



Negative memory bias predicts change in psychiatric problems in a naturalistic psychiatric patient sample

Pascal Fleurkens^{a,b,*}, Mike Rinck^{a,c}, Indira Tendolkar^{d,e,f}, Bauke Koekkoek^{b,g,h}, William J. Burk^a, Agnes van Minnen^{a,i}, Janna N. Vrijen^{d,f,j}

^a Behavioural Science Institute, Radboud University, Thomas van Aquinostraat 4, 6525 GD, Nijmegen, the Netherlands

^b Pro Persona Mental Health Care, Wolfheze 2, 6874 BE, Wolfheze, the Netherlands

^c Ruhr-University, Massenbergstraße 9-13, D-44787, Bochum, Germany

^d Radboud University Medical Center, Department of Psychiatry, Reinier Postlaan 10, P.O. Box 9101, 6500 HB, Nijmegen, the Netherlands

^e Department of Psychiatry and Psychotherapy, University Hospital Essen, Virchowstraße 174, 45147, Essen, Germany

^f Donders Institute for Brain, Cognition, and Behaviour, Radboud University Medical Centre, Thomas van Aquinostraat 4, 6525 GD Nijmegen, the Netherlands

^g Research Group Poorly Understood Behaviour and Society, University of Applied Science Arnhem-Nijmegen, Kapittelweg 33, 6525 EN, Nijmegen, the Netherlands

^h Police Academy, Deventerstraat 46, 7311 LX, Apeldoorn, the Netherlands

ⁱ Psychotrauma Expertise Centrum (PSYTREC), Professor Bronkhorstlaan 2, 3723 MB, Bilthoven, the Netherlands

^j Pro Persona Mental Health Care, Depression Expertise Center, Nijmeegsebaan 61, 6525 DX, Nijmegen, the Netherlands

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ABSTRACT

Self-referential negative memory bias contributes to depression and other psychiatric disorders. Co-morbidity between these disorders is highly common in clinical practice, but transdiagnostic predictors like negative memory bias are not well understood yet. Therefore, the present study aimed to investigate the predictive value of negative memory bias for long-term change in broad psychiatric problems. In a naturalistic psychiatric patient sample ($N = 202$), using a prospective design, we examined the predictive value of negative memory bias (Self-Referent Encoding Task, SRET) for change in psychiatric problems (Outcome Questionnaire-45, OQ-45) after one, two, three, and four years. More negative memory bias predicted more psychiatric problems three and four years later, even when controlling for baseline psychiatric problems and depression. Memory bias might be a transdiagnostic predictor of change in psychiatric problems. Including such neuropsychological measures in diagnostics and symptom course prediction may improve psychological interventions.

1. Introduction

Psychiatric problems are common and persistent, with a lifetime prevalence of 46.4% (Kessler et al., 2005). Psychiatric problems frequently reoccur, can take a chronic course (Scholten et al., 2016), and are associated with persistent functional and social impairments (Smith et al., 2018). Although psychotherapy and pharmacotherapy are effective in the treatment of diverse psychiatric problems (e.g., Carpenter et al., 2018), many patients do not improve (Hofmann et al., 2012). This calls for the identification of factors that contribute to psychiatric problems. One of these factors is negatively biased memory: easier recall of negative over positive information, which is assumed to contribute to the development and maintenance of psychiatric problems (LeMoult and Gotlib, 2018). Negative memory bias has frequently been found in depression (Everaert et al., 2022), and there is evidence for a

transdiagnostic role (e.g., Duyser et al., 2020).

Knowing if and how negative memory bias predicts the time course of psychiatric symptoms might improve clinical predictions, and perhaps targeted treatment selection. Indeed, memory bias seems to have predictive value for depression: depressed patients with stronger positive memory bias exhibited greater symptomatic improvement after nine months (Johnson et al., 2007). In remitted depressed patients, more negative self-referential recall predicted recurrence of depressive symptoms after six weeks (Lewis et al., 2017) and onset of a depressive episode within three years (LeMoult et al., 2017). Similarly, in youth and adolescent community samples, memory bias predicted increases in depressive symptoms (e.g., Connolly et al., 2015). Taken together, there is compelling evidence for memory bias as a predictor of depression.

Thus far, research on the predictive value of memory bias has included categorical patients groups or community samples, while

* Corresponding author. Behavioural Science Institute, Radboud University, Thomas van Aquinostraat 4, 6525 GD, Nijmegen, the Netherlands.

E-mail address: p.fleurkens@propersona.nl (P. Fleurkens).

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excluding or ignoring comorbidity. However, comorbidity is the rule rather than the exception in clinical practice (Lamers et al., 2011). Moreover, severity of comorbidity is associated with biased memory (Vrijzen et al., 2017), indicating a possible transdiagnostic mechanistic role of memory bias. This fits with contemporary conceptualizations of psychiatric problems highlighting shared underlying mechanisms (e.g., RDoC; Insel et al., 2010). Hence, studying whether negative memory bias predicts the time course of psychiatric problems across mental disorders may aid theory formation on shared psychiatric mechanisms, and it may identify candidate intervention targets for comorbid patient samples.

In line with clinical practice, we studied a large naturalistic sample of patients with a broad range of psychiatric problems, and we measured memory bias at baseline as well as psychiatric problems across four years. Our main aim was to conceptually replicate and extend previous findings on the predictive value of memory bias, including the study by LeMoult and colleagues (2017). We expected that negative memory bias would predict worsening in psychiatric problems after three years in our psychiatric patient sample, extending the previous findings to a transdiagnostic sample. Whether memory bias also predicted change in psychiatric problems after one, two and four years, was an exploratory question.

2. Methods

2.1. Participants

This study made use of the MATCH cohort (see Koekkoek et al., 2016). In total, 283 psychiatric patients participated in this study (age: 18–65 years old). They were recruited from three Dutch mental health institutions. Patients were eligible if they met the criteria of a psychiatric disorder according to the DSM-IV (American Psychiatric Association, 2000), but did not suffer from a primary psychotic, bipolar-I, or cognitive disorder. They had to be between 18 and 65 years old and show sufficient comprehension of the Dutch language.

Patients were interviewed using the Mini-International Neuropsychiatric Interview Plus (MINI Plus; Sheehan et al., 1998). Patients scoring above the cut-off on the Standardized Assessment of Personality-Abbreviated Scale Self-Report (SAPAS-SR; Germans et al., 2012), were assessed with the Structured Interview for DSM-IV Personality Disorders (SIDP-IV; Pfohl et al., 1995). For this study, specific disorders were grouped into nine diagnostic clusters: anxiety disorders, mood disorders, substance use disorders, manic disorders, psychotic disorders, eating disorders, somatoform disorders, personality disorders, and ADHD. Participants could suffer from one or more disorders in the same cluster. Those without any of the currently investigated disorders, which is not uncommon in mental health services (Druss et al., 2007; Lawrence et al., 2015), were not clustered within any of the diagnostic clusters. This was allowed because we aimed for a naturalistic patient sample.

Eleven patients with a current psychotic disorder and 4 patients with a bipolar-I disorder were excluded from the dataset because of the possible interference of these diagnoses with performing the cognitive tasks and responding to the questionnaires. Nine patients who did not complete the task were excluded. Nine patients who did not recall any words were also excluded from the analyses, because a bias score could not be computed. This resulted in a final sample of 250 patients.

Patients were rewarded for their participation with a gift certificate. All patients provided informed consent. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the local Medical Ethical Committee ("Commissie Mensgebonden Onderzoek regio Arnhem-Nijmegen"), registration number: 41139.091.12.

2.2. Sociodemographics

Patients' biological sex (female, male), age, and highest level of education finished with a diploma were assessed with an interview. Level of education was classified into seven categories, from low to high: lower education, lower vocational education, secondary general education, secondary vocational education, high school, higher vocational education, and university education.

2.3. Memory bias

Memory bias was measured with the computerized Self-Referent Encoding Task (SRET; Derry and Kuiper, 1981). The SRET has moderate to very high split-half and test re-test reliability (Dainer-Best et al., 2018). During the encoding phase, 24 adjectives (12 positive, 12 negative) were sequentially presented in a fixed random order on a computer screen. No more than two words of the same valence were presented sequentially. The participant was instructed to press the 'j' key ('ja' being Dutch for 'yes') on the keyboard if the word described them, and the 'n' key if not. After a brief (2–3 min) distraction with part A and B of the Trail Making Task (TMT; Reitan and Davison, 1974), the participant was instructed to type in as many words as (s)he could remember from the encoding phase within 3 min. Spelling errors and words with a similar semantic meaning were permitted. The first two and the last two words were not included in the test results to reduce primacy and recency effects on the negative memory bias index (cf. van Oostrom et al., 2012; Vrijzen et al., 2017). In accordance with a broad range of earlier studies (e.g. Duyser et al., 2020; Vrijzen et al., 2017), a negative memory bias index was calculated by dividing the number of negative words endorsed as self-descriptive and correctly recalled by the total number of words endorsed and recalled (Gotlib et al., 2004). For example, recalling 8 self-descriptive words of which 6 were negative, would yield a negative memory bias of .75 (6/8). The scores could range from 0 to 1, with higher scores representing more negative memory bias.

2.4. Level of psychiatric problems

The Outcome Questionnaire-45 (OQ-45; Lambert et al., 2004) was used to measure the level of psychiatric problems and difficulties in psychosocial functioning. It has three subscales: symptomatic distress, (problems in) interpersonal relationships, and (problems in) social role performance. The OQ-45 is intended to capture transdiagnostic psychiatric symptoms (de Jong et al., 2007; Lambert et al., 1996), and has proven its value in recent clinical research (Kist et al., 2023). The OQ-45 is sensitive to change over time, and research has shown high reliability and good validity (de Jong et al., 2007; Lambert et al., 1996). Total scores range from 0 to 180, with higher scores representing more psychiatric problems and difficulties in psychosocial functioning. For the current sample, internal consistency was very high, Cronbach's alpha $\alpha = .95$ at T3.

2.5. Procedure

The study had a prospective setup. The patients were diagnosed at baseline. The SRET, sociodemographics, and OQ-45 were completed at baseline (T0) and during four consecutive years (T1, T2, T3, and T4). On average, duration between timepoints was 322 days (SD = 54; for means and SDs for duration of the follow-up timepoints in relation to baseline, see Table S1 in the supplementary material). In the current study, we focused on T3. Baseline assessments were face-to-face, supervised by trained research assistants, and took place at one of the three participating institutions. Follow-up assessments were conducted by the research assistants by means of telephone interviews, and patients filled out online questionnaires. Patients without internet access completed the questionnaires on paper or by telephone. For further details on the procedure, see Koekkoek et al. (2016).

2.6. Statistical analyses

To examine our research question, we conducted a linear regression analysis with negative memory bias strength (SRET) as predictor, baseline psychiatric problems (OQ-45 Total Score at T0) as covariate, and psychiatric problems after three years (OQ-45 Total Score at T3) as dependent variable. To examine whether associations were specific to depression (as memory bias was mostly studied in depression), we added depression status as a predictor of psychiatric problems. This is also important because in a recent independent highly comorbid psychiatric sample evidence was found for the transdiagnostic nature of memory bias, but there was also some depression specificity (Duyser et al., 2020). In the present study, age, biological sex, and educational level were not significantly associated with psychiatric problems at T3 (all p -values $>.068$). Consequently, they were not included in the regression model.

3. Results

3.1. Sample descriptives

Means (SD), percentage and/or range of age, biological sex, and educational level of the baseline sample ($N = 250$) are presented in Table 1. 56 percent had one or more diagnoses in the anxiety disorder cluster, 30.4% in the mood disorder cluster, 18.4% in the substance use disorder cluster, 3.6% in the eating disorder cluster, 10.8% in the somatoform disorder cluster, 5.2% in the ADHD cluster, and 30.8% in the personality disorder cluster. 26.4% had one or more diagnoses in one cluster, 49.2% had one or more diagnoses in two or more clusters. 24.4% of the participants did not fulfill current criteria for any of the assessed diagnoses.

Means (SD) and range of the negative memory bias index at baseline, and psychiatric problems (OQ-45) at baseline, T1, T2, T3, and T4 are presented in Table 2. Note that OQ-45 scores are indicative of clinic symptom-levels (total score ≥ 63 ; Lambert et al., 2004) at all time points, and that there was no clinically reliable change over the course of four years ($RCI \geq 14$). Over the years, several participants dropped out, with $N = 250$ at baseline (T0), to $N = 223$ at T1, $N = 216$ at T2, $N = 202$ at T3, and $N = 196$ at T4. Thus, at T3, 48 participants had dropped out, resulting in 202 participants for analyses. Comparisons between completers and non-completers on demographic and clinical variables, and bivariate correlations between the main variables are presented in the supplementary material (S2 and S3, respectively). Although the mean OQ-45 total score decreased significantly from T0 to T3, with $t(201) = 2.45$, $p = .015$, many patients did not show a significant change, and several showed an increase. The following analyses were conducted to predict this increase.

3.2. Predictors of psychiatric problems after three years

In the regression model, negative memory bias strength was included as a predictor, with baseline psychiatric problems as covariate, to predict increase in psychiatric problems three years later. The model significantly predicted T0-to-T3 increase in psychiatric problems, with $F(2,199) = 51.71$, $p < .001$, $R^2 = .342$. Baseline psychiatric problems and negative memory bias significantly predicted an increase in psychiatric problems, with $B = .54$, $\beta = .49$, $p < .001$, and $B = 15.44$, $\beta = .17$, $p = .009$, respectively. Adding depression status as a predictor to the model yielded very similar results, with $B = .55$, $\beta = .50$, $p < .001$, for baseline

Table 2

Means (SD) and actual range for negative memory bias. (SRET) and OQ-45 Total Scores.

Variable	Mean (SD)	Range
Negative memory bias	.3 (.3)	0–1
OQ-45 Total Score		
Baseline (T0)	74.4 (24.6)	1–132
After one year (T1)	71.9 (25.5)	12–134
After two years (T2)	72.1 (27.5)	8–147
After three years (T3)	70.2 (27.3)	5–143
After four years (T4)	67.5 (29.3)	4–139

psychiatric problems and $B = 16.04$, $\beta = .18$, $p = .007$, for negative memory bias. Depression status was not a significant predictor ($B = -2.23$, $\beta = -.04$, $p = .561$). Relationships between baseline negative memory bias and change in symptomatic distress, (problems in) interpersonal relationships, and (problems in) social role performance at T3 are presented in the supplementary material (S4).

3.3. Explorative analyses: predictors of psychiatric problems after one, two, and four years

To explore possible relationships between baseline negative memory bias and change in psychiatric problems after one (T1), two (T2), and four years (T4), the regression analysis was repeated for these time points. Baseline psychiatric problems, but not baseline negative memory bias, significantly predict increase in psychiatric problems after one year, with $B = .65$, $\beta = .63$, $p < .001$, and $B = 7.18$, $\beta = .09$, $p = .149$, respectively, and after two years, with $B = .62$, $\beta = .55$, $p < .001$, and $B = 5.26$, $\beta = .06$, $p = .372$, respectively. Baseline psychiatric problems and baseline negative memory bias significantly predicted increase in psychiatric problems after four years, with $B = .64$, $\beta = .55$, $p < .001$, and $B = 14.62$, $\beta = .15$, $p = .018$, respectively.

4. Discussion

This study conceptually replicated previous evidence for the predictive value of negative memory bias for depression (LeMoult et al., 2017), extending these findings to a naturalistic patient sample where negative memory bias predicted change in psychiatric problems. The strength of the negative memory bias predicted the increase in psychiatric problems after three years, independent of baseline depression status. This is in line with recent evidence for the presence of negative memory bias in broader psychopathology (e.g., Duyser et al., 2020). The combined results indicate that memory bias may be a potential transdiagnostic predictor for reduced improvement or worsening of psychiatric problems.

Our findings conform to transdiagnostic models of biased information processing which focus on common principles and pathways in different psychiatric problems (e.g., RDoC; Insel et al., 2010; the Generic Cognitive Model; Beck and Haigh, 2014). In line with these models, we hypothesize that patients recall self-referential negative information more frequently and easily than positive information. This will in turn impede the flexible selection and implementation of the emotion regulation strategies that are needed for coping and adaptive behavior in the face of stress (see also Parsons et al., 2016). This process can lead to a vicious circle where easier recall of negative self-referential information increases negative mood, which then makes current experiences more negative and less enjoyable, and later on, these experiences are more easily recalled (see also LeMoult and Gotlib, 2018). Interestingly, the effects of negative memory bias may be long-lasting: In our study, memory bias predicted changes in psychiatric problems three and four years later, over and above the prediction of baseline level. Although we focus on the prediction by negative memory bias of psychiatric problems after three years, the finding that negative memory bias did not predict psychiatric problems after one and two years is surprising. We do not

Table 1

Means (SD) or %, and actual range for age, biological sex, and educational level.

Variable	Mean (SD) or %	Range
Age	38.0 (11.4)	19–61
Biological sex, female	70.8%	–
Educational level	4.68 (1.53)	1–7

have a definite explanation for this finding, and it would provide an interesting subject for follow-up research, in which memory bias should be measured at all time points. Beta values, however, were quite similar for the different time points, suggesting that memory bias may have predicted psychiatric problems after one or two years similar, yet in non-significant ways.

If these results can be replicated, future studies on transdiagnostic mechanisms may contribute to the development of more personalized health care, targeting patients' specific risk factors such as biased memory processing (Peeters, 2015). In this context, it is informative that a relatively simple and short computer task (SRET) has clinically relevant predictive value in a highly affected psychiatric patient sample. This supports recent attempts to assess transdiagnostic concepts such as negative memory bias and to develop corresponding therapeutic strategies (e.g. Todd et al., 2023). In the future, one might use the degree to which negative memory bias remains present after treatment as a predictor of continuation or recurrence of psychiatric problems (Vrijnsen et al., 2017). Moreover, if memory bias not only predicts psychiatric problems, but also contributes causally to them, the feasibility and effectiveness of so-called memory bias modification trainings should be investigated (c.f. positive memory enhancement training; Arditte et al. (2018), and positive autobiographical memory training; Bovy et al., 2022). In this respect, it should be taken into account that in the current study, predictive effects of memory bias were relatively small. Nevertheless, targeting memory with memory bias modification trainings, as an augmentation or enhancement strategy adjunctive to other treatments such as cognitive behavior therapy (CBT), might be helpful to address maintaining mechanisms involved in psychiatric problems (see also Vrijnsen et al., 2024). Indeed, Dalgleish and Hitchcock (2023) suggest to use memory protocols as augmentations of cognitive behavior therapy.

Of course the present study does not come without limitations. Due to the correlational design of the study, the observed long-term predictive value of memory bias does not imply causality. Second, for practical reasons we could not measure memory bias after T0, so we do not know if and how it changed over time, and whether changes in memory bias were related to changes in psychiatric problems. A possible psychometric limitation is that the memory bias score might be confounded with total recall performance on the SRET (c.f. Dainer-Best, 2023). Furthermore, although the OQ-45 was developed to capture common symptoms across a wide range of adult psychiatric disorders (de Jong et al., 2007; Lambert et al., 1996), it may be more suitable for certain patient groups or symptom profiles (e.g. depression; Levy et al., 2018). Finally, we consider our naturalistic sample as representative for clinical practice, but studying such a diverse group has disadvantages, too. Negatively biased processing, for example, can be both a susceptibility factor as well as a scar from previous depressive episodes or other psychiatric problems (Lewinsohn et al., 1981). Despite these limitations, the present results suggest that negative memory bias may be a valuable transdiagnostic predictor of psychiatric problems.

CRedit authorship contribution statement

Pascal Fleurkens: Writing – review & editing, Writing – original draft, Formal analysis. **Mike Rinck:** Writing – review & editing, Writing – original draft. **Indira Tendolkar:** Writing – review & editing, Methodology, Conceptualization. **Bauke Koekkoek:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization. **William J. Burk:** Writing – review & editing, Formal analysis. **Agnes van Minnen:** Writing – review & editing, Writing – original draft. **Janna N. Vrijnsen:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization.

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Declaration of competing interest

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Appendix A. Supplementary data

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