

Prefrontal cortical thickness, emotion regulation strategy use and COVID-19 mental health

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Abstract

Coronavirus disease 2019 (COVID-19) and associated restrictions have been linked to negative mental health outcomes across the globe. Cognitive emotion regulation strategies, neurally supported by prefrontal and limbic regions, constitute means to mitigate negative affects resulting from adverse life experiences. Variations in cognitive emotion regulation strategy use, anxiety, and depression were assessed in 43 adults (31♀/12♂, age = 35.14 ± 9.20 years) during the first months following COVID-19 onset and at the end of 2020 (seven assessments). Direct and indirect effects of emotion regulatory brain structures assessed prior to the pandemic and emotion regulation strategy use during the pandemic were assessed in relation to mental well-being. Varying levels of anxiety and depression were observed. While adaptive emotion regulation strategies were most frequently employed, maladaptive strategies explained the highest variation in anxiety and depression scores. The effectiveness of specific emotion regulation strategies varied. Momentary emotion regulation strategy use mediated the association between cortical thickness in right lateral prefrontal cortex assessed prior to the pandemic and mental health during the pandemic. Early mental health measures impacted later mental well-being. Maladaptive strategies have a negative effect on mental health during prolonged stress as induced by pandemics, providing possible targets for intervention.

Key words: emotion regulation; prefrontal cortex; mental health; COVID-19; cortical thickness

Introduction

Emotion regulation skills describe a set of abilities allowing control over the intensity, duration or extent of an emotional experience (Gross, 2002; Ochsner et al., 2012). Proficient emotion regulation skills have been linked to healthy social, physical, and psychological functioning, including one's own and others' physical and mental well-being (Tugade and Fredrickson, 2007). Reduced emotion regulation skills, however, have been linked to pathologies of childhood, adolescence or adulthood, including disruptive behavior disorders, depression or anxiety (Raschle et al., 2019; Megreya et al., 2020; Riaz et al., 2021). Healthy social functioning therefore relies on the interplay between mechanisms of emotion processing and cognitive control. Pandemics such as the coronavirus disease 2019 pandemic (COVID-19, named according to the year in which the outbreak was first identified and as recommended by the World Health Organization) can induce a significant amount of stress and negative affect (Lee et al., 2007; Shanahan et al., 2020; Veer et al., 2021). Prolonged negative feelings resulting from events that are a threat

to oneself, one's social status, self-identity or physical well-being increase the risk to develop physical or mental health problems (Cohen et al., 2019), highlighting the need for interventions that may mitigate such effects. An individual's strategy and ability for emotion regulation is considered an essential contributing factor for the etiology, maintenance and treatment of mental health disorders (Cisler et al., 2010; Cisler and Olatunji, 2012; Joormann and Stanton, 2016).

To date, the onset of COVID-19 and associated restrictions have been related to reduced general health and increases in neuropsychiatric symptoms, particularly anxiety and depression (Ensel and Lin, 1991; Ozamiz-Etxebarria et al., 2020; Shanahan et al., 2020; Borbás et al., 2021). First longitudinal assessments indicate that stress-related negative symptoms remained elevated during the first year following its onset (Gubler et al., 2020; de Quervain et al., 2020b; Barendse et al., 2021). Emotional distress tends to be highest in younger individuals, in individuals with chronic diseases or pre-existing health conditions, females and individuals living alone or in socioeconomic adversity

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(Adams-Prassl et al., 2020; Kwong et al., 2020; Ozamiz-Etxebarria et al., 2020; de Quervain et al., 2020b). Findings of increases in emotional distress are complemented by reports of the opposite pattern: groups of individuals with improved mental well-being, indicating the need to consider interindividual differences (Kuhn et al., 2020; de Quervain et al., 2020b; Achterberg et al., 2021).

In line with evidence demonstrating that a proficient use of adaptive emotion regulation skills may act as a possible buffer during adversity (Gross and John, 2003; John and Gross, 2004; Martin and Dahlen, 2005; Hu et al., 2014; Zahniser and Conley, 2018; Li et al., 2020; Shanahan et al., 2020), emerging evidence likewise indicates that the use of maladaptive emotion regulation strategies during the COVID-19 pandemic results in negative effects (Brehl et al., 2021; Muñoz-Navarro et al., 2021). This is in line with the notion that adaptive emotion regulation strategies are generally associated with better mental health, while the opposite is true for maladaptive skills (Garnefski et al., 2001). Adaptive skills include acceptance (being able to admit something took place), positive reappraisal (assigning positive meaning to an experience), refocus on planning (considering further steps and planning), positive refocus (attention shift toward something pleasant) and putting into perspective (setting an experience into context, for example, by comparing the event to other experiences and relativizing its impact). Maladaptive emotion regulation strategies include catastrophizing (sole focus on detrimental consequences), rumination (recurring thoughts about negative feelings), other-blame (blaming someone else) and self-blame (blaming oneself for the negative experience).

Prior research indicates that emotion regulation strategies are differently effective in the modulation of an emotional experience, and the direction of their effect on mental health outcomes may vary in dependence of context-specific factors (Balzarotti et al., 2016). For example, putting into perspective and acceptance are most commonly associated with beneficial outcomes; however, some studies report the opposite effect (Schroevers et al., 2007; Balzarotti et al., 2016). Such context-dependent variations might result from the type and intensity of the emotion experienced, vary with demographic characteristics of the individuals studied, but also depend on levels of controllability or the duration of the challenging circumstances (Martin and Dahlen, 2005; Aldao and Nolen-Hoeksema, 2012; McRae, 2016; Kobylińska and Kusev, 2019). Overall, the ability to adapt strategy use depending on context is considered beneficial for one's mental health (Kobylińska and Kusev, 2019). However, research on the temporal stability in the use of specific emotion regulation strategies is scarce. A study conducted in healthy participants investigated rumination and positive reappraisal over a 20 week period of everyday life, revealing relatively stable use of both strategies (Everaert and Joormann, 2020). To better understand the contextual effects on the efficacy of individual strategies, longitudinal studies are needed. Such repeated measures studies can add beyond the mere examination of large-scale cross-sectional designs (Klapwijk et al., 2020).

Research using structural and functional magnetic resonance imaging (MRI) indicates that emotion regulation skills are supported by brain regions associated with cognitive control (e.g. prefrontal regions) and emotion processing (e.g. limbic regions including the amygdala; Buhle et al., 2014; Kohn et al., 2014; Braunstein et al., 2017). Emotion regulation skill acquisition is paralleled by the maturation of corresponding brain regions and strengthened by the connectivity between these (Baum et al., 2020). The coordinated interplay of brain regions responsible for emotion processing and cognitive control thus allows use

of emotion regulation. Structural or functional alterations in any part of this network can lead to behavioral dysfunctions as reported for anxiety (Geng et al., 2016), depression (Zhang et al., 2018) or conduct disorder (Raschle et al., 2019). Varying levels of gray matter volume (GMV) or cortical thickness (CT) of prefrontal or limbic brain structures have been associated with emotion regulation skills or disruptions thereof (Kühn et al., 2011; Vijayakumar et al., 2014; Ferschmann et al., 2021). Furthermore, studies investigating functional and structural connectivity point toward the importance of effective communication between prefrontal and limbic brain structures (Salzman and Fusi, 2010).

The present study (i) first aims to investigate variations in the use of specific emotion regulation strategies and mental health (i.e. depression and anxiety levels) in adults as assessed during the first year of the COVID-19 pandemic in Switzerland. Secondly (ii), the association of specific emotion regulation strategies in relation to mental well-being during the first pandemic months or toward the end of 2020 (early and later effects) is examined. Thirdly (iii), structural brain correlates assessed before the pandemic associated with emotion regulation [i.e. lateral prefrontal cortex (lPFC) and amygdala; Phan et al., 2005; Raschle et al., 2019; Berboth and Morawetz, 2021] are investigated. More specifically, the mediating role of emotion regulation strategy use on the association of emotion regulatory brain structures assessed before pandemic onset and later mental well-being (beginning or end of the first year following COVID-19 onset) is investigated. Based on prior evidence (de Quervain et al., 2020a,b; Borbás et al., 2021), we expect that participants will report significant but varying levels of anxiety and depression. We anticipate that adaptive emotion regulation strategies are employed more often than maladaptive ones (Gross and John, 2003; Cohen et al., 2019; Cruz et al., 2020) and that adaptive emotion regulation strategies may buffer, while maladaptive strategies may increase the risk of negative outcomes (Butler et al., 2003; John and Gross, 2004; Martin and Dahlen, 2005; Hu et al., 2014). Furthermore, we test the hypothesis that the use of specific emotion regulation strategies may change across time (given scarce prior evidence a non-directional exploratory assessment of the link between specific strategy-use and psychological well-being is tested). Finally, we expect that emotion regulatory brain structures as assessed prior to COVID-19 support the use of specific emotion regulation strategies, which mediate the association between emotion regulatory brain structure and mental well-being during the pandemic (with adaptive strategies having a positive influence and maladaptive strategies having a negative influence on mental health).

Materials and methods

Participants and design

Participants who had previously taken part in a cross-sectional neuroimaging study and agreed to being re-contacted were invited to participate (Borbás et al., 2021). Study design and assessments relevant to the present investigation are presented in Figure 1. Baseline [2018–20; wave 1 (W1)] included behavioral testing and neuroimaging. All participants were of average intelligence or above (according to the International Standard Classification of Education (ISCED; Organisation for Economic Co-operation and Development, 1999). Forty-three participants (31♀/12♂; average age = 35.14 ± 9.20 years/range 22–51 years) agreed to participate in follow-up assessments. Retention rate per time point is reported in Supplementary Table 2.1.

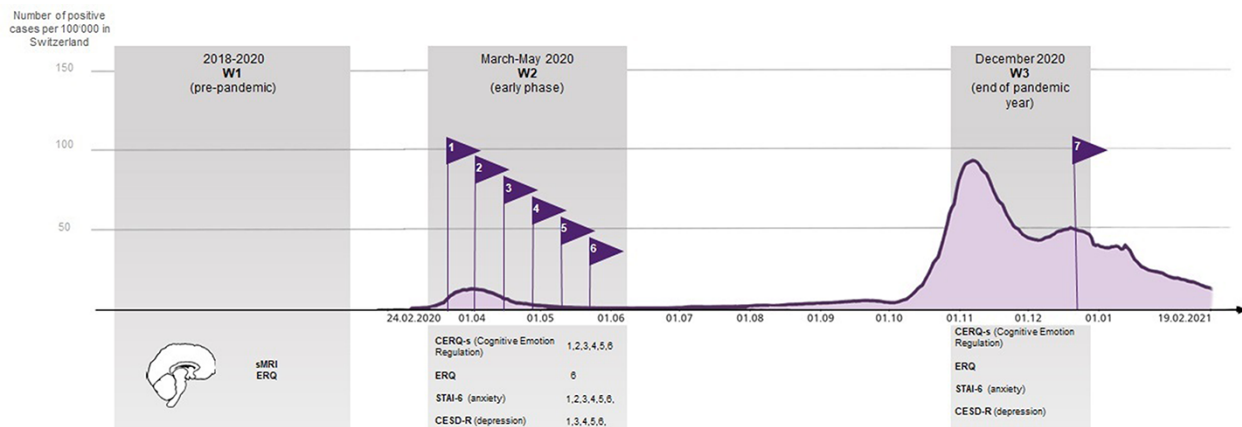


Fig. 1. Study design. Data acquisition during the first year after COVID-19 onset in Switzerland followed initial baseline testing prior to pandemic onset [wave 1 (W1)]. A second wave of assessments [wave 2 (W2)] included six biweekly testing spanning 11 weeks between March and May 2020 (T1–T6), and a third wave of assessments including one battery of questionnaires [T7; wave 3 (W3)] was completed at the end of the first pandemic year in December 2020. Assessments relevant to the present study including: brain structure (acquired before COVID-19 onset), emotion regulation skills and strategy use, and mental well-being (i.e., anxiety and depression) are listed below the respective wave; the bold line represents the daily incidence rate of individuals tested positive for COVID-19 per 100 000 in Switzerland.

All procedures were approved by the local ethics board (Ethikkommission Nordwest-und Zentralschweiz); participants signed an informed consent form.

Behavioral testing

The German short-form of the Cognitive Emotion Regulation Questionnaire (CERQ-s; [Garnefski and Kraaij, 2007](#)) was employed to assess state emotion regulation strategy use (six repeated assessments across W2: T1–T6, one testing at W3: T7). Mental well-being (W2–W3) was measured through the short-form of the State-Trait Anxiety Inventory (STAI-6; [Marteanu and Bekker, 1992](#)) and by the Center for Epidemiologic Studies Depression Scale–Revised (CESD-R; German; [Schmitt, 2016](#)). Trait emotion regulation skills were assessed once for each wave using the Emotion Regulation Questionnaire (ERQ; [Gross and John, 2003](#); [Abler and Kessler, 2009](#)). The full assessment list is provided in [Supplementary Methods and Supplementary Table 2.2](#).

Structural MRI

Structural T1-weighted magnetization-prepared rapid gradient-echo data were acquired on a Siemens 3T Prisma scanner (specifics in [Supplementary Methods](#)). Structural MRI data were preprocessed in FreeSurfer v7.1.0 (<https://surfer.nmr.mgh.harvard.edu/>) using the automated ‘recon-all’ stream including motion correction, intensity-normalization, Talairach-registration, skull-stripping, removal of non-brain tissue, segmentation, tessellation, smoothing and cortical parcellation ([Dale et al., 1999](#); [Fischl et al., 1999](#)). The quality of segmentation and reconstruction was visually inspected. CT and GMV were reckoned on the region level as defined in the Desikan/Killiany atlas ([Desikan et al., 2006](#)). Amygdala was defined through the automatic segmentation; bilateral IPFC regions of interest were derived based on average (for CT) or estimated total intracranial volume scaled sum (for GMV) of caudal middle frontal, rostral middle frontal regions, pars opercularis, pars triangularis and pars orbitalis, in line with [Boes et al. \(2012\)](#). We chose to investigate one key region of the emotion processing (i.e. amygdala) and one key region of the cognitive control network (i.e. IPFC) respectively, since the intricate interplay between neural structures

supporting emotion regulation and neural structures supporting affect processing has been suggested to best reflect the modal model of emotion regulation ([Gross, 1998](#); [Kohn et al., 2014](#)) and since this influence has been commonly reported for both key structures ([Kohn et al., 2014](#); [Raschle et al., 2019](#); [Berboth and Morawetz, 2021](#)).

Data analysis

Analysis of the behavioral data was based on an imputed dataset, where missing values were replaced using predictive mean matching as implemented in the Multivariate Imputation by Chained Equations package in R ([Buuren and Groothuis-Oudshoorn, 2010](#)). Repeated measures acquired biweekly during W2 (between March and May 2020) were combined into one average W2 score. All analyses were conducted in IBM SPSSv27 (IBM Corp, Armonk, NY, USA) and R (<https://www.r-project.org/>).

Early and late behavioral correlates during the first pandemic year

W2–W3 comparisons for anxiety, depression, and emotion regulation were conducted using one-way repeated measures analysis of covariance (ANCOVA; covariates: age and sex). The percentage of adults exceeding clinically relevant cut-off scores for anxiety (>40 for STAI-6 indicate the total score of STAI-6; [Spielberger, 1983](#); [Bekker et al., 2003](#)) and depression (>16 in CESD-R_{total}; <https://cesd-r.com/cesdr/>) is reported and number of people above clinically relevant thresholds at W2 and W3 were compared using chi-square tests.

Behavioral variations over time

To meet aim (i), variation in mental well-being and emotion regulation scores were examined by use of mixed-effect models and a bottom-up approach using the ‘lme4’ package in R ([Bates et al., 2012](#)) to test for linear and non-linear effects of time over the course of all seven repeated measurements collected. Subjects were entered as random effects accounting for non-independent data (i.e. same individuals participating at each time point), while weeks since the first assessment were entered as a fixed effect. The model allowed for random intercept (possible differences in scores at the start) and slope (since previous reports

support individuals reacting differently to the pandemic). Using the Satterthwaite approximation (Luke, 2017) and the 'lmerTest' package (Kuznetsova et al., 2014), P-values were obtained. Due to right skewness for anxiety, depression, maladaptive strategies, catastrophizing, other-blame, positive reappraisal, refocus on planning, rumination, self-blame, putting into perspective, and positive refocus data were log-transformed. The R-code used for imputing the missing values and examining the difference between early and late behavioral correlates during the first pandemic year, the illustration of and the statistical model describing the behavioral variance in cognitive emotion regulation strategy use and measures of psychological well-being over time is publicly available on OSF link in the parentheses to <https://osf.io/jgtq5/>. Furthermore, the frequency of adaptive and maladaptive CERQ-strategies employed at each assessment point was compared (paired sample t-tests for seven time points; significance level adjusted for multiple comparisons, $P < 0.007$).

Emotion regulation strategy use and mental well-being

To investigate aim (ii), testing the use of emotion regulation strategies in relation to variations in mental well-being, we employed multiple regression analyses. Anxiety or depression scores from the beginning (W2) and after 10 months past COVID-19 onset (W3) were entered as the dependent variable and the nine emotion regulation strategies were entered as predictors, while controlling for participants' sex and age.

To evaluate the relationship between maladaptive/adaptive emotion regulation strategies and mental well-being (anxiety and depression) across 2020, four bivariate correlations were calculated. Maladaptive or adaptive emotion regulation strategies (two scores per person per assessment point) and anxiety and depression (two scores per person per assessment point) were correlated.

Alpha-level significance was adjusted for multiple comparisons ($P < 0.0125$).

Brain structure, emotion regulation and mental well-being

To meet aim (iii), the association between structural brain markers assessed prior to COVID-19 pandemic (i.e. GMV and CT) in a priori defined emotion regulatory regions (bilateral lPFC and amygdala), emotion regulation strategies used, and mental health was assessed through mediation analyses while controlling for age, sex, months passed since individual MRI sessions, and ISCED (a proxy to socioeconomic status and intelligence quotient; Feinkohl et al., 2021). To identify the variables of interest: (i) the emotion regulation strategy explaining the highest degree of variation in anxiety or depression for W2 and W3 was selected; (ii) a priori defined structural brain measures explaining the highest degree of emotion regulation strategy use at W2 were selected. According to the hypothesized mediation framework (Figure 2), it is assumed that brain structure may be altered, as suggested by reports observing volumetric changes in healthy participants in anxiety- and stress-related brain regions following COVID-19 onset (Salomon et al., 2021). Consequently, brain structures entering the model in relation to later outcome (W3) remained the same, but mental well-being at W2 was further added as a mediator allowing for the testing of an indirect effect.

Mediation analyses were conducted using the PROCESS model 4 by Hayes (2017) to assess emotion regulation strategies as mediators of the relation between brain correlates (step 2) and W2-anxiety or W2-depression scores; covariates included age, sex, months passed since the neuroimaging session, and ISCED. Double mediations were performed through PROCESS model 6 to test whether emotion regulation strategies used at W3 and/or psychological well-being at W2 mediated the association between brain

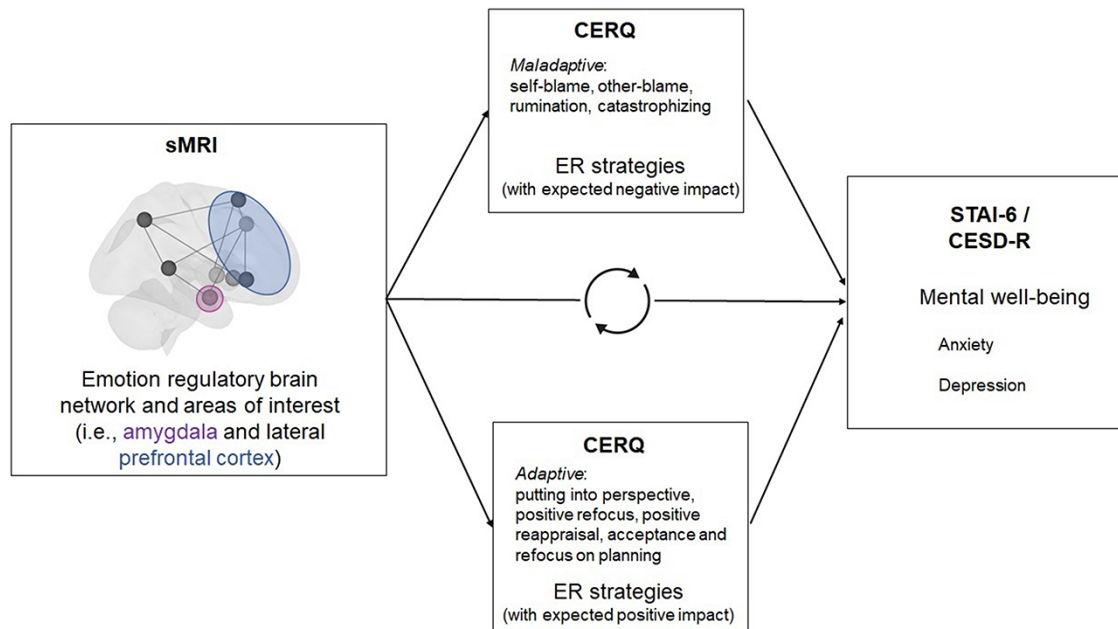


Fig. 2. Overview of the hypothesized parallel multiple mediation model. We tested the hypothesis that emotion regulatory structural brain characteristics (i.e. in prefrontal cortex and amygdala) assessed prior to COVID-19 onset enable the momentary use of adaptive and maladaptive cognitive emotion regulation strategies during the pandemic (Raschle et al., 2019; Berboth and Morawetz, 2021). Brain areas such as prefrontal cortex and the amygdala are key players within the emotion regulation networks for cognitive control and affect processing, respectively (Kohn et al., 2014). Positive (adaptive) or negative (maladaptive) strategies are expected to either positively or negatively mediate well-being as assessed by levels of anxiety or depression (Carver et al., 1993; Nowlan et al., 2015; McRae, 2016). The model acknowledges that prolonged use of maladaptive or adaptive emotion regulation strategies and long-term negative emotions may in turn impact brain structure (as indicated by circular arrows).

Table 1. Group characteristics and comparisons between the second (W2) and third (W3) assessment waves

N = 43; 31 females; mean age: 35.14 ± 9.20 years							
	W2	M ± s.d.	W3	M ± s.d.	F(1,40)	η ²	
Time since first testing	In months	18.76 ± 7.03	Time since first testing	In months	27.76 ± 7.03		
STAI-6	Anxiety	38.85 ± 8.13	STAI-6	Anxiety	41.32 ± 9.43	5.064*	0.020
CESD-R	Depression	9.53 ± 10.40	CESD-R	Depression	11.58 ± 12.15	2.765	0.009
ERQ	Cognitive reappraisal	4.64 ± 1.02	ERQ	Cognitive reappraisal	4.81 ± 0.96	1.684	0.008
	Expressive suppression	3.46 ± 1.05		Expressive suppression	3.11 ± 1.14	4.353*	0.034
CERQ-s	Self-blame	2.40 ± 0.97	CERQ-s	Self-blame	2.23 ± 0.57	2.585	0.011
	Acceptance	7.07 ± 1.71		Acceptance	6.98 ± 2.09	0.124	0.001
	Rumination	3.71 ± 1.27		Rumination	3.77 ± 1.34	0.189	0.001
	Positive refocusing	5.24 ± 1.66		Positive refocusing	5.30 ± 1.87	0.075	0.000
	Refocus on planning	5.09 ± 1.23		Refocus on planning	4.58 ± 1.62	3.507	0.033
	Positive reappraisal	5.29 ± 1.66		Positive reappraisal	5.14 ± 2.17	0.364	0.002
	Putting into perspective	5.88 ± 1.85		Putting into perspective	5.40 ± 2.01	2.438	0.016
	Catastrophizing	2.70 ± 0.93		Catastrophizing	2.58 ± 0.91	0.726	0.004
	Other-blame	3.25 ± 1.21		Other-blame	3.56 ± 1.44	2.230	0.014
CERQ-s	Adaptive strategies	5.71 ± 1.08	CERQ	Adaptive strategies	5.48 ± 1.27	2.191	0.010
Factors	Maladaptive strategies	3.01 ± 0.80	Factors	Maladaptive strategies	3.03 ± 0.71	0.056	0.000

*Indicates significance at $P < 0.05$.

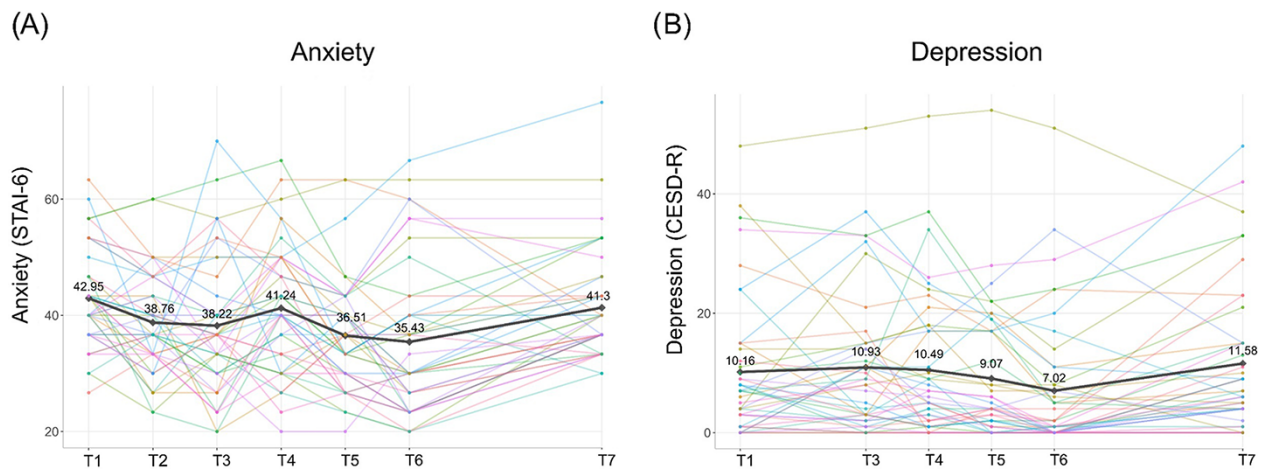


Fig. 3. Variation of mental health scores over time. Inter-subject variations (different colors) and group average (black, bold) are displayed. (A) Anxiety levels over seven time points after COVID-19 onset and (B) depression levels over six time points.

structure and psychological well-being at W3. Bootstrapping was set to 10 000 samples in each model.

Results

Early and late behavioral correlates during the first pandemic year

W2/W3-group characteristics and differences are provided in Table 1. One-way repeated measures ANCOVA (W2–W3 comparison) indicated significant differences in anxiety and use of expressive suppression. On average 34.88% of all participants surpassed clinically relevant anxiety levels at W2, 48.84% at W3 (percentages not statistically different). Subthreshold clinically relevant levels of depression were reported by 20.93% at W2 and W3.

Behavioral variations over time

In Figures 3 and 4 and the Supplementary Figure 3.1, the individual variations (differently colored lines) and group average (black line) over seven assessments for mental well-being (anxiety and depression scores), the nine cognitive emotion regulation

strategies, the adaptive and maladaptive strategies are depicted. Examining the effects of time revealed no significant variations for self-blame ($\beta = -0.001$), catastrophizing ($\beta = -0.001$), other-blame ($\beta = 0.002$), positive refocus ($\beta = 0.0003$), and cognitive reappraisal ($\beta = 0.001$).

Changes in anxiety ($\beta_{\text{linear}} = -0.02$, $\beta_{\text{quadratic}} = 0.0005$), adaptive strategies ($\beta_{\text{linear}} = -0.05$, $\beta_{\text{quadratic}} = 0.001$), acceptance ($\beta_{\text{linear}} = -0.08$, $\beta_{\text{quadratic}} = 0.002$), positive reappraisal ($\beta_{\text{linear}} = -0.02$, $\beta_{\text{quadratic}} = 0.0005$), refocus on planning ($\beta_{\text{linear}} = -0.03$, $\beta_{\text{quadratic}} = 0.0004$), and rumination ($\beta_{\text{linear}} = -0.01$, $\beta_{\text{quadratic}} = 0.0002$) were best described by quadratic models indicating a continuous significant decrease from T1 to T6 followed by a significant increase in scores to T7. Putting into perspective was also best characterized by a quadratic model, but the scores were increasing significantly from T1 to T6 and decreasing to T7 ($\beta_{\text{linear}} = 0.01$, $\beta_{\text{quadratic}} = -0.0003$). The use of maladaptive strategies was significantly declining from T1 to T6, but no further change was observed to T7 ($\beta_{\text{linear}} = -0.005$, $\beta_{\text{quadratic}} = 0.0001$).

Changes in depression scores were best described by a cubic model, with a significant increase between T1 and T3 then

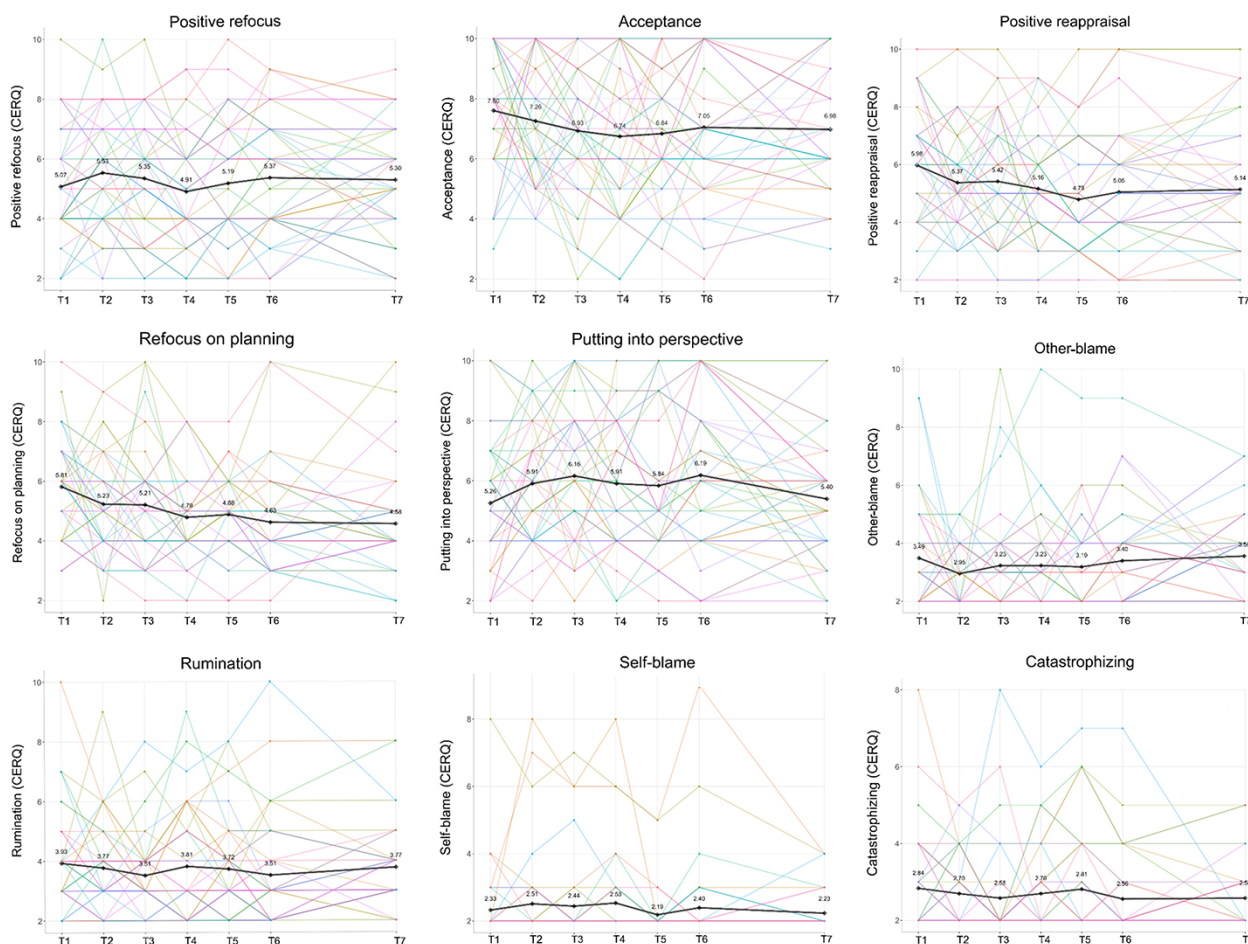


Fig. 4. Variation in the use of nine cognitive emotion regulation strategies over seven time points following COVID-19 onset in Switzerland. Inter-individual variations (different colors) and the group average (bold black) are displayed. The lowest employment of adaptive and maladaptive emotion regulation strategies is 2, while the highest possible use is 10.

a decrease to T6, but an increase anew to T7 ($\beta_{\text{linear}} = 0.12$, $\beta_{\text{quadratic}} = -0.02$, $\beta_{\text{cubic}} = 0.0005$; Table 2).

The employment of expressive suppression was significantly higher in the early (May 2020) compared to the late (December 2020) phase of assessments. However, when examining the trajectory of expressive suppression employment including all three time points (pre-pandemic, May 2020, December 2020; $\beta = 0.002$), no significant change was indicated. This discrepancy stems from the different analytical approaches. More specifically, an ANCOVA is handling time as a categorical variable, while in the mixed-effects model, time is regarded as a continuous variable, accounting for uneven spacing of data points. The results of both approaches should not be directly compared.

Paired t-tests comparing adaptive and maladaptive strategy use at each time point revealed significantly higher use of adaptive strategies at each time point (all $P < 0.001$; details in Supplementary Table 2.3).

Emotion regulation strategy use and mental well-being

Multiple regression analyses revealed that anxiety and depression during W2 (March–May 2020) were significantly predicted by rumination and positive reappraisal (variation in anxiety explained: 61.2%; depression: 49.2%). Rumination explained 41.5% of variation in anxiety ($F(4,38) = 15.001$, $P < 0.001$; $\beta = 0.730$,

$t(38) = 6.953$, $P < 0.001$), positive reappraisal explained 15.1% (negative association, $\beta = -0.396$, $t(37) = -3.849$, $P = 0.025$). The model for depression ($F(4,38) = 9.194$, $P < 0.001$) revealed a positive association of rumination ($\beta = 0.702$, $t(38) = 5.837$, $P < 0.001$; 40.6%) and negative association of positive reappraisal ($\beta = -0.275$, $t(38) = -2.338$, $P = 0.025$; 7.4%).

At W3 (December 2020), self-blame ($\beta = 0.510$, $t(39) = 3.661$, $P < 0.001$) explained 25.0% of the variance in anxiety ($F(3,39) = 4.887$, $P < 0.001$). The model for depression ($F(5,37) = 12.118$, $P < 0.001$) included three predictors, self-blame ($\beta = 0.485$, $t(37) = 4.308$, $P < 0.001$), rumination ($\beta = 0.286$, $t(37) = 2.591$, $P = 0.014$) and refocus on planning ($\beta = 0.251$, $t(37) = 2.357$, $P = 0.024$), explaining 38.3%, 8.3% and 5.7%.

Assessment of the relationship between adaptive or maladaptive strategy use and anxiety or depression revealed a significant link between higher use of maladaptive strategies and elevated levels of anxiety and depression. The use of adaptive strategies was negatively linked with anxiety (Figure 5), while the association between the use of adaptive strategies and depression was not significant.

Brain structure and early emotion regulation strategy use and mental well-being

Two simple mediation models were built testing how emotion regulation strategy use at W2 mediated the association of emotion

Table 2. Mixed models estimating the effect of time on individuals' mental health

Variables		Intercept	Duration (linear)	Duration (quadratic)	Duration (cubic)	ICC	N subjects/ observations
Anxiety (log)	Estimate (SE)	3.74 (0.03)	-0.02 (0.004)	0.0005 (0.0001)		0.46	43/301
	CI (95%)	3.68–3.81	-0.03–-0.01	0.0004–0.0008			
	P	<0.001	<0.001	<0.001			
Depression (log)	Estimate (SE)	1.87 (0.18)	0.12 (0.05)	-0.02 (0.01)	0.0005 (0.0001)	0.69	43/258
	CI (95%)	1.52–2.22	0.02–0.21	-0.03–-0.01	0.0002–0.0007		
	P	<0.001	0.017	<0.001	<0.001		
Adaptive strategies	Estimate (SE)	5.93 (0.18)	-0.05 (0.02)	0.001 (0.0004)		0.69	43/301
	CI (95%)	5.58–6.28	-0.09–-0.02	0.0003–0.002			
	P	<0.001	0.003	0.010			
Maladaptive strategies (log)	Estimate (SE)	1.39 (0.03)	-0.005 (0.003)	0.0001 (0.0001)		0.67	43/301
	CI (95%)	1.33–1.44	-0.01–0.001	-0.00001–0.0002			
	P	<0.001	0.017	0.079			
Cognitive reappraisal	Estimate (SE)	4.68 (0.13)	0.001 (0.001)				43/129
	CI (95%)	4.42–4.93	-0.002–0.004				
	P	<0.001	0.619				
Expressive suppression	Estimate (SE)	3.12 (0.16)	0.002 (0.001)			0.52	43/129
	CI (95%)	2.80–3.43	-0.001–0.004				
	P	<0.001	0.274				
Acceptance	Estimate (SE)	7.42 (0.30)	-0.08 (0.04)	0.002 (0.001)		0.52	43/301
	CI (95%)	6.48–8.00	-0.15–-0.01	0.0002–0.004			
	P	<0.001	0.020	0.028			
Positive reappraisal	Estimate (SE)	1.88 (0.04)	-0.02 (0.004)	0.0005 (0.0001)		0.70	43/301
	CI (95%)	1.79–1.96	-0.03–-0.01	0.0003–0.001			
	P	<0.001	<0.001	<0.001			
Positive refocus	Estimate (SE)	1.78 (0.04)	0.0003 (0.003)			0.68	43/301
	CI (95%)	1.69–1.87	-0.002–0.003				
	P	<0.001	0.809				
Refocus on planning	Estimate (SE)	1.86 (0.04)	-0.03 (0.004)	0.0004 (0.0001)		0.53	43/301
	CI (95%)	1.79–1.94	-0.03–-0.01	0.0002–0.001			
	P	<0.001	<0.001	<0.001			
Putting into perspective	Estimate (SE)	1.83 (0.05)	0.01 (0.01)	-0.0003 (0.0001)		0.60	43/301
	CI (95%)	1.73–1.92	0.001–0.02	-0.001–-0.0001			
	P	<0.001	0.032	0.013			
Rumination	Estimate (SE)	1.54 (0.04)	-0.01 (0.004)	0.0002 (0.001)		0.57	43/301
	CI (95%)	1.46–1.62	-0.02–-0.001	0.00002–0.0005			
	P	<0.001	0.039	0.030			
Self-blame	Estimate (SE)	1.19 (0.03)	-0.001 (0.001)			0.62	43/301
	CI (95%)	1.14–1.25	-0.002–-0.0004				
	P	<0.001	0.171				
Other-blame	Estimate (SE)	1.38 (0.04)	0.002 (0.001)			0.54	43/301
	CI (95%)	1.30–1.46	-0.0001–0.004				
	P	<0.001	0.066				
Catastrophizing	Estimate (SE)	1.27 (0.03)	-0.001 (0.001)			0.54	43/301
	CI (95%)	1.21–1.34	-0.003–0.001				
	P	<0.001	0.388				

Notes: SE: standard error, CI: confidence interval, ICC: intraclass correlation coefficient; N: number of participants/ observations, P-values are estimated employing Satterthwaite approximation; significant effects are indicated in bold.

regulatory brain structure assessed before the pandemic and anxiety (model 1) or depression (model 2) at W2. In step 1, rumination was identified as the strategy explaining most variance at W2 in anxiety and depression through multiple regression analyses. Next in step 2, the association of a priori-defined emotion regulatory brain structures and rumination revealed that only CT in the right lPFC (rlPFC_{CT}) remained a significant predictor of W2-rumination ($\beta = 0.540$, $t(37) = 3.221$, $P = 0.003$), explaining 20.7% of the variance within the model ($F(5,37) = 2.628$, $P = 0.039$, $R^2 = 0.262$).

Model 1 included rlPFC_{CT} as the predictor, W2-anxiety as the outcome and W2-rumination as the mediator (Figure 6A). rlPFC_{CT} was a significant positive predictor of W2-rumination ($b = 5.893$, $t(37) = 3.221$, $P = 0.003$, $R^2 = 0.262$). W2-rumination was also a significant predictor of W2-anxiety ($b = 3.349$, $t(36) = 3.958$, $P < 0.001$) and a significant mediator of the effect of rlPFC_{CT} on W2-anxiety ($b = 19.735$, $SE = 10.740$, 95% confidence interval (95% CI) [3.407, 44.950]). The direct effect of rlPFC_{CT} was not significant ($b = 20.811$, $SE = 10.655$, 95% CI [-0.798, 42.420]), thus a full mediation was observed. The full model explained

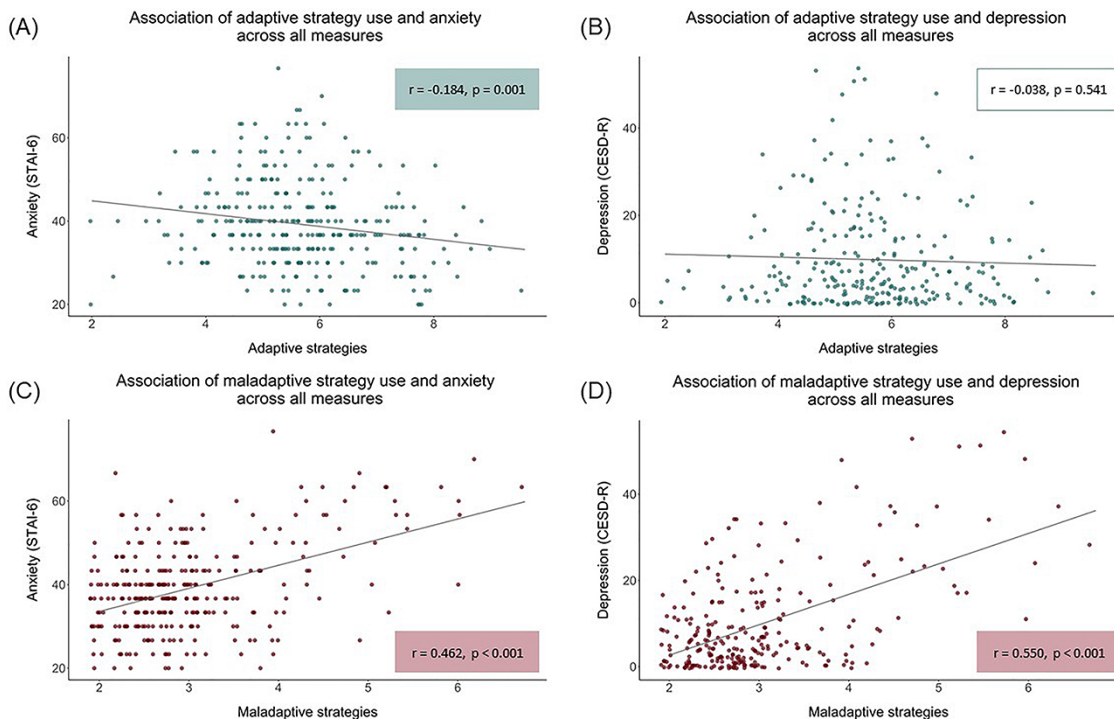


Fig. 5. Association between adaptive (A and B) or maladaptive (C and D) emotion regulation strategy use and mental well-being as represented by any answers given across the seven measurement time points by all individuals (total answer independent of person or testing point). Correlational displays indicate (A) a negative association between the use of adaptive strategies and anxiety levels; (B) no significant association between the use of adaptive strategies and depression levels; (C) a positive association between the use of maladaptive strategies and anxiety levels and (D) positive relations between the use of maladaptive strategies and depression levels. The lowest employment of adaptive and maladaptive emotion regulation strategies is 2, while the highest possible use is 10.

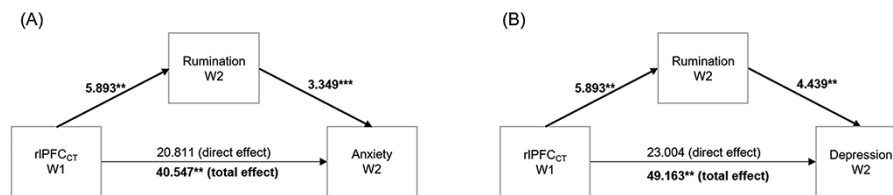


Fig. 6. Mediation models investigating the relationship between rIPFC_{CT} at W1 and mental well-being scores at W2. (A) Rumination at W2 mediates the relationship between rIPFC_{CT} at W1 and anxiety scores at W2 ($b = 19.735$, $SE = 10.740$, 95% CI [3.407, 44.950]); (B) rumination at W2 mediates the association between rIPFC_{CT} at W1 and depression levels at W2 ($b = 26.158$, $SE = 15.226$, 95% CI [3.530, 61.553]). Significant mediations are depicted as bold paths; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

53.72% of W2-anxiety score variations ($F(6,36) = 6.965$, $P < 0.001$, $R^2 = 0.537$).

Model 2 including depression as outcome (Figure 6B) revealed a significant positive prediction of rIPFC_{CT} on W2-rumination ($b = 5.893$, $t(37) = 3.221$, $P = 0.003$, $R^2 = 0.262$); however, it was not a direct predictor of W2-depression levels ($b = 23.004$, $SE = 14.655$, 95% CI [-6.718, 52.727]). Rumination was positively associated with depression ($b = 4.439$, $t(36) = 3.814$, $P = 0.001$) via the indirect path and significantly mediated the effect of rIPFC_{CT} on W2-depression ($b = 26.158$, $SE = 15.227$, 95% CI [3.530, 61.553]). The full model explained 46.43% of variance in W2-depression scores ($F(6,36) = 5.201$, $P = 0.001$, $R^2 = 0.464$).

Brain structure and late emotion regulation strategy use and mental well-being

Self-blame was the emotion regulation strategy explaining the highest degree of variance in anxiety and depression at W3 (step 1). rIPFC_{CT} was entered as a predictor. W3-anxiety

or W3-depression was the outcome variable in the two models, while W2-anxiety or W2-depression was included as a first mediator, and W3-self-blame as a second mediator. Double mediation for W3-anxiety (Figure 7A) revealed that rIPFC_{CT} was a significant positive predictor of W2-anxiety ($b = 40.547$, $t(37) = 3.644$, $P = 0.001$, $R^2 = 0.336$), not for W3-self-blame ($b = -0.088$, $t(36) = -0.060$, $P = 0.952$). W2-anxiety was a significant predictor for W3-self-blame ($b = 0.047$, $t(36) = 4.610$, $P < 0.001$) and W3-anxiety ($b = 0.647$, $t(35) = 3.192$, $P = 0.003$). W3-self-blame did not predict W3-anxiety ($b = 2.043$, $t(35) = 0.785$, $P = 0.438$). Without consideration of mediators, the effect of rIPFC_{CT} on W3-anxiety was significant ($b = 35.821$, $t(37) = 2.654$, $P = 0.012$). This effect was reduced in the full model, rendering the direct effect non-significant ($b = 5.778$, $t(35) = 0.456$, $P = 0.651$). W2-anxiety was a mediator in the relationship between rIPFC_{CT} and W3-anxiety ($b = 26.215$, $SE = 11.651$, 95% CI [8.400, 54.076]). Mediations between rIPFC_{CT} and W3-anxiety through W2-anxiety and W3-self-blame or through W3-self-blame only were not significant ($b = 3.927$, $SE = 9.010$, 95% CI [-14.202, 22.257];

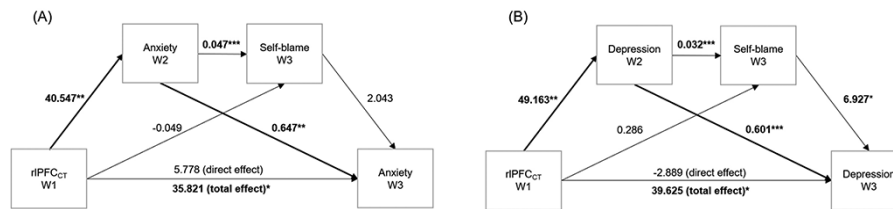


Fig. 7. Mediation models investigating the relationship between rIPFC_{CT} at W1 and mental well-being scores at W3. (A) Anxiety at W2 mediates the effect of rIPFC_{CT} at W1 on anxiety scores at W3 ($b = 26.215$, $SE = 11.651$, 95% CI [8.400, 54.076]). (B) Depression scores at W2 mediate the association between rIPFC_{CT} at W1 and depression at W3 ($b = 29.535$, $SE = 13.171$, 95% CI [6.407, 58.503]). Significant mediations are depicted as bold paths; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

$b = -0.100$, $SE = 3.296$, 95% CI [-6.606, 7.405]). The full model explained 55.40% of the variance in W3-anxiety ($F(7,35) = 6.211$, $P < 0.001$, $R^2 = 0.554$).

The double mediation of W3-depression (Figure 7B) revealed that rIPFC_{CT} positively predicted W2-depression ($b = 49.163$, $t(37) = 3.248$, $P = 0.003$, $R^2 = 0.248$); however, it did not directly predict W3-self-blame ($b = 0.286$, $t(36) = 0.348$, $P = 0.730$) nor W3-depression ($b = -2.889$, $t(35) = -0.217$, $P = 0.829$). The total effect of rIPFC_{CT} on W3-depression was significant ($b = 39.625$, $t(37) = 2.251$, $P = 0.030$), but not the full indirect path via W2-depression and W3-self-blame ($b = 10.997$, $SE = 8.982$, 95% CI [-4.518, 31.215]). Furthermore, W2-depression was a significant positive predictor of the W3-self-blame ($b = 0.032$, $t(36) = 4.103$, $P < 0.001$) and W3-depression ($b = 0.601$, $t(35) = 3.902$, $P < 0.001$). The relationship between W3-self-blame and W3-depression was significant ($b = 6.927$, $t(35) = 2.574$, $P = 0.015$); however W3-self-blame did not mediate rIPFC_{CT} effects on W3-depression ($b = 1.982$, $SE = 6.863$, 95% CI [-8.074, 19.704]). The relationship between rIPFC_{CT} and W3-depression was significantly mediated by W2-depression ($b = 29.535$, $SE = 13.171$, 95% CI [6.407, 58.503]). The full model explained 68.86% of variance in W3-depression scores ($F(7,35) = 11.056$, $P < 0.001$, $R^2 = 0.689$).

All data extracted for the relevant brain structures are provided in Supplementary Table 2.4. We further provide data from a child group that was part of the larger study (Borbás et al., 2021). This data set was too small for the here employed models but is provided in the Supplementary Children's Data section to further possible future pooled data analytic approaches.

Discussion

During the first year after COVID-19 onset, anxiety and depression levels varied significantly with different peaks during the assessment period. We demonstrate that adaptive strategies are more frequently employed when dealing with emotions; maladaptive strategies, however, explain most of the variance in negative mental health outcomes during the first year of the pandemic. Overall, the use of adaptive strategies was associated with reduced anxiety, but not depression, while maladaptive strategies were associated with elevated levels of both. The employment of rumination, acceptance, positive reappraisal, refocus on planning, and putting into perspective varied throughout the first year after COVID-19 onset. Rumination mediated the association between CT in right lPFC assessed prior to the start of the pandemic and mental health in the first months after COVID-19 onset. Mental well-being at the end of 2020 was, however, more strongly mediated by early correlates of mental well-being during the pandemic.

Mental well-being during the first pandemic year

Anxiety was highest after the onset of COVID-19 in Switzerland, was decreasing throughout the first months, but increased again significantly toward the end of the year. This trajectory might reflect an alarmed state and uncertainty at first, followed by an adaptation effect (Vinkers et al., 2020). However, though varying in intensity the prolonged negative experience may have led to a recurring increase in anxiety toward the end of the first pandemic year. Similarly, depression score initially increased and then decreased with a recurring increase at the end of the first pandemic year. At the start of the pandemic, 34.88%/20.93% of all participants reported clinically significant levels of anxiety or depression, respectively, and 48.84%/20.93% at the end of the pandemic year. Notably, prior research independent of the pandemic has noted seasonal effects for depressive symptoms in the general population (Oyane et al., 2008). Consequently, the significant increase in anxiety and depression scores observed here toward the end of the year may have similarly been influenced by factors other than those associated with the pandemic. Anxiety and depression scores in our participants during the first months after COVID-19 onset are comparable to larger-scale investigations (de Quervain et al., 2020a; González-Sanguino et al., 2021; Loosen et al., 2021; Pieh et al., 2021; Robinson and Daly, 2021; Salfi et al., 2021). Moreover, although the current study did not assess anxiety and depression prior to COVID-19, heightened scores have been observed worldwide in reports assessing mental health prior to and after COVID-19 onset retrospectively and prospectively (Ettman et al., 2020; de Quervain et al., 2020b). Contrary to our reports, some longitudinal studies reported a decline or stagnation for symptoms of anxiety and depression toward the end of the first pandemic year (Loosen et al., 2021; Pieh et al., 2021; Salfi et al., 2021). Such differences may be due to assessment timeframe, local restrictions, population studied or questionnaires used.

Emotion regulation strategy use and mental well-being

Over the course of the first pandemic year, the use of some emotion regulation strategies remained relatively constant, while the employment of others varied. Significant variations over time were observed for various adaptive emotion regulation strategies (i.e. acceptance, positive reappraisal, refocus on planning, and putting into perspective) and one maladaptive strategy (i.e. rumination). A higher variability in the use of adaptive strategies depending on situational context has been previously reported in cross-sectional studies (Aldao and Nolen-Hoeksema, 2012). In this context, we further demonstrated that adaptive strategies were employed more often than maladaptive ones; however, variations

in maladaptive strategy use were most strongly linked to worse mental well-being.

Some cognitive emotion regulation strategies were identified as significant predictors of mental health. Positive reappraisal had a buffering effect, while rumination aggravated symptoms of anxiety and depression during the early phase. Reassigning positive meaning to challenging events (positive reappraisal) has previously been reported to precede higher well-being (Garnefski and Kraaij, 2006; Haga et al., 2012; Nowlan et al., 2015) and is recognized in different treatment programs (Beck, 2005; Gratz et al., 2015). Anxiety levels at the end of 2020 were predicted by self-blame only, while depression scores were predicted by self-blame, rumination, and refocus on planning. Interestingly, increased use of all three strategies, including refocus on planning, which is usually considered an adaptive strategy, preceded higher depression scores. This is in line with prior research indicating that the effectiveness of specific adaptive strategies may depend on context, including length and nature of the stressful situation experienced (McRae, 2016; Kobylińska and Kusev, 2019). It has been suggested that in situations with low controllability, problem-focused strategies used to solve an adverse situation might not be adaptive (Lazarus, 1993). Contrariwise, the use of emotion-focused strategies that aim at changing the emotional state experienced is advised (Troy et al., 2013; Haines et al., 2016). It may thus be hypothesized that the problem-focused strategy of refocus on planning is less adaptive, because minimal control of pandemic circumstances exists. Our data indicate that across the whole group, the use of refocus on planning as an emotion regulation strategy was highest shortly after pandemic onset but less common toward the end of 2020. This might indicate that the negative effects of refocus on planning on mental health observed at the end of the first pandemic year were driven by a few individuals unable to adapt.

Mediating effects of brain structure and emotion regulation strategy use

Structural brain characteristics assessed prior to pandemic onset were hypothesized to be linked to emotion regulation strategy use consequently mediating levels of anxiety or depression. Bilateral LPFC (GMV or thickness) and amygdala (GMV) were considered; however, only right LPFC thickness remained a significant predictor. CT predicted psychological well-being by mediation through rumination at the start and through prior mental well-being at the end of the first pandemic year. LPFC is commonly implicated in cognitive control processes, including emotion regulation (Ochsner et al., 2012; Kohn et al., 2014; Raschle et al., 2019), and altered in clinical disorders, including anxiety or depression (Brühl et al., 2014). While supported by functional (Goldin et al., 2008; Ochsner et al., 2012; Kohn et al., 2014; Raschle et al., 2019) and structural neuroimaging evidence (Kühn et al., 2011; Vijayakumar et al., 2014; Ferschmann et al., 2021), the precise direction of findings remains under investigation, and differences in reports may be due to age or group characteristics studied. Greater LPFC cortical thinning was reported during adolescence paralleling an increased use of reappraisal (Vijayakumar et al., 2014; Ferschmann et al., 2021). Furthermore, the choice of emotion regulation strategy studied might impact outcome (Kühn et al., 2011). Our findings associating higher right LPFC thickness and maladaptive strategy use with worse mental health outcomes are in line with meta-analytic evidence investigating rumination and PFC volume in healthy participants (Kühn et al., 2012).

In the present analyses, rumination mediated the relationship between LPFC thickness and anxiety and depression levels in the early phase of the pandemic. The involvement of LPFC functioning in depression (Galynker et al., 1998; Koenigs and Grafman, 2009) and anxiety (Ball et al., 2013) has previously been reported, and prolonged depressive episodes and heightened anxiety have been associated with frequent use of rumination (Harrington and Blankenship, 2002; Sarin et al., 2005).

Double mediation models revealed a positive indirect link between right LPFC thickness and mental well-being at the end of 2020 via mental well-being assessed during the first months after pandemic onset. There was no direct association between CT assessed prior to COVID-19 onset and scores of anxiety or depression at the end of 2020. Additionally, early markers of well-being, as assessed during the first months after pandemic onset in Switzerland, predicted well-being at the end of the year better than individual predispositions (i.e. brain structure) or momentary emotion regulation strategy use. This is in line with Shanahan et al. (2020) reporting that emotional distress during the pandemic is best predicted by emotional distress prior to COVID-19. Furthermore, Brehl et al. (2021) demonstrated that anxiety scores during the pandemic were best predicted by a combination of pre-pandemic trait anxiety and maladaptive strategy use.

Limitations

Despite an extensive within-person data collection, the present findings should be interpreted with caution given the relatively small number of participants. Especially in mediation models, small sample sizes are associated with low power and the possibility for exceeding the recommended 5% for Type I error rate (Koopman et al., 2015; Liu and Wang, 2019). To reduce the conducted tests, an average score over six assessment points within W2 was used for the multiple regression and mediation models. Although we report varying effects of emotion regulation strategies on mental health depending on context, larger longitudinal studies are needed to inform about finer-grained time-dependent contextual changes.

Pre-pandemic clinical assessments were not available for all participants, therefore not allowing us to report on changes in anxiety and depression levels or to consider pre-pandemic health in the mediation models. Also, current analyses included education information (ISCED) as a proxy for IQ and Socioeconomic status as a covariate. Notably, IQ would be a superior choice in future analyses as it is a more stable indicator of cognitive abilities across the lifespan than education. Furthermore, since the global pandemic was experienced by all, no control group is available to deduce to which extent fluctuations in mental health were the consequence of COVID-19 and related restrictions. Additionally, the population studied includes a higher number of female participants. Females and males may be affected differently by stress associated with COVID-19 (Kwong et al., 2020), and the current group did not allow a balanced investigation or assessment of sex-specific effects.

Future studies may further investigate connectivity measures between cortical and limbic regions supporting emotion regulatory functions and investigate their association to successful emotion regulation abilities and mental health to enhance our understanding of the precise mechanisms impacting well-being. Lastly, data acquisition and analysis were not pre-registered due to the rapid response to capture and inform about the early effects of the pandemic-related circumstances.

Conclusions

The experience of prolonged negative life events such as a global pandemic can have a negative effect on mental health. Overall, the use of adaptive emotion regulation strategies was positively associated with mental well-being, while maladaptive strategies were negative for participants' mental health. While first evidence for contextual considerations were identified (e.g. varying effects of certain strategies across time), further research is needed. Our findings underline the potential of interventions minimizing maladaptive emotion regulation use in response to negative life events. Our results suggest that prefrontal CT assessed prior to the pandemic and emotion regulation strategies used after COVID-19 onset influence mental well-being during the pandemic. Due to substantial personal and societal costs associated with mental health disorders, such as anxiety and depression, an early identification of risk factors for the development and biological and psychological markers for treatment response are of great importance.

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Conflict of interest

The authors declared that they had no conflict of interest with respect to their authorship or the publication of this article.

Supplementary data

Supplementary data is available at SCAN online.

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