A body-mind map

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Trajectories of functional somatic, depressive and anxiety symptoms during adolescence and young adulthood

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ABSTRACT

Introduction: Functional somatic symptoms (FSS) frequently co-occur with depressive and anxiety symptoms in children, but it remains unclear how these symptoms simultaneously develop during adolescence. We studied how FSS co-develop with depressive and anxiety symptoms from late childhood to early adulthood in an explorative data-driven manner. We examined associations of this co-development with external factors.

Methods: We included 1,439 participants (56.4% female) of the Dutch TRacking Adolescents' Individual Lives Survey (TRAILS). FSS and depressive and anxiety symptoms were assessed with the Youth Self Report (11, 14 and 16 years) and the Adult Self Report (19, 22 and 26 years). Tucker 2 analysis was applied to capture heterogeneity across symptoms and persons to describe the co-development of symptoms. Correlations of different developmental patterns with sociodemographic characteristics, negative life events, and parenting style were computed.

Results: Symptom heterogeneity was decomposed into "functional somatic" and "depressive/anxiety" components. These symptom components followed similar as well as divergent developmental patterns from late childhood to early adulthood in specific individuals. Still, no person experienced increasing levels of the functional somatic and decreasing levels of the depressive/anxiety symptom component. Associations of developmental patterns with sociodemographic characteristics, negative life events, and parenting style were weak.

Conclusions: A parsimonious set of empirically derived components and their interactions explained a considerable part (explained variance=44%) of the variation of the co-development in FSS and depressive and anxiety symptoms. None of the external variables was associated with co-developmental patterns, indicating the complexity of the symptoms' development.

INTRODUCTION

Functional somatic symptoms (FSS) are somatic symptoms not conclusively explained by organic pathology [95]. The symptoms are reported by 25% of adolescents and can be greatly debilitating [96,97]. Furthermore, FSS have negative consequences for long-term mental health of youth [98]. FSS frequently co-occur with depressive and anxiety symptoms [51,99,100]. A review article concluded that a wide variety of FSS, including abdominal pain, headache, chest pain, musculoskeletal pain, and fatigue, were associated with an increased risk of depressive and anxiety symptoms in adolescents [51].

Three mechanisms have been suggested to explain the co-occurrence of FSS with depressive and anxiety symptoms in children and adolescents. The first mechanism is based on that many clinicians assume that children have difficulties recognizing and verbalizing emotions associated with depression and anxiety [49,50,101,102]. Still, children are aware of the physical sensations accompanying these emotions, which they are believed to present as FSS [95,101]. This concept is related to the condition of 'alexithymia' in adults (i.e., a reduced ability to experience, verbalize and differentiate between emotional feelings), but is believed to be a natural stage in the emotional development of children [103]. With naturally expanding emotional skills and maturation of brain areas during adolescence, reporting depressive and anxiety symptoms is believed to become easier for children [49,95,101,104]. This could be in line with the finding that at a population level the severity of FSS decreases during adolescence [96].

The second mechanism that could explain the association between FSS and depressive and anxiety symptoms includes that the symptom types directly cause and/or perpetuate each other [51]. One study investigated this mechanism in the large population sample of TRAILS and reported that depressive and anxiety symptoms predicted FSS after two years in adolescents, suggesting that they directly perpetuated the symptoms [105]. Although the reverse relation was less prominent [105], the predictive effect of FSS for depressive and anxiety symptoms has been indicated by other research [98].

The third mechanism suggested to underlie the co-occurrence is that FSS share risk factors with depressive and anxiety symptoms [51]. These could include genetic, hormonal as well as psychosocial factors [51]. Indeed, it has been shown that children with FSS and children with depressive and anxiety symptoms have other sociodemographic characteristics and have experienced a higher number of negative life events and a more negative parenting style compared to children without these symptoms [106-112]. Interestingly, these external factors have also been suggested to comprise the development of expression of affective states [49,113], suggesting that the relation of FSS with not fully developed affect expression could also be explained by common causes.

Although previous studies have given some clues about mechanisms that might underlie the co-occurrence of FSS with depressive and anxiety symptoms, much remains unclear about their specific role in the development of these symptoms. A first step to explore this is to examine the way FSS and depressive and anxiety symptoms co-develop from late childhood to young adulthood. For instance, the theory of changing affect expression would suggest that depressive and anxiety symptoms increase while FSS decrease during adolescence. If depressive and anxiety symptoms on themselves become more or less severe if a child matures, however, the explanation could lead to other developmental patterns (e.g., if depressive and anxiety symptoms decrease, one would expect to find a more extreme decrease in reported FSS levels). If FSS and depressive and anxiety symptoms directly reinforce each other, on the other hand, this would suggest that the symptom types follow similar developmental patterns such as parallel increasing or decreasing symptom levels. Finally, if the symptom types have common causes, parallel patterns would be expected with associations to sociodemographic characteristics, negative life events and/or perceived parenting style.

Although insight into the developments of FSS versus depressive and anxiety symptoms during adolescence is highly valuable to generate hypotheses about mechanisms underlying their co-occurrence, they have never been studied conjointly. This is important as developmental patterns of FSS and depressive and anxiety symptoms are heterogeneous. That is, it has been demonstrated that most FSS decrease during adolescence and young adulthood, but some types of FSS and particular individuals follow other developmental patterns (e.g., rising symptom levels for fatigue in girls [96,114]). Similarly, specific types of depressive and anxiety symptoms and persons show developmental patterns that differ from others (e.g., depressed mood increases while anhedonia decreases, with more prominent changes in girls than in boys [115]). To gain an understanding of the co-development of FSS and depressive and anxiety symptoms, it is therefore important to account for heterogeneity across symptoms and persons.

An analysis technique that distinguishes developmental patterns while capturing heterogeneity on different levels is Tucker 2 analysis [116,117]. This multi-way version of regular Principal Component Analysis (PCA) identifies a parsimonious number of components for symptoms and persons as well as their interactions in an integrated model [118,119]. As such, Tucker 2 can describe how persons differ in their developmental patterns on specific symptom domains [120,121]. An advantage of this technique compared to growth mixture models or latent class growth analysis is that is assigns flexible component scores rather than forcing symptoms or persons into specific trajectories. As the approach therefore allows each individual symptom and person to have a unique developmental pattern, the approach does more justice to the complexity of the development of FSS and depressive and anxiety symptoms in reality [121].

The current study explores the simultaneous development of FSS and depressive and anxiety symptoms during adolescence and young adulthood. Our main aim is to examine the association between changes in FSS and changes in depressive and anxiety symptoms while considering heterogeneity across symptoms and persons with Tucker 2 analysis. Secondly, we study the characteristics of developmental patterns by exploring their association with external factors.

METHODS

Participants

Data were derived from the TRacking Adolescents' Individual Lives Survey (TRAILS), a prospective cohort study of Dutch adolescents and young adults aiming to contribute to the understanding of the determinants of mental health and social development. The TRAILS study was approved by the Dutch Central Committee of Research Involving Human Subjects. Both parents and participants gave written informed consent. Detailed information about the study procedure is reported elsewhere [122].

Briefly, five municipalities in the North of the Netherlands were asked to give information from the community register of all citizens born between 1 October 1989 and 30 September 1990 (first two municipalities) or 1 October 1990 and 30 September 1991 (last three municipalities), yielding 3,483 names. All 135 schools within the municipalities were approached, and 123 (90.4%) agreed to participate. As school participation was a requirement for study participation, 3,145 adolescents were eligible for inclusion. A total of 210 of these adolescents were excluded due to mental retardation, a serious physical illness or handicap, or because they did not have a Dutch-speaking parent or guardian (except for Moroccan and Turkish parents, who were interviewed in their own language). Of all 2,935 adolescents who were approached for participation, 76.0% (N=2,230, mean age 11.1 years [SD=0.6], 51% female) participated in the first wave, which ran from March 2001 to July 2002. Follow-up waves were conducted every two to three years, with response rates of 96.4% at T2 (N=2,149, mean age 13.6 years [SD=0.5], 51% female), 81.4% at T3 (N=1,816, mean age 16.3 years [SD=0.7], 53% female), 84.3% at T4 (N=1,881, mean age 19.1 years [SD=0.6], 52% female), 79.7% at T5 (N=1,778, mean age 22.3 years [SD=0.7], 53% female), and 72.5% at T6 (N=1,617, mean age 25.7 years [SD=0.6], 55% female).

Participants with missing scores on all FSS and depressive and anxiety symptoms on more than one wave (N=791, 35.3%) were excluded from the study to avoid introducing bias by the multiple imputation procedure (see 'Missing data'). The main sample for this study therefore consisted of 1,439 participants. Excluded participants were less often

female (40.5% versus 56.4%, p<.001), older at study entry (11.2 versus 11.1 years, p<.001), and had lower baseline sum scores on the somatic (3.15 versus 3.25, p<.001), affective (3.26 versus 3.34, p<.001) and anxiety (1.89 versus 2.07, p<.001) problems scales than included participants.

Measures

FSS and depressive and anxiety symptoms

FSS and depressive and anxiety symptoms were assessed with self-report questionnaires from the Achenbach System of Empirically Based Assessment (ASEBA), using a version for adolescents (the Youth Self Report (YSR) [123]) at T1, T2 and T3 and a version for adults (the Adult Self Report (ASR) [124]) at T4, T5 and T6. The YSR and ASR have been shown to have high test-retest reliability and validity [123,124]. We included all items of the somatic problems scale (measuring somatic symptoms without a medical cause), the affective problems scale (measuring symptoms of DSM depressive disorders) and anxiety problems scale (measuring symptoms of DSM anxiety disorders) [125]. A total of 25 items were identical across the YSR and ASR and were included in the current study (see **Table 1**). Eight items (i.e. insomnia, fear of school, indecisiveness, feeling of failing, worry about the future, worry about family, palpitations and numbness or tingling in limbs) were not similar across scales and were therefore excluded. All symptoms during the past six months were scored on a 3-point scale (0='not at all', 1='a bit or sometimes', 2='a lot or often').

Due to a technical problem, the online version of the ASR at T4 (filled in by 82.3% of participants) assessed the somatic problems scale in a different way. In contrast to the other assessments, it included the screening question: "Did you experience any somatic symptoms without a medical cause?". If participants answered that they had never experienced such symptoms, the separate items on the somatic problems scale (i.e., dizziness, aches, headaches, stomachaches, nausea, eye problems, skin problems and vomits) were not shown to the participant and automatically scored as 'not at all'. As this resulted in lower scores on these symptoms at T4, we performed a sensitivity analysis (see 'Main analyses').

External factors

External factors included sociodemographic characteristics, negative life events, and perceived parenting style.

Table 1. Loadings of symptom components on specific symptoms.

	Functional somatic component	Depressive/anxiety component
Symptom	**Loading**	**Loading**
Headaches	**0.49**	0.00
Skin problems	**0.45**	-0.04
Stomachaches	**0.40**	-0.05
Vomits	**0.28**	-0.10
Aches	**0.28**	0.00
Dizziness	**0.21**	0.09
Nausea	**0.20**	-0.06
Overtired	-0.13	**0.42**
Worries	-0.03	**0.42**
Underactive	-0.07	**0.36**
Doesn't eat well	0.03	**0.28**
Nervous	0.14	**0.27**
Sad	-0.02	**0.27**
Sleep problems	0.10	**0.22**
Worthless	-0.03	**0.21**
Sleeps more	-0.05	**0.20**
Fears	0.14	**0.19**
Dependent	0.07	**0.17**
Cries	0.13	**0.16**
Fearful	0.07	**0.15**
Eye problems	0.14	0.06
Feels too guilty	0.13	0.10
Enjoys little	0.10	0.10
Talks suicide	0.05	0.03
Harms self	0.02	0.02

Loadings ≥0.15 are printed in bold font.

Sociodemographic characteristics

Sociodemographics of participants included sex and self-reported highest level of education at T6 (elementary education, lower tracks of secondary education, higher tracks of secondary education, senior secondary vocational training or higher vocational education/university). Socio-economic status of the parents was assessed by parent-report at T1 and T4 with the International Standard of Classification of Occupations, from which a self-computed standardized score by TRAILS was derived based on household income, education, and occupational level of both parents (higher scores indicate a higher parental socio-economic status) [126].

Negative life events

Whether participants had experienced parental divorce and/or the death of a parent or sibling was reported by parents at T1 and by participants at T2-T6 [127]. The experience

of sexual abuse, physical abuse or other trauma (e.g., having been involved in a life-threatening accident) ever during life was assessed at T4 with a questionnaire specifically designed for TRAILS [128] that was inspired by the Childhood Trauma Questionnaire [129].

Perceived parenting style

How participants perceived the style of parenting was measured with the overprotection, rejection and emotional warmth subscales of the Egna Minnen Beträffande Uppfonstran for Children (EMBU-C) [130] at T1. At T4, shortened versions of the rejection and emotional warmth subscales were assessed [131]. Average scores for perceived parenting style of the mother and the father were computed (ranging from 0 [lowest level of perceived overprotection, rejection and emotional warmth] to 4 [highest level of perceived overprotection, rejection and emotional warmth]).

Data analysis strategy

Missing data

Missing items were imputed in R version 3.4.3 with package Amelia II [132]. A total of 4.5% of data on FSS and depressive and anxiety symptoms were missing, which were imputed 20 times (for the analysis code, see https://www.researchgate.net/publication/336983768_Analysis_code_of_Chapter_2_Trajectories_of_functional_somatic_depressive_and_anxiety_symptoms_during_adolescence_and_young_adulthood). All analyses were conducted on each imputed dataset separately and summarized by averaging results and calculating their standard deviations across the imputed datasets to explore stability of the estimates.

Main analyses

To study the simultaneous development of FSS and depressive and anxiety symptoms, we applied Tucker 2 analysis [117]. This method summarizes heterogeneity in developmental patterns by identifying a limited set of components for symptoms and persons as well as their interactions in an integrated model. Interactions at each time point are summarized in a core array, from which basic patterns of the components can be obtained. The basic patterns function as standard developments by which numerous other developmental patterns occurring in the dataset can be described in a systematic way. Tucker 2 selects the basic patterns that can explain most variance in the dataset as opposed to developmental patterns that are most common or most extreme. Therefore, they can be interpreted as the processes that best summarize the heterogeneous developmental patterns of the symptoms in the dataset. Each symptom and person is assigned a component loading (measured on a continuous scale) indicating how much a symptom

or person follows the basic patterns characteristic for a specific component. This loading can be used to calculate developmental patterns for each symptom and person separately (positive loadings indicate developmental patterns in the same direction and negative loadings in the opposite direction as the basic developmental patterns in the component). As component loadings are non-standardized, no cut-offs for the interpretation of their absolute values are available. Rather, component loadings should be interpreted relative to each other. As Tucker 2 captures variation in item scores across participants and over time without assumptions about normality of the data, its results cannot be affected by skewed or low item scores in the dataset.

We conducted Tucker 2 analysis in R version 3.4.3 and Matlab version 2017b. Detailed information about the analytical procedure of Tucker 2 can be found elsewhere [117], and the analysis code used in this study is provided online **(**https://www.researchgate.net/publication/336983768_Analysis_code_of_Chapter_2_Trajectories_of_functional_somatic_depressive_and_anxiety_symptoms_during_adolescence_and_young_adulthood). First, we selected the number of components for symptoms and persons by balancing complexity with explained variance (% of explained sum of squares) using the generalized scree test in each imputed dataset [133]. The maximum number of components was set to six for symptoms and six for persons. Second, we applied the orthogonal Joint Orthomax rotation [134] to obtain interpretable component structures in each imputed dataset. Weights were set to 12.5 for symptom components (25 symptoms/2 symptom components, defined as “standard weight” [134]) and 0 for person components to maximize simplicity in the loadings on symptom components. Results were summarized over the imputed datasets using generalized Procrustes rotation [117,135,136]. Next, we explored the characteristics of the identified components. We inspected loadings of symptom components on individual symptoms and explored basic patterns of symptom and person components. Furthermore, we examined heterogeneity across persons in detail by inspecting their loadings on person components and calculating the developmental patterns of symptom components corresponding to these loadings. Associations of person components loadings with external factors were calculated using Pearson or Spearman correlations (absolute correlation coefficients of 0.1-0.3=weak, 0.3-0.5=moderate, >0.5-1=strong [137]). Finally, to test the effect of the screening question in the somatic problems scale at T4, we repeated the Tucker 2 procedure on data of all time points except T4 as a sensitivity analysis.

RESULTS

Sample characteristics

In our sample, 812 of the 1,439 (56.4%) adolescents were female and mean age at baseline was 11.1 (range=10.0-12.6) years (**Supplementary Table 1**). Mean symptom scores ranged from 0.0 for harms self at T5 to 0.7 for worries at T6 (scores ranging from 0-2).

Model selection

First, we selected the number of components. The generalized scree test indicated that the best balance of complexity and fit was found for the solution with two symptom and two person components (2,2-structure, mean fit=44.1% [ranging from 44.0% to 44.1% across the 20 imputed datasets]) and that with two symptom and three person components (2,3-structure, mean fit=45.7% [ranging from 45.7% to 45.8% in the different imputed datasets]). As the 2,3-structure had only 1.6% higher fit and the 2,2-structure was easier to interpret, the 2,2-structure was chosen.

Component characteristics

Subsequently, we applied the rotation to obtain better interpretable components and averaged results over the imputed datasets. Results were highly stable across imputed datasets, as reflected in small standard deviations (all <0.02) of the estimated component loadings.

Symptom components

The first symptom component was labeled the ‘functional somatic component’ as it had high loadings on somatic items without a medical cause such as headache and skin problems (**Table 1**). The second component was called the ‘depressive/anxiety component’ since it had high loadings on depressive and anxiety symptoms like sad and worries.

Person components

To interpret the developmental patterns that were identified, we first describe the person components that were found by the Tucker 2 analysis. Their basic patterns do not have any special value on their own but are standard developments from which the specific developmental patterns of individual participants can be constructed. We subsequently inspected loadings of all persons on the person components and explored their corresponding person-specific developmental patterns. Finally, associations of person components with external variables were examined.

Basic patterns

The first person component identified by Tucker 2 was called the 'parallel-course component'. Its basic pattern was characterized by moderate scores of the functional somatic component and the depressive/anxiety component at baseline, which both decreased over time (**Figure 1**). The second person component was called the 'divergent-course component'. The basic pattern of this component showed high baseline scores of the functional somatic component as well as the depressive/anxiety component. While scores of the functional somatic component decreased, those of the depressive/anxiety component increased.

Loadings and corresponding developmental patterns

Next, we inspected loadings of participants on the two person components. Loadings on person components differed considerably across participants (ranging from -0.12 to 0.11 on the parallel-course component and from 0.00 to 0.09 on the diverging-course component; **Figure 2**). Nearly all possible combinations of positive and negative loadings on the two person components were also found across persons, indicating that a high variety of developmental patterns was present in the dataset. Some examples of these developmental patterns include stable low scores of both symptom components (bottom panel in Figure 2), parallel increasing scores (left panel in Figure 2) and parallel decreasing scores of both symptom components (right panel in Figure 2), and decreasing scores of the functional somatic and increasing scores of the depressive/anxiety component (top panel in Figure 2). Despite the high number of combinations of loadings, negative loadings on the diverging-course trajectory did not occur. This indicates that variations of a trajectory with increasing scores of the functional somatic and decreasing scores of the depressive/anxiety component were absent.

Associations with external factors

In general, associations between loadings on the specific person components and external variables were weak (**Table 2**). Only the associations between diverging-course person component loadings and being female (r=0.34) and perceiving a rejective parenting style at T4 (r=0.31) were in the low range of moderate correlations. To explore whether these external factors were associated with specific combinations of loadings on the two person components, we inspected their distribution in a scatter plot (**Supplementary Figure 1**). No association with the combination of loadings on the two person components was observed.

Figure 1. Basic patterns in the parallel-course and diverging-course person component.

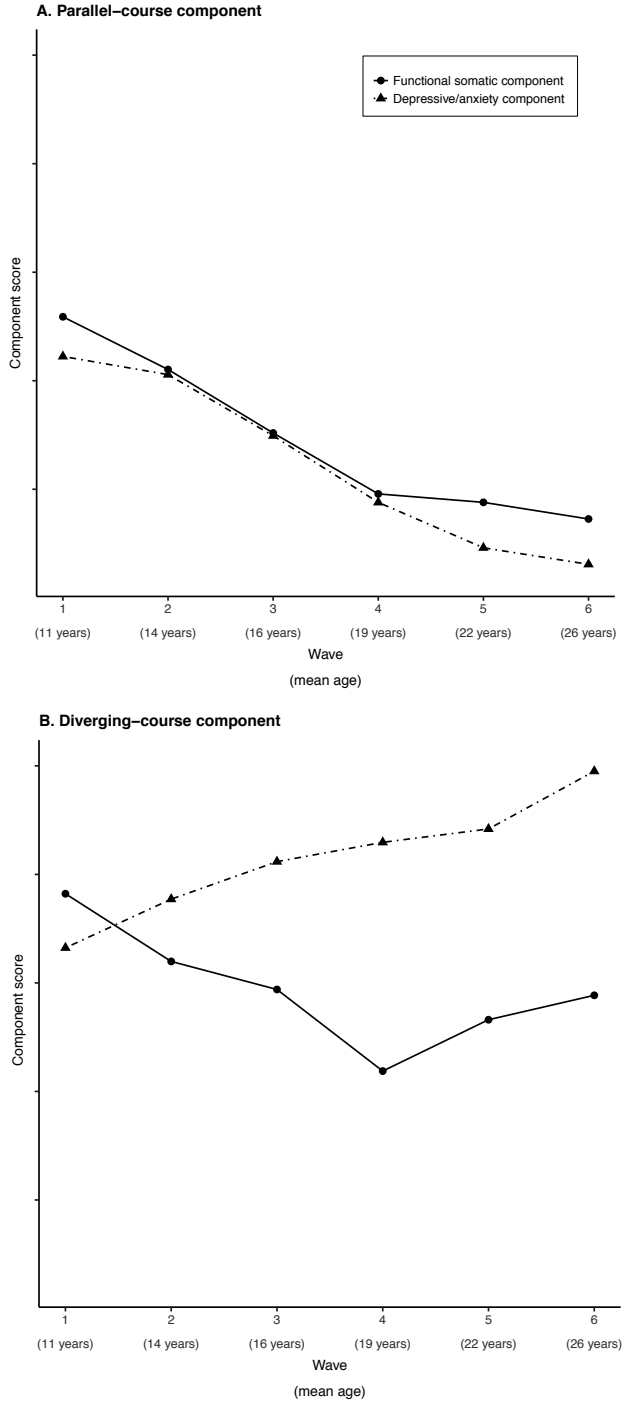
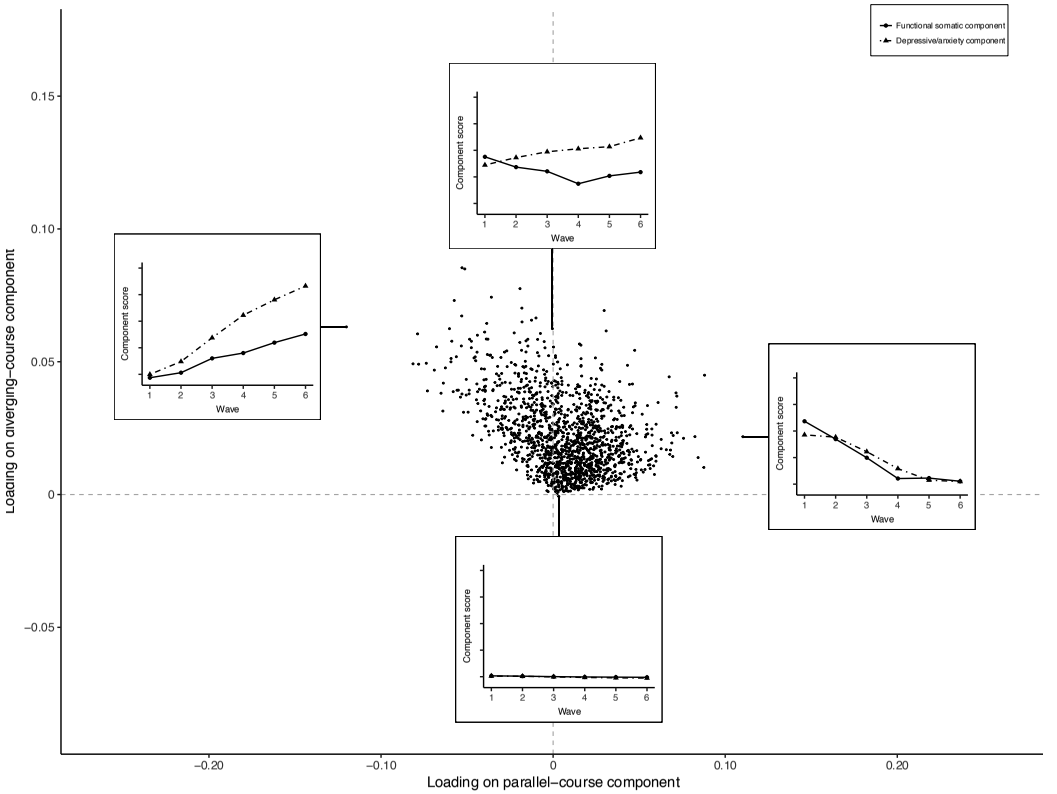


Figure 2. Loadings of specific participants on person components and their corresponding sets of developmental patterns.



The loadings of individual participants on the two person components are presented with dots. Four examples of trajectories corresponding to specific combinations of person component loadings are shown in the figure. Note that a high loading on the parallel-course component and a loading of 0 on the diverging-course component refers to the trajectory in **Figure 1A**, and a loading of 0 on the parallel-course component and a high loading on the diverging-course component to the trajectory in **Figure 1B**.

Table 2. Correlations of person component loadings with external factors.

	Parallel-course component loadings						Diverging-course component loadings					
	T1	**T2**	**T3**	**T4**	**T5**	**T6**	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**
Descriptive characteristics												
Sex (female)	-0.09						0.34					
Socio-economic status of parents	-0.01			0.01			-0.06			0.01		
Highest education						0.00						-0.08
Negative life events												
Parental divorce	-0.05	-0.06	-0.06	-0.05	-0.05	-0.05	0.09	0.09	0.09	0.09	0.09	0.10
Death of family member	-0.02	-0.03	-0.04	-0.05	-0.03	-0.02	0.04	0.05	0.06	0.07	0.08	0.06
Sexual abuse				-0.06						0.19		
Physical abuse				-0.09						0.21		
Other traumatic events				-0.01						0.13		
Perceived parenting style												
Overprotection	0.10						0.18					
Rejection	0.15			-0.09			0.16			0.31		
Emotional warmth	-0.07			0.03			-0.06			-0.17		

Correlations are presented for the wave at which an external variable was assessed (T1 to T6).

Sensitivity analysis

To examine the influence of the somatic problems scale screening question, we repeated the Tucker 2 analysis without T4 (**Supplement 1**). The results did not substantially differ. Still, given that the dip in scores of the functional somatic component at T4 in both person components disappeared, change became slightly more gradual over time.

DISCUSSION

This study identified different developmental patterns of FSS and depressive and anxiety symptoms from late childhood to early adulthood across persons. We found that nearly all possible patterns of parallel and divergent symptom co-development occurred in the dataset. However, a trajectory with increasing FSS and decreasing depressive and anxiety symptoms

was clearly absent. The developmental patterns did not show relevant associations with sociodemographic characteristics, negative life events, and perceived parenting style. Given the considerable proportion of explained variance by the model (explained variance 44%), the identified components and their interactions are highly valuable to summarize the complex co-development of FSS with depressive and anxiety symptoms.

An important strength of the current study is the prospective design in which assessments were conducted bi- to triennially for 15 years. Moreover, the population-based sample of 1,439 adolescents increased the generalizability of our results. Another strength is the use of Tucker 2 analysis, which allowed us to take into account heterogeneity of both symptoms and persons using a data-driven approach. The use of a data-driven algorithm to study symptom components is a considerable advantage given the conceptual overlap between FSS and depressive and anxiety symptoms that refer to the body (e.g., overtired) that complicates the categorization of these symptom before analysis. A limitation of the study is that the somatic problems scale of the ASR at T4 included a screening question, leading to lower symptom ratings at this wave. This may have led to a small drop in functional somatic component scores at T4 (age 19 years), but we showed that it did not affect the overall developmental patterns. Secondly, eight assessed FSS and depressive/anxiety symptoms could not be included in the analyses since they were not consistently measured across the YRS and ASR. Furthermore, all symptoms were assessed by self-report using the same instrument, which could have led to same-rater and same-instrument bias. We are also not certain that the self-reported FSS are indeed unexplained by somatic diseases. Still, the questionnaire clearly stated that the symptoms should occur without a medical cause or an obvious reason [123,124]. Moreover, scores on this scale were considerably higher than can be expected for explained symptoms given the low number of somatic diseases in the adolescent and young adult population [138].

This study is the first to examine the simultaneous development of FSS and depressive and anxiety symptoms from late childhood to early adolescence. The patterns of symptom development found in this study are comparable to previously found trajectories for FSS and depressive and anxiety symptoms separately. For example, that the functional somatic component followed stable, decreasing and increasing developmental patterns is in line with a previous TRAILS study using growth mixture models [114]. Similar developmental patterns of depressive and anxiety symptoms were also identified in other studies using growth mixture models [139,140]. As our study period was longer than in these studies (11-26 years as opposed to e.g. 11-17 years [114]), our findings provide insight into the continuation of these developmental patterns into young adulthood, which was characterized by similar changes in symptom levels as during adolescence. The use of Tucker 2 allowed us to capture more heterogeneity across persons than previous studies.

That developmental patterns differed considerably across persons indicates the strength of Tucker 2 to describe how these symptoms develop in varying patterns in real life [121]. We did not find relevant associations of symptom developmental patterns with external factors. Previous studies [110-112], some of which were based on the same sample [106,107,114,127,141], have found associations of these factors with trajectories of FSS and depressive and anxiety symptoms separately. Although these studies found statistically significant associations, the strength of associations in most studies was weak [110-112]. It is therefore not surprising that correlations of developmental patterns with external variables in the current study were also low. For some external variables, however, stronger associations with symptom trajectories have been identified in previous work [112,114]. For example, female sex has been associated with a five times increased risk of an unfavorable trajectory of FSS [114] and a two times higher risk of a unfavorable trajectory of depressive symptoms [142]. This inconsistency with our results could be explained by that previous studies focused on categories of extreme trajectories [112,114], while we identified components of developmental patterns along which persons and symptoms could vary. That we did not find relevant associations with external factors indicates that the symptoms' co-development is more complex than can be explained with such external factors alone. This contrasts with the development of cognitive depressive symptoms alone, which has been shown to be captured for a large part by scores on neuroticism [143]. This illustrates the value of the identified components and their interactions by Tucker 2 to summarize the way FSS and depressive and anxiety symptoms co-develop during adolescence.

The found developmental patterns of FSS and depressive and anxiety symptoms in this study could point to several potential mechanisms underlying their co-occurrence. First, they might be in line with the theory of developing affect expression during adolescence [49,95,101]. This theory could explain that some adolescents reported decreasing FSS and increasing depressive and anxiety symptoms while they matured. Depressive and anxiety symptoms can also become more or less severe over time on themselves [112] and, therefore, some adolescents could have experienced parallel increasing or decreasing FSS and depressive and anxiety symptoms even though their emotion expression skills developed. Supporting this suggestion is that within parallel developmental patterns, scores on the functional somatic component showed a less extreme increase or more prominent decrease than those of the depressive/anxiety component (as indicated by that negative and positive loadings on the parallel-course component occurred in combination with relatively high positive loadings on the diverging-course component). On the other hand, if no depressive or anxiety symptoms were present throughout the life of an adolescent, stable low symptom levels would have occurred.

Although other suggested mechanisms cannot explain all developmental patterns, it is possible that specific mechanisms underlie the co-development of the symptom

types in particular individuals. The diverging trajectory could for instance result from the presence of factors that negatively influence depressive and anxiety symptoms but not FSS. The parallel-course developmental patterns, in contrast, could be explained by two mechanisms. One possible mechanism is that FSS directly cause or perpetuate depressive or anxiety symptoms or vice versa [51]. Another mechanism that may underlie the parallel developmental patterns is that FSS and depressive and anxiety symptoms have common causes [51,110]. Although our findings indicated that sociodemographic characteristics, negative life events and perceived parenting style probably do not have a central role in this mechanism, it is possible that FSS and depressive and anxiety share genetic, hormonal or other psychosocial risk factors [51]. That the parallel developmental patterns were characterized by gradual changes over time rather than sudden changes suggests that age-independent factors such as insecure attachment constitute a more likely involved factor in this context than age-dependent risk factors such as pubertal hormonal changes [111].

As much remains unknown about the mechanisms underlying the co-occurrence of FSS and depressive and anxiety symptoms in adolescents, more research is warranted. Although previous studies have linked affect expression dysfunction to FSS [50,103,144] and depressive and anxiety symptoms [145-147], we are not aware of any studies that examined the relation between emotional development and patterns of FSS and depressive and anxiety symptoms in adolescents. This would be especially important as the previous literature is not conclusive about whether inadequate affect regulation and expression is a cause of, mediator of, or result of shared risk factors with the co-occurrence of FSS with depressive and anxiety symptoms [103]. As no assessments of language or cognitive development were conducted in TRAILS, we were not able to study it directly. One important direction for future studies is therefore to measure emotion regulation and expression skills as well as FSS and depressive and anxiety symptoms from early childhood onwards, as the development of important aspects of emotion understanding and expression occurs between early childhood and late childhood [148].

CONCLUSIONS

In summary, the current exploratory study demonstrated that FSS and depressive and anxiety symptoms show varying patterns of co-development from late childhood to young adulthood. More research is needed to investigate the mechanisms we hypothesized to underlie this co-developmental relation. One interesting direction for future studies is to directly measure development in emotion regulation and expression skills and examine if it is related with the onset and course of FSS and depressive and anxiety symptoms.

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Sample characteristics (N=1,439).

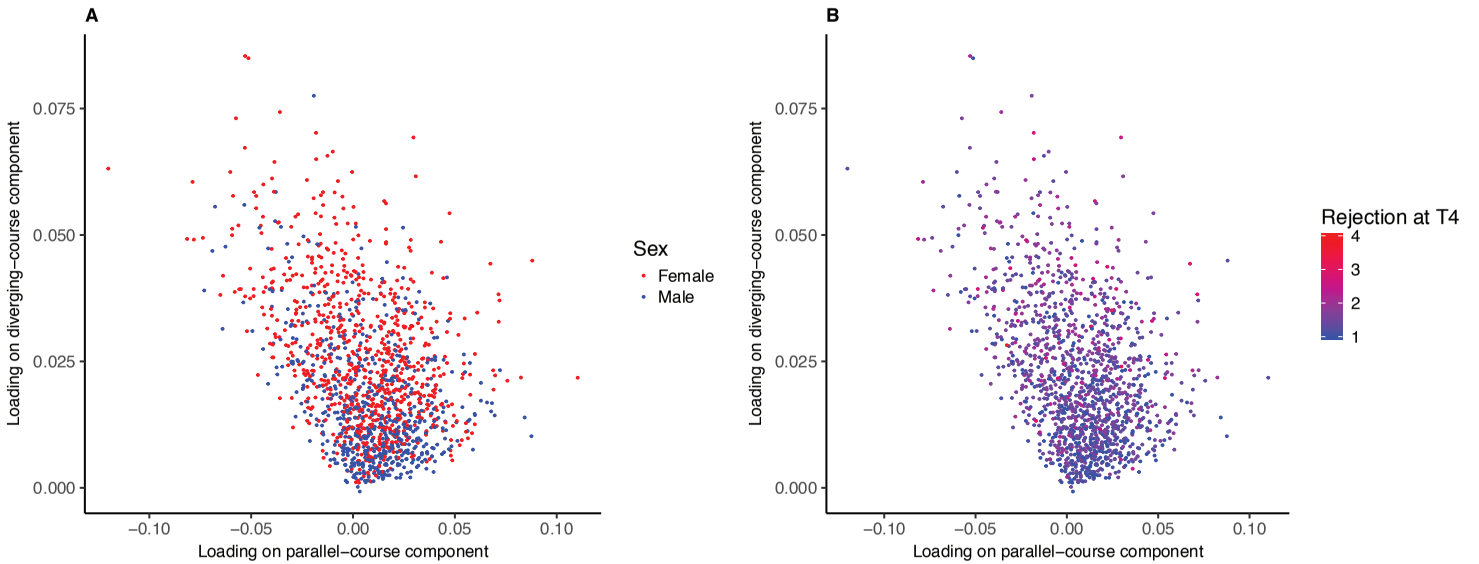
	T1	T2	T3	T4	T5	T6
	N (%)/Mean (range*)					
Symptoms (scores ranging from 0-2)						
Dizziness	0.36	0.39	0.35	0.26	0.22	0.26
Aches	0.44	0.28	0.25	0.13	0.19	0.23
Headache	0.75	0.61	0.53	0.17	0.44	0.47
Stomach ache	0.52	040	0.32	0.12	0.20	0.21
Nausea	0.27	0.05	0.06	0.03	0.05	0.08
Eye problems	0.28	0.23	0.23	0.09	0.21	0.30
Skin problems	0.64	0.47	0.35	0.14	0.27	0.30
Vomits	0.33	0.14	0.08	0.04	0.06	0.06
Enjoys little	0.30	0.23	0.22	0.17	0.17	0.24
Cries	0.42	0.31	0.29	0.31	0.34	0.32
Harms self	0.04	0.06	0.05	0.03	0.02	0.03
Doesn’t eat well	0.41	0.44	0.46	0.48	0.46	0.58
Worthless	0.21	0.20	0.20	0.22	0.24	0.32
Feels too guilty	0.33	0.27	0.22	0.19	0.20	0.25
Overtired	0.23	0.43	0.53	0.49	0.58	0.61
Sleeps more	0.24	0.15	0.20	0.29	0.29	0.34
Talks suicide	0.09	0.09	0.07	0.05	0.05	0.07
Sleep problems	0.44	0.34	0.38	0.37	0.45	0.45
Underactive	0.35	0.36	0.43	0.44	0.49	0.57
Sad	0.29	0.29	0.29	0.34	0.32	0.43
Dependent	0.34	0.37	0.33	0.31	0.30	0.38
Fears	0.50	0.61	0.34	0.49	0.41	0.39
Nervous	0.56	0.59	0.52	0.50	0.43	0.60

Supplementary Table 1. Continued.

	T1	T2	T3	T4	T5	T6
	N (%)/Mean (range*)					
Fearful	0.29	0.23	0.19	0.20	0.20	0.30
Worries	0.37	0.58	0.67	0.54	0.57	0.68
Sociodemographic characteristics						
Sex (female)	812 (56.4%)					
Age (in years)	11.08 (10.0-12.6)	13.52 (12.2-15.0)	16.23 (14-7-18.4)	19.01 (18.0-20.9)	22.25 (21.0-24.1)	25.63 (24.4-27.3)
Socio-economic status of parents	0.12 (-1.8-1.7)			-0.02 (-2.2-1.4)		
Highest education						
Elementary education						11 (0.8%)
Lower tracks secondary education						57 (4.0%)
Higher tracks secondary education						41 (2.8%)
Senior secondary vocational						443 (30.8%)
Higher vocational/university						887 (61.6%)
Negative life events						
Parental divorce	247 (17.2%)	301 (20.9%)	348 (24.2%)	388 (27.0%)	424 (29.5%)	445 (30.9%)
Death of family member	42 (3.1%)	56 (3.9%)	66 (4.6%)	81 (5.6%)	105 (7.3%)	128 (8.9%)
Sexual abuse				131 (9.1%)		
Physical abuse				387 (26.9%)		
Other traumatic events				350 (24.3%)		
Perceived parenting style						
Overprotection	1.83 (1.0-3.5)					
Rejection	1.48 (1.0-3.5)			1.46 (1.0-4.0)		
Emotional warmth	3.24 (1.1-4.0)			3.16 (1.0-4.0)		

*Range of all symptoms was 0-2.

Supplementary Figure 1. Distribution of A) sex and B) perceived parental rejection at T4 across different combinations of loadings on the two person components.



Supplement 1. Sensitivity analysis

To examine whether the screening question in the somatic problem scale at T4 had altered our conclusions, we repeated the Tucker 2 procedure excluding this wave. In line with the main analyses, a 2,2-structure was chosen.

Components

Symptom components
Similar to the main analyses, a functional somatic component and a depressive/anxiety component were found (**Supplementary Table 2**). Loadings were highly comparable to those found in the main analyses.

Person components
Person components included a parallel-course component and an diverging-course component, with similar basic patterns as in the main analyses (**Supplementary Figure 2**). As the dip in the functional somatic component at T4 disappeared in both person components, the decrease in this symptom component over time was more gradual than in the main analyses.

Supplementary table 2. Loadings of symptom components on specific symptoms in the analyses excluding T4.

	Functional somatic component	Depressive/anxiety component
Symptom	**Loading**	**Loading**
Headache	**0.44**	0.01
Skin problems	**0.43**	-0.06
Stomach ache	**0.39**	-0.07
Vomits	**0.28**	-0.14
Aches	**0.28**	-0.03
Dizziness	**0.23**	0.06
Fears	**0.23**	0.11
Nausea	**0.20**	-0.08
Cries	**0.17**	0.12
Overtired	-0.12	**0.45**
Worries	-0.02	**0.45**
Underactive	-0.05	**0.37**
Doesn't eat well	0.07	**0.26**
Nervous	**0.18**	**0.24**
Sad	0.00	**0.26**
Sleep problems	0.13	**0.20**
Worthless	-0.02	**0.22**
Sleeps more	-0.03	**0.19**
Dependent	0.09	**0.16**
Feels too guilty	0.14	0.09
Eye problems	0.11	0.08
Enjoys little	0.10	0.09
Fearful	0.08	0.14
Talks suicide	0.05	0.03
Harms self	0.03	0.02

Loadings ≥0.15 are printed in bold font.

Supplementary figure 2. Basic patterns in specific person components in the analyses excluding T4.