Trajectories of change in symptom distress in a clinical group of late adolescents: The role of maladaptive personality traits and relations with parents

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ABSTRACT

In this study, it was analysed whether trajectories of change in symptom distress could be identified in a clinical group of late adolescents with personality pathology. Furthermore, it was examined whether maladaptive personality traits and relations with parents were predictive of following one of these trajectories. Three latent classes emerged from growth mixture modelling with a symptom inventory (n = 911): a Stable High, a Strong Decreasing and a Moderate Decreasing trajectory. Subsequently, by using multinomial logistic regression analyses in a subsample of late-adolescents (n = 127), it was revealed that high levels of Negative Affectivity and Detachment were predictive of following the Strong Decreasing, and high levels of Detachment were predictive of following the Stable High trajectory. Support from or Negative Interactions with parents were not predictive of any of the trajectories. The current results contribute to the notion of individual trajectories of change in symptom distress and provide suggestions for screening patients on personality traits to gain insight in the course of this change. © 2018 The Authors Personality and Mental Health Published by John Wiley & Sons Ltd

Introduction

Adolescents differ with regard to change of symptom distress while receiving psychological care, such that divergent change trajectories may be distinguished[1–4]. Little is known, however, with regard to which specific factors contribute to individual differences in change in symptom distress. Several factors have been proposed, including pretreatment severity of the disorder[5], the therapeutic relationship[6] and the type of psychological care received[7]. However, as there is little evidence for superiority of one intervention over the other[8,9], both dispositional tendencies of the patient as well as contextual elements may be of additional interest for a deeper understanding of divergent change trajectories in youth. Especially because severity of psychopathology is strongly associated with specific personality traits, as well as with environmental adversities, a closer look at the specific role of maladaptive personality traits[10–12] and the individual's

social network[4,13,14] may increase our knowledge on why some adolescents recover more than others.

Associations between maladaptive personality traits and symptom distress

It is increasingly acknowledged that personality pathology is best described using a dimensional approach[15]. Although research using dimensional measures of personality pathology and relating this to change in symptom distress is limited, studies including five factor model-related trait measures showed that the combination of high Neuroticism, low Agreeableness, low Conscientiousness and low Extraversion is associated with higher levels of symptom distress[16]. Additionally, it has been shown that personality traits, especially emotional stability, are important predictors of treatment effect[9]. Moreover, these findings have been confirmed from a maladaptive trait perspective, indicating that especially high levels of Negative Affectivity are related to experiencing more distress[17,18].

Associations between parental relationship quality and symptom distress

In addition to (maladaptive) personality, social relations may be related to individual differences in symptom change. Specifically, experiencing support from parents may be an important determinant of decreases in symptom distress, for example, by promoting compliance with treatment[19,20], while conflict with parents may contribute to increased levels of symptom distress. However, evidence for such a link is limited and even less is known with regard to unique and potential complementary relations with mothers vs. fathers[21]. When looking at studies on more general psychological symptoms, some studies found a comparable impact of maternal versus paternal relations[22,23], whereas others found that support from mothers was most effective[24,25]. Alternatively, support from fathers has been

suggested to be more important, as mothers may have the tendency to co-ruminate with rather than support their child[26]. From a dynamic perspective, the effects of parental relationship quality may also interact with the effects of maladaptive personality traits. Previous research has suggested that patients with high levels of maladaptive traits who are involved in positive social interactions show an improved adjustment compared with patients who do not experience positive social interactions[27]. Therefore, a perspective considering both the unique and interactional effects of maladaptive personality and parental relationship quality is needed to increase our understanding of change in distress.

Current study

The first goal of this study is to examine trajectories of change in symptom distress in a clinical group of late adolescents with personality pathology. In line with previous findings on trajectories of symptom change in adults and adolescents[1–4], it is expected that different trajectories can be distinguished, with at least one that shows a decrease and one that shows no or very little decrease over time. In addition, preliminary evidence has outlined the role of individual (i.e. maladaptive traits) and contextual (i.e. social relations) factors, as well as their combined effects, on changes in symptom distress. Therefore, the second goal of this study is to examine whether and how maladaptive personality traits and relations with parents are predictive of trajectories of change in symptom distress. It is expected that patients with higher levels of maladaptive traits, and especially higher levels of Negative Affectivity, show high levels of symptom distress. Specifically, it is expected that higher levels of Negative Affectivity are related to a smaller decrease in symptom distress. Given the inconsistent results on social relations and psychological symptom distress, these associations will be explored.

Methods

Participants

For its first goal, the current study relies on a sample of 911 late-adolescent patients of the mental health institute Reinier van Arkel, who provided repeated measures of symptom distress (M_{age} = 20.2, SD = 2.4; 33% men). For its second goal, the current study relied on a subsample of patients who participated in a previous study and for whom maladaptive trait reports as well as parental relationship quality reports were additionally available (n = 127, M_{age} = 20.9 SD = 2.4; 27% men). This enabled us to explore how trajectories of change in symptom distress were related to dispositional and contextual factors. For a detailed sample description of this subsample, see Hessels, van Aken, de Castro, Laceulle, & van Voorst, (2016)[28]. Patients in this subsample received different kinds of psychological care, with 68 (54%) receiving some form of psychotherapy, and 50 (39%) receiving case-management, resulting from multidisciplinary guidelines on clinical decision making[29]. For nine patients (7%), no information regarding type of psychological care was available.

Procedure

The collection of routine outcome monitoring (ROM) data is a frequently used method in clinical practice in which a patient's treatment outcome, including symptom distress levels, is assessed at regular intervals[30]. For our study sample (n = 911), these intervals were on average 6 months. With regard to the subsample, in the period from September 2012 to October 2013, all new patients (n = 127) were invited to participate in an online study on personality pathology and social relations. The time between the base rate ROM measurement and the online survey was on average 2 months (SD = 6.2).

Measures

Symptom distress. All patients completed the Brief Symptom Inventory[31] as part of the ROM at four consecutive time points. The Brief Symptom Inventory is a 53-item self-report inventory in which patients rate their experience of symptom distress in the past week on a 4-point scale. The mean of the total items can be computed as the Global Severity Index (GSI) of symptom distress. Cronbach's alpha for the 51-item GSI score ranged from 0.96 to 0.97 across the four waves.

Maladaptive personality traits. The subsample of 127 patients completed the Personality Inventory for DSM-5[32,33], which measures an individual's level of maladaptive personality traits. The Personality Inventory for DSM-5 is a 220-item questionnaire and answers are given on a 4-point response scale. Five broad scales are distinguished, which are constructed from the three most defining facets: Negative Affectivity (23 items), Detachment (24 items), Antagonism (21 items), Disinhibition (22 items) and Psychoticism (33 items). Cronbach's alpha ranged from 0.88 to 0.94 across the five scales.

Quality of relationships with mother and father. Support (five items) and conflict (six items) in relations with parents was assessed in the subsample of 127 patients, relying on the Dutch translation of the Network of Relationships Inventory-Behavioural System Version[34,35]. Answers are given on a 5-point response scale. Cronbach's alpha ranged from 0.93 to 0.97 across scales and informants (fathers and mothers).

Data analytic strategy

First, data of the overall sample (n = 911) were used to determine the trajectories of change in symptom distress. Second, data of the subsample (n = 127) were used to examine the predictive value of maladaptive personality traits and parental relationship quality for the likelihood to display each of the defined change trajectories. Missing data in the full sample were handled by using robust maximum likelihood estimation in

Mplus and in the subsample with Relative Mean Substitution[36] in SPSS.

First, a latent growth curve model was analysed to determine whether change in the overall sample was best represented by a linear or a quadratic slope. Then, it was examined whether groups with different growth trajectories could be identified based upon the longitudinal trends, by assigning participants to different latent classes. Because individuals within groups might not follow strict homogeneous trajectories of change, a model allowing individual variation in both the intercept and linear slope within the latent classes was tested[37]. The final number of classes was determined by analysing which model best fit the data, based on a significant bootstrap likelihood ratio test, the lowest Bayesian information criterion (BIC) value, the difference in Akaike information criterion (AIC), a significant Lo–Mendell–Rubin likelihood ratio test (LMR-LRT), the highest posterior probabilities and logical reasoning[38,39]. Second, patterns of change in symptom distress were analysed using growth mixture modelling and class membership to the differential growth trajectories was saved. Third, descriptive statistics and bivariate correlations between the maladaptive personality traits and relations with parents were computed for the subsample in SPSS. Fourth, maladaptive traits and relations with parents were entered as predictors of class membership of the trajectories in multinomial logistic regression analyses, which controlled for the effect of treatment type and gender.

Results

Trajectories of change in symptom distress

The descriptive statistics of the general severity scores of the overall sample (n = 911) are presented in Table 1. Paired-samples *t*-tests showed that from wave 1 to wave 2 and from wave 2 to wave 3, the mean GSI-scores declined significantly *t* (M_{T1} = 1.27, M_{T2} = 1.04, d.f. = 614) = 9.46,

Table 1: Means and standard deviations of the general severity scores, maladaptive personality traits and parent support and conflict

		M	SD
Total sample	GSI_{T1}	1.24	0.68
	GSI_{T2}	1.04	0.67
	GSI_{T3}	1.05	0.68
	GSI_{T4}	1.04	0.69
Subsample	Negative Affectivity	2.73	0.51
	Detachment	2.18	0.53
	Antagonism	1.76	0.48
	Disinhibition	2.30	0.46
	Psychoticism	1.95	0.49
	$Support_{Mother}$	3.04	0.88
	$Conflict_{Mother}$	2.63	1.08
	$Support_{Father}$	2.47	0.98
	$Conflict_{Father}$	2.54	1.17

$p < 0.001$ and *t* (M_{T2} = 1.13, M_{T3} = 1.05, d. f. = 348) = 2.97, $p = 0.003$ respectively, but not from wave 3 to wave 4 *t* (M_{T3} = 1.11, M_{T4} = 1.04, d.f. = 187) = 1.80, $p = 0.067$. First, the fit of a Latent Growth Curve Model with a linear slope was analysed. The basic linear model produced an adequate fit; χ^2 = 34.08, $p < 0.001$, RMSEA = 0.080, CFI = 0.929. However, a model with both a linear and a quadratic slope fitted the data significantly better; Satorra–Bentler Scaled χ^2 = 29.79, $p < 0.001$; χ^2 = 4.17, $p = 0.041$, RMSEA = 0.059, CFI = 0.992. Analyses were continued with a model with a linear and a quadratic slope.

To identify trajectories of change in symptom distress, a Growth Mixture Model with ascending numbers of classes was fitted to the data. To increase interpretability, the quadratic slope was fixed to zero. In comparing the model fit between a 1-class (BIC: 3699.49), a 2-class [BIC: 3646.42, LMR-LRT: 77.50 ($p = 0.015$), Entropy: 0.67], a 3-class [BIC: 3610.66, ΔAIC = 55.03, LMR-LRT: 60.80 ($p = 0.024$), Entropy: 0.69] and a 4-class [BIC: 3616.09, ΔAIC = 13.84, LMR-LRT: 21.07 ($p = 0.840$), Entropy: 0.67] solution, a 3-class solution was selected as best fitting the data. This solution made the most valuable

distinction between classes based on statistical considerations and interpretability. The mean posterior probabilities of the three trajectories are presented in Table 2 and indicate a substantial separation among the profiles.

Also presented in Table 2 are the estimated parameters of the intercept, linear and quadratic slope of the trajectories (Figure 1). For descriptive purposes, we labelled the latent trajectories as Stable High ($n = 138$, 15%), starting with relatively high severity of symptom distress scores that do not change over time, Strong Decreasing ($n = 115$, 13%), starting with high severity scores that first decrease in a linear fashion that after some time is levelled out by the effect of a positive quadratic slope, and as Moderate Decreasing ($n = 658$, 72%), starting with moderate severity scores that moderately decrease in a linear way over time. ANOVA results showed that the three groups differed significantly from each other at the four time points [T_1: $F(2,908) = 712.48$, $p < 0.001$; T_2: $F(2,612) = 301.51$, $p < 0.001$; T_3: $F(2,346) = 195.43$, $p < 0.001$, T_4: $F(2,185) = 107.80$, $p < 0.001$; Table 3]. To increase interpretability of these trajectories in terms of the kind of patients they may represent, the percentage of patients with severe personality pathology in each trajectory was analysed (diagnosed and deferred). This was 93% of the patients in the Stable High, 87% in the Strong Decreasing and 73% in the Moderate Decreasing trajectory.

Maladaptive traits and relations with parents as predictors of the trajectories of change

Analyses on the predictive role of maladaptive traits and relations with parents for the likelihood
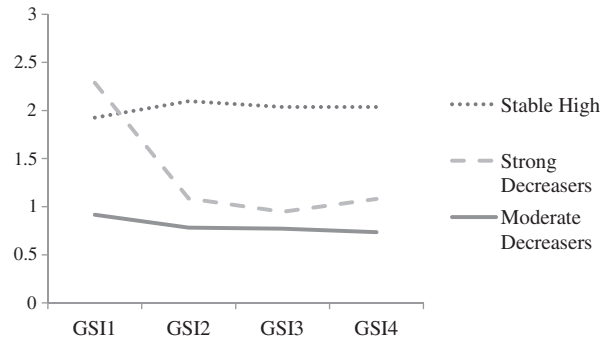

Figure 1: Three trajectories of change in general severity scores of symptom distress

to follow a specific trajectory of change were continued with data from a subsample, including their saved class membership. An ANOVA showed that there were no differences between the severity of symptom distress of the patients in the subsample ($n = 127$) and the rest of the sample ($n = 784$) at the four time points: $T1\Delta_{\text{total-subsample}}$: $F(1, 909) = 0.92$, $p = 0.337$; $T2\Delta_{\text{total-subsample}}$: $F(1, 613) = 0.01$, $p = 0.912$; $T3\Delta_{\text{total-subsample}}$: $F(1, 347) = 0.02$, $p = 0.882$; $T4\Delta_{\text{total-subsample}}$: $F(1, 186) = 0.03$, $p = 0.855$. Table 1 presents the descriptive statistics of the maladaptive traits and parent relations. Correlations between these variables are presented in Table 4. In the subsample, 22 patients were assigned to the Stable High (17%), 16 patients to the Strong Decreasing (13%) and 89 patients to the Moderate Decreasing trajectory.

First, it was found that the fit of a model with the five maladaptive traits as predictors of the three trajectories, and gender and treatment as covariates, was significantly better than the fit of a model with no predictors [χ^2 (14) = 61.37,

Table 2: Mean posterior probabilities and estimates for intercept linear and quadratic slopes

	Stable High	Strong Decreasing	Moderate Decreasing	Intercept	Linear	Quadratic
Stable High	0.74	0.14	0.12	1.86*	0.16	−0.05
Strong Decreasing	0.15	0.74	0.11	2.07*	−1.25*	0.31*
Moderate decreasing	0.05	0.05	0.90	0.91*	−0.14*	0.02

*$p < 0.05$.

Table 3: Means and standard deviations of general severity of symptom distress for the trajectories

	Stable High		Strong Decreasing		Moderate Decreasing	
	n	M (SD)	n	M (SD)	n	M (SD)
GSI_{T1}[1]	138	1.93 (0.42)[2]	115	2.29 (0.39)[2]	658	0.92 (0.44)[2]
GSI_{T2}[1]	98	2.10 (0.49)	86	1.09 (0.56)[3]	430	0.78 (0.46)[3]
GSI_{T3}[1]	69	2.04 (0.48)	49	.95 (0.46)	230	0.77 (0.47)[4]
GSI_{T4}[1]	37	2.04 (0.50)	26	1.08 (0.61)	124	0.74 (0.43)

Games Howell post hoc.
[1]Δall trajectories $p < 0.05$.
[2]ΔT1-T2 $p < 0.05$.
[3]ΔT2-T3 $p < 0.05$.
[4]ΔT3-T4 $p < 0.05$.

Table 4: Correlations between maladaptive personality traits, parent support and conflict

	Detach.	Antagon.	Disinhib.	Psycho.	Support M/F	Conflict M/F
Neg. Affect.	0.07	−0.02	0.22*	0.34**	0.09/−0.14	0.17/0.08
Detachment		0.03	0.16	0.35**	−0.22*/−0.22*	0.11/0.15
Antagonism			0.31*	0.39**	−0.06/−0.01	0.01/−0.09
Disinhibition				0.32**	−0.14/−0.18	0.26**/0.14
Psychoticism					−0.02/−0.10	0.16/0.09
Support$_{Mother}$					1.00/.28**	−0.35*/−0.18
Conflict$_{Mother}$					−0.35**/−0.09	1.00/.37**

*$p < 0.05$.
**$p < 0.001$.

$p < 0.001$, McFadden $R^2 = 0.32$]. Second, when analysing group differences, it appeared that higher levels of Detachment increased the chance of following the Stable High trajectory and higher levels of Negative Affectivity and Detachment increased the chance of following the Strong Decreasing trajectory, compared with the likelihood to display a Moderate Decreasing trajectory. Higher levels of Negative Affectivity also increased the chance of following the Strong Decreasing trajectory compared with the likelihood to display the Stable High trajectory.

Next, the predictive value of relations with parents for following one of the three trajectories was analysed, by adding these factors to the model. However, they appeared to be non-significant predictors. If only relations with parents were added, without controlling for the effect of maladaptive personality traits, this effect was the same. Parameter estimates are reported in Table 5. Concerning the effect of the covariates; using the reciprocal of the OR, it appeared that boys were 10 times more likely than girls to follow the Moderate Decreasing as opposed to the Stable High trajectory ($B = -2.32$, $SE = 1.13$, OR = 0.10, Wald = 4.21, $p = 0.040$). Moreover, boys were 14 times more likely to follow the Strong Decreasing as opposed to Stable High trajectory ($B = -2.67$, $SE = 1.34$, OR = 0.07, Wald = 3.93, $p = 0.047$). There were no gender differences between the Moderate Decreasing and Strong Decreasing group, and no differences between the types of treatment in any of the groups.

Table 5: Parameter estimates of the Stable High, the Strong Decreasing and the Moderate Decreasing trajectory

	Stable High vs. Moderate Decreasing			Strong Decreasing vs. Moderate Decreasing			Stable High vs. Strong Decreasing		
	B (SE)	OR	Sig.	B (SE)	OR	Sig.	B (SE)	OR	Sig
Intercept	−11.34 (3.47)		0.001	−20.36 (6.39)		0.001	9.02 (6.79)		0.184
Negative Aff.	0.66 (0.76)	1.94	0.386	4.21 (1.23)	67.63	0.001**	−3.55 (1.30)	0.03	0.006**
Detachment	1.87 (0.77)	6.47	0.015*	3.06 (1.24)	21.40	0.014*	−1.20 (1.34)	0.30	0.370
Antagonism	−0.62 (0.78)	0.54	0.426	0.17 (1.07)	1.19	0.872	−0.80 (1.15)	0.45	0.489
Disinhibition	1.22 (0.75)	3.38	0.104	−0.20 (0.81)	0.82	0.807	1.42 (0.93)	4.12	0.126
Psychoticism	0.89 (0.78)	2.43	0.253	−0.31 (0.90)	0.73	0.728	1.20 (1.03)	3.33	0.242
Support$_{mother}$	0.99 (0.52)	2.70	0.054	1.16 (0.79)	3.19	0.143	−0.17 (0.79)	0.85	0.832
Conflict$_{mother}$	0.43 (0.39)	1.53	0.278	1.07 (0.68)	2.91	0.116	−0.64 (0.69)	0.53	0.350
Support$_{father}$	−0.66 (0.53)	0.52	0.212	−0.57 (0.96)	0.56	0.549	−0.08 (0.96)	0.92	0.931
Conflict$_{father}$	0.19 (0.37)	1.21	0.608	−0.64 (0.67)	0.53	0.342	0.83 (0.70)	2.29	0.238

*$p < 0.05$.
**$p < 0.0$.

Discussion

Individual trajectories of change in symptom distress

In this study, change in symptom distress was empirically represented along a Stable High, a Strong Decreasing and a Moderate Decreasing trajectory. This is in line with previous studies that also describe one or two groups showing considerable decrease or stable levels of symptom distress[1–3]. The majority of the young patients followed the Moderate Decreasing trajectory, showing moderate initial severity of symptom distress that considerably improves over time. Patients that followed the Strong Decreasing trajectory started with the highest initial severity scores but showed a considerable decrease in symptom distress. This is in line with higher pretreatment severity showing significant relations with improvement[5]. Future studies could replicate these trajectories to see whether the decrease in symptom distress in these patients lasts or is limited to the first period of care. Vermote et al.[3] found that the decreasing trajectory in their study showed sustained improvement after 12 months. Patients in the Stable High trajectory showed no change in symptom distress despite receiving care as usual. This seems to be a problematic group, because a decrease in symptom distress is the target of psychological care. No change may point to a negative prognosis or treatment that does not fit the individual nor the complexity of their problems. The percentage of patients with severe personality pathology in the three trajectories seemed to confirm the severity of symptoms they represent. The percentage of patients with severe personality pathology was highest in the Stable High and lowest in the Moderate Decreasing trajectory.

Maladaptive personality traits as predictors of trajectories

Confirming our hypothesis, we found that patients with high levels of Negative Affectivity are more likely to experience the highest initial severity of symptom distress[17,18]. Levels of severity do tend to decrease the strongest in this group regardless of the type of care they receive. This may partly be due to the high levels of Negative Affectivity; and as such, represent a ceiling effect or a regression to the mean. However, this finding is in line with results of a recent systematic

review that demonstrates that individuals with high levels of Negative Affectivity or emotional instability respond best to therapy[9]. Furthermore, it could be that these patients were more likely to receive pharmacotherapy, which is known to have a short-term effect. Next, our findings show that high levels of Detachment increase the likelihood of following the Strong Decreasing, but also the Stable High trajectory. This is in line with a previous finding that Detachment, or the introversion dimension, is inflexible and the only trait that remains stable in childhood and adolescence, while other traits decline in a linear fashion[40]. It might be that patients with high levels of Detachment can be characterized by an insecure attachment style[11]. For patients in the Stable High trajectory, their attachment style may make them less likely to respond to treatment due to a reduced capacity for reflection and a tendency to withdraw and restrict expression of emotion[41]. Galatzer-Levi et al. also found that their non-remitting class was predicted by high avoidance symptoms[1].

Relations with parents as predictors of trajectories

We found no evidence that support from or conflict with any of the parents was predictive of the trajectories. Late adolescents, besides addressing their parents, may also turn to their friends or romantic partners when they are in need of support[42]. The influence of relationship quality with parents could therefore be exerted via indirect pathways by influencing the quality of later relations[25], which explains the lack of direct effects. Moreover, relations with parents might have been re-established in terms of autonomy and interdependency and therefore contain little conflict[43]. Future studies could replicate this effect in other age groups, whereby disentangling the possible differential effect of the relation with both parents.

In addition, the results suggested that patients with high levels of Detachment experienced less support from both parents and that there are predominantly girls in the Stable High trajectory, which is predicted by high levels of Detachment. Although sex differences were beyond the scope of the current study, it may be interesting for future studies to look at the interaction between maladaptive traits and relations with parents. This would be supported by the finding that relations with parents are directly related to levels of maladaptive traits and that the relation between emotional problems and (lack of) parental support is strongest for girls[14,44]. Our sample lacked the power to test this, but it can be expected that support from parents buffers and conflict exacerbates any negative effects of maladaptive traits on change in symptom distress[45].

Future research, strengths and limitations

This study gives insight in the predictive effect of maladaptive traits on the course of change in symptom distress in late adolescents with personality pathology. Moreover, this study sheds light on both individual traits as well as contextual factors. The results are closely related to clinical practice, using a large longitudinal sample with ROM data. Further research is needed to replicate these trajectories. Additionally, it is suggested that future studies with larger samples examine whether relevant factors can be distinguished that are predictive of the specific rates of change in symptom distress in these trajectories. This can be done by looking at the total change in symptom distress for patients within the trajectories. Because the final amount of patients within the trajectories for whom we could analyse any predictive effects was small, this was beyond the scope of this study. However, looking at the total change in symptom distress between the first and final measurement in the overall sample, this seems a very relevant direction for future studies. It could give important insights in differences in rates of improvement of particular patients, which could contribute to clinical decision making on treatment. Along these lines and based on the results

of this study, we suggest that future research focussing on important aspects related to shared decision making, takes into account which types of treatment might fit individuals with specific personality traits best.

This study also had some limitations. First, the personality and social relation scores were only available for a subgroup of 127 patients, and class sizes of the three groups were small. Results need to be interpreted with care. However, power was acceptable[46] and effects relatively large. Second, the time of assessment of symptom severity and the other measures varied between patients. This could have influenced the results to some extent, however, no drastic changes in personality traits are expected as they show quite some stability[47]. Third, this study used self-report ratings of parental relations, while additional observer or confederate ratings may have been of significant interest. It is suggested that future studies should rely on multi-informant designs in order to cover all relevant perspectives on an individual's social relationship quality.

Conclusion

In this study, trajectories of change in symptom distress were examined in a clinical group of late adolescents with personality pathology and three distinct trajectories were identified: A Stable High, a Strong Decreasing and a Moderate Decreasing trajectory. High levels of the maladaptive personality traits Negative Affectivity and Detachment were predictive of following the Strong Decreasing trajectory, and high levels of Detachment were predictive of following the Stable High trajectory. Support from and conflict with both parents were not predictive of any of the change trajectories. These results contribute to the notion of individual differences in change in symptom distress, as well as provide suggestions for screening patients on individual levels of specific personality traits to gain insight in the expected course of this change.

Conflict of interest

All authors declare that they have no conflict of interest.

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