Chapter 2

Negative and Positive Life Events are Associated With Small but Lasting Change in Neuroticism

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ABSTRACT

High neuroticism is prospectively associated with psychopathology and physical health. However, within-subject changes in neuroticism due to life experiences (LEs) or state effects of current psychopathology are largely unexplored. In this 2-year follow-up study, four hypotheses were tested: (i) positive LEs (PLEs) decrease and negative LEs (NLEs) increase neuroticism; (ii) LE-driven change in neuroticism is partly long-lasting; and (iii) partly independent of LE-driven changes in anxiety/depression; and (iv) childhood adversity (before age 16 years) moderates the influence of NLEs/PLEs on neuroticism scores in adult life. Data came from the Netherlands Study of Depression and Anxiety (NESDA, *n*= 2981, mean age 41.99 years, SD= 13.08, 66.6% women). At follow-up (T_2) we assessed PLEs/NLEs with the List of Threatening Experiences (LTE) over the prior 24 months and categorized them over recent and distant PLE/NLE measures (1–3 and 4–24 months prior to T_2 respectively) to distinguish distant NLE/PLE-driven change in trait neuroticism (using the Dutch version of the Neuroticism–Extroversion–Openness Five Factor Inventory, NEO-FFI) from state deviations due to changes in symptoms of depression (self-rated version of the 30-item Inventory of Depressive Symptomatology, IDS-SR30) and anxiety (Beck Anxiety Inventory, BAI). Distant NLEs were associated with higher and distant PLEs with lower neuroticism scores. The effects of distant LEs were weak but long-lasting, especially for distant PLEs. Distant NLE-driven change in neuroticism was associated with change in symptoms of anxiety/depression whereas the effect of distant PLEs on neuroticism was independent of any such changes. Childhood adversity weakened the impact of distant NLEs but enhanced the impact of distant PLEs on neuroticism. In sum, distant PLEs are associated with small but long-lasting decreases in neuroticism regardless of changes in symptom levels of anxiety/depression. Long-lasting increases in neuroticism associated with distant NLEs are mediated by anxiety/depression.

INTRODUCTION

Neuroticism is a superordinate domain in all major theories of personality and temperament [51,63]. Eysenck [132] defined neuroticism as the tendency to arouse quickly when emotionally stimulated and to inhibit emotions slowly, whereas Costa and McCrae [47] describe neuroticism as a general tendency to experience negative affects like fear, sadness, embarrassment, anger, guilt and disgust. High-neuroticism scores indicate an enhanced sensitivity to environmental stress and a cautious vigilant outlook [63]. High neuroticism is prospectively associated with psychopathology [3,52,273] and life-course outcomes across multiple domains, *e.g.* occupational attainment, divorce, and mortality [66]. Moreover, the economic burden of high neuroticism to society as a whole is enormous and at least twice that of all common mental disorders combined [55].

Albeit personality is conceptualized as a stable trait, the rank-order stability of neuroticism as indexed by test-retest correlations from age 21 drops steadily from .55 after a year, to .41 over 20 years, to .25 after 40 years [164,236,328]. Indeed, changes in neuroticism have been reported for all ages [64,329-333]. In a study across 40 years neuroticism scores decreased in 16% and increased in 13% of the individuals with more than half a standard deviation [231]. Moreover, both stability and change in neuroticism appears to be substantial influenced by environmental factors [91,230,328,334-337]. However, only few have examined the effects of specific environmental factors [172,338-340].

Prospective evidence implies that life events (LEs) influence neuroticism, especially those involving romantic relationships and work. For example, greater prestige, work-satisfaction, financial security [27,333,341], promotion, the beginning of regular work [339], greater relationship security, attachment and partner-satisfaction [333,342,343] have been associated with decreases in neuroticism. Unemployment, heavy physical work, night- and shift-work schedules [172], starting a new job, change in university studies, increased working hours [339], more relationship conflicts, partner abuse, marital tension [342,344], illness, self-harm, divorce/break-up, accidents, robbery, violent assault, failing an important exam and financial problems [239,339,345,346] have been associated with increases in neuroticism.

However, it remains unclear whether such observations reflect temporary shifts or lasting change in neuroticism. Prior research distinguishes three possible sources of variance for neuroticism: an allegedly stable set-point-neuroticism component representing the general trait-level of neuroticism, a transient state-deviation component which changes in response to LEs and current psychopathology, and an error component [114,347-349]. Individuals often rate themselves as more neurotic during depressive/anxious episodes [281,348,350]. This phenomenon has typically been interpreted

as a transient state-deviation in self-perception due to the state-effects of the patient's current psychopathology rather than real change in set-point-neuroticism [3,351-354].

Others, however, argued that this 'state-deviation' may reflect a true change in set-point-neuroticism [348,354,355]. Hence, when neuroticism-scores change after the experience of positive/negative LEs (PLEs/NLEs) this may reflect a transient state-deviation in neuroticism as a consequence of altered self-perception due to changes in anxiety/depression. Moreover, this change in neuroticism may be short-term, and levels may return to set-point-neuroticism when the effects of life events (LEs) on anxiety/depression decay. Therefore, it is important to examine LEs-effects on neuroticism both unadjusted and adjusted for possible state-deviations related to change in anxiety/depression.

Previous studies indicate that stressful-LEs may trigger an anxious/depressive episode typically within maximal three months [345,356-358], which indicates that taking timing of experienced SLEs into account is important. In the current study we distinguish between *recent-SLEs* that occurred up to three months before T_2 and *distant-SLEs* that occurred 4-24 months prior to T_2. Changes in neuroticism explained by recent-SLEs mark the "*short-term effects"* and by distant-SLEs the "*long-lasting effects"* which may indicate a persistent change in set-point-neuroticism.

Finally, early life adversities, such as sexual, physical or emotional maltreatment, trigger persistent changes in neurobiological systems, in this way increasing sensitivity to LEs later in adult life [302,359-361]. In the current study this developmental perspective is studied by testing if childhood adversity moderates the impact of LEs on neuroticism in adult life.

In sum, in the current study we test four hypotheses: (a) positive LEs decrease and negative LEs increase neuroticism-scores; (b) LE-driven change in neuroticism is partly long lasting; (c) part of LE-driven change in neuroticism is independent from short-term LE-driven changes in anxiety/depression; and (d) childhood adversity moderates the influence of LEs on neuroticism-scores in adult life.

METHODS

Study Sample

The data for this study were derived from the Netherlands Study of Depression and Anxiety (NESDA). The NESDA study design, sampling procedures, and non-response are in detail described elsewhere [362,363]. For this study, we used data from the baseline measurement wave (T_1, 2004-2006) and the follow-up wave (T_2, n= 2596, 87.1% response), two years later. Since this paper focused on the influence of LEs on change in neuroticism all participants with more than three missing items on the

neuroticism-scale (n= 38 at T_1, n= 67 at T_2) or LE-measure (n= 135) were excluded. After excluding these participants a final sample of 2356 participants remained (89% of T_2 sample, 79% of T_1 sample), with a mean age of 41.99 years (SD= 13.08) at T_1, and 66.6% women; comparable to the age and gender distribution of the original sample. Participants who did not participate at T_2 (n= 385) scored not significantly higher on neuroticism at T_1. However, when we imputed the missing items for participants who were excluded because they had more than three missing items (n= 38 at T_1 and n= 202 at T_2), results suggested that excluded participants scored higher on neuroticism (d= 0.29/0.17), reported more anxiety (d= 0.44/0.36) and depression (d= 0.43/0.23) symptoms and a higher childhood trauma score (d= 0.20). The NESDA study was approved by the Ethical Committees of participating universities, and all participants provided written informed consent.

Measures

Neuroticism

Neuroticism was measured at T_1 and T_2 with the validated Dutch version of the Neuroticism–Extroversion–Openness Five Factor Inventory (NEO-FFI, [47,364]). The 12 neuroticism items were scored on five-point scales ranging from (i) *strongly disagree* to (v) *strongly agree, and* aggregated into a neuroticism-score. Cronbach's alpha was 0.87.

Life Events

LEs were assessed at T_2 with the 20-item Brugha "List of Threatening Experiences" [365] that contains 7 PLEs and 13 NLEs (see Table 1). Kappas for six-month sensitivity and specificity were 0.89/0.74, with an inter-rater agreement of 0.70 [365]. Each LE was scored dichotomous (yes/no) with the exact month of the year in which it occurred. PLEs and NLEs were aggregated in separate measures. Since there is no consensus on the optimal way to calculate aggregated-LE-measures [268] we tested the robustness of our findings via aggregation over simple counts of reported LEs and the calculation of weighted PLEs- and NLEs-measures. This latter measure was based on earlier findings on social readjustment after experiencing LEs [366], in which was shown that the "impact" of infrequent LEs was significantly larger than that of the more common ones [367]. In analogy, the inverse of the prevalence of the LE was used to weigh its impact. For example, when 5.7% of the participants were "*sacked from their job*", the weight of this item was 0.943 (100-5.7)/100)).

To be able to test LE-driven change in neuroticism uncontaminated by state-deviations due to recent-LE prompted acute-changes in anxiety/depression; timing of LEs was taken into account. Previous studies indicated that the impact of LEs on anxiety/

Table 1. The prevalence (%) among the 2356 participants (67% women) of the negative and positive life events scored on the Brugha List; Pearson's correlations with neuroticism at baseline (N_1) or follow-up (N_2); and partial correlations with neuroticism at follow-up corrected for baseline neuroticism (ΔN, reflecting change in neuroticism) and additional corrections for change in depression and anxiety between baseline and follow-up (ΔN~ΔD&ΔA). Post-hoc, associations with ΔN stratified by gender.

Brugha negative life events	**%**	**N_1**	**N_2**	**ΔN**	**ΔN ~ΔD&ΔA**	**ΔN Men**	**ΔN Women**
Seriously ill, wounded or victim of violence	9.7	.05[b]	.06[a]	.03	.01	.04	.04
Seriously ill, wounded or victim of violence of family member	35.1	-.01	-.01	-.00	-.01	.07	-.03
Parent child, brother or sisters died	10.1	-.02	.00	.03	.02	.02	.04
Friend or family member died	29.2	-.04[b]	-.03	.00	.00	.02	-.01
Separation of partner	12.1	.06[a]	**.10**	**.08**	.06[a]	.06	**.09**
Broke up a longstanding relationship with a friend/relative	16.2	**.10**	**.13**	**.09**	**.08**	.06	**.10**
Serious problem with close friend, family member or neighbour	14.5	**.11**	**.13**	**.07**	.04	.09[b]	.06[b]
Became unemployed or looked for a job without result	12.5	**.08**	.05[b]	-.02	-.02	.04	-.05
Sacked from job or made redundant	5.7	.06[c]	.01	-.05[b]	-.05[b]	-.04	-.05[b]
Serious financial problems	9.4	**.15**	.15[*]	.05[b]	.02	-.01	.08[a]
Contact with police or justice by misdemeanour	4.0	-.01	-.01	-.01	-.00	.01	-.02
Something worthwhile or money was stolen or lost	8.8	.02	.01	-.00	.00	-.01	.00
Another serious negative life event	44.9	.01	.02	.02	-.00	-.02	.03
Total sample	100.0						
Brugha positive life events							
Recovery from serious illness of family member	16.0	-.02	-.05[b]	-.04[b]	-.05[a]	.01	-.07[a]
Found a new partner	10.7	.03	.02	-.01	.00	-.03	-.00
Befriended new people	54.5	-.04	**-.07**	**-.07**	-.06[a]	-.09[b]	-.07[a]
Started a new job or was promoted	33.0	.03	-.03	**-.10**	-.06[a]	-.09[b]	**-.10**
Formally finished school/course	14.9	-.06[a]	**-.08**	-.04[b]	-.03	-.11[a]	-.01
Major (positive) change in financial situation	20.5	-.03	-.05[b]	-.04[b]	-.01	-.05	-.04
Holiday	84.1	**-.13**	**-.16**	**-.09**	**-.08**	-.07[b]	**-.10**
Total sample	100.0						

Legend: $p < .001$ in bold, [a] $p < .01$, [b] $p < .05$ (two-tailed). N_1= neuroticism at baseline (T_1); N_2= neuroticism at follow-up (T_2); ~ΔD&ΔA= partial correlation corrected for ΔA or change in anxiety (A_2-A_1 (T_2-T_1)) and ΔD or change in depression (D_2-D_1); ΔN= change in neuroticism (N_2-N_1).
Men (n= 784) and women (n= 1566).

depression typically decays after three months [345,356-358]. Therefore, to take timing of the experienced LEs into account, the 24-months follow-up time between T_1 and T_2 was used to categorize the LEs into *recent-LEs,* which occurred within the three months before T_2, and *distant*-LEs, which occurred 3-24 months before T_2. Using this algorithm distant-LEs occurred on average 13.5 months before T_2 ((21/2) +3= 13.5).

Depressive Symptoms

Symptoms of depression (hereafter 'depression') were measured at T_1 and T_2 with the 30-item Inventory of Depressive Symptomatology [368]. The IDS-SR30 was designed to assess the self-reported severity of depression over the past week [368]. Responses were aggregated whereby appetite increase/decrease and weight increase/decrease were each treated as one item, and high-scores indicate greater severity [368]. Cronbach's alpha was 0.83.

Anxiety Symptoms

Symptoms of anxiety (hereafter 'anxiety') were measured at T_1 and T_2 with the 21-item self-report Beck Anxiety Inventory [369]. The BAI was designed to distinguish anxiety from depression while retaining convergent validity [370] and has high internal consistency (α= .92) and one-week test-retest reliability (r= .75) [369]. Participants rated how much each of the symptoms bothered them over the past week on a 4-point scale (0-3) that ran from 'not at all' to 'could barely stand it', and scores were aggregated. Cronbach's alpha was 0.81.

Childhood Adversity

The experience of the following childhood adversities before age 16 was assessed at T_1: 'emotional-neglect' (38.9%), 'psychological-abuse' (24.8%), 'physical-abuse' (13.8%), or 'approached in a sexual way against your will' (18.5%). Participants were asked to indicate if an adversity had occurred (yes/no) and how often it occurred (not, once, sometimes, regularly, often, or very often). Scores were recoded into 0= never, 1= once/sometimes and 2= regularly/often/very often. Following prior studies [371,372], a sum score of experienced number (0-4) and frequency (0-2) of the childhood adversity was calculated for each participant (range= 0-8). This sum score was recoded into a 5-category variable reflecting their level of exposure to childhood adversity: 0 (no adversity, n= 1264, 53.8%), 1 (1-2, n= 482, 20.5%), 2 (3-4, n= 333, 14.2%), 3 (5-6, n= 208, 8.9%) and 4 (7-8, n= 62, 2.6%), totaling 1085 individuals (46.2%) who had experienced some form of childhood adversity.

Statistical Analysis

All variables approached a normal distribution and were analyzed in SPSS (version 18.0, SPSS Inc., Chicago, Illinois). We used Pearson correlations to test the associations between the variables. Effect sizes are given as Cohen's *d*. As a heuristic, we indicate effect sizes of 0.20 as small, 0.50 as medium, and 0.80 as large (for correlations .10/.30/.50) [373]. The models are examined with multiple linear regression analyses ('forced entry method'), with separate parameter estimates for each block of predictors. To focus on within-subject changes in our analyses, T_2 measures of neuroticism, depression, and anxiety (N2/D2/A2) were predicted from T_1 measures ($N_{1/}D_{1/}A_1$). We present standardized regression coefficients (Beta-weights) which enable comparison of predictors because they indicate the change in outcome per SD change in the predictor (when the other independent variables are held constant). Second, intercepts and slopes of the regression analysis were used to interpret possible differences in baseline neuroticism and change in neuroticism, respectively.

To test our hypotheses about the influence of LEs on neuroticism, we fitted seven different models to the data, each numbered and fully described in Tables 4 and 5. First, we fitted a baseline model-1 wherein T_2 neuroticism (N_2) was predicted by T_1 neuroticism (N_1). We then examined differences and similarities between this baseline Model 1 and the other models that were fitted based on our hypotheses. The first hypothesis was tested in Model 2 (the 'life events model') wherein recent-NLEs/PLEs and distant-NLEs/PLEs were entered as predictors of change in neuroticism (Δneuroticism= N_2-N_1). Model 2 also allowed us to test hypothesis 2, *viz*., LE-driven Δneuroticism is partly long-lasting. If distant-NLEs/PLEs were not associated with Δneuroticism this hypothesis should be rejected.

Moreover, the relationship between LEs and Δneuroticism may be mediated by another variable [374], arguably symptom level of depression/anxiety. In Models 3-5 the third hypothesis was tested that distant-LEs-driven Δneuroticism is independent from change in symptom levels of anxiety/depression. The Δanxiety model tested change in anxiety (Δanxiety= A_2-A_1) as an additional predictor, the Δdepression model tested change in depression (Δdepression=D_2-D_1), and Model 5 tested both. If the variance predicted by LEs ceased when these models were applied this suggests mediation. The robustness of these mediation effects were tested with Preacher-Hayes bootstrap tests [375,376].

Model 6 serves as a baseline for Model 7, to test the fourth hypothesis, *viz*., that the association between LEs and Δneuroticism is moderated by childhood adversity. Model 7 consisted of baseline neuroticism, recent-NLEs/PLEs and distant-NLEs/PLEs, childhood adversity, and four interaction terms as predictors (each a function of a LE measure multiplied by childhood adversity). Significant interaction terms indicate that childhood adversity moderated the impact of LEs on Δneuroticism.

Finally, we repeated analyses after imputation of missing data with the means of the relevant variables. Since the results were highly comparable, only the analyses on the non-imputed data (n= 2356) are presented. Because the amount of correlations shown in the descriptives may inflate family-wise alpha we present only highly significant associations in bold (p< .01 for Table 1 and p< .001 for Table 3).

RESULTS

Descriptives and correlations between our variables are given in Table 2 and Table 3, respectively. Neuroticism, anxiety and depression decreased somewhat over time (d= 0.25/0.29/0.36). Older participants reported lower neuroticism and fewer distant-PLEs than younger participants, but age was not associated with the experience of distant-NLEs. Childhood adversity was associated with higher neuroticism, anxiety, and depression at both waves. Given the high test-retest correlations of all constructs, individual differences in neuroticism, anxiety, and depression were largely retained at

Table 2. The descriptives of the variables used from the NESDA cohort (n= 2356, 67% women). Means, standard-deviations (SDs), and ranges are given.

Variables	Mean	SD	Range
T_1 Neuroticism	35.71	9.40	12 – 60
T_2 Neuroticism	33.42	9.03	12 – 58
T_1 Depression	20.27	13.76	0 – 67
T_2 Depression	15.61	11.91	0 – 65
T_1 Anxiety	11.12	9.98	0 – 61
T_2 Anxiety	8.47	8.50	0 – 60
ΔNeuroticism	-2.29	6.16	-32 – 28
ΔDepression	-4.65	9.82	-47 – 44
ΔAnxiety	-2.64	7.43	-46 – 28
Childhood adversity	0.86	1.11	0 – 4
Number of negative life events	2.12	1.52	0 – 11
Number of positive life events	2.34	1.30	0 – 7
Recent negative life events	0.27	0.49	0 – 3.65
Recent positive life events	0.20	0.37	0 – 2.81
Distant negative life events	1.31	1.12	0 – 8.20
Distant positive life events	0.90	0.81	0 – 3.82

Note. T_1= baseline; T_2= follow-up; Δ= change, Δneuroticism, Δdepression, or Δanxiety reflect follow-up scores corrected for baseline scores. n= 2356 with a maximum deviation of 5 because of the exclusion criteria as formulated in the method section, where also details on the definition of the recent versus distant life events are given.

Table 3. Bivariate Pearson correlations between age, gender, neuroticism, symptoms of depression/anxiety, recent and distant life events, and childhood adversity among 2356 participants (67% women).

	Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1.	Age	—											
2.	Gender†	**-.09**	—										
3.	T_1 Neuroticism	**-.12**	**.10**	—									
4.	T_2 Neuroticism	**-.07**	**.09**	**.78**	—								
5.	T_1 Depression	.03	.04	**.77**	**.63**	—							
6.	T_2 Depression	**.09**	.04[b]	**.60**	**.74**	**.72**	—						
7.	T_1 Anxiety	.00	.05[a]	**.64**	**.51**	**.77**	**.59**	—					
8.	T_2 Anxiety	.06[a]	.05[b]	**.51**	**.63**	**.60**	**.80**	**.69**	—				
9.	Recent NLEs	.00	-.03	.04	**.07**	**.09**	**.12**	**.06**	**.13**	—			
10.	Recent PLEs	**-.16**	.02	-.03	-.05[a]	-.05[b]	**-.08**	-.04	-.04	**.10**	—		
11.	Distant NLEs	-.03	.04	**.11**	**.12**	**.16**	**.19**	**.13**	**.17**	-.02	.05[b]	—	
12.	Distant PLEs	**-.41**	.04[b]	-.02	**-.08**	**-.10**	**-.17**	**-.08**	**-.12**	.02	**-.07**	**.11**	—
13.	Childhood adversity	**.14**	**.11**	**.31**	**.27**	**.35**	**.32**	**.27**	**.27**	**.08**	-.01	**.18**	**-.08**

Note. † Men= 1, women= 2; T_1= baseline measure; T_2= follow-up measure; NLEs= number of negative life events; PLEs= number of positive life events.
Details on the definition of recent versus distant LEs-measures are given in the method section.
Significance at $p< .001$ in bold, [a] $p< .01$, [b] $p< .05$ (two-tailed)

follow-up, despite the drop in mean scores. Anxiety and depression scores were highly correlated, both cross-sectional and longitudinally.

Distant-NLEs showed a positive association with neuroticism, anxiety and depression at both waves, although associations with the T_2-outcomes were slightly stronger (d= 0.25/0.34/0.38, respectively). Distant-PLEs correlated negatively with neuroticism, anxiety and depression at T_2 (d= -0.15/-0.24/-0.33, respectively), and also, weakly, negatively with anxiety and depression at T_1. Neuroticism at T_1 predicted the occurrence of distant-NLEs (d= 0.24) but not distant-PLEs, whereas anxiety and depression at T_1 (weakly) predicted both more distant-NLEs (d= 0.29/0.35, respectively) and fewer distant-PLEs (d= -0.18/-0.22, respectively).

Life Events and Change in Neuroticism

In Table 4 and Table 5 the results of our regression analyses are presented. Model 1 is the baseline model. Model 2 is the LEs-model and indicated that distant-NLEs predicted an increase and distant-PLEs a decrease in neuroticism (d's= 0.19/-0.23). Although both effects were weak, the betas for the distant-PLEs were slightly higher compared to those of the distant-NLEs. However, both distant-effects were significant and thus indicated that distant-LEs (occurring on average a year before follow-up (361.6 days, SD= 2.84)) still affected neuroticism.

Table 4. Regression models with standardized regression coefficients (and 95% CI) for effects of recent and distant negative and positive life events on change in neuroticism, and mediation thereof by change in anxiety and change in depression. Outcome is neuroticism at follow-up, *n*= 2356 in all models.

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Baseline	**Life Events**	**ΔAnxiety**	**ΔDepression**	**ΔAnxiety & ΔDepression**
Predictors	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**
T_1 Neuroticism	0.777***	0.767***	0.837***	0.879***	0.885***
	(0.752, 0.802)	(0.742, 0.792)	(0.813, 0.861)	(0.855, 0.903)	(0.862, 0.909)
Recent NLEs		0.049***	0.030*	0.035**	0.030**
		(0.024, 0.074)	(0.006, 0.054)	(0.013, 0.057)	(0.008, 0.052)
Recent PLEs		-0.039**	-0.034**	-0.022*	-0.023*
		(-0.064, -0.014)	(-0.058, -0.010)	(-0.046, 0.002)	(-0.045, -0.001)
Distant NLEs		0.043***	0.028*	0.021	0.019*
		(0.018, 0.068)	(0.004, 0.052)	(-0.003, 0.045)	(-0.003, 0.041)
Distant PLEs		-0.067***	-0.055***	-0.041***	-0.041***
		(-0.092, -0.042)	(-0.079, -0.031)	(-0.065, -0.017)	(-0.063, -0.019)
ΔAnxiety			0.248***		0.105***
			(0.224, 0.272)		(0.076, 0.134)
ΔDepression				0.313***	0.250***
				(0.301, 0.325)	(0.221, 0.279)
Adjusted R^2	0.603[x]	0.611*	0.667*	0.696*	0.702*
$\Delta R^{2\,\dagger}$		0.008*	0.064*	0.093*	0.099*
$\Delta F^{\dagger}$		12.75***	400.63***	658.46***	362.07***

Note. †= ΔR^2 and ΔF reflect changes from the baseline Model 1; ΔR^2= proportion of variation in the response variable that can be accounted for by the predictors, adjusted for the number of explanatory terms in the model (always ≤ R^2); ΔF= statistic of the F-test; T_1= baseline; Δanxiety= change in anxiety between T_1 and T_2; Δdepression= change in depression between T_1 and T_2; NLEs= number of negative life ; PLEs= number of positive life events. Details on the definition of recent versus distant LEs-measures are given in the method section.*** $p< .001$, ** $p< .01$, * $p< .05$ (two-tailed).

The regression results of Models 2 to 5 indicate that the magnitude of association between distant-NLEs and Δneuroticism decreased when Δanxiety (Model 3) was added, but even more when Δdepression (model-4) or Δanxiety and Δdepression simultaneously (Model 5) were added to the model. This suggests mediation; especially by Δdepression, since the drop of the betas in these models was larger, and the predictive effect of distant-NLEs lost statistical significance. Nevertheless, Model 3 suggests that the association between recent and distant-LEs and Δneuroticism is also partially mediated by Δanxiety. The robustness of these mediation effects of Δanxiety and Δdepression on the associations between distant-LEs and neuroticism were tested

Table 5. Regression models with standardized regression coefficients (and 95% CI) for effects of recent and distant negative and positive life events on change in neuroticism, and moderation thereof by childhood adversity (CA).

Predictors	Model 6 Adversity Baseline		Model 7 Adversity Moderation	
	β	**(95% CI)**	***β***	**(95% CI)**
T_1 Neuroticism	0.767***	(0.740, 0.794)	0.761***	(0.734, 0.788)
Recent NLEs			0.036*	(0.003, 0.069)
Recent PLEs			-0.018*	(-0.049, 0.013)
Distant NLEs			0.064***	(0.031, 0.097)
Distant PLEs			-0.047**	(-0.078, -0.016)
Childhood adversity	0.031*	(0.004, 0.058)	0.088***	(0.035, 0.141)
Recent NLEs*CA			0.021	(-0.016, 0.058)
Recent PLEs*CA			-0.038*	(-0.073, 0.035)
Distant NLEs*CA			-0.055*	(-0.104, -0.006)
Distant PLEs*CA			-0.042*	(-0.083, 0.000)
Adjusted R^2	0.604		0.612	
$\Delta R^{2\,\dagger}$			0.009	
ΔF ?			7.23***	

Note. Outcome is neuroticism at follow-up, *n*= 2356 in all models. †= ΔR^2 and ΔF reflect changes from the childhood adversity baseline reported in Model 6; ΔR^2= proportion of variation in the response variable that can be accounted for by the predictors, adjusted for the number of explanatory terms in the model (always ≤ R^2); ΔF= statistic of the F-test; CA= childhood adversity; NLEs= number of negative life events; PLEs= number of positive life events. Details on the definition of recent versus distant LEs-measures and childhood adversity are given in the method section. *** *p*< .001, ** *p*< .01, * *p*< .05 (two-tailed)

with Preacher-Hayes bootstrap tests (*k*= 5000). Results confirmed that the positive association between distant-NLEs and Δneuroticism was mediated by Δdepression (for 0.017 or 40% of the beta of 0.043 in Model 2 in Table 4 (95% CI= 0.008 to 0.027)) and Δanxiety (for 0.007 or 16% of the beta of 0.043 (95% CI= 0.002 to 0.012)), and suggest a non-significant independent path (for 0.019 or 44% of the beta of 0.043 (95% CI= 0.008 to 0.027), but *p*= .09). The negative association between distant-PLEs and Δneuroticism was also mediated by Δdepression (for -0.021 or 32% of the beta of -0.067 in Model 2 in Table 4 (95% CI= -0.031 to -0.012)) and Δanxiety (-0.005 or 7% of the beta of -0.067 (95% CI= -0.010 to -0.001)), but was mainly independent (-0.041 or 61% of the beta of -0.067 (95% CI= -0.053 to -0.030), *p*< .0005).

Moderation by Childhood Adversity

Model 6 in Table 5 served as a baseline for Model 7. The results of Model 7 indicate that childhood adversity moderated the associations between LEs and Δneuroticism. Compared to participants without such experiences, those who experienced childhood

adversity had higher baseline neuroticism (intercept= 0.85 *vs*. 0.76), less increase in neuroticism after distant-NLEs (slopes of 0.01 *vs*. 0.06), but more decrease in neuroticism after distant-PLEs (slopes of -0.09 *vs*. -0.05). However, childhood adversity (Models 6 and 7) explained little additional variance in Δneuroticism not already covered by Model 1 and 2 (+0.1%, see Table 4). Moreover, part of the association between childhood adversity and Δneuroticism is mediated by the experience of LEs; the more childhood adversity participants reported the more NLEs and fewer PLEs they reported.

Repeating analyses in Tables 4 and 5 with simple counts of PLEs/NLEs as predictors of Δneuroticism showed only minor changes in the results reported above. The effects of distant-PLEs were slightly stronger (*e.g*., beta -0.079 in Model 2, $p< .001$), the interaction term for the recent-PLEs (recent-PLE*Adversity) in Model 6 lost statistical significance, whereas distant-PLEs became more predictive for Δneuroticism. Nevertheless, the magnitudes of the long-lasting effects of distant-LEs were highly comparable. Moreover, Model 2, with LEs predictors that were not partitioned over distant-LEs and recent-LEs, gave highly comparable results (beta's 0.055 for NLEs and -0.085 for PLEs, respectively, both $p< .001$).

Post-hoc Analysis

To check on possible influence of gender and age on Δneuroticism, analyses were repeated with these covariates and the interactions between them and the four LE-measures as additional predictors (*e.g*., gender*distant-PLEs). The results in Appendix Table A1 show that all predictors were non-significant and the estimates were highly comparable to the ones given in Tables 4 and 5. This suggests that influences of gender and age on neuroticism are already represented in baseline neuroticism and that gender and age neither affect change in neuroticism nor modify the effect of PLEs/NLEs on neuroticism.

Finally, because our results suggest that distant-LE-driven Δneuroticism is partly independent from Δanxiety and Δdepression, we examined the extent to which LE-driven Δanxiety and Δdepression are independent from Δneuroticism (statistical results available on request, but an indication can be found in Appendix Table A2). Although the effects of LEs, in particular distant-NLEs, on Δanxiety and Δdepression are somewhat stronger than on Δneuroticism, the pattern is similar. When adjusted for Δneuroticism, the effects of distant-PLEs/NLEs on Δanxiety and Δdepression weaken but remain statistically significant ($p< .001$), which indicates that effects of distant-LEs on Δanxiety and Δdepression are fairly independent from concomitant Δneuroticism. Gender specific associations were added to Table 1.

DISCUSSION

Four main findings emerge from this study; (a) PLEs predict small decreases and NLEs increases in neuroticism; (b) part of the LEs-driven change in neuroticism is long-lasting (at least a year); (c) the effect of PLEs on change in neuroticism is relatively independent from reductions in depression/anxiety, whereas the effect of NLEs on change in neuroticism appears to be largely mediated by increases in depression and, to a lesser extent, by anxiety. These findings suggest that only the effect of distant-PLEs on neuroticism, and not that of distant-NLEs, is independent from the individuals' 'current' psychopathology. The effects of LEs on change in neuroticism and depression/anxiety seem to overlap, both cross-sectional and longitudinally. Finally, (d) childhood adversity weakens the impact of distant-NLEs on neuroticism but enhances that of distant-PLEs.

Strong points of our design include the large sample size, the longitudinal approach, and the examination of both recent-NLEs/PLEs and distant-NLEs/PLEs. This categorization allows for studying the timing of LE-effects [223], which is a relatively new approach, and helpful for studying the underlying mechanism causing fluctuations in neuroticism. Doing so, we could disentangle state-deviations in neuroticism as a consequence of recent-LE-driven change in depression/anxiety from lasting distant-LE-driven change in the set-point of neuroticism.

The reported findings should be viewed in light of the following limitations; retrospective self-reports of LEs inherently incorporate response components such as cognition, appraisal, interpretation, and recall, which may be influenced by current mental state [268,269,377]. Furthermore, the focus on the number of LEs rather than their ecological context is a simplification. The stress and impact of various events depend on a variety of non-assessed factors regarding resources, age, skills, social support, unpredictability, magnitude of change/disruption produced, or potential to exhaust the individual physically [268,269,366,378-380]. Also, ongoing difficulties were not assessed in this study but may also impact on neuroticism [380]. Finally, LEs may elicit mixed emotional responses (*e.g.*, move house), NLEs/PLEs may have complementary longitudinal relationships (*e.g.*, divorce and remarriage [381]), and PLEs may buffer the impact of NLEs [269,382-384].

Future research may take aforementioned limitations into account by using measures of 'life change' or 'context ratings' in a life-chart interview like the "Life Events and Difficulties Schedule" by Brown and Harris [385]. This may also enable a better distinction between the positive and negative valence of an experience. However, conducting interviews is more time-consuming and costly than assessing questionnaires and may consequentially lead to smaller samples and fewer studies [377]. Addition-

ally, participants may be less likely to report embarrassing information or information that may have negative consequences if reported (*e.g.*, physical or sexual abuse [386]).

Explanations for the mechanism behind the observed stronger effects of distant-PLEs compared to distant-NLEs on neuroticism remain speculative. PLEs may elicit change in positive biases, which are reported for never-depressed high-neurotic individuals [32], and lead to more favourable cognitions [387,388]. Moreover, PLEs seem more central to individual's life stories and identity than NLEs [389] and might therefore have more potential for lasting change. However, it is also possible that the composition of our sample explains part the effects of distant-PLEs, as most participants were included because of their depression/anxiety symptoms (see methods). This may have created a ceiling-effect that made decreases in neuroticism more likely when individuals experience the natural course of symptoms, that is, towards recovery. Change in neuroticism may be partly due to antidepressant medication or cognitive treatment [351,390], which was not controlled. However, note that we *did* control for change in anxiety/depression symptoms in our analyses.

LEs explained 2% of change in neuroticism (distant-NLEs d= 0.19, distant-PLEs d= -0.23). This is a rather small effect, but similar to what has been reported in the literature [292]. However, in this study we assessed only 20 specific LEs, whereas participants must have experienced many others as well. Hence, it is likely that we report an underestimation of the magnitude of LEs-driven change in neuroticism. The key observation that part of the lasting change in neuroticism, and especially that of distant-PLEs, is independent from change in anxiety/depression corresponds with other findings in the field [391,392]. Hence, our results suggest that LE-driven change in neuroticism is more than a transient state-deviation of self-perception due to current psychopathology [351-353], and may indeed be interpreted as a true change in the set-point of neuroticism [94,348,354,355].

Our findings are relevant for the interpretation of intervention studies of depression [351-354]. For example, neuroticism level is reported to moderate the impact of PLEs on depression i.e. PLEs have a greater impact on high-neurotic depressed individuals [393-398] whereas high neuroticism is reported to exacerbate the impact of NLEs on depressive mood [33,399]. Additionally, interventions that elicit a decrease in neuroticism may not only reduce the risk of a relapse of depression but may also help to cut back the societal costs of neuroticism *itself* [55].

In line with previous research, childhood adversity was positively associated with neuroticism in adults. However, in contrast to reports thus far [400,401], adult individuals who experienced childhood adversity increased less in neuroticism after distant-NLEs and decreased more after distant-PLEs. Generally, researchers argue that early life adversity enhances hypothalamic-pituitary-adrenal-axis activity and emotional reactivity [361,401,402]. In contrast with the literature, participants who experienced

childhood adversity did not show an enhanced acute reaction after recent-NLEs in this study (see Model 7, Table 5). In addition, our observation that the lasting effect of distant-NLEs on neuroticism appears to be blunted for individuals who experienced childhood adversity suggests a temporal difference, and requires replication.

Although some changes in neuroticism must be persistent given the steady drop in differential stability with time, most changes in neuroticism will tend to regress to baseline (set-point-neuroticism) after an adaptation period, a process known as the dynamic-equilibrium-hypothesis [94,155,403-406]. However, some experiences may elicit persistent shifts in neuroticism in some individuals (*e.g.*, via changed personality-environment feedback-loops). Since this study lasted only 24 months, additional waves would be needed to examine such conjectures.

To conclude, high-neuroticism is an important indicator of risk for the development of full-blown psychological disorders and can, to some extent, be viewed as sub-threshold psychopathology. The independent relationships between PLEs and neuroticism in this study indicate that neuroticism does not fully overlap with anxiety/depression. Thus as a relatively stable personality trait, neuroticism is of interest in its own, and cannot be substituted by measures of anxiety/depression. Finally, this study showed that experiences can elicit long-lasting change in neuroticism, and thereby influence, potentially, the risk for development of psychopathology. Future studies that focus on the mechanisms behind PLE-driven long-lasting change in neuroticism and demonstrate such effects in intervention studies may confluence into prevention strategies focused on decreases in neuroticism.

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