ORIGINAL ARTICLE



Anxiety in Early Adolescence: Heterogeneous Developmental Trajectories, Associations with Risk Factors and Depressive Symptoms

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Abstract

This study aimed: (1) to identify heterogeneous trajectories of anxiety symptoms in early adolescence; (2) to analyze the relationships between risk factors and identified trajectories; (3) to study the association between anxiety symptom trajectories and depression symptom course. Anxiety and depressive symptoms of 825 participants (44.40% boys; mean initial age = 13.01, SD = 0.56) was assessed every 6 months over an 18-month period. Trajectory identification relied on latent-variable approach. As a result, 2–4 trajectories were identified for social phobia (SP), generalized anxiety (GA) and panic symptoms, revealing at least a low-symptom course and a trajectory of elevated symptoms (at-risk trajectory). Being girl and sibling cohabitation were related to at-risk trajectories, and a course of low effortful control and heightened negative affectivity. Finally, SP and GA symptoms were related to heightened depressive symptom courses. Relevant implications towards tailored prevention and intervention are highlighted to promote a healthy development across adolescence.

Keywords Anxiety symptoms · Development · Temperament · Adolescence · Growth mixture modeling

Introduction

Almost one in five adolescents may develop an anxiety disorder over the adolescence [1, 2]. Adolescent anxiety disorders (ADs) have a dramatic impact on daily adjustment and constitute a risk factor for severe mental disorders in adolescence and later in life, such as depression and drug use disorders [3–5]. Many studies on developmental psychopathology have focused on depicting how anxious symptomatology evolves across adolescence, as an attempt to uncover

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specific pathways to AD onset [6–9]. Unfortunately, most of these studies have systematically focused on determining overall course, overlooking heterogeneity among individuals in symptom course.

According to Weems [10], "a functional model of continuity and change in anxious emotion must also take into consideration the reality that ideographic or individually experienced factors will also shape the expression of anxious emotion" (p. 494). In recent years, person-specific issues are receiving increasing attention, and several studies have highlighted the presence of different relatively heterogeneous courses of AD symptomatology throughout adolescence. Most of studies have identified between two to five person-specific courses of symptoms [11, 12]. For instance, Allan et al. [13] identified three heterogeneous trajectories underlying the overall AD symptom decline over the early adolescence. Nivard et al. [14] found five developmental courses of internalizing symptoms (comprising anxiety and depression symptoms) across adolescence.

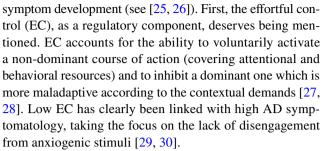
Another issue to note is the time-specific expression of anxiety symptoms. Theorists on anxiety development highlight that specific time frames may be associated with predominant expression of concrete subtypes of anxiety symptoms across childhood and adolescence [1, 10]. Unfortunately, most of studies are focused on overall anxiety



symptoms [7, 11, 13, 14] and very few studies have analyzed the heterogeneous trajectories of AD subtype symptoms over the adolescence [15, 16]. Moreover, results between these studies are quite inconsistent. For instance, Ohannessian et al. [17] found five developmental courses of social phobia symptoms from middle to late adolescence, as well as four trajectory classes for generalized anxiety symptoms. Conversely, Nelemans et al. [12] identified two developmental courses for generalized anxiety, separation anxiety and school anxiety, and three trajectories for social phobia across adolescence. On the other hand, most of studies assessed anxiety symptoms either annually, biannually or even longer intervals between measurement occasions [7, 14, 15]. This could mask the effects of maturational and environmental factors on anxiety symptom course that may occur in a shorter time scale (e.g., months), for instance, adjustment to a new school [18]. Finally, most studies did not take into account the mutual influence of anxiety and depression symptoms in longitudinal terms (i.e., how a trajectory of anxiety symptoms may influence the trajectory of depressive ones). A special mention deserves the high comorbidity between depression and generalized anxiety disorder over adolescence, sharing some common symptoms, such as ruminative thought (see [1, 8]).

Early adolescence constitutes a sensitive period for the development of ADs, and some (vulnerability) factors may have a decisive influence on individual's brain plasticity towards the emergence or exacerbation of anxiety symptoms [14, 19, 20]. Individual (e.g., sex, maturational timing) and family factors show a decisive influence on anxiety symptomatology course. For instance, sex has been identified as a critical factor in terms of adolescent anxiety development. In the sense, girls have systematically showed higher levels of symptoms across adolescence [12, 21]. This could be probably related to sexually-mediated biological mechanisms and socialization processes [22]. On the other hand, negative family events (e.g., divorce) have also been associated with trajectories of high anxiety symptoms [1, 5], because of derived conflicting emotions and changes in household environment (e.g., new distribution of family roles, visiting arrangements). In this line, adolescents from single-parent households often exhibit increasing levels of anxiety symptoms with age [8, 9]. Sibling cohabitation is also relevant to take into account. Thus, anxiety symptom emergence and aggravation (especially social phobia) have been association with sibling cohabitation due to influence of sibling conflicts and social contagion (i.e., it is very likely that adolescents mimic siblings' ways of expression) effects [23, 24].

Besides, temperamental characteristics, considered to be a precursor of adult personality traits, have a strong influence on anxiety (also in depression symptoms) throughout adolescence [9, 15, 25]. In this regard, reactive and regulatory temperament components are highly involved in anxiety



On the other hand, Rothbart highlighted the influence of negative affectivity (NA), a reactive temperament component strongly related to neuroticism, on anxiety [27, 31]. NA is defined as the expression of an unpleasant affect as a consequence of confronting potentially aversive stimuli. High NA has strongly been linked with anxious symptomatology and the development of full-blown ADs [25, 28, 32].

EC and NA measured cross-sectionally have been associated with heightened or increasing courses of anxiety symptoms [11, 12, 33]. However, temperamental factors must be considered dynamically throughout adolescence, as they are under maturation towards adult personality. Fluctuations in these temperamental factors over time have been linked with subsequent onset of ADs [34–36].

The study of person-specific anxiety courses deserves special attention because it could lead to the identification of specific pathways towards the emergence of AD and comorbid disorders (e.g., depressive disorder) across the lifespan. That is particularly relevant in periods as critical to the expression of anxiety as the early adolescence is. Additionally, a fine-grained approach should be taken to study anxiety symptom course (i.e., shorter interval across measurement occasions) in this period of adolescence. This study aimed to answer this question: how many symptom trajectories may exist in early adolescence? We expected to find varying trajectories (between two and five trajectory classes in line with scientific literature on this field [12, 15, 17, 37]) for each subtype of symptomatology, under a 6-month measurement follow-up approach.

Moreover, we aimed to study the relationship of individual, family and temperamental risk factors and the AD symptom trajectory classes. In this regard, we hypothesized that sex, family composition, NA and EC (concretely, being girl, living in monoparental households and showing high NA and low EC across assessments) would help to explain the developmental trajectories of high levels of symptoms among early adolescents. More concretely, sibling cohabitation would be more related to at-risk trajectories of social phobia symptoms due to the influence of social contagion effects. Sex and living in a monoparental household would influence on all AD subtype symptom course. In addition, trajectories of heightened symptoms would be related to courses of elevated NA and attenuated EC, regardless of subtypes of AD.



Finally and as a secondary aim, it intended to study how trajectory membership across AD subtype symptoms would be related with depressive symptom course as a way of shedding light on internalizing symptom comorbidity. It is expected that adolescents with at-risk trajectories of generalized anxiety symptoms would show at-risk trajectory of depressive symptoms due to the high comorbidity between both disorders.

Methods

Participants

This 4-wave longitudinal study with assessments every six months is part of a wider research project (see [38]). A sample of 934 Spanish adolescents (45.40% boys; 13.01 years old on average at the first assessment point, SD = 0.56, range = 11.65-15.25; and 14.50 at the last follow-up, SD = 0.56, range = 13.15–16.75) was invited to participate in this study. All of them were Caucasians, attended state schools, and came from middle-class families. Most of participants lived with their both parents (74.59% of sample) and siblings (78.09% of participants). Participants were recruited from the first level of secondary education of 20 high schools (45% from rural areas) across the Majorca island (Spain). All of the participants were able to write, read, and speak fluently in both Spanish and Catalan, and each handed in a written consent form signed by themselves and their legal guardians. None of the participants showed severe physical or intellectual disabilities, or neurological disorders according to parents and school board reports.

Sample who accepted to participate (N=852) and completed the questionnaires at baseline (T1) comprised 816 participants (response rate = 99.77%). Moreover, 68 new participants were enrolled in the second assessment point (T2) and 50 participants in the third assessment point (T3). A total of 731 participants completed the questionnaires at T2 (response rate = 85.79%); 727 participants at T3 (response rate = 85.33%), and 623 participants at T4 (response rate = 73.12%). Because our statistical approach allowed for handling longitudinal data series with intermittent missing data (see further details in the Data analysis section), our final sample included 825 participants (13.01 years old on average, SD = 0.56; 51.80% of participants from high schools in rural areas). In terms of sex, 44.40% of participants were boys (M = 13.07 years old, SD = 0.61; 45% from schools in rural areas), and the rest were girls (M = 12.94 years old, SD = 0.50; 50.39% from schools inrural areas). No significant differences were found in terms of non-responders (participants with two or more missing assessment points and therefore ruled out for analyses) and responders for any sociodemographic, or temperamental- or anxiety-related variables.

Psychological Instruments

Family Composition

A brief sociodemographic questionnaire was completed by participants. The questionnaire comprised questions about family members that lived with respondents (both parents and siblings).

Internalizing Symptomatology

The Revised Child Anxiety and Depression Scale (RCADS; [39, 40]) consists of 47 self-report items on a 4-point response scale. This questionnaire evaluates symptomatology of four different ADs (separation anxiety disorder, social phobia, generalized anxiety disorder, panic disorder), obsessive compulsive disorder and depression. Due to study purposes, we just used the AD and depression scales of RCADS. Reliability levels were satisfactory across assessment points for these scales (Cronbach's alpha from 0.67 to 0.87). Correlations between points of measurement ranged from Pearson's r = 0.31 (between the T1 and T4 assessment points) to r = 0.75 (between the T2 and T3 assessment points), for all the scales across the four sample points in our study (see Figure F1 in the Supplementary material).

Temperamental Factors

The Early Adolescence Temperament Questionnaire (EATQ-Revised long form [41, 42]) is comprised of 103 items on a 5-point Likert scale. The EATQ-R allows for 13 different domains and four principal temperamental factors (negative affectivity, effortful control, affiliativeness, and surgency) to be assessed. Due to the goals of this study, we considered EC and NA. Regarding psychometrical properties, levels of reliability similar to reference studies (see [41, 43]) were observed for the factors of interest across assessment points (Cronbach's alpha from 0.60 to 0.71), and levels of correlation between points were ranged from Pearson's r=0.43 (between the T1 and T4 assessment points) to r=0.74 (between the T3 and T4 assessment points) for all the scales within our sample (all p<0.05).

Procedure

The University Bioethics Committee approved all the study procedures. The research project was presented to school boards. Afterwards, students were invited to participate. Once participants provided the written consent forms, they were gathered in a classroom. Two 1-h sessions were carried



out in which participants filled out the questionnaires, which were presented to participants in a counter-balanced order (in the same classroom, a random set of participants filled out the EATQ-R 1 day and the other group completed the family-composition questionnaire and the RCADS; the questionnaires that each group did not fill out were completed on the following day). Measurement points were scheduled every 6 months across four assessment waves (starting when adolescents were in the third trimester of the first year of secondary school) and spanned three academic years of secondary schooling.

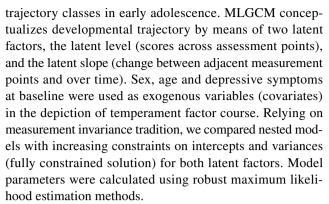
Data Analysis

To test the first hypothesis, we used the latent class mixed modeling (LCMM), a growth mixture approach, based on the robust maximum likelihood framework [44, 45]. This approach (as a person-centered approach) relaxes the assumption of a unitary course of AD symptoms for all individuals and allows for the identification of the varying latent trajectory classes (see [45]). In turn, subject-specific variability is better captured by LCMM than other group-based growth models, such as latent class growth analysis [44, 46, 47].

First, we tested whether each AD subtype symptom course evolved under a linear or quadratic growth. Second, we compared the fit of models with an increasing number of trajectory classes until finding either two consecutive unstable solutions (models without convergence) for criterion or increasingly higher fit index values. Two indices were used to test goodness of fit [44, 48, 49]: the sample-adjusted Bayesian information criterion (SABIC) and the consistent Akaike information criterion (CAIC). Smaller model SABIC and CAIC values signify a better fit. Regarding class membership, mean of posterior probabilities of belonging to a concrete class should be greater than 0.70; and each class should have a meaningful percentage of participants (at least 5% of sample).

Logistic (binary or multinomial) regression was used to study the relationship between trajectory class membership and individual (age and sex) and family factors (parent cohabitation and sibling cohabitation). Trajectory class membership (being the low-symptom trajectory as the reference class) was used as a criterion and a separate regression analysis was conducted for each subtype of AD symptoms. A lower Akaike information criterion (AIC) for the model with individual and family factors (in comparison to unconstrained models) indicated a better model fit. Z-based Wald tests were used to test factor loading estimates being significantly different from zero.

Finally, multigroup latent growth curve modeling (MLGCM; [50, 51]) was used to study how temperamental factors (NA and EC) may evolve according to AD symptom



Good fit of each individual model was shown by scaled χ^2 statistic being significant [52]; a scaled root mean square error of approximation index (RMSEA) lower than 0.080; a scaled comparative fit index (CFI) and a scaled Tucker-Lewis index (TLI) higher than 0.95; and the standardized root mean square residual (SRMR) lower than 0.080. Additionally, we conducted comparisons between nested models by means of the incremental RMSEA (Δ RMSEA) and incremental CFI (Δ CFI). An Δ RMSEA > 0.015 (in absolute value) and Δ CFI < -0.01 would reflect the lack of measurement invariance, and better fit of a more constrained model [53, 54].

Finally, to test whether the trajectories of AD symptoms were associated with depressive symptom course, MLGCM was used under the same rationale than the one followed for temperamental factor course. Age at baseline and sex were used as exogenous variables (covariates). AD symptom trajectory membership was used as a multigroup factor.

To run the analyses, R x64 3.0.1 (lcmm and lavaan packages) and STATA v. 14 were used.

Results

Mean scores and standard deviations of anxious symptomatology and temperamental factors are displayed in Table 1. Moderate correlations between temperamental factors were found across assessment points (Pearson's r at T1 = -0.58, p > 0.01; r at T2 = -0.51, p > 0.01; r at T3 = -0.52, p > 0.01; r at T4 = -0.52, p > 0.01). Correlation matrix between all symptom and temperament variables is provided in Figure F1 (Supplementary material).

Trajectory Class Identification

LCMM model comparison revealed that the course of the AD subtype symptoms was better depicted by quadratic growth solutions, but linear growth for social phobia (see Table 2). Regarding the social phobia symptomatology, the 4-trajectory class model showed a better fit with mean of posterior probabilities in each class between 0.70 and 0.85.



Table 1 Scores in anxiety scales and temperament across the study measurement points

	Measurement point			
	T1	T2	Т3	T4
Anxiety				
Social phobia	11.63 (5.85)	10.27 (5.65)	9.98 (5.65)	9.56 (5.92)
Separation anxiety	2.53 (2.79)	2.33 (2.89)	2.03 (2.80)	1.87 (2.75)
GAD	7.67 (3.71)	7.07 (3.63)	6.44 (3.54)	6.27 (3.66)
Panic anxiety	6.06 (5.03)	5.75 (4.93)	5.51 (4.83)	5.06 (4.69)
Depression	7.95 (5.30)	7.99 (5.48)	8.08 (5.50)	8.24 (5.62)
Temperament				
NA	3.07 (0.53)	3.00 (0.57)	3.02 (0.57)	3.00 (0.57)
EC	4.41 (0.49)	4.43 (0.49)	4.42 (0.52)	4.40 (0.51)

Mean and standard deviations (between brackets) are displayed for each scale

Measurement points were scheduled each 6 months

GAD generalized anxiety disorder symptomatology, NA negative affectivity, EC effortful control

The four identified classes were (see Fig. 1): a class consisting of 54.92% (n = 452) of the sample (the so-called lowanxiety class or normative class) with decreasing levels of symptoms across assessment points due to a negative slope of time (B = -0.23, Wald's test with z = -5.20, p < 0.01);also, it identified a class made up of 24.91% (n = 205) of participants (the decreasing-anxiety class) with a significant intercept (all the estimates are displayed in the Supplementary table S2) and steep negative effect of time (time slope, B = -0.64, z = -5.04, p < 0.01). Participants classified into this class showed levels of symptoms surpassing the cutoff point of clinically relevant symptoms in the three first assessment points. Another class (the heightened-anxiety class), comprising 10.81% of sample (n=89), was identified. For this class, a significant intercept was observed, but time slope estimate was not significant (B = -0.05, z = -0.66, p = 0.51). Participants in this class showed clinically relevant levels of symptoms in all the assessment waves. Finally, the increasing-anxiety class was uncovered (n = 77). This class was featured by a significant intercept and positive time slope (B = 0.56, Wald's test with z = -5.20, p < 0.01), pointing to increasing levels of symptoms across assessment points. Participants in this class showed clinically relevant levels of symptoms from the second assessment point.

For generalized anxiety, the 2-class model (mean of posterior probabilities for each class between 0.79 and 0.90) under a quadratic shape fitted better than the nested growth solutions. Thus, it identified a group (the low-anxiety class or normative class) with 82.75% of participants (n = 681) and a significant intercept and a negative coefficient for the linear term of time (B = -0.54, Wald's test with z = -2.69,

Table 2 Mixed model solutions for the anxious symptomatology courses

	LL	CAIC	SABIC	%part		
Social phobia						
Linear growth						
Class = 1	-7590.44	15221.16	15202.10	100		
Class = 2	-7554.95	15170.32	15141.73	18.95-81.04		
Class = 3	-7547.76	15176.08	15137.96	9.23-62.94		
Class = 4	-7532.51	15165.74	15118.08	54.92-9.36		
Class = 5	-7524.46	15169.77	15112.58	3.52-53.95		
Class = 6	-7521.72	15184.44	15117.73	2.79-40.34		
Quadratic growth						
Class = 1	-7575.23	15185.84	15217.61	100		
Class = 2	-7538.42	15126.36	15170.83	17.62-82.38		
Class = 3	-7528.88	15121.43	15178.61	10.33-58.32		
Class = 4	-7528.88	15135.57	15205.46	0-54.43		
Class = 5	-7506.34	15104.66	15187.25	4.01-48.60		
Class = 6	-7490.44	15087.00	15182.30	3.64-49.80		
Generalized ar	nxiety					
Linear growt	h					
Class = 1	-6553.76	13147.80	13128.74	100		
Class = 2	-6538.27	13136.96	13108.37	15.67-84.33		
Class = 3	-6534.11	13148.79	13110.67	11.30-52.73		
Class = 4	-6534.11	13168.93	13121.28	0-64.64		
Class = 5	-6534.11	13189.07	13131.89	0-64.16		
Class = 6	-6508.77	13158.53	13091.82	2.55-44.59		
Quadratic gro	owth					
Class = 1	-6541.40	13149.94	13118.17	100		
Class = 2	-6524.50	13143.00	13098.53	17.25-82.75		
Class = 3	-6521.63	13164.12	13106.94	11.66-55.16		
Class = 4	-6512.20	13172.11	13102.22	1.58-55.04		
Class = 5	-6512.34	13199.26	13116.66	2.19-46.54		
Panic anxiety						
Linear growt	h.					
Class = 1	-7233.30	14506.88	14487.82	100		
Class = 2	-7142.45	14345.31	14316.72	16.30-83.70		
Class = 3	-7142.45	14365.45	14327.33	0-83.09		
Class = 4	-7142.45	14385.59	14337.94	0-83.09		
Class = 5	-7127.75	14376.34	14319.15	3.89-78.34		
Class=6	-7110.60	14362.18	14295.47	8.64-81.51		
Quadratic gro	owth					
Class = 1	-7228.92	14524.97	14493.20	100		
Class = 2	-7134.10	14362.18	14317.71	15.33-84.67		
Class = 3	-7093.65	14308.14	14250.95	7.30-83.21		
Class = 4	-7093.65	14334.99	14265.10	0-81.99		
Class = 5	-7134.10	14442.74	14360.14	0-81.39		
Class = 6	-7067.94	14337.27	14241.97	0-81.75		
Separation and	kiety					
Linear growth						
Class = 1	-6021.67	12083.62	12064.56	100		
Class=2	-6021.67	12103.76	12075.17	41.19–58.81		
Class = 3	-5888.79	11858.14	11820.02	0-95.26		



Table 2 (continued)

	LL	CAIC	SABIC	%part		
Class=4	-5888.79	11878.28	11830.63	0-94.90		
Class = 5	-5833.43	11787.71	11730.53	0-82.38		
Class = 6	-5833.43	11807.86	11741.14	0-81.89		
Quadratic gro	Quadratic growth					
Class = 1	-6010.43	12088.00	12056.23	100		
Class = 2	-6010.43	12114.86	12070.38	38.52-61.48		
Class = 3	-5876.07	11872.99	11815.81	0-95.14		
Class = 4	-5876.07	11899.85	11829.96	0-94.77		
Class = 5	-5876.07	11926.71	11844.11	0-94.77		
Class=6	-5818.95	11839.33	11744.02	0-84.08		

Models in bold face showed the best fit for each anxiety disorder symptomatology

For every criterion, the unconstrained solutions were modelled considering the time passage as predictor

LL maximum log-likelihood estimator for model convergence, CAIC consistent Akaike information criterion, SABIC sample-adjusted Bayesian information criterion, %part range of percentages of participants by trajectory classes

p < 0.01). Also, 17.25% of sample (n = 142) was assigned to the so-called heightened-anxiety (or at-risk) class, with no significant predictors (see Fig. 1). This means that heightened-anxiety class participants showed relatively same levels of panic symptoms across assessment points. Participants in this class showed clinically relevant levels of symptoms in all assessment waves.

On the other hand, the 3-class model under quadratic growth showed a better fit compared to the nested models, for panic anxiety course (mean of posterior probabilities in each class ranged from 0.81 to 0.96). The three identified classes were (Fig. 1): the so-called low-anxious or normative class (83.21% of sample, n = 684), showing a significant intercept and non-significant estimates for the time components (see the Table S2); the stable-anxiety class (9.49% of sample, n = 78), with no significant predictors. These results pointed to some stability (around the cut-off point for clinical meaningfulness) in symptom levels across assessment points for these two classes (low levels in the low-anxious class and elevated levels in the decreasing anxiety class, respectively). Finally, the increasing-anxiety class (7.30% of sample, n = 60) was uncovered. This class was featured by a significant intercept and a positive coefficient for the quadratic term of time (B=0.32, z=2.97, p<0.01), indicating an increasing pattern of symptoms across assessment points. Participants in this class showed clinically relevant levels of symptoms from the third assessment point.

Most of participants (65.90%) showed low-anxiety or decreasing-anxiety trajectories across the aforementioned AD subtypes of symptoms; 19.10% were classified into an at-risk trajectory class for one AD subtype of symptoms

(either increasing-anxiety, heightened-anxiety classes across AD subtypes or decreasing-panic anxiety class); 9.55% showed at-risk trajectories for two AD subtypes of symptoms (46.20% with at-risk social-phobia symptom and generalized-anxiety trajectory classes; 37.20% showing at-risk social-phobia symptom and panic symptom trajectory classes; and 16.70% with at-risk generalized-anxiety symptom and panic symptom trajectory classes). Finally, 5.45% of participants showed at-risk symptom trajectories in all the AD subtypes. Trajectory of each symptom classes across AD subtypes showed a similar shape after excluding individuals with at-risk trajectories in more than one of symptom subtypes (see Supplementary material).

With regard to separation anxiety symptoms, the 1-class model (under quadratic growth) fitted better than the other nested models. This model did not show significant predictors. Levels of separation anxiety symptoms were quite low and stable across the assessment points.

Risk Factor Analysis

Regarding the social phobia class membership, multinomial regression revealed that the model with predictors (AIC = 1017.55) fitted better than the unconstrained one (AIC = 1880.44). A significant effect of sibling cohabitation (reference category = living with siblings) was found for the increasing-anxiety class membership (in comparison to normative class membership), with relative risk ratio (RRR) = 0.35, Z = -2.02, p < 0.05. Sex (reference category = being boy) explained heightened-anxiety class membership, RRR = 7.83, Z = 3.76, p < 0.01. In terms of generalized anxiety class membership, again the model with covariates (AIC=418.27) fitted better than the unconstrained one (AIC = 758.98). However, no significant loadings of predictors were observed. Finally, panic anxiety class membership was better explained by the model with covariates (AIC = 541.45) in comparison to the unconstrained model (AIC = 938.89). In this case, sex was found to be significant when comparing the decreasing-anxiety class and the normative one, RRR = 3.14, Z = 2.95, p < 0.01.

Analyses excluding participants with at-risk symptom trajectories in more than one AD subtypes were conducted (see the Supplementary material). As a result, it uncovered a discriminant role of sex in symptom-trajectory class characterization for social phobia and panic anxiety. However, sibling cohabitation did not show differences across social phobia symptom trajectory classes.

MLGCM revealed a lack of measurement invariance for the EC and NA courses across AD-subtype symptom classes (see Table 3 and Supplementary Table S3, for parameters). In terms of EC, a lack of residual (fully constrained) measurement invariance was shown across social phobia trajectory classes (Δ CFI=-0.005; Δ RMSEA=0.000) and



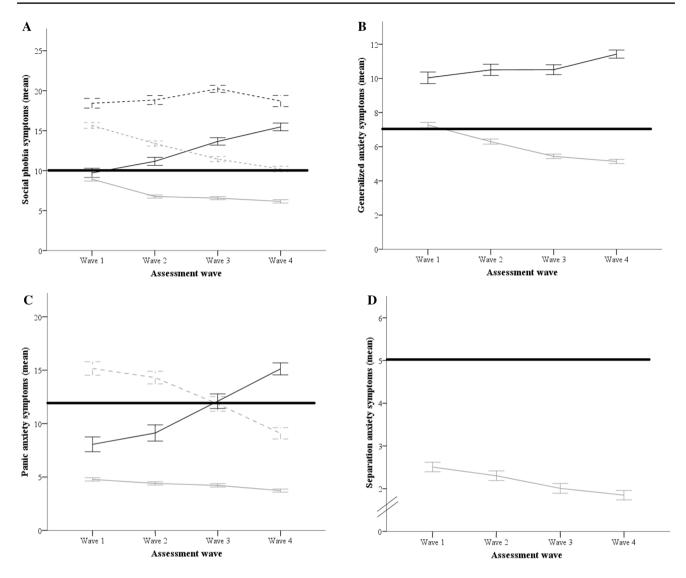


Fig. 1 Heterogeneous trajectories of anxious symptomatology in early adolescence. *Note* Figure in the **a** box depicts the trajectory of the social phobia classes. Figure in the **b** box depicts the trajectory of the generalized anxiety classes. Figure in the **c** box depicts the trajectory of the panic anxiety classes. Figure in the **d** box depicts the overall trajectory of the separation anxiety symptoms. Error bars depict

the standard error of the mean. Bold line=cut-off point for clinical symptomatology (see Chorpita et al. [55]). Dark dashed line=heightened symptom trajectory. Grey dashed line=decreasing symptom trajectory (stable symptom trajectory in the case of panic symptoms). Grey solid line=low symptom trajectory. Dark solid line=increasing symptom trajectory

across generalized anxiety trajectory classes, $\Delta CFI = 0.001$; $\Delta RMSEA = -0.004$ (see Fig. 2). This result indicates that different latent means and variances must be considered in terms of level and growth slope across social phobia and generalized anxiety symptom trajectories. This was related to observable scores across waves. By and large, participants classified into at-risk trajectory classes (either increasing-anxiety, heightened-anxiety classes or decreasing-panic anxiety class) showed lower levels of EC across assessment points.

Regarding the NA course, a lack of fully constrained invariance was shown for generalized anxiety trajectory membership, $\Delta CFI = 0.002$; $\Delta RMSEA = -0.005$; and

for panic anxiety class membership, $\Delta CFI = -0.001$; $\Delta RMSEA = -0.003$. Again, different latent means and variances must be considered in terms of level and growth slope across symptom trajectories. Moreover, participants showing at-risk trajectory classes (either increasing-anxiety, heightened-anxiety classes or decreasing-panic anxiety class) scored higher in NA across assessment points. On the other hand, a lack of mean constrained invariance was shown for social phobia trajectory membership, $\Delta CFI = 0.001$; $\Delta RMSEA = -0.005$. In this sense, latent means (but not latent variances) were found across symptoms trajectories. Social phobia at-risk trajectory class



Table 3 Model fit summary of multigroup models for the temperament factors

	χ^2 (df)	RMSEA (CI ₉₀)	CFI	TLI	SRMR
Effortful control					
Social phobia					
Unconstrained (linear)	73.66 (44)	0.079 (0.046, 0.110)	0.964	0.941	0.055
Unconstrained (quadratic)	69.07 (44)	0.073 (0.037, 0.104)	0.970	0.951	0.051
Constrained means (quadratic)	74.37 (50)	0.066 (0.031, 0.096)	0.971	0.959	0.052
Fully constrained (quadratic)	78.16 (56)	0.061 (0.022, 0.091)	0.973	0.966	0.055
Generalized anxiety					
Unconstrained (linear)	39.43 (22)	0.062 (0.028, 0.092)	0.979	0.965	0.045
Unconstrained (quadratic)	38.09 (22)	0.059 (0.024, 0.090)	0.980	0.968	0.043
Constrained means (quadratic)	40.03 (24)	0.056 (0.022, 0.085)	0.981	0.972	0.044
Fully constrained (quadratic)	40.42 (26)	0.051 (0.014, 0.081)	0.983	0.976	0.046
Panic anxiety					
Unconstrained (linear)	71.16 (33)	0.089 (0.060, 0.117)	0.954	0.925	0.054
Unconstrained (quadratic)	71.08 (33)	0.088 (0.060, 0.116)	0.955	0.927	0.053
Constrained means (quadratic)	78.67 (37)	0.084 (0.058, 0.110)	0.954	0.932	0.054
Fully constrained (quadratic)	84.06 (41)	0.082 (0.057, 0.107)	0.952	0.937	0.057
Negative affectivity					
Social phobia					
Unconstrained (linear)	68.33 (44)	0.072 (0.035, 0.104)	0.963	0.939	0.043
Unconstrained (quadratic)	69.76 (44)	0.074 (0.038, 0.106)	0.961	0.936	0.046
Constrained means (linear)	75.23 (50)	0.069 (0.033, 0.100)	0.961	0.944	0.049
Fully constrained (linear)	92.61 (56)	0.078 (0.048, 0.105)	0.945	0.93	0.068
Generalized anxiety					
Unconstrained (linear)	44.93 (22)	0.071 (0.041, 0.101)	0.966	0.944	0.04
Unconstrained (quadratic)	46.82 (22)	0.074 (0.044, 0.103)	0.963	0.940	0.045
Constrained means (linear)	47.83 (24)	0.069 (0.040, 0.098)	0.965	0.947	0.042
Fully constrained (linear)	48.07 (26)	0.064 (0.035, 0.093)	0.967	0.955	0.044
Panic anxiety					
Unconstrained (linear)	52.55 (33)	0.065 (0.028, 0.098)	0.970	0.951	0.041
Unconstrained (quadratic)	56.45 (33)	0.071 (0.037, 0.102)	0.965	0.942	0.044
Constrained means (linear)	59.28 (37)	0.066 (0.032, 0.096)	0.966	0.95	0.047
Fully constrained (linear)	63.25 (41)	0.063 (0.029, 0.092)	0.966	0.955	0.054

Models with a better fit are in bold face

All the growth solutions were modelled taking into account the influence of sex, age and depressive symptoms at baseline on temperament trajectories

members scored higher in NA across assessment points than normative class members (see Fig. 2).

Analyses excluding participants with at-risk trajectories in more than one AD subtype went in this same line (see the Supplementary material for further details).

Depressive Symptom Course and AD Symptom Trajectories

MLGCM revealed the lack of fully constrained measurement invariance when either generalized anxiety trajectory



All χ^2 -based tests were significant with a p < 0.05

 $[\]chi^2$ Satorra–Bentler χ^2 test, df degrees of freedom, RMSEA robust root mean square error of approximation index (scores below 0.080 depict reasonable model fit), CI confidence interval at 90%, CFI robust comparative fit index, TLI robust Tucker-Lewis index (scores of 0.95 or more indicate satisfactory model fitting, for TLI and CFI), SRMR standardised root mean square residual (scores above 0.080 depict poor fit)

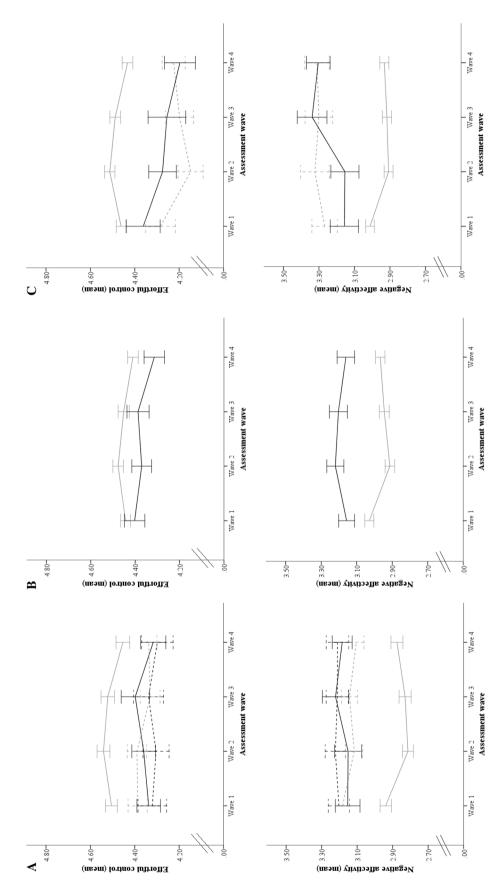
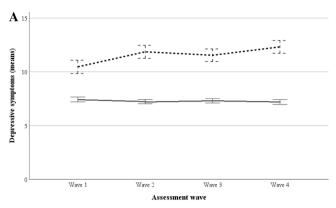


Fig. 2 Trajectories of temperament factors according to anxiety symptom class. Note. Figures in the a boxes depict the trajectory of effortful control (at the top) and negative affectivity (at the bottom) according to generalized anxiety class. Figures in the c boxes depict the trajectory of effortful control (at the top) and negative affectivity (at the bottom) according to panic anxiety class. Error bars depict the standard error of the mean. Dark dashed line=heightened symptom trajectory. Grey dashed line=decreasing symptom trajectory (stable symptom trajectory in the case of panic disorders). Grey solid line=low symptom trajectory. Dark solid line = increasing symptom trajectory





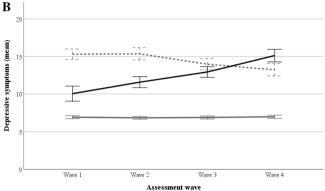


Fig. 3 Course of depressive symptoms according to generalized anxiety and panic trajectories. *Note*. Figure in the **a** box depicts the course of depressive symptoms according to generalized anxiety trajectory class membership. Figure in the **b** box depicts the course of depressive symptoms according to panic anxiety trajectory class membership.

ship. Error bars depict the standard error of the mean. Dark dashed line=heightened symptom trajectory. Grey dashed line=stable symptom trajectory. Grey solid line=low symptom trajectory. Dark solid line=increasing symptom trajectory

class or panic anxiety trajectory class were considered (see Fig. 3 and Table S4 in the Supplementary material). However, means of latent intercept and slope were not significantly different from zero across groups for both subtypes of AD symptoms (for generalized anxiety: constrained intercept, B = -4.02, SE = 7.51, Z = -0.53, p > 0.59; and slope, B = 2.85, SE = 2.29, Z = 1.24, p > 0.21; for panic classes: intercept, B = 2.80, SE = 6.28, Z = 0.45, p > 0.66; and slope, B = 3.31, SE = 2.43, Z = 1.36, p > 0.17). In other words, no difference in symptom course parameters could be revealed.

Analyses when removing overlapping, revealed the influence of social phobia trajectory membership and generalized anxiety disorder on depressive symptom course (see the Supplementary material for further details). At-risk trajectories for both subtypes of AD symptoms were associated with more elevated courses of depressive symptoms (in comparison to normative trajectories).

Discussion

This study aimed to depict the developmental course of anxiety symptomatology in early adolescence, from a person-centered approach. We conducted a 4-wave longitudinal study with assessments every 6 months to examine the person-specific trajectories of the different AD subtypes of symptoms. Further, we aimed to study the relationships of individual (i.e., sex and age), family composition and temperamental factors (negative affectivity and effortful control) with the adolescents' symptom trajectories. Finally, we were interested in studying the relationship of AD-specific symptom trajectories with depressive symptoms course in an attempt to address internalizing disorder comorbidity issues.

By and large, a decreasing overall trajectory of symptoms across the assessment points was uncovered. In this line, Weems [10] postulated that overall, undifferentiated anxiety decreases longitudinally overtime. Our results are consistent with some studies examining developmental trajectories of anxiety during early adolescence and showing similar decreasing patterns [8, 13].

Additionally, Weems [10] pointed to heterogeneous developmental trajectories of symptoms across AD subtypes. Accordingly, we found more than two different trajectory classes for social phobia symptoms, panic anxiety and generalized anxiety, underlying the overall developmental course. For all these subtypes of symptoms, we identified a low-symptom trajectory class, with most of participants showing low levels of symptoms across the assessment points; and at least a class with participants showing either increasing or heightened levels of symptomatology across assessment points (at-risk trajectories), with clinical levels in some points of assessment (see [55]). More concretely, we found that almost 35% of participants showed at-risk trajectories of symptoms. Note that we also considered the stable panic anxiety class as an at-risk trajectory because time effect was not significant in this class (i.e., members in this class showed sustained levels of symptoms, which were around the clinical meaningfulness cut-off point across assessment waves [55]). Trajectories showed similar shapes after removing individual at risk of higher symptoms across various AD subtypes.

The fact that we uncovered at-risk symptom trajectories for social phobia, generalized anxiety and panic anxiety may suggest early adolescence to be a crucial period in the development of these subtypes of AD. Conversely, a unitary trajectory depicted better the developmental course of separation anxiety symptoms over our studied period. According



to Weems [10], separation anxiety and animal fear symptoms are more characteristic in children aged 6–9 years. We uncovered a unitary trajectory of separation anxiety symptoms, which showed quite low levels across assessment points. In this vein, our results provide some support on maladaptive anxious emotion being manifested in other ways of expression in early adolescence (e.g., social phobia or generalized anxiety), as postulated Weems ([10] p. 491).

It could be surprising to see that our study revealed different classes of symptom trajectories for all criteria than other studies [15, 17, 56]. Even though comparability with these and other studies was quite limited for several reasons. First, it is important to consider that our study was focused on early adolescence. Early adolescence is featured by relevant maturational changes influencing emotion decoding and expression [20, 21]. Accordingly, a more fine-grained approach was followed by assessing participants every 6 months. Most of studies focused on anxiety symptom trajectories conducting assessments either annually or biannually (e.g., [7, 13]); this could mask the actual developmental course of anxiety symptoms. Second, most of studies covering early adolescence examined overall anxiety symptom trajectories (e.g., [11, 13, 57]), overlooking the heterogeneity of anxious emotion expression across adolescence (see [10]).

In terms of risk factor analysis, we found that sex (being girl) was related to membership in the heightened social phobia symptom trajectory class and the stable panic anxiety class. In other words, it seems that being girl was associated with at-risk trajectories of social phobia and panic anxiety symptoms. This result was consistent even after removing participants showing at-risk trajectories for various AD subtypes. Sex-related differences in AD have been shown more consistently than in other disorders [58], due to sex influence on all the biological processes involved in puberty and learning-derived social processing [19, 22]. Surprisingly, we found that sex did not show a significant explanatory role for the generalized anxiety at-risk trajectory. However, proportion of girls (65.49%) in this class was higher than boys. Some studies have reported similar results (i.e., the lack of sex influence on generalized anxiety in the early adolescence) [2, 59]. We speculated that a sex-related effect on generalized anxiety may be unfolded later in life (e.g., late adolescence). On the other hand, living with siblings was related to show an increasing trajectory of social phobia symptoms. This could be related to social avoidance learning at home, by peer modeling and imitation (see [24, 60]). Atrisk trajectory co-occurrence may also explain this effect, as it was no longer observed when removing individuals classified in at-risk trajectory class for two or more AD subtypes.

In terms of temperamental factors, it uncovered different courses of NA and EC across trajectories of social phobia, generalized anxiety and panic symptoms. These

findings show high level of robustness as sex- age and depression symptom-related effects were controlled on temperament course depiction. Additionally, these results remained similar after controlling for at-risk trajectory co-occurrence across AD subtypes. More concretely, social phobia and generalized trajectory classes were associated with varying trajectories of EC and NA across waves (i.e., attenuated EC and heightened NA across waves were observed for at-risk class participants). On the other hand, panic symptom trajectories were related to different NA courses (the at-risk trajectories were related to heightened NA courses). The lack of fit of the EC model considering panic symptom trajectory membership may account for differences in heterogeneous development shapes across both AD-subtype trajectory classes.

Our findings go in line with some evidence from community sample studies [26, 61, 62]. EC is a high-order component highly involved in self-regulation [63, 64]. Individuals with social phobia and generalized anxiety problems often show deficient emotion regulation strategies (e.g., poor recognition of emotions, recurrent avoidance of intense emotions), especially when dealing with social stimuli (see [65, 66]). We suggest that these common self-regulation deficits may mediate the onset of both full-blown disorders from atrisk trajectories of symptoms over the adolescence.

On the other hand, NA was proved to show a heightened course in individuals with at-risk trajectories of social phobia, generalized anxiety and panic anxiety symptoms. Our results support similar findings uncovered by studies considering NA (or related constructs) cross-sectionally [11, 12, 33]. All these AD subtypes share some expression features, especially those related to physiological activation and lack of affective flexibility (see [67–70]).

Regarding the relationship between AD symptom trajectories and depressive symptom course, we found that participants with at-risk trajectories of social phobia and generalized anxiety symptoms showed more elevated courses of depressive symptoms, when removing members with AD polyrisk (i.e., showing at-risk trajectories in more than one type of symptomatology). Depression and AD show many common risk factors (e.g., stressful events, NA) and symptoms (e.g., ruminative thoughts, low self-esteem), and some neurobiological and endocrine substrates (e.g., the cingulate cortex and the hypothalamus-pituitary-adrenals axis) are involved in both disorders (see [71–73]). In this line, we speculate that a reciprocal relationship exists between both types of AD symptoms and depressive symptom trajectories. The lack of association between panic trajectories and depression symptom course deserves a special mention. In this line, Cummings et al. [71] stated that relationships between panic and depression may be mediated by either physiological issues (e.g., depressive patients showed much lower levels of physiological arousal than those with panic



anxiety in) and comorbidity with other AD (i.e., separation anxiety).

To sum up, the developmental course of anxious symptomatology displayed a decreasing trajectory in early adolescence, but AD-specific symptomatology must be considered separately. Varying trajectories were identified for most AD-specific symptomatology. The role of sex and family factors were significant in depicting the person-specific trajectories of anxiety. Heightened NA and attenuated EC courses were related to at-risk trajectories of anxiety across assessment points. Finally, a relationship between social phobia and generalized anxiety symptoms with depressive symptom course was uncovered as an attempt to longitudinally study depression-anxiety symptom comorbidity.

Strengths, Limitations, and Directions for Future Research

As a main strength, this study provides a piece of evidence on how anxiety symptomatology evolves during a sensitive period for the development of ADs, following a person-centered approach. Moreover, monitoring adolescents every six months allows clinicians and researchers to uncover relevant emotional changes in anxiety symptomatology over time. This could otherwise have gone unnoticed if larger intervals between assessments (e.g., annual or biannual assessments) had been used. As a consequence, a more accurate picture on how anxiety evolves was obtained. Also noteworthy was the use of a robust methodological approach (relied on structural equation modeling) that provided strong support for our findings. Also in this regard, analysis of potential risk factors, some of them considered longitudinally (by means of the MLGCM), serves as a way to support trajectory class enumeration robustness (see [74, 75]). Finally, the subtypes of AD-specific symptom trajectory, not just overall anxiety, were addressed due to their relevance for development in adolescence.

As a limitation, this study was based on self-report assessments. This means that a partial view on how anxiety evolved over time was considered. However, some of our factors of interest (e.g., temperament, anxiety symptoms) are better studied using self-reports (see [76, 77]). Additionally, our instruments showed low-to-moderate levels of reliability, but similar to reference studies. Moreover, the sole use of self-reports to collect information on our relevant variables might bias the results obtained, due to common-method variance effect. Future studies should integrate other assessment sources to make assessment more accurate and valid (parent and teacher reports, etc.).

On the other hand, our sample was quite homogeneous in terms of race, ethnicity, and socioeconomic status. Moreover, our results relied on a high-functioning sample, due to they were recruited on a community basis. These issues may have implications for generalizability of findings to other populations. Furthermore, we did not analyze the influence of contextual factors (e.g., experience of bullying or peer relationships) on the course of anxiety symptomatology. While our interest was on the influence of individual and family factors, regular contextual events might predictably influence the maturing adolescents (e.g., the adjustment to school). However, further research should be conducted in order to determine how contextual events may affect the time course of anxiety. Similarly, biological correlates of maturational processes (e.g., scores on a maturity scale) could have been added to provide information on the specific stage of adolescence that each participant was. Age was our determinant in this regard. Nevertheless, further research should include more biological biomarkers of adolescent maturity. Finally, our MLGCM-based analyses did not allow studying measurement invariance at an item level (the so-called second-order MLGCM), because of sample size requirements. Future studies should extend results from this study on larger samples.

Adolescence is a crucial time for physical and psychological development, and it influences adult wellbeing and health. Our study provides some valuable evidence in terms of health promotion and prevention. For instance, the inclusion of therapeutic components targeting temperamental factors (e.g., EC and NA) in early intervention programs may be decisive to prevent the development of a full-blown syndrome. Moreover, therapeutic components to deal with family conflictive situations (e.g., conflicts between siblings) may contribute to hinder AD symptom escalation. Finally, intervention on AD symptoms may also lead to decreases in depressive symptoms due to symptom overlap and comorbidity.

Summary

This study highlights the individual-specific nature of anxiety symptomatology over the early adolescence, as well as its AD-specific nature, in terms of development. We found heterogeneous trajectories of social phobia, generalized anxiety and panic anxiety symptoms, respectively. More than 15% of adolescents showed at-risk trajectories across the aforementioned subtypes of anxiety symptoms. These results go in line with those pointing to heterogeneous developmental pathways of anxiety development in adolescence [1, 10]. Results remained similar after removing participants showing at-risk trajectories in two or more subtypes of symptoms. As explanatory factors, we found that sex (being girl) and a course of heightened NA and attenuated EC, in terms of temperament, were related to at-risk trajectories of anxiety across subtypes of symptoms. These findings go in line with those supporting that girls are at higher risk of anxiety



disorder development due to biological and socialization factors [19, 22]; and cross-sectional and other longitudinal studies pointing to strong relationships between higher negative emotionality trait and lower trait capacity to disengage from anxiety-related stimuli and anxiety disorder development [26, 30, 34, 35]. Finally, the at-risk trajectories of social phobia and generalized anxiety symptoms were associated with courses of more elevated levels of depressive symptoms, as a way to study depression-anxiety comorbid patterns. To conclude, this study provides some robust evidence towards the promotion of prevention programs to tackle with anxiety symptom escalation and temperament-based interventions in adolescence.

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Compliance with Ethical Standards

Conflict of interests The authors of this manuscript declare that they have no conflict of interests.

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