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Depression recurrence after recovery: Prognostic value of implicit and explicit self-depressed associations☆

Lonneke A. van Tuijl[a,e,*], Klaske A. Glashouwer[a,b], Hermien J. Elgersma[a,b], Claudi L.H. Bockting[a,c], Brenda W.J.H. Penninx[d], Peter J. de Jong[a]

[a] Department of Clinical Psychology and Experimental Psychopathology, University of Groningen, The Netherlands
[b] Accare, Child and Adolescent Psychiatry, Center for Eating Disorders, Groningen, The Netherlands
[c] Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[d] Department of Psychiatry, VU University Medical Center, Amsterdam, The Netherlands
[e] Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

Major depressive disorder and dysthymia are some of the most prevalent lifetime disorders, with prevalence rates reported as high as 16.6% and 2.5%, respectively (Kessler et al., 2005). Depression is persistent with high rates of recurrence (i.e., return of symptoms following at least six months of no symptoms; e.g., 42% within 20 years Hardeveld, Spijker, Graaf, Nolen, & Beekman, 2013) and relapse (i.e., return of symptoms following a symptom-free period of less than six-months; Frank et al., 1991). Periods of recovery decreases with each episode (Hardeveld et al., 2013), while the risk for recurrence increases with each episode (e.g., Mueller et al., 1999). Given the highly recurrent nature of depression, it imposes high personal and societal costs. It is therefore critical to understand the mechanisms that are potentially involved in the recurrence of depression.

Dysfunctional thoughts and attitudes about the self ("negative self-associations") have been proposed as central factors that may contribute to the development and persistence of depression symptomatology (e.g., Beck, 2002). Dual-process models highlight the importance of distinguishing between more explicit self-associations and automatic (implicit) self-associations (Gawronski & Bodenhausen, 2006) as these can differ (e.g., Briñol, Petty, & Wheeler, 2006), and can manifest in different types of behaviours (Strack & Deutsch, 2004). Specifically, explicit self-associations are related to more deliberate behaviours, while implicit self-associations have been linked to more spontaneous behaviours (e.g., Rudolph, Schröder-Abé, Riketta, & Schütz, 2010). It has been theorized that implicit associations moderate mood and behaviour in response to stressors through the unintentional and fast activation of associated constructs in memory networks (Beevers, 2005). This in turn can trigger symptoms of depression (e.g., feelings of worthlessness, sad mood) which may trigger other symptoms of depression (e.g., change in appetite). If explicit associations are positive, they may correct negative implicit associations, thereby resulting in positive moods and behaviours, and offering protection from depression. However, if explicit associations are also negative, they may worsen the effect of negative implicit associations (or weaken the effect of positive implicit associations), and consequently facilitate the emergence of depressive symptoms. Furthermore, even when explicit associations are positive, they may fail to correct negative implicit associations if there are insufficient cognitive resources (e.g., constrained working memory due to high stress), limited time, or lack of motivation (e.g., a person is not aware of persistent negative thoughts which may not be true; Elgersma, Glashouwer, Bockting, Penninx, & de Jong, 2013). A negative feedback loop can develop between negative self-associations and symptoms of depression which in relatively healthy individuals may be corrected through positive explicit associations (e.g., purposefully thinking of the things that have been done well recently). Therefore, negative implicit associations and explicit associations are considered distinct, yet related mechanisms through which depressive symptoms may be triggered or worsened.

During a period of depression, negative self-views emerge when reduced cognitive control fails to break a spiral between excessive self-focused thinking (e.g., rumination) and triggering of negative self-schemas (e.g., De Raedt, Remue, Loeys, Hooley, & Baeken, 2017). Associations between concepts of depression (e.g., hopelessness, worthlessness) and the self are particularly salient during this period, therefore becoming stronger at the explicit level, and with time, at the implicit level. This is supported by the observation that implicit self-depressed associations (SDA) and explicit SDA were stronger in those with a current depression in comparison to those with an anxiety disorder and those who had never had a depression or anxiety disorder (Glashouwer & de Jong, 2010). While recovery marks a period where symptoms of depression have reduced to non-clinical levels for at least six months, it is feasible that SDA remain strong. This might be

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* Corresponding author. Department of Clinical Psychology and Experimental Psychopathology, University of Groningen, Grote Kruisstraat 2/1, 9712, TS Groningen, The Netherlands.
E-mail address: L.A.van.tuijl@rug.nl (L.A. van Tuijl).

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particularly so for implicit self-associations, which require time and consistent explicit self-associations to change (see Gawronski & Bodenhausen, 2006, for a review of implicit and explicit attitude change). Indeed, those with a previous depression still showed stronger explicit SDA and implicit SDA than a never-depressed comparison group (Glashouwer & de Jong, 2010). Furthermore, where depression was present for a longer period, or where there is a history of relatively many depressive episodes, explicit SDA and implicit SDA were stronger (Elgersma et al., 2013). In the presence of stressors, SDA may facilitate the re-emergence of depressive symptoms by triggering dormant negative self-schemas. It is therefore feasible that remaining SDA in those who have recovered from a major depressive disorder or dysthymia may represent a cognitive vulnerability ("scar") increasing risk for recurrence by facilitating the triggering of depressive symptoms. If SDA does represent a scar following depression, then it should "independently predict future recurrences" (Burcusa & Iacono, 2007, p. 16). Therefore, the first main aim of the current study was to test whether SDA in recovered depressed individuals indeed predict the recurrence of depression.

Not everyone who recovers from a depression will experience another episode, and therefore scars may not be present in everyone with a history of depression. As such, some appear to recover better than others. SDA following a depression regardless of changes may be a poorer predictor of recurrence than persistence of SDA from a current depression into recovery as the latter may be indicative of slower recovery or uncorrected SDA. The second aim was therefore to test whether SDA during a depression that persists into recovery is related to an increased risk for recurrence.

It has been argued that relatively negative self-associations as a *consequence* of the depressive episode represents a scar that lowers the threshold for the development of a new episode (i.e., the scar hypothesis; Lewinsohn, Steinmetz, Larson, & Franklin, 1981). However, for a construct to be considered a scar related to recurrence risk, it is important to differentiate between recurrence risk that is a consequence of a depressive episode from recurrence risk that existed *before* the onset of the depressive episode (Burcusa & Iacono, 2007). It is feasible that factors preceding the onset of a depression (i.e., first episode) already predict who will have a more recurrent course of depression (Bockting, Hollon, Jarrett, Kuyken, & Dobson, 2015). To identify whether SDA following a period of depression represents a scar or a premorbid vulnerability, an explorative analysis was conducted in a small subsample of those where onset of first episode of depression occurred during the study.

The first main hypothesis of this study was that implicit SDA and explicit SDA would predict recurrence in those with a history of major depressive disorder or dysthymia. The second main hypothesis is that persistent SDA (i.e., relatively less improvement) into recovery would particularly increase risk for recurrence. Finally, we included an explorative analysis to test whether SDA following a period of depression was best understood as a scar increasing the likeliness of recurrence, or a pre-episode factor predicting a recurrent course of depression. Understanding factors relating to recurrence may highlight potential targets for preventative interventions.

1. Method

1.1. Participants

The Netherlands Study of Depression and Anxiety (NESDA; www.nesda.nl) is an ongoing longitudinal cohort study. At baseline (2004–2007), participants were included in the study based on meeting the age criterion (18–65 years) and the presence of a depression or anxiety disorder (n = 1701), or if they were at-risk for or had a history of depression or anxiety (n = 907). A further 373 participants were included as the comparison group who reported no depression or anxiety currently or in the past, resulting in a final total sample of 2981. Participants who met the criteria for other psychiatric disorders (e.g., psychotic disorder, severe addiction) or did not have a fluent command of the Dutch language were excluded from the study. A thorough overview of NESDA has been described elsewhere (Penninx et al., 2008). All participants provided written consent, and all participating institutions granted ethical approval (VU University Medical Center, Protocol number: 2003/183).

The present study makes use of data collected at baseline, the two-year follow-up (T2), the four-year follow-up, and the six-year follow-up. Participants were selected to form two groups: i) History of Depression; and ii) Recently Recovered. Diagnoses were determined with the Composite International Diagnostic Interview (CIDI; Robins et al., 1988, see measures section).

The history of depression subsample was determined by: 1) Selecting all participants who reported a history of either MDD and/or dysthymia at baseline and had not met the criteria for a depression for at least six months (n = 815); 2) Excluding those who had not completed measures of implicit SDA and explicit SDA at baseline (e.g., participation via telephone; n = 63); 3) excluding those missing at the two-year follow-up (n = 74) or missing at a later wave before recurrence was determined (n = 62). In the final sample of 616, 314 remained depression free in the six-year follow-up (51%) and 302 had an onset of a new depressive episode (49%; MDD and/or dysthymia).

The recently recovered subsample included participants who 1) reported MDD and/or dysthymia in the last month at baseline and no dysthymia and MDD for at least six months at the two-year follow-up (n = 332); 2) had completed measures of SDA at both baseline and T2 (excluded n = 77); 3) were not missing at follow-up before recurrence was determined (excluded n = 35). Of the final 220, 112 remained depression free at the four-year follow-up (51%), and 108 had a recurrence of depression (MDD and/or dysthymia) in the four-year follow-up (49%).

For the explorative analysis testing the pre-morbid vulnerability and scar hypotheses, participants were selected who 1) never had an episode of MDD or dysthymia at baseline, met the criteria for depression between baseline and the two-year follow-up (n = 98), and 2) had been depression free for at least six months at the two-year follow-up (n = 27). Four were missing at follow-up before recurrence could be determined and four had not completed measures of SDA at both baseline and the two-year follow-up. These were excluded from the relevant analysis. Of the 23 where recovery was determined, 19 remained depression free at the six-year follow-up and 4 had a recurrence of depression.

1.2. Measures

Implicit Association Test (IAT; Greenwald, McGhee, & Schwartz, 1998). A thorough overview of the depression IAT given at baseline and T2 in NESDA has been described previously (Glashouwer & de Jong, 2010). In brief, the depression IAT is a computer-based word-sorting task where words are presented from two target categories: *I* (I, myself, self, my, own) and *other* (other, you, they, them, themselves); and two attribute categories: *depressed* (useless, pessimistic, inadequate, negative, meaningless) and *elated* (positive, optimistic, active, valuable, cheerful; translated from Dutch). Participants sorted *depressed*- and *I*-related words with the same key and *elated*- and *other*-related words with the other key (pairing 1). This was repeated for two blocks of 20 trials. In the next test block, *elated*- and *I*- related words (and *depressed*- and *other*-related words) were sorted with the same key (pairing 2). Response and reaction time were recorded for each trial. The premise of the IAT is that the attribute and target categories that are more strongly associated for the participant are easier to sort when they share a key. A person with strong self-depressed associations is therefore expected to find it easier to sort words when *I* and *depressed* share a key than when *I* and *elated* share a key. For all participants, an anxiety IAT was given before the depression IAT (see Glashouwer & de Jong, 2010, for

description of anxiety IAT), and the IATs given at baseline and T2 were identical.

The IAT was scored based on the D_4-measure (Glashouwer, Smulders, de Jong, Roefs, & Wiers, 2013). First, trials with reaction times longer than 10,000 ms were discarded. Reaction times on error trials were replaced with the mean of the correct answers for that participant in that block, with an added 600 ms error penalty. The mean reaction time for pairing 1 was then subtracted from the mean reaction time for pairing 2, and subsequently divided by the pooled standard deviation of both pairings to control for individual variation. This was done for the practice blocks first, then the test blocks, before calculating the average between the two. Higher scores were therefore indicative of a relatively fast response for pairing 1, thus indicating stronger implicit self-depressed associations. Participants were excluded from any analysis involving IAT scores when more than 10% of trials were faster than 300 ms, an error rate of over 20%, or where more than 1% of trials were longer than 10,000 ms (History of depression: 3 excluded from baseline IAT; Recently recovered: 5 & 5 from the depression IAT at baseline & T2, respectively; Greenwald & Farnham, 2000; Greenwald, Nosek, & Banaji, 2003). Spearman-Brown corrected correlations between test halves were previously calculated to be 0.92 and 0.91 (depression IAT), and 0.86 and 0.84 (anxiety IAT) for the complete sample at baseline and T2, respectively (test halves based on trials 1, 2, 5, 6, etc., and 3, 4, 7, 8, etc.; Glashouwer et al., 2013).

Explicit self-associations. Two measures of explicit self-associations were created for NESDA at baseline and T2, one for depressed (vs. elated) and one for anxious (vs. calm). Participants scored from 1 "hardly/not at all" to 5 "very much" how much each word from the depression IAT and anxiety IAT attribute categories described themselves. Scores for elated/calm attributes were subtracted from depressed/anxious attributes. Higher scores indicated stronger explicit self-depressed/self-anxious associations. These measures showed excellent internal consistency across the complete NESDA sample in a previous study (Cronbach's $\alpha = 0.94$ & 0.95 for self-anxious and self-depressed, respectively at baseline, Glashouwer & de Jong, 2010). Furthermore, the explicit self-depressed associations measure showed good test-retest reliability with a two year follow-up ($r = 0.56$, Elgersma et al., 2013), good specificity (i.e., pronounced in those with a depression and not in those with an anxiety; Glashouwer & de Jong, 2010), and good predictive validity concerning time to remission in depression over and above a well-validated depression symptomatology measure (Glashouwer, de Jong, & Penninx, 2012).

Composite International Diagnostic Interview v2.1 (CIDI; Robins et al., 1988; Wittchen, 1994). Depressive disorders were determined using a semi-structured CIDI based on criteria from the DSM-IV. Interviews were conducted by trained research staff. Number of previous MDD episodes was asked at baseline when participants indicated a history of MDD and capped at 96. Number of MDD episodes prior to baseline was missing for 63 and 13 participants from history of depression and recently recovered, respectively, either due to non-response or no history of MDD. Comorbid anxiety disorder was qualified as meeting the criteria for social anxiety disorder, panic disorder (with/without agoraphobia), agoraphobia or generalized anxiety disorder in the last six months at baseline.

Inventory of Depressive Symptomatology – self-report (IDS; Rush et al., 1986). The IDS was used to measure depressive symptomatology in the preceding seven days, based on the DSM-IV criteria for MDD. The version used contained 28 items. For each of the 28 items (e.g., "Feeling sad") there were four corresponding answers from "0" which indicated no depressive symptom (e.g., "I do not feel sad") to "3" referring to a more severe depressive symptom (e.g., "I feel sad nearly all the time"). For history of depression, three had too many missing answers (> 6 items) at baseline, and were excluded from any relevant analysis. Five had too many missing answers at the two-year follow-up in recently recovered. Previous studies have shown the IDS to have excellent internal consistency (e.g., Cronbach's $\alpha = .94$, Rush, Gullion, Basco, Jarrett, & Trivedi, 1996).

1.3. Procedure

Participants completed computer tasks, self-reported questionnaires, interviews and biological assessments in one sitting lasting three to 5 h (see Penninx et al., 2008). For all participants, the IATs were completed before measures of explicit self-associations. In return for participation, travel expenses and a 15-euro gift voucher was given to each participant.

1.4. Statistical analysis

Univariate (single-predictor models) and multivariate (multi-predictor models) binary logistic regressions were conducted to predict recurrence during the six- and four-year follow up in history of depression and recently recovered, respectively. For the recently recovered group, the strongest predictors (i.e., largest odds ratio) from the two-year follow-up (e.g., T2 IAT scores) and corresponding change variables (e.g., T2 IAT scores – baseline IAT scores) were included in the adjusted model to prevent theoretical multicollinearity. Binary predictors were contrasted so that odds refer to female (compared to male) and presence of a comorbid anxiety disorder (compared to absence). In all adjusted models, where SDA was a significant predictor, the analysis was rerun with self-anxious associations in place of SDA to test the specificity of self-related associations. The relatively few missing values were dealt with by pairwise deletion. In the adjusted models, this totalled to 76 missing from the history of depression group and 18 missing from the recently recovered group. To explore whether SDA may be a pre-morbid vulnerability factor, depressive symptoms at the four- and six-year follow-up were correlated with explicit SDA and implicit SDA prior to depression onset (pre-morbid) and after an episode of depression (scar). Significant correlations for scar were rerun controlling for pre-morbid SDA.

2. Results

2.1. History of depression

Descriptives. Means and standard deviations of the demographics and relevant variables are presented in the left side of Table 1. Spearman's rank correlations were calculated between relevant baseline variables and recurrence are displayed in Table 2. Recurrence was correlated with symptoms of depression and number of previous depressive episodes.

Prediction of Recurrence between Baseline and T6. Univariate and multivariate logistic regressions were conducted to predict recurrence. In the unadjusted model, both explicit SDA and implicit SDA, and depressive symptoms were predictive of depressive recurrence in a positive direction (left side of Table 4). That is, stronger explicit SDA, stronger implicit SDA, more depressive symptoms and the presence of a comorbid anxiety disorder at baseline were related to increased odds of recurrence. However, once adjusting for the other variables, only depressive symptoms at baseline remained a significant predictor (right side of Table 4). The multivariate model was significant, $X^2(6) = 84.93$, Nagelkerke $R^2 = 0.19$.

2.2. Recently recovered

Descriptives. Means and standard deviations of the demographics and relevant variables are presented in the right side of Table 1. Correlations were calculated between relevant baseline and T2 variables and are displayed in Table 3. In those who had recurred, depressive symptoms as indexed by the IDS at the two-year follow-up were higher, and implicit SDA and explicit SDA were stronger. Two paired-samples t-tests were conducted to see whether implicit SDA and explicit SDA

Table 1
Means (standard deviations; unless otherwise specified) for Descriptive and Predictor Variables.

	History of Depression		Recently Recovered	
	Non-recurrence (n = 314)	Recurrence (n = 302)	Non-recurrence (n = 112)	Recurrence (n = 108)
Female (%)	69%	74%	63%	65%
Baseline				
Comorbid Anxiety (%)	27%	44%	58%	69%
Age	44.08 (13.01)	42.25 (12.46)	40.36 (13.55)	42.09 (12.59)
#MDD episodes	3.16 (8.38)	3.96 (8.19)	4.34 (6.24)	8.01 (17.93)
Median	1.00	2.00	2.00	2.00
IAT	−0.31 (0.39)	−0.24 (0.39)	−0.21 (0.39)	−0.13 (0.39)
EA	−2.05 (1.21)	−1.43 (1.34)	−0.68 (1.37)	0.03 (1.55)
IDS	13.82 (8.88)	21.03 (9.62)	29.49 (10.28)	33.79 (10.26)
Two-year follow-up				
IAT	−0.34 (0.38)	−0.24 (0.38)	−0.32 (0.34)	−0.20 (0.37)
EA	−2.27 (1.06)	−1.43 (1.37)	−1.81 (1.13)	−1.09 (1.36)
IDS	10.96 (7.84)	19.73 (10.97)	15.70 (8.06)	20.42 (9.55)

Note. History of depression = depression free for at least six months at baseline; Recently recovered = current depression at baseline, depression free for at least six months at follow-up. IDS = Inventory of Depressive Symptomatology; IAT = implicit association test (higher scores = stronger self-depressed associations); EA = explicit associations (higher scores = stronger self-depressed associations); MDD = major depressive disorder.

Table 2
Spearman's rank correlations between baseline predictors in history of depression.

Baseline variables	2.	3.	4.	5.
1. IAT	.25*	.15*	.08	.08
2. EA	–	.63*	.15*	.24*
3. IDS	–	–	.15*	.38*
4. # MDD episodes	–	–	–	.13*
5. Recurrence (yes/no)	–	–	–	–

Note. IDS = Inventory of Depressive Symptomatology; IAT = implicit association test (higher scores = stronger self-depressed associations); EA = explicit associations (higher scores = stronger self-depressed associations); MDD = major depressive disorder. Missing and excluded scores omitted listwise.
*$p < .01$.

decreased from baseline to T2 (i.e., from current depression to remission). For explicit SDA, there was a significant decrease in strength (current depression: M = −0.33, SD = 1.50, recovered depression: M = −1.46, SD = 1.30), t (219) = 11.31, $p < .001$, Cohen's d = 0.81. Implicit SDA also became weaker (current depression: M = −0.17, SD = 0.39, recovered depression: M = −0.27, SD = 0.35), t (209) = 3.40, $p = .001$, Cohen's d = 0.35.

Prediction of Recurrence between T2 and T6. Univariate and multivariate logistic regressions were conducted to predict recurrence in those who had been depressed in the last two years (Table 5). For implicit SDA, explicit SDA, and depressive symptomatology, scores at the two-year follow-up were stronger univariate predictors than changes in scores from current to recovered depression. Stronger explicit SDA, implicit SDA and more depressive symptoms after a depression increased the odds of a recurrence. In the adjusted, multivariate model, only explicit SDA predicted recurrence. The multivariate model was a significant predictor of recurrence in those who recently recovered, X^2 (6) = 16.39, Nagelkerke R^2 = 0.10. To test the specificity, the analysis was rerun with implicit and explicit self-anxious associations in place of SDA. Neither of these variables was significant, and only depressive symptoms were predictive of recurrence.

Table 3
Pearson's Bivariate Correlations (unless otherwise specified) between Predictors in Recently Recovered.

		2.	3.	4.	5.	6.	7.[a]	8.
	1. #MDD episodes [a]	.05	-.06	-.02	0	.03	.07	-.01
	2. Recurrence (yes/no)	–	.10	.24**	.21**	.17*	.29**	.26**
Baseline	3. IAT	–	–	.26**	.20**	.40**	.12	.06
	4. EA	–	–	–	.54**	.21**	.44**	.22**
	5. IDS	–	–	–	–	.09	.26**	.34**
Two-year follow-up	6. IAT	–	–	–	–	–	.25**	.14*
	7. EA [a]	–	–	–	–	–	–	.55**
	8. IDS	–	–	–	–	–	–	–

Note. IDS = Inventory of Depressive Symptomatology; IAT = implicit association test (higher scores = stronger self-depressed associations); EA = explicit associations (higher scores = stronger self-depressed associations); MDD = major depressive disorder. Missing and excluded scores omitted listwise.
*$p < .05$.
**$p < .01$.
[a] Spearman's rank correlations due to significant skew.

Table 4
Coefficients from univariate and multivariate logistic regression models in Predicting Recurrence in the six-year follow-up in those with a History of Depression.

	Univariate model			Multivariate model		
Baseline variables	OR	95% CI	*p*	OR	95% CI	*p*
IAT	1.51	[1.00–2.28]	.05	1.19	[0.74–1.92]	.47
EA	1.47	[1.29–1.67]	< .001	1.04	[0.86–1.25]	.70
IDS	1.09	[1.07–1.11]	< .001	1.09	[1.06–1.11]	< .001
Sex	1.26	[0.89–1.79]	.72	1.25	[0.82–1.89]	.30
# MDD episodes	1.01	[0.98–1.04]	.58	0.99	[0.97–1.02]	.55
Comorbid anxiety	2.06	[1.47–2.88]	< .001	1.11	[0.74–1.69]	.61

Note. History of Depression = depression free for at least six months at baseline; IDS = Inventory of Depressive Symptomatology; IAT = implicit association test (higher scores = stronger self-depressed associations); EA = explicit associations (higher scores = stronger self-depressed associations); MDD = major depressive disorder; comorbid anxiety = presence of anxiety disorder in previous six months at baseline.

Table 5
Coefficients from univariate and multivariate logistic regression models in Predicting Recurrence in the four-year follow-up in those Recently Recovered.

	Univariate model			Multivariate model[a]		
	OR	95% CI	*p*	OR	95% CI	*p*
Change IAT	1.15	[0.59–2.23]	.68			
T2 IAT	2.70	[1.24–5.90]	.01	1.14	[0.52–2.50]	.74
Change EA	1.01	[0.84–1.21]	.94			
T2 EA	1.60	[1.27–2.01]	< .001	1.29	[1.01–1.63]	.04
Change IDS	1.00	[0.98–1.03]	.74			
T2 IDS	1.06	[1.03–1.10]	< .001	1.01	[0.98–1.05]	.49
Sex	1.12	[0.64–1.92]	.72	0.91	[0.49–1.71]	.78
# MDD episodes	1.03	[1.00–1.05]	.08	1.02	[0.99–1.05]	.13
Comorbid anxiety	1.64	[0.94–2.86]	.08	1.35	[0.71–2.54]	.36

Note. T2 = two-year follow-up; IDS = Inventory of Depressive Symptomatology; IAT = implicit association test (higher scores = stronger self-depressed associations); EA = explicit associations (higher scores = stronger self-depressed associations); MDD = major depressive disorder; comorbid anxiety = presence of anxiety disorder in previous six months at baseline.
[a] The strongest predictor of the change and corresponding T2 variables was entered into the multivariate model. In this case, all T2 variables (IAT, EA, and IDS) were stronger predictors than the change variables.

2.3. Pre-morbid vulnerability vs. scar (explorative analysis)

To explore whether SDA represents a scar following a depression or a pre-morbid vulnerability, a number of Spearman-rank correlations were conducted to see whether explicit SDA and implicit SDA before (pre-morbid) and after (scar) a depression predicted depressive symptoms at the two-, four-, and six-year follow-up. Pre-morbid explicit SDA correlated with depressive symptoms at the four-year follow-up, $\rho(25) = 0.42$, $p = .03$, and six-year follow-up, $\rho(21) = 0.45$, $p = .03$. While explicit SDA scar only predicted symptoms at the four-year follow-up, $\rho(21) = 0.46$, $p = .03$, and not the six-year follow-up, $\rho(17) = 0.24$, $p = .33$, this disappeared when controlling for pre-morbid explicit SDA, $\rho(18) = 0.37$, $p = .09$. Pre-morbid implicit SDA did not predict depressive symptoms at the four-year follow-up, $\rho(24) = 0.02$, $p = .93$, but did predict symptoms at the six-year follow-up, $\rho(20) = 0.60$, $p = .003$. Implicit SDA scar did not predict symptoms at the four-year follow-up, $\rho(19) = 0.07$, $p = .76$, nor at the six-year follow-up, $\rho(15) = 0.35$, $p = .17$. These results should be interpreted tentatively given the very small sample sizes.

3. Discussion

The present large-scale, longitudinal study is the first to test the hypothesis that the strength of self-depressed associations in those recovered from MDD or dysthymia would increase the risk for recurrence. To test this, large samples of recovered depressed participants were followed-up for 4–6 years. The findings from the main analyses indicated: i) Explicit SDA predicted recurrence in those with a history of depression; ii) In those who recently recovered, both explicit SDA and implicit SDA during recovery were significant predictors of recurrence; and iii) Persistence of SDA from current depression to recovery did not have predictive value for recurrence.

Furthering previous studies observing stronger SDA in recovered depression (Glashouwer & de Jong, 2010) and an association between past depression severity and strength of SDA (Elgersma et al., 2013), the current study found explicit SDA to be predictive of recurrence in those who had recovered from depression. In those who were recently recovered, explicit SDA showed predictive value for recurrence over and above symptoms of depression. Specifically, the extent that participants considered themselves “useless”, “pessimistic”, “inadequate”, “negative”, and “meaningless” compared to “positive”, “optimistic”, “active”, “valuable”, “cheerful” shortly after a depressive episode, was related to recurrence. However, the means presented in Table 1 would suggest that explicit SDA were not particularly strong. This is consistent with the direction of the means presented by Glashouwer and de Jong (2010). Negative means suggest that, on average, relatively elated adjectives were considered better self-descriptors than relatively depressive adjectives. Therefore, it seems better to conclude that stronger self-elated associations than weak self-depressive associations offer protection from recurrence. It was theorized that explicit SDA may be a facilitating mechanism through which depressive symptoms may arise due to a failure to correct implicit SDA, and by moderating behavioural and mood reactions to stressors (e.g., Elgersma et al., 2013). The current findings do not negate this, but it seems more apt to suggest, specifically, that self-elated associations offer protection potentially by correcting implicit SDA and dampening (rather than amplifying, as suggested with self-depressed associations) the behavioural and mood effects of stressors (e.g., through positive interpretation). Decreasing self-depressed associations so that self-elated associations are stronger, or strengthening self-elated associations where self-depressed associations are relatively weak may therefore reduce risk for recurrence. While implicit SDA also showed predictive value for recurrence in an unadjusted model, it is not possible to draw similar conclusions based on the negative group averages as method variance (e.g., order effects) means that zero is not meaningful (i.e., it is not possible to say there was an absence of implicit SDA because reaction times in the I + depressed block were similar to reaction times in the I + elated block). Future studies should test whether weakening explicit SDA and implicit SDA, either by strengthening self-elated associations or weakening self-depressed associations, leads to a decreased risk for recurrence.

When controlling for depressive symptoms, explicit SDA remained a significant predictor of recurrence particularly in those who have recovered recently. It may be that other factors are better predictors of recurrence in individuals who have been recovered for quite some time. It is also possible to argue that controlling for residual depressive symptoms over-adjusts for the role of potential mechanisms (like SDA) in depression recurrence, particularly in those who have recovered for some time. Recent focus on the interplay between symptoms have highlighted that the concept of depression as a latent construct causing symptoms is erroneous, and depression is better conceptualised as the concurrent presence of several related symptoms. In this vein, researchers aim to identify which symptoms may trigger other symptoms, with the potential to personalise treatment by targeting symptoms that seem to have the largest influence (e.g., Borsboom & Cramer, 2013). It therefore stands to reason that potential mechanisms may trigger just one symptom that with time escalates to a depression (i.e., the presence of several symptoms). In controlling for depressive symptoms, one may conclude that residual symptoms might be a better predictor of recurrence, but it does not offer any insight into what prevention interventions should target. More specific processes, like SDA, have clearer targets for clinical interventions, even if these fail to hold when controlling for residual symptoms. As such, although explicit SDA no longer had predictive value in those with a history of depression when controlling for residual symptoms, targeting explicit SDA may still lead to the prevention of recurrence. Indeed, post-hoc analysis suggests that explicit SDA was a better predictor than depressive symptoms as the odds ratio for standardised explicit SDA (1.83) was larger than the odds ratio for standardised depressive symptoms (1.74) in unadjusted models.

Change scores showed no predictive validity for recurrence. The lack of support for persistence of SDA into recovery may be explained by differences already apparent in SDA during depression. Indeed, the means for recently recovered at baseline would suggest that those who recur following recovery appear to have stronger SDA during a depression than those who will not recur in the four years after recovery. Change scores therefore do not adequately distinguish between those with persistent strong SDA and those with persistent weak SDA thereby obscuring the potential role of persistent strong SDA in recurrence. Furthermore, differences in SDA during a depression may reflect differences in SDA prior to depression onset. Within the recently recovered group, 46% were currently in an index MDD episode (i.e., first episode) of which approximately half had a depression recurrence during follow-up. We compared post-hoc explicit SDA during the depression between those who recurred following recovery from the first depressive episode ($M = 0.23$, $SD = 1.67$) to those who did not ($M = -0.66$, $SD = 1.28$). Results indeed suggest that these differed, $t(94) = 2.94$, $p < .01$, $d = 0.61$. This supports the notion that SDA represents a pre-morbid vulnerability predicting depression recurrence as the stronger SDA during depression in those who recurred cannot be explained by prior depressive episodes. Pre-morbid SDA (or lack of self-elated associations) is also supported by the exploratory analysis in the present study. Although the subsample was very small, both implicit and explicit pre-morbid SDA predicted depressive symptoms four years after recovery. Future studies should aim to test whether SDA prior to or after the first episode of depression predicts a recurrent course of depression in larger samples. The current study shows tentative support for pre-morbid vulnerability based on explorative analysis and post-hoc testing. Establishing pre-morbid vulnerabilities for recurrent depression may have an important role in identifying those who require relapse prevention interventions following the first episode of depression, before the depression becomes increasingly recurrent, and subsequently,

treatment-resistant.

3.1. Limitations

The present study used an IAT to measure implicit SDA. Although the IAT showed excellent reliability in terms of internal consistency and acceptable consistency over a two-year follow-up, the IAT is not without its critics (e.g., Fiedler, Messner, & Bluemke, 2006). Perhaps most important, it has been shown that the IAT effect may also be sensitive to non-associative stimulus features (Rothermund & Wentura, 2004). In addition, the IAT effect is silent with regard to the exact nature of the associations between targets and attributes; in other words a strong self-elated association could indicate that people associate themselves very strongly with elated concepts but could also reflect the wish to be elated (e.g., I would like to be elated; Remue, De Houwer, Barnes-Holmes, Vanderhasselt, & De Raedt, 2013). All in all, it is feasible that the IAT only partially captures implicit self-related associations.

Furthermore, the results in the adjusted models are limited to those who provided valid data for all measures. In those with a history of depression, 12% were excluded from the final model, with missing data on number of previous MDD episodes being the most common reason. Despite this, we retained relatively large sample sizes. It is possible that participants were unable to recount all periods of depression in their life, and those who did report the number of episodes may be influenced by response and memory biases. Previous missing analysis would suggest that those missing at the two-year follow-up were younger, had lower education, non-European ancestry, and were more likely to have a depressive disorder (Lamers et al., 2012). As such, our findings are biased to those who completed all measures and were not lost at follow-up.

4. Conclusion

In the present study, explicit SDA and implicit SDA predicted recurrence, particularly in those who recently recovered. Scores would suggest that not stronger self-depressed associations increase risk for recurrence, for example, by amplifying mood and behavioural responses to stressors, but the absence of relatively strong self-elated associations. It is possible that self-elated associations dampen the effect of stressors. This would suggest that future studies should aim to strengthen self-elated associations, particularly at the explicit level, either by targeting this directly or by weakening self-depressed associations. In doing so, this may decrease risk for recurrence. Furthermore, there was some support that SDA may represent a premorbid vulnerability factor predictive of a more recurrent depression. This requires further testing in larger samples in which SDA is measured before and after the first MDD episode. Replicating this finding may indicate that stronger SDA, or weak self-elated associations, may be used to identify those individuals who will have a more recurrent aetiology and may best benefit from longer treatment or specific preventative interventions.

References

Beck, A. T. (2002). In R. L. Leahy, & E. T. Dowd (Vol. Eds.), *Cognitive models of depression: Vol. 14*, (pp. 29–61). New York: Springer Pub. Co.

Beevers, C. G. (2005). Cognitive vulnerability to depression: A dual process model. *Clinical Psychology Review, 25*(7), 975–1002. https://doi.org/10.1016/j.cpr.2005.03.003.

Bockting, C., Hollon, S. D., Jarrett, R. B., Kuyken, W., & Dobson, K. (2015). A lifetime approach to major depressive disorder: The contributions of psychological interventions in preventing relapse and recurrence. *Clinical Psychology Review*. https://doi.org/10.1016/j.cpr.2015.02.003.

Borsboom, D., & Cramer, A. O. J. (2013). Network Analysis: An integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology, 9*(1), 91–121. https://doi.org/10.1146/annurev-clinpsy-050212-185608.

Briñol, P., Petty, R. E., & Wheeler, S. C. (2006). Discrepancies between explicit and implicit self-concepts: Consequences for information processing. *Journal of Personality and Social Psychology, 91*(1), 154–170. https://doi.org/10.1037/0022-3514.91.1.154.

Burcusa, S. L., & Iacono, W. G. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*(8), 959–985.

De Raedt, R., Remue, J., Loeys, T., Hooley, J. M., & Baeken, C. (2017). The effect of transcranial direct current stimulation of the prefrontal cortex on implicit self-esteem is mediated by rumination after criticism. *Behaviour Research and Therapy, 99*, 138–146. https://doi.org/10.1016/j.brat.2017.10.009.

Elgersma, H. J., Glashouwer, K. A., Bockting, C. L. H., Penninx, B. W. J. H., & de Jong, P. J. (2013). Hidden scars in depression? Implicit and explicit self-associations following recurrent depressive episodes. *Journal of Abnormal Psychology, 122*(4), 951–960. https://doi.org/10.1037/a0034933.

Fiedler, K., Messner, C., & Bluemke, M. (2006). Unresolved problems with the 'I', the 'a', and the 'T': A logical and psychometric critique of the implicit association test (IAT). *European Review of Social Psychology, 17*, 74–147. https://doi.org/10.1080/10463280600681248.

Frank, E., Prien, R. F., Jarrett, R. B., Keller, M. B., Kupfer, D. J., Lavori, P. W., et al. (1991). Conceptualization and rationale for consensus definitions of terms in major depressive disorder: Remission, recovery, relapse, and recurrence. *Archives of General Psychiatry, 48*(9), 851–855. https://doi.org/10.1001/archpsyc.1991.01810330075011.

Gawronski, B., & Bodenhausen, G. V. (2006). Associative and propositional processes in evaluation: An integrative review of implicit and explicit attitude change. *Psychological Bulletin, 132*(5), 692–731.

Glashouwer, K. A., & de Jong, P. J. (2010). Disorder-specific automatic self-associations in depression and anxiety: Results of The Netherlands study of depression and anxiety. *Psychological Medicine, 40*(7), 1101–1111. https://doi.org/10.1017/S0033291709991371.

Glashouwer, K. A., de Jong, P. J., & Penninx, B. W. J. H. (2012). Prognostic value of implicit and explicit self-associations for the course of depressive and anxiety disorders. *Behaviour Research and Therapy, 50*(7–8), 479–486.

Glashouwer, K. A., Smulders, F. T. Y., de Jong, P. J., Roefs, A., & Wiers, R. W. H. J. (2013). Measuring automatic associations: Validation of algorithms for the Implicit Association Test (IAT) in a laboratory setting. *Journal of Behavior Therapy and Experimental Psychiatry, 44*(1), 105–113. https://doi.org/10.1016/j.jbtep.2012.07.015.

Greenwald, A. G., & Farnham, S. D. (2000). Using the implicit association test to measure self-esteem and self-concept. *Journal of Personality and Social Psychology, 79*(6), 1022–1038. https://doi.org/10.1037/0022-3514.79.6.1022.

Greenwald, A. G., McGhee, D. E., & Schwartz, J. L. K. (1998). Measuring individual differences in implicit cognition: The implicit association test. *Journal of Personality and Social Psychology, 74*(6), 1464–1480. https://doi.org/10.1037/0022-3514.74.6.1464.

Greenwald, A. G., Nosek, B. A., & Banaji, M. R. (2003). Understanding and using the implicit association test: I. An improved scoring algorithm. *Journal of Personality and Social Psychology, 85*(2), 197–216. https://doi.org/10.1037/0022-3514.85.2.197.

Hardeveld, F., Spijker, J., Graaf, R. D., Nolen, W. A., & Beekman, A. T. F. (2013). Recurrence of major depressive disorder and its predictors in the general population: Results from The Netherlands mental Health survey and incidence study (NEMESIS). *Psychological Medicine, 43*(1), 39–48. https://doi.org/10.1017/S0033291712002395.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National comorbidity survey replication. *Archives of General Psychiatry, 62*(6), 593–602.

Lamers, F., Hoogendoorn, A. W., Smit, J. H., van Dyck, R., Zitman, F. G., Nolen, W. A., et al. (2012). Sociodemographic and psychiatric determinants of attrition in The Netherlands study of depression and anxiety (NESDA). *Comprehensive Psychiatry, 53*(1), 63–70. https://doi.org/10.1016/j.comppsych.2011.01.011.

Lewinsohn, P. M., Steinmetz, J. L., Larson, D. W., & Franklin, J. (1981). Depression-related cognitions: Antecedent or consequence? *Journal of Abnormal Psychology, 90*(3), 213–219. https://doi.org/10.1037/0021-843X.90.3.213.

Mueller, T. I., Leon, A. C., Keller, M. B., Solomon, D. A., Endicott, J., Coryell, W., et al. (1999). Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. *The American Journal of Psychiatry, 156*(7), 1000–1006.

Penninx, B. W. J. H., Beekman, A. T. F., Johannes, H. S., Zitman, F. G., Nolen, W. A., Spinhoven, P., et al. (2008). The Netherlands study of depression and anxiety (NESDA): Rationale, objectives and methods. *International Journal of Methods in Psychiatric Research, 17*(3), 121–140. https://doi.org/10.1002/mpr.256.

Remue, J., De Houwer, J., Barnes-Holmes, D., Vanderhasselt, M.-A., & De Raedt, R. (2013). Self-esteem revisited: Performance on the implicit relational assessment procedure as a measure of self- versus ideal self-related cognitions in dysphoria. *Cognition & Emotion, 27*(8), 1441–1449. https://doi.org/10.1080/02699931.2013.786681.

Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., et al. (1988). The composite International diagnostic interview: An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Archives of General Psychiatry, 45*(12), 1069–1077.

Rothermund, K., & Wentura, D. (2004). Underlying processes in the implicit association Test: Dissociating salience from associations. *Journal of Experimental Psychology: General, 133*(2), 139–165.

Rudolph, A., Schröder-Abé, M., Riketta, M., & Schütz, A. (2010). Easier when done than said!: Implicit self-esteem predicts observed or spontaneous behavior, but not self-reported or controlled behavior. *Zeitschrift Für Psychologie Journal of Psychology, 218*(1), 12–19. https://doi.org/10.1027/0044-3409/a000003.

Rush, A. J., Giles, D. E., Schlesser, M. A., Fulton, C. L., Weissenburger, J., & Burns, C. (1986). The inventory for depressive symptomatology (IDS): Preliminary findings.

Psychiatry Research, 18(1), 65–87. https://doi.org/10.1016/0165-1781(86)90060-0.
Rush, A. J., Gullion, C. M., Basco, M. R., Jarrett, R. B., & Trivedi, M. H. (1996). The inventory of depressive symptomatology (IDS): Psychometric properties. *Psychological Medicine, 26*(3), 477–486. https://doi.org/10.1017/S0033291700035558.
Strack, F., & Deutsch, R. (2004). Reflective and impulsive determinants of social behavior. *Personality and Social Psychology Review, 8*(3), 220–247. https://doi.org/10.1207/s15327957pspr0803_1.
Wittchen, H.-U. (1994). Reliability and validity studies of the WHO-composite International diagnostic interview (CIDI): A critical review. *Journal of Psychiatric Research, 28*(1), 57–84.