SUPPLEMENTARY INFORMATION

Positive memory specificity reduces adolescent vulnerability to depression

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Supplementary Methods:

Participant Recruitment

Uptake from the schools was generally high (about 1:2; 1707 invited, 990 consented, 937 did school interview, 905 remained after exclusion, 888 after dropout at baseline). The main sample studied here with 427 adolescents were those who had data on all measures including cortisol, stemming from an overall cohort of 575 adolescents who had data on all measures excluding cortisol.

Types of Negative Life Events

1. Losses, involving only death or permanent separation from a valued other.
2. Disappointments, involving failure of previously held expectations and/or hopes, including breakdown of a romantic relationship or examination failure (affecting self), or loss of a job, new financial difficulties or an extramarital affair (affecting others).
3. Dangers to the self, involving a clear expectation or occurrence of a physical threat to the youth, including being affected by an illness or accident.
4. Dangers to others, similar events including an illness or accident affecting a parent, friend or significant other.

Cortisol Assay Specifications

Cortisol was measured by enzyme-linked immunosorbent assay (ELISA) on 20-µL samples of saliva without extraction (antibody; Cambio). Intraassay variation was 5.7 % and interassay variation was 5.6 %.

Supplementary Results:

Confirmatory Factor Analysis of Morning Cortisol

To acquire a stable trait-like measure of morning cortisol, a latent factor was extracted from morning cortisol across four sampling days at both baseline and follow-up. The confirmatory factor analysis (CFA) of morning cortisol (see Supplementary Figure 1; n = 427) showed good model fit at baseline without any modifications (robust model fit indices: X^2_2 = 2.817, P = .244, CFI = 0.998, TLI = 0.994, RMSEA = 0.035, 90 % CI [0.000, 0.120], SRMR = 0.013). However, the CFA at follow-up did not show good model fit (robust model fit indices: X^2_2 = 21.689, P < .001, CFI = 0.943, TLI = 0.828, RMSEA = 0.175, 90 % CI [0.113, 0.244], SRMR = 0.039). The model was re-specified once (MI = 30.307), freeing the path between day one and two at follow-up (improved model fit, ANOVA: X^2_2 = 28.168, P < .001). The modified model showed good model fit (robust model fit indices: X^2_1 = 0.285, P = .593, CFI = 1, TLI = 1.016, RMSEA = 0, 90 % CI [0.000, 0.133], SRMR = 0.004). Strong longitudinal measurement invariance was established between baseline and follow-up (see Supplementary Table 2).

Validation of the Specific / Categorical Positive Memory Specificity Ratio

To validate the use of the ratio between positive specific and positive categorical responses as our predictor, we investigated the main findings of the path model for specific and categorical responses separately. In these analyses, we found support for the idea that specific and categorical responses tap into the same underlying construct; specific responses to positive cues predicted less negative self-cognitions during low mood at follow-up (Estimate = -0.196, S.E. = 0.054, z = -3.607, P < .001) and lower morning cortisol (Estimate = -0.399, S.E. = 0.177, z = -2.249, P = .025), whereas categorical responses to positive cues predicted more negative self-cognitions (Estimate = 0.212, S.E. = 0.082, z = 2.601, P = .009)

and higher morning cortisol at follow-up (Estimate = 0.577, S.E. = 0.264, z = 2.183, P = .029). Specifically; specific responses to positive cues at baseline were related to less negative self-cognitions during low mood at follow-up (Pearson's r effect size = -.16, 95 % CI [-.25, -.07], Estimate = -0.188, S.E. = 0.056, *z* = -3.389, P = .001), but not at baseline (r = -.04, 95 % CI [-.13, .06], Estimate = -0.059, S.E. = 0.070, *z* = -0.835, P = .404). Specific responses to positive cues were related to lower morning cortisol at follow-up (r = -.11, 95 % CI [-.20, -.02], Estimate = -0.433, S.E. = 0.188, *z* = -2.304, P = .021), but not at baseline (r = -.08, 95 % CI [-.17, .01], Estimate = -0.396, S.E. = 0.235, *z* = -1.681, P = .093). On the other hand, categorical responses to positive cues were related to more negative self-cognitions during low mood at follow-up (r = .10, 95 % CI [.01, .19], Estimate = 0.165, S.E. = 0.080, *z* = 2.070, P = .038), but not at baseline (r = .04, 95 % CI [-.06, .13], Estimate = 0.075, S.E. = 0.093, *z* = 0.807, P = .420). Categorical responses to positive cues were related to higher morning cortisol at follow-up (r = .12, 95 % CI [.03, .21], Estimate = 0.692, S.E. = 0.278, *z* = 2.492, P = .013), but not at baseline (r = .07, 95 % CI [-.03, .16], Estimate = 0.485, S.E. = 0.339, *z* = 1.430, P = .153).

Controlling for Related Cognitive Factors: Rumination and Positive Self-Esteem

Memory specificity and rumination are interacting cognitive vulnerability factors, especially in a context of recent stressors[1,2]. Moreover, positive self-esteem may have similar effects on depressive vulnerability after stressors as specific positive memories[3]. To disentangle positive memory specificity from other related cognitive factors, we ran all models with self-esteem and mood-related rumination at baseline as covariates. For these analyses, we utilised the total score of the Responses Style Questionnaire (RSQ)[4], a 39-item self-report scale where participants report what they think, feel and do when they experience depressed mood, which has good psychometric properties[4]. For self-esteem, we utilised the

total score on the Rosenberg Self-Esteem Questionnaire[5], a 10-item self-report questionnaire that measures global self-worth and feelings about the self.

We found that mood-related rumination was correlated with depressive symptoms (baseline: r = .40, P < .001, follow-up: r = .47, P < .001), negative self-cognitions (baseline: r = .59, P < .001, follow-up: r = .40, P < .001). Mood-related rumination was not associated with morning cortisol at baseline (r = .05, P = .296), and had a small correlation with morning cortisol at follow-up (r = .13, P = .008). Positive self-esteem was strongly related to depressive symptoms (baseline: r = -.50, P < .001, follow-up: r = -.39, P < .001), negative self-cognitions (baseline: r = -.46, P < .001, follow-up: r = -.35, P < .001), but was not related with morning cortisol (baseline: r = -.09, P = .059, follow-up: r = -.04, P = .417).

When we added both mood-related rumination and self-esteem as covariates in our path model, all results remained. Positive memory specificity independently predicted less negative self-cognitions during low mood (Effect = -0.106, S.E. = 0.04, z = -2.863, P = .004, r = -.14, 95 % CI [-.23, -.05]) and lower morning cortisol at follow-up (Effect = -0.347, S.E. = 0.13, z = -2.637, P = .008, r = -.13, 95 % CI [-.22, -.04]). Furthermore, both the moderation of the path between positive memory specificity and negative self-cognitions by negative life events ($F_{9,415}$ = 8.319, P = .004) and the moderated mediation with negative self-cognitions as the mechanism protecting against depressive symptom formation remained unchanged (Index = -3.057, S.E. = 1.372, 95 % CI [-5.641, -0.661]).

Cross-Sectional Correlations in the Moderation and Moderated Mediation Models

To facilitate interpretation of the conditional process results, we report the cross-sectional correlations in the moderation and moderated mediation models. Correlations between negative life events and other follow-up measures were small to moderate (negative self-cognitions: r = .17, 95 % CI [.08, .26], P < .001; dysphoric mood: r = .23, 95 % CI [.14,

.32], P < .001; depressive symptoms r = .22, 95 % CI [.13, .31], P < .001; morning cortisol r = .11, 95 % CI [.02, .20], P = .028). The correlation between negative self-cognitions and depressive symptoms was large (r = .69, 95 % CI [.64, .74], P < .001).

Group Differences: Gender

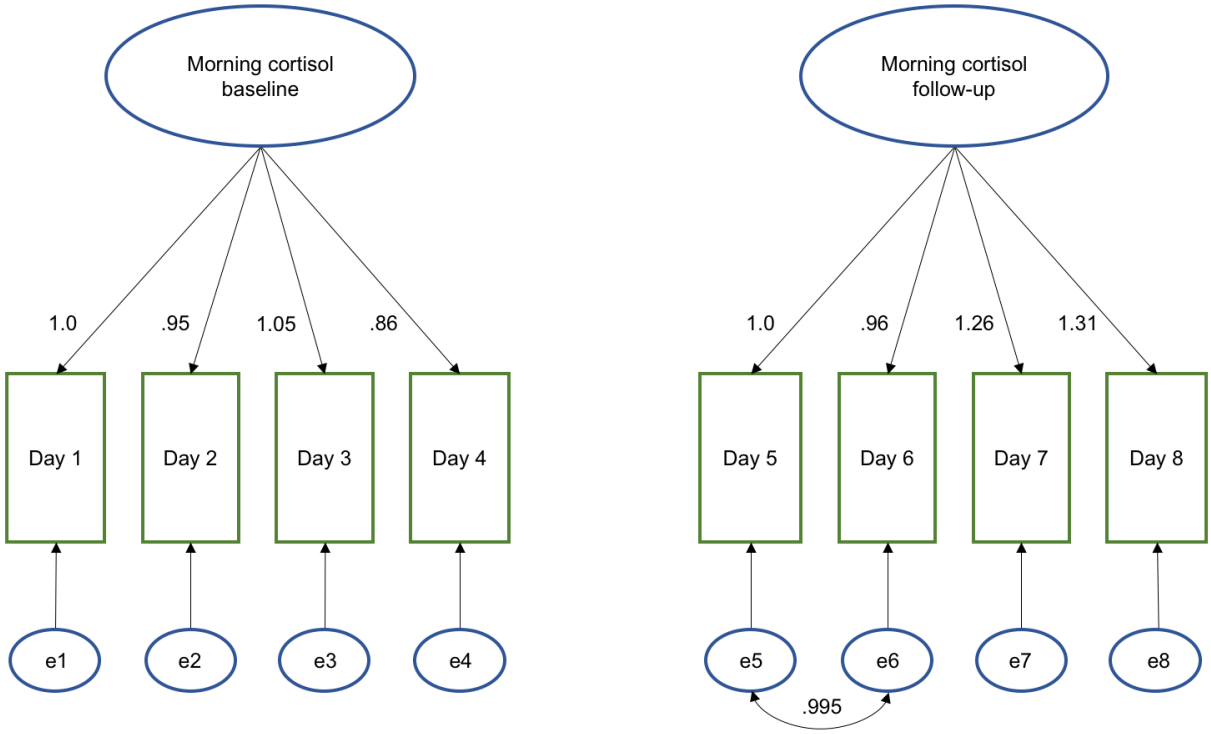
Gender affected morning cortisol both cross-sectionally and longitudinally in our path model (see Table 1 in the main manuscript). As we found that positive memory specificity predicted morning cortisol at follow up, we therefore examined whether gender affected this relationship using a bias-corrected moderation analysis with 5,000 bootstrapped samples. This analysis showed that gender did not significantly affect the relationship between positive memory specificity and morning cortisol over time ($F_{1,419}$ = 2.398, P = .122).

Group Differences: Major Depression

To investigate whether there were group differences between adolescents who developed (vs did not) major depression at follow up, we examined whether there were group differences on morning cortisol, negative self-cognitions and positive memory specificity at follow-up between the group that developed major depression (n = 41) vs those who did not (n = 386). Univariate analyses of variance (ANOVAs) without covariates showed that adolescents who developed major depression had higher morning cortisol ($F_{1,426}$ = 5.730, P = .017), and more negative self-cognitions at follow-up ($F_{1,426}$ = 21.605, P < .001), but did not differ in positive memory specificity ($F_{1,426}$ = 1.199, P = .274). Because positive memory specificity did not differ with major depression status, we did not run any further moderation analyses.

References

1. Hamlat, E. J. *et al.* Rumination and Overgeneral Autobiographical Memory in Adolescents: An Integration of Cognitive Vulnerabilities to Depression. *J. Youth Adolesc.* **44,** 806–818 (2015).
2. Williams, J. M. G. *et al.* Autobiographical memory specificity and emotional disorder. *Psychol. Bull.* **133,** 122–148 (2007).
3. Dumont, M. & Provost, M. A. Resilience in adolescents: Protective role of social support, coping strategies, self-esteem, and social activities on experience of stress and depression. *J. Youth Adolesc.* **28,** 343–363 (1999).
4. Nolen-Hoeksema, S. Responses to depression and their effects on the duration of depressive episodes. *J. Abnorm. Psychol.* **100,** 569–82 (1991).
5. Rosenberg, M. *Society and the adolescent self-image.* (Princeton University Press, 1965).



Supplementary Figure 1. Confirmatory factor analysis of morning cortisol. Extraction of a stable factor of morning cortisol over four days at baseline and at one-year follow-up. Values are factor loadings on each indicator. The double-headed arrow between day 5 and day 6 indicates the modification to the model at follow-up.

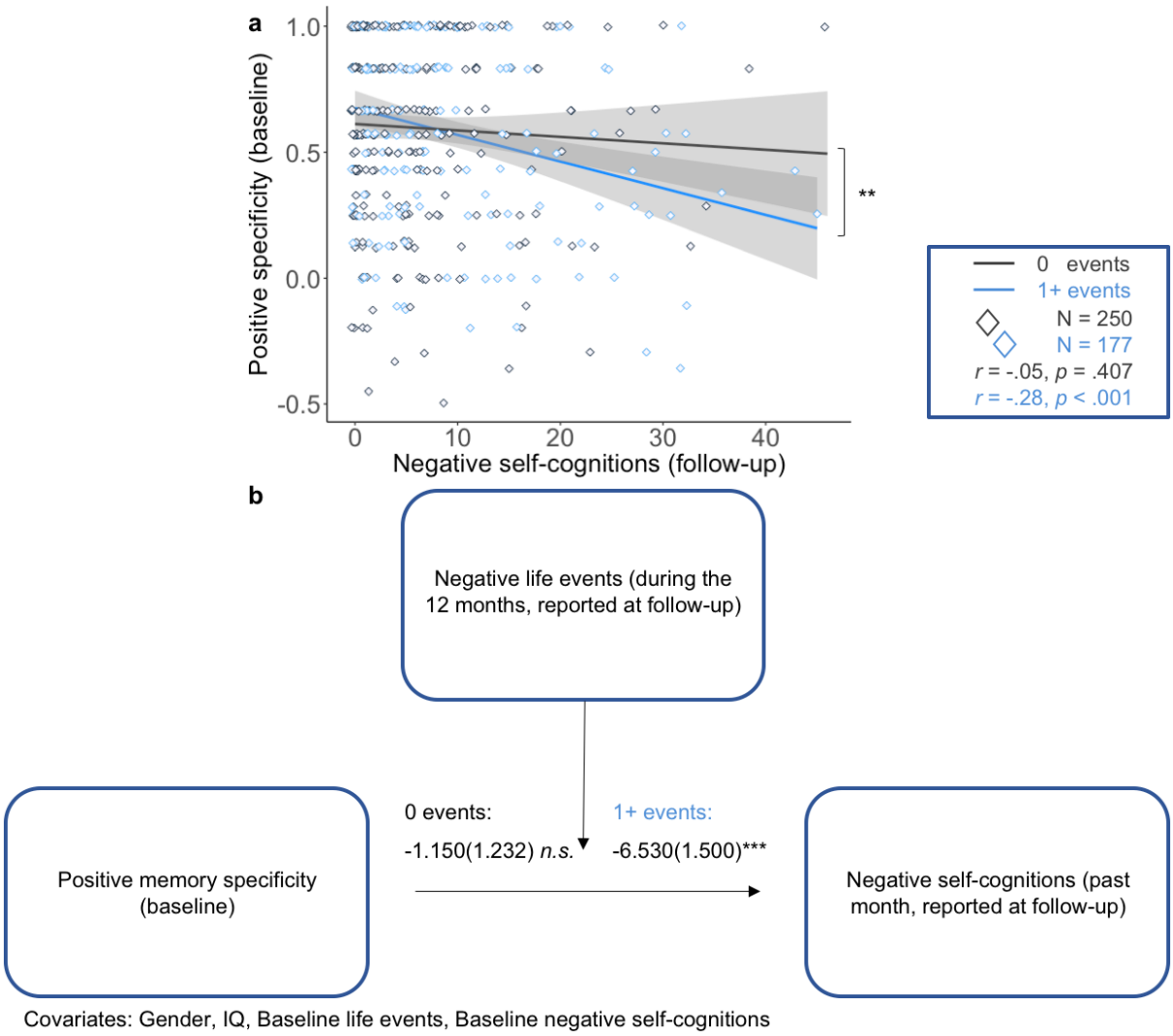


Figure 2. Positive memory specificity lowers negative self-cognitions after recent negative life events. Plot **a** is showing a significant interaction where the effect of positive memory specificity on negative self-cognitions depends on exposure to recent negative life events. Specifically, positive memory specificity is related to lower negative self-cognitions in those exposed to one or more recent negative life events (during the 12 months following baseline of the study; blue line). The relationship is not significant in those not exposed to recent negative life events (black line). Lines show raw correlations and grey bands show confidence intervals. Figure **b** shows these results as a moderation model. Path values represent unstandardized coefficients and bootstrapped standard errors; *P < .05; **P < .01; ***P < .005; *n.s.* not significant.

Supplementary Table 1. Descriptive statistics, and comparison of variable means between full sample (n = 575) and subsample (n = 427).

	Subsample (n = 427)			Full sample (n = 575)			
Variable	M	SD	Min-max	M	SD	Min-max	P
Age baseline	13.70	1.17	12 - 16	13.70	1.15	12 - 16	.807
Age follow-up	14.70	1.17	13 - 17	14.70	1.15	13 - 17	.719
Positive memory specificity	0.59	0.36	-0.5 - 1	0.59	0.37	-0.5 - 1	.874
IQ	102.80	16.62	59 - 151	101.80	16.32	59 - 151	.343
Depressive symptoms baseline	17.89	9.24	0 - 55	18.24	9.19	0 - 55	.548
Depressive symptoms follow-up	14.66	9.35	0 - 58	14.99	9.14	0 - 58	.578
Negative self-cognitions/mood ratio baseline	0.41	0.33	0 - 2.5	0.42	0.33	0 - 2.5	.521
Negative self-cognitions/mood ratio follow-up	0.34	0.31	0 - 1.6	0.34	0.28	0 - 1.6	.977
Negative life events baseline	0.96	1.10	0 - 4	0.97	1.14	0 - 4	.938
Negative life events follow-up	0.67	1.03	0 - 7	0.67	1.03	0 - 7	.982

M = mean, SD = standard deviation

Supplementary Table 2. Longitudinal measurement invariance of morning cortisol. The configural model is the baseline comparison model, in which all parameters are freely estimated. In the metric model, all parameters are freely estimated apart from factor loadings, which are constrained to be equal across time points. The scalar model constrains the mean of each observed variable over time. If this step is satisfied, strong measurement invariance can be established. The means model constrains the mean of the latent factor over time, indicating whether there are any significant mean differences across measurements.

Model	X^2	df	P	CFI	RMSEA	CFI delta	RMSEA delta
Configural	23.754	14	NA	0.991	0.040	NA	NA
Metric vs Configural	28.612	17	.183	0.989	0.040	0.002	0.000
Scalar vs Metric	28.731	20	.989	0.992	0.032	0.003	0.008
Means vs Scalar	29.326	21	.440	0.992	0.030	0.000	0.002

Model = four hierarchical (nested) steps of increasingly more strict equality constraints, X^2 = chi square difference, df = degrees of freedom, CFI = comparative fit index, RMSEA = the root mean squared error of approximation, CFI delta = difference in comparative fit index**,** RMSEA delta = difference in root mean squared error of approximation. Differences less than RMSEA delta = .015, or CFI delta = .01 are not considered significant, which indicates measurement invariance for that particular nested model comparison.

Supplementary Table 3. Path model without outliers: positive memory specificity predicting negative self-cognitions and morning cortisol.

Outcome	Predictors	Estimate	S.E.	*z*-value	P(>|z|)
Morning cortisol (b)	Positive memory specificity (b)	-0.226	0.159	-1.426	.154
	Negative life events (b)	-0.047	0.047	-0.987	.324
	Gender (b)	0.759	0.115	6.610	**.001**
	IQ (b)	0.000	0.004	0.078	.938
Morning cortisol (f)	Morning cortisol (b)	0.212	0.040	5.319	**.001**
	Positive memory specificity (b)	-0.303	0.119	-2.539	**.011**
	Negative self-cognitions/mood (b)	0.192	0.148	1.296	.195
	Negative life events (b)	-0.021	0.043	-0.474	.635
	Negative life events (f)	0.137	0.051	2.681	.007
	Gender (b)	0.339	0.096	3.523	**.001**
	IQ (b)	0.008	0.003	3.301	**.001**
Negative self-cognitions/mood (b)	Positive memory specificity (b)	-0.048	0.039	-1.238	.216
	Negative life events (b)	0.025	0.015	1.710	.087
	Gender (b)	0.037	0.029	1.273	.203
	IQ (b)	-0.000	0.001	0.087	.931
Negative self-cognitions/mood (f)	Negative self-cognitions/mood (b)	0.446	0.044	10.180	**.001**
	Positive memory specificity (b)	-0.095	0.034	-2.797	**.005**
	Morning cortisol (b)	-0.017	0.012	-1.507	.132
	Negative life events (b)	0.017	0.011	1.516	.130
	Negative life events (f)	0.024	0.016	1.570	.116
	Gender (b)	0.007	0.029	0.249	.804
	IQ (b)	0.000	0.001	0.480	.631
Morning cortisol (b) ~~	Negative self-cognitions/mood (b)	0.017	0.015	1.128	.259
Morning cortisol (f) ~~	Negative self-cognitions/mood (f)	-0.011	0.010	-1.122	.262

n = 390. (b) = baseline, (f) = follow-up. Boys are coded as 1, girls as 2. Significant paths are bolded. Robust model fit indices (acceptable fit): X^2_2 = 3.871, P = .144, CFI = 0.992, TLI = 0.883, RMSEA = 0.051, 95 % CI [0.000, 0.128], SRMR = 0.015. Estimate = unstandardised coefficient, S.E. = robust standard error, *z*-value = standardised coefficient.

Supplementary Table 4. To rule out selective attrition as an explanation for the results, we ran a structural equation model using the Full Information Maximum Likelihood method and a robust estimator to handle missing data. The model is penalised for all estimated parameters.

Outcome	Predictors	Estimate	S.E.	*z*-value	P(>|z|)
Morning cortisol (b)	Cortisol day 1 (b)	1.000			
	Cortisol day 2 (b)	1.021	0.075	13.555	**.001**
	Cortisol day 3 (b)	1.090	0.082	13.339	**.001**
	Cortisol day 4 (b)	0.923	0.074	12.544	**.001**
Morning cortisol (f)	Cortisol day 1 (f)	1.000			
	Cortisol day 2 (f)	0.935	0.114	8.175	**.001**
	Cortisol day 3 (f)	0.924	0.111	8.340	**.001**
	Cortisol day 4 (f)	0.934	0.110	8.527	**.001**
Morning cortisol (b)	Positive memory specificity (b)	-0.270	0.148	-1.821	.069
	Negative life events (b)	-0.048	0.047	1.008	.313
	Gender (b)	0.779	0.111	7.028	**.001**
	IQ (b)	0.006	0.003	2.076	**.038**
Morning cortisol (f)	Morning cortisol (b)	0.620	0.123	5.048	**.001**
	Positive memory specificity (b)	-0.419	0.192	-2.183	**.029**
	Negative self-cognitions/mood (b)	0.405	0.216	1.874	.061
	Negative life events (b)	0.036	0.064	0.566	.571
	Negative life events (f)	0.002	0.059	0.027	.978
	Gender (b)	0.342	0.151	2.270	**.023**
	IQ (b)	0.009	0.004	2.362	**.018**
Negative self-cognitions/mood (b)	Positive memory specificity (b)	-0.060	0.036	-1.649	.099
	Negative life events (b)	0.020	0.011	1.850	.064
	Gender (b)	0.063	0.024	2.641	**.008**
	IQ (b)	-0.000	0.001	-0.694	.488
Negative self-cognitions/mood (f)	Negative self-cognitions/mood (b)	0.408	0.048	8.426	**.001**
	Positive memory specificity (b)	-0.080	0.033	-2.453	**.014**
	Morning cortisol (b)	-0.008	0.010	-0.861	.389
	Negative life events (b)	0.013	0.009	1.548	.122
	Negative life events (f)	0.021	0.010	2.154	**.031**
	Gender (b)	0.032	0.024	1.343	.179
	IQ (b)	-0.001	0.001	-0.838	.402
Morning cortisol (b) ~~	Negative self-cognitions/mood (b)	0.002	0.016	0.142	.887
Morning cortisol (f) ~~	Negative self-cognitions/mood (f)	-0.000	0.017	-0.004	.997

(b) = baseline, (f) = follow-up. Boys are coded as 1, girls as 2. Significant paths are bolded. Robust model fit indices: X^2_{63} = 89.826, P = .015, CFI = 0.984, TLI = 0.976, RMSEA = 0.024, 95 % CI [0.011, 0.034], SRMR = 0.025. Estimate = unstandardised coefficient, S.E. = robust standard error, *z*-value = standardised coefficient.

Supplementary Table 5. Results of moderation and moderated mediation models without covariates. The index of the moderated mediation (ab) is significant for confidence intervals that do not include 0. All significant values are bolded.

Path	Predictor	Moderator	Mediator	Outcome	Effect	S.E.	df	t	95% CI	P(>|z)
c1	Pos memory	0 events		Neg cognitions	-1.079	1.411	423	-0.765	[-3.853, 1.694]	.445
c2	Pos memory	1+ events		Neg cognitions	-7.433	1.741	423	-4.270	**[-10.855, -4.012]**	**.001**
a1	Pos memory	0 events	Neg cognitions		-1.079	1.411	423	-0.765	[-3.853, 1.694]	.445
a2	Pos memory	1+ events	Neg cognitions		-7.433	1.741	423	-4.270	**[-10.855, -4.012]**	**.001**
b			Neg cognitions	Dep sympt	0.754	0.039	424	19.170	**[0.676, 0.831]**	**.001**
ab	Pos memory	Neg events	Neg cognitions	Dep sympt	-4.788	1.859	424		**[-8.541, -1.255]**	
c’	Pos memory	Neg events	Neg cognitions	Dep sympt	-0.060	0.918	424	-0.065	[-1.865, 1.745]	.948
a1	Pos memory	0 events	Dep sympt		-1.238	1.565	423	-0.791	[-4.314, 1.837]	.429
a2	Pos memory	1+ events	Dep sympt		-5.005	1.930	423	-2.593	**[-8.799, -1.211]**	**.010**
b			Dep sympt	Neg cognitions	0.616	0.032	424	19.170	**[0.553, 0.679]**	**.001**
ab	Pos memory	Neg events	Dep sympt	Neg cognitions	-2.321	1.740	424		[-5.849, 0.954]	
c’	Pos memory	Neg events	Dep sympt	Neg cognitions	-1.934	0.825	424	-2.344	**[-3.555, -0.312]**	**.020**

Predictor: baseline, moderator: between baseline and follow-up, mediator and outcome: follow-up. Pos memory = positive memory specificity, Neg events = negative life events, Neg cognitions = negative self-cognitions, Dep sympt = depressive symptoms. Levels of the moderator are 0 (no events) and 1+ (one or more events). Path a1/a2 = conditional effect of predictor on mediator, b = relationship between mediator and outcome, ab = indirect effect of predictor on outcome, through mediator, c’ = direct effect of predictor on outcome controlling for the indirect effect, c1/c2 = conditional direct effect of predictor on outcome. Effect = standardised coefficient, S.E. = bootstrapped standard error, df = degrees of freedom, 95 % CI = 95 % bootstrapped confidence interval of the estimate.

Supplementary Table 6. Results of moderation and moderated mediation models with outliers excluded. The index of the moderated mediation (ab) is significant for confidence intervals that do not include 0. All significant values are bolded.

Path	Predictor	Moderator	Mediator	Outcome	Effect	S.E.	df	t	95% CI	P(>|z)
c1	Pos memory	0 events		Neg cognitions	-1.549	1.096	382	-1.413	[-3.705, 0.607]	.159
c2	Pos memory	1+ events		Neg cognitions	-6.064	1.380	382	-4.394	[-8.778, -3.350]	**.001**
a1	Pos memory	0 events	Neg cognitions		-1.335	1.076	381	-1.240	[-3.450, 0.781]	.216
a2	Pos memory	1+ events	Neg cognitions		-5.773	1.355	381	-4.260	**[-8.437, -3.108]**	**.001**
b			Neg cognitions	Dep sympt	0.497	0.048	382	10.277	**[0.402, 0.592]**	**.001**
ab	Pos memory	Neg events	Neg cognitions	Dep sympt	-2.206	1.034	382		**[-4.301, -0.291]**	
c’	Pos memory	Neg events	Neg cognitions	Dep sympt	0.242	0.830	382	0.292	[-1.389, 1.874]	.771
a1	Pos memory	0 events	Dep sympt		-0.816	1.160	381	-0.703	[-3.097, 1.465]	.482
a2	Pos memory	1+ events	Dep sympt		-1.973	1.461	381	-1.351	[-4.845, 0.899]	.178
b			Dep sympt	Neg cognitions	0.436	0.042	382	10.277	**[0.352, 0.519]**	**.001**
ab	Pos memory	Neg events	Dep sympt	Neg cognitions	-0.504	0.909	382		[-2.485, 1.063]	
c’	Pos memory	Neg events	Dep sympt	Neg cognitions	-2.501	0.766	382	-3.264	**[-4.007, -0.995]**	**.001**

Predictor: baseline, moderator: between baseline and follow-up, mediator and outcome: follow-up. Pos memory = positive memory specificity, Neg events = negative life events, Neg cognitions = negative self-cognitions, Dep sympt = depressive symptoms. Levels of the moderator are 0 (no events) and 1+ (one or more events). Path a1/a2 = conditional effect of predictor on mediator, b = relationship between mediator and outcome, ab = indirect effect of predictor on outcome, through mediator, c’ = direct effect of predictor on outcome controlling for the indirect effect, c1/c2 = conditional direct effect of predictor on outcome. Effect = standardised coefficient, S.E. = bootstrapped standard error, df = degrees of freedom, 95 % CI = 95 % bootstrapped confidence interval of the estimate.