Archival Report

In the Face of Potential Harm: The Predictive Validity of Neural Correlates of Performance Monitoring for Perceived Risk, Stress, and Internalizing Psychopathology During the COVID-19 Pandemic

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ABSTRACT

BACKGROUND: The COVID-19 pandemic is a major life stressor posing serious threats not only to physical but also to mental health. To better understand mechanisms of vulnerability and identify individuals at risk for psychopathological symptoms in response to stressors is critical for prevention and intervention. The error-related negativity (ERN) has been discussed as a neural risk marker for psychopathology, and this study examined its predictive validity for perceived risk, stress, and psychopathological symptoms during the COVID-19 pandemic.

METHODS: A total of 113 individuals who had participated as healthy control participants in previous electroencephalography studies (2014–2019) completed a follow-up online survey during the first COVID-19 wave in Germany. Associations of pre-pandemic ERN and correct-response negativity (CRN) with perceived risk regarding COVID-19 infection, stress, and internalizing symptoms during the pandemic were examined using mediation models.

RESULTS: Pre-pandemic ERN and CRN were associated with increased perceived risk regarding a COVID-19 infection. Via this perceived risk, the ERN and CRN were associated with increased stress during the pandemic. Furthermore, risk perception and stress mediated indirect effects of ERN and CRN on internalizing psychopathology, including anxiety, depression, and obsessive-compulsive symptoms, while controlling for the effects of pre-pandemic symptom levels.

CONCLUSIONS: In summary, heightened pre-pandemic performance monitoring showed indirect associations with increases in psychopathological symptoms during the first COVID-19 wave via effects on perceived COVID-19 risk and stress. These results further strengthen the notion of performance monitoring event-related potentials as transdiagnostic neural risk markers and highlight the relevance of stress as a catalyst for symptom development.

https://doi.org/10.1016/j.bpsgos.2021.08.004

In March 2020, the World Health Organization declared the outbreak of COVID-19 as a worldwide pandemic. Since then, this pandemic has had a profound impact on life, requiring individuals to adapt to changing circumstances and new hardships. A growing number of reports suggest that the COVID-19 pandemic has led to increased levels of anxiety and distress (1–6). At the same time, psychopathological effects of the pandemic differ across individuals, and our understanding of the pathways to anxiety and depression and the identification of individuals at risk for mental illness is critical for the development of targeted intervention and prevention.

Neuroscience methods, including event-related potentials (ERPs), are gaining importance for studying mechanisms that lead to mental disorders. This line of research strives to identify biomarkers informing models of pathomechanisms and predictions of future psychopathology (7), particularly under conditions of stress (8–12). The error-related negativity (ERN)

(13) is of particular interest in this regard and has been highlighted as a promising transdiagnostic risk marker (14). The ERN is a well-validated neural marker of error processing with good psychometric properties (15), observable as a sharp negativity over frontocentral brain regions after errors. The corresponding ERP on correct responses, the correct-response negativity (CRN), has been studied to a lesser extent. Existing findings point toward the CRN representing broader general performance monitoring functions shared between both correct and incorrect actions, whereas an additional error-specific process is present only after incorrect responses (16,17). Both ERPs are assumed to be generated by activity in the midcingulate cortex, specifically the anterior cingulate cortex (18,19), and are thought to prompt adaptive responses with the aim to avoid harm (20,21). Variations in ERN and CRN are assumed to be trait like, shaped by genes (22), learning history (23–25), and situational demands

(13,26–28). Furthermore, variations in ERN magnitude have been linked to individual differences in harm avoidance (14), anxious apprehension (29), or threat sensitivity (30). Similarly, increased ERN amplitudes are shared by disorders such as obsessive-compulsive disorder (OCD) and various anxiety disorders, including generalized and social anxiety disorder [e.g., (31,32)]. In contrast to ERN, CRN variations have been less frequently studied in relation to traits and psychopathology, and alterations have been reported less consistently. However, one exception is an association between elevated CRN and OCD, which has been shown repeatedly (33), suggesting changes not only in error-specific but also in general performance monitoring processes (16) and a possible association with increased concern about the correctness of actions even in the absence of errors.

Beyond this observed cross-sectional association of the ERN with psychopathology, a growing number of studies support that alterations in ERN magnitude represent a neural vulnerability marker preceding symptom development. Alterations in ERN are present in healthy individuals with increased familial risk for OCD or anxiety (14,34,35), and increased ERN amplitudes persist after symptom improvement by psychotherapy in OCD and anxiety (36–39), suggesting that they are not a consequence of symptoms. Moreover, the ERN can be used to predict symptom onset across different disorders (9,11,40). In concert, these findings underscore that ERN alterations can lead to maladaptive behaviors and mental disorders, further highlighting its critical role in mental health. However, the relationship between alterations in performance monitoring and the development of symptoms is complex, and its role in psychopathological trajectories is still poorly understood. Existing findings highlight the ERN as a potential endophenotype for internalizing psychopathology [e.g., (14)], suggesting that it may play an important mediating role on the pathways from genetic risk to psychopathological phenotypes (41,42). More recently, the role of stress as a catalyst in this relationship has been emphasized (11,43). Few studies to date have used ERPs to investigate reactions to real-life stressors. One study in children showed that the ERN prospectively predicted response to a natural disaster in that youths with initially higher ERN amplitudes showed stronger increases in anxiety after the event (8). Similarly, an increased ERN has been shown to render individuals more susceptible to the adverse effects of interpersonal stress during transition to university, thereby increasing risk for heightened anxiety (8). This growing evidence supports an involvement of the ERN in the emergence of stress susceptibility (43). Nevertheless, the mechanisms by which performance monitoring ERPs influence stress susceptibility and symptom development remain poorly understood, a research gap that this study aims to address.

The COVID-19 pandemic, as a major real-life stressor, provides a unique research environment to investigate the hypothesis that overactive performance monitoring (i.e., ERN and CRN) translates into psychopathology through heightened risk perception and its effects on stress. We explored the association of pre-pandemic ERN and CRN in previously healthy participants (2014–2019) (14,44,45) with self-reported perceived risk,

stress, and psychopathological symptom dimensions, such as anxiety, depression, and obsessive-compulsive symptoms during the first COVID-19 wave in Germany.

METHODS AND MATERIALS

Participants

We invited 317 adults who had participated as healthy comparison participants in three previous electroencephalography studies conducted at Humboldt-Universität zu Berlin (14,44,45) to an online survey and clinical phone interview. The invitation was accepted by 140 participants (44.2%), but only 123 (38.8%) completed all questionnaires and 121 (38.2%) could be interviewed on the phone. Two participants reported that they had tested positive for COVID-19 at that time and were omitted from data analysis because asking for the perceived risk of an infection or severe course became obsolete. In addition, 8 participants were excluded because <6 error segments were available for ERN assessment (46). The final sample consisted of 113 participants (62.8% female) aged 20–63 years (mean = 33.47, SD = 10.35). These participants did not differ from the full participant pool in age (t_{315} = −0.699, p = .485), gender ($\chi^2_{3,317}$ = 3.058, p = .080), trait anxiety (Spielberger State-Trait Anxiety Inventory [STAI-T]) (t_{315} = 0.034, p = .973), depressive symptoms (Beck Depression Inventory-II [BDI-II]) (t_{315} = 0.227, p = .820), obsessive-compulsive symptoms (Obsessive-Compulsive Inventory-Revised [OCI-R]) (t_{315} = 0.266, p = .790), CRN (t_{311} = −0.32, p = .751), and ERN (t_{296} = −0.07, p = .947).

Procedure

Baseline assessments were conducted during study participation in previous projects, between 0.83 and 5.38 years (mean = 2.87, SD = 1.51) prior to this investigation. Electrophysiological data of all participants had been recorded using a flanker task, and detailed study information and cross-sectional results have been reported elsewhere (14,44,45). However, raw data were reprocessed for this study to ensure identical procedures (details below). Participants who had agreed to be recontacted for future studies during initial study participation received information of the objectives and methods of this investigation. Those who agreed to participate then completed several online questionnaires and were interviewed via phone based on the Structured Clinical Interview for DSM-IV (47). Clinical data were collected between February 11 and May 19, 2020, while COVID-19 infection rates and media reports were rising across Europe and in Germany. For reference, the first case of COVID-19 infection in Germany was confirmed on January 29, 2020, and federal contact restrictions were implemented on March 23, 2020. The study procedures were in accordance with the Declaration of Helsinki as approved by the local ethics committee. Participants gave informed consent prior to the baseline and follow-up assessment and received a monetary compensation of €15 for the follow-up assessment.

Measures

The follow-up online survey consisted of several questionnaires: depressive symptoms were assessed with BDI-II (21

items; 4-point Likert scale 0–3; Cronbach's α = 0.90) (48,49), obsessive-compulsive symptoms with OCI-R (18 items; 5-point Likert scale 0–4; α = 0.88) (50,51), and trait anxiety using the trait subscale of STAI-T (4-point Likert scale 1–4; α = 0.92) (52,53). Stress was assessed using the Stress and Coping Inventory (SCI) (21 items; 5-point Likert scale 1–7; α = 0.88) (54), including the subscales strain, stress symptoms, and coping strategies. Perceived COVID-19 risk was measured by the average of 2 items (Likert scale 0–100; α = 0.69) asking participants to rate "How likely do you think you will become infected with COVID-19 within the next month?" and "How likely do you think you would experience a severe course of COVID-19, if you were infected?" As a measure of objective risk regarding COVID-19, participants were asked to self-categorize whether or not they have an increased risk of infection, including occupation (e.g., employment in health care, retail, or public transportation) and risk of a more severe course due to known medical risk factors (e.g., age over 60 years, overweight, hypertension).

Task

At the initial assessment, participants performed a modified arrow version of the flanker task (36) presented on a 19-inch liquid crystal display monitor in a dimly lit, electrically shielded cabin. Sets of 5 vertically aligned arrows, including 1 target and 4 flanker arrows (set size approximately 2.5° × 2.5°), were presented using Presentation Software (Neurobehavioral Systems, Inc.) with a fixation phase (200–1200 ms), stimulus presentation (100 ms), and a response window (maximum 1000 ms). Half of the stimuli were incongruent (i.e., target arrow pointed in the opposite direction); 480 stimuli were presented pseudorandomly. Participants were instructed to indicate direction of the target arrow as fast and accurately as possible. One study (44) provided performance feedback to the participants in between blocks, whereas the other two studies repeated the instruction irrespective of performance. Elicited ERPs did not differ between projects, neither for ERN ($F_{2,110}$ = 1.02, p = .365) nor for CRN ($F_{2,110}$ = 2.30, p = .106).

Electrophysiological Recording and Processing

Electrophysiological activity was recorded using 64 Ag/AgCl electrodes and two 32-channel BrainAmp amplifiers (Brain Products GmbH). Electrodes were mounted on a cap with equidistant layout (Easycap). Additional electrodes were placed at nasion, neck, and left infraorbital site and a ground electrode on the right cheek; Cz served as recording reference. Impedances were kept below 5 kΩ. The continuous signal was recorded with a low-cutoff time constant of 10 seconds and a high-cutoff frequency of 250 Hz. Sampling rate was 1000 Hz.

Data were processed with Brain Vision Analyzer 2.2 (Brain Products GmbH). The electroencephalogram was filtered by zero phase shift Butterworth bandpass filters from 0.1 to 30 Hz (24 dB/octave roll-off) and a 50-Hz notch filter. Ocular artifacts were removed using independent component analysis (55); components were semiautomatically identified by visual inspection. After re-referencing electroencephalography data to the common average of all scalp electrodes, response-locked segments were epoched from −500 to 1000 ms and baseline corrected using the −500 to −300-ms interval (15). Segments

with artifacts were automatically removed if there was a voltage step >50 μV between data points, the absolute voltage range exceeded ±200 μV, or the voltage was <0.5 μV within 100-ms intervals. Average data loss due to artifact rejection was small (mean = 0.57%, SD = 1.22), and no participant had >25% excluded segments. Segments were discarded (mean = 12.24%, SD = 13.68) if response times were <100 or >800 ms; remaining segments were averaged separately for correct and erroneous responses. The ERN and CRN were scored as the mean activity from 0 to 100 ms after response at electrode FCz, where signals were maximal. Both ERPs had excellent psychometric properties as reflected by the Spearman-Brown–corrected split-half reliability of odd and even trials (r_{ERN} = 0.87, r_{CRN} = 0.99).

Data Analysis

Statistical analyses were conducted with SPSS version 25.0 (IBM Corp.) using a two-tailed α = 0.05. Pearson correlations were conducted to determine associations between variables at baseline and follow-up.

Exploratively, a series of mediation models was tested to examine effects of baseline ERPs on risk, stress, and symptoms during the pandemic. Mediation analyses were conducted using the PROCESS Macro for SPSS, version 3.5 (56), applying model 4 for simple mediation and model 6 for the serial mediation models to calculate 95% confidence intervals (CIs) around the indirect effect with 5000 bootstrap resamples. Because time between baseline and follow-up varied between participants, this was included as covariate in all mediation models. We used separate mediation models using the ERN and CRN, respectively, as predictors and self-reported experienced stress during the pandemic as outcome, with perceived COVID-19 risk as the mediator. In addition, specificity was examined by computing similar models with objective risk as the mediator and other ERPs as predictors.

Because experienced stress was closely related to symptoms during the pandemic (Table 1), we additionally tested indirect effects of ERN and CRN via perceived risk and stress on these symptoms in another set of models including two serial mediators. Baseline ERN or CRN, respectively, were used as predictors, while follow-up perceived COVID-19 risk and self-reported stress were included as serial mediators in the prediction of symptoms. Separate models were applied to predict symptoms of anxiety, OCD, and depression at follow-up, while controlling for the respective symptoms at baseline as covariates.

RESULTS

Table 1 shows demographic and clinical characteristics; Table S1 presents frequencies of new-onset diagnoses. Pearson correlation coefficients for associations between ERPs at baseline and symptoms measured at baseline and follow-up are presented in Table 2. A depiction of individual symptom changes between time points is shown in the Supplement (Figure S1). Neither the ERN nor CRN assessed at baseline was directly related to stress (SCI) or symptoms (BDI-II, STAI-T, OCI-R). However, significant negative correlations between ERN and CRN and perceived COVID-19 risk at follow-up were present, indicating that larger (i.e., more negative) ERN

Table 1. Demographic, Self-report/Clinical, and ERP Data in the Baseline and Follow-up Sample

Variable	Baseline	Follow-up
Demographic Data		
Gender, female/male, n	71/42	71/42
Age, years	30.84 (10.17)	33.47 (10.35)
Clinical Data		
BDI-II	5.07 (5.97)	6.05 (6.56)
OCI-R	9.07 (8.31)	9.10 (8.64)
STAI-T	36.96 (9.08)	36.89 (9.27)
SCI	–	43.25 (16.71)
COVID-19 perceived risk[a]	–	23.01 (20.67)
COVID 19 objective risk, risk/no risk[b]	–	38/75
ERP Data		
CRN at FCz, μV	0.62 (2.70)	–
ERN at FCz, μV	−4.55 (4.06)	–

Values are presented as mean (SD) unless otherwise indicated. $N = 113$.

BDI-II, Beck Depression Inventory-II; CRN, correct-response negativity; ERN, error-related negativity; ERP, event-related potential; OCI-R, Obsessive-Compulsive Inventory-Revised; SCI, Stress and Coping Inventory; STAI-T, Spielberger State-Trait Anxiety Inventory– Trait subscale.

[a]Averaged perceived risk of infection and severe course of disease.

[b]Dichotomous self-categorization of personal risk for COVID-19 based on occupation and medical factors.

and CRN amplitudes were associated with higher perceived COVID-19 risk estimates. The scatterplots for the associations between pre-pandemic ERN and CRN and perceived COVID-19 risk, as well as grand averages incorporating a median split regarding risk estimates to further visualize these associations, are shown in Figure 1. Perceived risk showed a significant positive correlation with objective risk. However, objective risk was not related to the ERN and CRN. Furthermore, perceived stress (SCI) during the pandemic was significantly correlated with depressive (BDI-II), anxious (STAI-T), and obsessive-compulsive (OCD-R) symptoms, whereas perceived COVID-19 risk was only correlated with BDI-II scores. Among the three symptom dimensions, STAI-T and BDI-II were strongly correlated with each other, while both were only moderately correlated with OCI-R.

A mediation model testing perceived risk as mediator between pre-pandemic ERN and stress at follow-up indicated a significant total model ($F_{3,109} = 4.591$, $p = .005$, $R^2 = 0.112$) (see Figure 2 for all coefficients). Importantly, while the direct effect of baseline ERN and stress at follow-up was not significant ($c' = 0.605$, SE = 0.380, $t = 1.591$, $p = .115$, 95% CI −0.149 to 1.358), the indirect effect of baseline ERN and stress during the pandemic via the perceived COVID-19 was significant (ab = −0.240, SE = 0.120, 95% CI −0.497 to −0.032). The analogous mediation model with baseline CRN as predictor of stress at follow-up was also significant ($F_{3,109} = 3.665$, $p = .015$, $R^2 = 0.092$). Again, there was no significant direct effect on stress ($c' = -0.049$, SE = 0.594, $t = -0.083$, $p = .934$, 95% CI −1.226 to 1.128), but the indirect effect via perceived COVID-19 risk was significant (ab = −0.437, SE = 0.260, 95% CI −1.034 to −0.036).

To examine potential distinct contributions of the ERN and CRN, we used the residualized ERN (residuals from a regression of CRN on ERN) as predictor of stress via risk perception. This model was not significant (Figure S2), suggesting that these results are rather driven by the overlap of both components than an error-specific process. Accordingly, a mediation model using the arithmetic mean of the ERN and CRN as predictor indicated a significant indirect effect on stress via

Table 2. Bivariate Correlations of ERPs With COVID-19 Risk, Stress, and Symptom Measures

Variable	1	2	3	4	5	6	7	8	9	10	11
Baseline											
1 ERN	0.87	–	–	–	–	–	–	–	–	–	–
2 CRN	0.62[a]	0.99	–	–	–	–	–	–	–	–	–
3 BDI-II	0.11	−0.03	0.90	–	–	–	–	–	–	–	–
4 OCI-R	0.14	0.01	0.35[a]	0.86	–	–	–	–	–	–	–
5 STAI-T	0.13	0.02	0.72[a]	0.44[a]	0.92	–	–	–	–	–	–
Follow-up											
6 COVID-19 objective risk	0.11	0.04	0.17	0.12	0.24[b]	0.03	–	–	–	–	–
7 COVID-19 perceived risk	−0.19[b]	−0.25[c]	0.01	0.06	0.05	0.33[a]	0.69	–	–	–	–
8 SCI	0.08	−0.10	0.39[a]	0.36[a]	0.47[a]	0.30[c]	0.27[c]	0.88	–	–	–
9 BDI-II	0.07	−0.14	0.59[a]	0.40[a]	0.52[a]	0.26[c]	0.24[b]	0.66[a]	0.90	–	–
10 OCI-R	0.04	−0.04	0.25[c]	0.63[a]	0.34[a]	0.12	0.08	0.47[a]	0.40[a]	0.88	–
11 STAI-T	0.13	−0.01	0.65[a]	0.43[a]	0.74[a]	0.22[b]	0.15	0.57[a]	0.78[a]	0.43[a]	0.92

Baseline refers to pre-pandemic assessment. Follow-up refers to assessment during pandemic. COVID-19 objective risk refers to averaged objective risk for COVID-19 based on occupation and medical factors, and COVID-19 perceived risk refers to averaged perceived risk of infection and severe course of disease. Correlations are displayed as Pearson's r; psychometric properties depicted in the diagonal with Spearman-Brown–corrected split-half reliability for ERP data and Cronbach's alpha for questionnaire data. $N = 113$.
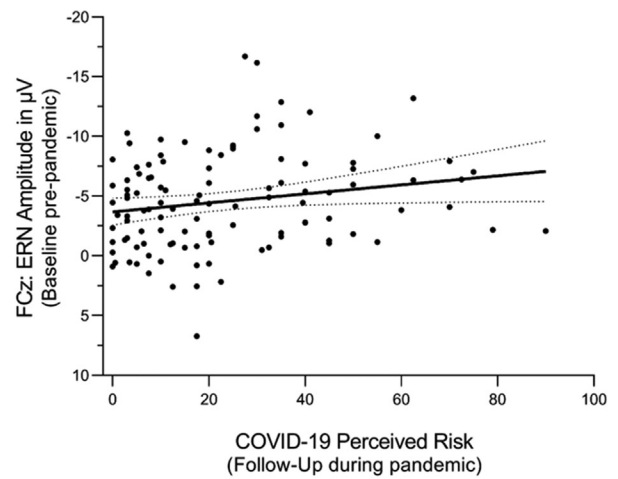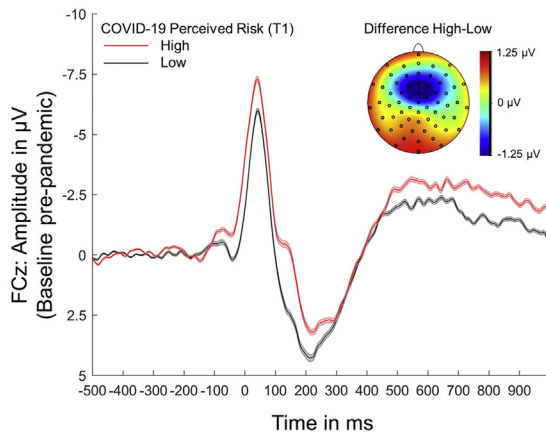
BDI-II, Beck Depression Inventory-II; CRN, correct-response negativity; ERN, error-related negativity; OCI-R, Obsessive-Compulsive Inventory-Revised; SCI, Stress and Coping Inventory; STAI-T, Spielberger State-Trait Anxiety Inventory–Trait subscale.
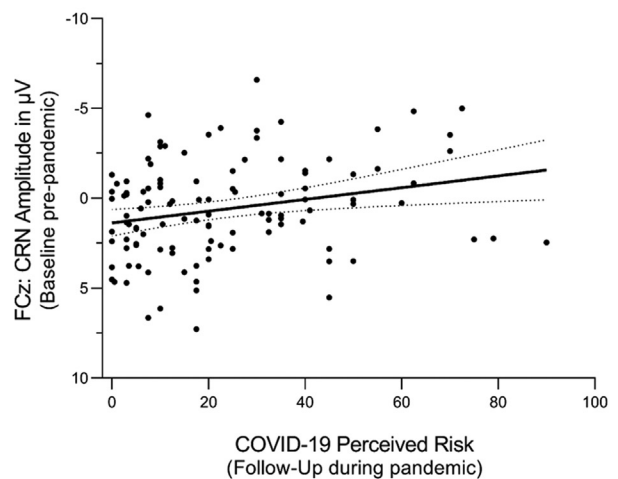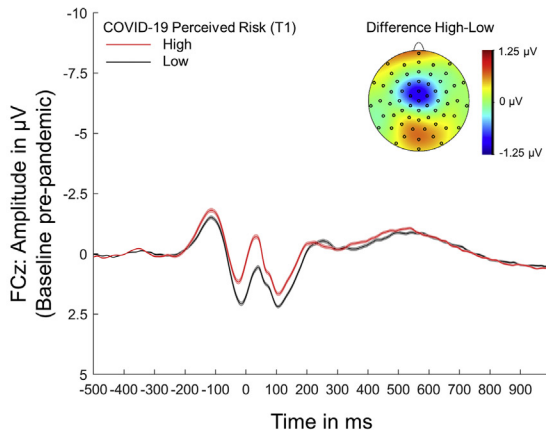
[a]$p < .001$.

[b]$p < .05$.

[c]$p < .01$.

Figure 1. Grand average waveforms for error and correct trials as a function of COVID-19 risk (median split in high and low) and scatterplots for the error-related negativity (ERN) and the correct-response negativity (CRN) with COVID-19 risk. **(A)** The upper left panel shows grand average waveforms for error trials measured before the pandemic, split by individuals indicating high (i.e., above median) and low (i.e., below median) perceived COVID-19 risk, and scalp distribution of the high vs. low-risk difference (0–100 ms). Shading around waveforms indicates standard errors at the respective time point. The upper right panel displays the scatterplot for the association of the ERN at the pre-pandemic baseline and perceived COVID-19 risk at follow-up. **(B)** The lower left panel shows grand average waveforms and scalp distribution for correct trials; the lower right panel displays the respective scatterplot for the CRN and perceived COVID-19 risk. T1, follow-up during pandemic.

perceived risk (Figure S3). Furthermore, mediation models examining whether objective risk mediated an association between pre-pandemic ERN or CRN and stress at follow-up did not reach significance, supporting a specific role of

perceived risk (Figures S4 and S5). To further probe specificity for the ERN and CRN, Pe on error trials and stimulus-locked N2 for correct trials were tested as predictors. None of these models reached significance (Tables S5 and S6).
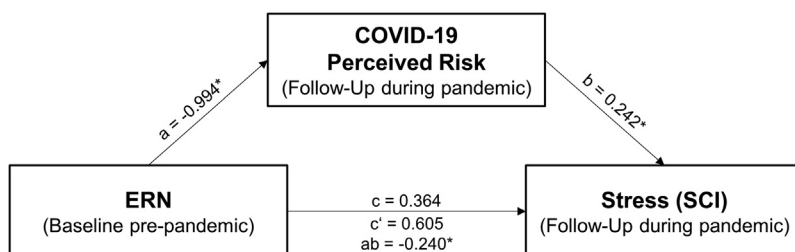

Figure 2. Mediation model with pre-pandemic error-related negativity (ERN) as predictor of stress at follow-up and COVID-19 risk as mediator. Time between baseline and follow-up is controlled for by implementation as covariate in the model. *$p < .05$. SCI, Stress and Coping Inventory.

Using serial mediation models, we examined the indirect effects of ERN and CRN on psychopathology while correcting for the respective baseline symptoms. For the three models using STAI-T, BDI-II, and OCI-R at follow-up as outcome variables, an indirect effect of ERN on symptoms, mediated via perceived risk and stress, was observed (Table 3 for all coefficients and Figure 3 for the exemplary model). Similarly, the serial mediation models to predict symptoms from the CRN at baseline indicated indirect effects through perceived COVID-19 risk and stress (Table 4).

DISCUSSION

To our knowledge, this study is among the first longitudinal studies to investigate the utility of neural correlates to predict behavioral and clinical outcomes in the context of the COVID-19 pandemic. Previous research has identified overactive performance monitoring ERPs (i.e., ERN and CRN) as risk markers for internalizing disorders (9,14,31,38), but the underlying pathways and the role of stress are still largely unclear (11,43). This study revealed the following key findings. Both the ERN and CRN were prospectively associated with risk perception regarding COVID-19. Moreover, this perceived COVID-19 risk functioned as mediator for indirect effects of pre-pandemic ERN and CRN on stress during the pandemic. Finally, indirect effects of ERN and CRN on psychopathological symptoms during the first COVID-19 wave were observed, mediated by effects on perceived risk and stress. Notably, these associations were independent of pre-pandemic symptom levels, indicating a prediction of stress-related changes in symptoms.

Individuals with higher (i.e., more negative) pre-pandemic ERN or CRN amplitudes reported an increased perceived risk for an infection and a severe course of COVID-19 disease during the pandemic. This association with risk estimation complements previous knowledge, specifically studies linking reduced ERN amplitudes or reduced activity of the anterior cingulate cortex, i.e., the main generator of the ERN, to

heightened risk taking (57,58) and increased anterior cingulate cortex activity to risk aversion during decision making (58). Furthermore, an association between ERN and risk perception corresponds with findings that conceptualize an elevated ERN as a low-threshold alarm signal in line with a better safe than sorry logic (20,59,60) and suggest relationships to harm avoidance (14) and threat sensitivity (30). Moreover, alterations in the ERN, and less consistently the CRN, have been observed across disorders such as OCD and generalized anxiety disorder [e.g., (32)], known to be characterized by cognitive biases such as overestimation of threat and risk aversion (61–63). In addition, interventions aimed at reducing attentional bias to threatening information have been shown to decrease the ERN (45,64). Collectively, these findings support an association of heightened ERN/CRN with alterations in risk perception. The risk measure used here was tailored specifically to the COVID-19 pandemic, but the fit with previous findings suggests that similar associations might apply to risk estimation of other life stressors as well.

The ERN and CRN also predicted individual stress levels during the pandemic, mediated via effects on risk perception. With regard to potential underlying mechanisms, this seems to suggest that individual differences in performance monitoring might influence how individuals appraise risk for harm when confronted with real-life stressors, which then determines resulting stress levels. In line with previous reports, this may suggest an effect of the ERN on susceptibility to stress (11). However, it may also indicate that ERPs of performance monitoring influence which individuals are more likely to experience stress, i.e., in the sense of dependent stressors (i.e., stressors to which an individual contributes). Finally, experiencing stress may in turn affect the function of the performance monitoring system [e.g., (23–25)]. Future research is needed to improve our understanding of the complex relationship between increased performance monitoring and stress, possibly incorporating more objective stress measures, e.g., cortisol responses.

Table 3. Coefficients for the Mediation Models With the ERN as Predictor, Perceived COVID-19 Risk and Stress as Serial Mediators, and Symptoms (STAI-T, OCI-R, or BDI-II) as Outcomes, Controlling for Respective Symptoms at Baseline and Time Between Baseline and Follow-up as Covariates

	STAI-T: Coefficient (95% CI)	OCI-R: Coefficient (95% CI)	BDI-II: Coefficient (95% CI)
Paths			
a_1	−1.073[a] (−2.031 to −0.114)	−1.075[a] (−2.034 to −0.117)	−1.022[a] (−1.979 to −0.064)
a_2	0.294 (−0.395 to 0.983)	0.381 (−0.349 to 1.111)	0.412 (−0.299 to 1.123)
b_1	0.023 (−0.034 to 0.076)	−0.017 (−0.079 to 0.046)	0.034 (−0.009 to 0.076)
b_2	0.145[a] (0.068 to 0.223)	0.151[a] (0.070 to 0.232)	0.187[a] (0.131 to 0.243)
d_{21}	0.208[a] (0.074 to 0.341)	0.217[a] (0.076 to 0.358)	0.230[a] (0.091 to 0.367)
Effects			
c	0.070 (−0.223 to 0.364)	−0.091 (−0.411 to 0.218)	0.007 (−0.244 to 0.258)
c′	0.084 (−0.196 to 0.366)	−0.131 (−0.443 to 0.180)	0.008 (−0.202 to 0.218)
a_1b_1	−0.024 (−0.110 to 0.065)	0.018 (−0.044 to 0.098)	−0.036 (−0.115 to 0.018)
a_2b_2	0.043 (−0.063 to 0.142)	0.058 (−0.054 to 0.157)	0.077 (−0.046 to 0.201)
$a_1d_{21}b_2$	−0.032[a] (−0.079 to −0.002)	−0.035[a] (−0.077 to −0.004)	−0.044[a] (−0.106 to −0.004)

N = 113.

BDI-II, Beck Depression Inventory-II; OCI-R, Obsessive-Compulsive Inventory-Revised; ERN, error-related negativity; STAI-T, Spielberger State-Trait Anxiety Inventory–Trait subscale.
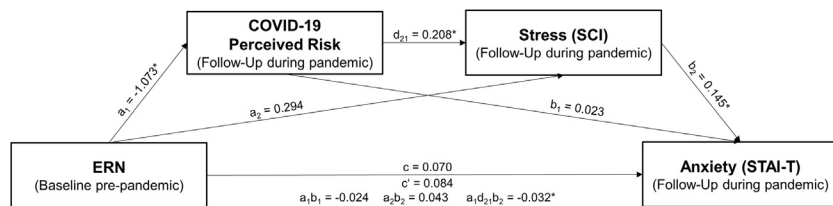
[a]Significant at $p < .05$.

Figure 3. Exemplary depiction of mediation model to examine the error-related negativity (ERN) at baseline as a predictor of anxiety symptoms at follow-up, with perceived COVID-19 risk and stress as mediators. Baseline Spielberger State-Trait Anxiety Inventory (STAI-T) (trait anxiety) and time between baseline and follow-up is controlled for by implementation as covariates in the model. *$p < .05$. SCI, Stress and Coping Inventory.

Consistent with vulnerability stress models (65), self-reported stress further closely related to multiple internalizing symptoms, including anxiety, depression, and OC symptoms. By this, the performance monitoring ERPs could be used to indirectly predict the development of internalizing symptoms via their effect on perceived risk and stress. This holds even when controlling for the effects of initial symptoms, supporting a predictive utility of performance monitoring ERPs for psychopathological symptoms above and beyond preexisting symptoms. It should be noted that in this study, no direct association was observed between variations in ERN and CRN and internalizing symptoms at follow-up, which is at odds with some previous reports of direct predictions [e.g., (66)] but in line with the notion that the association might be stronger or even limited to clinical groups (67). Instead, the connections observed in this study appear to be more complex, and mediating factors, such as perceived risk and stress, need to be considered. Notably, in this complex mechanistic model encompassing risk perception and stress as mediators, indirect prediction of psychopathology includes increases in depressive symptoms, whereas findings regarding direct associations of ERN/CRN alterations with depression are still rather mixed (68–70). However, the rather unspecific predictive effects across different symptoms can be explained by the indirect effects of ERN and CRN on psychopathology acting through a common mechanism in which stress plays a key role. Such a model also aligns with findings that suggest the ERN as a transdiagnostic risk marker (31,32) preceding psychopathological symptoms (9,11,66,71).

These results showed that both ERN and CRN variations were associated with risk perception and indirectly predicted symptom development, pointing to an association with increases in performance monitoring after erroneous and correct responses. In line with this, the arithmetic mean of both ERPs also acted as a significant predictor. These findings support the interpretation of alterations in a general performance monitoring process shared across both ERPs (16) being implicated in risk perception, stress reactivity, and ultimately psychopathology. In future studies on stress reactivity, the role of the CRN, which is often given little attention, should thus be considered alongside the ERN. Collectively, the results suggest that ERPs of performance monitoring represent a promising target for interventions aimed to improve symptoms or prevent psychopathology (45,72) that can be applied transdiagnostically.

This investigation has several limitations. Most importantly, the analyses are primarily exploratory, and while the results provide insight into the complex relationship between performance monitoring and psychopathology, consolidation in future studies is needed. Because the follow-up measures (i.e.,

Table 4. Coefficients for the Mediation Models With the CRN as Predictor, Perceived COVID-19 Risk and Stress as Serial Mediators, and Symptoms (STAI-T, OCI-R, or BDI-II) as Outcomes, Controlling for Respective Symptoms at Baseline and Time Between Baseline and Follow-up as Covariates

	STAI-T: Coefficient (95% CI)	OCI-R: Coefficient (95% CI)	BDI-II: Coefficient (95% CI)
Paths			
a_1	−2.064[a] (−3.487 to −0.640)	−2.041[a] (−3.462 to −0.620)	−2.012[a] (−3.436 to −0.587)
a_2	−0.335 (−1.390 to 0.721)	−0.191 (−1.308 to 0.926)	−0.069 (−1.164 to 1.026)
b_1	0.019 (−0.038 to 0.076)	−0.013 (−0.076 to 0.051)	0.028 (−0.014 to 0.071)
b_2	0.147[a] (0.070 to 0.225)	0.147[a] (0.067 to 0.228)	0.187[a] (0.131 to 0.242)
d_{21}	0.185[a] (0.049 to 0.320)	0.195[a] (0.051 to 0.339)	0.211[a] (0.070 to 0.352)
Effects			
c	−0.141 (−0.583 to 0.301)	−0.124 (−0.604 to 0.357)	−0.311 (−0.686 to 0.063)
c′	0.003 (−0.428 to 0.434)	−0.062 (−0.536 to 0.412)	−0.162 (−0.480 to 0.156)
a_1b_1	−0.039 (−0.218 to 0.130)	0.025 (−0.095 to 0.170)	−0.056 (−0.214 to 0.050)
a_2b_2	−0.049 (−0.247 to 0.101)	−0.028 (−0.216 to 0.127)	−0.013 (−0.241 to 0.161)
$a_1d_{21}b_2$	−0.056[a] (−0.154 to −0.002)	−0.059[a] (−0.142 to −0.003)	−0.079[a] (−0.211 to −0.006)

$N = 113$.

BDI-II, Beck Depression Inventory-II; CRN, correct-response negativity; OCI-R, Obsessive-Compulsive Inventory-Revised; STAI-T, Spielberger State-Trait Anxiety Inventory–Trait subscale.

[a]Significant at $p < .05$.

COVID-19 risk, stress, and symptoms) were assessed at the same time, direction of the associations cannot be discerned and the indirect paths, albeit significant and plausible, can only suggest potential mechanisms pending further replication in fully prospective investigations. In addition, the COVID-19–related risk measures used here have not been validated yet, and the observed associations need replication. Moreover, we examined psychopathology dimensionally, and it needs to be determined whether similar results can be seen with regard to clinical outcomes. Nonetheless, this approach allows for the prospective investigation of symptom development among previously healthy individuals. Moreover, although there was variability in symptoms at both assessments, no overall increase in symptoms during the pandemic was apparent in this sample. This might indicate that despite being a major life stressor, the COVID-19 pandemic did not affect all participants uniformly with regard to increases in stress and psychopathology symptoms. Finally, our results showed rather small effects, which is typical for multifactorial, complex processes such as the development of psychopathology, but again, replication in well-powered samples will be essential.

Conclusions

The COVID-19 pandemic constitutes a global health crisis with profound impact on mental health. With this study, we adopted a longitudinal approach to study mechanisms and neural predictors of such effects. Results suggest that pre-pandemic ERPs of performance monitoring (i.e., ERN and CRN) may contribute to predict risk perception, stress, and exacerbation of internalizing symptoms during such a real-life stressor. Specifically, individuals with increased neural sensitivity to errors and correct responses experienced heightened risk perception, which was further connected to elevated stress levels during the first COVID-19 wave. Through these potential mediators, the ERN and CRN were also related to increases in internalizing symptoms (anxiety, depression, and OC symptoms). These findings bear clinical relevance because they demonstrate predictive utility of performance monitoring ERPs for identification of individuals at risk for mental health issues under real-life stressors, and the mechanisms elucidated here can offer vantage points for targeted prevention efforts.

ARTICLE INFORMATION

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