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Genetic and environmental contributions to psychopathological symptoms stability and change across the COVID-19 pandemic

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ABSTRACT

Several longitudinal studies investigated changes in mental health related to the pandemic event. However, little research has focused on the mediating role of environmental and genetic factors. The current prospective study aimed to evaluate the genetic and environmental contributions to the stability of symptoms of depression, anxiety and stress during the COVID-19 crisis. A total of 798 adult twins, previously enrolled in the Italian Twin Register, participated in the study and completed on-line questionnaires sent out on June 2020 and December 2020. The nine-item Patient Health Questionnaire (PHQ-9), the six-item State-Trait Anxiety Inventory (STAI-6), and the Impact of Event Scale - Revised (IES-R) were administered to assess depressive and anxiety symptoms, and pandemic-related subjective distress, respectively. A considerable longitudinal stability was observed for each trait (range: 0.57, STAI-6 - 0.67, PHQ-9). Bivariate Cholesky decomposition indicated that genetic factors explained from 53% (IES-R) to 61% (STAI-6) of between-wave covariance and that genetic overlap between the two waves was almost complete (range: 0.91, STAI-6 – 0.99, PHQ-9). Our findings support the hypothesis, at least over the 6-month period examined, of a genetic stability between waves and of an environmental discontinuity due to changes in life conditions during the pandemic.

1. Introduction

Depression and anxiety are the two most prevalent psychiatric disorders and cause substantial disease burden, accounting for more than 10% of years lived with disability worldwide (Vigo et al., 2016).

Twin and family studies suggested that genetic factors have a substantial role in liability to these disorders, with heritability estimates between 30 and 50% for both depression and anxiety (Nivard et al., 2015; Hettema et al., 2001; Sullivan et al., 2000; Boomsma et al., 2000). Further, they argued that these disorders have a common genetic source (Mather et al., 2016). In adulthood, heritability of anxiety and major depression was estimated around 40% (Sullivan et al., 2000). Similarly, Kendler et al. (2006) reported that the heritability of major depression in a large sample of Swedish adult twins was 42% for women and 29% for men, with individual-specific environment contributing most of the remaining liability. However, given that other studies have not found gender differences in heritability (Kendler et al., 2008; Nivard et al., 2015), gender difference needs to be further studied (Zhao et al., 2020; Trzaskowski et al., 2019).

Moreover, the available research mostly indicated that genetic effects contribute greatly to the stability in depression and anxiety throughout the life span (Nivard et al., 2015). Several studies revealed that after age 18, genetic effects on both depression and anxiety are highly stable (Gillespie et al., 2004; Cerda et al., 2010; Nivard et al., 2015), which suggests that the risk of depression and anxiety over adult life is largely of genetic origin (Burcusa and Iacono, 2007).

On the other hand, conflicting information exists about the stability of environmental risk factors. Some studies suggest that the effects of non-shared environmental factors have mostly short-term effects on anxiety and depression, which disappear in as short a time period as 1-3 months (Dunn et al., 2015). Consistently, other twin studies have indicated no (Torvik et al., 2017) or low (Kendler and Gardner, 2010, 2017) stability in environmental contributors to major depression and anxiety in adulthood (Waszczuk et al., 2016). In particular, Kendler and Gardner (2017) reported that the percentage of stable environmental influences over 8 years of follow-up on major depression corresponded to

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about 17%, while the remainder was occasion-specific. In a more recent study with a larger sample size covering a wider age-span, Torvik et al. (2019) found 2% stability in environmental risk of major depression over a similar length of time. Overall, these studies indicate that environmental factors are not responsible for longer-term stability of risk of depression and anxiety disorders.

In contrast, other studies suggest that environmental factors, especially non-shared environmental factors, contribute primarily to short-term stability, and that with increasing age the contribution to stability of these environmental factors increases (Nivard et al., 2015), reaching a plateau after adolescence (Kendler et al., 2011). Accordingly, two twin studies found long-lasting unique environmental effects from adolescence into adulthood and beyond (Gillespie et al. 2004; Kendler et al., 2008). Further, a meta-analysis of longitudinal studies which assessed monozygotic twins (spanning an age range of 10–66 years) showed that within-pair differences between MZ twins in anxiety and depression increased from childhood into late adulthood, with middle adulthood environmental factors contributing substantially to stable individual differences (Kendler et al., 2011).

Overall, to date, knowledge regarding the contributions of genetic and environmental factors to the stability of anxiety and depression is still scarce, as the majority of relevant studies with genetically informative designs have been limited to cross-sectional analyses. Moreover, the available longitudinal studies had mostly a long time interval between follow-ups, so they were not able to investigate short- and medium-term stability. To what extent the environment contributes to short/medium-term stability of depression and anxiety, and whether the impact of environment lasts longer as people age, remain issues that need to be further investigated.

Given this, the present study, which has a longitudinal design, aimed to gain further insight into the aetiology of the stability/variation in symptoms of anxiety, depression, and stress assessed in twins aged 18-93 years, over a 6-month span during the course of the COVID-19 pandemic. It should be noted that in Italy the trend of symptoms may have been affected, at least on average, by the spread evolution of the pandemic especially during the second semester of 2020. In fact, the first pandemic wave had its peak of 26,575 new infections on the 14th of March 2020 and ended within the last two weeks of July. The second wave started to grow in August and increased faster from the last week of September onwards. It presented a number of incident cases even higher compared to the first wave with a peak of 60,425 infections on the 12-th of November, and was stable at about 41,500 between the 17th and the 29th of December (Ferrante, 2021).

First, the present study aimed at assessing the relative contribution of genetic and environmental influences on individual differences in those symptoms at each time point to investigate the extent to which such influences are stable over a 6-month period. Then, the study aimed at elucidating the genetic and environmental contributions to stability and change. The majority of non-genetically informed research to date focused on changes in psychopathology during the COVID-19 crisis. However, a fundamental aspect of these changes was ignored, that is, if they are mostly environmental or genetic in origin. The present study allows a more robust test of the causal underpinning of those changes.

This kind of results may provide relevant information for the understanding of the bases of a trait's longitudinal pattern, and therefore for evaluating the feasibility of strategies aimed to alter this pattern. In particular, if the analysis shows that time changes are mainly environmental in origin, then subsequent research will be encouraged to identify modifiable factors that may impact on trait's trajectory, for example producing favourable effects on symptoms' evolution in the case of a psychopathological condition.

2. Methods

2.1. Participants

Adult twins, previously enrolled in the Italian Twin Register (ITR) (Medda et al., 2019) were contacted by e-mail and were invited to participate in this longitudinal study (Medda et al., 2022). Living abroad during the Italian lockdown was the only exclusion criterion. The baseline survey (wave 1) was in June 2020 (immediately after the end of the first Italian lockdown), while the follow-up survey (wave 2) was in December 2020 (when Covid-19 cases were increasing, and vaccination was not yet available). Participants completed online questionnaires regarding socio-demographic characteristics, Covid-19 symptoms and diagnosis (the latter in participants themselves or in their household), as well as validated assessment instruments to measure depressive, anxiety, and stress symptoms. A total of 1751 adult twins participated in both waves, and 798 twins from 399 complete twin pairs (258 MZ, 141 DZ) were included in the analysis. The study was approved by the Ethical Committee of the Istituto Superiore di Sanità (May 2020), and all subjects signed an online informed consent to participate.

2.2. Assessment instruments

Participants were administered the following questionnaires: (i) the nine-item Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001) to assess depressive symptoms; (ii) the six-item State-Trait Anxiety Inventory (STAI-6) (Marteau and Bekker, 1992) to measure anxiety symptoms; (iii) the Impact of Event Scale - Revised (IES-R) (Weiss and Marmar, 1997) to assess pandemic-related subjective distress. Total scores for these scales were computed and used in statistical analyses. More precisely, the PHQ-9 score ranged from 0 to 27 [9 items scored from 0 (not at all) to 3 (nearly every day)], the STAI-6 score ranged from 20 to 80 [6 items scored from 1 (not at all) to 4 (very much); the total score was divided by 6 and multiplied by 20 to obtain the same range as in the original 20-item scale], and the IES-R score ranged from 0 to 88 [22 items scored from 0 (not at all) to 4 (extremely)]. For all instruments, a higher score indicates more severe symptoms.

2.3. Statistical analyses

Means and proportions were used to summarize continuous and categorical variables, respectively, and means scores on assessment instruments were compared between waves by the Student's t-test. Original total scores were considered for descriptive purposes, while log-transformed scores were used in statistical modelling to better approximate normal distribution. The modelling procedure was based on the twin design (Neale and Cardon, 1992), and was aimed to explore the longitudinal patterns of the scales across the two study waves along with etiological factors underlying these patterns. More precisely, for each scale, the following correlations were estimated: (i) (within-pair) correlation between twin and cotwin at each wave (referred to as "cross--twin/within-wave" correlation), separately for MZ and DZ pairs, which is informative on etiological factors affecting phenotype's expression at a given wave; (ii) (within-individual) correlation between the two waves, to assess the degree of longitudinal stability/variation; (iii) (within-pair) correlation between twin at one wave and cotwin at the other wave (referred to as "cross-twin/cross-wave" correlation), separately for MZ and DZ pairs, which is informative on etiological factors affecting the within-individual longitudinal correlation. Subsequently, for each scale, a bivariate Cholesky model was fitted to the two waves to decompose total variance at each wave and covariance between waves into contributions due to additive genetic effects (A) (i.e., additive effects of all gene variants influencing the phenotype, without interactive effects), common environmental effects (C) [i.e., effects of environmental factors that are shared by the twins within the family, particularly during childhood and adolescence (e.g., rearing environment,

family socio-economic status, parental behaviours, etc.), or that are shared in the womb (e.g., hormonal exposures)], and unique (individual-specific) environmental effects (E) [i.e., effects of environmental factors that specifically act on an individual (e.g., lifestyles, relations with peers, infections, etc.), including measurement error] (Neale and Cardon, 1992). Relevant statistics that can be derived from this model include phenotype's (*narrow*) *heritability* at each wave (i.e., the proportion of variance at a given wave that is explained by additive genetic variance), *bivariate heritability* between waves (i.e., the proportion of between-wave covariance that is explained by additive genetic covariance), and *genetic correlation* between waves (i.e., the extent to which the same genes affect the phenotype at both waves; e.g., a value of 0 would mean that completely different genes affect the phenotype at the two waves, while a value of 1 would indicate that exactly the same genes are involved over the longitudinal window). The same statistics can be estimated for common (C) and unique (E) environmental effects. The Full ACE model encompassing all three sources of variance/covariance was compared with reduced models (AE, CE) by chi-square likelihood-ratio test; in case of non-significant chi-square tests, the reduced model with the lowest Akaike Information Criterion (AIC) was retained as the best-fitting model (principle of parsimony), under which parameters' estimates were reported. Correlation and model-fitting analyses included age at baseline and gender as covariates. Descriptive analyses were performed by the Stata software version 16 [Stata Corporation, College Station, TX, USA], while model-fitting analyses were conducted by the Mx software (Neale at al., 2006).

3. Results

3.1. Sample characteristics

Descriptive statistics about socio-demographic characteristics and scores on the assessment instruments are reported in Table 1. Socio-demographic and Covid-19 characteristics (i.e., age, education, occupation, Covid-19 symptoms/diagnosis) did not differ between the complete-pair study sample and the unmatched twins (n=953) who were not included in the analyses; the only exception was gender, with a higher proportion of women among complete pairs (73% vs 59%). Moreover, no differences in the level of depression, anxiety, and stress were observed between matched and unmatched twins (respectively, 4.9 vs 4.6; 41.2 vs 40.6; 16.1 vs 15.3). Psychopathology showed an increase from wave 1 to wave 2 (p=0.01 for PHQ-9, p<0.001 for STAI-6, p<0.001 for IES-R). All instruments showed more than adequate internal consistency at both waves, with Chronbach's alpha values of about 0.85-0.87 for PHQ-9 and STAI-6, and about 0.90-0.92 for IES-R.

Table 1
Socio-demographic characteristics of the participants and symptom scores by study period.

	Wave 1		Wave 2		p
	Mean ± SD	*%*	*Mean ± SD*	*%*	
Age	45.8 ± 15.2				
Gender (Female)		72.9			
Zygosity					
MZ		64.7			
DZ		35.3			
Education					
- Diploma or below		44.17			
- Bachelor's degree		10.29			
- Master's degree		45.54			
Depression	4.86 ± 4.21		5.16 ± 4.51		0.01
Anxiety	41.18 ± 11.31		45.34 ± 12.71		<0.001
Stress	16.09 ± 11.75		19.58 ± 13.16		<0.001

Abbreviation: SD: Standard Deviation; MZ, monozygotic; DZ, dizygotic. ^Longitudinal comparison of Total scores observed at Wave 1 and Wave 2.

3.2. Correlation and model-fitting analyses

Table 2 shows correlation patterns and best-fitting model estimates for the three scales. For each of the scales, a higher "cross-twin/within-wave" correlation in MZ compared to DZ pairs pointed to genetic effects at each wave; furthermore, a considerable longitudinal stability was observed [range of "within-twin/cross-wave" correlation: 0.57 (STAI-6) – 0.67 (PHQ-9)], with a higher "cross-twin/cross-wave" correlation in MZ than in DZ pairs suggesting a genetic role in the stability.

For each assessment instrument, the best-fitting (reduced) model of the full ACE Cholesky was the one incorporating only additive genetic and unique environmental effects (AE model). Under this model, scales' heritability was moderate and remained basically unchanged across the two waves. Furthermore, genetic factors explained from 53% (IES-R) to 61% (STAI-6) of between-wave covariance, with genetic correlations indicating a complete (PHQ-9) or almost complete (STAI-6, IES-R) genetic overlap between the two waves. For all three instruments, unique environmental factors, compared to genetic factors, provided a higher contribution to individual differences at each wave, and varied qualitatively between the two waves, as indicated by unique environmental correlations below 0.50.

4. Discussion

To our knowledge, this is the first genetic epidemiological study in twin adults that investigated with a longitudinal design the genetic and environmental contributions to the stability of and change in anxious, depressive, and psychological stress symptoms during the COVID-19 pandemic, at two time points.

It should be acknowledged that this study has a number of limitations, such as the exclusive reliance on self-reported measures, the small sample size and especially the small number of DZ twin pairs, the impossibility to control for gender effects in the analyses, and the data collection limited to only two time points. Although all the assessment instruments used in the present study are valid and reliable and have been widely used in research practice for decades, it has been suggested that there are stable individual differences in self-reported symptoms (McCrae and Costa, 2008), which include measurement error that can lead to underestimation of environmental stability. Future research should complement self-completed instruments with observer-rated measures in order to reduce random and systematic error effects.

Future genetically informed studies examining psychopathological symptoms variation would also benefit from explicitly testing and comparing models separately for men and women, although previous studies did not indicate support for potential differences in heritability estimates, which makes it unclear whether differences in sizes and sources of genetic and environmental effects are to be expected (Kendler et al., 2008; Nivard et al., 2015; Zhao et al., 2020; Thorp et al., 2020). Finally, future studies should collect longitudinal data over three or more time points, in order to explore symptom stability over the medium term.

While these limitations suggest some caution in interpreting our findings, this study yielded a number of significant results. The first research question was the relative contribution of genetic and environmental influences on individual differences in symptoms at two time points over a 6-month interval. Results of the bivariate Cholesky decomposition model analysis showed that both additive genetic and non-shared environmental influences explain the variance in each symptom dimension. Specifically, genetic effects explained from 30 to 40% of phenotypic variance in depression, anxiety, and stress at wave 1 and from 38 to 43% at wave 2, with the remaining variance explained by the non-shared environmental component, which was substantial both at wave 1 (from 60 to 70%) and wave 2 (from 57 to 62%). These results indicated that both genetic and environmental contributions remain substantially stable across time. Therefore, the underlying genetic and environmental causes of variance did not shift during the early phases of

Table 2
Correlation patterns and best-fitting models' estimates.

Depression							
Correlations							
Cross-Twin/Within-Wave				**Within-Twin/Cross-Wave**		**Cross-Twin/Cross-Wave**	
Wave 1		Wave 2				MZ	DZ
MZ	DZ	MZ	DZ				
0.38	0.20	0.41	0.32	0.67		0.41	0.22
Best-fitting (AE) model estimates							
Proportions of variance				**Proportions of covariance**		**A/E correlations**	
Wave 1		Wave 2		A	E	A	E
A	E	A	E				
0.38	0.62	0.43	0.57	0.60	0.40	0.99	0.45
(0.28-0.48)	(0.52-0.72)	(0.34-0.52)	(0.48-0.66)	(0.49-0.70)	(0.30-0.51)	(0.89-1.00)	(0.36-0.54)
Anxiety							
Correlations							
Cross-Twin/Within-Wave				**Within-Twin/Cross-Wave**		**Cross-Twin/Cross-Wave**	
Wave 1		Wave 2				MZ	DZ
MZ	DZ	MZ	DZ				
0.38	0.29	0.38	0.18	0.57		0.35	0.20
Best-fitting (AE) model estimates							
Proportions of variance				Proportions of covariance		A/E correlations	
Wave 1		Wave 2		A	E	A	E
A	E	A	E				
0.40	0.60	0.38	0.62	0.61	0.39	0.91	0.36
(0.29-0.49)	(0.51-0.71)	(0.27-0.47)	(0.53-0.73)	(0.48-0.73)	(0.27-0.52)	(0.78-1.00)	(0.26-0.45)
Stress							
Correlations							
Cross-Twin/Within-Wave				**Within-Twin/Cross-Wave**		**Cross-Twin/Cross-Wave**	
Wave 1		Wave 2				MZ	DZ
MZ	DZ	MZ	DZ				
0.27	0.24	0.43	0.23	0.63		0.32	0.24
Best-fitting (AE) model estimates							
Proportions of variance				**Proportions of covariance**		**A/E correlations**	
Wave 1		Wave 2		A	E	A	E
A	E	A	E				
0.30	0.70	0.43	0.57	0.53	0.47	0.94	0.46
(0.19-0.40)	(0.60-0.81)	(0.32-0.52)	(0.48-0.68)	(0.40-0.65)	(0.35-0.60)	(0.81-1.00)	(0.37-0.55)

Abbreviation: MZ, monozygotic; DZ, dizygotic; A, additive genetic effects; E, unique environmental effects.
Numbers in parentheses are 95% CIs of best-fitting models' estimates.

the COVID-19 crisis, given that genetic effects explaining individual differences were not be substantially amplified or reduced. The sizes of the estimates of genetic and environmental effects fall within the range reported in previous studies using a variety of anxiety and depression measures (Sullivan et al., 2000; Kendler et al., 2006; Franz et al., 2011; Nivard et al., 2015; Torvik et al., 2019) or measures of psychological distress. For example, in a two-wave study of adult female twins (aged 18–79, mean age 47.7), Rijsdijk et al. (2003) reported heritability estimates of 44% and 51% for the total GHQ-28 score. Also, consistently with our findings, in an eight-wave study of twins (aged 12-63 years), Nivard et al. (2015) reported heritability from 30 to 40% during adulthood for the total Adult Self-Report score (ASR; Achenbach and Rescorla, 2003).

Psychopathological symptoms appeared to be substantially correlated, with longitudinal phenotypic correlations for the different symptoms ranging from 0.57 (anxiety symptoms) to 0.67 (depression symptoms), which suggests that liability to psychopathological symptoms was largely stable across a 6-month time interval. In a recent longitudinal twin study (Rimfeld et al., 2021) addressing mental health of young adults in their mid-twenties, prior to the COVID-19 pandemic and during the COVID-19 pandemic (in April, July, and October 2020, and in March 2021), the authors found comparable phenotypic correlations, although they used different measures. For example, they found an average correlation of 0.69 for anxious and 0.66 for depressive symptoms between April 2020 and October 2020.

The size of the cross twin-cross wave correlations (from 0.32 to 0.41 for MZ twins and from 0.20 to 0.24 for DZ twins) indicated that the phenotypic correlations were due to both genetic and, to a lesser extent, non-shared environmental factors.

The causes of stability/change in psychopathological symptoms over time were the second research question of this study.

The contribution of genetic factors to the covariance in psychopathology between the two waves was substantial, ranging from 53% (stress) to 61% (anxiety), while the covariance in psychopathology between waves due to environmental factors was only moderate (from 39% to 47%). This suggests that genetic influences more than environmental influences were contributing to stability and that the individual-specific environment did not have, even across a medium span of time, a substantial stable component, thus contributing more to change than stability across time. This suggests that immediate life circumstances mostly do not produce enduring changes on liability to symptoms of anxiety, depression, and stress, and that these effects are not generally cumulative over time. One may hypothesize that pandemic effects played a smaller role in the persistence of symptoms as compared with genetic factors. The exposure to the pandemic did not seem to change a person's genetic risk of the psychopathological symptoms that we examined. Though we cannot rule out that long-term environmental effects exist and are relevant for certain individuals experiencing

particularly severe life events, such as natural disasters or pandemics, these effects did not seem to have major importance in explaining psychopathological symptoms in our sample.

Longitudinal correlations shed light on the relative overlap of genetic and environmental effects between the waves. The finding of very high genetic correlations (ranging from 0.91 to 0.99) indicated a quasi-perfect overlap for non-additive effects between the two time points. These results indicate that the same genetic factors contributing to individual differences endured across the measurement points. In other words, almost all the genetic factors influencing mental health in June 2020 also contributed to mental health in December 2020, which suggests that mental health was not affected by the interplay of genetic risk and the environment. In contrast, the findings suggest a substantial change in non-shared environmental influences, given the moderate (from 0.36 to 0.46) overlap for the environment influences between the two time points. Therefore, it may speculate that some *new* individual-specific environmental experiences may have played a key role in precipitating the observed rise in anxiety and stress levels. It should be noted, in fact, that the average differences between the waves showed a statistically significant, although moderate from a clinical point of view, increase in anxious and stress symptoms from June 2020 to December 2020, and a statistically significant increase in depressive symptoms, although very small in size and as such of limited meaningfulness from a clinical point of view. The occurrence of this increase some months after the beginning of the pandemic suggests that as Italy progressed through the pandemic and the economic and social consequences of lockdown increased, simultaneously an increased risk of symptoms emerged, especially in some population groups. Among women, for example, an increased risk of symptoms may be explained by several factors which are more likely to affect women, such as greater responsibility for supervision and education of children and increased burden of care for ill family members, (COVID-19 Mental Disorders Collaborators, 2021). It is likely that, as the pandemic continued and a state of socio-economic crisis persisted, several brackets of the population have been affected by decreases in household income or job instability or various other disadvantages. Even in the group of employed people, many individuals may have feared losing their job, or have been forced to work in ways that exposed them to COVID-19 infection. At the end of the 2020, many persons might have also experienced an exacerbation of mental health difficulties because of interruption of any form of government emergency assistance (such as unemployment benefits and temporary financial assistance for needy families), which could not last indefinitely.

The picture of the aetiology of the course of psychopathological symptoms provided by this study is consistent with previous studies reporting stable genetic influences in depression and anxiety during adulthood, although the majority of those studies were carried out over a longer span of time (Gillespie et al., 2004; Cerda et al., 2010; Nivard et al., 2015; Rijsdijk et al., 2003) and only few examined shorter time periods (Kendler and Gardner, 2017; Dunn et al., 2015). Our findings are also consistent with previous studies which suggested considerable transient influences from environmental factors and life events (Torvik et al., 2017, 2019; Kendler and Gardner, 2010, 2017), though they do not corroborate previous findings of a substantial contribution of environmental factors to stable and predictable individual differences in anxiety and depression in adult life (Gillespie et al., 2004; Kendler et al., 2011).

5. Conclusions

Using a genetically-informed longitudinal design, our study suggested that at the individual level the liability to symptoms of anxiety, depression, and stress was quite stable during the early phases of the COVID-19 pandemic, and that this stability was largely attributable to stable genetic factors. Also, the findings suggest that the interplay between genetic and environment factors was quite small, at least over the short/medium-term period that we examined.

Non-shared environmental influences were mostly responsible for the change in psychopathological symptoms, although much of these influences seemed to be transient. This finding supports the conceptualization that non-shared environmental influences on emotional behaviours may be largely unsystematic (Turkheimer and Waldron, 2000), particularly in low-risk unselected populations.

The evidence presented in our study could also have potential clinical significance. From a clinical perspective, the finding of genetic stability underpinning psychopathological symptoms should not be viewed deterministically; stable genetic influence does not preclude the possibility of effective treatment. It is important to note that environmental influences substantially contribute to change. This suggests that an improvement in psychopathological symptoms can be induced by positive environmental experiences, such as positive life events, and that an increase in symptoms can be caused by negative experiences, such as adverse life events or conditions. It should also be noted that adverse life events can elicit negative effects which could endure over an extended period of time among individuals who are already suffering from psychopathological symptoms or are at higher risk for exposure to negative life events (Middeldorp et al., 2008). This underlines the importance of helping individuals with symptoms by means of clinical support strategies that emphasize modification of the current environment (e.g., increasing social support or involving significant others or reducing social risk factors). For psychotherapy research and practice, these findings may be informative especially if we consider that personal change originates not only from specific psychotherapeutic techniques in the session, but also from the capacity of the therapeutic relationship to promote modification outside the framework of the session, that is, in the environment where the individual lives (Fonagy and Allison, 2014). In closing, it should be noted that the time-specific and stability nature of environmental influence on psychopathological symptoms suggests that, for clinical interventions to be successful in the long-term, they may need to be actively maintained.

Author contributions

Antonella Gigantesco: Conceptualization, Writing - original draft & review. Corrado Fagnani: Conceptualization, Formal analysis, Methodology Writing - original draft & review. Angelo Picardi: Conceptualization, Writing - original draft & review. Maria Antonietta Stazi: Conceptualization, Writing - review. Emanuela Medda: Conceptualization; Methodology, Formal analysis, Methodology, Writing - original draft & review & editing.

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Declaration of Competing Interest

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