Preventive Medicine Reports 37 (2024) 102559

Contents lists available at ScienceDirect

Preventive Medicine Reports

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

Connecting psychosocial and personality characteristics with mental health outcomes. An Italian co-twin control study

Corrado Fagnani [a], Antonella Gigantesco [a], Gianmarco Giacomini [a,b], Emanuela Medda [a,*]

[a] Centre of Reference for Behavioural Sciences and Mental Health, Istituto Superiore di Sanità, Viale Regina Elena, 299, Rome 00161, Italy
[b] Department of Public Health Sciences and Pediatrics, University of Turin, via Santena 5 bis, 10126 Turin, Italy

ARTICLE INFO

Keywords:
Anxiety
Depression
Stress
Mental health
COVID-19
Twin

ABSTRACT

Exposure to stressful life events is common, and it is linked to increased psychological issues. As most likely people respond to stressors depending on environmental and genetic factors, we assessed in a twin study the association of some personal characteristics such as resilience and self-perception with anxiety, depression and stress in the late Covid pandemic period, to verify the underlying genetic and shared familial components. With this design, the strength of the associations was compared between individual-level and intrapair-level analyses. From June 2020 to December 2021, the Italian Twin Registry conducted a three-wave longitudinal study among adult twins using validated questionnaires, and 1,763 adult twins participated in the study (mean age 46 years, 67 % females, 70 % monozygotic). A regression-based within-pair differences model was applied to control for genetic and shared environmental confounding. Results showed that anxiety was linked negatively with resilience, social support and perceived health, and positively with risk perception and hypochondria. Depression was associated negatively with resilience, social support and perceived health, and positively with financial concern and hypochondria. Stress was associated negatively with resilience and perceived health, and positively with financial concern, risk perception and hypochondria.

These results suggest potential etiological effects of the above-mentioned risk factors. While our findings need to be confirmed by longitudinal studies, they propose potential etiological models for mental disorders, indicating that addressing in the clinical practice factors such as self-perception, personality traits (resilience), environmental resources (social support), and comorbid disorders (hypochondria) could have therapeutic benefits while treating certain common mental disorders.

1. Introduction

Exposure to stressful life events is common, and it is linked to an increase in mental health issues, such as anxiety, perceived stress and depression (Jacoby et al., 2021). The study of connection between stressful life events and worst mental health has gained relevance as our world has faced the common COVID-19 stressor. People respond to stressors in different ways: while someone could experience severe psychiatric symptoms, others may remain asymptomatic (Jacoby et al., 2021). Factors influencing adaptation to adversities include environmental conditions, past experiences, personal resources, gender, and culture (Jacoby et al., 2021). Some factors, as explained below, are known from previous literature to be associated with anxiety, perceived stress and depression expression, but there is still very limited understanding of the role of genetic and environmental factors in explaining those associations.

Resilience, defined as an individual's ability to overcome stress while maintaining psychophysical functioning, plays a major role in stress response (Sheerin et al., 2018). It has been shown, in prior studies, to be protective against stressful exposures such as widowhood (King, 2019) and adults' reactivity to adverse events such as onset of new chronic illness (Manning et al., 2016). Also, in the COVID-19 era, an important role has been attributed to resilience in contrasting the worsening of people's mental health (Zhang et al., 2020). It should be noted, however, that a recent longitudinal study has evidenced that resilience had no influence on both subjective and biological stress markers during the first wave of the Covid-19 pandemic (Engert et al., 2021). Perceived social support is known to protect against depressive and anxiety symptoms, as well as suicidal ideation and attempts, even in individuals who experienced mental health problems (Scardera et al., 2020).

* Corresponding author at: Centre for Behavioural Sciences and Mental Health, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy.
E-mail address: emanuela.medda@iss.it (E. Medda).

https://doi.org/10.1016/j.pmedr.2023.102559
Received 18 July 2023; Received in revised form 11 December 2023; Accepted 12 December 2023
Available online 14 December 2023
2211-3355/© 2023 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Economic conditions and physical health are also pivotal and influence subjective well-being and life satisfaction, which are the key components of positive mental health (Diener et al., 2009). Consistently, some studies have documented that individuals who reported moderate or poor health condition had significantly higher odds ratios for anxiety or depression than those who reported good health condition (Tran et al., 2017; Ibrahim et al., 2013). Low socioeconomic status has been also established as a risk factor for poor mental health (Lorant et al., 2003; Marmot et al., 1991). Finally, increased health risk perception and health anxiety were found to be associated with poorer stress management and poor mental health (Mousavi et al., 2021; Fitzpatrick et al., 2020; Lee et al., 2020; Montano and Acebes, 2020).

On the basis of the above-mentioned studies, one may speculate that specific psychosocial factors could causally influence mental health outcomes. However, the analysis of the relationship between those factors and mental health problems can be influenced by familial confounders. Using genetically informative data from twins allows for optimal control of confounding effects. Some previous twin studies further supported the association between financial problems and increased risk of depression (Kendler et al., 2010; Kendler & Gardner, 2014; Kendler and Halberstadt, 2013; Lam et al., 2019). A prospective population-based twin cohort study has revealed that poor or moderate self-rated health was an independent predictor of mental disorders after accounting for genetic and familial confounders (Samuelsson et al., 2013). While accounting for genetic and environmental factors, two twin studies provide mixed evidence for the association between social support and mental health problems. One study has shown that the levels of social support from the co-twin, other relatives, parents, and the spouse were strongly associated with the risk for depression (Kendler, 2005), while a subsequent discordant monozygotic twin study has showed that the effect of perceived social support was neither a significant antecedent to, nor sequela of depression (Coventry et al., 2009).

In the present study, we contributed to the limited existing work by analyzing data from a twin dataset, using indicators (for the most part validated questionnaires and scales) of psychological resilience, social support, self-perception of physical health condition, financial status and subjective perception of risk to acquire SARS-CoV-2 infection, and validated measures of anxiety, depression and stress. We suppose that there are not strong pleiotropic effects between those indicators and mental health outcomes, indicative of shared genetic susceptibility between them. In partial consistence with previous limited research, we expect, when controlling for genetic and environmental shared factors between those constructs, to find significant unshared possible direct causal effects of those psychosocial factors on anxiety, depression and stress outcomes.

2. Materials and methods

2.1. Study design and participants

At the end of the Italian lockdown, the Italian Twin Register (ITR, Medda et al., 2019) started a longitudinal study to investigate prospectively the effect of the Covid-19 pandemic on the general population, and conducted three online surveys in June 2020, December 2020 and December 2021. About 7000 adult twins (age 18–92 years) previously enrolled in the ITR, residing in Italy at the time of the pandemic, and contactable by email were selected and invited to participate in the survey. Each selected twin received a personal link via email to be able to take part in the study, and once used, the access to the platform was blocked to avoid duplication or fraudulent use. A reminder was sent to those who did not respond within a 3-week period.

A total of 2,164 adult twins joined the survey, resulting in a response rate of 31%. This rate is in line with other studies conducted by the ITR; however, to exclude major selection biases, the main socio-demographic characteristics were compared between participants and non-participants.

All the twins filled-out the Italian versions of the questionnaires online through the LimeSurvey platform (LimeSurvey GmbH).

This research was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the Ethical Committee of the Istituto Superiore di Sanità (ISS Ethical Committee approval PRE BIO CE n.0020797, June 6, 2020).

Before filling out the online questionnaire, all the twins were invited to read the information note and sign the informed consent form. The request for consent was also reiterated at the end of the questionnaire completion. The ITR systematically stimulates the participation of twins by emphasizing the importance of their contribution to public health, and sometimes at the end of the study, the twin's willingness is acknowledged and rewarded with a small and low-value gadget (as in this study) or with the return of health-relevant information.

2.2. Measurements

The online survey included the following validated self-reported questionnaires:

1) Patient Health Questionnaire (PHQ-9), a 9-item psychological screening test for depression in the previous two weeks. The score ranges from 0 to 27 (Kroenke et al., 2001). The Italian validated translation of the PHQ-9 showed to possess good psychometric properties (Mazzotti et al., 2003).

2) State-Trait Anxiety Inventory (STAI-6), a 6-item questionnaire measuring symptoms of anxiety. The score ranges from 20 to 80 (Marteau & Bekker, 1992). It derives from the original full form of the STAI-Y (Spielberger, 1983). The Italian version of the STAI-Y shows high internal consistency (alpha Cronbach = 0.91) and good test–retest reliability (Spearman correlation = 0.49; $p < 0.01$) (Pedrabissi and Santinello, 1989).

3) Impact of Event Scale - Revised (IES-R), a 22-item questionnaire assessing subjective distress in the previous seven days. The score ranges from 0 to 88 (Weiss & Marmar, 1997). The Italian translation of the IES-R showed satisfactory internal consistency in studies on different at-risk populations, as reported by Craparo et al. (2013) (Intrusion, $\alpha = 0.78$; Avoidance, $\alpha = 0.72$; Hyperarousal, $\alpha = 0.83$) and Converso & Viotti (2014) (Intrusion, $\alpha = 0.91$; Avoidance, $\alpha = 0.81$; Hyperarousal, $\alpha = 0.87$).

4) Dispositional Resilience Scale (DRS-15), a 15-item instrument measuring subject's resilience or hardiness, with a 0–45 score range (Bartone, 2007). A relatively recent study provided evidence of both validity and reliability for the Italian version of the DRS-15 (Picardi et al., 2012).

5) Health Anxiety Questionnaire (HAQ), a 21-item questionnaire to identify individuals with high levels of concern about their health. Total score ranges from 21 to 84 (Lucock & Morley, 1996). The Italian version of the HAQ demonstrated excellent internal consistency (alpha = 0.91) and a good stability over time ($r = 0.89$); the factor analysis highlighted the presence of four main dimensions, which together account for 58.4% of the total variance: fear of death and diseases, interference with daily activities, worries about health condition, and need for reassurance (Melli et al., 2007).

6) Level of financial concern was measured using four questions (1. *My or my family's financial situation will get much worse over the next 12 months*; 2. *I am worried about my or my family's financial situation over the next 12 months*; 3. *I am worried about providing for myself financially over the next 12 months*; 4. *I have enough means to secure food and housing for myself or my family over the next 12 months*). Participants rated their agreement with each of the four questions on a six-point Likert scale. A total score ranging from 4 to 24 was obtained by summing responses across the four questions.

7) Multidimensional scale of perceived social support (MSPSS), a 12-item questionnaire to measure perceived social support from others. Total score ranges from 12 to 84 (Zimet, 1988). The Italian version of the instrument has good psychometric properties (Grassi et al., 2000) and

Table 1
Descriptive statistics of levels of anxiety, depression and stress in adult twins at Wave 1 (Italy, June 2020), Wave 2 (Italy, December 2020) and Wave 3 (Italy, December 2021) in the first and fourth quartiles for each risk factor.

	Resilience - Lower 25th percentile			Resilience - Upper 75th percentile		
	N	Mean	SD	N	Mean	SD
Anxiety – Wave1	353	43.692	11.507	244	37.454	10.643
Anxiety – Wave2	352	48.483	12.814	247	39.341	11.309
Anxiety – Wave3	364	48.797	11.717	258	38.204	10.191
Depression – Wave1	360	6.303	4.909	249	3.098	3.482
Depression – Wave2	350	6.764	5.044	249	3.075	3.400
Depression – Wave3	363	6.867	5.226	256	2.441	2.468
Stress – Wave1	359	17.484	11.556	247	12.793	10.583
Stress – Wave2	350	21.495	13.548	249	15.755	13.420
Stress – Wave3	366	20.251	14.099	258	14.641	12.464
	Risk Perception - Lower 25th percentile			Risk Perception - Upper 75th percentile		
	N	SD	Mean	N	Mean	SD
Anxiety – Wave1	428	38.886	10.809	177	42.927	11.567
Anxiety – Wave2	432	41.347	11.560	183	49.505	13.270
Anxiety – Wave3	434	40.848	10.987	186	48.208	11.906
Depression – Wave1	434	4.042	3.893	181	5.024	4.153
Depression – Wave2	431	4.484	4.364	183	6.048	5.030
Depression – Wave3	433	4.206	4.187	187	5.742	4.894
Stress – Wave1	433	12.443	10.133	179	18.724	11.876
Stress – Wave2	432	16.090	12.605	184	25.242	14.504
Stress – Wave3	434	14.141	12.038	188	25.667	15.289
	Social Support - Lower 25th percentile			Social Support - Upper 75th percentile		
	N	Mean	SD	N	Mean	SD
Anxiety – Wave1	328	44.411	12.097	281	38.195	10.989
Anxiety – Wave2	328	47.728	12.936	283	41.060	11.799
Anxiety – Wave3	340	47.741	12.375	291	40.751	11.562
Depression – Wave1	336	6.026	5.005	284	3.695	3.576
Depression – Wave2	329	6.680	5.133	284	3.654	3.650
Depression – Wave3	339	6.613	5.520	290	3.148	3.203
Stress – Wave1	334	17.126	12.107	283	13.699	10.996
Stress – Wave2	328	22.186	14.283	286	17.659	13.486
Stress – Wave3	342	21.453	15.443	292	15.403	13.177
	Health anxiety - Lower 25th percentile			Health anxiety - Upper 75th percentile		
	N	Mean	SD	N	Mean	SD
Anxiety – Wave1	374	37.018	10.226	272	45.887	12.516
Anxiety – Wave2	382	39.127	10.885	284	52.556	13.224
Anxiety – Wave3	366	39.778	10.461	269	48.947	13.044
Depression – Wave1	377	3.235	3.364	280	6.809	5.098
Depression – Wave2	385	3.290	3.604	284	7.902	5.078
Depression – Wave3	365	3.385	3.653	269	6.727	4.957
Stress – Wave1	378	10.280	8.778	280	23.278	13.493
Stress – Wave2	384	11.417	9.442	284	32.014	14.528
Stress – Wave3	368	12.782	11.242	271	27.188	15.198
	Financial concern - Lower 25th percentile			Financial concern - Upper 75th percentile		
	N	Mean	SD	N	Mean	SD
Anxiety – Wave1	474	38.203	10.421	229	44.626	12.774
Anxiety – Wave2	481	41.027	11.989	229	49.909	13.126
Anxiety – Wave3	471	40.599	10.876	227	47.421	11.978
Depression – Wave1	481	3.790	3.743	232	6.235	5.059
Depression – Wave2	481	3.768	3.909	232	7.427	5.216
Depression – Wave3	467	3.452	3.592	227	6.502	4.827
Stress – Wave1	481	13.271	10.701	232	18.352	12.198
Stress – Wave2	480	16.073	12.337	232	25.051	15.781
Stress – Wave3	470	14.713	12.289	227	22.483	14.734

Abbreviation: SD, Standard Deviation

has been used in many previous studies (Picardi et al., 2005; Picardi et al., 2013).

8) General self-perceived health was measured by a single question (i.e., *Please choose one point in this 0–10 scale, which can best represent your health today – 0 means the worst and 10 means the best*).

2.3. Statistical methods

Data were analyzed with Stata version 16 (Stata Corporation, College Station, TX, USA).

To obtain a higher sample homogeneity, only monozygotic (MZ) and same-sex dizygotic (DZ-SS) twin pairs participating in the third wave of the survey were included in the analyses.

The cumulative exposure distribution of risk factors – i.e., resilience, social support, financial concern, risk perception and hypochondria – was divided into quartiles. Means (standard deviations) of outcome variables – i.e., anxiety, depression and stress – were estimated for subjects in the first and fourth quartiles, and were then compared using

Table 2
Beta coefficients estimated using individual and intra-pair differences regression models by zygosity with respect to anxiety, depression and stress assessed in adult twins (Italy, 2021).

	Individual model Beta coefficient (95 %CI)	Intra-pair model – DZ-SS Beta coefficient (95 %CI)	Intra-pair model - MZ Beta coefficient (95 %CI)
ANXIETY (STAI-6)			
Financial concern	0.697 (0.536; 0.857)	0.384 (−0.206; 0.974)	0.264 (−0.103; 0.631)
Resilience	−0.699 (−0.797; −0.601)	−0.720 (−1.040; −0.401)	−0.747 (−0.983; −0.511)
Social Support	−0.245 (−0.295; −0.195)	−0.238 (−0.407; −0.070)	−0.177 (−0.281; −0.072)
Risk Perception	1.402 (1.108; 1.696)	1.348 (0.166; 2.529)	0.691 (0.052; 1.330)
Self-perceived health	−3.695 (−4.163; −3.226)	−2.613 (−3.904; −1.323)	−2.808 (−3.804; −1.811)
Health anxiety	0.379 (0.310; 0.450)	0.486 (0.254; 0.719)	0.288 (0.119; 0.458)
DEPRESSION (PHQ-9)			
Financial concern	0.313 (0.253; 0.374)	0.212 (−0.005; 0.429)	0.174 (0.041; 0.307)
Resilience	−0.308 (−0.348; −0.269)	−0.236 (−0.352; −0.120)	−0.316 (−0.400; −0.232)
Social Support	−0.127 (-0.147; −0.107)	−0.151 (-0.207; −0.095)	−0.072 (−0.110; −0.033)
Risk Perception	0.411 (0.284; 0.539)	0.558 (0.145; 0.971)	0.171 (−0.060; 0.403)
Self-perceived health	−1.581 (−1.763; −1.398)	−1.243 (−1.690; −0.799)	−1.172 (−1.525; −0.820)
Health anxiety	0.154 (0.126; 0.182)	0.147 (0.060; 0.234)	0.152 (0.093; 0.212)
STRESS (IES-R)			
Financial concern	0.804 (0.620; 0.988)	0.352 (−0.286; 0.989)	0.593 (0.199; 0.986)
Resilience	−0.496 (−0.620; −0.371)	−0.241 (-0.631; 0.149)	−0.337 (−0.610; −0.063)
Social Support	−0.181 (−0.244; −0.119)	−0.087 (−0.279; 0.106)	−0.001 (−0.119; 0.117)
Risk Perception	2.086 (1.691; 2.481)	2.555 (1.305; 3.805)	1.115 (0.394; 1.836)
Self-perceived health	−3.077 (−3.671; −2.483)	−1.645 (−3.069; −0.220)	−1.254 (−2.375; −0.132)
Health anxiety	0.578 (0.498; 0.658)	0.602 (0.363; 0.841)	0.333 (0.152; 0.513)

Statistically significant coefficients are indicated in bold ($p < 0.05$).
Abbreviation: 95 %CI, 95 % Confidence intervals; MZ: monozygotic twin pairs; DZ-SS same-sex dizygotic twin pairs.

t-tests.

Initially, a linear regression model based on twins as individual subjects was applied to estimate the association between risk factor variables and mental health outcomes, adjusting for the non-independence of observations within twin pairs. To investigate if the observed associations between risk factors and outcomes persisted after adjustment for genetic and shared (familial) environmental confounding (thus being consistent with possible direct causal effects), the regression-based within-pair differences model was fitted. According to this model, causal evidence was tested in MZ pairs (i.e., perfect genetic and familial matching scenario) by regressing within-pair differences of outcome scores on within-pair differences of risk factor scores, and evaluating both the magnitude and the significance of the association. Furthermore, the intra-pair differences regression model in DZ-SS pairs (i.e., partial genetic and perfect familial matching scenario) and the individual-level regression model (i.e., no matching scenario) were also applied: in the presence of causality, association estimates from all three models should be significant and of similar magnitude (McGue et al., 2010).

3. Results

3.1. Participants and measurements

A total of 1,763 twins, belonging to MZ and DZ-SS pairs, completed the questionnaires. Mean age was 46 years, 33% of subjects were male, and more than half were from Northern Italy. Seventy percent of the subjects were MZ. No significant differences in the main socio-demographic characteristics were found between participants and non-participants, as well as between early and late respondents (i.e., between participants who filled out the questionnaire immediately after receiving the email and those who did it after a reminder). Cronbach's alpha has been calculated as 0.85 for PHQ-9 and STAI-6, 0.90 for IES-R, 0.79 for DRS-15, 0.93 for HAQ, 0.82 for level of financial concern, and 0.93 for MSPSS.

3.2. Associations between risk factors and outcomes

For subjects participating in all three waves of the longitudinal Covid survey, the pattern of variation in outcomes (i.e., anxiety, depression, and stress) according to variation in risk factors was consistent across the waves. For each wave, mean anxiety score was lower for subjects in the upper 75th percentile compared to subjects in the lower 25th percentile of both resilience and social support scores (risk factors); similar patterns emerged for depression and stress. Opposite pattern of variation in outcomes was observed for each wave according to financial concern, risk perception, and hypochondria (risk factors) (Table 1).

According to these patterns, outcome scores (i.e., anxiety, depression, and stress scores) were negatively associated with resilience, social support, and self-perceived health, whereas they were positively associated with financial concern, risk perception, and health anxiety (Table 2, Individual model).

3.3. Adjusted associations between risk factors and outcomes: The within-pair differences analysis

With respect to anxiety, regression models showed a negative (i.e., protective) effect of resilience, social support and perceived health, and a positive effect of risk perception and hypochondria; these effects were detected both at individual level and within MZ and DZ pairs.

As regards depression, a negative effect of resilience, social support and perceived health, and a positive effect of financial concern and hypochondria persisted in within-pair analyses.

As for stress, a negative association with resilience (at individual level and within MZ pairs) and perceived health (in all types of analysis) was found. A positive association with financial concern (at individual level and within MZ pairs), as well as with risk perception and hypochondria (in all types of analysis) emerged from regression models (Table 2).

4. Discussion

4.1. Interpretation of results and comparison with previous studies

Using a co-twin control study, we found that there were significant outcomes differences within twin pairs who were exposed to different levels of resilience, social support, financial condition, perception of one's health status and perception of risk for SARS-CoV-2 infection. This suggested possible causal effects since the magnitude of the exposure effects were controlled for genetic and shared environmental influences.

Significant associations provided evidence that the relationships of

financial concerns with depression and stress were not attributable to genetic and shared environmental confounding. This is in line with previous genetically informative studies that have found increased depression risk associated with financial problems (Kendler et al., 2010; Kendler & Gardner, 2014; Kendler and Halberstadt, 2013; Lam et al., 2019) and suggests that financial hardship is an important risk factor with probable causal influence on depression. With regard to stress, our result corroborates previous findings from non-genetically informative literature, which have demonstrated that financial hardship is typically accompanied by considerable stress (Cole et al., 2011). The observed initial association between financial concerns and risk of anxiety in the full sample vanished in the within-pair analyses, suggesting that the association was probably due to confounding by genetic factors or family environment. To our knowledge, no previous genetically informative studies have implicated financial concerns as risk factor for anxiety, or specifically reported within-twin pair estimates of a probable association.

Dispositional resilience was associated, in a potentially causal way, with anxiety, depression and stress symptoms. As stated before, resilience has been shown, in prior studies, to be protective against stressful exposures (King, 2019; Manning et al., 2016). Resilience has become even more relevant as our world has faced the common COVID-19 stressor. Our findings align with the limited existing literature of longitudinal investigations of the buffering effects of resilience against major depressive disorder and generalized anxiety disorder (Hjemdal et al., 2006; Sheerin et al., 2018). On the other hand, the observed association between resilience and stress is in contrast with the findings of a recent longitudinal study, which evidenced that resilience, irrespective of its conceptualization as a dynamic state or trait, had no influence on both subjective and biological stress markers during the first wave of the Covid-19 pandemic (Engert et al., 2021). However, in that study, some personality traits (e.g., neuroticism and extraversion) were also included in the regression model of analysis. As suggested by the same authors, it is possible that above and beyond the variance explained by those personality traits, resilience made no additional contribution to the pandemic stress load (Engert et al., 2021).

The significant within-pair effects of social support on depression suggested that the association could be of causal origin, consistently with the available genetically informative literature (Kendler et al., 2005) and with recent cohort research suggesting that poor social support and loneliness might underlie anxiety and depression symptoms (Matthews et al., 2022). However, as previously mentioned, this result does not align with a previous discordant monozygotic twin study, which showed that the effects of perceived social support on depression were not causal, although the same study found in males that perceived support in the face of multiple stressors was an antecedent mitigating subsequent depression (Coventry et al., 2009).

The relationship between social support and stress was likely to reflect shared familial and genetic effects, rather than causal effects. Some previous non-genetically informative research showed that personality traits (e.g., extraversion, agreeableness, conscientiousness, and neuroticism) might influence perceived stress because of the tendency to gain perceived or actual social support as resources to cope with stressful situations or not (Bowling et al., 2005; Swickert et al., 2002). This indicates that the experience of stress related to social support may be at least partially attributable to personality factors, whose genetic components were found to make substantial contribution to the genetic variance in perceived stress (Roberts et al., 2009). Therefore, the genetic and shared familial confounding effects that we observed in the association between social support and stress might be partially due to higher-order relations between personality facets and stress, and could attest to the notion of social support as a resource that has much in common with personality traits.

A possibly causal association of health status concerns with depression and anxiety symptoms was also found. Self-rated health has been found to be moderately heritable (Svedberg et al., 2005; Stevens et al., 2020). This shows the importance of accounting for potential familial confounding when studying the associations between self-rated health and mental disorders. Our findings align with the limited existing literature based on prospective population-based twin cohort studies which has revealed that poor or moderate self-rated health is an independent predictor of mental disorders even after accounting for genetic and familial confounders (Samuelsson et al., 2013).

A causal association between perceived risk of getting infected with SARS-CoV-2 and anxiety symptoms and stress appears in consonance with prior observed associations between specific worries and fear relating to the COVID-19 pandemic and increases in anxiety and stress (Fitzpatrick et al., 2020; Lee et al., 2020; Montano and Acebes, 2020).

Hypochondria was possibly causally associated with anxiety, stress and depressive symptoms. While hypochondria is known to overlap with several other psychiatric disorders, it has been proposed as a construct on its own (Scarella et al., 2016). In this regard, our findings demonstrate that individual differences in hypochondria could increase or attenuate the likelihood of reporting anxiety and depressive symptoms during COVID-19 pandemic, and this likelihood reflects personal history of exposure to hypochondria more that genetic/shared familial risk. Consistently, previous non-twin research (Mousavi et al., 2021) mentioned sense of vulnerability to disease and injury and job stress as probable consequences of corona-induced hypochondria.

4.2. Limitations

This study has some limitations. First of all, although the co-twin control design increases control over genetic and shared environmental confounders, it is unable to control for non-shared confounders that only affect one twin, which can bias estimated effects (Kendler & Gardner, 2010). Second, although we observed that the main sociodemographic characteristics did not differ between participants and non-participants, it cannot be ruled out that the low response rate (31%) may have resulted in residual selection bias. Moreover, the cross-sectional nature of the data did not allow us to draw a definitive conclusion about the causal relationship between the examined variables, and therefore our results should be confirmed by longitudinal studies. In particular, it should be noted that, given the considerable comorbidity of hypochondria with other psychiatric disorders, especially anxiety disorders, differentiating hypochondria from these disorders in terms of which disorder is antecedent and which is subsequent is somewhat arbitrary. There are also limitations inherent to the self-report assessment. We did not have measures of mental health that were not self-reported, and it would be important for future studies to include measures that do not rely solely on participant's subjective perception of her/his current mental status. This common method bias, that includes social desirability bias, was partially minimized by participant anonymity. Finally, although our findings are in line with a causal model, we cannot rule out more complex mechanisms underlying the associations. Future studies could test whether the observed effects are influenced by gene-environment correlation and interactions, which were not analyzed here.

5. Conclusions

Our study supported previous findings linking resilience, social support, and self-perceived health to mental health outcomes, and extended these findings by making use of a twin design that minimized the risks of genetic and familial confounding. The present twin investigation suggests potential etiological models for some mental disorders. Factors like self-perception (subjective perception of health status and risk to acquire infections), personality traits (resilience), environmental resources (social support) and comorbid disorders (hypochondria), may prove as compelling as major underlying unshared environmental triggers of common mental disorders and stress.

While our findings require confirmation in longitudinal studies, they

preliminarily suggest that in clinical practice, targeting specific hypochondriac thoughts, health status and social relationships concerns, may have specific therapeutic benefits in the treatment of depression, anxiety and stress. Individuals low in social support, for example, may benefit particularly from group counseling sessions.

From a public health point of view, study findings also highlight the need for calling all the relevant actors to implement training health programs to control anxiety and depression especially in vulnerable populations, such as people experiencing loneliness or who become worried about their health condition for the first time or have a progressive exacerbation of the perception to be at risk, and support them, in times of crisis and/or epidemic with tailored psychosocial interventions aimed at fostering adaptive coping as means of prevention for serious mental health sequelae.

Further, integrated policies should be recommended, which include education, research, and welfare, and engage a wide range of stakeholders within and beyond health in order to promote mental health. For example, school-based mental health promotion programs that optimize self-efficacy, resilience and satisfaction with life, which are fundamental components of positive mental health, could play a role in minimizing the burden that may be caused by stressful life events among young people. The hypothesis is that promoting the emotional strength of an individual, such as self-esteem and resilience, could act as a protective factor, in particular against anxiety and depression. This also concords with cognitive theories that posit negative views of the self, the world, and the future as fundamental aspects characterizing worst mental health.

Funding

No grants were received to accomplish this study.

CRediT authorship contribution statement

Corrado Fagnani: Writing – original draft, Methodology, Formal analysis. **Antonella Gigantesco:** Writing – original draft, Methodology. **Gianmarco Giacomini:** Writing – original draft, Visualization. **Emanuela Medda:** Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

We thank Sabrina Alviti, Cristina D'Ippolito, Maurizio Ferri, and Miriam Salemi for technical support and data collection management of Italian Twin Registry data.

References

Bartone, P.T., 2007. Test-retest reliability of the dispositional resilience scale-15, a brief hardiness scale. Psychol. Rep. 101 (3 Pt 1), 943–944. https://doi.org/10.2466/pr0.101.3.943-944.

Bowling, N.A., Beehr, T.A., Swader, W.M., 2005. Giving and receiving social support at work: the roles of personality and reciprocity. J. Vocat. Behav. 67, 476–489. https://doi.org/10.1016/j.jvb.2004.08.004.

Cole, J., Logan, T.K., Walker, R., 2011. Social exclusion, personal control, self-regulation, and stress among substance abuse treatment clients. Drug Alcohol Depend. 113 (1), 13–20. https://doi.org/10.1016/j.drugalcdep.2010.06.018.

Converso, D., Viotti, S., 2014. La reazione post-traumatica tra bancari vittime di rapina sul luogo di lavoro: Il ruolo dei fattori pre-trauma e peri-trauma. Med. Lav. 105, 243–254.

Coventry, W.L., Medland, S.E., Wray, N.R., Thorsteinsson, E.B., Heath, A.C., Byrne, B., 2009. Phenotypic and discordant-monozygotic analyses of stress and perceived social support as antecedents to or sequelae of risk for depression. Twin Res. Hum. Genet. 12 (5), 469–488. https://doi.org/10.1375/twin.12.5.469.

Craparo, G., Faraci, P., Rotondo, G., Gori, A., 2013. The impact of event scale–revised: psychometric properties of the italian version in a sample of flood victims. Neuropsychiatr. Dis. Treat. 9, 1427. https://doi.org/10.2147/NDT.S51793.

Diener, E., Oishi, S., Lucas, R.E., 2009. Oxford handbook of positive psychology, (2nd ed.). 187–194 (Oxford University Press, US.

Engert, V., Blasberg, J.U., Köhne, S., Strauss, B., Rosendahl, J., 2021. Resilience and personality as predictors of the biological stress load during the first wave of the Covid-19 pandemic in Germany. Translational Psychiatry 11 (1). https://doi.org/10.1038/s41398-021-01569-3.

Fitzpatrick, K.M., Harris, C., Drawve, G., 2020. Fear of COVID-19 and the mental health consequences in America. Psychol. Trauma 12 (S1), S17–S21. https://doi.org/10.1037/tra0000924.

Grassi, L., Rasconi, G., Pedriali, A., Corridoni, A., Bevilacqua, M., 2000. Social support and psychological distress in primary care attenders. Psychother. Psychosom. 69 (2), 95–100. https://doi.org/10.1159/000012372.

Hjemdal, O., Friborg, O., Stiles, T.C., Rosenvinge, J.H., Martinussen, M., 2006. Resilience predicting psychiatric symptoms: a prospective study of protective factors and their role in adjustment to stressful life. Clin. Psychol. Psychother. 13 (3), 194–201. https://doi.org/10.1002/cpp.488.

Ibrahim, A.K., Kelly, S.J., Adams, C.E., Glazebrook, C., 2013. A systematic review of studies of depression prevalence in university students. J. Psychiatr. Res. 47 (3), 391–400. https://doi.org/10.1016/j.jpsychires.2012.11.015.

Jacoby, R., Barsky, K.G., Porat, T., Harel, S., Miller, T.H., Goldzweig, G., 2021. Individual stress response patterns: preliminary findings and possible implications. PLoS One 16 (8), e0255889.

Kendler, K.S., Gardner, C.O., 2010. Dependent stressful life events and prior depressive episodes in the prediction of major depression: the problem of causal inference in psychiatric epidemiology. Arch. Gen. Psychiatry 67 (11), 1120–1127. https://doi.org/10.1001/archgenpsychiatry.2010.136.

Kendler, K.S., Gardner, C.O., 2014. Sex differences in the pathways to major depression: a study of opposite-sex twin pairs. Am. J. Psychiatry 171 (4), 426–435. https://doi.org/10.1176/appi.ajp.2013.13101375.

Kendler, K.S., Halberstadt, L.J., 2013. The road not taken: life experiences in monozygotic twin pairs discordant for major depression. Mol. Psychiatry 18 (9), 975–984. https://doi.org/10.1038/mp.2012.55.

Kendler, K.S., Myers, J., Prescott, C., 2005. Sex differences in the relationship between social support and risk for major depression: a longitudinal study of opposite-sex twin pairs. Am. J. Psychiatry 162 (2), 250–256. https://doi.org/10.1176/appi.ajp.162.2.250.

Kendler, K.S., Kessler, R.C., Walters, E.E., MacLean, C., Neale, M.C., Heath, A.C., Eaves, L.J., 2010. Stressful life events, genetic liability, and onset of an episode of major depression in women. Focus 8 (3), 459–470. https://doi.org/10.1176/foc.8.3.foc459.

King, B., M., Carr, D., C., Taylor, M., G. Depressive symptoms and the buffering effect of resilience on widowhood by gender (2019). Gerontologist, 59(6), 1122-1130. doi: 10.1093/geront/gny115.

Kroenke, K., Spitzer, R.L., Williams, J.B.W., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16 (9), 606–613. https://doi.org/10.1046/J.1525-1497.2001.016009606.X.

Lam, J.R., Tyler, J., Scurrah, K.J., Reavley, N.J., Dite, G.S., 2019. The association between socioeconomic status and psychological distress: a within and between twin study. Twin Res. Hum. Genet. 22 (5), 312–320. https://doi.org/10.1017/THG.2019.91.

Lee, S.A., Jobe, M.C., Mathis, A.A., Gibbons, J.A., 2020. Incremental validity of coronaphobia: coronavirus anxiety explains depression, generalized anxiety, and death anxiety. J. Anxiety Disord. 74, 102268 https://doi.org/10.1016/J.JANXDIS.2020.102268.

LimeSurvey GmbH, Hamburg, Germany. URL http://www.limesurvey.org.

Lorant, V., Deliege, D., Eaton, W., Robert, A., Philippot, P., Ansseau, M., 2003. Socioeconomic inequalities in depression: a meta-analysis. Am. J. Epidemiol. 157, 98–112. https://doi.org/10.1093/aje/kwf182.

Lucock, M.P., Morley, S., 1996. The health anxiety questionnaire. Br. J. Health Psychol. 1, 137–150. https://doi.org/10.1111/j.2044-8287.1996.tb00498.x.

Manning, L.K., Carr, D.C., Kail, B.L., 2016. Do higher levels of resilience buffer the deleterious impact of chronic illness on disability in later life? Gerontologist 56 (3), 514–524. https://doi.org/10.1093/geront/gnu068.

Marmot, M.G., Stansfeld, S., Patel, C., North, F., Head, J., White, I., Smith, G.D., 1991. Health inequalities among British civil servants: the Whitehall II study. Lancet 337, 1387–1393. https://doi.org/10.1016/0140-6736(91)93068-k.

Marteau, T.M., Bekker, H., 1992. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). Br. J. Clin. Psychol. 31 (3), 301–306. https://doi.org/10.1111/J.2044-8260.1992.TB00997.X.

Matthews, T., Bryan, B.T., Danese, A., Meehan, A.J., Poulton, R., Arseneault, L., 2022. Using a loneliness measure to screen for risk of mental health problems: a replication in two nationally representative cohorts. Int. J. Environ. Res. Public Health 19 (3). https://doi.org/10.3390/IJERPH19031641.

Mazzotti, E., Fassone, G., Picardi, A., Sagoni, E., Ramieri, L., Lega, I., Camaioni, D., Abeni, D., Pasquini, P., 2003. II Patient Health Questionnaire (PHQ) per lo screening dei disturbi psichiatrici: Uno studio di validazione nei confronti della Intervista

Clinica Strutturata per il DSM-IV asse I (SCID-I). Italian J. Psychopathol. 9 (3), 235–242.
McGue, M., Osler, M., Christensen, K., 2010. Causal inference and observational research: the utility of twins. Perspect. Psychol. Sci. 5 (5), 546–556. https://doi.org/10.1177/1745691610383511/ASSET/IMAGES/LARGE/10.1177_1745691610383511-FIG2.JPEG.
Medda, E., Toccaceli, V., Fagnani, C., Nisticò, L., Brescianini, S., Salemi, M., Ferri, M., D'Ippolito, C., Alviti, S., Arnofi, A., Stazi, M.A., 2019. The Italian twin registry: an update at 18 years from its inception. Twin Res. Hum. Genet. 22 (6), 572–578. https://doi.org/10.1017/THG.2019.75.
Melli, G., Coradeschi, D., Smurra, R., 2007. The Italian version of health anxiety questionnaire: reliability and factorial analysis. Psicoterapia Cognitiva e Comportamentale 13, 37–48.
Montano, R.L.T., Acebes, K.M.L., 2020. Covid stress predicts depression, anxiety and stress symptoms of Filipino respondents. International Journal of Research in Business and Social Science 9 (4), 78–103. https://doi.org/10.20525/ijrbs.v9i4.773.
Mousavi, S.M., Yazdanirad, S., Jahadi Naeini, M., Abbasi, M., Sadeghian, M., 2021. The role of individual factors on corona-induced hypochondriasis and job stress: a case study in workplace. Med. J. Islam Repub. Iran 35 (1), 87–94. https://doi.org/10.47176/mjiri.35.11.
Pedrabissi, L., Santinello, M., 1989. Verifica della validità dello STAI forma Y di Spielberger [Verification of the validity of the STAI, Form Y, by Spielberger]. Giunti Organizzazioni Speciali 191–192, 11–14.
Picardi, A., Mazzotti, E., Gaetano, P., Cattaruzza, M.S., Baliva, G., Melchi, C.F., Biondi, M., Pasquini, P., 2005. Stress, social support, emotional regulation, and exacerbation of diffuse plaque psoriasis. Psychosomatics 46 (6), 556–564.
Picardi, A., Bartone, P.T., Querci, R., Bitetti, D., Tarsitani, L., Roselli, V., Maraone, A., Fabi, E., De Michele, F., Gaviano, I., Flynn, B., Ursano, R., Biondi, M., 2012. Development and validation of the Italian version of the 15-item dispositional resilience scale. Riv. Psichiatr. 47 (3), 231–237. https://doi.org/10.1708/1128.12446.
Picardi, A., Miglio, R., Tarsitani, L., Battisti, F., Baldassari, M., Copertaro, A., Mocchegiani, E., Cascavilla, I., Biondi, M., 2013. Attachment style and immunity: a 1-year longitudinal study. Biol. Psychol. 92 (2), 353–358. https://doi.org/10.1016/j.biopsycho.2012.10.001.
Roberts, B.W., Jackson, J.J., Fayard, J.V., Edmonds, G., Meints, J., 2009. Conscientiousness. In: Handbook of Individual Differences in Social Behavior. The Guilford Press, pp. 369–381.
Samuelsson, Å., Ropponen, A., Alexanderson, K., Svedberg, P., 2013. A prospective cohort study of disability pension due to mental diagnoses: the importance of health factors and behaviors. BMC Public Health 13 (1), 1–11. https://doi.org/10.1186/1471-2458-13-621/TABLES/4.
Scardera, S., Perret, L.C., Ouellet-Morin, I., Gariépy, G., Juster, R.P., Boivin, M., Turecki, G., Tremblay, R.E., Côté, S., Geoffroy, M.C., 2020. Association of social support during adolescence with depression, anxiety, and suicidal ideation in young adults. JAMA Netw. Open 3 (12), e2027491–e. https://doi.org/10.1001/JAMANETWORKOPEN.2020.27491.
Scarella, T.M., Laferton, J.A.C., Ahern, D.K., Fallon, B.A., Barsky, A., 2016. The relationship of hypochondriasis to anxiety, depressive, and somatoform disorders. Psychosomatics 57 (2), 200–207. https://doi.org/10.1016/J.PSYM.2015.10.006.
Sheerin, C.M., Lind, M.J., Brown, E.A., Gardner, C.O., Kendler, K.S., Amstadter, A.B., 2018. The impact of resilience and subsequent stressful life events on MDD and GAD. Depress. Anxiety 35 (2), 140–147. https://doi.org/10.1002/DA.22700.
Spielberger, C.D., 1983. Manual for the State-Trait-Anxiety Inventory: STAI (form Y). Consulting Psychologists Press, Palo Alto, CA.
Stevens, S.M., Gustavson, D.E., Fang, B., Tu, X., Logue, M., Lyons, M.J., Reynolds, C.A., Kremen, W.S., Franz, C.E., 2020. Predicting health-related quality of life in trauma-exposed male veterans in late midlife: a 20 year longitudinal study. Int. J. Environ. Res. Public Health 17 (12), 4554. https://doi.org/10.3390/ijerph17124554.
Svedberg, P., Gatz, M., Lichtenstein, P., Sandin, S., Pedersen, N.L., 2005. Self-rated health in a longitudinal perspective: a 9-year follow-up twin study. The Journals of Gerontology 60 (6), S331–S340. https://doi.org/10.1093/geronb/60.6.s331.
Swickert, R.J., Rosentreter, C.J., Hittner, J.B., Mushrush, J.E., 2002. Extraversion, social support processes, and stress. Pers. Individ. Differ. 32, 877–891. https://doi.org/10.1016/S0191-8869(01)00093-9.
Tran, A., Tran, L., Geghre, N., Darmon, D., Rampal, M., Brandone, D., Gozzo, J.M., Haas, H., Rebouillat-Savy, K., Caci, H., Avillachm, P., 2017. Health assessment of French university students and risk factors associated with mental health disorders. PLoS One 12 (11), e0188187.
Weiss, D.S., Marmar, C.R., 1997. The Impact of Event Scale—Revised. In: Assessing Psychological Trauma and PTSD. The Guilford Press, pp. 399–411.
Zhang, J., Yang, Z., Wang, X., Li, J., Dong, L., Wang, F., Li, Y., Wei, R., Zhang, J., 2020. The relationship between resilience, anxiety and depression among patients with mild symptoms of COVID-19 in China: a cross-sectional study. J. Clin. Nurs. 29 (21–22), 4020–4029. https://doi.org/10.1111/JOCN.15425.
Zimet, G., 1988. The multidimensional scale of perceived social support pursuit of the three cs: confident, concise and consistent health care provider recommendations for adolescent vaccines view project. Article J. Pers. Assess. https://doi.org/10.1207/s15327752jpa5201_2.