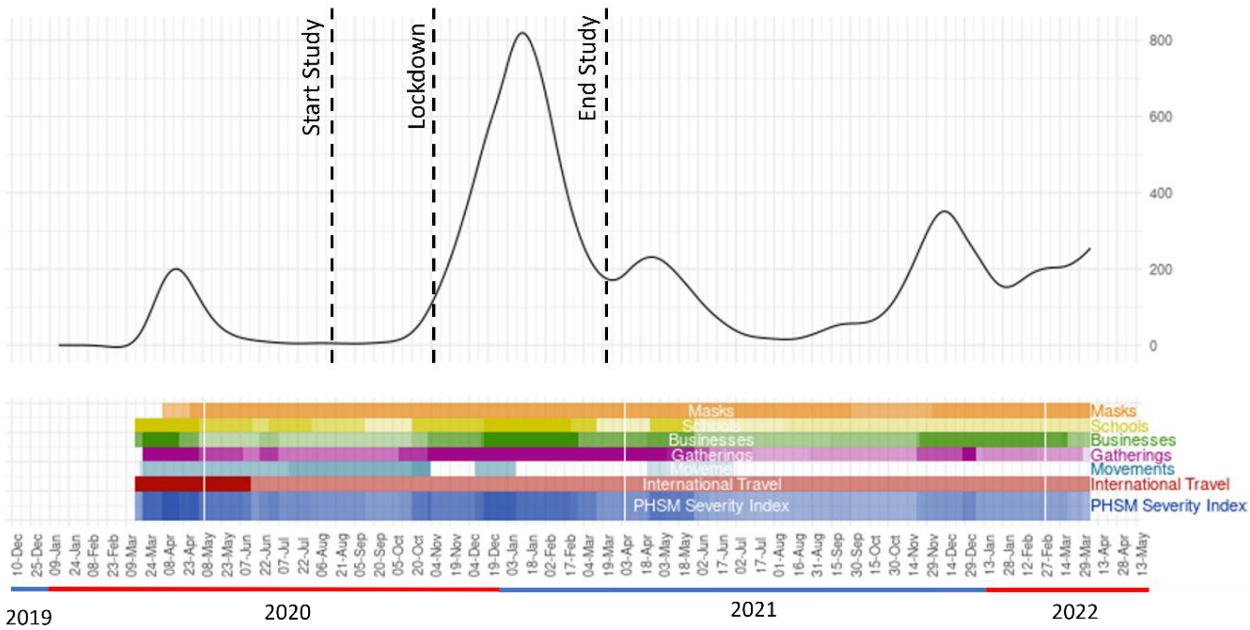


To contain the COVID-19 pandemic Germany implemented federal and state guidelines via the Infection Protection Act (Infektionsschutzgesetz, IfSG), which allows state governments to issue pandemic-related protective regulations, including curfews (Deutsche Welle, 2021a). The common National Pandemic Plan (Nationaler Pandemieplan) describes the public health measures in response to the COVID-19 pandemic (Robert Koch Institut, 2020). These measures had four targets: 1. Reduction of morbidity and mortality, 2. Ensure treatment of infected people, 3. Keeping up essential public services, 4. Provision of reliable and accurate information for decision makers, medical personnel, media and public.

Measures taken by institutions, local and national government to decrease the spread of a disease can be called public health and social measures (PHSM; WHO 2022b). The

WHO (2022b) developed a PHSM severity scale consisting of six indicators: 1. Wearing of masks or facial coverings, 2. Adapting or closing schools, 3. Adapting or closing offices, businesses, institutions and operations, 4. Restrictions on gatherings, 5. Restrictions on domestic movement, 6. Restrictions on International travel. Together these six indicators form a total PHSM Severity Index Score. The PHSM severity and timing in Germany during this dissertation project can be seen in **Figure 3**.

Figure 3. PHSM severity (WHO, 2022b) and timing against the 7-day average count of reported deaths in Germany. Six types of PHSM scores displayed according to the response policy's degree of intensity and scope, darker shades indicate more severe measures. Ref: WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020. Available online: https://covid19.who.int/ (last accessed: 10.09.2022).



The pandemic and associated public health measures had a large impact on the German economy and employment. During the first quarter of 2020, Germany's economy shrunk by 2.2%, which led to a recession (Deutsche Welle, 2020). In January 2022, the German Economic Institute estimated the economic loss resulting from the pandemic to be 350 billion euros (Deutsche Welle, 2022a). Moreover, the unemployment rate rose to 6.1%, with a year-on-year unemployment increase by 577,000 (Deutsche Welle, 2020b). To minimize infection risks, many workers shifted to telework and home office. A survey by

Eurofound (2021) conducted in April 2020, showed that 36.6% of Germans worked from home because of the COVID-19 pandemic.

Moreover, there was a disruption in the deliverance of mental health and educational services. A WHO survey (2021b) found that 60% of countries reported disruption of mental health services, mostly caused by closure of outpatient and community-based services in psychiatric and general hospitals. A total of 67% of countries were reporting disruption of psychotherapy and counselling, and 35% reporting disruption of emergency intervention. During the first pandemic wave telemedicine was routinely used by approximately 20% of German health care providers (Peine et al., 2020). In addition, to halt the spreading virus, childcare facilities and schools were closed in Germany. School closures across German states lasted on average 38 weeks (UNESCO, 2021). Moreover, school children spend an average of 3.6 hours per day in school during school closure in spring 2020, compared to 7.4 hours per day prior to the school closure (Grewenig, Lergetporer, Werner, Woessmann, & Zierow, 2021). Considering all these situational factors, the COVID-19 pandemic and associated lockdown measures likely led to a decline of the general population’s mental health. In the following section, I will outline the empirical evidence for a pandemic effect on mental health.

2.2 The COVID-19 pandemic impact on mental health

After the declaration of the global COVID- 19 pandemic on March 11, 2020, concerns were raised that the pandemic and associated public health and social measures (PHSM) will lead to a parallel mental health crisis (Holmes et al., 2020; Liu, Heinz, Haucke, & Heinzel, 2021; Pfefferbaum & North, 2020). This seemed likely, as prior pandemics (e.g., 2009 H1N1 influenza, “swine flu”) have led to an increase in anger, anxiety and worry in the general population (Caleo et al., 2018; Goodwin, Gaines, Myers, & Neto, 2011; Jones & Salathé, 2009). Early evidence for the pandemic impact on mental health stems from online surveys conducted in China during the initial COVID-19 outbreak (Cao et al., 2020; Li, Wang, Xue, Zhao, & Zhu, 2020; Liu et al., 2020; Qiu et al., 2020; Wang et al., 2020; Wang, Di, Ye, & Wei, 2021; Zhang & Ma, 2020). These findings indicate that prevalence rates of psychological distress ranged from 7% to 54%. Indicators of psychological distress were anxiety, depression, stress, insomnia, worries about one’s own and family health, general life dissatisfaction, avoidance, impairment of social functioning as well as physical symptoms (for a review see Talevi et al., 2020). A meta-analysis by Liu et al. (2021) including 71 studies in

European, American, and Asian countries found a total prevalence of following symptoms during the first COVID-19 wave: anxiety 32.60% (95% Confidence Interval (CI): 29.1-36.30), depression 27.60% (95% CI: 24.00–31.60), insomnia 30.30% (95% CI: 24.60–36.60) and post-traumatic stress disorder (PTSD) symptoms 16.70% (95% CI: 8.90–29.20). Subpopulations that were identified to be especially vulnerable to the mental health impact of the COVID-19 pandemic were health care workers (Huang, Han, Luo, Ren, & Zhou, 2020; J. Lai et al., 2020), women (Liu et al., 2020; C. Wang et al., 2020), young people (Qiu et al., 2020), people with insecure employment and lower income (Liu, Heinzel, Haucke, & Heinz, 2021) and people with preexisting health conditions (Wang et al., 2020). In sum, mental health of the general population significantly declined in most countries during early stages of the COVID-19 pandemic. Yet, to estimate the overall impact of the pandemic on mental health, it is necessary to look beyond the early pandemic stage.

A meta-analysis including 65 longitudinal European and North American cohort studies, compared mental health status prior and during the COVID-19 pandemic (Robinson et al. 2022). The results indicate an overall increase in mental disorder symptoms during March-April 2020 (standardized mean change (SMC) = .102, 95% CI: .026 to .192), which then declined and became non-significant in May- July 2020 (SMC = .067, 95% CI: -.022 to .157). Moreover, a review of longitudinal studies (Daly & Robinson, 2021) found that there was a rather small increase of mental disorder symptoms directly after the outbreak of COVID-19, which then decreased to a pre-pandemic level during May-July 2020. The authors concluded that the early mental health decline was a rather acute response followed by a period of psychological resilience.

Yet, depressive symptoms in Europe and North America were rising again towards the European winter in 2020 (OECD, 2021). For example, survey data from the United Kingdom Office for National Statistics (2022) shows an increase of life dissatisfaction of 12.5% in January 2021, compared to 9.2% in September 2020. In addition, these surveys show that life dissatisfaction seems to decline to 8.2% with the beginning of the European summer 2022. In Germany, the second lockdown during the Winter 2021/2022 started with less rigorous measures than the first lockdown; however, anxiety and depressive symptoms still increased (Brito, Andrade, Rojas, Martinez, & Alfaro, 2022; Moradian et al., 2021). So far mental health data for the third wave in Germany is limited (Mauz et al., 2022).

To summarize, there seems to be a peak in psychological distress during the early stages of the pandemic (March-April), followed by a decline during European summer and an increase towards the European winter. Therefore, mental health issues might be linked to peaks of COVID-19 related cases and associated periods of stringent PHSM. Importantly, the effects of the COVID-19 pandemic on mental health differed across countries, due to different COVID-19 case numbers and implemented PHSM. The heterogeneity of study contexts limits the extent to which an overall decline of mental health is generalizable to other timepoints or/and countries. Thus, an understanding of underlying psychological mechanisms causing a decline of mental health during the COVID-19 pandemic and PHSM is needed. To further understand the impact of lockdown measures on mental health, I will outline the role of central pandemic-related cognitions and behaviors, as well as loneliness.

2.3 COVID-19-related cognitions, behaviors and mental states

Loneliness can be crucial to understand the COVID-19 pandemic impact on mental health. Every social interaction is potentially contagious during the COVID-19 pandemic (Maheshwari & Albert, 2020), therefore most PHSM focused on decreasing physical contacts (WHO, 2022b). These measures included the closure of sites with regular social gatherings (e.g., leisure facilities, educational facilities and working places), mobility restrictions and prohibitions of private and public gatherings. In addition, self-isolation became an altruistic behavior, as every social contact might lead to the spreading of the virus. In line with this, a multinational survey during March 2020 found that physical distancing was done by 90% of the respondents (Mækelæ et al., 2020). In the following section I will describe the concept of loneliness and outline the empirical evidence for increased feelings of loneliness during the pandemic.

Loneliness has been of interest since a long time, the first scientific publication on loneliness dates back to an article by Zimmermann (1784) “Über die Einsamkeit”. Moreover, the “need to belong” is said to be one of the most fundamental motivations that drive human thoughts, emotions and behaviors (Baumeister & Leary, 2017). People who are unable to hold satisfying interpersonal relationships, often experience psychological difficulties, such as depression, anger and anxiety (Heinrich & Gullone, 2006). Being alone can been distinguished into social isolation, solitude, and loneliness. Loneliness is defined as the subjective perception that one’s desired interpersonal relationships do not match one’s actual interpersonal relationships (Cacioppo & Cacioppo, 2018b). Social isolation, on the other hand, has an objective connotation and refers to the number of social contacts (Andersson, 1998). Thus, one can feel lonely because one’s social relationships, despite being plentiful, are not satisfying (Cacioppo & Cacioppo, 2018b). Finally, solitude refers to the act of being alone voluntarily, and is associated with more pleasant feelings, such as being “free from people’s scrutiny and demands” (p. 157, Larson, 1990) and providing time for contemplation, creativity and personal growth (Andersson, 1998; Larson, 1990). In sum, there are different ways to refer to the state of “being alone”, which can be an objective number of social interactions (social isolation), positive and even enriching experience (solitude) or a rather aversive subjective experience (loneliness).

Loneliness can have a severe impact on one’s mental and physical health and has been associated with an 26% risk increase of premature death (Cacioppo & Cacioppo, 2018a). A meta-analysis indicates that loneliness has comparable effects on mortality risks as smoking 15 cigarettes per day and exceeds the mortality risk of obesity (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015). Loneliness has been linked to a range of mental disorders, such as social anxiety disorder (Anderson & Harvey, 1988; Lim, Rodebaugh, Zyphur, & Gleeson, 2016; Moore & Schultz, 1983), schizophrenia (Deniro, 1995; Lim, Gleeson, Alvarez-Jimenez, & Penn, 2018) and depression (Erzen & Çikrikci, 2018; Nolen-Hoeksema & Ahrens, 2002). In addition, loneliness increases the rate of suicidal ideation, suicide attempts and suicide completion (Lasgaard, Goossens, & Elklit, 2011; Stravynski & Boyer, 2001). Considering these harmful effects, it is crucial to investigate whether the COVID-19 pandemic increased loneliness in the general population.

An Eurofound survey (2017) conducted during a pre-pandemic time in 2016 found that 12 % of EU citizen felt lonely more than half of the time. This amount doubled to 25% during the first COVID-19 outbreak, with 15.5% more people feeling “lonely more than half of the time” (Eurofound, 2020). Before the COVID-19 pandemic, in 2016, older people reported the highest amount of loneliness (Eurofound, 2017). After the COVID-19 pandemic onset, young adults reported the highest amount of loneliness, with loneliness quadrupling among the 18 to 25-year-olds. In addition, compared to the pre-pandemic level in 2016, being single increased loneliness by 22% (Eurofound, 2020).

However, there is also evidence against a COVID-19 pandemic effect on loneliness. A longitudinal survey (Luchetti et al., 2020) between January and April 2020 indicates that mean-levels of loneliness did not increase. Similarly, McGinty, Presskreischer, Han, and Barry (2020) compared average loneliness scores between 2019 and 2020 and found only a slight increase in loneliness, which led the authors conclude “*Because loneliness increased only slightly from 2018 to 2020, other factors may be driving psychological distress during* *the COVID-19 pandemic*." (p. 94). A large German survey (Beutel et al., 2021) including over 2,500 participants found no significant increase in loneliness, when comparing loneliness scores between 2018 and spring 2020. Moreover, there was only a slight increase in loneliness reported in a Dutch study comparing loneliness score between October 2019 and March 2020 (Van Tilburg, Steinmetz, Stolte, Van der Roest, & de Vries, 2021). However, these studies assessed different samples during and prior to the pandemic. Moreover, these studies relied on average based assessments of loneliness. This assessment does not allow to investigate harmful consequences of loneliness, which happen on a neuroendocrine level, and/or which may develop over time. Time sensitive assessment and analysis can be crucial to advance psychological theorizing (Sonnentag, 2012) and to understand how the COVID-19 lockdown impacts mental health. In this dissertation, I used a temporal dynamic network approach, to estimate how loneliness affects subsequent pandemic-related cognitions, behaviors, and mental states. Moreover, I examine how a lockdown stage affects the association between loneliness and hypothalamic–pituitary–adrenal (HPA) axis functioning.

Moreover, I assessed pandemic-related news consumption, physical activity, perceived restriction and COVID-19 related worries. Worries are a form of repetitive thought, which is the process of thinking attentively, repetitively, or frequently about oneself and the world (Segerstrom, Stanton, Alden, & Shortridge, 2003). Specifically, worries are an attempt to engage in mental problem-solving of an issue with an uncertain outcome, which contains the possibility of one or several negative outcomes (Borkovec, Robinson, Pruzinsky, & DePree, 1983). Worries focuses on future potential threat and involves imagined catastrophes, uncertainties and risks (Watkins, 2008). There is a strong link between worries and negative mental health outcomes (for a review see Davey & Tallis, 1994). Exaggerated amount of worries are a core symptom of most anxiety disorders, such as Social Anxiety Disorder and Generalized Anxiety Disorder (American Psychological Association, 2013). Worries about the impact of COVID-19 and associated lockdown measures might have a rather passive focus on unchangeable causes, as the pandemic affects situational factors that can be perceived as uncontrollable (Brochu & Zhou, 2009). Moreover, worries about the dangerous health effects and the socioeconomic consequences of COVID19 can cause fear and distress (Taylor et al., 2020; Fitzpatrick, Drawve, & Harris, 2020; Ye et al., 2020).

COVID-19 related news consumption might be an important pandemic-related behavior that can decline mental health. A cross sectional study during the first COVID-19 outbreak in China (Gao et al., 2020) showed that 80% of participants were exposed to COVID-19 related news. On the one hand, COVID-19 news consumption can have a negative impact on mental health. For example, greater COVID-19 media consumption was associated with anxiety (Gao et al., 2020) and increased psychological distress, via an increased perception of COVID-19 related threat (Stainback, Hearne, & Trieu, 2020). On the other hand, exposure to reliable information, based on experts and health authorities, can increase COVID-19 vaccination intentions (Gehrau, Fujarski, Lorenz, Schieb, & Blöbaum, 2021). Thus, although reliable information about COVID-19 and its effects on health might be necessary to induce behavioral changes, unfiltered and constant media consumption likely leads to detrimental mental health effects.

The perception of COVID-19 related restrictions might induce feelings of uncertainty about the future, a lack of control over one's life and a feeling of threat. A multinational study (Mækelæ et al., 2020) has found that most respondents were affected by COVID-19 restrictions. Moreover, respondents reporting higher levels of restriction also reported higher levels of severe disruption of their daily life. School closings were reported to have the strongest effect on one's daily life. The less satisfied the respondent was with the government's response, the higher was the reported worry and fear about the COVID-19 pandemic. Moreover, a Chinese survey indicates that perceived restrictions in daily essentials (e.g., food, medicine) and social activities increase mental health problems during the pandemic (Liu, Liu, Lin, & Zhao, 2022).

The COVID-19 pandemic and public health measures severely restricted people's choice of daily activities and might lead to prolonged staying at home and decreased physical activity (Woods et al., 2020). However, physical activity can be crucial for physical and mental health (Fox, 1999; Vancampfort et al., 2017), because it increases neuroplasticity, especially in hippocampal and cortical regions relevant for depression (Firth et al., 2018; Li et al., 2017; Zheng et al., 2019) Moreover, exercise is associated with adaptive improvements in cerebral blood flow, increasing the delivery of neurotrophic factors and oxygen (Bailey et al., 2013; Maass et al., 2015; Pereira et al., 2007). Exercise can reduce inflammatory factors (Fedewa, Hathaway, Ward-Ritacco, Williams, & Dobbs, 2018; Lin et al., 2015) and increase resistance to oxidative stress, associated with depression (Bloomer, 2008; de Sousa et al., 2017). Finally, exercise can improve self-efficacy and self-esteem (Anderson, Murphy, Murtagh, & Nevill, 2006; Feuerhahn, Sonnentag, & Woll, 2014; Moore, Mitchell, Bibeau, & Bartholomew, 2011; Sani et al., 2016).

Despite these positive health effects, lockdown measures might have reduced engagement in physical activity. During the first COVID-19 lockdown time spent for moderate (by 2.6%) and vigorous activities (by 16.8%) decreased in comparison to a pre-lockdown stage. Moreover, walking time reduced by 58.2% and sedentary time increased by 23.8% (Castañeda-Babarro, et al. 2020). Yet, this study was based on a retrospective questionnaire and thus might be subject to memory bias. Thus, there is a lack of studies that investigate how the pandemic affected physical activity with an objective measure, such as actigraphy devices (i.e., a wrist-worn device that obtains objective measures of physical activity in a natural environment; Rowlands et al., 2015). Therefore, in this dissertation project I employed actigraphy devices across lockdown stages.

In sum, to better understand the mental health decline caused by the pandemic, this dissertation investigates the impact of lockdown on pandemic-related cognitions, behaviors and mental states on a temporal and neuroendocrine level. It extends the previously described literature in the following ways: Firstly, I estimate within-person time sensitive processes which might be overlooked by previous average-based assessment. This also allows to assess which cognitions, behaviors and mental states have the largest impact within a temporal dynamic network and might need to be prioritized by mental health interventions. Secondly, I investigate how a lockdown impacts the association between pandemic related cognitions and behaviors and hypothalamic–pituitary–adrenal (HPA) axis functioning, indexed by salivary cortisol. This allows to examine the biological basis of the pandemic impact on mental health. In the next section, I will describe the estimation of temporal effects and the endocrine stress response in more detail and describe how it can help to advance our understanding of the pandemic consequences for mental health.

3 Estimating the temporal and endocrine impact of the COVID-19 pandemic

3.1 Ecological momentary assessment

Ecological momentary assessment (EMA) involves the repeated sampling of a subject's current psychological, behavioral and physiological states in their real-world environment (Smyth & Stone, 2003). EMA often involves smartphone-based assessment, because most people already carry these devices in their everyday life and there is a range of software available to trigger and store questionnaires (e.g., movisensXS). Although EMA studies are increasingly popular, so far most clinical psychological research focused on global, summarized, and retrospective self-reports of mental states or behavior (Joseph, Jiang, & Zilioli, 2021; Shiffman, Stone, & Hufford, 2008). This lab-based assessment can introduce some bias, most notably retrospective recall bias caused by faulty memory (Bradburn, Rips, & Shevell, 1987; Tourangeau, 1999; Tversky & Kahneman, 1973). For example, negative mood can increase the recall of negatively valanced information (Clark & Teasdale, 1982). Moreover, experimental or survey studies often require participants to be in research settings or at home, possibly decreasing the ecological validity of the sampled data (i.e. as behaviors and experiences are likely affected by the context in which they occur; Araujo, Davids, & Passos, 2007). EMA on the other hand allows to study how behavior, mental states and physiological processes vary over time within a subject (i.e., the temporal dynamics) and across ecologically valid situations (Shiffman et al., 2008). Therefore, it has the advantages to measure momentary data within a person and in a natural environment, which allows to approximate temporal dynamic changes.

3.2 Estimating temporal effects via time series analysis

"*The ability to shed light on dynamic processes and situational influences is potentially the most critical contribution of EMA methods to clinical psychology*," (p. 10; Shiffman et al., 2008)

To better understand how the COVID-19 pandemic changes behaviors, cognitions, and mental states, I will estimate temporal parameters in this dissertation project. The estimation of temporal effects requires mathematical models that account for time series data. Time series can be defined as a time-ordered sequence of observations (Wei, 2006). An example time series is the sequence of the variable "bad mood" (denoted as "x"), with x_1, x_2 and x_3, which means that bad mood was measured at time point 1 (x_1), at time point 2 (x_2), and at time point 3 (x_3). We can define the variables "bad mood" by using x_t, with t indexing the different time points. Importantly, in time series observations are correlated, which means that the value at time point t (x_t), is influenced by past values (x_t-1, x_t-2, etc.; Geoghegan, 2006). A collection of time indexed random variables (x_t) is also called a stochastic process (Geoghegan, 2006). Referring to our example, we can assume that if one is in a very bad mood an hour earlier, it will have an impact on the mood the person experiences right now. Thus, the values of x_t depend in a significant way on the value of x_{t-1}. Most standard statistical methods based on random samples cannot effectively estimate time series data. The main difference between a time series and a random sampling with a known mean and standard deviations is that the value of the series at time t, say x_t, depends in some significant way on past values, thus their mean and /or variance change over time in a non-random pattern. The three basic characteristics of time series data are: 1. variation (i.e., trend, cycles, irregular variation and seasonality) 2. stationarity (i.e., the mean, variance and autocorrelation structure do not vary over time) and 3. autocorrelation (Jebb, Tay, Wang, & Huang, 2015). I explain variation and stationarity in more detail in the *Appendix*.

If a psychological variable is correlated with itself across time points, it exhibits autocorrelation. Autocorrelation is similar to a regular Pearson correlation, only that it describes the correlation of a variable with itself at a previous point in time, also called the lag (i.e., lag-1 is the correlation with the immediately preceding observation of that variable; Jebb et al., 2015). In a regular correlation we collect two series of observations and want to test whether there is a relationship between them. Autocorrelation is almost identical, except that we do not measure two random variables (x and y), but we measure the correlation between a variable with itself at different lags (shift in time). That is, we use the same value but separate it in time for k-number of lags. The autoregressive (AR) model can capture autocorrelated processes with random components. In these models a response variable in the previous time period (e.g., immediately preceding time point: lag-1) becomes the predictor (see *Appendix*).

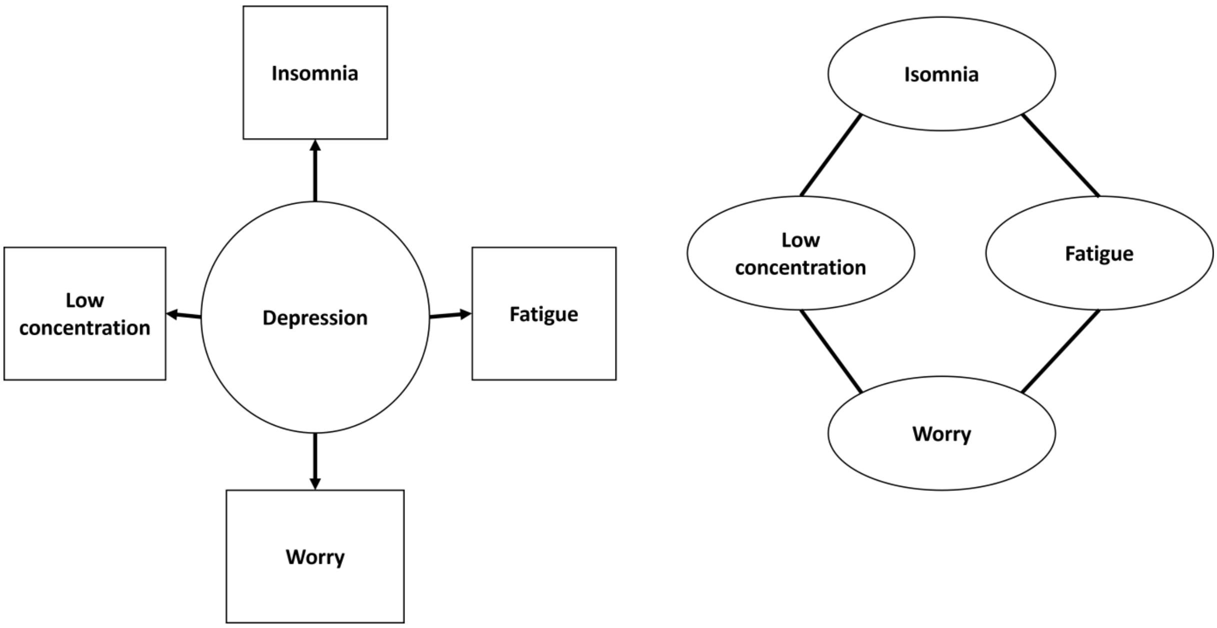
Previously, autocorrelation parameters have been used as an indicator for mood and affect regulation. In this context, an autoregressive parameter is called inertia of affect and indicates how much negative affect at one time point affects negative affect at the next time point (i.e., affect scores are regressed on themselves over time). Values are interpreted as carry-over effect, indicating affect regulation (de Haan-Rietdijk, Kuppens, & Hamaker, 2016). Similarly, autoregressive effects have been investigated to study mood homeostasis, which refers to the regulation of mood via mood-modifying activities over time. Here, autoregressive effect of mood is indicative for whether a person is able to stabilize their mood (Taquet, Quoidbach, Gross, Saunders, & Goodwin, 2020). This autoregressive effect of mood can be used as an indicator for depressive symptoms. People with impaired mood homeostasis have been more often depressed, and it can lead to a higher amount and longer duration of depressive episodes (Taquet et al., 2020). Thus, depression can be seen as a process developing over time, in which the person is unable to effectively regulate their mood. Thus, autoregressive effect can be used to extend our understanding of how mental health problem develop and are maintained, which might be overlooked using average-based assessment.

Yet, there is a lack of studies that use autoregressive models to study the impact of the COVID-19 pandemic on mental health. Because a lockdown stage restricts the extent people can engage in mood-modifying activities, mood homeostasis can help to understand how the pandemic affects mental health. So far, the only study that investigated mood homeostasis during the COVID-19 pandemic has found that mood homeostasis was impaired during a lockdown stage, compared to a pre-lockdown stage (Taquet, Quoidbach, Fried, & Goodwin, 2021). To see whether mood regulation remains impaired after the lockdown measures have ended, in Study 1, I will estimate the mood inertia effect during a no-lockdown period. In Study 2, I used time series data to build temporal dynamic networks, to investigate how a lockdown changes the temporal dynamics between COVID-19 related behavior, cognition, and mental states.

3.3 Temporal network approach

The temporal network perspective differs from the common conceptualization of mental health disorders, called the disease model (Hyland, 2011). The disease model proposes that psychological symptoms (e.g., depressive symptoms) stem from the disorder itself (e.g., depression), comparable to a physical disease, such as a brain tumor causing nausea, dizziness or headaches. According to the disease model, symptoms of depression result from the underlying disorder. In contrast, the network perspective proposes that symptoms exist, because they are causally connected within a complex system, rather than caused by a latent disorder (Borsboom & Cramer, 2013) (see **Figure 4**).

Figure 4. On the left side one can the disease model, assuming a latent cause of symptoms. On the right side, is the network approach assuming that symptoms arise and persist due to their complex interaction, without any latent cause. Adapted from Borsboom & Cramer (2013).



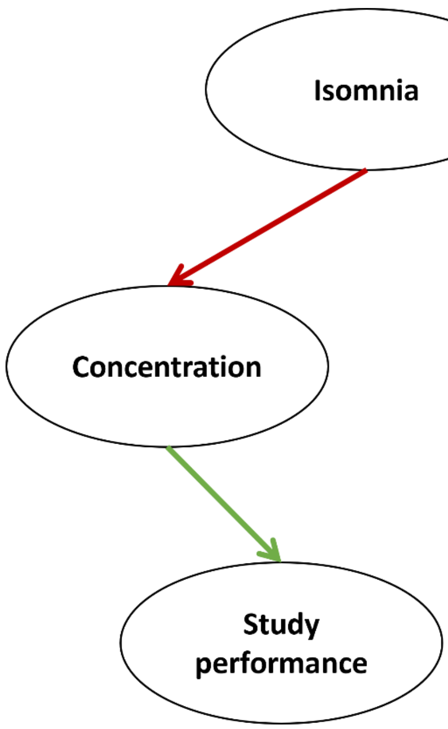
The overall decline of mental health caused by the pandemic and associated measures can be explained by a change of the temporal interconnection between a range of stress-related cognitions and behavior. The temporal dynamic network perspective advances previous studies in the following ways: Firstly, it allows to investigate how the pandemic impacts time-sensitive psychological processes. Secondly, it allows to examine the temporal association between a range of pandemic related variables, controlling for all other time-lagged association. For example, does loneliness at 3 P.M. lead to more COVID-19-related worries at 6 P.M., controlling for all other measured time-lagged associations? And is this effect stronger during a lockdown than during a no-lockdown? Thirdly, we can analyze the structure of a network to find variables that have a relatively more central role. The identification of these more central symptoms in the network can be one step towards informed mental health interventions. Finally, a temporal network can indicate causal pathways, as it approximates the temporal requirement of causality, called Granger causality (i.e., the cause precedes the effect; Granger, 1969). Yet, temporal causality can only be approximated and never established via temporal dynamic networks, because many questions remain: Did we measure our variables in the right time frame to capture specific time sensitive processes (Robinaugh, Haslbeck, Ryan, Fried, & Waldorp, 2021)? Did we measure the construct with reliable and valid measures? Did we model all variables that are relevant to the network (i.e., excluding the possibility that a third unmeasured variable z causes the observed relation between x and y; De Ron, Fried, & Epskamp, 2019)? Thus, to establish causality we would need further empirical evidence, for example via measuring the effectiveness of mental health interventions based on temporal networks. Despite their potential, temporal networks have been barely used to study the pandemic impact on mental health.

Network approaches have been used for two kinds of data, cross-sectional data (i.e., multiple subjects measured once) and time series data (i.e., one subject or multiple subjects measures at several time points; Epskamp, Waldorp, Mõttus, & Borsboom, 2018). To account for measuring multiple participants, one can use a multilevel approach to vector autoregressive (VAR) modelling (Bringmann et al., 2016). The vector autoregressive model is an extension of the previously described autoregressive model because it has more than one dependent time series variable (Geoghegan, 2006). Thus, vector autoregressive (VAR) models are a multivariate (allowing for n-variables and n-equations models) extension of the univariate (a single equation model) autoregressive (AR) model (see *Appendix*). In a VAR model, variables are regressed on the time-lagged variable and all other variables that have been entered into the network. In addition, the multilevel approach to VAR (mlVAR) modeling allows the VAR coefficient to differ across individuals, and therefore can be applied to data with a nested structure that violates the assumption of independent observation (Bringmann et al., 2013). In Study 2 mlVAR models were estimated and compared between lockdown stages, to examine how a lockdown changes the temporal association between stress-related cognitions and behavior.

The residual structure of mlVAR analyses can be modelled using the Gaussian graphical model (GGM), which is an undirected network of partial correlation coefficients. An undirected network model is called Markov random field, if the data is Gaussian normally-distributed it is called Gaussian graphical model (Epskamp et al., 2018). This can be used to model temporal networks, which shows how variables predict each other over time. A temporal network is a directed network of regression coefficients between the time-lagged and current variables (Epskamp et al., 2018). That is, to construct the temporal dynamic networks, we can use the regression coefficients of the time-lagged associations among the variables computed via autoregressive multilevel modeling.

The partial correlation matrix of the multilevel VAR model is graphically displayed in a temporal network, in which each variable is represented as a node (i.e., graphical VAR). Moreover, a temporal network displays the partial correlation as the connection between two variables (edges). An edge within a temporal network indicates a node predicting another node (or its time-lagged self) at the next measurement point, controlling for all other nodes at the previous measurement point (Epskamp et al., 2018). Positive associations are often visualized with blue or green edges, negative ones with red, while the absolute strength of a partial correlation is represented with the width or saturation of an edge. Zero or non-significant partial correlations have no edges (Epskamp, Cramer, Waldorp, Schmittmann, & Borsboom, 2012a). Thus, a GGM is a network of conditional associations, in which an edge signals the relation between two variables after controlling for all other variables in the network (see **Figure 5**).

Figure 5. An example of a simplified temporal network in which there are three nodes (insomnia, concentration and study performance) and two edges (insomnia negatively predicts concentration over time (using *k*-lags), controlling for all other time-lagged associations; Concentration positively predicts study performance over time, controlling for all other time-lagged associations).



To analyze the structure of networks, we can estimate the inter-connectedness of variables within the network via centrality indices (Kolaczyk & Csárdi, 2014; for an overview see Lü et al., 2016). In temporal networks, using vector autoregressive models, one can differentiate between instrength and outstrength. Instrength is the sum of absolute values of edge weight that come into a node. Thus, a node with the highest instrength is the node that receives the most edges. Outstrength is the sum of absolute edge weights that a node sends to other nodes. Thus, the node that sends the most edges has the highest outstrength (Wasserman & Faust, 1994). Centrality measures have been applied to highlight mental disorder symptoms with a relatively central role in the network (Groen et al., 2019; Klippel et al., 2018). The identification of these central symptoms could help to decide on which symptoms mental health interventions or clinical practice should focus on (Borsboom & Cramer, 2013).

Previously two published studies examined temporal dynamic networks during the COVID-19 pandemic. Fried, Papanikolaou and Epskamp (2020) investigated undergraduate students during the first COVID-19 pandemic stage and found vicious cycles (i.e., feedback loops) between negative mental health states (e.g., depression, anxiety, distress) and being alone, which also predicted concerns about COVID-19. In addition, Ebrahimi, Burger, Hoffart, and Johnson (2021) found that the main mechanism which increased depressive symptoms during COVID-19 lockdown was the feeling of helplessness. So far there has not been a study that compared the change of time-lagged association and network characteristic between lockdown stages. However, this is needed to estimate the impact a pandemic lockdown on temporal networks, which in turn, allows to find the change of time-sensitive psychological processes that causes a decline of mental health. Thus, in this dissertation, I will compare the moment-to-moment time-lagged associations between pandemic-related cognitions, behaviors, and mental health states and network diagnostics (instrength and outstrength) of two separately estimated temporal networks during a lockdown and no-lockdown stage. I do this via permutation testing, which does not require parametric assumptions about the null distribution of test statistics (Klippel et al., 2018). During the permutation procedure, I compared the results of the actual observed data with a distribution that is derived from repeated permutation of the data under the null hypothesis.

Not only a temporal, but also a biological perspective can help to understand the pandemic impact on mental health. Therefore, I investigated whether a lockdown increases hypothalamic–pituitary–adrenal (HPA) axis activity, indexed by salivary cortisol. In addition, I investigated how a lockdown changes the association between COVID-19 related stressors and salivary cortisol.

3.4 The pandemic effect on hypothalamic–pituitary–adrenal (HPA) axis functioning

The COVID-19 pandemic is a major adverse life event for most people and can lead to chronic stress, that is associated with an activation of the hypothalamic–pituitary–adrenal (HPA) axis, indexed by glucocorticoids (e.g., cortisol). Thus, the COVID-19 pandemic can challenge the dynamic equilibrium between behavioral, mental, and physiological adaptive responses (Chrousos, 2009). One such adaptive response is the regulation of neuroendocrine hormones (Charmandari, Tsigos, & Chrousos, 2005). Neuroendocrine hormones are central to the regulation of basal homeostasis and the response to threat. They target neural activity (e.g., executive functioning, reward and fear systems), growth and reproductive thyroid hormone axes, as well as cardiorespiratory, metabolic and immune functioning (Chrousos, 2009). Therefore, excessive or chronic stress can lead to a state of cacostasis (i.e., dyshomeostasis), which in turn, can lead to a range of behavioral and somatic disorders (e.g., anxiety, depression, sleep disorders, metabolic disorders and immune dysfunction (Chrousos, 2009).

There are two neuroendocrine axes that are involved in a stress response, the hypothalamic-pituitary-adrenocortical (HPA) axis, and the sympathetic adrenomedullary (SAM) axis, leading to the release of cortisol and norepinephrine (Cacioppo & Cacioppo, 2018b). The SAM axis leads to a relatively rapid release of noradrenaline and adrenaline. It includes the prefrontal cortex and limbic regions (e.g., amygdala, bed nucleus), which send signals to the brain stem and hypothalamus, which, in turn, activate the sympathetic nervous system (Hermans, Henckens, Joëls, & Fernández, 2014). The sympathetic nervous system (SNS) consists of sympathetic nerve fibers connected to most major organs which release norepinephrine, and an adrenal-medullary component which secretes catecholamines and epinephrine (Hermans, Henckens, Joëls, & Fernández, 2014). On the other hand, the HPA axis is characterized by a relatively slow release of glucocorticoids. It consists of hormone secreting glands from the nervous and endocrine system: the hypothalamus, the pituitary gland and the adrenal glands (Cacioppo & Cacioppo, 2018b). HPA axis is activated by a cascade of signals from the hypothalamus and limbic regions to the paraventricular nucleus of the hypothalamus, which then secretes corticotropin releasing hormones (CRH) into the hypophyseal portal circulatory system. CRH, in turn, signals the anterior pituitary glands to secrete adrenocorticotropic hormone (ACTH), which travel to the adrenal cortex, which triggers secretion of glucocorticoid hormones, such as cortisol (Hermans, Henckens, Joëls, & Fernández, 2014).

Only a small proportion of glucocorticoids are biologically active (i.e., being able to bind to receptors), because most glucocorticoids are already bound to proteins, such as globulin and albumin (Cacioppo & Cacioppo, 2018b). Moreover, the proportion of biologically active glucocorticoids differs between tissue (e.g., salivary, urine, blood). Salivary samples are often used for research purposes, because salivary cortisol correlates to unbound plasma or serum cortisol levels (Cacioppo, Cacioppo, Capitanio, & Cole, 2015). Moreover, glucocorticoids follow a circadian rhythm, with highest levels in the morning and lowest in the evening, to regulate physiological processes, such as immune and reproductive functions, inflammation and energy mobilization (Sapolsky, Romero, & Munck, 2000). Despite their circadian rhythm, glucocorticoids are still affected by acute psychological stressors that occur during the day, for example socio-evaluative stress (Dickerson & Kemeny, 2004). If cortisol levels are chronically and excessively elevated by stressors, they can lead to physical and mental disorders (Chrousos, 2009).

Thus, increased HPA axis activity, indexed by salivary cortisol, could explain a relationship between mental disorders and the COVID-19 pandemic. Yet. there have been only a few studies with mixed findings about if and how a lockdown impacts HPA axis functioning. On the one hand, greater loneliness in young people during the first wave of the COVID-19 pandemic was associated with higher levels of salivary cortisol upon awakening (Jopling et al., 2021). In addition, a study including mothers and their children showed that maternal hair cortisol was positively associated with COVID-19 related news exposure and social isolation, whereas child hair cortisol was associated with job loss in their family and social isolation (Perry, Donzella, Troy, & Barnes, 2022). Moreover, compared to pre-pandemic times, there was an increase in hair cortisol in nurses during the first COVID-19 pandemic wave (Rajcani, Vytykacova, Solarikova, & Brezina, 2021). In addition, there was an association between burnout status and cortisol levels in healthcare professionals (Marcil et al., 2022). One the other hand, Feneberg et al. (2022) found that, during a lockdown stage, hair cortisol concentrations (HCC) decreased. The mixed findings might result from the usage of HCC as a marker of HPA axis functioning, which is a rather long-term and retrospective biological marker and has a relatively low association with self-reported stress in non-clinical populations (Stalder et al., 2017).

Study 3 in this dissertation advances the previous research on the pandemic effect of cortisol levels in the following ways: 1. including time sensitive salivary cortisol and EMA measures, 2. comparing the impact of different lockdown stages on salivary cortisol and 3. investigating how different lockdown stages change the association between COVID-19 stressors and HPA axis functioning. This allows to find a neuroendocrine explanation for the mental health decline during a lockdown.

4 Aim and design of the dissertation project

The COVID-19 pandemic is a severe health crisis, leading to mental health problems worldwide (Liu et al., 2021). Previous studies using averaged-based assessment found mixed results on the pandemic impact on mental health and loneliness (Beutel et al., 2017; Liu, Heinzel, et al., 2021; Liu et al., 2021; Luchetti et al., 2020; McGinty et al., 2020; Van Tilburg et al., 2021). To explain how the pandemic affects mental health, this dissertation projects investigated how lockdown measures affect the temporal dynamics of mental health and the neuroendocrine stress response.

The studies in this dissertation are part of a research project funded by the Berlin University Alliance and investigated temporal factors that might be important to understand the effects on mental health: mood regulation during a post-lockdown stage and the impact of a lockdown on the temporal dynamics of COVID-19 related stressors and loneliness. Investigating moment-to-moment changes in mental states and behaviors allows to estimate the directionality over time, which can lead to insights, which would not be possible with average based assessment. In addition, by comparing temporal dynamic networks, I can examine whether a lockdown affects the centrality of loneliness or other specific pandemic-related behaviors and cognitions (i.e., a more central variable has more and stronger connections to other variables within the network). This, in turn, can help to identify central triggers of stress-inducing behaviors and cognitions that should be prioritized by mental health interventions. In addition, I investigated the mood inertia (i.e., the effect of negative mood at time point 1 on negative mood at time point 2) and the persistence of COVID-19 related stressors in times of eased lockdown measures. This helps to understand whether and how mental health needs to be protected after lockdown measures have ended.

Lastly, I investigate the impact of lockdown and associated stress-relevant cognitions and behaviors on stress responsive hypothalamic-pituitary-adrenal (HPA) axis functioning, indexed by glucocorticoids (i.e., cortisol). Excessive levels of glucocorticoids influence a range of physiological processes, such as immune system functioning, and neuronal functioning, which can explain if and how lockdown measures increase risk of mental disorders. Thus, it is an objective biological marker that helps to further understand the reasons for mental health decline during the pandemic. Finally, COVID-19 related stressors associated with salivary cortisol can hint to important mental health intervention targets. On a broader level, this dissertation project helps to estimate the temporal and endocrine effects of forced social isolation on mental health. Importantly, I referred to the no-lockdown stage as post lockdown in Study 1, because during the time of the assessment of Study 1, we did not know that there would be another lockdown stage. To summarize, the three studies in this dissertation investigated:

1. Mood inertia, COVID-19 related distress and loneliness during a post lockdown stage in Germany.

Haucke, M., Liu, S., & Heinzel, S. (2021). The persistence of the impact of COVID-19–related distress, mood inertia, and loneliness on mental health during a post lockdown period in germany: an ecological momentary assessment study. *JMIR Mental Health, 8*(8), e29419.

2. The impact of lockdown stages on the temporal dynamic association between COVID-19 related cognitions, daily activities, and stress.

Haucke, M., Heinz, A., Liu, S., & Heinzel, S. (2022). The Impact of COVID-19 Lockdown on Daily Activities, Cognitions, and Stress in a Lonely and Distressed Population: Temporal Dynamic Network Analysis. *Journal of medical Internet research, 24*(3), e32598.

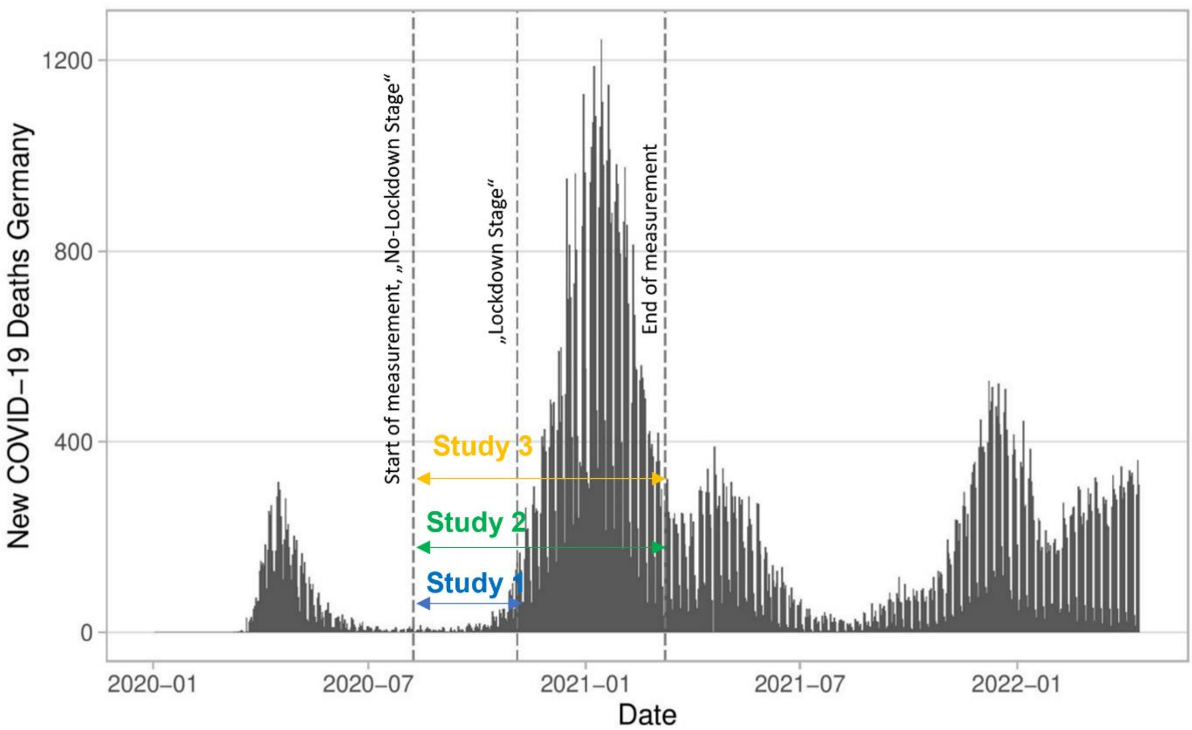
3. The impact of lockdown staged and associated mental health mechanisms on the stress-regulating hypothalamic–pituitary–adrenal (HPA) axis activity.

Haucke, M., Golde, S., Saft, S., Hellweg, R., Liu, S., & Heinzel, S. (2022). The effects of momentary loneliness and COVID-19 stressors on hypothalamic–pituitary adrenal (HPA) axis functioning: A Lockdown stage changes the association between loneliness and salivary cortisol. *Psychoneuroendocrinology, 145*, 105894.

To achieve the above-mentioned research goals, I conducted a smartphone-based ecological momentary assessment (EMA). In addition, I measured physical activity via the “GENEActiv” Original (Activinsights) monitor (dynamic range ±8 g, sampling frequency range 10-100 Hz). Saliva was collected using cotton rolls (Salivettes, Sarsteddt, Nuembrecht, Germany). The study was approved by the ethics committee at Charité–Universitätsmedizin Berlin (reference EA2/143/20) and Freie Universität Berlin (reference 030/2020).

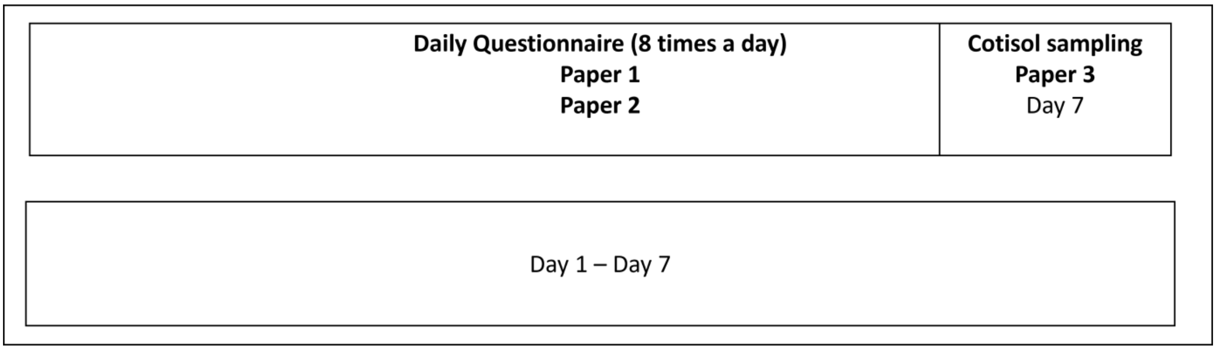
This dissertation project was conducted in Germany, between August 8, 2020, and March 9, 2021, amid the COVID-19 pandemic. In total, the project covers 213 days between a no-lockdown period (8 August – 1 November 2020) and a lockdown period (2 November 2020 – 9 March 2021; **Figure 6**).

Figure 6. The three studies included in this dissertation, which were conducted during the COVID-19 pandemic. The 7-day average of COVID-19 related deaths is displayed. Ref: WHO COVID-19 Dashboard. Geneva: World Health Organization, 2022. Available online: https://covid19.who.int/



I recruited participants across Germany who reported at least mild levels of loneliness (ULS-8; Hays & DiMatteo, 1987; cutoff score = 16) and COVID-19 related distress (CPDI; Liu & Heinz, 2020; cutoff score = 28). Participants were recruited via online advertisements on university websites, Twitter and eBay classifieds. In total 1549 participants were screened, of which 45% met both cut-offs. The study lasted 7 days, during the last day participants were instructed to take cortisol samples (**Figure 7**).

Figure 7. The sampling days the respective studies.



In the following section the three publications, which can be found in **Chapter 11 Publications**, are summarized.

5 Summary of empirical studies

5.1 Mood inertia, COVID-19 related distress and loneliness during a post lockdown stage in Germany (Study 1)

This chapter is a summary of 'Haucke, M., Liu, S., & Heinzel, S. (2021). The persistence of the impact of COVID-19–related distress, mood inertia, and loneliness on mental health during a post lockdown period in germany: an ecological momentary assessment study. *JMIR Mental Health, 8*(8), e29419.' DOI: https://doi.org/10.2196/29419

Research question:

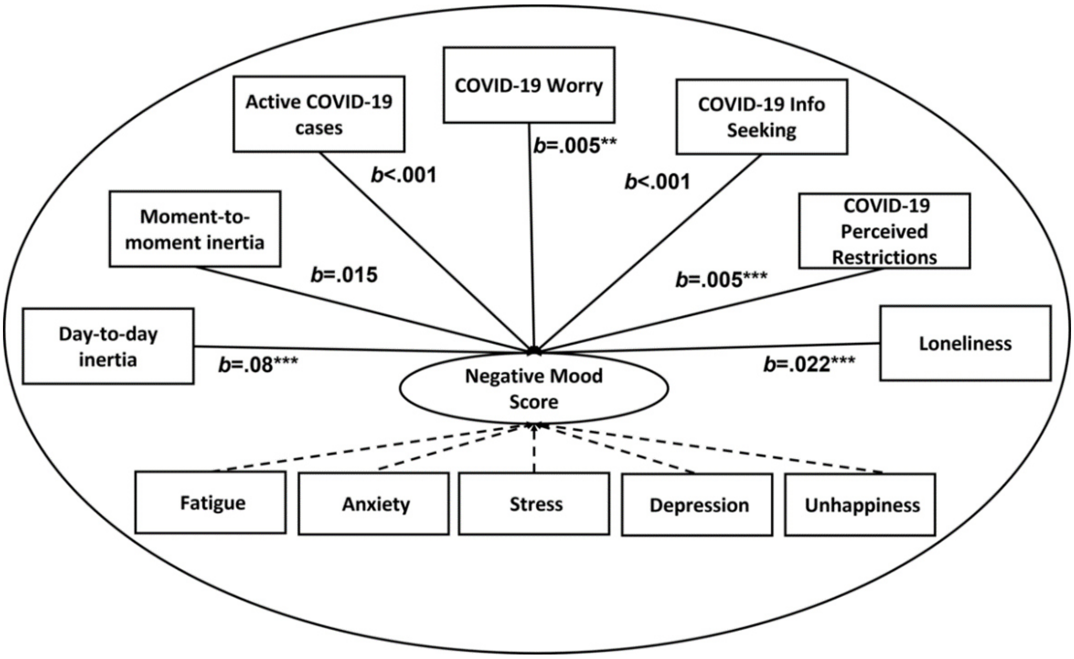
I investigated which COVID-19 related stressors during the first lockdown (Kämpfen et al., 2020; Mækelæ et al., 2020; Talevi et al., 2020; Wilson, Lee, & Shook, 2021), continue to impact mental health after the first major lockdown in Germany had ended. Due to social distancing measures and the resulting severe socioeconomic impact, it has been postulated that the COVID-19 pandemic impact on mental health will be long-term (Galea, Merchant, & Lurie, 2020; Kathirvel, 2020), some authors even expected a "tsunami of psychiatric illness" (Tandon, 2020). Yet, there is a lack of studies that investigate mood homeostasis (i.e., the regulation of mood via mood-modifying activities over time), as well as the effects of COVID-19 related distress and loneliness after the lifting of COVID-19 lockdown measures. Therefore, I investigated the following hypotheses:

1. The carryover effects of negative mood (indicating impaired mood homeostasis) will persist during a no-lockdown stage.
2. COVID-19–related stressors (i.e., momentary COVID-19–related worry, COVID-19 information seeking and perceived restriction), loneliness and daily reported COVID-19 cases will persist to increase momentary negative mood during a no-lockdown.

Main results and discussion:

A total of 131 participant were included in the study. I found that not COVID-19 information seeking or COVID-19 case numbers, but COVID-19-related worries, feeling restricted, and loneliness continued to increase negative mood. In addition, I found that there was not a moment-to-moment, but a day-to-day carry over effect of negative mood (i.e., mood inertia; see **Figure 8**)

Figure 8. Loneliness, COVID-19 worries, perceived restriction, and day-to-day mood inertia statistically significantly increased negative mood. Moment-to-moment mood inertia, active COVID-19 cases, and COVID-19 information seeking did not significantly increase negative mood. *p<.05, **p<.01, ***p<.0001 (two-tailed). N=131.



A possible reason for the continued impact of COVID-19 worries is that the negative economic consequences and the possibility of a virus resurgence remain beyond lockdown stages (Schiøler, Knudsen, Brøndum, Stoustrup, & Bøgsted, 2021; Liu, Heinzel, et al., 2021). Moreover, day-level mood inertia and perceived restrictions persist because people might limit their daily activities by choice. Although official restrictions are not in place anymore, the fear of infection could remain. Moreover, people's everyday habits and social networks might need to be rebuild after the disruptions caused by the first lockdown. In contrast to findings from the first lockdown (Ebrahim et al., 2020; Lüdecke & von dem Knesebeck, 2022), neither COVID-19 information seeking, nor active COVID-19 cases continued to impact mental health during a no-lockdown stage. Due to low case numbers, news reports might have been relatively positive compared to a more severe pandemic stage. To conclude, mental health might remain to be challenged by COVID-19-related stressors and impaired day-level mood homeostasis, even after strict lockdown measures have ended. Thus, this study highlights the need to protect mental health during a post-lockdown time.

However, due to a lack of comparison to a lockdown stage in Study 1, I cannot estimate whether the impact of loneliness on mental health was increased during the no-lockdown stage. This was done in Study 2, in which I compare the effect of lockdown stage on the temporal dynamic network structure of loneliness and other COVID-19 related behaviors and cognitions.

5.2 The impact of lockdown stages on the temporal dynamic association between COVID-19 related cognitions, daily activities, and stress (Study 2)

This chapter is a summary of 'Haucke, M., Heinz, A., Liu, S., & Heinzel, S. (2022). The Impact of COVID-19 Lockdown on Daily Activities, Cognitions, and Stress in a Lonely and Distressed Population: Temporal Dynamic Network Analysis. *J. Med. Internet Res., 24*(3), e32598.' DOI: https://doi.org/10.2196/32598

Research question:

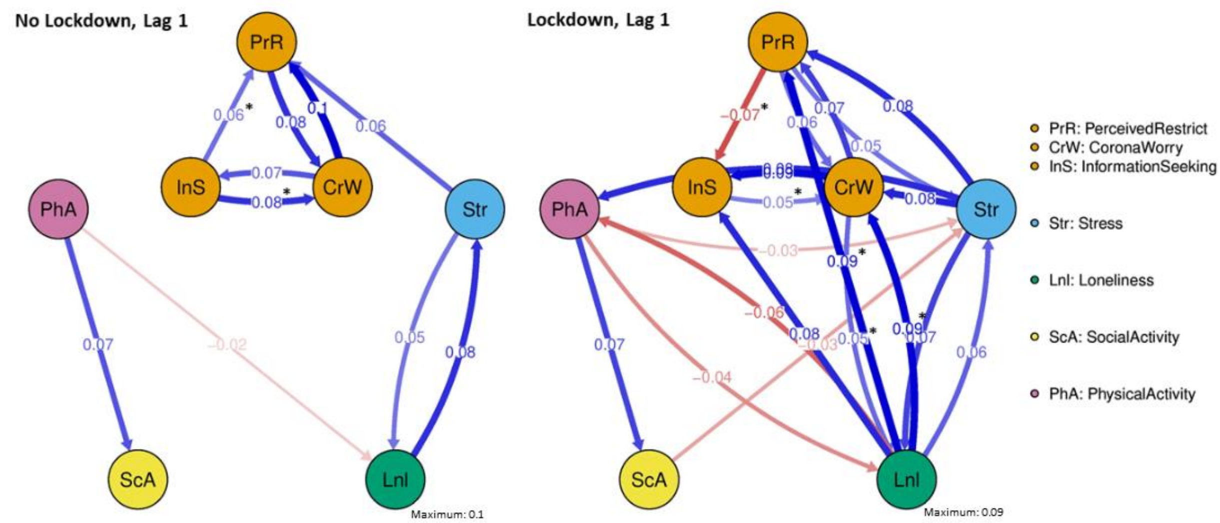
Although the COVID-19 pandemic and its associated lockdown measures impacted mental health worldwide, the temporal dynamics of mental health during a lockdown stage are not well understood. To do so, I estimated moment-to-moment time-lagged associations between loneliness and COVID-19-related cognitions, behavior, and stress. Moreover, I examined whether and how a lockdown changes the temporal association and centrality (i.e., a more central variable has more or/and stronger connections to other variables in the network) of loneliness and specific COVID-19-related behaviors and cognitions. This allows to identify the most protective or detrimental influences on mental health during a lockdown, which can help to prioritize mental health intervention targets. I investigated the following hypotheses:

1. Stress and loneliness will have a stronger influence on COVID-19–related worries, COVID-19 information seeking and perceived restriction, during a lockdown than during a no-lockdown stage.
2. A lockdown, in comparison to a no-lockdown period, will increase the network centrality of stress, physical activity, social contacts, and loneliness.

Main results and discussion:

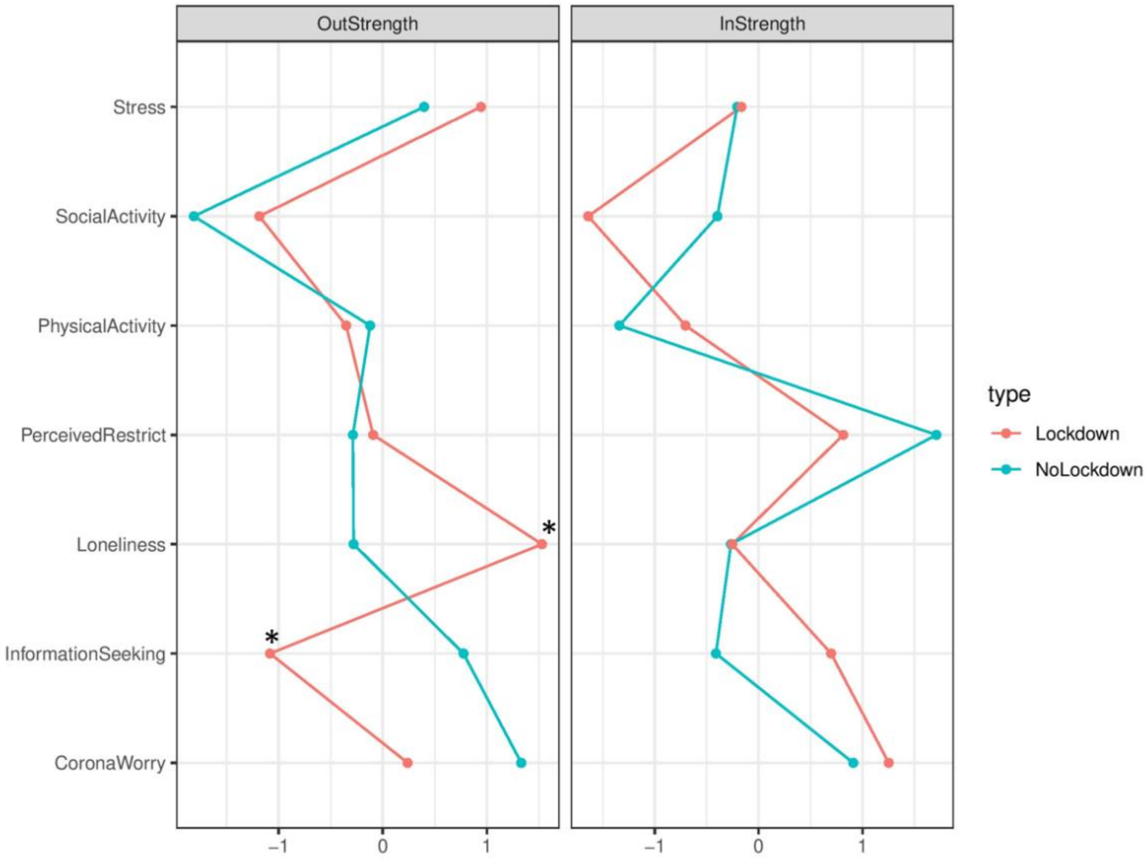
A total of 258 participant were included in the study (127 during a lockdown, 131 during a no-lockdown stage). I found that a lockdown stage, compared to a no-lockdown stage, increases the impact of loneliness on subsequent stress-inducing COVID-19-related cognitions (e.g., COVID-19-related worries) and behaviors (e.g., less physical activity, COVID-19-related information seeking, see **Figure 9**). These pandemic related cognitions and behaviors then reinforced each other over time and increased stress. In addition, during a lockdown stage, loneliness at one measurement point decreases stress-buffering physical activity at the next measurement point. Thus, loneliness can indirectly increase distress by decreasing stress-reducing behaviors.

Figure 9. Temporal dynamic networks in a no-lockdown (n=131) and a lockdown stage (n=127). Temporal associations among variable are estimated via multilevel vector autoregressive models. Nodes are variables and edges (arrows connecting nodes) are statistically significant (α<.05) temporal associations among variables. Thicker edges depict stronger relations; positive relations are blue and negative relations are red. Temporal associations that are statistically significantly different between the no-lockdown and lockdown stages (permutation testing using a two-sided p value at the uncorrected α level) are marked with an asterisk.



Moreover, a lockdown increases the centrality of loneliness. This means, during a lockdown, participants who reported feeling lonely at one measurement point, report more stress-inducing COVID-19-related cognitions and behaviors at the next measurement point (**Figure 10**). On the other hand, a lockdown decreases the centrality of COVID-19 information seeking. This means, during a lockdown, people who report COVID-19 information seeking at one measurement point, report less stress-inducing loneliness, COVID-19 related cognitions and behaviors at the next measurement point.

Figure 10. The standardized centrality indices out-strength and in-strength of the temporal networks of the no-lockdown (n=131) and lockdown stage (n=127). The statistically significant indices (permutation tests using a two-sided P value at the uncorrected α level) are marked with asterisks.



In line with my findings, two previous temporal dynamic network studies (Fried et al., 2020; Ebrahimi et al., 2021) found vicious cycles between negative mental health states (e.g., depression, anxiety, distress) and loneliness. Although these studies did not compare temporal networks across lockdown stages, they indicate that loneliness plays the most central role in the temporal dynamics of mental health during the first COVID-19 pandemic stage. In sum, results suggest that, during lockdown, loneliness becomes the central trigger of stress-related behaviors and cognitions and therefore should be prioritized in pandemic mental health interventions.

In addition to the temporal effect of lockdown stage, in study 3, I investigated whether a lockdown stage moderates the association between loneliness and hypothalamic–pituitary–adrenal (HPA) axis functioning.

5.3 The impact of lockdown on hypothalamic–pituitary–adrenal (HPA) axis functioning (Study 3)

This chapter is a summary of ‘Haucke, M. N., Golde, S., Saft, S., Hellweg, R., Liu, S., & Heinzel, S. (2022). The effects of momentary loneliness and COVID-19 stressors on hypothalamic–pituitary adrenal (HPA) axis functioning: A Lockdown stage changes the association between loneliness and salivary cortisol. *Psychoneuroendocrinology, 145*, 105894.’ DOI: https://doi.org/10.1016/j.psyneuen.2022.105894

<u>Research question</u>:

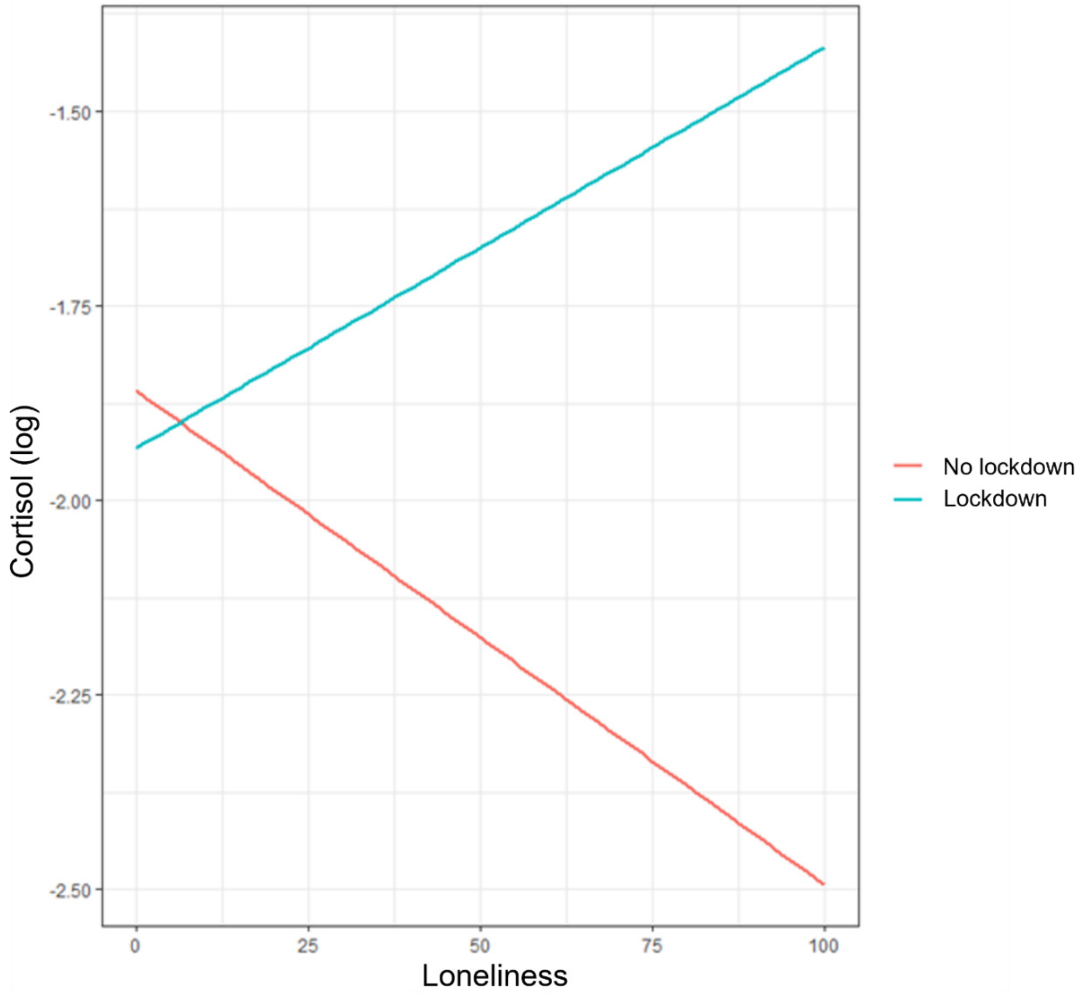
Excessive hypothalamic–pituitary–adrenal (HPA) axis activity can lead to chronically high glucocorticoid levels, which in turn, can increase risk for a range of physical (e.g., endocrine, metabolic, autoimmune dysfunction) and mental disorders (Charmandari et al., 2005). So far there are mixed results on the impact of COVID-19 pandemic and cortisol levels (Feneberg et al., 2022; Jopling, Rnic, Tracy, & LeMoult, 2021). Therefore, I investigated the following hypotheses:

1. Salivary cortisol will be higher during a lockdown stage than during a no-lockdown stage.
2. Loneliness and COVID-19-related stressors will be positively associated with salivary cortisol
3. Loneliness and COVID-19-related stressors will be more positively associated with salivary cortisol during a lockdown, than during a no-lockdown stage

<u>Main results and discussion</u>:

A total of 250 participants were included in the study (127 during a lockdown, 123 during a no-lockdown stage). I found higher levels of salivary cortisol during a lockdown, than during a no-lockdown stage. Furthermore, I found that a lockdown stage moderates the association between loneliness and salivary cortisol. During a no-lockdown stage loneliness was associated with decreased salivary cortisol, whereas during a lockdown stage, loneliness was associated with increased salivary cortisol (**Figure 11**).

Figure 11. Lockdown stage moderates the association between loneliness and cortisol. Cortisol is displayed as a function of loneliness during no-lockdown stage (red) versus lockdown stage (blue). More loneliness was associated with higher cortisol, specifically during a lockdown.



The results might be explained by the finding from Study 2. Loneliness during a lockdown might become a central trigger for other stress inducing behaviors and cognitions (e.g., worrying about the pandemic), while decreasing stress-buffering activities (e.g., physical activity). Thus, loneliness during a lockdown might has a more negative effect on HPA axis activity. Moreover, if stressors build up and ultimately exceed the adaptive resources of an individual, they can be perceived as uncontrollable and are strongly associated with an excessive and sustained endocrine stress response (Bornstein & Chrousos, 1999; Habib, Gold, & Chrousos, 2001). Moreover, a qualitative study conducted during the first lockdown stage indicates that the social restriction led to the perception that loneliness was outside of participants' personal control (McKenna-Plumley, Graham-Wisener, Berry, & Groarke, 2021). Thus, during a lockdown stage loneliness might be experienced as more uncontrollable, resulting in activation of the stress responsive HPA axis. In sum, loneliness can explain a mental health decline during the COVID-19 lockdown. Moreover, this study gives further evidence that loneliness should be a priority for mental health interventions during a lockdown stage.

The reasons for the different endocrine and temporal impact of loneliness during a no-lockdown and a lockdown stage are discussed in the following sections.

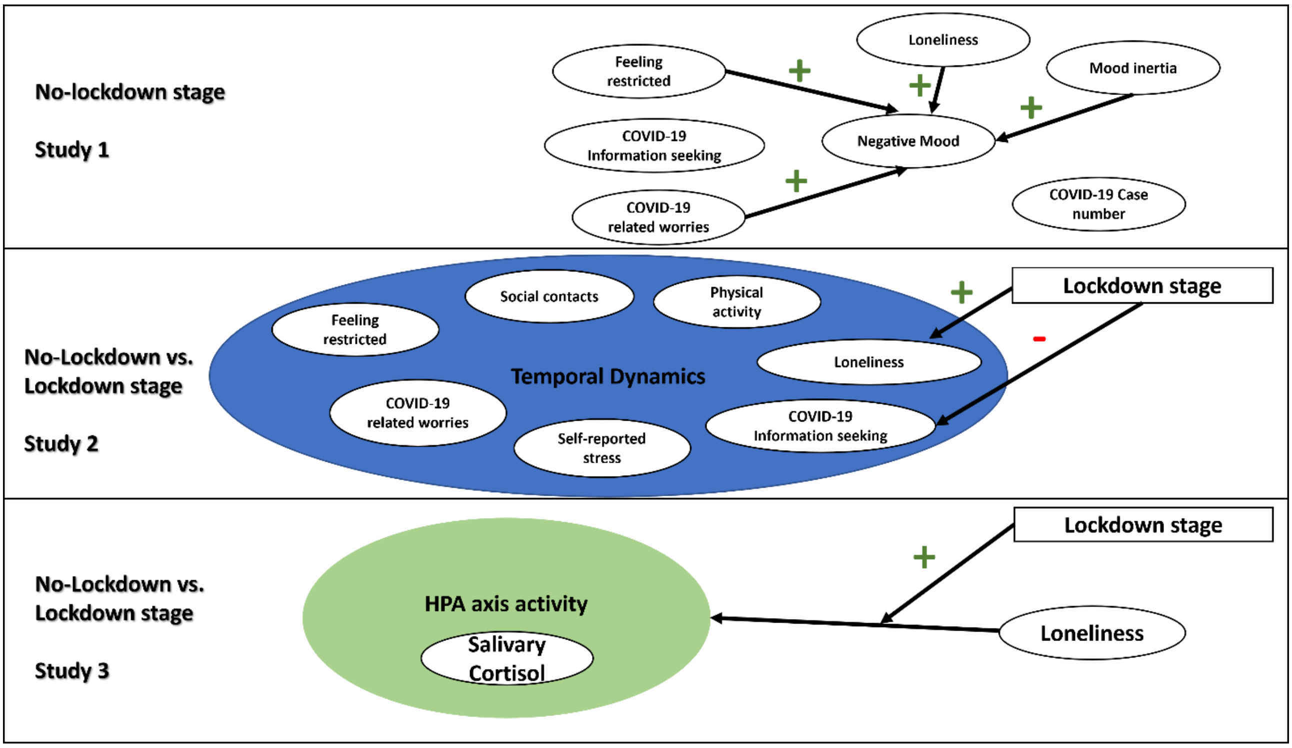
6 General discussion

The COVID-19 pandemic and associated public health measures have led to a decline of the general population's mental health (Holmes et al., 2020; Liu, Heinz, et al., 2021; Pfefferbaum & North, 2020). However, multiple factors (e.g., implemented public health measures, average-based assessment of loneliness and distress) lead to conflicting evidence on the magnitude of the pandemic impact on mental health (Beutel et al., 2021; Liu et al., 2021; Luchetti et al., 2020; Robinson et al., 2022). Thus, the dissertation project set out to better understand how the pandemic affects mental health, find effective mental health intervention targets during a pandemic, and advance our understanding of the impact of forced social isolation on temporal dynamics of mental health and the neuroendocrine system. The three studies in this dissertation investigated: 1) whether the pandemic and lockdown effect will continue to impact mental health beyond a lockdown stage, 2) how a lockdown impacts the temporal dynamic of COVID-19 related stressors and loneliness and 3) whether and how a lockdown is associated with stress-regulating pituitary-adrenal (HPA) axis functioning.

The three main results of this dissertation project are: Firstly, I found that after lockdown measures have ended, the negative effects of a majority of measured COVID-19 related stressors and mood inertia persist. Thus, there is a need for continued effort to protect mental health, after a lockdown stage has ended. Secondly, my study suggests that a lockdown stage, compared to a no-lockdown stage, increases the impact of loneliness on subsequent COVID-19 related cognitions and behaviors, which build up to a vicious, stress-inducing cycle. In addition, loneliness is the central trigger for other COVID-19 related stressors during a lockdown stage. Thus, when strict lockdown measures are in place, loneliness can set behaviors and cognitions in motion, which can lead to mental health decline. Thirdly, compared to no-lockdown, during lockdown I found evidence for changed hypothalamic-pituitary-adrenal (HPA) activity, indexed by salivary cortisol. My results suggest that lockdown measures moderate the association between loneliness and HPA axis activity. During a no-lockdown stage, loneliness is associated with decreased levels of salivary cortisol, whereas during a lockdown stage, loneliness is associated with increased levels of salivary cortisol. Thus, loneliness is a central reason for the mental health decline during a lockdown stage and should be prioritized by mental health interventions.

I found two temporal effects associated with the impact of the COVID-19 pandemic on mental health: impaired mood homeostasis indicated by day level mood inertia (Study 1), and an increased temporal dynamic impact of loneliness on stress-related behavior (Study 2). In addition, I found evidence for a neuroendocrine effect associated with the COVID-19 pandemic: a lockdown stage can moderate the relationship between loneliness and salivary cortisol level, that is, loneliness was positively related to cortisol levels specifically during lockdown (Study 3). **Figure 12** shows a summary of the results.

Figure 12. Overview of the main results of the three research results involved in this dissertation.



In the following chapters I will discuss in more detail why loneliness has a different impact on mental health during a lockdown stage.

6.1 Interim conclusion

A range of studies comparing the average amount of loneliness prior and during lockdown stages showed that there was no, or a negligible increase in loneliness (Beutel et al., 2021; Liu, et al., 2021; Luchetti et al., 2020; McGinty et al., 2020; Van Tilburg et al., 2021). These findings led McGinty et al. (2020) to conclude "*Because loneliness increased* *only slightly from 2018 to 2020, other factors may be driving psychological distress during the COVID-19 pandemic*" (p. 94). Yet, this dissertation project indicates that although the average amount of felt loneliness does not necessarily increase, the temporal and endocrine impact of loneliness can change. The results of the presented research projects open some intriguing questions: Why does loneliness become a central trigger of other stress-inducing behaviors during a lockdown, but not during a no-lockdown? Why does loneliness increase salivary cortisol during a lockdown, but decreases salivary cortisol during a no-lockdown? In the following section I will try to give a possible explanation by proposing a new model of loneliness.

6.2 Integration of results - a new hypothetical model of loneliness

To explain why a lockdown changes the impact of loneliness on subsequent stress-inducing cognitions, behaviors (Study 2) and the neuroendocrine stress response (Study 3), I propose the following three factors: The type of lacking relationships, perception of control over loneliness and different prior experiences with loneliness. In the following section, I will summarize previous conceptualizations of loneliness, then I will explain what the lockdown taught us about the negative mental health impact of loneliness. Finally, I will propose the "contextual and cognitive model of loneliness".

Loneliness can be classified according to positive and negative forms. A common way to define negative loneliness is the subjectively experienced discrepancy between desired and actual interpersonal relationships (Perlman & Peplau, 1984). A rather objective description of a situation in which there is an absence of interpersonal relationships is called social isolation (de Jong Gierveld, Van Tilburg, & Dykstra, 2006). Thus, social isolation does not necessarily lead to higher amount of loneliness, or the experience of negative loneliness. A rather positive form of loneliness has been called solitude, which describes a fundamental human experience, involving phases of self-confrontation. That is, the individual in solitude becomes aware of her/his values and self-identity, which can lead to self-growth (Moustakas, 2016).

Loneliness can be further distinguished between more short term and long-term forms. On the one hand, loneliness can be experienced temporarily, which is often linked to life events, such as moving to a new city. One the other hand, loneliness can also take more chronic forms, which is strongly associated with detrimental consequences for mental health (de Jong et al., 2006). Weiss (1973) has further proposed forms of loneliness that can cause distinct emotional consequences: social and emotional loneliness. Emotional loneliness results from a lack of close and intimate relationships, evoking anxiety and emptiness. On the other hand, social loneliness results of a lack of a social network, such as friends who share the same interests, evoking feelings of aimlessness and boredom (Russell, Cutrona, Rose, & Yurko, 1984). However, not only the form of loneliness can be important for mental health consequences, but the way loneliness is perceived.

According to the cognitive discrepancy approach to loneliness (Perlman & Peplau, 1981), the mental health consequences of loneliness are modulated by a person's perception of control, social comparison and causal attribution. Following the approach by Weiner (2012), loneliness can be attributed to the dimensions "locus of causality" (internal vs. external), "stability" (stable vs. instable) and "control" (uncontrollable vs. controllable). For example, the statement "I am lonely because I am an uninteresting person" would represent an internal, stable, and uncontrollable attribution, whereas "I am lonely because I moved to a new city" would be an external, unstable, and rather controllable attribution. If loneliness attributions are stable, internal and uncontrollable, loneliness can have a more detrimental impact on mental health, such as increased levels of depression (Michela, Peplau, & Weeks, 1982; Newall et al., 2009). Loneliness experienced during a lockdown might be perceived as rather external, instable and uncontrollable.

Perlman and Peplau (1981) propose that personal control over one's relationship influences the experience of loneliness. For example, perceived control over loneliness decreases experienced loneliness in elderly nursery home residents (Moore & Schultz, 1987). Moreover, nursing home residents report less loneliness if they had control over the visiting hours (Schulz, 1976) and relationship partners who initiated the breakup with their partners felt less distressed by loneliness than their counterpart (Hill, Rubin, & Peplau, 1976). Due to social distancing measures and people's avoidance of possibly contagious social contacts, lockdown might have changed the perception of control over one's loneliness. In line with this, a qualitative study conducted during the first lockdown stage found that respondents indicated a lack of agency and choice when describing their social life (McKenna-Plumley et al., 2021). Finally, the cognitive discrepancy approach to loneliness proposed that social comparisons influence the experience of loneliness (Perlman & Peplau, 1981). Accordingly, by comparing oneself to others (peers or former relationships) one estimates how large or important one's social deficits are.

In sum, loneliness can vary across these dimensions: 1. positive vs. negative, 2. chronic vs. short term, 3. the type of lacking relationships. The type of loneliness, in turn, is processed and perceived by an individual via 1. attribution process 2. social comparison processes and 3. perception of control. The processed loneliness then leads to behavioral and cognitive consequences.

According to Hawkley and Cacioppo (2010), loneliness induces a feeling of being unsafe, which induces hypervigilance towards social threats. That is, loneliness induces a cognitive bias, causing people to overly attend to, expect, and remember social threatening information. This, in turn, elicits behavior in other people, which tends to confirm the negative expectation, creating a self-fulfilling prophecy. Moreover, this implicit hypervigilance toward social threats decreases a person's ability to engage in self-regulatory behaviors, such as regulation of feelings (e.g., maintenance and increase of positive emotions; Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006), behaviors (e.g., physical activity; Hawkley, Thisted, & Cacioppo, 2009) and thoughts (e.g., worries about one's social performance; Maes et al., 2019). Finally, the lack of self-regulatory behavior, together with the distress of prolonged stress-increasing behaviors and cognitions, can increase physical and mental disease risk.

Moreover, there are two central models that explain why loneliness affects mental and physical health (Cacioppo et al., 2015). On the one hand, the "main effects" models propose that social relationships encourage healthy behaviors, including exercise, restricted drug and alcohol consumption or engaging in a healthy diet (Umberson, 1992) and model healthy behaviors, and therefore establish a social norm (Holt-Lunstad, Smith, & Layton, 2010). On the other hand, loneliness could have a direct effect on physiological functioning by activating stress-responsive physiological systems, such as the hypothalamic–pituitary–adrenal (HPA) axis (Bosch, Nair, Ahern, Neumann, & Young, 2009; Castro & Matt, 1997; Pournajafi-Nazarloo et al., 2011). If this physiological stress response persists, it can lead to chronically high levels of glucocorticoids, affecting physiological functions, which in turn, can directly increase the risk for physical and mental disorders (Charmandari et al., 2005).

In line with Hawkley and Cacioppo (2010), my study indicates that loneliness can set in motion a range of stress-inducing and self-reinforcing negative behaviors (lower physical activity, more COVID-19 related information seeking) and cognitions (more COVID-19-related worry, more perception of restriction). That is, loneliness can trigger worrying and rumination (e.g., "Why am I lonely?", "Will I lose my job?", "Why is the pandemic so hard for me?”), which might not have a clear answer and therefore can continue for a long time, which in turn leads to a self-reinforcing loop of stress-inducing cognitions. Moreover, my results indicate that the effect of loneliness on the stress—responsive physiological system are partially caused by a negative effect of loneliness on stress-regulating behaviors (e.g., physical activity). Yet, the factors that decide on whether loneliness triggers stress-relevant behaviors and cognitions were present during lockdown, but not during a no-lockdown stage. Therefore, my results indicate that an advanced understanding of the health impact of loneliness requires a combination of the loneliness models by Hawkley and Cacioppo (2010) and the cognitive discrepancy model by Perlman and Peplau (1981). That is, not only the amount of loneliness, but the context and how it is perceived, decide on whether loneliness triggers other stress-inducing behaviors and cognitions.

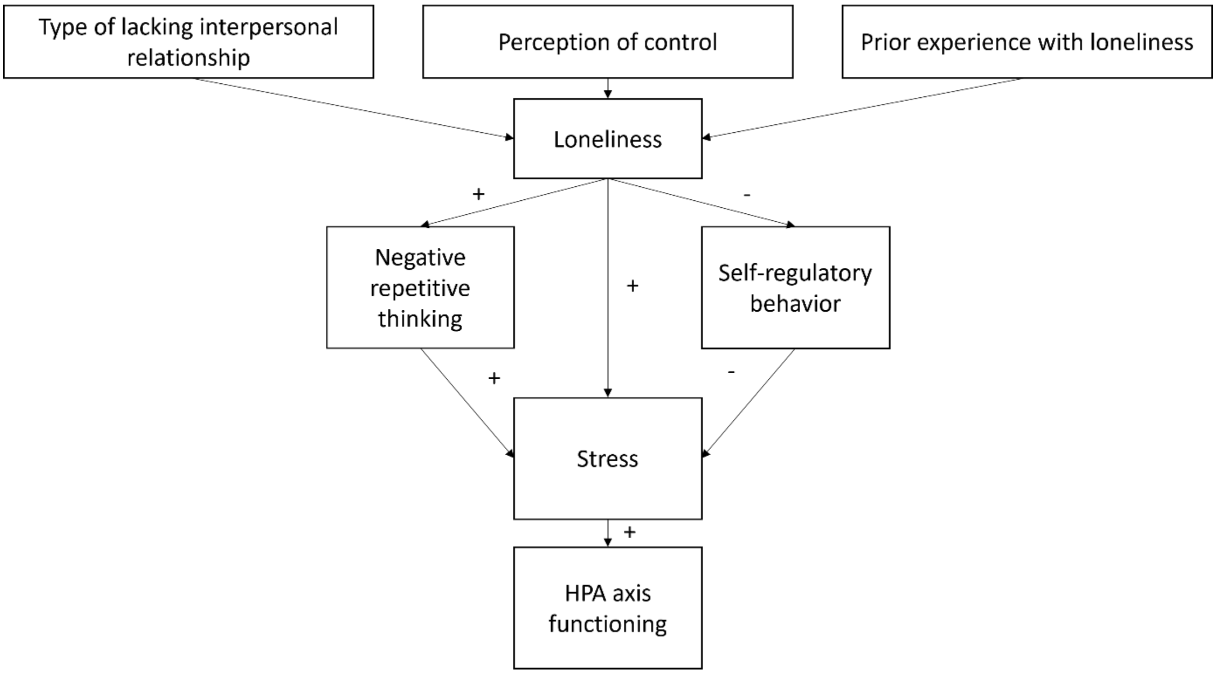
The lockdown might have impacted three factors that are decisive for whether loneliness triggers subsequent stress-inducing behaviors and cognitions and affect HPA axis functioning. Firstly, lockdown measure and forced social isolation might change the type of interpersonal relationship one is lacking: Missing close family members or relationship partners vs. missing friends or acquaintances. A qualitative study (McKenna-Plumley et al., 2021) indicates there was a general increase of emotional loneliness during lockdown, as public health measures and fear of infecting others limited the visits of close family members (e.g., elderly parents and grand-parents), which would normally be accessible. Moreover, respondents stated that lockdown measures have made it harder to meet romantic partners. So far, there is a lack of studies that investigated whether a lockdown leads to more emotional than social loneliness. A German study indicates that there was no general increase in emotional loneliness (Landmann & Rohmann, 2022), yet it only covers the first 8 weeks of lockdown.

Secondly, a lockdown might confront people with loneliness, who have not experienced it before. Extroverted and younger individuals, who usually report less loneliness (Buecker, Maes, Denissen, & Luhmann, 2020), reported higher levels of loneliness during a lockdown (Landmann & Rohmann, 2022). People who are used to being alone might be more capable to regulate their need for social contacts without engaging in social interactions. For example, compared to people in relationships, single people rely less on social networks and focus more on their careers and professions when feeling lonely (Rokach & Brock, 1998). This might be an effective strategy in times of physical distancing.

Thirdly, governmental enforced and self-chosen physical distancing during the first lockdown can increase the perception that loneliness is uncontrollable (McKenna-Plumley et al., 2021). A range of psychological theories propose that perceived control or agency over a stressful situation is a central mechanism that explains the occurrence of subsequent thought, behavior, and physiological stress reactions (Bandura, 1982; Perlman & Peplau, 1981; Seligmann, 1975).

To explain why a lockdown changes the effect of loneliness on subsequent behaviors, cognitions, and HPA axis activity, I propose the "*contextual and cognitive model of loneliness"*. This time-sensitive model states that 1. the type of lacking interpersonal relationships, 2. the perception of control over one's loneliness and 3. prior experience with loneliness influence the current experience of loneliness, which in turn, can lead to a cascade of other stress-inducing behaviors and cognitions. That is, these three factors can influence whether loneliness triggers negative repetitive thinking (i.e., worry about the cause of loneliness) and decreases stress-regulating activities (e.g., hobbies, physical activity). In addition to the direct effect of loneliness, these cognitions and behaviors then lead to the subjective experience of distress, which affects hypothalamic–pituitary–adrenal (HPA) axis functioning, see **Figure 13.**

Figure 13. A *contextual and cognitive model of loneliness*. This time-sensitive model proposes that contextual and cognitive factors can influence whether loneliness leads to a cascade of other stress-including behaviors and cognitions and ultimately to distress on a subjective and physiological level.



This model is based on a times-sensitive assessment of loneliness, which allows to estimate the triggering effects of loneliness on other subsequent behaviors and cognitions. Accordingly, the total amount of felt loneliness is not sufficient to predict whether loneliness impacts mental health. Finally, the model could be applied within psychotherapeutic settings to decide on the harmful consequences of being alone.

For example, one could ask:

1. What kind of relationships are you missing: romantic partners, family members, friends?
2. Do you feel in control of your loneliness? Is your current loneliness unchangeable?
3. Have you experienced loneliness before? Do you have strategies against it?

Importantly, my results might not be representative beyond the COVID-19 lockdown. The COVID-19 lockdown has a direct influence on the subsequent cognitions and behaviors, by restricting the choice of daily activities a person can engage in (e.g., being hesitant to meet people, not being allowed to engage in one's sport class) and by creating the situational context in which specific personal worries arise (i.e. the economic impact of lockdown, one's health status and the health status of one's family members).

Moreover, I did not measure the three proposed factors, thus how the experience of loneliness was changed by a lockdown stage remains speculative.

6.3 Future studies and implications

Large pandemics such as the COVID-19 pandemic have been part of human history for a long time. In the last century humanity faced the Spanish flu (1918-1920), the severe acute respiratory syndrome (SARS, 2002-2003), the “Swine” flu (2009) and Ebola (2013-2014). In fact, the probability of a major epidemic outbreak might increase between 0.3% to 1.8% per year, that is, a person born in 2000 has a 38% likelihood of experiencing a major pandemic in their lifetime (Marani, Katul, Pan, & Parolari, 2021). In addition, the risk of future pandemics increases due to factors such as population growth, international travel, climate change, environmental degradation and the resulting contact between humans and disease-harboring animals (Daszak, Cunningham, & Hyatt, 2001; Marani et al., 2021). Thus, the results from this research projects can inform mental health interventions for future pandemics.

A next step in using the network approach to decide on mental health intervention targets is the adaption of a mixed method approach (Shorten & Smith, 2017). While gathering data to estimate the temporal dynamics between mental health related behaviors and cognitions, one can conduct qualitative interviews with the respective participants. This approach would allow to understand how a person experiences loneliness and the content of a person’s worries, beyond their temporal associations.

Moreover, it remains important to investigate whether the stressor during the pandemic persists and whether the pandemic will lead to permanent lifestyle changes. For example, a survey with over 1,700 businesses (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin; BAUA 2020) has shown that 18% of respondents planned to increase working from home after the pandemic. Homeoffice and telework can offer a range of benefits for the employee; however, it can also decrease one’s social network and can lead to increased work-family conflicts (Oakman, Kinsman, Stuckey, Graham, & Weale, 2020).

Moreover, the role of loneliness in triggering stress-inducing behaviors and cognitions and its impact on HPA axis function need to be investigated in other contexts of involuntary social isolation. One such context could be loneliness experienced by refugees who were forced to leave their homes to escape an armed conflict, violation of human rights and natural or human made disaster. Currently, there are 15 million people claiming refugee status, who often arrive in foreign countries and experience high levels of social isolation (Johnson, Bacsu, McIntosh, Jeffery, & Novik, 2019; Solmaz, Karataş, Kandemir, & Solmaz, 2021).

My research project indicates that mental health interventions during a pandemic should focus on loneliness. But how can we design mental health interventions for future pandemics? Interventions aimed at reducing loneliness have four primary goals: 1. Providing social skills (e.g., psychoeducation, social skills groups), 2. increasing social support (e.g., telehealth, support groups), 3. increasing social interactions opportunities (e.g., a sport club) and 4. changing maladaptive social cognition (e.g., unrealistic relationship expectations, dysfunctional thoughts, and beliefs about being alone; de Jong Gierveld et al., 2006). A meta-analysis (Masi, Chen, Hawkley, & Cacioppo, 2011) has shown that the most effective intervention to reduce loneliness was the treatment of maladaptive social cognition. Thus, the way loneliness is perceived and evaluated might be an important pathway to reduce its harmful effect.

During the pandemic the ways to reduce loneliness are limited by social distancing measures. However, there are three potential pathways to decrease loneliness: Firstly, engaging with social contacts via online media. Accordingly, the World Health Organization (2020) recommended using digital media such as telephone, e-mail, social media platforms, or video conference to stay connected with one's social network in times of physical distancing. In line with this, the usage of social media in socially isolated groups (e.g., elderly in nursing homes) has been shown to decrease a sense of social isolation (Hajek & König, 2019). Secondly, adapting personal standards to the new situation. Adapting one's personal demands, desires, goals, or norms of interpersonal relationships can be effective if the loneliness provoking situation is unchangeable (Bouwman, Aartsen, van Tilburg, & Stevens, 2017). This includes readapting expectation toward friendships and one's behaviors to reevaluate the situation ("I do not want to transmit the virus to a friend or family members; thus, I want to accept that I cannot directly meet my friends or family."). Finally, one could reduce the perceived importance of loneliness, without necessary altering or reducing the feelings of loneliness. That is, loneliness is allowed to persist, but its importance is reduced by accepting that the problem cannot be directly solved and by putting one's attention away from it (e.g., one could create a list of attractive solitude activities; Bouwman et al., 2017). In line with this proposition, engagement in pleasurable solitary activities (e.g., reading, watching TV) can decrease feelings of loneliness (Rook, 1984; Stevens, 2001).

6.4 General limitations of the studies

Intensive ecological momentary assessment allows to investigate psychological processes that happen in people's everyday life over the course of the day (Shiffman et al., 2008). Yet, EMA also causes an interference in people's everyday life, leading to a decrease of compliance rates (Wen, Schneider, Stone, & Spruijt-Metz, 2017). Therefore, I used single-item questions, rather than an extensive questionnaire, which limits the way I can capture the concept under investigation. For example, I cannot make statements about the content of COVID-19-related worries. Moreover, I have a single-item measure of loneliness, which might be insufficient to measure this complex construct. On the other hand, in Study 1, I used an aggregated score of stress, depression, anxiety, fatigue and happiness ("negative mood"), which averages out effects that might be specific to a unique outcome.

Moreover, there are several important limitations associated with my estimation of temporal dynamic networks via univariate models (Bringmann et al., 2013). Estimation via univariate models involves the sequential estimation of multiple autoregression models, which allows to simplify the calculation and makes it feasible to conduct via an open-source statistical software (i.e., R Software). However, univariate models do not allow to estimate all correlation of random effect in the same models, thus some potentially important correlations of random effects are ignored (Epskamp et al., 2012a). Secondly, this approach does not allow a reliable estimation beyond eight nodes, which limits the method's applicability to larger datasets (Epskamp, Cramer, Waldorp, Schmittmann, & Borsboom, 2012b). Related to the limited estimation capacity is the possibility that I omitted a variable that was central to the estimated network, which might have caused the observed temporal dynamics (De Ron et al., 2019).

In Study 1 I assessed day-to-day mood inertia (i.e., the impact of mood at time point 1 on mood at time point 2), which can indicate impaired mood homeostasis. Mood homeostasis refers to a person's ability to modulate their mood via mood modifying activities (e.g., meeting friend when being sad). Importantly, I did not directly test for the impact of mood modifying activities on mood inertia, thus it remains possible that participants engaged in mood modifying activities, without effectively changing their mood.

Moreover, there are at least two limitations caused by the way I sampled salivary cortisol. Firstly, although self-collection of salivary cortisol increases ecological validity, it does not allow to fully control for the adherence to the sampling protocol (Stalder et al., 2016). Since salivary cortisol has a strong variation during the day (sharp increase within 30-45 minutes after morning awakening, followed by a flattening towards nighttime) the correct sampling time points are crucial (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). Although I controlled for the adherence by comparing the written waking up times with the estimated waking up times via actigraphy devices (Van Hees et al., 2015), I cannot rule out non-adherence to sampling protocol for later measurement points.

This dissertation project was conducted during a severe stage of the COVID-19 pandemic with high amounts of COVID-19 cases and COVID-19-related deaths in Germany, leading to strict social isolation measures. This limits the generalizability to other countries, pandemic stages, and to other forms of involuntary social isolation (e.g., elderly people who have lost their romantic partners or imprisonment). In addition, the effects of high amounts of COVID-19 case numbers and the associated lockdown measures are highly intertwined, which makes it hard to distinguish between a specific lockdown and a severe pandemic effect. A final complication is that COVID-19 cases are driven by seasonal changes, causing differences in behavior (e.g. meeting people indoors with bad ventilation) and a change of the virus' survival rate (e.g. SARS-CoV-2 survives best in cold and dry climate conditions) (Mallapaty, 2020; Merow & Urban, 2020). Thus, I cannot exclude the possibility that the observed effects of loneliness are caused by seasonal changes, rather than the lockdown stages. Finally, I focused on a vulnerable group that reported at least mild levels of distress as well as loneliness (approximately 45% of the recruited participants), which limits the generalizability of my findings to the entire population.

Despite their limitations, this dissertation project has been conducted during one of the most severe pandemics of the century. Thus, it offers a unique insight into the impact of a pandemic and involuntary social isolation on the neuroendocrine system and the temporal dynamics between loneliness and mental health.

6.5 Conclusion

The main aim of this dissertation project was to understand how the COVID-19 pandemic and lockdown stage impact mental health. Moreover, the dissertation project sets out to find effective targets for mental health interventions and to further understand the impact of forced social isolation on temporal dynamics of mental health and the neuroendocrine system. In a first study the following research questions were examined:

Do COVID-19–related stressors, loneliness and daily reported COVID-19 cases persist to increase momentary negative mood during a no-lockdown? And is mood homeostasis impaired during a no-lockdown stage?

I found that COVID-19-related worries, perceived restrictions, and loneliness, as well as day-level mood inertia continued to affect mental health. In contrast to findings from the first lockdown, I did not find that COVID-19 information seeking, nor COVID-19 cases continued to affect mental health during a no-lockdown stage.

To identify the most protective or detrimental influences on mental health during a lockdown, I estimated and compared moment-to-moment time-lagged associations between pandemic-related cognitions, behaviors, and mental states between lockdown stages. I examined whether and how a lockdown changes the centrality (i.e., a more central variable has more or/and stronger connections to other variables in the network) of loneliness and specific pandemic-related behaviors and cognitions. Thus, in a second study the following research questions were examined:

Does a lockdown, in comparison to a no-lockdown period, increase the network centrality of stress, physical activity, social contacts, and loneliness? And will stress and loneliness have a stronger influence on COVID-19–related worry, COVID-19 information seeking and perceived restriction?

I found that during a lockdown stage loneliness was the central trigger for subsequent stress-inducing behaviors and cognitions. Moreover, during lockdown loneliness increased in centrality. That is, during lockdown, participants who report feeling lonely at one measurement point, report more COVID-19 related cognitions and behaviors at the next measurement point. These pandemic related cognitions and behaviors then reinforced each other over time building vicious cycles and increasing stress. In addition, during a lockdown stage, loneliness at one measurement points decreased stress-buffering physical activity at the next measurement point. Finally, I looked at the effect of lockdown on the stress-regulating endocrine system (i.e., hypothalamic–pituitary–adrenal (HPA) axis). In a third study the following research questions were examined:

Are salivary cortisol levels higher during a lockdown stage than during a no-lockdown stage? And does a lockdown change the association between salivary cortisol and COVID-19-related stressors as well as loneliness?

In study 3, I found that salivary cortisol levels were increased during a lockdown stage. Moreover, a lockdown moderates the association between loneliness and salivary cortisol. During a lockdown, loneliness was positively associated with salivary cortisol, whereas during a no-lockdown loneliness was negatively associated with salivary cortisol. Thus, a change on the experience of loneliness might be a central mechanism that explains the impact of the pandemic and associated lockdown stages on HPA axis functioning.

Taken together, my findings highlight the need to protect mental health, even after lockdown measures have ended. A key factor explaining the impact of lockdown on mental health is loneliness. Firstly, a lockdown can increase the temporal dynamic impact of loneliness on subsequent stress-inducing behaviors and cognitions. Secondly, a lockdown stage can lead to higher amount of cortisol levels which indicates changed HPA axis activity during a lockdown. In addition, a lockdown stage was found to moderate the relationship between momentary loneliness and salivary cortisol levels, i.e., loneliness was positively related to cortisol levels specifically during a lockdown stage. This result further supports the conclusion that loneliness should be a priority for mental health intervention during times of lockdown. A more complex and time-sensitive model of how loneliness affects subsequent stress-inducing behaviors, cognitions and HPA activity is needed to fully understand the impact of forced isolation on mental health.

7 Appendix

Further explanation of time series models

In a time series, a trend is the systematic change of the long-term direction. That is, the direction and slope (rate of change) change during a time series. Seasonality describes repeating patterns of increase or decrease in a time series. In other words, seasonality is the cyclical pattern of movement associated with seasonal factors, such as month, quarts of a year or days of a week (Jebb et al., 2015). Cycles are non-seasonal component of time series data that vary in recognizable patterns (e.g., business cycles) (Jebb et al., 2015). Thus, cycles are similar to seasonality, however their pattern are not of fixed duration (i.e., length varies from cycle to cycle), nor are they related to naturally occurring time periods, such as day/weeks/months.

A time series is called stationary when its mean, variance and autocorrelation structure do not vary over time (Cowpertwait & Metcalfe, 2009). Thus, stationarity is important because the descriptive statics of a time series, such as its mean and variance, only reflect population estimates accurately if they remain constant (Cowpertwait & Metcalfe, 2009). Stationarity is "the most important assumption" when one tries to predict future values from past operation, and most time series models assume stationarity or can be transformed to be stationary (e.g., logarithmic transformation if the variance is not constant over time; Cryer & Chan, 2008). A common formal statistical test for stationarity is the augmented Dickey–Fuller test (ADF; Said & Dickey, 1984).

Time series analysis can be further subdivided into a time domain and frequency domain approach (Wei, 2006). The Frequency domain approach uses spectral functions to investigate variation in time series via a mixture of sines and cosine with varying frequency (e.g., astronomers deduce the speeds of galaxies relative to our own via spectral analysis, for more details see Jenkins & Priestley, 1957). Whereas, in the time domain approach, time function such as the autocorrelation function (ACF) and the partial autocorrelation function (PACF) are used to represent time series-processes via time-lagged relationships (Wei, 2006).

Variation in time series analysis, which is completely random (i.e., not autocorrelated) is called white noise in time series terminology, which is the same as the error term in other types of statical models (Jebb et al., 2015). Thus, in a time series analysis that has accounted for all pattern in the data, the residual error should be white noise with a mean of zero and constant variance (Geoghegan, 2006). Therefore, in time series analysis every systematic error must be accounted for by either explicitly modeling it or removing it through mathematic transformation (Geoghegan, 2006).

The autocorrelation coefficient across many lags is called the autocorrelation function (ACF). We can plot the autocorrelation function (correlation coefficient as a function of lag k), which indicates if correlation between that shifted and original time series will decline. Related to this is the partial autocorrelation function (PACF), the particle autocorrelation at lag k is the autocorrelation between yt and yt-k that is not accounted for by lags 1 through k-1. Thus, the PACF is a way to remove intermediary effects and isolate the portion of the lag between yt and yt-k that doesn't depend on other time steps. PACF is used to identify the correct order (k) of an autoregressive model.

The autoregressive (AR) model can capture autocorrelated processes with random components. In these models a response variable in the previous time period (e.g., immediate time point: t-1) becomes predictor and the error have usual normal distribution assumption. The formula for a time series (x_t) as an autoregressive process of order p, summarized as AR(*p*) can also be written as:

$$x_t = \alpha_1 x_{t-1} + \alpha_2 x_{t-2} + \ldots + \alpha_p x_{t-p} + w_t$$

In this formula w_t is white noise, α_i are the model parameter. The order of an AR model is the number of immediately preceding values in the time series that is used to predict a value at time point t. For example, and AR(1) model would only use the immediately preceding values at time time (t-1). A second order AR models AR(2) would predict the values at time xt, from the values at times (t-1) and (t-2). So AR(k) is a multiple linear regression in which the values of the series at time point t is a linear function of the values at times t-2,t-2…,t-k.

Other types of time series models are the autoregressive moving average (ARMA) model or autoregressive integrated moving average (ARIMA) model. The current values in a time series can be determined by two factors: 1. The prior value, and 2. random errors (i.e., "random shocks"; Jebb et al., 2015). This random error (i.e., white noise) results from interacting unobserved variable varying across time and impacting our observed values. In moving averages models, autocorrelation is explained by the persistence of this lingering random error (i.e., unobserved random shocks). Or put differently, a moving average term is the values of x_t as the function of a mean w_t and a time-lagged random noise components $w_{(t-1)}$, which can be written as:

$$x_t = w_t + \beta_1 w_{t-1} + \ldots + \beta_q w_{t-q}$$

Autoregressive moving average (ARMA) models may include any combination of autoregressive as well as moving average terms (Cryer & Chan, 2008). A time series (xt) follows a autoregressive moving average (ARMA) process of order (p,q), denoted as:

$$x_t = \alpha_1 x_{t-1} + \alpha_2 x_{t-2} + \ldots + \alpha_p x_{t-p} + w_t + \beta_1 w_{t-1} + \beta_2 w_{t-2} + \ldots + \beta_q w_{t-q}$$

An ARIMA model is not only constituted by an AR(p) and MA(q) component, but also by an added integrated (I[d]) portion, which indicates the order of differencing that has been applied to the time series, to remove trend or render stationarity. For a detailed guide on how to specify an ARIMA model see Jebb et al. (2015).

An extension of the autoregressive (AR) model is the vector autoregressive mode (VAR model), which allows to include more than one dependent variable. An example for a VAR model with two variables (yt and xt), and autocorrelation terms (yt-1, xt-1), as well as two white noise component (ut, vt) can be seen below:

$$y_t = a_1 + b_{11} y_{t-1} + b_{12} x_{t-1} + u_t$$

$$x_t = a_2 + b_{21} y_{t-1} + b_{22} x_{t-1} + v_t$$

Which can also be written in a matrix representation.

$$\begin{bmatrix} y_t \\ x_t \end{bmatrix} = \begin{bmatrix} a_1 \\ a_2 \end{bmatrix} + \begin{bmatrix} b_{11} & b_{12} \\ b_{21} & b_{22} \end{bmatrix} \begin{bmatrix} y_{t-1} \\ x_{t-1} \end{bmatrix} + \begin{bmatrix} u_t \\ v_t \end{bmatrix}$$

8 References

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9 List of abbreviation

COVID-19 = Corona virus disease 2019

HPA = Hypothalamic–pituitary–adrenal

EMA = Ecological momentary assessment

RKI = Robert Koch Institut

WHO= World Health Organization

PHSM = Public health and social measures

UNESCO = United nations educational, scientific and cultural organization

CI = Confidence interval

PTSD = Post-traumatic stress disorder

AR = Autoregression

VAR = Vector autoregression

mlVAR = Multilevel vector autoregression

GGM = Gaussian graphical model

SAM = Sympathetic adrenomedullary

SNS = Sympathetic nervous system

CRH = Corticotropin releasing hormones

ACTH = Adrenocorticotropic hormone

HCC = Hair cortisol concentrations

ULS- 8 = University of California Los Angeles loneliness scale

CPDI = COVID-19 peritraumatic distress index

10 List of figures

Figure 9. Temporal dynamic networks in a no-lockdown (*n*=131) and a lockdown stage (*n*=127). Temporal associations among variable are estimated via multilevel vector autoregressive models. Nodes are variables and edges (arrows connecting nodes) are statistically significant (α<.05) temporal associations among variables. Thicker edges depict stronger relations; positive relations are blue and negative relations are red. Temporal associations that are statistically significantly different between the no-lockdown and lockdown stages (permutation testing using a two-sided p value at the uncorrected α level) are marked with an asterisk.

Figure 10. The standardized centrality indices out-strength and in-strength of the temporal networks of a no-lockdown (*n*=131) and lockdown stage (*n*=127). The statistically significant indices (permutation tests using a two-sided P value at the uncorrected α level) are marked with asterisks.

Figure 11. Lockdown moderates the association between loneliness and cortisol. Cortisol is displayed as a function of loneliness during no-lockdown stage (red) versus lockdown stage (blue). More loneliness was associated with higher cortisol, specifically during a lockdown.

Figure 12. Overview of the main results of the three research results involved in this dissertation.

Figure 13. A *contextual and cognitive model of loneliness*. This time-sensitive model proposes that situational, personal and cognitive factors can influence whether loneliness leads to a cascade of other stress-including behaviors and cognitions and ultimately to distress on a subjective and physiological level.

11 Publications

Haucke, M., Liu, S., & Heinzel, S. (2021). The persistence of the impact of COVID-19–related distress, mood inertia, and loneliness on mental health during a postlockdown period in germany: an ecological momentary assessment study. *JMIR Mental Health, 8*(8), e29419.

Haucke, M., Heinz, A., Liu, S., & Heinzel, S. (2022). The Impact of COVID-19 Lockdown on Daily Activities, Cognitions, and Stress in a Lonely and Distressed Population: Temporal Dynamic Network Analysis. *J. Med. Internet Res., 24*(3), e32598.

Haucke, M. N., Golde, S., Saft, S., Hellweg, R., Liu, S., & Heinzel, S. (2022). The effects of momentary loneliness and COVID-19 stressors on hypothalamic–pituitary adrenal (HPA) axis functioning: A Lockdown stage changes the association between loneliness and salivary cortisol. *Psychoneuroendocrinology*, *145*, 105894.

11.1 Study 1: The persistence of the impact of COVID-19-related distress, mood inertia and loneliness on mental health during a postlockdown period in germany

Published as: Haucke, M., Liu, S., & Heinzel, S. (2021). The persistence of the impact of COVID-19–related distress, mood inertia, and loneliness on mental health during a postlockdown period in germany: an ecological momentary assessment study. *JMIR Mental Health*, *8*(8), e29419. doi: 10.2196/29419

11.1.1 Abstract

Background: The first wave of the COVID-19 pandemic in early 2020 increased mental health problems globally. However, little is known about mental health problems during a low-incidence period of the pandemic without strict public health measures.

Objective: We aim to investigate whether COVID-19-related risk factors for mental health problems persist beyond lockdown measures. We targeted a vulnerable population that is at risk of developing low mental health and assessed their daily dynamics of mood and emotion regulation after a strict lockdown.

Methods: During a postlockdown period in Germany (between August 8, 2020, and November 1, 2020), we conducted an ecological momentary assessment with 131 participants who experienced at least mild COVID-19-related distress and loneliness. To estimate negative mood inertia, we built a lag-1 three-level autoregressive model.

Results: We found that information exposure and active daily COVID-19 cases did not have an impact on negative mood amid a postlockdown period. However, there was a day-to-day carryover effect of negative mood. In addition, worrying about COVID-19, perception of restrictions, and feeling lonely increased negative mood.

Conclusions: The mental health of a vulnerable population is still challenged by COVID-19-related stressors after the lifting of a strict lockdown. This study highlights the need to protect mental health during postpandemic periods.

11.1.2 Introduction

The COVID-19 pandemic and its associated socioeconomic consequences increased global mental health problems [1, 2]. Negative mental health outcomes of the COVID-19 pandemic are associated with fear of becoming infected [3, 4] and various mitigation strategies to curb virus spreading (e.g., curfew and restriction to public life). These measures can disrupt regular routines, impair mood homeostasis [5-7] and impose economic hardship (e.g., income loss and unemployment) [8], which can fuel anxiety, depression, and loneliness [9-12]. However, it is unclear whether these effects continue after lockdown measures have been eased. As variants emerge and cause sudden spikes in COVID-19 case numbers (e.g., the B.1.1.7 variant in the United Kingdom in late 2020), fear of getting infected and/or another lockdown could persist. Moreover, after the pandemic and lockdown measures end, socioeconomic uncertainty remains [13]. Chronic psychological distress and social isolation are risk factors for developing mental disorders such as psychosis, substance abuse disorder and affective disorder [14-17]. To investigate whether COVID-19-related stressors remain beyond lockdown measures, we set up an ecological momentary assessment (EMA) study in Germany during a postlockdown period. We focus on a group at high risk of poor mental health: those who experienced at least mild psychological distress and loneliness amid the COVID-19 pandemic. We expect a carryover effect of negative mood from one measurement to the next (mood inertia) and assume that COVID-19-related stressors (i.e., momentary COVID-19-related worry, COVID-19 information seeking and perceived restriction, loneliness, and daily reported COVID-19 cases) result in an increase in momentary negative mood (for more background information see *Supplement A).*

11.1.3 Methods

Study Design and Sampling

We conducted an EMA that involves repeated sampling of individuals' current behaviors and experiences in real time and in their natural environments [18] during a postlockdown period (from August 8, 2020, to November 1, 2020) in Germany, when restrictions were lenient (e.g., no private or public meeting restrictions, reopening of most leisure facilities, bars, and catering facilities, see *Supplement B*). EMA aims to minimize recall bias, maximize ecological validity, and approximate temporal causality (i.e., Granger causality) and allows researchers to study microprocesses that influence behavior in real-world contexts [19]. Participants were recruited via online advertisements on universities' websites, Twitter and eBay classifieds. Participants had to fill in an online prequestionnaire on the Siuvo Intelligent Psychological Assessment Platform. After an initial contact via phone or email, we sent participants our study information, informed consent and a QR code (to install a smartphone app) by mail.

We targeted vulnerable individuals who reported at least mild psychological distress and sometimes felt lonely amid the COVID-19 pandemic. We used the COVID-19 Peritraumatic Distress Index (CPDI [20]; cutoff score=28, indicating mild distress) questionnaire and the short-form version of the UCLA Loneliness Scale (ULS-8 [21]; cutoff score=16, indicating mild loneliness), respectively. Other inclusion criteria were being at least 18 years of age, not working night shifts, not currently infected with COVID-19, using an Android smartphone, and speaking fluent German. The CPDI was designed to evaluate changes in mental health status, cognitive skills, avoidance and compulsive behavior, physical symptoms, and loss of social functioning due to the COVID-19 pandemic. The questionnaire has been previously validated in a sample in Germany [20].

Data collection

We used a smartphone app called "movisensXS" (movisens GmbH) which was developed for research purposes. The app is compliant with the General Data Protection Regulation (European Union) and Berlin Data Protection Act (Berliner Datenschutzgesetz – BlnDSG). Participants completed a 20-minute baseline assessment, followed by 7 consecutive days in which they received 8 randomized prompts between 8 A.M. and 10 P.M. The study procedure was approved by the Ethics Committees of Charité – Universitätsmedizin Berlin (ref: EA2/143/20) and Freie Universität Berlin (ref: 030/2020).

Measurements

To quantify COVID-19-related distress, we measured worries about the COVID-19 pandemic, perceived restrictions due to the COVID-19 pandemic, COVID-19 information exposure and feelings of loneliness. Finally, we measured respondents' momentary negative mood (anxiety, depression, fatigue, stress and unhappiness). All questions were measured on a visual analogue scale ranging from 0 (not at all) to 100 (very much). To account for the steady increase in active COVID-19 active cases in Germany during the time of measurement [22], we included daily COVID-19 cases as a predictor in our analysis. Our smartphone study consisted of a sociodemographic assessment (i.e., age, gender, years of education) and the EMA. The exact EMA items can be found in *Supplement E* and online at [23].

Statistical Analysis

All statistical analyses were conducted in R (version 3.5.3; R Foundation for Statistical Computing [24). To consider the hierarchical data structure and autoregressive parameters, we performed model selection using autoregressive (AR) multilevel models with the dependent variable negative mood. We followed the approach by Haan-Rietdijk et al. [25], details about the model selection procedure can be found in *Supplement D* and online at [23].

11.1.4 Results

We assessed 755 people for eligibility in an online questionnaire. The final sample size was 131 (18%; recruitment flow is shown in **Figure 1** and sample characteristics shown in **Table 1**, for power estimation see *Supplement C*). No participant filled in less than 28 (50%) of the daily questionnaires, while 40 (<0.01%) of the total sent daily questionnaires were not answered by the participants.

Figure 1. Recruitment flow.

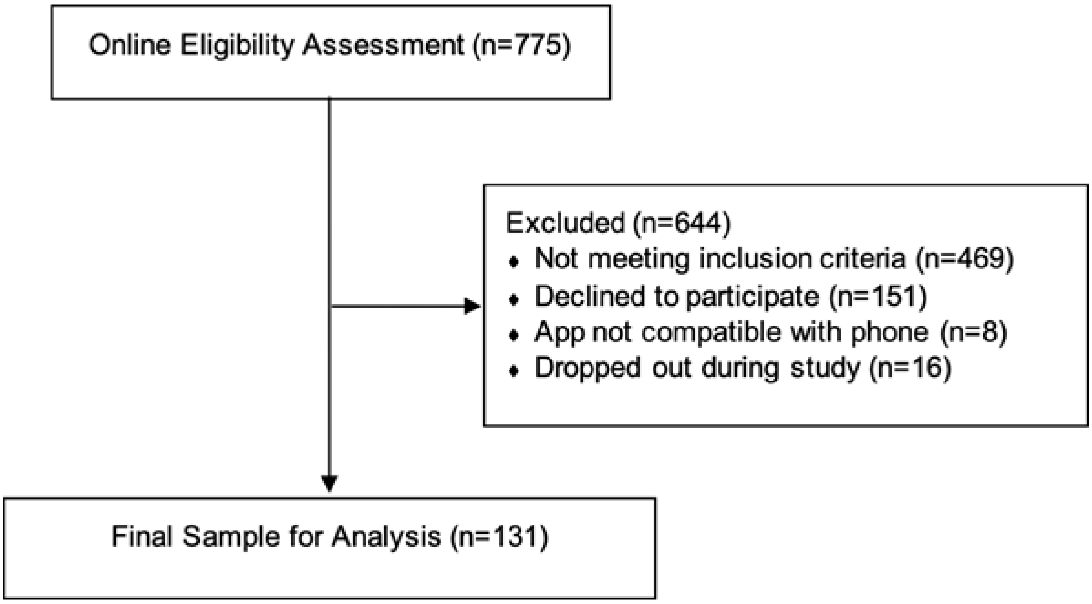


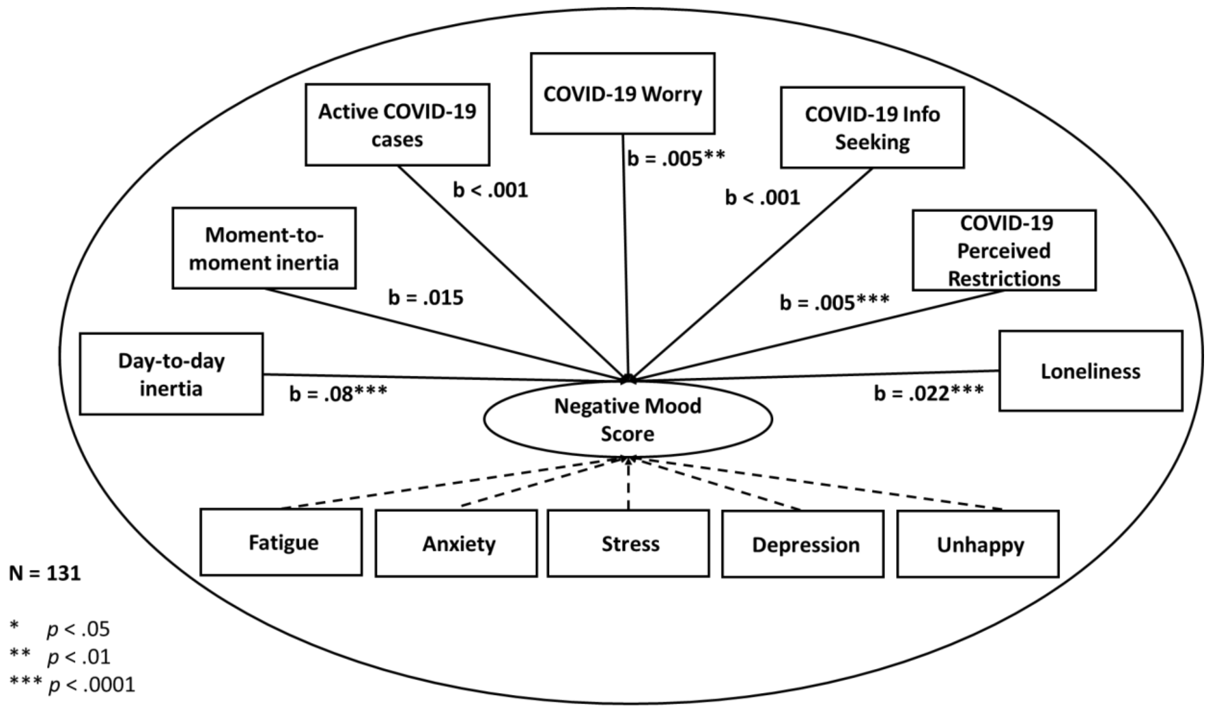
Table 1. Demographics and sample characteristics.

Parameter	Values
COVID-19 Peritraumatic Distress Index score, mean (SD)	48.42 (16.31)
UCLA Loneliness Scale score, mean (SD)	22 (4.03)
Education (in years), mean (SD)	15.08 (3.66)
Age (in years), mean (SD)	31.62 (10.76)
Gender, n (%)	Male: 49 (37); female: 82 (63)

We used a lag-1 three-level AR model, which allows us to separate the variance of negative mood scores into variance at the person level (level 3), variance at the day level (level 2), and variance at the questionnaire level (level 1). We created two lagged variables, a within-day centered predictor at questionnaire level and a within-person centered lagged predictor at the day level. The very first beep of each day (i.e., the time period between the previous day's beep and next day's beep) was excluded from the analysis, to remove possible unexplained carryover effects resulting from the night (e.g., lack of sleep). This model includes mood inertias, COVID-19 worries, COVID-19 information seeking, perceived restrictions, and loneliness during the last hour, as well as daily active COVID-19 cases as random effects. The momentary negative mood score was built by averaging momentary feelings of fatigue, anxiety, depression, unhappiness, and stress. A graphical check indicated a positive skew of negative mood; therefore, we performed a square root transformation on this variable. The analysis script can be found online at [23]

We found that loneliness (b=.022, $t_{3713.83}$=18.68, P<.001), COVID-19 perceived restriction (b=.005, $t_{129.84}$=3.65, P<.001), COVID-19–related worry (b=.005, $t_{132.74}$=2.87, P=.001), and day-to-day mood inertia (b=.078, $t_{134.58}$=3.96, P=.001) increased negative mood scores. Active daily COVID-19 case numbers (b<.001, $t_{92.17}$=–0.27, P=.87), COVID-19–related information seeking (b<.001, $t_{88.41}$=0.73, P=.47), and moment-to-moment inertia (b=.015, $t_{42.19}$=0.17, P=.87) did not increase negative mood scores (see **Figure 2**).

Figure 2. Loneliness, COVID-19- worries, perceived restriction and day-to-day mood inertia increased negative mood. Moment-to-moment mood inertia, active COVID-19 cases and COVID-19 information seeking did not increase negative mood.



11.1.5 Discussion

We found that negative effects of the COVID-19 pandemic on mental health outlast lockdown measures. In line with findings from the first COVID-19 wave [8, 26-30], we found that loneliness, worrying about COVID-19, and perceived restrictions increased negative mood during a postlockdown phase. Similar to the Ebola pandemic [31], possible reasons for the lasting effect of the COVID-19 pandemic might be worries about the negative economic consequences, concern about resurgence of the virus, struggles to rebuild social networks, and/or deliberately withdrawing from social contacts to avoid infection.

Furthermore, we found a negative carryover effect of mood between days (mood inertia), indicating dysfunctional mood regulation. Restrictive policies during the COVID-19 pandemic can impact mental health possibly due to impaired mood homeostasis (i.e., failure to positively regulate mood via mood-modifying activities) [7]. Importantly, our results show that even when the acute threat and restrictive measures are less pronounced, negative daily mood inertia remains.

Neither COVID-19 information seeking, nor active COVID-19 cases increased negative mood. This contrasts with previous findings from lockdown periods [6, 32]. For example, an EMA study during the first lockdown in Germany and Austria, reported increased perceived COVID-19-related restrictions that were positively associated with increased daily news consumption, especially in individuals living alone [32]. In addition, an EMA study conducted in New Jersey in the United States between April 24 and May 26, 2020, showed that undergraduates felt more anxious about COVID-19 on days when the number of new cases and deaths due to COVID-19 were higher [6]. Our opposing finding might be caused by the relatively low domestic case numbers and associated news during the postlockdown period. Moreover, negative COVID-19 news might have less impact on mood over the course of the pandemic as people get accustomed to it.

Limitations

We did not make explicit comparisons to participant status before the COVID-19 outbreak or to a control group, which limits generalizability to other populations. Furthermore, we did not measure adaptability, which has been associated with positive mood (e.g., optimism and satisfaction) [33]. Finally, we did not assess the nature of COVID-19 worries and the perceived restrictions.

Conclusions

Even if cases are low and lockdown policies are lenient, mental health is still challenged by COVID-19-related stressors. Although COVID-19 information seeking and daily COVID-19 cases had no impact on mood, we found a day-to-day carry-over effect of negative mood. Moreover, COVID-19-related restriction, worry about COVID-19 and loneliness increased negative mood. Thus, the negative impact of the COVID-19 pandemic on mental health outlasts lockdown measures and mental health challenges will likely continue after the pandemic.

11.1.6 References

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11.1.7 Appendix

Supplementary Material A: Further Background Information

The coronavirus disease 2019 (COVID-19) is continuing to spread around the world. The World Health Organization (WHO) reports, as of May 2021, 164,523,894 confirmed cases and 3,412,032 deaths [1]. To mitigate the spread of the COVID-19 virus, most countries enforced lockdown measures, including social restrictions, travel bans, stay-at-home orders, and business shutdown. These measures had major impact on the mental health of the general population and may have profound and long-lasting consequences [2]. Negative mental health outcomes of the COVID-19 pandemic are associated with fear of becoming infected [3, 4]. A survey during the initial outbreak of the COVID-19 outbreak in China found that 53.8% of respondents rated the psychological impact of the outbreak as moderate or severe [5]. Previous studies during the Ebola outbreak have shown that the fear of the virus is associated with the experience of intense distress and pose a risk factor for long-term mental and psychosocial problems, such as anxiety, mood disorder as well as acute stress reactions [6]. Moreover, public health responses (i.e., closing off business and prohibiting physical contact) disrupt daily routines, impair mood homeostasis [7-9] and impose economic hardship (e.g., income loss and unemployment) [10] which, in turn, can increase anxiety, depression and loneliness and distress [11-14]. Chronic psychological distress and social isolation are risk factors for developing mental disorders, such as psychosis, substance abuse disorder and affective disorder [15-18]

We measured three COVID-19 related stressors: firstly, feelings of restriction in everyday life, secondly, seeking information about the pandemic, and thirdly, worrying about the pandemic and its impact on one's life. Worries about the COVID-19-related economic downfall, and the possible health impact on oneself or others can increase psychological distress [10, 19]. In addition, anxiety, psychological distress, and worries increase with the common public health measure of physical distancing [20, 21]. Moreover, if people are staying at home more often, they will more likely be exposed to pandemic related digital and social media information, which in turn increases anxiety and stress [8, 22]. To conclude, there are three stressors central to the pandemic: COVID-19 related feelings of restriction, information seeking and worry.

Social restrictions and other lockdown measures help limit the spread of COVID-19; however, during the first wave of the pandemic, these measures have also led to an increase in feelings of loneliness [10, 23]. Loneliness can be defined as an aversive state resulting from a discrepancy between an individual's desired and realized social relationships [24]. Loneliness has severe impacts one people's health, increasing cardiovascular disease and immune dysfunction, depression, anxiety, and suicidal ideation [25].

In Germany, there is an increased demand in psychological counseling because of the COVID-19 pandemic and lockdown measures [26]. This increase indicates heightened loneliness, anxiety, and even suicidal ideation and is more pronounced in German federal states that implemented stricter measures [26]. It is unclear whether the negative effects of COVID-19 will continue after lockdown measures have been eased. As variants occur with a sudden spike in COVID-19 case numbers (e.g., India in April 2021 [27]), fear of getting infected and another lockdown could persist. Moreover, after the pandemic and lockdown measures are over, socio-economic uncertainty remains [28]. To investigate whether COVID-19 related stressors remain beyond lockdown measures, we set up an ecological momentary assessment (EMA) study in Germany during a post-lockdown phase.

Supplementary Material B: Lockdown measures

Summary of measures to counteract the pandemic in Germany between August 8, 2020 and November 1, 2020 (https://www.deutschland.de/en/news/german-federal-government-informs-about-the-corona-crisis)

1. Nationwide, a distance of at least 1.5 meters must be maintained, hygiene rules must be observed, and masks must be worn in shops and on public transport. There was no general restriction on public meetings.

2. Institutions and leisure facilities (i.e., theatres, concert halls, cinemas, and fitness studios) opened.

3. Sports and recreational activities indoor and outdoor were permitted.

4. Restaurants, bars, pubs, cafés, and other catering establishments opened.

All above-mentioned policies must act in strict compliance with hygiene and infection control regulations.

5. Governmental financial aid for those that suffered economic losses during the time of the pandemic.

Supplementary Material C: Power estimation

Based on within-subject reliability of assessments performed on a smartphone, power analyses are recommended based on even smaller effect sizes [29]. Conventional power analyses for multiple regression models indicate a sample size of N = 115 for detecting small effect sizes (f = .05) using predictor sets of up to 7 variables. Considering a drop-out rate of 25%, a total size of 144 is required.

Supplementary Material D: Modell building process

To determine whether a two-level and three-level lag- 1 autoregressive (AR1) models is more appropriate for our data, we followed a model selection procedure using the Akaike Information Criterion [30] described by de Haan-Rieddijk and colleagues [31].

First, we build the most basic, empty (or intercepts-only) two-level model (**2-l. empty**), which accounts for the fact that we have measurements within persons, but which does not include an autoregressive parameter. Then, we build the two-level AR(1) model, in which each affect score is regressed on the immediately preceding affect score of that person. For this two-level AR (1) model, we build a model in with a correlation between random effects (**2-l. AR(1)**), and a constrained model where the correlation is fixed at zero (**2-l. AR(1) no corr**.), which is achieved by explicitly separating the random intercept and the random predictor.

We build a three-level AR(1) model (**3-l. empty**), which accounts for the fact that the beeps (each questionnaire) are nested within persons, and for the multi-day structure of the data. This results in distinct inertia parameters for the carry-over from day to day and from moment to moment. Thus, we can partition the variance in the affect scores into variance at the person level (level 3), variance at the day level (level 2), and variance at the beep level (level 1). Again, two models were constructed, one with a correlation between random effects (**3-l. AR(1)**), and one constrained model where the correlation is fixed at zero (**3-l. AR(1) no corr**.).

We created two lagged variables, a within-day centered predictor at questionnaire level, and a within-person centered lagged predictor at the day level. The first day and the first questionnaire of each day were excluded from the analysis of the three-level model to exclude carry over-effects resulting from processes prior to the study and from the night. To compare the AIC of the AR(1) models, the two-level AR(1) models were refitted to the smallest of the data, to those cases that could also be used in the three-level AR(1) model with day-level inertia. Based on the AIC, we selected the model **3-l. AR(1) no corr** (see **Table 1**).

Table 1. The models are estimated on the smallest suitable subset of data to ensure equal sample size. The bold model indicates the model that was selected for the final analysis.

Model	AIC
2-l. empty	13376
3-l. empty	12956
2-l. AR(1) no corr.	13310
2-l. AR(1)	13312
3-l AR(1) no corr	**12895**
3-l AR(1)	12898

Adding more predictors:

Finally, we added the predictors COVID-19 worries, information seeking, perceived restrictions, and loneliness during the last hour as well as COVID-19 case numbers as random effects. The outcome variable momentary negative mood score was built by averaging momentary feelings of fatigue, anxiety, depression, unhappiness, and stress.

Supplementary Material E: EMA Items

Mood Items

In diesem Moment...

In this moment….

<u>Unhappy</u>:

.. fühle ich mich unglücklich.

.. I feel unhappy.

<u>Fatigue</u>:

..fühle ich mich müde.

..I feel tired.

Stress:

…habe ich das Gefühl, unter Stress zu stehen.

..I feel stressed.

Anxiety:

...fühle ich mich ängstlich.

.. I feel anxious.

Depression:

.. fühle ich mich niedergeschlagen.

.. I feel depressed.

COVID-19 and loneliness Items

In der letzten Stunde...

During the last hour…

Corona restriction:

...in welchem Ausmaß haben Sie sich durch die Pandemie in Ihrem Alltag eingeschränkt gefühlt?

… to which extent did you feel constrained by the pandemic in your everyday life?

Corona worry:

...in welchem Ausmaß haben Sie darüber nachgedacht wie die Pandemie Ihre persönliche Lebenssituation beeinflusst?

.. to which extent did you worry about how the pandemic affects your personal situation?

Corona Information Seeking:

...in welchen Ausmaß haben Sie Informationen zur Corona Pandemie gelesen/gesehen?

.. to which extent did you read/see Information about the Corona pandemic?

Loneliness:

.. wie sehr fühlten Sie sich einsam?

.. how lonely did you feel?

Supplementary Material F: Supplementary References

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11.2 Study 2: The Impact of COVID-19 Lockdown on Daily Activities, Cognitions, and Stress in a Lonely and Distressed Population: Temporal Dynamic Network Analysis

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11.2.1 Abstract

Background: The COVID-19 pandemic and its associated lockdown measures impacted mental health worldwide. However, the temporal dynamics of causal factors that modulate mental health during lockdown are not well understood.

Objective: We aimed to understand how a COVID-19 lockdown changes the temporal dynamics of loneliness and other factors affecting mental health. This is the first study that compares network characteristics between lockdown stages to prioritize mental health intervention targets.

Methods: We combined ecological momentary assessments with wrist-worn motion tracking to investigate the mechanism and changes in network centrality of symptoms and behaviors before and during lockdown. A total of 258 participants who reported at least mild loneliness and distress were assessed 8 times a day for 7 consecutive days over a 213-day period from August 8, 2020, through March 9, 2021, in Germany, covering a "no-lockdown" and a "lockdown" stage. COVID-19-related worry, information-seeking, perceived restriction and loneliness were assessed by digital visual analog scales ranging from 0 to 100. Social activity was assessed on a 7-point Likert scale, while physical activity was recorded from wrist-worn actigraphy devices.

Results: We built a multilevel vector autoregressive model to estimate dynamic networks. To compare network characteristics between a no-lockdown stage and a lockdown stage, we performed permutation tests. During lockdown, loneliness had the highest impact within the network, as indicated by its centrality index (i.e., an index to identify variables that have a strong influence on the other variables). Moreover, during lockdown, the centrality of loneliness significantly increased. Physical activity contributed to a decrease in loneliness amid the lockdown stage.

Conclusions: The COVID-19 lockdown increased the central role of loneliness in triggering stress-related behaviors and cognition. Our study indicates that loneliness should be

prioritized in mental health interventions during lockdown. Moreover, physical activity can serve as a buffer for loneliness amid social restrictions.

11.2.2 Introduction

The outbreak of COVID-19 is an unprecedented global health challenge; as of November 2021 there are 259,502,031 confirmed cases and 5,183,003 deaths globally [1]. To mitigate the spread of SARS-CoV-2, most countries enforced lockdown measures, including social restrictions, travel bans, stay-at-home orders, and business shutdown. Together with the pandemic per se, these lockdown measures increased global mental health problems [2-3]. Reasons for this are an increase of distress and loneliness during the COVID-19 lockdown [4-7], yet most studies are overlooking the directionality between behavior and cognition over time. Recently, a network approach to psychopathology proposed that changes in mental health result from a temporal dynamic interaction between mental states, such that one mental state at one moment in time (e.g., worry) can trigger other mental states at the next moment in time (e.g., feeling stressed) [8]. We set out to examine whether lockdown measures can alter the dynamic network structure of behavior (e.g., physical activity) and pandemic-related mental states (e.g., worry). To do so, we compared differences between moment-to-moment time-lagged associations of pandemic-related cognitions, behaviors, and mental health, and tested for changes in centrality between lockdown stages. Comparing centrality (i.e., an index to identify variables that have a strong influence on the other variables) can be informative in finding the most protective or detrimental temporal influence on mental health amid a lockdown [9-10]. This knowledge can be transferred to prioritize targets for pandemic-related mental health care interventions.

Psychological distress and social isolation are risk factors for developing mental disorders [11-15]. Therefore, we focused on a subpopulation who were experiencing at least mild levels of psychological distress and loneliness amid the COVID-19 pandemic. Moreover, we gathered real-life data using ecological momentary assessment (EMA) via smartphone technology and measured objective physical activity via wrist-worn actigraphy devices. We investigated the temporal associations between loneliness, stress, physical and social activity, and COVID-19-related behaviors and cognitions.

We measured three COVID-19-related cognitions: perceived restriction in everyday life due to the pandemic, seeking information about the pandemic, and worrying about the pandemic's impact on one's life. Worries about the COVID-19-related economic downfall and the possible health impact on oneself or others can increase psychological distress [7, 16]. In addition, distress, anxiety, depression, and anger are further increased by physical and social distancing measures [17-18]. People who stayed at home often acquired more COVID-19-related information through digital media, which increased anxiety and psychological distress [19-21]. Thus, COVID-19-related worrying, perceptions of restrictions and information-seeking can be central causes of mental health issues.

Prior to the COVID-19 pandemic, loneliness was already recognized as one of the most pressing issues in modern societies [23]. Loneliness is an aversive state resulting from a discrepancy between an individual's desired and realized social relationships [24]. Limiting social contacts and closing off social spaces can help to halt the spread of COVID-19; however, they also increase feelings of loneliness [7, 25]. Loneliness has serious consequences for health, including increasing the risk of cardiovascular disease and immune dysfunction, depression, anxiety and suicidal ideation [26]. To buffer against feelings of loneliness during lockdown, it can be essential to receive social support and engage in digital social activities [27,28].

A second buffer against mental health problems during the pandemic might be physical activity. Physical activity can relieve stress [29] enhance cognitive abilities [30] and reduce the risk of diabetes [31] and cardiovascular disease [32], cancer [33], and mental disorders [34, 25]. Conversely, sedentary behavior, defined as low-energy-expenditure behavior (≤ 1.5 metabolic equivalents), increases the risk for negative health outcomes, including type 2 diabetes mellitus, cardiovascular disease, and all-cause mortality [36-38]. Physical activity can lead to physiological reactions associated with decreased depression, such as an increase in neuroplasticity, cerebral blood flow, delivery of neurotrophic factors and oxygen, and resistance to oxidative stress [39]. Finally, exercise can improve self-efficacy and self-esteem [40]. We assessed physical activity through actigraphy (i.e., a wrist-worn device that obtains objective measures of physical activity) [41].

Our study was performed in Germany during a no-lockdown stage (August 8 to November 1, 2020) and a lockdown stage (November 2, 2020, to March 9, 2021). During the no-lockdown stage, the restrictions were lenient (e.g., no private or public meeting restrictions and leisure facilities, bars and catering facilities were open). To counter the steep increase in active COVID-19 cases, the German government announced a lockdown on November 2, 2020, including social restrictions, travel bans, closing of restaurants, cinemas, and business shutdowns. In addition, these lockdowns measures were further tightened on 16 December (e.g., closing of most retail; see *Supplement A*).

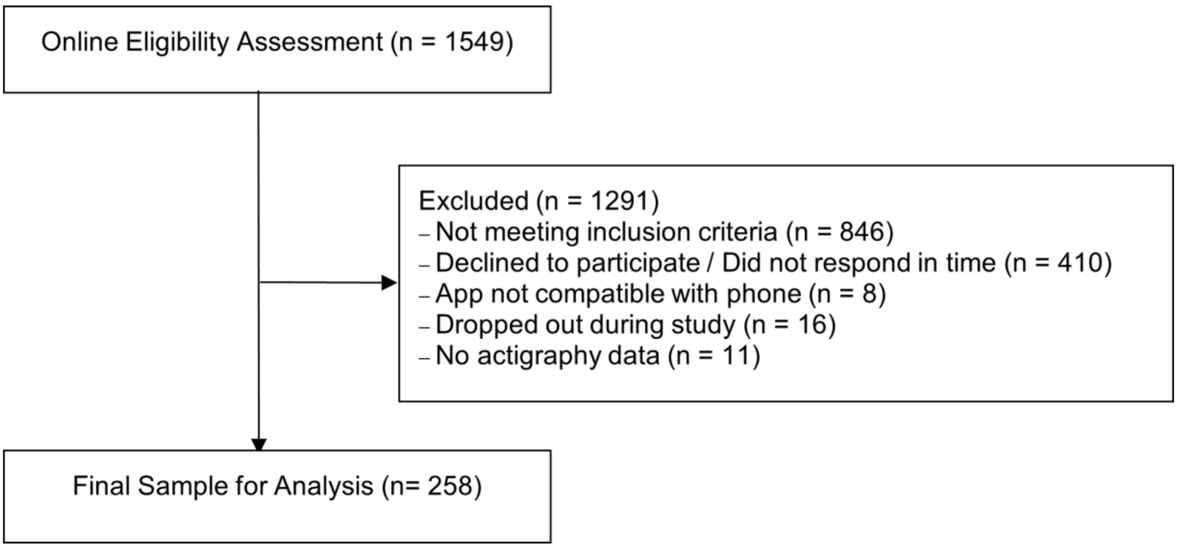
The aim of this study was to examine the temporal dynamic interplay between COVID-19 pandemic-related cognitions, behaviors, and mental health states. This is the first study to use a dynamic network approach to compare moment-to-moment time-lagged associations between pandemic-related cognitions, behaviors, and mental health states between lockdown stages. Moreover, we examined whether the lockdown affects the centrality of loneliness and specific pandemic-related behaviors and cognitions (i.e., a more central variable has more and stronger connections to other variables). This helps to identify the most protective or detrimental influences on mental health during a lockdown. This knowledge, in turn, can be used to prioritize mental health intervention targets. Specifically, we hypothesized that a lockdown, in comparison to a no-lockdown period, increases the centrality of stress, physical activity, social contacts and loneliness. Finally, we hypothesized that stress and loneliness will have a stronger influence on COVID-19 related behaviors and cognitions during lockdown than during no-lockdown.

11.2.3 Methods

Participants and sampling

We assessed 1549 participants for eligibility in an online questionnaire. The final sample size was 258 (see **Figure 1** for the recruitment flow). On average participants missed 17.5% of the questionnaires, no participants missed more than 50% of the send questionnaires and 117 data points were marked by the GGIR package [42] as "non-wear"[1] and subsequently excluded from the analyses.

Figure 1. Recruitment flow.



Inclusion criteria were (1) a minimum age of 18 years, (2) not working a night shift, (3) not being infected by COVID-19, (4) using an Android smartphone, and (5) speaking fluent German. Moreover, we targeted individuals who reported (6) perceived mild to moderate psychological distress and (7) sometimes felt lonely during the COVID-19 pandemic. We used the COVID-19 Peritraumatic Distress Index (CPDI [43], cut-off score=28, indicating mild distress) questionnaire and the short-form of the University of California Los Angeles Loneliness Scale (ULS-8 [44], cut-off score=16, indicating mild loneliness), respectively. The

[1] Accelerometer non-wear score is estimated based on the standard deviation and the value range of the raw data from each accelerometer axis. See van Hees VT, Renström F, Wright A, et al. Estimation of daily energy expenditure in pregnant and non-pregnant women using a wrist-worn tri-axial accelerometer. *PloS one.* 2011;6(7):e22922.

CPDI was designed for evaluating changes in mental health status, cognitive skills, avoidance and compulsive behavior, physical symptoms, and loss of social functioning due to the COVID-19 pandemic. The questionnaire has been previously validated in Germany [43].

Study design and procedure

The study was conducted in Germany over a 213-day period between August 8, 2020, and March 9, 2021, covering a no-lockdown and a lockdown stage. Participants were recruited via online advertisements on university websites, Twitter and eBay classifieds. Participants had to fill in an online screening questionnaire on the Siuvo Intelligent Psychological Assessment Platform. After an initial contact via phone or email, we sent participants our study information, accelerometer, informed consent and a QR code (to install a smartphone app) by mail. After they completed the study, participants sent back the study material by mail.

We conducted the EMA via the smartphone app “movisensXS” (movisens GmbH, Karlsruhe, Germany) developed for research purposes. This app is compliant with the General Data Protection Regulation (European Union) and Berlin Data Protection Act (Berliner Datenschutzgesetz – BlnDSG). The app consists of a sociodemographic assessment (e.g., age, gender, and years of education) and measures participants’ current experiences in real time. Participants filled in questionnaires for 7 consecutive days, in which they received 8 prompts (randomized within 1 hour and 45 minute blocks between 8 A.M. and 10 P.M.). We performed an EMA that involves repeated sampling of individuals’ current behaviors and experiences in real time and in their natural environments. EMA minimizes recall bias, maximizes ecological validity and allows approximating temporal causality (i.e., Granger causality) [45]. A time series X is said to Granger-cause Y if it can be shown, usually through a series of t tests and F tests on lagged values of X (and with lagged values of Y also included), that the X values provide statistically significant information about future values of Y [46].

Moreover, we measured physical activity via the "GENEActiv" Original (Activinsights) monitor (dynamic range ±8 g, sampling frequency range 10-100 Hz). Participants wore the actigraphy devices on the left wrist. The study was approved by the ethics committee at Charité – Universitätsmedizin Berlin (ref: EA2/143/20) and Freie Universität Berlin (ref: 030/2020).

Measures

EMA items. Stress was measured with the following question: "In this moment I feel stressed." Other items started with "During the last hour..." followed by "to which extent did you feel constrained by the pandemic in your everyday life?" (perceived restriction), "to which extent did you worry about how the pandemic affects your personal situation?" (worry), "to which extent did you seek information about the Corona pandemic?" (information-seeking) and "to which extent did you feel lonely" (loneliness). Each of these items was measured on a visual analog scale (0–100: 0 = not at all, 100 = most frequent or severe). Duration of social activity was measured with the question "How long did your last social contact last?" via a Likert Scale ranging from 1 = "0 minutes", to 7 = "50-60 minutes.

Actigraphy Data. Physical activity data were collected using the actigraphy devices worn by each participant on the left wrist.

Statistical Analysis

Overview

All analyses were performed using R statistical software (version 3.5.3). In this section, we describe the data preparation procedures, averaged values of our measured items, estimation of the dynamic networks and the permutation procedure used to test for group differences in centrality indices and dynamic association.

Data preparation

We calculated the Euclidean norm (vector magnitude) of the raw signals of the three-measurement axis, which is a summary score of body acceleration and a validated measure for physical activity [47]. The Euclidean norm minus one (ENMO) is defined as ri–1000 [48], where

$$r_i = \sqrt{x_i^2 + y_i^2 + z_i^2} = i^{th}\ vector\ magnitude\ at\ each\ time\ point$$

The actigraphy data from GENEActiv (100 Hz; .bin files) were downloaded using GENEActiv PC software V3.3. The GENEActiv .bin files were then exported into R statistical software V4.0.3 for processing using the GGIR package V1.2-0. We autocalibrated the raw triaxial accelerometer signals and computed the average ENMO metric for 1 hour before each beep. To exclude time frames in which participants did not wear their actigraphy device, we used the nonwear score of the GGIR package. We excluded time frames above the cut-off score of 1. As the EMA items were nonnormally distributed, we transformed all variables using the nonparanormal transformation [49]. To test for nonstationarity, we calculated a two-level autoregressive model for each lockdown group, in which each score of the variable included in our model was regressed on the immediately preceding score of that variable (i.e., moment-to-moment inertia). A moment-to-moment inertia value larger than 1 indicates a nonstationary process [50]. We assumed stationarity, as the average moment-to-moment inertia ranged between 0.13 and 0.37 for all 7 included variables for each lockdown group (see *Supplement B*). In addition, a Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test was performed separately for every subject and variable. The KPSS test indicated that the data were stationary (approximately 99.9%). The R code of the statistical analyses is available online [51].

Dynamic Network Estimation

We built a first-order vector autoregressive model (VAR) with the R-package mlVAR. Each variable at time point *t* was predicted by all variables (including itself) at the next time point of measurement (lag 1). The results of the network models consisted of nodes (variables) and directed edges (statistical relations) that were visualized via the R package qgraph [52]

Permutation testing of centrality indices and edge differences

Permutation tests were used to compare individual path and network centrality between the lockdown and no-lockdown stages. The permutation procedure was developed by Wolfgang Viechtbauer and compares the results of the observed data with a distribution derived from repeated permutation (100,000) of the data under the null hypothesis [53-55]. To assess the importance of specific variables in the network of two groups, in-strength and out-strength were calculated from all (including nonsignificant) edges in the network. In-strength reflects the sum of ingoing edge weights, whereas out-strength reflects the sum of outgoing edge weights to the specific node [56, 57]. A detailed description of the permutation procedures can be found in *Supplement C*.

11.2.4 Results

Sociodemographics

Sociodemographic characteristics of the final sample (N=258), as well as results of independent t tests or χ^2 tests comparing these characteristics between a no-lockdown and a lockdown are shown in **Table 1**. As we had more women in our lockdown group, we tested the effect of Gender on all measured variables (see *supplement G)*. We found that, except for social duration, gender did not statistically significantly affect our variables.

Table 1. Sociodemographic characteristics of participants

Characteristic	Total (August 8, 2020, to March 9, 2021; N=258)	No-lockdown period (August 8 to November 1, 2020; n=131)	Lockdown period (November 2 to March 9, 2021; n=127)	*P* value[a]
Age (years), mean (SD)	30.78 (11.16)	31.18 (10.52)	30.16 (11.67)	.55
Education (years), mean (SD)	15.28 (3.69)	15.1 (3.69)	15.46 (3.69)	.44
Gender, n (%)				.008
Male	77 (29.8)	49 (37.4)	28 (22.0)	
Female	178 (70.0)	82 (62.6)	96 (75.6)	
Diverse	3 (1.2)	0 (0)	3 (2.4)	
Family status, n (%)				.93
Single	114 (44.2)	61 (46.6)	53 (41.7)	
In relationship	92 (35.7)	45 (34.4)	47 (37.0)	
Married	48 (18.6)	23 (17.6)	25 (19.7)	
Other	4 (1.6)	2 (1.5)	2 (1.6)	
Number of children, mean (SD)	1.77 (0.78)	1.7 (0.78)	1.88 (0.78)	.38
Number living with others, mean (SD)	2.56 (2.15)	2.5 (1.29)	2.62 (2.77)	.65
Health status (1=very bad, 5=very good), mean (SD)	3.74 (0.86)	3.65 (0.91)	3.83 (0.81)	.09
COVID-19 risk group, n (%)	64 (24.8)	33 (25.2)	31 (24.4)	.80
COVID-19 distress (CPDI[b]), mean (SD)	47.56 (14.79)	48.32 (16.34)	46.76 (13.31)	.41
Loneliness (ULS-8[c]), mean (SD)	22.57 (3.97)	22.01 (4.01)	23.15 (3.85)	.02

[a]Based on independent *t* test or χ^2 test; unequal variance was assumed, and we applied the Welsh approximation to the degrees of freedom.
[b]CPDI: COVID-19 Peritraumatic Distress Index.
[c]ULS-8: University of California Los Angeles Loneliness Scale.

Average based lockdown differences

To compare the no-lockdown and lockdown stages, we performed independent *t* tests using overall averages for each person. As shown in **Table 2**, the lockdown statistically significantly increased COVID-19 worries, perceived restriction, and duration of social contacts. Moreover, the lockdown significantly decreased physical activity. There was no significant influence of lockdown on information-seeking, stress, and loneliness.

Table 2. Difference between No-Lockdown and Lockdown Stages.

Variables	No-lockdown period (n=131), mean (SD)	Lockdown period (n=127), mean (SD)	*P* value[a]
EMAb items			
Loneliness	22.62 (20.82)	21.45 (19.80)	.64
COVID-19 worries	24.59 (18.36)	29.12 (17.33)	.04
COVID-19 perceived restriction	23.86 (17.83)	28.16 (17.05)	.05
COVID-19 information-seeking	22.85 (15.57)	23.46 (13.94)	.74
Social contacts	2.64 (0.95)	3.05 (1.00)	<.001
Stress	35.05 (18.43)	33.25 (17.34)	.42
Physical activity from actigraphy (microgravity)	40.15 (13.37)	35.24 (11.42)	.002

[a]*t* test; unequal variance was assumed and we applied the Welsh approximation to the degrees of freedom.
[b]EMA: ecological momentary assessment.

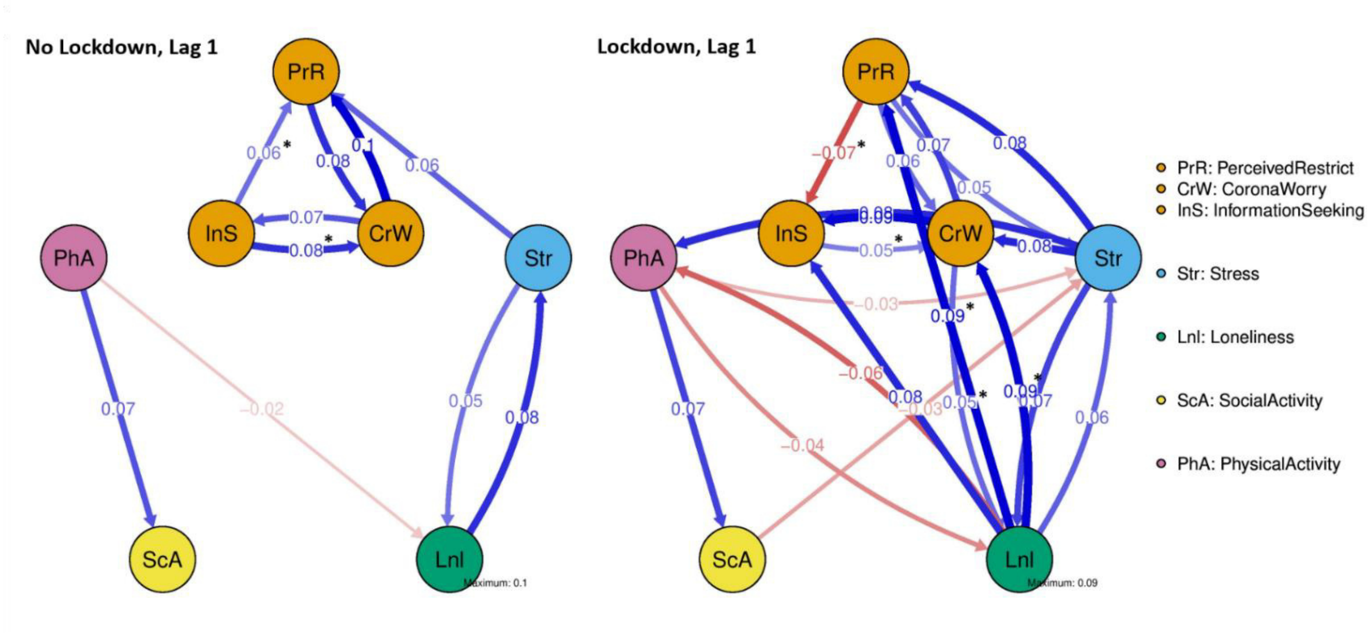
Network Estimation

We wanted to investigate how a lockdown affects the temporal dynamics of pandemic-related cognitions, behaviors, and mental health states. To do so, we first estimated the temporal (i.e., time-lagged) and bidirectional associations between detrimental and beneficial factors via multilevel vector autoregressive (mlVAR) models [58-60]. These VAR models were then used to estimate temporal dynamic networks for a lockdown and a no-lockdown stage. Permutation testing was used to test for group differences in individual paths and the network centrality of pandemic-related detrimental and beneficial mental health factors between the lockdown and no-lockdown stage. Moreover, the exploratory results of a permutation test for the difference in overall connectivity are provided in *Supplement C*.

Edge differences between groups

Figure 2 displays the 'full' dynamic symptom networks for the lockdown and no-lockdown groups, which include only statistically significant *edges* (i.e. time-lagged partial correlations with $\propto < 0.05$). Permutation tests revealed that 7 of the edges were significantly different between the no-lockdown and lockdown groups at the uncorrected α level (indicated with an asterisk in **Figure 2**).

Figure 2. Temporal dynamic networks for a no-lockdown and a lockdown stage. Temporal relations among EMA and physical activity data, measured by actigraphy devices, are estimated with a multilevel vector-autoregressive model. These relations are depicted as a graph, where nodes are variables, and edges (arrows connecting nodes) are statistically significant (α < 0.05) partial correlations among variables. Thicker and more saturated edges depict stronger relations, positive relations are in blue, negative relations are in red. Associations that are statistically significantly different between a no-lockdown and a lockdown stage (permutation testing using two-sided *P* value at the uncorrected α level) are marked with an asterisk.



Compared to no-lockdown, in a lockdown, participants showed a stronger connection from "loneliness" to "perceived restriction" (difference –0.114, *P*<.001) and from "loneliness" to "COVID-19–related worry" (difference –0.0767, *P*=.03).

Compared to no-lockdown, in a lockdown, participants showed a weaker connection from "information-seeking" to "perceived restriction" (difference 0.0609, *P*=.02) and from "information-seeking" to "COVID-19–related worry" (difference 0.0477, *P*=.05). In addition, information-seeking led to less information-seeking in the next moment (i.e., weaker autocorrelation; difference 0.0754, *P*=.02).

Compared to no-lockdown, during the lockdown, participants showed a stronger connection from “COVID-19–related worry” to “loneliness” (difference –0.0444, *P*=.05).

Compared to no-lockdown, during the lockdown, participants showed a weaker connection from “perceived restriction” to “social activity” (difference 0.0065, *P*=.01).

More information on the time-lagged partial correlations (ie, edges) that were significantly different during the lockdown can be found in **Table 3** (all, including nonsignificant, edge differences are shown in *Supplement F*).

Table 3. Significant edge differences of time-lagged partial correlation coefficients between lockdown and no-lockdown.

Predictor (1-lag)	Outcome	Partial correlation coefficients		Difference in partial correlation coefficient	P value
Information-seeking	Perceived restriction	0.0548	-0.0062	0.0609	.02
Loneliness	Perceived restriction	0.001	0.115	-0.114	< .001
Information-seeking	COVID-19-related worry	0.0689	0.0212	0.0477	0.05
Loneliness	COVID-19-related worry	0.0274	0.1042	-0.0767	0.03
Information-seeking	Information-seeking	0.1721	0.0967	0.0754	0.02
COVID-19-related worry	Loneliness	-0.0129	0.0315	-0.0444	0.05
Perceived restriction	Social activity	0.0043	-0.0021	0.0065	0.01

Centrality indices results

In-strength is the sum of *ingoing* edge weights to a specific node and *out-strength* is the sum of the *outgoing* edge weights to a specific node. During the no-lockdown stage, worrying about COVID-19 had the highest out-strength, indicating that when a participant reports worries about COVID-19 at one measurement occasion, it is likely that this participant will report other COVID-19-related behaviors and cognitions at the next measurement occasion. During lockdown, loneliness had the highest out-strength, indicating that when a participant reports feeling lonely in one moment, this participant is likely to report COVID-19 related behaviors and cognitions in the next momentary assessment.

Permutation tests revealed a significant higher out-strength for “loneliness” during lockdown (difference –0.1975, P=.04) and significant lower out-strength for “information-seeking” (difference 0.1452, P=.03) at the uncorrected α level (as indicated by asterisks in **Figure 3**). More information on centrality indices that were significantly different can be found in **Table 4** (all, including nonsignificant, differences between centrality indices can be found in *Supplement E*).

Figure 3. The standardized centrality indices out-strength and in-strength among EMA and physical activity data, within the networks of the no-lockdown and lockdown stages. The statistically significant indices (permutation tests using a two-sided *P* value at the uncorrected *α* level) are marked with asterisks.

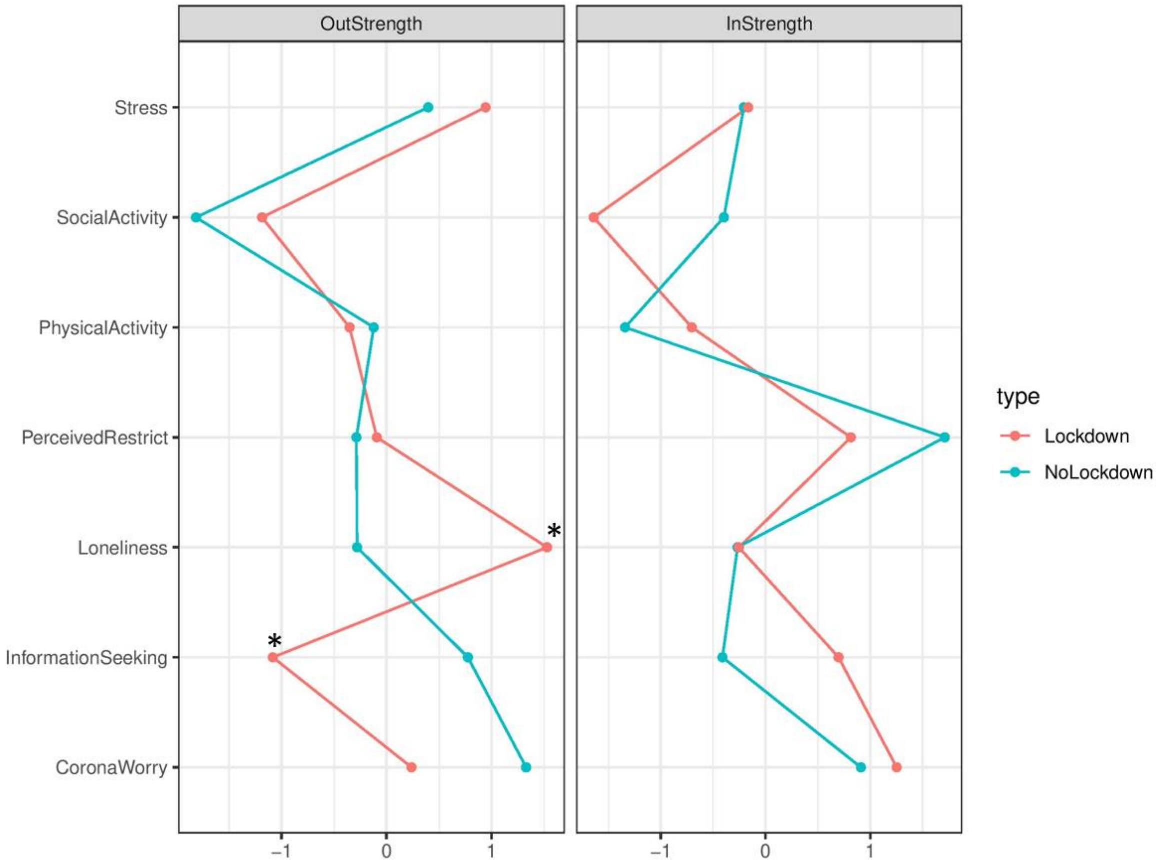


Table 4. Significant differences in variable out-strength between lockdown and no-lockdown stage.

Variable	Out-strength		Difference	*P* value
	No-lockdown	Lockdown		
Information-seeking	0.3129	0.1677	0.1452	.03
Loneliness	0.4109	0.6084	–0.1975	.04

11.2.5 Discussion

The COVID-19 pandemic increased mental health problems worldwide [2, 61]. Our study sheds light on the mechanisms with which a lockdown affects mental health during the COVID-19 pandemic. Compared to no-lockdown, during lockdown loneliness had a stronger impact on pandemic-related cognitions and behaviors, such as perceived restrictions and worries about the pandemic. In turn, pandemic-related cognitions and behaviors, reinforced each other and increased stress across lockdown stages. Finally, we found engaging in daily physical activity to be an effective strategy against feelings of loneliness during lockdown. In sum, our results suggest that when strict lockdown measures are in place, loneliness is the central trigger of stress-related behaviors and cognitions. Thus, loneliness should be prioritized in mental health interventions in the context of pandemic-related psychological distress.

Loneliness is a distressing emotional state in which one experiences a discrepancy between the desired and perceived quantity and quality of social relations [62]. Previous studies showed that lonely individuals exhibit a negative information bias, such as increased attention for social threatening stimuli, negative and hostile intent attributions, expectation of rejection and rumination [63]. We found that during lockdown, feelings of loneliness had the highest out-strength, indicating that loneliness is the central trigger of stress-related behaviors and cognitions. Compared to a no-lockdown, a lockdown increased the out-strength of loneliness, which indicates that loneliness has a more central role in affecting stress-related cognitions and behaviors during lockdown. Moreover, during lockdown, the influence of loneliness on perceptions of restriction and COVID-19-related worry increased. Thus, a lockdown changes the way loneliness interacts with pandemic-related behaviors and cognitions.

COVID-19-related-worries, feelings of restriction and information seeking were mutually reinforcing over time in both the no-lockdown and lockdown stages, resulting in a vicious stress-inducing cycle from which it can be increasingly difficult to escape. Information-seeking had less out-strength during lockdown compared to the no-lockdown stage, which indicates that COVID-19-related information seeking has a more central role during a no-lockdown period. During lockdown, information-seeking at one moment led to less information-seeking at the next moment (i.e., weaker autocorrelation) and its influence on perceived restrictions and COVID-19-related worry decreased. These findings contrast earlier reports concluding a more significant influence of information seeking during lockdown, based on findings of increased averaged information-seeking [19, 21]. Moreover, during the no-lockdown stage, perceived restrictions increased information-seeking, whereas during lockdown, perceived restrictions decreased information seeking. This suggests that during a no-lockdown stage, people are in a type of information approach state, whereas during lockdown, people are more likely to be in an information avoidance state. Therefore, the best moment to communicate COVID-19-relevant information, such as safety behaviors, might be an early pandemic stage when no lockdown measures are in place.

Physical activity increased social activity in both the no-lockdown and lockdown stages. This association might result from public health recommendations that suggest meeting people only outside enclosed spaces. During COVID-19, people might have combined physical and social activity (i.e., they found a companion to go for a walk or hike outside). Physical activity can also help to form interpersonal relationships (e.g., attending a virtual group fitness class). Moreover, physical activity decreased feelings of loneliness during lockdown. A possible reason is that physical activity can mediate contextual influences on loneliness (e.g., being in nature and physically active rather than sitting at home and leading a sedentary lifestyle) [64]. Meeting more people did not decrease feelings of loneliness in either of the lockdown stages. A potential explanation is that feelings of loneliness are not caused by the number of social contacts but rather the perception that current relationships do not match desired relationships (e.g., the other person being attentive to one's needs) [65]. Finally, physical activity and social activity were associated with decreased stress only during the lockdown stage, indicating that during lockdown these stress-buffering behaviors become effective.

Perspectives on mental health interventions

We found that loneliness has the highest temporal effect on all measured moment-to-moment pandemic-related cognition and behaviors during lockdown. This, in turn, suggests that loneliness can be a central trigger of stress-related behaviors and cognitions. Our study suggests that mental health interventions during the pandemic lockdown should prioritize the feeling of loneliness rather than pandemic-related worry, perception of restriction or information-seeking. This could be achieved by a digital mental health approach (e.g., online therapy or smartphone-based interventions) that fosters a sense of belonging and community [66-70]. To our knowledge this is the first study to use a temporal network model comparison approach to identify and refine mental health intervention targets. This approach might be valuable to identify possible temporal causal trigger variables for negative cognitions and behaviors in other types of mental health interventions as well.

Limitations

This was a natural experiment with high ecological validity but low control for extraneous variables, including seasonal effects [71]. Moreover, we cannot exclude the possibility that the observed interactions are influenced by other unmeasured underlying factors [72]. In addition, we have independent samples for comparing the lockdown and no-lockdown stages. Thus, we cannot exclude the possibility that differences in sample characteristics may have influenced the results. However, except for the loneliness score and gender distribution, the samples did not differ in any of the measured variables. We assume that the slightly higher loneliness measure (ULS-8) in the lockdown sample was due to the lockdown. However, it cannot be ruled out that we recruited participants who were generally lonelier in the lockdown sample by chance. Gender did not have an influence on any of the measured variables, except for time spent on social activities. Here, women reported higher values than men or diverse genders. Taken together, it is unlikely that there is a major bias in our central findings due to differences in sample characteristics.

Conclusion

To develop effective pandemic mental health interventions, it is crucial to understand the temporal dynamics of mental health factors during a COVID-19 lockdown. In comparison to a no-lockdown stage, a lockdown increased the central role of loneliness in triggering pandemic related behaviors and cognition. In turn, pandemic-related cognitions and behaviors, such as perceived restrictions and worries about the pandemic, reinforced each other and increased stress. In addition, we found that physical activity can be an effective buffer against stress and loneliness during lockdown. Our results suggest that loneliness can be the central trigger for stress-related behaviors and cognitions during lockdown and therefore should be prioritized in mental health interventions.

11.2.6 References

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11.2.7 Appendix

Supplement A: Lockdown Stages

Summary of most important changes in public health measures to counteract the pandemic in Germany between August 2020 and March 2021 (End of measurement, not end of lockdown) (https://www.deutschland.de/en/news/german-federal-government-informs-about-the-corona-crisis)

No-Lockdown Stage	**Lockdown Stage**
8 August 2020 – 1 November 2020	2 November 2020 - 9 March 2021
1. Nationwide, a distance of at least 1.5 meters must be maintained, hygiene rules must be observed, and masks must be worn in shops and on public transport. There was no general restriction on public meetings. 2. Institutions and leisure facilities (i.e., theatres, concert halls, cinemas and fitness studios) opened. 3. Sports and recreational activities indoor and outdoor were permitted. 4. Restaurants, bars, pubs, cafés and other catering establishments opened. All of above-mentioned policies must act in strict compliance with hygiene and infection control regulations 5. Governmental financial aid for those that suffered economic losses during the time of the	1. Only 2 households are allowed to meet, maximal 10 people. 2. Institutions and leisure facilities (i.e., theatres, concert halls, cinemas and fitness studios) had to close. 3. Sports and recreational activities indoor and outdoor were not allowed. 4. All service sectors are closed (e.g., tattoo shops, cosmetic shop), except hairdresser and medically needed treatment, such as ergo- or physiotherapy. 5. Travel restriction abroad and inland. Hotels and pensions are not allowed to receive guests. 6. Schools and kindergartens remained open, as well as youth welfare services. 7. Home office required if possible.

pandemic.	From 16 December 2020 onwards: 1. Only 2 households are allowed to meet, maximal 5 people. 2. Further closing of service sectors (including hairdresser). 3. Closing of most retail, some exception, such as grocer's shop, pharmacies, post offices, banks and gas station. 4. Closing of schools and kindergarten.

Supplement B. Test for stationarity

To test for non-stationarity, we calculated a two-level AR(1) model, in which each score of the variable included in our model is regressed on the immediately preceding score of that person, resulting in a moment-to-moment inertia score.

The two level AR(1) model can be formulated as following:

Level 1 : $y_{bi} = \mu_i + \phi_i (y_{b-1,i} - \mu_i) + e_{bi}$

Level 2 : $\mu_i = \gamma_{00} + \mu_{0i}$

$\phi_i = \gamma_{10} + \mu_{i1}$

Where μ_0 represents th mean/trait level of person i, e_{bi} their deviation from this trait level at measurement occasion b that cannot be explained by the autoregression. The lagged Predictor $(y_{b-1,i} - \mu_i)$ is centered around the person's trait level and the parameter ϕ_i represents how much the variable affects itself from one moment to the next moment. Each variable was square root transformed to achieve a normal distribution. The R code for the test for stationarity can be found online at https://osf.io/zskgm/.

Moment-to-moment inertia larger than 1 indicate a non-stationary process [1] results are shown in **Table 1**. We see that the average moment-to-moment inertia is between 0.13 and 0.37 for all 7 included variables, with standard errors ranging from 0.002 to 0.18.

Table 1. Overview of average trait level and averaged moment-to-moment inertia for each of the seven variables and for each lockdown group. The standard errors for the fixed effects are given between parentheses.

Group	Two-level AR mode	Notion	Perceived restriction	Corona Worry	Information seeking	Stress	Loneliness	Social activity	Physical activity
No-lockdown	Avg. trait level	γ_{00}	3.80 (0.18)	3.88 (0.19)	3.68 (0.17)	5.11 (0.17)	3.72 (0.20)	1.50 (0.03)	0.19 (0.003)
	Avg. moment-to-moment inertia	γ_{10}	0.26 (0.02)	0.25 (0.02)	0.19 (0.02)	0.28 (0.02)	0.28 (0.02)	0.24 (0.02)	0.16 (0.02)
Lockdown	Avg. trait level	γ_{00}	4.35 (0.18)	4.40 (0.18)	3.68 (0.16)	4.85 (0.17)	3.54 (0.21)	1.66 (0.06)	0.178 (0.002)
	Avg. moment-to-moment inertia	γ_{10}	0.27 (0.02)	0.24 (0.02)	0.13 (0.02)	0.37 (0.02)	0.29 (0.02)	0.26 (0.02)	0.16 (0.02)

Supplement C. Permutation Procedure.

Centrality indices. The centrality indices in-strength and out-strength were used in this study. These centrality indices were based on all estimated coefficient in the multilevel autoregressive model (including non-significant one's). These measures can quantify the importance of each variable within the network.[5] In-strength reflect the sum of ingoing absolute edge weights (i.e., the sum of predictor's coefficient for a specific outcome) and out-strength reflect the sum of outgoing absolute edge weights to the specific node (i.e., the sum of the coefficients between specific predictor and all other outcomes). To create a permutation distribution, the group label was randomly assigned to participants, then centrality indices were calculated (i.e., in-strength and out-strength), this was repeated 100,000 times. Statistical significance was determined by counting the occurrence of out-strength/in-strength difference as extreme or more extreme than the differences based on the observed data. This count was divided by the total amount of iteration and doubled to gain a two-sided p-value. We considered difference scores with a (two-sided) p-value below 0.05 as statistically significant.

Edge differences. Statistical significance for group differences in network edges was determined by comparing the size of the edge-differences based on the actual data to a permutation distribution. To create a permutation distribution, the group label was randomly assigned to participants, then random coefficients were taken from both groups. This was repeated 100,000 times. Statistical significance was determined by counting the occurrence of coefficient difference as extreme or more extreme than the differences based on the observed data. This count was divided by the total amount of iteration and doubled to gain a two-sided p-value. We considered differences with a (two-sided) p-value below 0.05 as statistically significant.

Exploratory Analysis: Overall connectivity. Overall network connectivity was calculated as the mean strength of absolute connection of weight between nodes.[2] Networks with stronger overall connectivity are thought to be more vulnerable, as nodes are more likely to trigger each other more easily and strongly.[3] Previous studies have found that stronger overall connectivity signal vulnerability for psychopathology.[2,4] Group differences in connectivity were calculated by subtracting the connectivity estimates of the no-lockdown stage from the connectivity estimates of the lockdown stage. First, we saved connectivity differences based upon the regression coefficients from a model with the actual data. To create a distribution under a null hypothesis, the group variable (Lockdown, No-lockdown) was randomly assigned to individuals, and subsequently connectivity differences were estimated based on regression coefficients derived from modelling the reshuffled data. This was repeated 100,000 times, statistical significance was determined by counting the occurrence of connectivity difference as extreme or more extreme than the connectivity differences based on the observed data. This count was divided by the total amount of iteration and doubled to gain a two-sided p-value. We considered differences with a (two-sided) p-value below 0.05 as statistically significant.

Permutation tests revealed no statistically significant difference between the two groups in overall network connectivity (i.e., absolute values of all edges; difference = -0.403, *P* = .514; no-lockdown group B = 1.31; lockdown group B = .91). These two groups did also not differ significantly in inter-node connectivity (i.e., cross-regressive edges; difference = .0028, *P* = .865; no-lockdown B = .211; lockdown B = .208) nor intra-node connectivity (i.e., autoregressive effects; difference = .4692, *P* = .515; no-lockdown B= 1.49; lockdown B= 1.03) (see Supplement D).

Supplement D. Overall connectivity permutation test results between no-lockdown and lockdown group.

	b.diff.obs	**b.nolockdown**	**b.lockdown**	**p-perm.def2**
grp1_vs_grp2_all	0.4025	1.311358	0.9088197	0.5144
grp1_vs_grp2_diag	0.0028	0.210771	0.2080003	0.8651
grp1_vs_grp2_off	0.4692	1.494789	1.025623	0.5148

Supplement E. Permutation results centrality indices in-strength and out-strength between no-lockdown and lockdown group.

Supplement Table E. Permutation results of centrality indices in-strength and out-strength between no-lockdown and lockdown group. Results that are statistically significant (two-sided p value at the uncorrected α level) are marked in bold and with asterisk.

Variables	**Out-Strength**			**In-Strength**		
		No-lockdown	**Lockdown**		**No-lockdown**	**Lockdown**

	Difference	B	B	Difference	B	B
Perceived restriction	-0.063063	0.2542236	0.3172868	4.748569	5.588932	0.8403637
Corona worry	0.041758	0.3822933	0.3405358	2.738025	7.007971	4.269947
Information seeking	**0.145194***	0.3129435	0.1677495	20.103076	23.43126	3.32818
Stress	-0.120391	0.4190705	0.5394615	-10.880732	3.980051	14.86078
Loneliness	**-0.197533***	0.4109139	0.6084465	3.245508	20.088	16.84249
Social activity	-0.757939	0.9260614	1.684	-0.254114	4.046562	4.300676
Physical activity	20.676352	61.55104	40.87468	0.024048	0.1137732	0.08972553

Supplement F. Permutation results of dynamic associations between variables for the no-lockdown and lockdown group.

Supplement Table F. Associations between variables for the no-lockdown and lockdown group, and the differences in associations between groups. Results that are statistically significant (permutation testing using two-sided p value at the uncorrected α level) are marked with bold font and asterisks.

	No-lockdown	**Lockdown**	**Difference No-Lockdown vs. Lockdown**
Perceived restriction (outcome)			

Perceived restriction	0.168361167	0.209280080	-0.0409
Corona worry	0.093930687	0.058423729	0.0355
Information seeking	0.054766023	-0.006164548	**0.0609** *
Stress	0.057600390	0.076000884	-0.0184
loneliness	0.000990697	0.114984496	**-0.114***
Social activity	-0.034224490	-0.199609564	0.1654
Physical activity	-5.179058957	-0.175900440	-5.0032
Corona worry (outcome)			
Perceived restriction	0.04961000	0.03815016	0.0115
Corona worry	0.19130966	0.17582498	**0.0155***
Information seeking	0.06893197	0.02120137	**0.0477***
Stress	0.02685971	0.05706330	-0.0302
loneliness	0.02744843	0.10418599	**-0.0767***
Social activity	-0.01084773	-0.17633630	0.1655
Physical activity	-6.63296364	-3.69718455	-2.9358
Information seeking			
Perceived restriction	-0.009187084	-0.03182693	0.0226
Corona worry	0.068932020	0.06828975	6e-04
Information seeking	0.172070557	0.09671964	**0.0754***
Stress	0.016648518	0.01513835	0.0015
loneliness	-0.004302592	0.04524142	-0.0495
Social activity	-0.089219118	-0.19994264	0.1107
Physical activity	-23.070896004	-2.87102164	-20.1999
Stress			

Perceived restriction	0.009905426	0.029978702	-0.0201
Corona worry	0.014639647	-0.004817997	0.0195
Information seeking	0.013378323	0.026506587	-0.0131
Stress	0.281292472	0.349809306	-0.0685
loneliness	0.082897759	0.076983545	0.0059
Social activity	-0.236783136	-0.508308587	0.2715
Physical activity	3.341154199	-13.864377864	17.2055
Loneliness			
Perceived restriction	0.01281949	0.005914085	0.0069
Corona worry	-0.01293064	0.031500069	**-0.0444***
Information seeking	-0.00250844	-0.016125181	0.0136
Stress	0.03531339	0.038755178	-0.0034
loneliness	0.29161681	0.266552851	0.0251
Social activity	-0.29704402	-0.331087923	0.034
Physical activity	-19.43576336	-16.152552853	-3.2832
Social activity			
Perceived restriction	0.0043388190	-0.0021206610	**0.0065***
Corona worry	-0.0005405175	0.0016629806	-0.0022
Information seeking	-0.0012475821	-0.0010179940	-2e-04
Stress	-0.0013483639	-0.0026195790	0.0013
loneliness	-0.0036485525	-0.0004227891	-0.0032
Social activity	0.2574926656	0.2685007186	-0.011
Physical activity	3.7779456112	4.0243313946	-0.2464
Physical activity			
Perceived restriction	0.000001567147	0.00001617310	-1.460595e-05

Corona worry	0.000010136284	0.00001625251	-6.116226e-06
Information seeking	0.000040654396	-0.00001414608	5.480048e-05
Stress	0.000007707282	0.00007489472	-6.718744e-05
loneliness	-0.000009045968	-0.00007541477	6.63688e-05
Social activity	0.000450261913	0.00021419024	0.0002360717
Physical activity	0.113253876221	0.08931445475	0.0239

Supplement G. Testing for the effect of gender.

Because we had more female participants in our lockdown group compared to the no-lockdown group, we are tested the effect of gender on each measured variable. For each participant, we calculated an average score for every variable included in our network analyses. Gender consisted of three levels: male, female and diverse.

Stress. A one-way ANOVA revealed that there was no significant difference of stress scores among different genders ($F(2, 255) = 0.27$, $P = 0.764$).

COVID-19 related worry. A one-way ANOVA revealed that there was no significant difference of levels of COVID-19 related worry among different genders ($F(2, 255) = 0.727$, $P = 0.484$).

Perceived restriction. A one-way ANOVA revealed that there was no significant difference of levels of perceived restriction among different genders ($F(2, 255) = 0.961$, $P = 0.384$).

Information seeking. A one-way ANOVA revealed that there was no significant difference of levels of information seeking among different genders ($F(2, 255) = 0.294$, $P = 0.745$).

Loneliness. A one-way ANOVA revealed that there was no significant difference of loneliness scores among different genders ($F(2, 255) = 2.757$, $P = 0.065$).

Physical activity. A one-way ANOVA revealed that there was no significant difference of levels of perceived restriction among different genders ($F(2, 255) = 0.297$, $P = 0.743$).

Social activity. A one-way ANOVA revealed that there was no significant difference of duration of social activity among different genders ($F(2, 255) = 11.62$, $P = < 0.001$). Tukey's HSD Test for multiple comparisons found that females spent more time on social activity than males ($P < 0.001$, 95% C.I. of difference score = [0.3095, 0.9228], Male: M = 2.41, SD = 0.886, Female: M = 3.02, SD = 0.886, Diverse: M = 3.33, SD = 1.17).

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11.3 Study 3 :The effects of momentary loneliness and COVID-19 stressors on hypothalamic–pituitary adrenal (HPA) axis functioning

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12 Publication list

Haucke, M., Golde, S., Heinzel S. (2022). *The Socio-evaluative N-Back Task (SENT): Developing and testing a paradigm to investigate how acute socio-evaluative stress impacts working memory in social anxiety.* [in preparation].

Haucke M., Gutmann, G., Wilbertz, G., Heinzel S., (2022). *Near-miss inference – testing a paradigm for a cognitive correlate of pathological anxiety.* [in preparation].

Haucke M., Heinz A., Heinzel S., Liu. S. (2022). *Mechanism of everyday alcohol consumption in times of COVID-19 in a distressed and lonely population: Worries about COVID-19 leads to higher alcohol consumption amid lockdown*. [in preparation].

Liu, S., Wegner, L., Haucke, M., Gates, J., Adam, M., Bärninghausen, T. (2022). *An entertainment-education video and written messages to alleviate loneliness in Germany*. [Manuscript submitted for publication].

Golde, S., Ludwig, S., Lippoldt, S., Rimpel, J., Schulze, L., Haucke, M., Renneberg, B., Heinzel S. (2022). *Negative and positive self-beliefs in social anxiety: the strength of believing mediates the affective response.* [Manuscript submitted for publication].

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13 Eidesstattliche Versicherung (statement of authorships)

Hiermit erkläre ich, die vorliegende Dissertation selbstständig verfasst und ohne unerlaubte Hilfe angefertigt habe.

Alle Hilfsmittel, die verwendet wurden, habe ich angegeben. Die Dissertation ist in keinem früheren Promotionsverfahren angenommen oder abgelehnt worden.

Berlin, 22. September 2022

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Matthias Haucke