Positive memory specificity is associated with reduced vulnerability to depression

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Depression is the leading cause of disability worldwide[1]. Early life stress exposure increases risk for depression[2], and has been proposed to sensitise the maturing psychophysiological stress system to later life stress[3]. In response to stress, positive memory activation has been found to dampen cortisol responses and improve mood in humans[4], and to reduce depression-like behaviour in mice[5]. Here we used path modeling to examine whether recalling specific positive memories predicts reduced vulnerability to depression (i.e., high morning cortisol[6–9] and negative self-cognitions during low mood[10–12]) in adolescents at risk due to early life stress (n = 427, age: 14 years)[8]. We found that positive memory specificity was associated with lower morning cortisol and fewer negative self-cognitions during low mood over the course of one year. Moderated mediation analyses demonstrated that positive memory specificity was related to lower depressive symptoms through fewer negative self-cognitions in response to negative life events reported in the one-year interval. These findings suggest that recalling specific positive life experiences may be a resilience factor[13] that helps lowering depressive vulnerability in adolescents with a history of early life stress.

Remembering specific positive life experiences, as single, temporally limited instances from the past, may be an important protective process when stress occurs[4]. People engage in reminiscing about past events quite frequently in their everyday lives[14], and evidence suggests that healthy individuals use recall of positive memories as one of many strategies to repair sad mood[15]. Positive emotions, for instance generated by such memories, in turn appear to facilitate physiological and emotional stress recovery, particularly in resilient individuals[16,17]. Recalling positive memories may be a protective mechanism in most adolescents, which may be disturbed in individuals who are vulnerable to depression[18]. In support of this, adolescents who were in remission from a recent depressive episode recalled more categorical positive memories[19]. Furthermore, it was recently found that depressed, at-risk and healthy adolescents show a gradient of positive memory deficits after a negative mood induction[20]. These findings together imply that less specific responses to positive cues in particular ('positive memory specificity') constitute a trait-like marker of depressive vulnerability in at-risk adolescents. In addition, having a tendency toward more categorical, overgeneral memories (i.e., lacking in defining characteristics) that are not fixed in time or place, is characteristic of depression[21]. Low memory specificity is a trait-like characteristic of individuals at risk for depression[6,22], those currently depressed[19], and those in remission from depression[23]. Crucially, low memory specificity predicts the onset and course of depression[23], especially in response to stress[24]. Thus, low memory specificity may comprise a cognitive mechanism through which stress increases the risk of developing depression. Here we examined whether positive memory specificity is related to lower cognitive and physiological vulnerability to depression at baseline and over time in adolescents at risk due to high emotionality and/or exposure to early life stress.

We examined whether positive memory specificity is associated with reductions in two types of vulnerability for depression: negative self-cognitions during low mood[10–12] and high morning cortisol[6–9]. Negative self-cognitions refer to the tendency to blame and be derogatory about oneself ("I am useless"). Negative self-cognitions can be reactivated during in stress in individuals who are in remission from depression[12] and have been shown to prospectively predict first incidence of depression[25]. In individuals at risk for depression with a negative thinking style, negative life events may be particularly detrimental. The capacity to recall positive memories, however, may attenuate the interactive risks conferred by stress-exposure and negative self-cognitions. Morning cortisol is a physiological marker of vulnerability to depression; high morning cortisol is associated with familial risk for[9], onset[6,8], presence[7] and history of[7] major depression. Recently, morning cortisol was shown to interact with stressful life events leading to more depressive symptoms in adolescent girls[26]. Recalling positive memories, in contrast, has been shown to dampen the cortisol response to stress[4]. Here, we therefore hypothesised that positive memory specificity would be associated with fewer negative self-cognitions during low mood and lower morning cortisol at baseline and over time. That is, we investigated the putative relationships between positive memory specificity and two distinct vulnerability pathways for depression; one cognitive and the other physiological[27].

In this study, the role of positive memory specificity was investigated prospectively in a sample of adolescents at-risk for depression due to early life stress and/or high emotionality. Here, early life stress was operationalised as the presence of any early risk factor including current marital disharmony or past breakdown, moderately to severely negative life events, parental psychiatric illness, and/or the loss of a close relative or friend. In this letter, we use the term more broadly when referring to studies that examined childhood emotional, physical

or sexual abuse and/or neglect. High emotionality was defined as scoring over the 80th percentile on this trait[28]. All participants (n = 427, 200 girls, age 14; see descriptive statistics in Supplementary Table 1) completed the experimental cued recall Autobiographical Memory Test at baseline[29]. We used the ratio of total specific divided by total categorical (overgeneral) responses to positive cues as our predictor variable. The rationale for using this ratio was that specific and categorical responses are thought to tap into the same underlying construct of positive memory specificity (see Supplementary Results for analyses validating this ratio). At baseline and 1-year follow-up, all participants reported the frequency of moderate to severe negative life events during the last 12 months in a semi-structured interview. At both times, all participants reported depressive symptoms during the last two weeks (Mood and Feelings Questionnaire[30]), and negative self-cognitions and dysphoric mood experiences during episodes of low mood in the past month[12]. In accordance with Teasdale's Differential Activation hypothesis[12], we used the ratio of negative self-cognitions divided by dysphoric mood as our measure of cognitive vulnerability to depression. 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 (see Supplementary Results and Supplementary Figure 1). The morning cortisol factor showed strong measurement invariance over time, therefore, changes in cortisol can be meaningfully interpreted (see Supplementary Table 2).

We used path modeling in R (*lavaan*[31]) to examine whether positive memory specificity was related to fewer negative self-cognitions during low mood and lower morning cortisol currently and/or one year later. IQ and gender were specified as covariates since they have been associated with cognitive and physiological vulnerability for depression[6,32]. We also included negative life events as a covariate in the model because we were interested in depressive vulnerability relative to the extent of exposure to recent life stress[33]. These

variables deviated from a normal distribution (see Supplementary Table 3). Therefore, we employed a robust estimation method which accounts for this non-normality. We found that positive memory specificity at baseline was related to fewer negative self-cognitions during low mood at follow-up (Effect = -0.115, S.E. = 0.039, z = -2.983, P = 0.003, Pearson's effect size r = -0.144, 95% CI = -0.235, -0.050), but not at baseline (Effect = -0.048, S.E. = 0.046, z = -1.038, P = 0.299, r = -0.050, 95% CI = -0.144, 0.050). Positive memory specificity was also related to lower morning cortisol at follow-up (Effect = -0.360, S.E. = 0.131, z = -2.747, P = 0.006, r = -0.133, 95% CI = -0.225, -0.039), but not at baseline (Effect = -0.305, S.E. = 0.165, z = -1.851, P = 0.064, r = -0.090, 95% CI = -0.183, 0.004). Model fit was excellent (see Figure 1 and Table 1). The findings were not influenced by outliers (see Supplementary Table 4) or selective attrition (see Supplementary Table 5). The absence of cross-sectional relations was not due to the inclusion of follow-up assessments in the model, as post hoc analyses showed no significant raw correlations between positive memory specificity and baseline cortisol (Spearman's rank correlation, rho_{425} = -0.067, bootstrap 95% CI = -0.166, 0.023, P = 0.169) or negative self-cognitions during low mood (rho_{425} = -0.073, bootstrap 95% CI = -0.163, 0.012, P = 0.131).

Insert Figure 1 about here

Next, we examined whether the relationships in the path model (Figure 1 and Table 1) were due to memory specificity in general (and also found for negative memory specificity), or specific to positive memory specificity. We ran an exploratory model with both negative and positive memory specificity as predictors. In this model, there was a relation between positive memory specificity and negative self-cognitions/mood (Effect = -0.122, S.E. = 0.041, z = -2.979, P = 0.003, r = -0.144, 95% CI = -0.235, -0.050) and morning cortisol at follow-up

(Effect = -0.368, S.E. = 0.146, z = -2.523, P = 0.012, r = -0.122, 95% CI = -0.214, -0.028). In contrast, negative memory specificity was unrelated to negative self-cognitions/mood (Effect = 0.018, S.E. = 0.043, z = 0.422, P = 0.673, r = 0.020, 95% CI = -0.075, 0.114) and morning cortisol at follow-up (Effect = 0.021, S.E. = 0.153, z = 0.134, P = 0.893, r = 0.007, 95% CI = -0.087, 0.101). Relationships between positive memory specificity and negative self-cognitions/mood (Effect = -0.033, S.E. = 0.049, z = -0.649, P = 0.497, r = -0.031, 95% CI = -0.125, 0.064) and morning cortisol were not significant at baseline (Effect = -0.263, S.E. = 0.179, z = -1.469, P = 0.142, r = -0.071, 95% CI = -0.164, 0.024). Negative memory specificity was unrelated to negative self-cognitions/mood (Effect = -0.038, S.E. = 0.049, z = -0.774, P = 0.439, r = -0.038, 95% CI = -0.132, 0.057) and morning cortisol at baseline (Effect = -0.108, S.E. = 0.169, z = -0.640, P = 0.522, r = -0.031, 95% CI = -0.125, 0.064). Robust fit statistics indicated good fit for the model with both predictors (X^2_2 = 1.361, P = 0.506, CFI = 1, TLI = 1.041, RMSEA = 0, 95% CI = 0.000, 0.087, SRMR = 0.007). In this model, constraining the negative memory specificity paths to zero did not affect model fit, suggesting that negative memory specificity was not needed to explain our data (robust chi-square difference: X^2_2 = 0.189, P = 0.910). The strength of the evidence against the model with negative memory specificity included was very strong (BIC = 10252 for the comparison model with both included; BIC = 10240 for the nested model with negative memory specificity constrained; BIC difference > 10)[34]. Robust fit statistics still indicated good fit when negative memory specificity was constrained: X^2_4 = 1.558, P = 0.816, CFI = 1, TLI = 1.078, RMSEA = 0, 95% CI = 0.000, 0.045, SRMR = 0.008. On the other hand, constraining the positive memory specificity paths to zero significantly lowered model fit (robust chi-square difference: X^2_2 = 16.214, P < 0.001). Compared to the model with both included, the evidence against the model with positive memory specificity constrained was positive, despite the lower complexity (BIC = 10252 for the comparison model with both included; BIC =

168 10255 for the nested model with positive memory specificity constrained; BIC difference 3)[34].
169 Robust fit statistics indicated poor model fit when positive memory specificity was
170 constrained: X^2_4 = 16.869, P = 0.002, CFI = 0.947, TLI = 0.605, RMSEA = 0.086, 95% CI =
171 0.047, 0.131, SRMR = 0.020). Furthermore, the lack of an effect of negative memory
172 specificity was not due to the inclusion of positive memory specificity in the same model.
173 When positive memory specificity was constrained to zero, negative memory specificity was
174 unrelated to negative self-cognitions/mood (Effect = -0.035, S.E. = 0.041, *z* = -0.844, P =
175 0.399, r = -0.041, 95% CI = -0.135, 0.054) and morning cortisol at follow-up (Effect = -0.139,
176 S.E. = 0.136, *z* = -1.020, P = 0.308, r = -0.049, 95% CI = -0.143, 0.046). Overall, positive but
177 not negative memory specificity contributed to the path model, so negative memory
178 specificity was not needed as a predictor.
179
180 *Insert Table 1 about here*
181
182 Accessing specific positive memories in the face of stress may activate a cognitive
183 mechanism that 'disconfirms' negative self-cognitions, leading indirectly to mood
184 improvement over time. To test this mechanistic hypothesis, we first ran a moderation
185 analysis with prospective negative life events as a moderator of the relationship between
186 positive memory specificity at baseline and negative self-cognitions at follow-up. We
187 conducted a moderation analysis using the PROCESS macro in SPSS[35]. This analysis
188 supported our hypothesis (see Table 2 and Supplementary Figure 2), showing a significant
189 overall moderation ($F_{1,419}$ = 7.927, P = 0.005, R^2 change = 0.013), controlling for IQ, gender,
190 negative life events and negative self-cognitions at baseline. In this model, positive memory
191 specificity was associated with fewer negative self-cognitions in those who experienced at
192 least one negative life event (Effect = -6.530, S.E. = 1.500, t = -4.353, P < 0.001, r = -0.208,
193 95% CI = -0.297, -0.116), but not in those who did not experience any negative life events

(Effect = -1.150, S.E. = 1.232, t = -0.934, P = 0.351, r = -0.046, 95% CI = -0.140, 0.049). In contrast, post hoc analyses showed that negative life events did not moderate the relationship between positive memory specificity and dysphoric mood ($F_{1,419}$ = 1.785, P = 0.182, R^2 change = 0.003), depressive symptoms ($F_{1,419}$ = 1.534, P = 0.216, R^2 change = 0.002), or morning cortisol ($F_{1,419}$ = 0.271, P = 0.603, R^2 change = 0.001) at follow-up, controlling for IQ, gender, negative life events and baseline values of the outcomes. Next, we explored whether negative self-cognitions mediated an indirect relationship between positive memory specificity and later depressive symptoms depending on exposure to negative life events (i.e., a moderated mediation with 5,000 bootstrap samples; Figure 2B). In line with the path model in Figure 1, we controlled for baseline depressive symptoms and negative self-cognitions in this analysis to focus on differences over time, in addition to IQ, gender and negative life events. This analysis (see Table 2, Figure 2A and Figure 2B) showed a significant indirect effect of positive memory specificity through lower negative self-cognitions on depressive symptoms, depending on exposure to negative life events (Index = -3.026, S.E. = 1.290, 95% CI = -5.752, -0.704).

Insert Figure 2 about here

The moderation model showed the same results without any covariates ($F_{1,423}$ = 8.039, P = 0.005, R^2 change = 0.018; see Supplementary Table 6) and with outliers excluded ($F_{1,382}$ = 6.755, P = 0.010, R^2 change = 0.012; see Supplementary Table 7). Also, the moderated mediation model showed the same results without any covariates (Index = -4.788, S.E. = 1.859, 95% CI = -8.541, -1.255; see Supplementary Table 6) and with outliers excluded (Index = -2.206, S.E. = 1.034, 95% CI = -4.301, -0.291; see Supplementary Table 7). Importantly, the moderated mediation model was specified on data from two and not three

waves (see correlations between the cross-sectional measures in the model in Supplementary Results). However, a moderated mediation model with the mediator and outcome interchanged showed that depressive symptoms did not mediate the relationship between positive memory specificity and negative self-cognitions (Index = -1.184, S.E. = 1.167, 95% CI = -3.630, 0.962; see Table 2).

Insert Table 2 about here

In this study, we find that positive memory specificity is associated with reduced cognitive and physiological vulnerability to depression over time in at-risk adolescents. We further identify a potential cognitive mechanism whereby specific positive memories predict lower negative self-cognitions in response to stress. As such, it may be that specific positive memories help form boundaries to the scope of negative self-cognitions, thereby reducing the likelihood of the emergence of depressogenic symptoms[36]. We recently showed that emphasising the value of positive social experiences as part of a brief psychological treatment programme can lead to depressive symptom reduction on par with existing treatments in depressed adolescents[37]. Encoding of current positive social experiences may increase both the availability of specific positive memories and the probability of positive memories being retrieved later in life, which may disconfirm negative self-cognitions arising from low mood.

We propose that positive memory specificity may be an adaptive mnemonic mechanism that may be especially relevant in adolescents at risk for depression. Early adverse experiences confer risk in part because being recurrently told ‘you are worthless’ and/or ignored are associated with the emergence of negative self-cognitions[38]. These comprise a cognitive vulnerability to depression which is ‘activated’ in the face of stress[11], leading to subsequent

low mood. Early adversities have also been found to alter activation of brain areas involved in the specification of positive memories (i.e., reduced hippocampal activation), suggesting a neural substrate of lower positive memory specificity after early life stress[39]. Here, we find support for the idea that positive memory specificity may act as a naturalistic defence against the negative cognitive consequences emerging from new incoming stress in at-risk adolescents.

Our findings conceptually replicate and extend findings that positive memory recall lowers acute cortisol and mood responses to stress induction in the laboratory, where mood improvements were particularly seen in resilient individuals[4]. This conceptual replication is important given calls to triangulate research findings with multiple methods and lines of evidence[40]. The relationship between positive memory specificity and depressive symptoms was dependent on exposure to stressful events as they occurred naturally over time. This conditional relationship is in line with findings in a recent longitudinal community study, which did not find an association between low memory specificity and subsequent depression; however, the study did not take the potential interaction with recent life events into account[41]. Importantly, we found that positive memory specificity was only associated with fewer negative self-cognitions during low mood and lower morning cortisol over time, and not at baseline. Our results complement research finding a delayed symptomatic and morning cortisol reduction after positive attentional bias modification training[42]. The effect of a positive memory and/or attentional bias may unfold over time by regulating responses to new life events. This notion is in line with our finding that positive memory specificity was related to lower depressive symptoms through fewer negative self-cognitions in response to negative life events. Positive memory specificity may similarly be associated with dampened cortisol responses to everyday hassles over time. Compared to such everyday stressors, the

negative life events measured here may have been too infrequent to affect the relationship between positive memory specificity and morning cortisol[43].

We have previously demonstrated that in this sample, high morning cortisol predicts conversion to major depression only in boys with high subclinical depressive symptoms[6], and similar results have been obtained in adolescent girls[26]. Here, we find that positive memory specificity is associated with reduced morning cortisol over time, thus potentially regulating an important physiological vulnerability marker of depression (note that this effect is present for both genders; see Supplementary Results). Together, these findings suggest that positive memory specificity in adolescents who are at risk, but not yet clinically unwell, may reduce depressive vulnerability associated with elevated morning cortisol levels. Furthermore, this physiological pathway to depressive vulnerability appeared to be relatively distinct from our measure of cognitive vulnerability, which was unrelated to cortisol in the path model (see Figure 1). This dissociation is in accordance with recent research findings, where pharmacological blockade of the Hypothalamic-Pituitary-Adrenal (HPA) axis stress response had no influence on subjective mood and self-esteem responses to stress[44]. Thus, while recent theory suggests that negative biases and cortisol may be interlinked in depression[27], we find a dissociation of cognitive and physiological vulnerability to depression in this study. Positive memory specificity may be associated with alleviated depression vulnerability through distinct pathophysiological mechanisms in different individuals. As of yet unidentified, intermediate neural pathways may link these mechanisms. Reward-related neural circuitry may be a promising candidate, which is related to both mood and cortisol reactivity, and is activated during positive memory recall, facilitating resilient responses to stress[4].

Currently, we do not know the precise mechanisms through which positive memory specificity is associated with reduced cortisol levels over time in the developing adolescent. However, there is some evidence to support a potential mediating role of reward processing in the effects of positive memory recall on mood and cortisol[4]. Blunted reward processing arising from the striatum is one of the strongest effects of early life stress on the developing adolescent brain[45]. The intrinsically rewarding properties of positive memories (where activation of the striatum underpins rekindling of positive emotion) may be lowered in depressed individuals[46], possibly as a consequence of blunted striatal responses to reward in major depression[47]. Thus, the protective effects associated with positive memory specificity in these at-risk individuals may be in part due to successful engagement of corticostriatal reward circuits. The amygdala, hippocampus and ventral striatum may be particularly important in regulating the HPA axis due to their direct connections with the paraventricular nucleus, which regulates signals to the HPA axis[48]. Lower daily cortisol output is associated with sustained corticostriatal activation to positive stimuli[49], and decreased amygdala signal coupled with increased ventromedial prefrontal activation during emotion regulation[50]. Thus, improved reward and positive emotion processing may lead to lower morning cortisol levels. Updating of reward-based learning over time through the activation of positive memories could further explain our findings of longitudinal, but not cross-sectional, relations between positive memory specificity and morning cortisol.

In a striking homology, stimulation of positive memory engrams reduced stress-induced depression-like behaviour in preclinical mouse models[5]. Optogenetic reactivation of positive memory engrams in the dentate gyrus triggered the reward system, including parts of the striatum and the amygdala, which again acted as a mechanism of the antidepressant effect. Importantly, optogenetic reactivation of engrams which encoded the memory of a positive

experience (i.e., meeting a female mouse), but not simple exposure to the positive situation, lowered depression-like behaviour in male mice. This suggests that recalling specific positive memories, with concurrent activation of neural systems involved in emotion and reward processing, may facilitate resilient responses to stress[51]. This benefit of positive emotion and reward activation was additionally supported by a recent neurofeedback study where the effect of positive memory recall on depressive symptoms was mediated by increased amygdala activity after training[52]. In sum, recalling specific positive memories may rekindle positive emotion and regulate cortisol output over time. The possibility that this effect is mediated by reward processing should be investigated in future research.

Positive memory specificity may be a resilience factor that facilitates adaptive responses to stress. An international consortium recently proposed a resilience framework where resilience is defined as *'The maintenance or quick recovery of mental health following an adverse life event or a period of adversity'*[13]. In this framework, stable pre-existing factors (resilience factors) facilitate resilient responses to future stress. These are distinguished from resilience mechanisms, which reflect adaptive responses to stress. Our findings suggest that positive memory specificity comprises a pre-existing resilience factor[6,22] that confers adaptive responses to stress (lower negative self-cognitions after negative life events; the resilience mechanism). This process may in turn help the maintenance or quick recovery of mental health (i.e., lower depressive symptoms) after stressful life events.

Notably, we showed no cross-sectional relation between positive memory specificity and both negative self-cognitions during low mood and morning cortisol. These findings are in accordance with the resilience framework, which suggests that resilient outcomes can only be measured after some form of life stress[13]. Depressive vulnerability was stress-emergent in this

study; positive memory specificity was only associated with fewer negative self-cognitions and, indirectly, lower depressive symptoms in the presence of at least one negative life event. This is in line with an emerging animal literature finding hormonal, neural and epigenetic adaptations to experimental stress, which facilitate future beneficial outcomes[53]. Based on this literature, it has been suggested that the process underlying resilient responses to stress is dynamic and interacting rather than a stable property of an organism which can be measured in a cross-sectional manner[53]. Our findings could be explained by similar adaptive processes over time, and support a dynamic conceptualisation of resilience.

Our findings may have important clinical implications. One possibility is that training in recalling specific positive memories may lower risk of developing depression. Such training has already shown promise[54]. For example, real-time amygdala neurofeedback during positive memory recall improved positive memory specificity and in turn lowered depressive symptoms after training[52]. Training may address the disturbed specificity and vividness of positive memory recall observed in depressed and recovered individuals (hampering the experience of "reliving" positive memories and thereby its mood-repairing effects)[18]. A recent study of positive memory enhancement training which emphasised specific positive memory recall provided preliminary support for this hypothesis. This study found higher memory specificity and higher perceived ability to "relive" positive memories after training, improving mood in depressed individuals[55]. The mechanistic role of negative self-cognitions in our study suggests that in particular, training in accessing specific self-affirming positive memories[56] may result in lower depressive symptoms in at-risk adolescents. Thus, our findings support ongoing work exploring the effects of targeting autobiographical memory processing on vulnerability to emotional disorders[54,57].

The current findings should be interpreted with the caveat that we did not have experimental control over the studied variables, thereby limiting the causal inferences that can be drawn. Although path models cannot establish causality from associations alone[58], they can examine whether a given hypothesised causal model is provisionally compatible with (i.e., not rejected by) the data, and whether it is more or less plausible than models that specify competing causal accounts. In doing so, temporal precedence is the most important criterion for causal models in the absence of experimental manipulation[59]. In our analyses, we aimed to establish temporal precedence by taking baseline measures into account (together with important confounds). In addition, we conceptually replicate findings from an experimental study[4], which provided a foundation for our hypothesis about causal direction. Finally, reduced morning cortisol associated with positive memory specificity may be interpreted as meaningful, because we established strong longitudinal measurement invariance of the cortisol assessments. However, we cannot fully discount the alternative causal explanation that cortisol moderated positive memory specificity[60]. In sum, although the present data seem to be compatible with our proposed causal model, we cannot conclude from these analyses that the relationships are causal. Future work should test whether manipulating positive memory specificity affects cognitive and physiological vulnerability to depression.

There are also some methodological limitations to consider. The relatively low number of cue words (i.e., 12) in the Autobiographical Memory Test may have reduced the reliability of the measure, particularly as responses to positive and negative cue words were analysed separately. It should further be noted that as only current and not previous psychopathology was among the exclusion criteria, it is possible that 'scarring' effects from previous episodes of psychopathology affected the results. However, this issue is limited by that participants were recruited in early adolescence, before the age of onset of many depressive disorders[61].

Moreover, the pattern of results did not differ in individuals who were diagnosed with major depression at follow-up (see Supplementary Results). Furthermore, exploratory analyses showed that all relationships between depressive vulnerability and positive memory specificity were independent of variation in self-esteem and mood-related rumination (see Supplementary Results). However, it should be noted that there may be other confounding variables underlying these associations (e.g., a general positive processing bias) not measured in this study.

A limitation of the cortisol sampling protocol was that cortisol was assessed at 08.00 am with a variable time interval from waking across four mornings at baseline and follow-up. However, if the measure was highly variable due to confounding from awakening times, the latent factor of morning cortisol would be expected to reflect state characteristics and not be highly stable over time. This was not the case, as morning cortisol showed strong longitudinal measurement invariance (see Supplementary Results).

A final caveat of our study is that in the exploratory moderated mediation models, the mediator and outcome variables were assessed at the same time. However, if shared measurement variance fully explained the mediating role of negative self-cognitions with depressive symptoms as the outcome, one would assume to find a significant mediation when the variables were interchanged. Yet, depressive symptoms did not mediate the relationship between positive memory specificity and negative self-cognitions at follow-up. Similarly, participants reported both negative life events in the last 12 months and depressive symptoms in the last two weeks at the same time point at follow-up, possibly inflating their (small to moderate) interrelation. This may have been affected in part by recall bias, where participants with high depressive symptoms may have overestimated the occurrence of recent negative life

418 events. However, negative life events were ascertained in a validated semi-structured
419 interview with particular emphasis on reducing recall bias, showing high parent-child and
420 panel agreement in previous reports[62]. Also, any time-invariant recall bias was taken into
421 account by controlling for baseline reporting of negative life events. Finally, the moderated
422 mediation analyses were exploratory, and need to be replicated in independent samples. With
423 the above caveats in mind, we tentatively suggest that lower negative self-cognitions may
424 comprise a cognitive mechanism through which positive memory specificity is associated
425 with decreased vulnerability to depression in response to stress in at-risk adolescents.
426
427 In sum, we show that positive memory specificity is associated with lower morning cortisol
428 and fewer negative self-cognitions during low mood over time in at-risk adolescents. We
429 propose that positive memory specificity may comprise a resilience factor in at-risk
430 adolescents, potentially through moderating cognitive and physiological pathways to
431 depressive vulnerability after life stress. Our findings conceptually replicate and extend
432 previous experimental work[4], showing the potential role of positive memory specificity in
433 regulating responses to stressors as they occur naturally over time. These findings may have
434 important clinical implications, highlighting the role of remembering specific positive life
435 experiences in adolescent mental health resilience.
436
437 **Methods**
438 The analyses were carried out on data from the Cambridge Hormones and Mood Project[8]. We
439 used a subsample of participants with data available for all measures (n = 427), and these did
440 not significantly differ from the full sample (n = 575; see Supplementary Table 1). No
441 statistical methods were used to pre-determine the sample size. However, our sample size is
442 larger than those reported in previous publications[24,41,63]. The exclusion criteria were: current

443 mental illness, current medical illness, pervasive developmental disorders, history of epilepsy
444 or central neurological disease or non-English speaking. Data was collected at secondary
445 schools in the county of Cambridgeshire in the middle 1990s (see Supplementary Methods for
446 information about recruitment). Interviews were conducted in the school setting, which
447 increases generalisability to a context relevant for early interventions. Parents and youths
448 gave written informed consent to join the study. The study was approved by the Cambridge
449 Local ethics committee and was conducted in accordance with the first revision of the
450 Declaration of Helsinki (Tokyo, 1975).
451
452 Adolescents at risk of developing depression due to high emotional temperament or exposure
453 to early adversity were selected and followed up over 12 months. Emotional temperament was
454 assessed with the EAS scales (Emotionality, Activity, Sociability and Shyness)[28] completed
455 by parents. Emotionality is associated with development of clinical depression[64]. At-risk
456 status was defined as having at least one early risk factor, which could be: scoring high (over
457 the 80th percentile) on the emotionality scale; current marital disharmony or past breakdown;
458 loss of/ permanent separation from a close relative or friend; history of parental psychiatric
459 disorder; moderately to severely undesirable events in the past twelve months. Moderate to
460 severe negative life events in the past 12 months were assessed by semi-structured interview
461 at baseline and follow-up[62]. A clear benefit over self-report were objective panel ratings of
462 severity, taking factors such as social context into account (see Supplementary Methods for an
463 overview of the types of events).
464
465 The Autobiographical Memory Test (AMT)[29] was developed to assess the content of
466 memories evoked by an experimental cued recall procedure. The AMT is validated and shows
467 good psychometric properties in young adolescents[65]. Participants were presented with one of

six positive and six negative cues at a time (e.g., 'happy') and instructed to recall a specific episode in relation to that cue. 60 seconds were allowed to produce a response. Memories were coded by research assistants trained by Professor Mark Williams, who created the Autobiographical Memory Test[29]. All ambiguous / uncertain codings were discussed at a consensus meeting of trained researchers and a coding was agreed upon. Inter-rater agreement, using the same scoring procedure, has previously been reported as excellent (99.3 % for categorical responses)[19]. Specific memories were defined as an episode with a specific time and place lasting no longer than a day. Responses were coded as categorical if they referred to repeated events. We used the ratio of specific to categorical responses to positive and negative cues in our analyses.

The Depressed States Checklist[12] is a measure of negative self-cognitions and dysphoric experience during episodes of low mood. Participants were asked to report how they felt when their mood went down at an occasion in the last month and rate their experience on 28 adjectives (i.e., not at all; slightly; moderately; very; or extremely) of which 14 were dysphoric mood descriptors (e.g., "sad") and 14 assessed negative self-cognitions (implying a globally negative view of the self, e.g., "useless"). The distinct and interactive nature of these two components of dysphoric experience has been supported[12].

The Moods and Feelings Questionnaire (MFQ) is a 33-item measure of self-reported depressive symptoms for use in children and adolescents[30]. Participants rated their symptoms over the last two weeks on a three-point Likert scale (*0 = not true*, *1 = sometimes*, *2 = true*). The scale has good psychometric properties ($\alpha = 0.91$, test-retest: $r = 0.84$)[66].

Morning cortisol was measured at 08.00 am at four occasions within a week after the baseline measurements (see Supplementary Methods for information about assay technique). The same procedure was followed 12 months later. Participants took samples on four consecutive schooldays and recorded their time of waking. The mean time from waking to sampling was 50 minutes. Morning cortisol is relatively stable over time in this cohort (estimated to 48-60% using latent state-trait modeling[6]).

Adolescents' current mental state was ascertained with the Kiddie Schedule for Affective Disorders and Schizophrenia patient version[67] and history of psychiatric illness was assessed by semi-structured interview with both adolescents and parents. General cognitive ability (IQ) was estimated from a short version of the Wechsler Intelligence Scale for Children–II[68] including the block design and vocabulary subtests.

Path modeling, confirmatory factor analyses (CFA) and structural equation modeling (SEM) were carried out in R version 3.4.1 ('Single Candle') using the packages *ggplot2*[69] and *lavaan*[31] (see the Supplementary Software for R code). CFA is a confirmatory latent variable technique where a theorised latent construct ('morning cortisol') load on separate indicators (cortisol assessments across several mornings), which also have a unique variance not accounted for by the latent factor (i.e., 'error'; see Supplementary Figure 1). Path modeling is a more flexible and powerful extension to the regression model where directional hypotheses about linear relationships between independent variables (i.e., positive memory specificity) and dependent variables can be tested (i.e., morning cortisol and negative self-cognitions during low mood)[70]. It should be noted that path modelling does not provide evidence for the causality of such relationships. However, it may indicate whether the causal model under investigation is compatible with the data[58]. Results were validated in a structural equation

model (which combines the principles behind CFA and path modeling) using the Full Information Maximum Likelihood method (FIML; see Supplementary Table 5). FIML yields unbiased parameter estimates assuming data is missing at random or missing completely at random[71]. The path model described in the main analyses had 32 free parameters, which is above the common guideline of minimum 10 observations per parameter (n = 427)[72].

The moderation and moderated mediation analyses were conducted in PROCESS 3.0 (model 1 and 7 respectively; processmacro.org) using IBM SPSS Statistics Version 25.0. These analyses were based on the ordinary least squares method. We followed the recommendations of Hayes[35] for these analyses, given its superior power and conceptual advantages over the traditional causal steps approach[73]. Using percentile bootstrap confidence intervals, PROCESS offers computation of a single index testing the significance of the moderated mediation model, removing the need for separate significance tests of each path.

To account for deviations from multivariate normality we use a robust robust maximum likelihood estimator ('MLR' in *lavaan*) which computes robust standard errors and a scaled test statistic[31]. Furthermore, the bootstrap confidence intervals in the moderated mediation analyses are customised to the distribution of the data[35]. Finally, we report non-parametric Spearman's rank correlations with bootstrap confidence intervals. Tests of equality of variances, based on the median to account for non-normality, is reported for statistical analyses of group differences.

Removing 37 outliers with *z*-scores ± $\geq$3 did not change any of the main findings reported (see Supplementary Tables 4 and 7 for results with outliers removed). All hypothesis tests conducted were two-tailed. Effect sizes reported here (Pearson's r) represent conservative

estimates, as they were calculated based on *z* and *t* scores from the baseline-adjusted longitudinal models.

We report chi-square (X^2) fit statistics, the root mean squared error of approximation (RMSEA) with its 90 % confidence interval, and standardized root mean square residual (SRMR). RMSEA of less than 0.05 and an SRMR below 0.1 implies a good fit[70]. We also report the comparative fit index (CFI) and the Tucker-Lewis index (TLI), where values of CFI and TLI over 0.95 represent good fit[70]. For model comparisons, we report the robust (scaled) Satorra-Bentler chi-square difference test. We also report the Bayesian Information Criterion (BIC), which is penalised for the number of freely estimated parameters, favouring the least complex model. As a rule of thumb, a BIC difference over 10 is considered very strong evidence against the model with the highest BIC, 6 to 10 is considered strong evidence, 2 to 6 is considered positive evidence and 0 to 2 is considered negligible evidence[34].

Data availability statement

The data supporting the analyses presented in this paper is available at the University of Cambridge research repository [https://doi.org/10.17863/CAM.23436][74], and the corresponding authors' websites (www.annelauravanharmelen.com & www.adriandahlaskelund.com).

Code availability statement

The code supporting the analyses presented in this paper is available at the University of Cambridge research repository [https://doi.org/10.17863/CAM.23436][74], and the corresponding authors' websites (www.annelauravanharmelen.com & www.adriandahlaskelund.com).

References

1. Barber, R. M. *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* **386,** 743–800 (2015).
2. Green, J. G. *et al.* Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: Associations with first onset of DSM-IV disorders. *Arch. Gen. Psychiatry* **67,** 113–123 (2010).
3. McLaughlin, K. A., Conron, K. J., Koenen, K. C. & Gilman, S. E. Childhood adversity, adult stressful life events, and risk of past-year psychiatric disorder: A test of the stress sensitization hypothesis in a population-based sample of adults. *Psychol. Med.* **40,** 1647–1658 (2010).
4. Speer, M. E. & Delgado, M. R. Reminiscing about positive memories buffers acute stress responses. *Nat. Hum. Behav.* **1,** 0093 (2017).
5. Ramirez, S. *et al.* Activating positive memory engrams suppresses depression-like behaviour. *Nature* **522,** 335–339 (2015).
6. Owens, M. *et al.* Elevated morning cortisol is a stratified population-level biomarker for major depression in boys only with high depressive symptoms. *Proc. Natl. Acad. Sci.* **111,** 3638–3643 (2014).
7. Vreeburg, S. A. *et al.* Major depressive disorder and hypothalamic-pituitary-adrenal axis activity. *Arch. Gen. Psychiatry* **66,** 617–626 (2009).
8. Goodyer, I. M., Herbert, J., Tamplin, A. & Altham, P. M. E. First-episode major depression in adolescents. *Br. J. Psychiatry* **176,** 142–149 (2000).
9. Mannie, Z. N., Harmer, C. J. & Cowen, P. J. Increased waking salivary cortisol levels in young people at familial risk of depression. *Am. J. Psychiatry* **164,** 617–621 (2007).

10. Teasdale, J. D. Cognitive vulnerability to persistent depression. *Cogn. Emot.* **2,** 247–274 (1988).

11. Alloy, L. B., Abramson, L., Stange, J. & Rachel, S. Cognitive vulnerability and unipolar depression. in *The Oxford Handbook of Mood Disorders* (eds. DeRubeis, R. J. & Strunk, D. R.) (Oxford University Press, 2017).

12. Teasdale, J. D. & Cox, S. G. Dysphoria: self-devaluative and affective components in recovered depressed patients and never depressed controls. *Psychol. Med.* **31,** 1311–1316 (2001).

13. Kalisch, R. *et al.* The resilience framework as a strategy to combat stress-related disorders. *Nat. Hum. Behav.* **1,** 784–790 (2017).

14. Killingsworth, M. A. & Gilbert, D. T. A wandering mind is an unhappy mind. *Science (80-.).* **330,** 932 (2010).

15. Josephson, B. R., Singer, J. A. & Salovey, P. Mood regulation and memory: Repairing sad moods with happy memories. *Cogn. Emot.* **10,** 437–444 (1996).

16. Tugade, M. M. & Fredrickson, B. L. Resilient individuals use positive emotions to bounce back from negative emotional experiences. *J. Pers. Soc. Psychol.* **86,** 320–333 (2004).

17. Ong, A. D., Bergeman, C. S., Bisconti, T. L. & Wallace, K. A. Psychological resilience, positive emotions, and successful adaptation to stress in later life. *J. Pers. Soc. Psychol.* **91,** 730–749 (2006).

18. Joormann, J., Siemer, M. & Gotlib, I. H. Mood regulation in depression: Differential effects of distraction and recall of happy memories on sad mood. *J. Abnorm. Psychol.* **116,** 484–490 (2007).

19. Park, R. J., Goodyer, I. M. & Teasdale, J. D. Categoric overgeneral autobiographical memory in adolescents with major depressive disorder. *Psychol. Med.* **32,** 267–276

(2002).

20. Begovic, E. *et al.* Positive autobiographical memory deficits in youth with depression histories and their never-depressed siblings. *Br. J. Clin. Psychol.* **56,** 329–346 (2017).

21. Williams, J. M. G. *et al.* Autobiographical memory specificity and emotional disorder. *Psychol. Bull.* **133,** 122–148 (2007).

22. Young, K. D., Bellgowan, P. S. F., Bodurka, J. & Drevets, W. C. Behavioral and neurophysiological correlates of autobiographical memory deficits in patients with depression and individuals at high risk for depression. *JAMA Psychiatry* **70,** 698–708 (2013).

23. Sumner, J. A., Griffith, J. W. & Mineka, S. Overgeneral autobiographical memory as a predictor of the course of depression: A meta-analysis. *Behav. Res. Ther.* **48,** 614–625 (2010).

24. Sumner, J. A. *et al.* Overgeneral autobiographical memory and chronic interpersonal stress as predictors of the course of depression in adolescents. *Cogn. Emot.* **25,** 183–192 (2011).

25. Alloy, L. B. *et al.* Prospective incidence of first onsets and recurrences of depression in individuals at high and low cognitive risk for depression. *J. Abnorm. Psychol.* **115,** 145–156 (2006).

26. Schuler, K. L. *et al.* Diurnal cortisol interacts with stressful events to prospectively predict depressive symptoms in adolescent girls. *J. Adolesc. Heal.* **61,** 767–772 (2017).

27. Beck, A. T. The evolution of the cognitive model of depression and its neurobiological correlates. *Am. J. Psychiatry* **165,** 969–977 (2008).

28. Buss, A. H. & Plomin, R. Theory and measurement of EAS. in *Temperament: Early Developing Personality Traits* 84–104 (Lawrence Erlbaum Associates, 1984).

29. Williams, J. M. G. & Broadbent, K. Autobiographical memory in suicide attempters. *J.*

642 *Abnorm. Psychol.* **95,** 144–149 (1986).
643 30. Costello, E. J. & Angold, A. Scales to assess child and adolescent depression:
644 Checklists, screens, and nets. *J. Am. Acad. Child Adolesc. Psychiatry* **27,** 726–737
645 (1988).
646 31. Rosseel, Y. lavaan: An R package for structural equation modeling. *J. Stat. Softw.* **48,**
647 1–36 (2012).
648 32. Koenen, K. C. *et al.* Childhood IQ and adult mental disorders: A test of the cognitive
649 reserve hypothesis. *Am. J. Psychiatry* **166,** 50–57 (2009).
650 33. van Harmelen, A. L. *et al.* Adolescent friendships predict later resilient functioning
651 across psychosocial domains in a healthy community cohort. *Psychol. Med.* **47,** 2312–
652 2322 (2017).
653 34. Kass, R. E. & Raftery, A. E. Bayes factors. *J. Am. Stat. Assoc.* **90,** 773–795 (1995).
654 35. Hayes, A. F. *Introduction to Mediation, Moderation, and Conditional Process*
655 *Analysis*. (Guilford Press, 2013).
656 36. Hitchcock, C., Rees, C. & Dalgleish, T. The devil's in the detail: Accessibility of
657 specific personal memories supports rose-tinted self-generalizations in mental health
658 and toxic self-generalizations in clinical depression. *J. Exp. Psychol. Gen.* **146,** 1286–
659 1295 (2017).
660 37. Goodyer, I. M. *et al.* Cognitive behavioural therapy and short-term psychoanalytical
661 psychotherapy versus a brief psychosocial intervention in adolescents with unipolar
662 major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind,
663 randomised controlled trial. *The Lancet Psychiatry* **4,** 109–119 (2017).
664 38. van Harmelen, A.-L. *et al.* Child abuse and negative explicit and automatic self-
665 associations: the cognitive scars of emotional maltreatment. *Behav. Res. Ther.* **48,** 486–
666 494 (2010).

39. McCrory, E. J. *et al.* Autobiographical memory: a candidate latent vulnerability mechanism for psychiatric disorder following childhood maltreatment. *Br. J. Psychiatry* **211,** 216–222 (2017).

40. Munafò, M. R. & Davey Smith, G. Repeating experiments is not enough. *Nature* **553,** 399–401 (2018).

41. Gutenbrunner, C., Salmon, K. & Jose, P. E. Do overgeneral autobiographical memories predict increased psychopathological symptoms in community youth? A 3-year longitudinal investigation. *J. Abnorm. Child Psychol.* **46,** 197–208 (2018).

42. Browning, M., Holmes, E. A., Charles, M., Cowen, P. J. & Harmer, C. J. Using attentional bias modification as a cognitive vaccine against depression. *Biol. Psychiatry* **72,** 572–579 (2012).

43. Hallford, D. J., Austin, D. W., Raes, F. & Takano, K. A test of the functional avoidance hypothesis in the development of overgeneral autobiographical memory. *Mem. Cogn.* **46,** 895–908 (2018).

44. Ali, N., Nitschke, J. P., Cooperman, C. & Pruessner, J. C. Suppressing the endocrine and autonomic stress systems does not impact the emotional stress experience after psychosocial stress. *Psychoneuroendocrinology* **78,** 125–130 (2017).

45. Hanson, J. L., Hariri, A. R. & Williamson, D. E. Blunted ventral striatum development in adolescence reflects emotional neglect and predicts depressive symptoms. *Biol. Psychiatry* **78,** 598–605 (2015).

46. Speer, M. E., Bhanji, J. P. & Delgado, M. R. Savoring the past: Positive memories evoke value representations in the striatum. *Neuron* **84,** 847–856 (2014).

47. Pizzagalli, D. A. *et al.* Reduced caudate and nucleus accumbens response to rewards in unmedicated subjects with major depressive disorder. *Am. J. Psychiatry* **166,** 702–710 (2009).

692 48. Haber, S. N. & Knutson, B. The reward circuit: Linking primate anatomy and human
693 imaging. *Neuropsychopharmacology* **35,** 4–26 (2010).
694 49. Heller, A. S. *et al.* Sustained striatal activity predicts eudaimonic well-being and
695 cortisol output. *Psychol. Sci.* **24,** 2191–2200 (2013).
696 50. Urry, H. L. Amygdala and ventromedial prefrontal cortex are inversely coupled during
697 regulation of negative affect and predict the diurnal pattern of cortisol secretion among
698 older adults. *J. Neurosci.* **26,** 4415–4425 (2006).
699 51. Dillon, D. G. & Pizzagalli, D. A. Mechanisms of memory disruption in depression.
700 *Trends Neurosci.* **41,** 137–149 (2018).
701 52. Young, K. D. *et al.* Randomized clinical trial of real-time fMRI amygdala
702 neurofeedbackfor major depressive disorder: Effectson symptoms and autobiographical
703 memory recall. *Am. J. Psychiatry* **174,** 748–755 (2017).
704 53. Russo, S. J., Murrough, J. W., Han, M.-H., Charney, D. S. & Nestler, E. J.
705 Neurobiology of resilience. *Nat. Neurosci.* **15,** 1475–1484 (2012).
706 54. Hitchcock, C., Werner-Seidler, A., Blackwell, S. E. & Dalgleish, T. Autobiographical
707 episodic memory-based training for the treatment of mood, anxiety and stress-related
708 disorders: A systematic review and meta-analysis. *Clin. Psychol. Rev.* **52,** 92–107
709 (2017).
710 55. Arditte Hall, K. A., De Raedt, R., Timpano, K. R. & Joormann, J. Positive memory
711 enhancement training for individuals with major depressive disorder. *Cogn. Behav.*
712 *Ther.* **47,** 155–168 (2018).
713 56. Werner-Seidler, A. & Dalgleish, T. The Method of Loci improves longer-term
714 retention of self-affirming memories and facilitates access to mood-repairing memories
715 in recurrent depression. *Clin. Psychol. Sci.* **4,** 1065–1072 (2016).
716 57. Dalgleish, T. & Werner-Seidler, A. Disruptions in autobiographical memory

processing in depression and the emergence of memory therapeutics. *Trends Cogn. Sci.* **18,** 596–604 (2014).

58. Bollen, K. A. & Pearl, J. Eight Myths About Causality and Structural Equation Models. in *Handbook of Causal Analysis for Social Research* 301–328 (Springer, Dordrecht, 2013). doi:10.1007/978-94-007-6094-3_15

59. Biddle, B. J. & Marlin, M. M. Causality, confirmation, credulity, and structural equation modeling. *Child Dev.* **58,** 4–17 (1987).

60. Abercrombie, H. C. *et al.* Neural signaling of cortisol, childhood emotional abuse, and depression-related memory bias. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* **3,** 274–284 (2018).

61. Kessler, R. C. *et al.* Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch. Gen. Psychiatry* **62,** 593–602 (2005).

62. Goodyer, I. M., Herbert, J., Secher, S. M. & Pearson, J. Short-term outcome of major depression: I. Comorbidity and severity at presentation as predictors of persistent disorder. *J. Am. Acad. Child Adolesc. Psychiatry* **36,** 179–187 (1997).

63. Gibbs, B. R. & Rude, S. S. Overgeneral autobiographical memory as depression vulnerability. *Cognit. Ther. Res.* **28,** 511–526 (2004).

64. Goodyer, I. M., Ashby, L., Altham, P. M., Vize, C. & Cooper, P. J. Temperament and major depression in 11 to 16 year olds. *J. Child Psychol. Psychiatry.* **34,** 1409–23 (1993).

65. Heron, J. *et al.* 40,000 memories in young teenagers: Psychometric properties of the Autobiographical Memory Test in a UK cohort study. *Memory* **20,** 300–320 (2012).

66. Sund, A. M., Larsson, B. & Wichstrøm, L. Depressive symptoms among young Norwegian adolescents as measured by the Mood and Feelings Questionnaire (MFQ).

Eur. Child Adolesc. Psychiatry **10,** 222–229 (2001).

67. Chambers, W. J. *et al.* The assessment of affective disorders in children and adolescents by semistructured interview: Test-retest reliability of the Schedule for Affective Disorders and Schizophrenia for School-Age children, Present Episode Version. *Arch. Gen. Psychiatry* **42,** 696–702 (1985).

68. Wechsler, D. *Manual for the Wechsler Intelligence Scale for Children, Revised*. (Psychological Corporation, 1974).

69. Wickham, H. ggplot2: elegant graphics for data analysis. *J. R. Stat. Soc. Ser. A (Statistics Soc.* **174,** 245–246 (2009).

70. Kline, R. B. *Principles and Practice of Structural Equation Modeling*. (Guilford Press, 2011).

71. Enders, C. K. & Bandalos, D. L. The relative performance of full information maximum likelihood estimation for missing data in structural equation models. *Struct. Equ. Model.* **8,** 430–457 (2001).

72. Nunnally, J. C. *Psychometric Theory*. (McGraw-Hill Book company, 1967).

73. Baron, R. M. & Kenny, D. A. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J. Pers. Soc. Psychol.* **51,** 1173–1182 (1986).

74. Askelund, A. D., Schweizer, S., Goodyer, I. M. & van Harmelen, A.-L. Data and code supporting the paper 'Positive memory specificity is associated with reduced vulnerability to depression'. *University of Cambridge data repository* (2018). doi:https://doi.org/10.17863/CAM.23436

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777 Author Contributions

778 A.D.A., I.M.G and A.L.v.H conceptualised the study. All authors contributed to the study
779 design. A.D.A. analysed the data and drafted the paper under the supervision of A.L.v.H. S.S.
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783 Competing Interests

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785

Figure 1. Positive memory specificity is related to lower cognitive and physiological vulnerability over time. n = 427. Path model showing that positive memory specificity is associated with both fewer negative self-cognitions during low mood and lower morning cortisol at follow-up. Broader arrows indicate stronger relationships. *z* = standardised path coefficient, r = Pearson's r effect size, 95% CI = 95% confidence interval of the effect size.

Figure 2. Positive memory specificity is associated with reduced depressive symptoms after life stress. n = 427. 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 moderately related to lower negative self-cognitions in those exposed to one or more recent negative life events (during the 12 months of the study; blue line). The relationship is small and not significant in those not exposed to recent negative life events (black line). Lines show unadjusted regression lines for illustration purposes, and grey bands show 95% confidence intervals. Figure **b** shows a moderated mediation model where positive memory specificity at baseline is associated with decreased depressive symptoms indirectly over time. The relationship is mediated by negative self-cognitions, depending upon exposure to negative life events. *Path a:* Relationship between positive memory specificity and negative self-cognitions, depending on exposure to recent negative life events; *Path b:* Relationship between negative self-cognitions and depressive symptoms; *Path c':* Relationship between positive memory specificity at baseline and depressive symptoms at follow-up, controlling for the indirect effect; *Path ab:* the index of the conditional indirect effect of positive memory specificity on depressive symptoms. The 95% confidence interval (CI) for this indirect path does not include 0, suggesting that the moderated mediation is significantly different from 0 (at $P < 0.05$). Path values represent unstandardised coefficients and bootstrap standard errors.

Positive memory specificity is associated with fewer negative self-cognitions and lower morning cortisol. n = 427. (b) = baseline, (f) = follow-up. Boys are coded as 1, girls as 2. Significant paths are bolded. Robust model fit indices: X^2_2 = 1.353, P = 0.508, CFI = 1, TLI = 1.036, RMSEA = 0, 90% CI = 0.000, 0.087, SRMR = 0.008. Estimate = unstandardised path coefficient, S.E. = robust standard error, *z*-value = standardised path coefficient, r = Pearson's r effect size, 95% CI = 95% confidence interval of the effect size.

Table 1.

Outcome	Predictor	Estimate	S.E.	*z*-value	P(>|z|)	r	95 % CI
Morning cortisol (b)	Positive memory specificity (b)	-0.305	0.165	-1.851	0.064	-0.090	-0.183, 0.004
	Negative life events (b)	0.012	0.060	0.198	0.843	0.010	-0.084, 0.104
	Gender (b)	0.677	0.115	5.878	**0.001**	**0.285**	**0.196, 0.369**
	IQ (b)	-0.000	0.003	-0.087	0.931	-0.004	-0.098, 0.090
Morning cortisol (f)	Morning cortisol (b)	0.363	0.081	4.483	**0.001**	**0.217**	**0.125, 0.305**
	Positive memory specificity (b)	-0.360	0.131	-2.747	**0.006**	**-0.133**	**-0.225, -0.039**
	Negative self-cognitions/mood (b)	0.144	0.137	1.054	0.292	0.051	-0.044, 0.145
	Negative life events (b)	0.008	0.053	0.156	0.876	0.008	-0.086, 0.102
	Negative life events (f)	0.083	0.048	1.726	0.084	0.084	-0.010, 0.177
	Gender (b)	0.288	0.106	2.730	**0.006**	**0.132**	**0.038, 0.224**
	IQ (b)	0.011	0.003	3.772	**0.001**	**0.183**	**0.090, 0.273**
Negative self-cognitions/mood (b)	Positive memory specificity (b)	-0.048	0.046	-1.038	0.299	-0.050	-0.144, 0.045
	Negative life events (b)	0.022	0.016	1.433	0.152	0.069	-0.026, 0.162
	Gender (b)	0.032	0.032	1.002	0.317	0.049	-0.046, 0.143
	IQ (b)	-0.001	0.001	-0.802	0.423	-0.039	-0.133, 0.056
Negative self-cognitions/mood (f)	Negative self-cognitions/mood (b)	0.399	0.071	5.631	**0.001**	**0.273**	**0.183, 0.358**
	Positive memory specificity (b)	-0.115	0.039	-2.983	**0.003**	**-0.144**	**-0.235, -0.050**
	Morning cortisol (b)	-0.012	0.012	-0.978	0.328	-0.047	-0.141, 0.048
	Negative life events (b)	0.015	0.012	1.288	0.198	0.062	-0.033, 0.155
	Negative life events (f)	0.015	0.013	1.180	0.238	0.057	-0.038, 0.151
	Gender (b)	0.019	0.030	0.627	0.531	0.030	-0.065, 0.124
	IQ (b)	0.000	0.001	0.512	0.609	0.025	-0.070, 0.119
Morning cortisol (b) ~~	Negative self-cognitions/mood (b)	0.026	0.019	1.370	0.171	0.066	-0.029, 0.159
Morning cortisol (f) ~~	Negative self-cognitions/mood (f)	0.000	0.013	0.036	0.972	0.002	-0.092, 0.096

Results of moderation and moderated mediation models. n = 427. All significant values are bolded. Moderation: Positive memory specificity predicting negative self-cognitions depending on negative life events. Moderated mediation 1: Positive memory specificity predicting depressive symptoms through negative self-cognitions depending on negative life events. Moderated mediation 2: Positive memory specificity predicting negative self-cognitions through depressive symptoms depending on negative life events. The index of the moderated mediation (ab) is significant for confidence intervals that do not include 0. Predictor: baseline, moderator: between baseline and follow-up, mediator and outcome: follow-up. Levels of the moderator are 0 (no events) and 1+ (one or more events). Pos memory = positive memory specificity, Neg events = Negative life events, Neg self = Negative self-cognitions, Dep sympt = Depressive symptoms. 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. = bootstrap standard error, df = degrees of freedom, 95% CI = 95% bootstrap confidence interval of the estimate, R^2 = variance explained, MSE = mean squared error.

Table 2.

Path	Predictor	Moderator	Mediator	Outcome	Effect	S.E.	df	t	95% CI	P(>|z|)
Moderation: R^2 = 0.335, MSE = 48.978, $F_{7,419}$ = 30.165, P < 0.001										
c1	Pos memory	0 events		Neg self	-1.150	1.232	418	-0.934	-3.571, 1.271	0.351
c2	Pos memory	1+ events		Neg self	-6.530	1.500	418	-4.353	**-9.479, -3.582**	**0.001**
Moderated mediation 1: R^2 = 0.373, MSE = 46.301, $F_{8,418}$ = 31.073, P < 0.001										
a1	Pos memory	0 events	Neg self		-0.773	1.200	418	-0.644	-3.132, 1.585	0.520
a2	Pos memory	1+ events	Neg self		-5.968	1.463	418	-4.080	**-8.843, -3.092**	**0.001**
b			Neg self	Dep sympt	0.583	0.044	419	13.370	**0.497, 0.668**	**0.001**
ab	Pos memory	Neg events	Neg self	Dep sympt	-3.026	1.290	419		**-5.752, -0.704**	
c'	Pos memory	Neg events	Neg self	Dep sympt	0.265	0.858	419	0.309	-1.422, 1.951	0.758
Moderated mediation 2: R^2 = 0.403, MSE = 53.216, $F_{8,418}$ = 35.295, P < 0.001										
a1	Pos memory	0 events	Dep sympt		-0.466	1.286	418	-0.362	-2.995, 2.062	0.717
a2	Pos memory	1+ events	Dep sympt		-2.772	1.568	418	-1.768	-5.855, 0.310	0.078
b			Dep sympt	Neg self	0.513	0.038	419	13.370	**0.438, 0.589**	**0.001**
ab	Pos memory	Neg events	Dep sympt	Neg self	-1.184	1.167	419		-3.630, 0.962	
c'	Pos memory	Neg events	Dep sympt	Neg self	-2.133	0.799	419	-2.670	**-3.703, -0.562**	**0.008**