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The role of genetic and environmental factors in covariation between anxiety and anger in childhood

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ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical committee of each participating institution accepted the procedures and the parents of all participants signed informed consent.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation and data collection were performed by Corrado Fagnani, Maria Antonietta Stazi, Marco Battaglia. Analysis was performed by Simona Scaini, Giulio Centorame, Francesca Lissandrello, Stella Sardella and Chiara Brombin. The first draft of the manuscript was written by Simona Scaini and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Abstract

Higher levels of anger expression, as well as lower levels of anger control, have been reported for adults with anxiety disorders compared to individuals without anxiety disorders. Differently to research on adults, very few studies examined the relationship between anxiety and anger in childhood.

In our study, we investigated in 398 Italian twin pairs (74 MZ male, 70 MZ female, 134 same-sex dizygotic-53 male, 81 female-, and 120 unlike-sex dizygotic twin pairs), aged 8–17 (mean 13.06±2.59): i) the heritability of a childhood anger phenotype; ii) the association between five anxiety domains and anger; iii) the role of possible common etiological factors in explaining the observed comorbidity and overlap in risk between anxiety phenotypes and anger. The study demonstrated that anger, assessed by CBCL items, is heritable in children at a similar rate to prior studies (40%). Our research found low to moderate rate of correlation between anger and anxiety (from 0.10 to 0.19). Finally, the present study found that the majority of etiological influences on anxiety and anger are independent of each other. Data showed that shared environmental influences have some small effects on the phenotypic covariation between the anxiety phenotypes and anger (12%); whereas unique environmental influences have an almost negligible effect (1%). Our analyses did not reveal the effect of genetic effects in explaining the covariation between these phenotypes.

Key words: anger, anxiety, twin study, childhood

Introduction

Higher levels of internal anger, external anger expression, and trait anger, as well as lower levels of anger control, have been reported for adults with different anxiety disorders [1, 2]. For example, a subset of individuals with social anxiety disorder exhibits externalizing behaviour, including outwardly directed anger expression [3, 4], especially in response to criticism or negative evaluation (angry reaction) and without provocation (angry temperament) [5]. The elevated level of anger is an important clinical indicator of psychopathological symptoms' severity, as it is associated with worse impairment, including problematic substance use [4], greater risk for suicide [6] and higher incidence of depression [7].

Differently from research on adults, very few studies investigated this relationship in childhood. Empirical research has shown that internalizing symptoms are associated with aggressive behaviour among children [8] and adolescents [9, 10]. Moreover, a pattern of behaviour called the Child Behavior Checklist Dysregulation Profile [11], consisting of attention problems, aggressive behaviour, and higher anxious or depressed scores at the Child Behavior Checklist (CBCL), has been proposed in literature. This profile has been described by several studies as a potential marker for severe childhood psychopathologies [12-14], and as a predictor of negative adult outcomes [15]. Children with this profile exhibit elevated levels of anxiety and disruptive behaviour disorders [16, 17], marked impairment [18] and suicidality [17].

After a period in the 1970s, in which anger and fear were thought to be mutually exclusive, Rothenberg [19] revised these theories positing that an individual is bound to experience anxiety, but his response to this state of anxious arousal can either be to escape and avoid the situation (anxiety) or to attack (anger). Thus, anger is theorized as always preceded by anxiety. More recently, in the Cognitive Neoassociation model [20], a component of the general aggression model [21], Berkowitz theorizes that, while in a situation of threat, the activation of the flight response is experienced as fear, but the fight response produces irritation and anger.

Several possible scenarios have been hypothesized by literature on the nature of the relationship. Some contributions [22] speculate that anxiety increases the risk for disruptive behaviour disorders, exacerbating oppositional or non-compliant behaviours. One possible explanation of why anxiety may confer risk for the development of reactive aggression is the frustration-aggression model [23]. This model proposes that reactive aggression results from frustration. In addition, this frustration and the associated negative emotions (e.g., anxiety) stem from blocking of the individual's goals [22]. Conversely, evidence from literature also support the hypothesis that disruptive behaviours moved by anger confer risk for anxiety symptoms [22]. In terms of processes, different hypotheses have been proposed. Frick and colleagues (1999) hypothesized that engaging in antisocial behaviours may engender recurrent state anxiety. A second explanation involves peer processes (e.g., peer rejection) as a possible mediator. In fact, it is possible that reactive aggression leads to peer rejection,

which then may lead to anxiety symptoms. In this direction, contributions focused on irritability suggested that phenotypes with significant irritability expression predict the development of anxiety and depression symptoms [12, 24]. For example, results of the longitudinal study of Savage et al. [25] were inconsistent with a model where internalizing symptoms cause irritability or both are caused by an unmeasured third variable, leaving the possibility that irritability could play a causal role in the expression of anxiety/depression symptoms. A third explanation of the co-occurrence of anger and anxiety suggests the presence of shared risk factors. With regard to child-specific factors, genes involved in some aspects of dopaminergic and serotonergic function have been implicated in the association between anxiety and externalizing behaviours [26]. In terms of shared environmental factors, several causes have been supposed. For example, literature seems to suggest that some parent-child interaction styles are similar among families of children with anxiety and anger problems [22]. Parents of anxious or aggressive children are less likely to agree with their children and are less likely to acknowledge positive consequences of situations, as compared to parents of nonclinical children [27, 28]. Other evidence seem to indicate neighborhood violence as a shared risk factor. In fact, exposure to neighborhood violence may confer risk for disruptive behavior disorders as well as anxiety symptoms perceived as uncontrollable [29]. Other possible shared risk factors could be difficult temperamental styles and negative emotionality, common information processing models (e.g hypervigilance to threat) and information-processing biases (for a review see Bubier & Crdabick, 2009 [22]). For example, individuals high on neuroticism present high level of irritability, anger, sadness, anxiety, worry, hostility, self-consciousness, and vulnerability that have been found to be substantially correlated with one another in factor analyses [30, 31]. Finally, some evidence suggest autonomic hyperarousal in stress situations as a shared correlate of anxiety and aggressive behaviours [32].

Although several theoretical contributions examined the issue in adulthood or in anger-close phenotypes, empirical childhood research not often inquired the nature of the association between anxiety and anger. In particular, to our knowledge, child and adolescent multivariate twin studies focused only on the relationship between the construct of irritability and anxiety, and not on anger phenotypes. For example, Savage [25] reported that common genetic and environmental factors may influence irritability and internalizing symptoms from middle childhood to young adulthood. Moreover, a very recent contribution by Rappaport et al. [33] indicated that there is substantial overlap among the genetic and environmental factors that influence individual differences in irritability and those that increase liability for depression and anxiety symptoms in children.

However, anger and irritability could be conceptualized as two close but different constructs.

Following Kassinove and Sukhodolsky's (1995) [34] definition, 'anger' refers to 'a label given to a constellation of specific uncomfortable subjective experiences and associated cognitions (e.g., thoughts, beliefs,

images) that have variously associated verbal, facial, bodily, and autonomic reactions'. Anger is an affective state experienced as the motivation to act in ways that warn, intimidate, or attack those who are perceived as challenging or threatening [35]. Differently, the term 'irritability' represents a complex hypothetical construct, defined as a phenomenological experience (and possibly a trait), a complex construct that involves increased sensitivity to environmental stimulation that causes physiological arousal and tension, *without cognitive mediation*, and that results in a lowered threshold to experience anger, and/or impulsive, but not premeditated, aggression [36].

Because of this blank in literature, a further in-depth inspection of the relationship between anger and anxiety and of the possible presence of common and differential genetic and environmental overlap may clarify this association also in childhood.

Our purpose was to elucidate the nature of the relationship between anger and different subtypes of anxiety. In fact, in the light of recent literature, the choice of adopting a single global scale could not constitute the best choice to study a phenomenon that is multifaceted as anxiety in children. Clinical and community studies have well established the presence of different subtypes of anxiety from early childhood [37-39]. Moreover, previous meta-analytic data (e.g. [40], in addition to specific results on this sample [41]), have shown differences in etiological contributions of genes and environment in explaining variance for different anxiety subtypes. Therefore, it is important to assess different subtypes of anxiety, in order to evaluate the presence of differences in genetic and environmental contributions in orchestrating the relationships between five specific alternative anxiety phenotypes (Generalized Anxiety, Separation Anxiety, Social Anxiety, School Phobia and Panic/Somatic Anxiety) and anger.

In particular, this study addresses knowledge gaps by attempting to investigate: i) the heritability of a childhood anger phenotype; ii) the association between anxiety phenotypes and anger; iii) the role of possible common etiological factors in explaining the observed comorbidity and overlap in risk between anxiety symptoms and anger. Due to the lack of empirical evidence in favour of a clear relationship between them, we compared different multivariate models [42] to investigate how genetic and environmental components could (or could not) explain the covariation between anger and Panic/Somatic Anxiety, Generalized Anxiety, Separation Anxiety, and Social Anxiety symptoms. We implemented three different multivariate models of twin method: the first model assumes that common genetic and/or environmental factors may cause the covariation between anxiety and anger; the second one presupposes that both common and specific genetic and environmental effects influence the covariation; the third one assumes a latent psychometric factor mediating both common and specific genetic and environmental effects. Given the nature of anger and its expression across a number of anxiety dimensions, a better understanding of the genetic and environmental contributions to

its expression, as well as of the co-occurrence with anxiety, could inform the extant literature and promote the development of psychological and pharmacological therapeutics.

Method

Participants

This study is part of a project involving the Italian Twin Registry. The Italian Twin Registry is a database of all possible twins in the Italian general population set up in 2001 [43-45].

The families of 2,015 possible twins living in the provinces of Milano and Lecco were invited by mail to participate in the survey: across three steps, 973 families (48%) confirmed the presence of a twin pair among their offspring; 707 of the 973 families agreed to participate in surveys of various nature, and 407 (57.5%) of these families agreed to complete a psychometric survey, made of questionnaires for children and one of the parents. Because nine couples were excluded due to missing data, the final sample consisted of 398 twin pairs aged 8–17 (mean 13.06±2.59). The parent-rated Goldsmith [46] questionnaire was employed to assign zygosity: According to its algorithm (accuracy of determination: > 94% [47], there were 74 monozygotic (MZ) male, 70 MZ female, 134 same-sex dizygotic (DZS, 53 male, 81 female), and 120 discording-sex dizygotic (DZU) twin pairs. Seventy-seven percent of CBCL/6-18 questionnaires were completed by the mother of the twins and 23% by the father.

The response rates across these three steps did not differ between families living in the industrialized Milan province when compared with those living in the suburban Lecco province. The mean age of children and parents did not differ between families who agreed to participate in the psychometric survey versus the remaining families (respectively, 13.06 ± 2.60 versus 13.11 ± 2.31, $p = .62$ for children 46.06 ± 0.23 versus 46.71 ± 0.35, $p = .10$ for mothers). The educational level and percentage of full-time employment were similar for mothers of twins participating compared with those of twins not participating in the psychometric survey (university degree of mothers: respectively, 17.7% versus 16.3% $p = .65$). In the final sample we registered the following higher educational level for fathers: 0% primary school, 3.7% secondary school, 23.1% vocational school, 50.1% high-school, 23.1% university degree and for mothers: 0.3% primary school, 2.4% secondary school, 23.2% vocational school, 55.9% high-school, 18.3% university degree. Table 2 shows demographics data and the mean values of anxiety and anger scores in twins considered as individuals and divided by sex and zygosity groups.

The procedures were accepted by the ethics committee. For all of the participants, parents signed a declaration of consent.

Measures

Child Behavior Checklist/6-18 (CBCL/6-18). The CBCL/6-18 [48] is a standardized questionnaire made up of 113 items. A parent should rate the behavioural and emotional problems of his child on the basis of his conduct in the last 6 months. Each item is rated on a 3-point Likert scale.

To build an empirical, concise index of behavioural anger, a scale based on CBCL items was created. Similarly to the *top-down* approach, used to create DSM-oriented scales (i.e., agreement in experts' ratings of the pre-existing items' consistency with DSM-oriented scales from experts' ratings of the items' consistency [49], the Delphi method [50] has been implemented to develop the anger index. Four authors coded the CBCL items to be included in the anger scale (see Table 1) independently. In case of disagreements, the consensus was reached via discussion, ending with Cohen's Kappa coefficient of inter-rater reliability ranging 0.71-0.88. Finally, 14 CBCL items were included in the anger scale (see Table 1), with Cronbach's coefficient for the retained items of 0.78.

Screen for Child Anxiety Related Emotional Disorders (SCARED). The Italian version of the SCARED questionnaire was used to estimate anxiety symptoms through 41 items [41, 51]. This is a screening instrument for childhood anxiety disorders. Despite the SCARED questionnaire was originally developed to assess anxiety disorders in clinical populations [52, 53], its validity is demonstrated also in the general population [54, 55]. Children should assess the frequency of each symptom on a 3-point Likert scale. In the original factorial structure of the SCARED questionnaire, the 41 items are clustered in 5 subscales [53]: (1) Panic/Somatic Anxiety (cut-off: 7), (2) Generalized Anxiety (cut-off: 9), (3) Separation Anxiety (cut-off: 5), (4) Social Anxiety/Social Phobia (cut-off: 8), and (5) School Phobia (cut-off: 3). When a cut-off point of 25 was applied to the total score endorsed by subjects across these five factors, data showed good sensitivity (70%) and good ability to discriminate between children with anxiety disorders versus those without anxiety disorders (specificity: 67%), and between children with anxiety disorders versus those with depression, or disruptive disorders: 61 and 71%, respectively [56, 57]. Finally, in a meta-analytic study, Hale et al. (2011) [58] found that internal consistency for the total score was good ($\alpha = 0.89–0.91$) although substantial variation was found in the internal consistency of the subscales ($\alpha = 0.43–0.93$). In this study, we included only scales based on the DSM-5 anxiety disorders classification (Panic/Somatic Anxiety (PD), Generalized Anxiety (GAD), Separation Anxiety (SA), Social Anxiety/Social Phobia (SP)).

Data Analyses

Phenotypic and cross-twin/within-trait correlations for the SCARED anxiety subscales and the empirically derived anger scale were calculated.

Then, multivariate twin models were applied to data with OpenMx [59] with the aim to investigate the possible causes of covariation between the anxiety subscales and the anger scale.

The maximum-likelihood theory was used to estimate parameters, with models fitted to quantitative raw data. Through multivariate twin design both variance and covariance of the phenotypic traits were split into fractions of i) additive genetic factors (A), ii) shared environmental factors (C), and iii) unique (specific for each subject) environmental factors (E).

Before applying genetic modelling, a saturated model requiring a free parameter for every observed statistic was fitted to the data. We constrained it in successive steps: equal means and variances of each phenotype for twin 1 and twin 2 in each pair, and for MZ and DZ pairs. Successively, three multivariate models were applied, with the anger score entered as the last variable: the Cholesky model, the Common Pathway model, and the Independent Pathway model. All the models were firstly compared with saturated models. Then, Cholesky model was used as a saturated model against which the fit of more restrictive models (Common Pathway model, Independent Pathway model) were compared [42, 60]. The $\chi 2$ statistic and the Akaike information criterion (AIC) were used to obtain information about the fit of more parsimonious models.
The Cholesky model (Figure S1) represents the associations between measures due to the presence of common genetic and/or environmental factors. For *n* variables, a Cholesky decomposition includes *n* independent genetic and environmental factors: the first factor loads on all traits, the second one loads on all traits but the first, the third factor loads on all traits but the first two, and so on. Genetic and environmental influences on covariation are not limited by this model, supplying the fullest explanation of data. The Independent Pathway (Figure S2) model postulates that each measure has specific and common genetic and environmental factors directly influencing the covariation. It does not consider mediating factors. The Common Pathway Model (Figure S3), assumes a shared pathway in which covariation is due both to genetic and environmental common factors, which influence a latent variable that has effects on all the model's measures. Moreover, it specified scale-specific genetic and/or environmental factors. The latent intervening variable designed in the Common Pathway model can be interpreted as one or multiple connecting (patho-) physiological mechanisms, or multiple systems of variables shared by Anxiety phenotypes and Anger.

Multivariate genetic analysis of the last two models can be seen as a simultaneous factor analysis of genetic and environmental variances and covariances [61]. These models discriminate between common causal factors and scale-specific causal factors. Phenotypic covariance is explained by common genetic and environmental factors; residual variance (i.e., not shared by the various scales) is explained by specific factors that are unique to each scale.

Before proceeding with model fitting analyses, variables were log-transformed to approximate our data to a normal distribution. Age and sex were included as covariates in the models.

Results

The within-individual phenotypic correlation and within-pair twin correlation coefficients for the anxiety subscales and the anger are shown in Table 3. Only those SCARED subscales that were significantly correlated with Anger (PD, GAD, and SP) were analysed afterwards. Table 4 shows the results of the biometric model fitting. The Cholesky decomposition model was used as a base level of fitting to compare the most parsimonious Common and Independent Pathway models. The Independent Pathway model did not produce a significant decrease in fitting compared to the Cholesky model and fitted better than the Common Pathway model.

Figure 1 shows the Independent Pathway model and Table 5 reports genetic and environmental contributions accounted for by common and specific causal agents and univariate estimates.

The majority of etiological influences on anger and anxiety are independent of each other, and the common shared environmental influences contribute very little to all the phenotypes, while the common additive genetic factors do not show influences on the anger phenotype. The model included significant specific genetic factors for PD, GAD and Anger and specific unique environmental factors for each variable except GAD.

More in detail, the common shared environmental variables affect Anger (12% of the phenotype variation) as well as PD (24%), GAD (15%), and SP (8%). Covariation among phenotypes is also determined by unique environmental factors: E influence GAD (accounting for 45% of total variance) and explain a little variance in PD, SP, and Anger (respectively, 7%, 2% and 1%). Finally, common genetic factors explain PD (15% of total variation), GAD (14%), and SP (23%).

Discussion

The primary aim of the current study was to determine the nature of the relationship between anger and anxiety symptoms and evaluate the role of possible common etiological factors in explaining the observed comorbidity between anger and anxiety syndromes. The collected data displayed small-to-moderate positive correlations between anger and three specific anxiety subscales (Panic/Somatic Anxiety, Generalized Anxiety, and Social Anxiety), but not with the Separation Anxiety subscale. Consistently with findings of several previous studies [2, 62], these correlations found in a population-based sample support a small, but significative, association between anxiety problems and anger in childhood. These associations could suggest the appropriateness of anger assessment among anxious children and vice versa. Many interventions focus on improving individual's ability to manage anxiety without addressing anger management or the development of appropriate expressions of anger [63, 64]. On the other hand, programs for the prevention or the treatment of

externalizing symptoms should include a module aimed at improving an individual's awareness and regulation of anxiety and internalizing emotions.

The univariate heritability estimate obtained for anger was 0.40 with the remaining variance accounted for 0.25 by shared environment and 0.35 by unique environment. Our estimate is consistent with heritability reported in previous studies on anger (e.g. [65, 66]) and in some reports on anger-close phenotypes, such as irritability [25]. However, in considering our results we should keep in mind that our estimate is based on a parent- report. In fact, although the present study demonstrated a consistent estimate of heritability in comparison with studies on irritability based on parent-report [25], this is somewhat higher than what was found in studies that derived an irritability score from child-report (e.g [33, 67]). Moreover, our study is based on a specific behavioral aspect of anger. In literature, in addition to trait and state anger, several dimensions of anger have been considered: hostility (the cognitive component of anger), aggression (the behavioural component of anger), internalized anger expression (the tendency to suppress angry feelings), externalized anger expression (the tendency to outwardly express angry feelings), and anger control (the ability to regulate anger)[1, 36]. Thus, in future research, it would be interesting to study genetic and environmental contributions for every specific anger phenotype, as well as the relationship between these components and anxiety in childhood.

Model-fitting analyses showed that the phenotypic covariation in our sample is better explained by the Independent Pathway model. This is not surprising since the phenotypic correlations between anger and anxiety scales are low. The majority of etiological influences on anxiety and anger are independent of each other and the common shared environmental influences contribute very little to the overall variance. Specifically, data showed that shared environmental influences have some small effects on the phenotypic covariation between the anxiety subscales and anger (12%), whereas unique environmental influences have an almost negligible effect (1%). This findings suggest that components of the shared environment that cause twins to be similar exert small influence on the co-occurrence of anger and anxiety symptoms expression. Therefore, for a small amount common shared environmental causal influences can be held responsible for the simultaneous development of anxiety symptoms and high levels of anger. The fact that there were no common unique environmental factors influencing the comorbidity suggests a shared environmental (e.g. family, neighborhood, peers) liability to both anger and anxiety psychopathology. Our analyses did not reveal the effect of genetic effects in explaining the covariation between anger and anxiety phenotypes. The individual differences for PD, GAD and Anger are due to specific genetic factors, while specific unique environmental influences affect the variance of the phenotypes of PD, SP and Anger.

Differently to our results, the recent contributions of Rappaport [33] and Savage [25] on the relationship between irritability and some internalizing phenotypes, found that a common set of both genetic and environmental factors influence the etiology of irritability and internalizing syndromes. In the study of

Savage [25] a single set of common environmental factors (C) had an impact on both irritability and anxious/depressed symptoms only at the first wave (8-9 years).

In accordance with the literature, even in our study, correlations between the anxiety subscales are affected by genetic and environmental components.

Some potential limitations should be taken into account when our findings are interpreted. The first limitation is the scale used to assess anger: the measure is created ad hoc, and this could have consequences in term of validity and reliability. In addition, anger and irritability are very close constructs. In definitions and measures of irritability, causes often seem interchangeable with the causes of other constructs, especially anger, making it difficult to distinguish between the two constructs [68]. Thus, it is possible that, although we aimed at assessing anger, we have implemented a scale partially focused on irritability. The second one is the cross-sectional nature of our study: a longitudinal design is a more appropriate way to provide an evaluation of the relationship between anger and anxiety symptoms, and their relationship over time. Furthermore, the sample size is relatively small, making difficult to give a likely estimation of the variance and covariance components in case of small effects and preventing us from investigating sex differences in these variables.

Despite that, univariate estimates are coherent with previous findings on anxiety [69-72] and anger in children samples [66, 73]. However, some studies found that unique environmental contribution for anger phenotypes are usually higher than additive genetic effects [66, 73]. It must be kept in consideration that, given the nature of a twin study, the estimation of environmental contributions to the phenotype are not measured directly; thus, they may be affected by further biases related to the methods. Moreover, a recent meta-analysis on the environmental contributions to developmental psychopathology [74] found that the estimates of shared environment were higher for studies based on maternal and paternal reports, rather than the ones based on child reports. Since our anger scale was based on parent-report measures, this could have influenced the results.

In considering results we should keep in mind that our estimates have been calculated considering only a specific age range. Since previous studies found an increase of heritability with age for symptoms of internalizing and externalizing disorders [75, 76], future studies should investigate the variation in the magnitude of genetic and environmental influences on covariation between anger and anxiety across different ages. It could be possible that in late adolescence and in early adulthood the role of genetic factors in influencing the covariation increases in accordance with neurobiological models on adults theorizing that anger and anxiety may be related through underlying biological vulnerabilities [20, 77].

In conclusion, the present study demonstrates that anger, assessed by CBCL items, is heritable in children at a similar rate to prior studies. Moreover, the present study investigated, for the first time in literature, the nature of the relationship between anger and several anxiety phenotypes in children and adolescents. Our research found low to moderate rate of correlation between anger and anxiety. Finally, the present study found

that the majority of etiological influences on anxiety and anger are independent of each other. The common shared environmental influences contribute very little to the overall, whereas unique environmental influences have an almost negligible effect.

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Table 1. CBCL items included in the empirical Anger scale.

CBCL ITEM
3. Argues a lot
20. Destroys his/her own things
21. Destroys things belonging to his/her family or others
37. Gets in many fights
45. Nervous, high strung, or tense
57. Physically attacks people
65. Refuses to talk
68. Screams a lot
86. Stubborn, sullen, or irritable
87. Sudden changes in mood or feelings
88. Sulks a lot
90. Swearing or obscene language
95. Temper tantrums or hot temper
97. Threatens people

Table 2. Demographic characteristics, SCARED total score, Panic/Somatic Anxiety (PD), Generalized Anxiety (GAD), Separation Anxiety (SA) and Social Anxiety (SP) subscales values and Anger score, by sex and zygosity.

	Age	SCARED	PD	GAD	SA	SP	Anger
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Entire Sample (n 796)	13.06 (2.59)	22.62 (10.11)	4.03 (3.08)	7.27 (3.84)	3.92 (2.86)	6.03 (3.40)	3.58 (3.18)
Girls (n 422)	13.10 (2.58)	23.62 (10.29)	4.25 (3.16)	7.51 (4.00)	4.15 (2.90)	6.25 (3.42)	3.50 (3.01)
Boys (n 374)	13.00 (2.61)	21.48 (9.80)	3.79 (2.98)	6.99 (3.64)	3.66 (2.79)	5.79 (3.36)	3.67 (3.37)
MZ (n 288)	13.21 (2.59)	23.68 (10.01)	4.21 (3.05)	7.67 (3.76)	3.98 (2.96)	6.53 (3.54)	3.55 (3.17)
DZ (n 508)	12.96 (2.59)	22.01 (10.13)	3.93 (3.10)	7.03 (3.87)	3.89 (2.80)	5.76 (3.28)	3.60 (3.19)

Table 3. Phenotypic and Within-Pair Twin Correlations among variables. Mean and Standard Deviation are presented in parentheses.

	SCARED TOTAL (22.62±10.11)	PANIC/ SOMATIC ANXIETY (4.03±3.08)	GENERALIZED ANXIETY (7.27±3.84)	SEPARATION ANXIETY (3.92±2.86)	SOCIAL ANXIETY (6.04±3.40)	ANGER (3.58±3.18)
Phenotypic Twin Correlations						
SCARED TOTAL	1	-	-	-	-	-
PANIC/SOMATIC ANXIETY	.76**	1	-	-	-	-
GENERALIZED ANXIETY	.78**	.49**	1	-	-	-
SEPARATION ANXIETY	.61**	.40**	.24**	1	-	-
SOCIAL ANXIETY	**.70****	.33**	.41**	.28**	1	-
ANGER	.18**	.14**	.19**	.04	.10**	1
Within-Pair Twin Correlations						
MZ	.61**	.45**	.47**	.63**	.56**	.67**
DZ	.43**	.35**	.37**	.43**	.31**	.41**

** p< .01

Table 4. Model-fitting analyses.

Model	compared to model	ep	-2LL	df	AIC	diffLL	diff.df	*p* value
Comparison to Saturated Model								
1. Saturated	-	88	46.59	3020	-5993.41	-	-	-
2. Cholesky	1	34	108.36	3074	-6039.64	61.77	54	0.22
3. Independent pathway	1	28	112.38	3080	-6047.62	65.79	60	0.28
4. Common pathway	1	23	128.81	3086	-6043.19	82.22	66	0.09
Comparison to Cholesky Model								
3. Independent pathway	2	28	112.38	3080	-6047.62	4.02	6	0.67
4. Common pathway	2	23	128.81	3086	-6043.19	20.45	12	0.06

ep:estimated parameters; 2LL:likelihood statistic; df:degrees of freedom; AIC:Akaike information criterion; diff.LL:difference in log likelihood statistic; diff.df:difference in degrees of freedom.

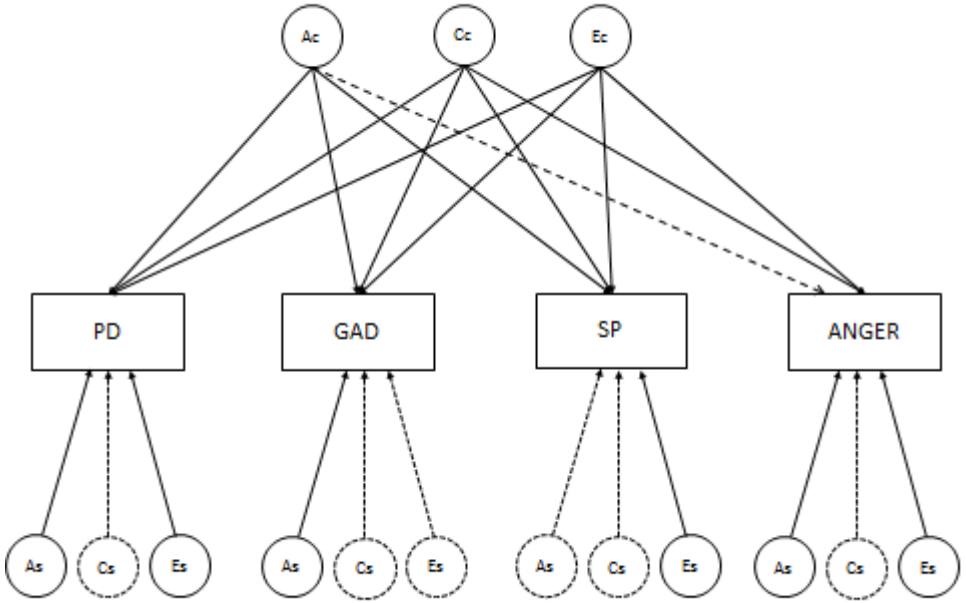
Table 5. Genetic and Environmental Contributions accounted for by common and specific causal agents under the best-fitting and univariate estimates.

	Genetic and Environmental Contributions								
	Va_c	**Va_s**	**Vc_c**	**Vc_s**	**Ve_c**	**Ve_s**	**Va**	**Vc**	**Ve**
PANIC/SOMATIC ANXIETY	0.15 (0.00;0.39)	0.18 (0.00;0.29)	0.24 (0.05;0.43)	0.00* (-0.14;0.14)	0.07 (0.03;0.15)	0.36 (0.28; 0.45)	0.33 (0.08;0.56)	0.24 (0.05;0.43)	0.43 (0.34;0.55)
GENERALIZED ANXIETY	0.14 (0.00;0.40)	0.26 (0.13;0.37)	0.15 (0.03;0.30)	0.00* (-0.09;0.09)	0.45 (0.26;0.57)	0.00* (-0.20; 0.20)	0.40 (0.19;0.58)	0.15 (0.03;0.30)	0.45 (0.34;0.57)
SOCIAL ANXIETY	0.23 (0.03;0.61)	0.27* (-0.43;0.43)	0.08 (0.00;0.22)	0.00* (-0.13;0.13)	0.02 (0.00;0.06)	0.40 (0.32;0.50)	0.50 (0.30;0.63)	0.08 (0.00;0.22)	0.42 (0.33;0.52)
ANGER	0.00* (-0.09;0.12)	0.40 (0.15;0.63)	0.12 (0.01;0.37)	0.13* (-0.34;0.34)	0.01 (0.00;0.04)	0.34 (0.27; 0.44)	0.40 (0.16; 0.63)	0.25 (0.05; 0.44)	0.35 (0.28;0.45)

Vac: variance explained by common additive genetic influence; Vas: variance explained by specific additive genetic influences; Vcc: variance explained by common shared environmental factors; Vcs: variance explained by specific shared environmental factors; Vec: variance explained by common unique environmental factors; Ves: variance explained by specific unique environmental influences; Va: variance explained by additive genetic factors; Vc: variance explained by shared environmental factors; Ve: variance explained by unique environmental factors.

*Parameters can be dropped in subsequent sub-models without any loss in fit.

Fig. 1 Independent pathway multivariate model for PD, GAD, SP and ANGER. Non-significant paths are indicated with a dashed line. Proportion of variance accounted for by common and specific factors are reported in table 5.



Observed variables are depicted in squares and latent variables in circles

A = additive genetic influences; C = shared environmental influences; E = unique environmental influences. C subscript = common factor; S subscript = factor specific for each observed variable

PD= Panic/Somatic Anxiety; GAD= Generalized Anxiety; SP= Social Anxiety