Vulnerability Before, During, and After a Major Depressive Episode

A 3-Wave Population-Based Study

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**Background:** Vulnerability as defined by high levels of neuroticism, low self-esteem, and poor coping skills characterizes individuals with a history of major depressive episodes (MDEs).

**Objective:** To separate postmorbid vulnerability into (1) trait effects (i.e., the continuation of premorbid vulnerability); (2) state effects of subthreshold (residual) symptoms on personality or its perception; and/or (3) scar effects (i.e., negative personality change that develops during an MDE and persists beyond MDE remission).

**Methods:** Data come from the Netherlands Mental Health Survey and Incidence Study, a prospective Dutch psychiatric population-based survey. We obtained psychiatric (Composite International Diagnostic Interview) and personality data on neuroticism, depressive coping style, self-esteem, and mastery from 4796 respondents at 3 time points (T1, T2, and T3), 12 and 24 months apart. Between- and within-subjects differences were tested with repeated-measures analysis of variance and adjusted for sex, age, and time.

**Results:** After T1, 409 respondents developed an MDE, of whom 334 were MDE-free at T3. In comparison with individuals without any lifetime MDE, the 262 subjects with a first MDE had higher premorbid T1 vulnerability scores on each personality measure (0.38-0.83 effect size units). During the MDE, vulnerability scores further increased (0.33-0.52 effect size units) but returned to premorbid levels after MDE remission. We found no scar effects among subgroups with severe or long-lasting MDEs. Subthreshold residual symptoms at T3 biased comparisons between T1 and T3 if the premorbid period of T1 to MDE onset was longer than the postmorbid period of MDE remission to T3, misleadingly suggesting scar effects. We obtained similar results in the 147 subjects with recurrent MDEs.

**Conclusions:** There was no evidence of a negative change from premorbid to postmorbid assessment for any of the personality traits. Postmorbid vulnerability reflected the continuation of premorbid vulnerability. Pre-post MDE comparisons are sensitive to prodromal and residual symptoms. Our findings suggest 2 independent simultaneous processes: (1) the ongoing expression of vulnerability as a personality deviance; and (2) synchrony of change between severity of depressive symptoms and personality deviance.

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U NIPOLAR MAJOR DEPRESSION and personality traits have complex relationships.1-8 Several studies have consistently documented that personality traits in the domain of neuroticism, low self-esteem, and poor mastery are risk factors for the onset of major depressive episodes (MDEs).2-14 In this article, we use the concept of vulnerability to indicate the personality characteristics associated with an increased risk of depression. Ample evidence shows that during an MDE, the scores for neuroticism are increased and those for self-esteem and mastery are reduced, an effect usually denoted as the state effect of depression.2,15-18 It is unclear whether the state effect is limited to the MDE or whether it persists beyond MDE remission (i.e., postmorbidly). Many investigators use the concept of scarring to indicate postmorbid vulnerability that was not present premorbidly (i.e., before the MDE).2,19-21 We follow this definition. The evidence of scarring is limited and contradictory, with some evidence in favor2,19 and some against it.20,21 Postmorbid vulnerability, however, could also be due to the continuation of premorbid vulnerability. In that case, premorbid personality characteristics (as true trait factors) would still be present after the MDE. We define this as the trait effect. Finally, postmorbid vulnerability could reflect mild state effects caused by subthreshold residual symptoms.

To separate postmorbid vulnerability into state, trait, and scar effects, a prospective multiwave population study was...
required to identify first and recurrent MDEs with assessments of vulnerability before, during, and after the MDE. First MDEs were needed to obtain premorbid vulnerability scores for individuals who were going to develop an MDE but had had no history of depression. Recurrent MDEs were needed to examine whether state, scar, and trait effects occurred in recurrent depression. In addition, the timing of premorbid and postmorbid vulnerability assessment was important. If the premorbid assessment took place long before MDE onset but the postmorbid assessment was performed shortly after MDE remission, the pre-post comparison could be biased by residual symptoms and might wrongly suggest scarring. The opposite could occur if the postmorbid period was longer than the premorbid period. Such bias might account for the inconsistent findings for scarring.

Using the 3-wave Netherlands Mental Health Survey and Incidence Study (NEMESIS)22-25 conducted in the Dutch general population, we tested, for first and recurrent MDEs separately, 3 hypotheses: (1) Vulnerability scores are higher during the MDE than before (state effect); (2) Vulnerability scores are higher after the MDE than before (scar effect); and (3) Premorbid vulnerability scores for those who developed a first MDE after the first wave (time point 1 [T1]) are higher than the vulnerability scores of those who never had an MDE (trait effect). Individuals with a history of depression who developed an MDE after T1 (recurrent MDE) were contrasted with individuals who also had a history of depression but did not develop a recurrent MDE after T1. To examine the state effects of subthreshold residual symptoms, we had to use an indirect approach because a measure of residual symptoms at T3 was not available. The indirect approach used the time elapsed from remission of the MDE until T3, assuming that residual symptoms generally decrease with time.

Scarring may not routinely occur.26-28 It might occur only in people who experience a severe or long-lasting MDE so that the negative effect on personality is sufficiently severe and prolonged to solidify and persist.26,28 or only in people with a history of depression26,27 owing to the demoralizing effects of a recurrent MDE, or only in high-risk subjects26,28 as a possible result of traumatic childhood events or a family history of depression. Hence, we examined scarring in various subgroups.

**METHODS**

**SAMPLE**

We obtained the data presented in this article from NEMESIS. The design, sample, and instruments of NEMESIS have been extensively described elsewhere.22,23 Briefly, NEMESIS was a prospective psychiatric epidemiologic survey in the Dutch adult general population (aged 18-64 years) with assessments in 1996 (T1), 1997 (T2), and 1999 (T3). It used a multistage, stratified, random-sampling procedure. From each household, we randomly selected 1 respondent. Interviewers made up to 10 telephone calls or visits to a household at different times of day and on various days of the week. For each subject, the interviews were 12 months (T1-T2) and 24 months (T2-T3) apart and were administered in the same month of the year to prevent season-related bias. The fieldwork of each assessment wave extended from February to December. Each interview included the Composite International Diagnostic Interview (CIDI)29,30 and self-report personality measures.

In the first wave, we obtained data from 7076 persons, a response rate of 69.7%. At T2, 1458 respondents (20.6%) dropped out; at T3, a further 822 (14.6%) were lost. We obtained General Health Questionnaire data from 44% of the T1 nonresponders.24 The T1 nonresponders had a slightly lower mean score on the General Health Questionnaire (1.6 vs 1.22, suggesting better mental health), a lower mean age (40.2 vs 41.2 years), and a higher proportion of women (54.4 vs 53.3). Their psychiatric morbidity (estimated with a logistic regression model) did not differ from that of the respondents.22-25 Attrition at T2 and T3 was weakly associated with younger age, lower level of education, urbanization, living alone, being unemployed, and being born outside the Netherlands.25 After adjustment for these demographic variables, mental health status as defined by absence vs presence of any disorder according to the DSM-III-R25 was not associated with attrition, but major depression at T2 weakly predicted attrition at T3 (odds ratio=1.37; 95% confidence interval, 1.05-1.54). Our study used the 4796 respondents who participated in all 3 waves.

At T1, 1-month, 12-month, and lifetime prevalence rates of major depression for women were 3.4%, 7.5%, and 20.1%, respectively; for men they were 1.9%, 4.1%, and 10.9%, respectively.23

**DIAGNOSTIC INSTRUMENT**

We used the World Health Organization–authorized Dutch version of the CIDI, version 1.1,29,30 and its diagnostic computer program to assign diagnoses according to the DSM-III-R. The CIDI has acceptable interrater and test-retest reliability for most nonpsychotic diagnoses, including major depression.26 At T2 and T3, the CIDI lifetime framework was adapted to the 1-year interval from T1 to T2 and the 2-year interval from T2 to T3.

We assigned DSM-III-R diagnoses without the use of hierarchical exclusion rules or application of the functional impairment criterion. Persons with bipolar disorder were not included in the MDE group.

**ASSESSMENT OF MDEs AND CONSTRUCTION OF GROUPS**

The lifetime prevalence of MDEs according to the T1 CIDI indicated whether or not there was a history of MDEs. The occurrence of an MDE during the 1-year T1-to-T2 interval was determined by the 12-month prevalence of MDEs at the T2 CIDI and during the 2-year T2-to-T3 interval by the 24-month prevalence of MDEs at the T3 CIDI. The presence of an MDE at T1 was determined by the 1-month prevalence of MDEs at the T1-CIDI. We excluded subjects with a 1-month prevalence of MDEs at the T1 CIDI from all analyses (see Figure). The presence of an MDE at T1 and T3 was determined by the 1-month prevalence of MDEs at the T2 and T3 CIDI, respectively. On the basis of lifetime history, we classified each MDE occurring after T1 as a first episode (first MDE) or recurrence (recurrent MDE). An MDE remission was determined by a negative 1-month prevalence of MDEs at the T2 or T3 CIDI, according to which interval the MDE occurred.

We constructed several groups from the CIDI data obtained at T1, T2, and T3 (Figure). The “never MDE” group (A in Figure) refers to respondents who never had an MDE (T1 CIDI) and did not develop one during the T1-to-T3 interval according to the T2 and T3 CIDI. The “history of MDE but no MDE after T1” group (B) refers to respondents who had at least 1 MDE before T1 (T1 CIDI) but did not develop a recurrence.
SEVERITY AND DURATION OF MDES

We categorized MDES in terms of severity, designated as mild, moderate, or severe according to the CIDI and DSM-III-R criteria (thus, mild MDES still met DSM-III-R criteria for MDE). We calculated duration using data from the Life Chart Interview (LCI), administered at T3. Complete LCI data were available for just 54% of all MDES that occurred in the T1-to-T3 interval, largely because the LCI was administered only to those who responded affirmatively at T3 to the LCI probe question of whether they had felt depressed for more than 2 weeks after T1. The LCI rated the presence of MDE symptoms per 3-month period. This measure defined remission as no or only subthreshold depressive symptoms in a 3-month period. We calculated duration by summing the 3-month periods with MDE symptoms until the 3-month period occurred with no or only subthreshold symptoms. We used both a continuous measure of duration and a dichotomized version (split at the mean duration of 6 months).

PERSONALITY TRAITS

We administered 4 brief personality questionnaires in the same order at each of the assessment waves. We assessed neuroticism with the short form of the Neuroticism scale from the Amsterdam Biographic Inventory. The Amsterdam Biographic Inventory, based on the Maudsley Personality Inventory, was one of the most frequently used personality questionnaires in the Netherlands during the last decades. A high score indicates high levels of neuroticism or negative affectivity. Prototypical items include the following questions: Does it happen often that you make a decision too late? Are you often too burdened by disappointments that you cannot put them out of your head? Do you ever have nightmares? Do you ever feel terribly unhappy, without knowing why? The internal consistency of the 14-item Neuroticism scale was satisfactory (Cronbach α = .79-.83). We assessed depressive coping style with the Utrecht Coping Scale. A high score indicates a depressive coping style in response to stressors; for example, “Problems overwhelm me” or “Problems tend to make me pessimistic” (Cronbach α = .64-.67). We assessed self-esteem with the 10-item Rosenberg Self-esteem Scale. A high score indicates high levels of neuroticism or negative affectivity. Prototypical items include the following questions: Does it happen often that you make a decision too late? Are you often too burdened by disappointments that you cannot put them out of your head? Do you ever have nightmares? Do you ever feel terribly unhappy, without knowing why? The internal consistency of the 14-item Neuroticism scale was satisfactory (Cronbach α = .79-.83). We assessed depressive coping style with the Utrecht Coping Scale. A high score indicates a depressive coping style in response to stressors; for example, “Problems overwhelm me” or “Problems tend to make me pessimistic” (Cronbach α = .64-.67). 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Table 1. Evaluating State Effects: Personality Scores Before and During the MDE for Subjects With First and Recurrent MDEs

<table>
<thead>
<tr>
<th>Personality Measure</th>
<th>Premorbid (T1)</th>
<th>During MDE (T2 or T3)</th>
<th>Effect Size Difference (95% CI)</th>
<th>F Statistic†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroticism</td>
<td>21.85 (6.32)</td>
<td>25.00 (5.75)</td>
<td>−0.52 (−0.69 to −0.35)</td>
<td>141.17</td>
</tr>
<tr>
<td>Depressive coping style</td>
<td>5.72 (2.00)</td>
<td>6.71 (1.78)</td>
<td>−0.52 (−0.76 to −0.28)</td>
<td>33.22</td>
</tr>
<tr>
<td>Self-esteem</td>
<td>29.91 (5.15)</td>
<td>28.30 (4.50)</td>
<td>0.33 (0.11 to 0.55)</td>
<td>13.97</td>
</tr>
<tr>
<td>Mastery</td>
<td>17.18 (4.25)</td>
<td>15.54 (4.02)</td>
<td>0.40 (0.20 to 0.59)</td>
<td>27.74</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>23.83 (6.78)</td>
<td>27.06 (6.78)</td>
<td>−0.50 (−0.79 to −0.21)</td>
<td>64.54</td>
</tr>
<tr>
<td>Depressive coping style</td>
<td>5.69 (1.72)</td>
<td>6.65 (1.85)</td>
<td>−0.54 (−0.85 to −0.23)</td>
<td>17.17</td>
</tr>
<tr>
<td>Self-esteem</td>
<td>30.24 (5.02)</td>
<td>28.12 (4.11)</td>
<td>0.46 (0.17 to 0.76)</td>
<td>21.31</td>
</tr>
<tr>
<td>Mastery</td>
<td>16.35 (4.14)</td>
<td>14.80 (3.63)</td>
<td>0.40 (0.20 to 0.60)</td>
<td>20.68</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MDE, major depressive episode; T, time point.

*The effects represent time × group interactions (adjusted for sex and age), with time being the difference between premorbid personality scores and scores obtained during the MDE, and group being subjects with a current MDE (first MDEs: n = 85; recurrent MDEs: n = 54) vs controls (never MDE: n = 3736; history of MDE but no MDE after T1: n = 533). To take into account that some subjects had an MDE at T2 and others at T3, a similar proportion of the control group’s personality scores were measured at T2 and T3. Data are presented as mean (SD) unless otherwise indicated.

†df = 1; P < .001.

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**SCAR EFFECT**

We evaluated scar effects for subjects with remitted first (E in Figure) and recurrent (F) MDEs separately by comparing premorbid T1 with postmorbid T3 personality scores. Higher postmorbid vulnerability scores would suggest scar effects. The findings were negative: T1 and T3 scores did not differ for subjects with first (Table 3, row E) or recurrent (row F) MDEs.

Although these results suggest that scarring does not routinely occur in first and recurrent MDEs, it might occur in particular subcategories. We examined, for first and recurrent MDEs separately, scarring in the subcategories of severe MDEs, MDEs lasting more than 6 months, and severe MDEs lasting more than 6 months. We also examined scarring in the subcategories of individuals who experienced potentially traumatic childhood events or had a biological parent with a history of depression. With 1 exception, the results of all subgroup tests were negative (data not presented). The exception was depressive coping style in the subcategory of recurrent MDEs lasting more than 6 months (F1 = 6.95; P = .02). Given the number of subgroup tests, we consider this a chance finding.

**EFFECTS OF UNEQUAL PREMORBID AND POSTMORBID PERIODS**

Table 3 also presents T1-to-T3 effect size differences in personality scores for subgroups of those with first remitted MDEs with equal (E1 and E2) and different (E3 and E4) premorbid and postmorbid periods. In E1 and E2, pre-post episode vulnerability scores did not differ, but they did in E3 and E4. In subgroup E3, in which the premorbid period was longer than the postmorbid period, we found higher levels of neuroticism and depres-
sive coping style (negative effect size) and lower self-esteem and mastery (positive effect size) at T3 than at T1. Given the longer premorbid than postmorbid period, this is probably due to fewer prodromal symptoms at T1 than residual symptoms at T3. The reverse occurred in subgroup E4, in which the premorbid period was shorter than the postmorbid period. Subgroups F1 to F4 of subjects with recurrent MDEs yielded similar results to the E1 to E4 subgroups of those with first MDEs, although the vulnerability scores in F4 showed only a trend toward lower vulnerability at T3 as compared with T1 (data not presented). Collectively, these results suggest that pre-post MDE comparisons in which the premorbid and postmorbid period differ in length may misleadingly suggest scarring or its opposite.

Whereas personality-related vulnerability (high levels of neuroticism and depressive coping style with low self-esteem and mastery) was present more than 1 year before and further increased during the MDE, it returned to its premorbid level after remission of the MDE. Our results confirm earlier findings of a state effect\(^2,15-18\) of depression on personality traits in the domain of neuroticism and control as well as a risk factor effect\(^2,9-14\) of these traits on depression. Our results, however, do not support the scar hypothesis. The findings are consistent with results reported from the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression\(^11\) and extend these separately to larger and more representative samples of first and recurrent MDEs. Our findings point to 2 independent but simultaneous processes: (1) the ongoing expression of vulnerability for depression in increased neuroticism and depressive coping style as well as reduced self-esteem and mastery, collectively denoted as personality deviance; and (2) synchrony of change between severity of depressive symptoms and severity of personality deviance.

Pre-post MDE personality comparisons may misleadingly suggest scarring if the premorbid period is longer than the postmorbid period (and the opposite if shorter). We attribute this to a state effect of subthreshold residual symptoms on self-reported personality. If the premorbid period is longer than the postmorbid period, residual symptoms will likely outnumber prodromal symptoms. State effects are not limited to the MDE itself but extend to the prodromal and residual symptom phases. The few studies reporting scar effects\(^2,19\) may have had longer premorbid than postmorbid periods on average, favoring an excess of residual symptoms at the postmorbid personality assessment relative to the level of prodromal symptoms at the premorbid assessment. Nothing is known about possible time lags in the synchrony of change between personality and symptom severity.

LIMITATIONS AND STRENGTHS

Findings and interpretations should be considered in the context of several limitations. The most serious limitation is the lack of a measure of current symptoms at the times the respondents took the CIDI and personality measures (T1, T2, and T3) because the CIDI version 1.1 has no cross-sectional symptom assessment. Hence, we cannot rule out that premorbid and postmorbid personality deviance might be entirely due to (chronic) subthreshold symptoms. However, we do not think that this is the case for 2 reasons, and our data support the notion of premorbid and postmorbid personality deviance as an expression of trait vulnerability to depression. First, personality deviance was already present more than 1 year before the first lifetime MDE. Second, if chronic subthreshold symptoms are present years before and after the MDE and they produce personality deviance or are produced by it, it is more appropriate to consider these symptoms as an integral part of the personality and an expression of underlying trait vulnerability.

The second limitation is that we could not discriminate between 2 competing explanations of state effects: real albeit temporary personality changes vs reporting bias due to the effects of depression on self-perception and recall processes.\(^43-45\) Other limitations include the retrospective assessment at T3 of the duration of only 53% of MDEs occurring in the T1-to-T3 interval, the lack of reliability data for the measures of childhood adversity and parental depression, and the slightly selective attrition. We do not believe that attrition threatened the validity of our findings because of the large sample size and the fact that approximately 80% of all individuals with an MDE participated again at the next assessment wave, including those with first and recurrent as well as remitted and nonremitted MDEs. Hence, attrition probably did not reduce the variation in course. Finally, because detailed treatment data are lacking, we cannot exclude the possibility that at the group level, effective treatment may have reduced the personality deviance of some so much that this neutralized the scar effects of nontreatment in others.

Although scarring does not routinely occur after an MDE, it may occur in MDEs that require inpatient treatment. These patients are different from the average subject with MDE in a community study. In the NEMESIS study, 2% received inpatient psychiatric care, 22% specialty outpatient mental health care, and 23% only primary care in the year following onset. We also cannot rule out that scarring occurs in childhood or adolescent depression or that forms of scarring exist that self-report personality measures do not pick up.\(^19\) Challenge tests to detect latent scars would have strengthened the study, but given the large sample size, the costs would have been exorbitant.

The major strengths of our study are its sample size, random population sample, structured diagnostic assessment procedures, and prospective longitudinal design made possible by assessment in 3 waves during a 3-year period. This way we could identify 334 individuals with an MDE that started after the first personality assessment and remitted before the last one, avoid referral filter and lead time bias, and assess personality prior to, after, and during the MDE.

IMPLICATIONS

The occurrence of MDEs is common, with a 1-year incidence in the Netherlands of 1.72 for men and 3.90 for
women per 100 people at risk.66 About 50% of these episodes do not remit within a few months.32 Thus, the finding that there is no evidence of negative personality change from premorbid to postmorbid assessment is good news. The bad news is the continuation of premorbid personality-related vulnerability after the MDE. If treatments would not only achieve remission of the MDE but would also normalize levels of neuroticism, coping style, mastery, and self-esteem, relapse and recurrence rates would probably fall.

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