Limited Functioning After Remission of an Anxiety Disorder as a Trait Effect Versus a Scar Effect:

Results of a Longitudinal General Population Study

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ABSTRACT

Objective: After remission of an anxiety disorder, subjects often experience persistent functional impairments. We examined whether impairments in mental and physical functioning following remission are a continuation of premorbid lower functioning (trait effect), due to impairments that develop during the anxiety disorder and persist beyond recovery (scar effect), or both.

Methods: Data were derived from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), a prospective psychiatric epidemiologic study among the general population with a 3-wave design (6-year follow-up, with the study starting in 2007 and ending in 2015). *DSM-IV* anxiety disorders were measured with the Composite International Diagnostic Interview. Functioning was assessed with the Medical Outcomes Study 36-Item Short Form Health Survey. We evaluated trait effects using between-subjects comparison and scar effects using within-subjects comparisons.

Results: Compared to healthy controls, individuals with anxiety disorders had showed significant impairment in mental functioning (β = −11.6 [SE = 0.78]; $P < .001$) and physical functioning (β = −12.1 [SE = 1.14]; $P < .001$) prior to the onset of the anxiety disorder (n = 199), indicating a trait effect. In those who developed an anxiety disorder that remitted within the 6-year follow-up (n = 92), functioning after remission (at second follow-up) was similar to functioning before onset (at baseline), indicating that a scar effect was absent. A trend toward mental scarring was visible in the subgroup with recurrent anxiety disorders ($P = .03$).

Conclusions: Persistent functional limitations following remission largely reflect a preexisting trait effect. Since lower levels of functioning are associated with relapse, investments in functional improvement seem worthwhile. Relapse prevention might help to prevent mental scarring.

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Anxiety disorders are among the most prevalent[1] and the most burdensome[2–5] disorders worldwide if both mental and physical disorders are taken into account. When anxiety symptoms remit, the level of functioning improves.[6–8] However, subjects often still experience impairments after remission.[6,9] These impairments may feed the cycle of chronicity of anxiety disorders, as the level of functioning after remission of an anxiety disorder is predictive for relapse.[10–13] Hence, understanding the origin of these persistent functional limitations could help improve treatment strategies and may contribute to breaking the cycle of chronicity.

To date, it is not clear how functioning and anxiety symptoms are connected. Some suggest functioning can be seen as part of symptoms of an overall anxiety disorder syndrome,[11] whereas others regard limited functioning as a psychosocial vulnerability.[13,14] Two distinct explanations for prolonged impairment in subjects with a remitted disorder include a trait effect and a scar effect. A trait effect is the situation in which subjects with a remitted disorder already had functional limitations before the onset of their disorder. Alternatively, a scar effect means that the disorder causes persistent functional damage, with levels of functioning not returning to premorbid levels after remission.

Prolonged functional impairments following remission are present in other forms of psychopathology as well, including schizophrenia,[15] bipolar disorder,[16,17] and major depressive disorder (MDD).[16,18] Regardless of the type of disorder, a trait effect was present in these disorders,[19,20] suggesting that limited functioning may be a nonspecific vulnerability factor for the development of psychopathology. If so, a trait effect will be present in anxiety disorders as well. A scar effect is generally present in schizophrenia[21] and bipolar disorder,[22,23] both of which are characterized by severity and recurrence of psychopathology. In schizophrenia, the duration of the illness has significantly and permanently impacted functional outcome.[21] Likewise, in bipolar disorder, the number of episodes appears to be associated with a decline in cognitive functioning,[22] which in turn has influenced the level of psychosocial functioning in the euthymic phase[23] and the progression of the disease.[24] By contrast, in MDD, scarring does not occur routinely, but is present only in a subgroup of subjects that have suffered from a severe recurrent episode.[18] These findings might lead to the hypothesis that the occurrence of scarring depends on severity or unfavorable course trajectories of psychopathology. If so, scarring will not occur routinely in anxiety disorders because anxiety disorders are heterogeneous regarding severity and course,[25] like MDD.[26] Scarring, then, will be present in those with unfavorable course trajectories and a severe episode of anxiety.

Clinical Points

- Functional impairments may persist after remission of an anxiety disorder, though until now it was not clear whether this persistence reflects a trait or a scar effect.
- Mental and physical functioning are already significantly impaired prior to the development of an anxiety disorder, reflecting the presence of a trait effect. Mental scarring may occur in those with a recurrent anxiety disorder.
- Because functional impairments are associated with relapse, investing in optimizing levels of functioning, besides symptom reduction, seems an appropriate goal and may be especially beneficial in those with recurrent anxiety disorders.

To our knowledge, no study has yet examined whether functional limitations following remission of anxiety disorders reflect a trait effect, a scar effect, or both. The Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2) is a prospective psychiatric epidemiologic study among the general population. Its 3-wave design with both subjects with anxiety disorders and subjects without common mental disorders enables us to examine the following:

1. If levels of functioning of subjects prior to the development of an anxiety disorder differ from those of healthy controls (trait effect); we hypothesized such a trait effect to be present.
2. If functioning returns to premorbid levels after remission of the anxiety disorder (scar effect); we expected no scarring in general.
3. Whether the presence of a trait or scar effect differs for mental and physical domains of functioning.
4. Whether the presence of a trait or scar effect differs between subgroups, ie, between severe versus moderate versus mild disorders, and between recurrent and first-incident cases; we hypothesized scarring to be present in a subgroup with severe and/or recurrent symptoms.

METHODS

Sample

NEMESIS-2 is a psychiatric epidemiologic cohort study of the Dutch general population aged 18–64 years at baseline. It is based on a multistage, stratified random sampling of households, with 1 respondent randomly selected in each household. The face-to-face interviews were computer-assisted. In the first wave (T_0), performed from November 2007 to July 2009, 6,646 persons were interviewed (response rate: 65.1%). This sample was nationally representative, although younger subjects were somewhat underrepresented.[27] Three years after T_0 (ie, T_1), 5,303 persons could be reinterviewed (response rate: 80.4%).[28] Three years after T_1 (ie, T_2), 4,618 persons were interviewed again (response rate 87.8%).[28] The study was approved by a medical ethics committee. After having been informed about the study aims, respondents provided written informed consent at each wave. For a more comprehensive description of the design, see de Graaf et al.[27]

Diagnostic Instrument

Psychiatric disorders according to *DSM-IV* were diagnosed using the Composite International Diagnostic Interview (CIDI) version 3.0, a fully structured lay-administered diagnostic interview. The CIDI 3.0 version[29] used in NEMESIS-2 was an improvement of the Dutch version used in the World Mental Health Survey Initiative. Clinical calibration studies in various countries[30] found that the CIDI 3.0 assesses mood, anxiety, and substance use disorders with generally good validity in comparison to blinded clinical reappraisal interviews. The CIDI assessed a 12-month diagnosis and a lifetime framework. At all waves, the 12-month diagnosis was assessed. The lifetime framework was assessed at T_0. At T_1 and T_2, the framework was adapted to the 3-year T_0–T_1 and T_1–T_2 intervals. In the current study, anxiety disorders included panic disorder with or without agoraphobia, agoraphobia without panic disorder, social phobia, and generalized anxiety disorder.

Functioning

To assess level of functioning, the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)[31] was administered at each wave, assessing level of functioning during the previous 4 weeks. The SF-36 consists of 36 items and 8 scales.[32] The 8 SF-36 scales were combined into mental health functioning and physical health functioning subscales, with scores ranging from 0 (poor) to 100 (good). The mental health component (MHC) includes psychological health, psychological role functioning, social role functioning, and vitality (at T_0 and T_2, Cronbach $\alpha = .78$; at T_1, $\alpha = .79$). The physical health component (PHC) includes general health, physical health, physical role functioning, and physical pain; (at T_0, Cronbach $\alpha = .79$; at T_1 and T_2, $\alpha = .81$).

Covariates

Covariates consisted of sociodemographic and clinical variables. Sociodemographic variables were assessed at baseline and included age (< 35 years vs ≥ 35 years), sex, and education. Education was defined as either low (primary, basic vocational, and low secondary education) or high (high secondary education, higher professional education, and university).

Clinical variables included presence of comorbid mood disorder, first-incident or recurrent anxiety disorder, severity of the anxiety disorder, and presence of any somatic disorder. Presence of comorbid mood disorder (yes/no) was defined as 12-month MDD, dysthymia, or bipolar disorder according to the CIDI. Presence was assessed at all 3 waves, as it may change over time. The distinction between first-incident and recurrent anxiety disorder was determined according to the absence or presence of a lifetime history of any anxiety disorder at T_0. Severity of the anxiety disorder was assessed at T_1 and was based on criteria used in previous studies.[33–35]

Severe impairments in at least 2 areas of role functioning on the Sheehan Disability Scale (SDS)[36] were classified as severe, moderate role impairment in any domain of the SDS were classified as moderate, and the remaining were classified as mild. Any somatic disorder was assessed at all 3 waves and regarded as present if 1 or more of 17 chronic somatic disorders from a standard checklist was reported present and had been treated or monitored by a medical doctor in the previous 12 months. Comparisons between self-reports of chronic somatic disorders and medical records show moderate to good concordance.[37,38]

Statistical Analysis

Trait effect. To examine the presence of a trait effect, we compared the level of functioning at baseline between healthy controls (n = 2,826) and subjects that developed an anxiety disorder between baseline and T_1 (the anxiety disorder group; n = 199). Healthy controls were subjects who had no 12-month anxiety, mood, or substance use disorder at T_0 and who developed none within the T_0–T_1 interval. Subjects with an anxiety disorder were defined as those who did not have a 12-month anxiety disorder at T_0 but who developed an anxiety disorder between T_0 and T_1. The category thus encompasses first-incident and recurrent cases. Baseline characteristics between healthy controls and the anxiety disorder group were examined using 2-tailed χ^2 tests. To assess the presence of a trait effect, MHC and PHC at T_0 (thus prior to the development of the anxiety disorder) were compared between the anxiety disorder group and healthy controls using linear regression analyses. After the unadjusted analyses, the analyses were adjusted for sociodemographics. The analysis on MHC was additionally adjusted for comorbid mood disorders, and the analysis on PHC was additionally adjusted for somatic disorders, since these could be confounders. We further examined if results differed between the incident subgroup and the recurrent subgroup and between those who developed a mild versus a moderate versus a severe anxiety disorder. Because severity could be assessed only in those who had an anxiety disorder at T_1, we restricted these latter analyses to the 152 subjects with a 12-month diagnosis at T_1 (of the total of 199 in the anxiety disorder group). Multiple tests were conducted, with a maximum of 10 tests for each outcome parameter. To ensure that the cumulative type I error remained below 0.05, an effect was considered significant if the *P* value was .005 or smaller.

Scar effect. To assess the presence of a scar effect, we compared the level of functioning prior to onset of an anxiety disorder with the level of functioning following remission of the anxiety disorder. We selected subjects without a 12-month anxiety disorder at T_0 who had a 12-month anxiety disorder at T_1 and who had no 12-month anxiety disorder T_2 (ie, were remitted at T_2).

This sample consisted of 92 subjects. To account for the longitudinal design of the data, linear mixed models were performed with mental and physical functioning as dependent variables, defining restricted maximum likelihood.[39] First, we examined a model with time only. For MHC, this resulted in a model with a random intercept, a random slope for time T_1, and an independent structure for covariance. For PHC, the same model without random slopes was the most optimal. Following the unadjusted analyses with time as independent variable, we adjusted for sociodemographics and additionally for comorbid mood disorders (when studying MHC) and somatic disorders (when studying PHC). When a scar effect was present after remission, a significant negative effect of time at T_2 would be present compared to the situation at T_0, indicating worse functioning at T_2 compared to T_0. Finally, we examined the presence of a scar effect in specific subgroups (first-incident vs recurrent disorder; mild, moderate, or severe disorder; time of onset within or after 1 year after T_0) by adding an interaction of the subgroup to the model with time and adjusting for age, gender, education, comorbid mood disorder (when the dependent variable was MHC), or any somatic disorder (when studying PHC). Like for the trait analyses, an effect was considered significant if the *P* value was .005 or smaller.

Table 1. Baseline Characteristics of the Subjects Who Developed an Anxiety Disorder Between T_0 and T_1 (the anxiety disorder group) and Healthy Controls, as Used to Examine a Trait Effect[a]

Variable	Anxiety Disorder Group (n = 199)	Healthy Controls (n = 2,826)	Test Statistics χ^2	Test Statistics *P* Value
Age < 35 y	29.2 (58)	20.8 (589)	7.6	.006
Female	71.9 (143)	54.4 (1,538)	22.9	< .001
Low education	35.7 (71)	29.8 (843)	3.0	.082
Comorbid mood disorder at T_0	19.1 (38)	0	546.5	< .001
Any somatic disorder at T_0[b]	46.4 (89)	32.0 (892)	16.7	< .001

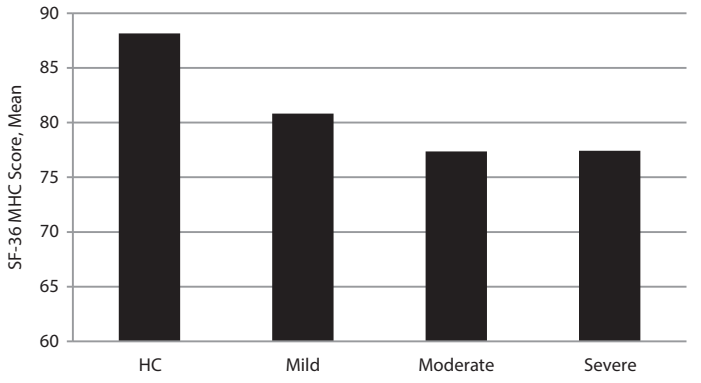
[a]Values shown as % (n).
[b]Data missing for some subjects.
Abbreviations: T_0 = baseline, T_1 = first follow-up.

RESULTS

Trait Effect

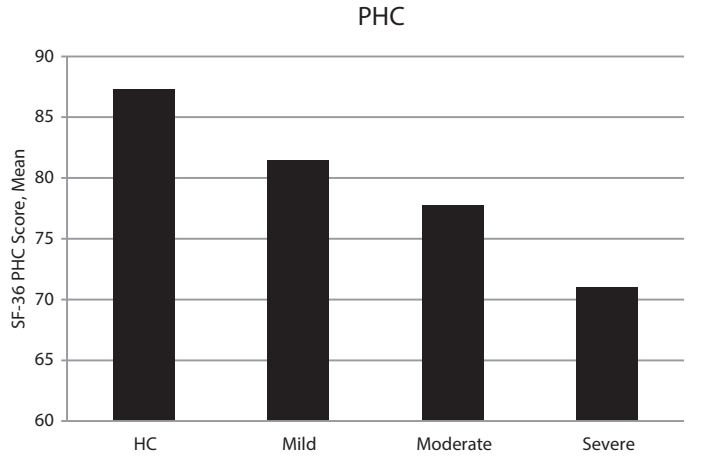
To examine the trait effect, the level of functioning at T_0 was compared between subjects who developed an anxiety disorder at T_1 (the anxiety disorder group) and healthy controls. Baseline characteristics are presented in Table 1. Regression analyses showed that mean (SD) SF-36 mental functioning scores at T_0, ie, before the disorder developed, were significantly lower in the anxiety disorder group as compared to the healthy controls (MHC anxiety disorder group: 76.7 [17.6]; MHC healthy controls: 88.3 [9.9]; $\beta = -11.6$ [SE = 0.78], $P < .001$). Results were similar for physical functioning (PHC incident anxiety disorder group: 75.3 [21.9]; PHC healthy controls: 87.4 [14.9]; $\beta = -12.1$ [SE = 1.14], $P < .001$). Adjusting the analyses for age, gender, education, and mood comorbidity (for MHC) or any somatic disorder (for PHC) did not change these results for MHC ($\beta = -8.51$ [SE = 0.85], $P < .001$) or for PHC ($\beta = -9.55$ [SE

Figure 1. Mean Baseline Score on the Mental Health Component (MHC) of the SF-36 Among Healthy Controls (HCs) and Subjects in 3 Anxiety Disorder Severity Groups at First Follow-Up Controlled for Gender, Age, Education Level, and Comorbid Mood Disorder[a]



[a]Actual values and comparisons were as follows:
Mean (SD): HC: 88.14 (0.20), mild: 80.82 (1.77), moderate: 77.37 (1.47), severe: 77.43 (1.45).
Statistical comparisons: overall: $F_7 = 47.72$, $P < .001$; mild vs HC: $\beta = -7.33$ (SE = 1.78), $P < .001$; moderate vs HC: $\beta = -10.77$ (SE = 1.49), $P < .001$; severe vs HC: $\beta = -10.71$ (SE = 1.47), $P < .001$; moderate vs mild: $\beta = -3.45$ (SE = 2.27), $P = .129$; severe vs mild: $\beta = -3.39$ (SE = 2.24), $P = .131$; severe vs moderate: $\beta = 0.06$ (SE = 1.93), $P = .975$.
Abbreviation: SF-36=Medical Outcomes Study 36-Item Short-Form Health Survey.

Figure 2. Mean Baseline Score on the Physical Health Component (PHC) of the SF-36 Among Healthy Controls (HCs) and Subjects in 3 Anxiety Disorder Severity Groups at First Follow-Up Controlled for Gender, Age, Education Level, and Somatic Disorder[a]



[a]Actual values and comparisons were as follows:
Mean (SD): HC: 87.31 (0.27); mild: 81.48 (1.98); moderate: 77.71 (1.61); severe: 70.97 (1.54).
Statistical comparisons: Overall $F_7 = 110.44$, $P < .001$; mild vs HC: $\beta = -5.84$ (SE = 2.45), $P = .02$; moderate vs HC: $\beta = -9.60$ (SE = 1.91), $P < .001$; severe vs HC: $\beta = -16.34$ (SE = 1.83), $P < .001$; moderate vs mild: $\beta = -3.77$ (SE = 3.08), $P = .221$; severe vs mild: $\beta = -10.51$ (SE = 3.03), $P = .001$; severe vs moderate: $\beta = -6.74$ (SE = 2.61), $P = .010$.
Abbreviation: SF-36=Medical Outcomes Study 36-Item Short-Form Health Survey.

1.06], $P < .001$). Thus, in subjects who developed an anxiety disorder, both mental and physical functioning were already impaired prior to the onset of the anxiety disorder.

Further analyses, dividing the anxiety disorder group into the first-incident subgroup (71%, n = 142) and the recurrent subgroup (29%, n = 57), showed that both MHC and PHC at baseline were significantly lower in both the first-incident and the recurrent subgroup as compared to healthy controls (adjusted analyses, all P values < .001). No significant difference was found between the first-incident and the recurrent subgroup (MHC: $\beta = 1.41$ [SE = 1.66], $P < .394$; PHC: $\beta = 2.69$ [SE = 2.25], $P < .232$; adjusted analyses).

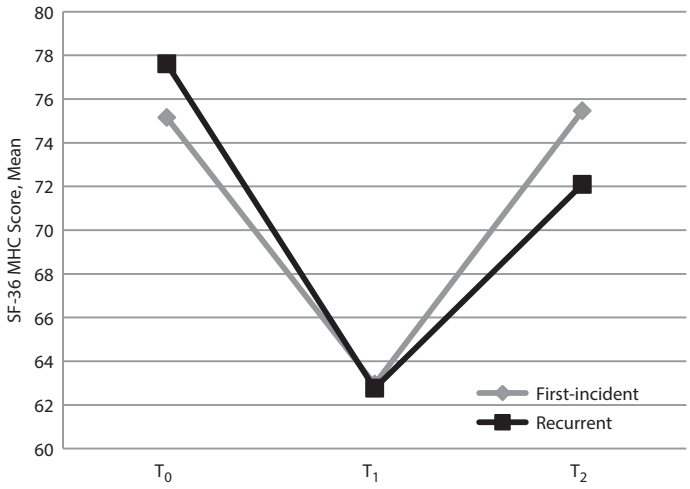
Additionally, we examined whether the severity of the anxiety disorder impacted the results. As mentioned previously, we restricted these analyses to 152 subjects with a 12-month diagnosis at T_1 because disorder severity was assessed only if a disorder was present at T_1. Of our sample, 23% (n = 35) had a mild, 36% (n = 55) had a moderately severe, and 41% (n = 62) had a severe anxiety disorder. In adjusted analyses, both MHC and PHC were significantly lower in all severity groups compared to the healthy controls (MHC: $P < .001$, see Figure 1; PHC: $P = .02$ [for mild] and $P < .001$ [for moderate and severe], see Figure 2). A trend showed that the more severe the anxiety disorder, the lower the functioning prior to disorder onset. Regarding mental functioning, differences between severity subgroups were not significant. By contrast, the mild and moderate subgroups had higher levels of physical functioning compared to the severe subgroup ($P = .001$ and $P = .01$ [trend], respectively). Thus, those who developed the most severe anxiety disorders also had the worst level of physical functioning prior to the onset of the disorder.

Scar Effect

To examine a scar effect, mental and physical functioning at T_0 were compared to levels of functioning at T_2 in the 92 subjects without an anxiety disorder at T_0 who had developed a 12-month anxiety disorder at T_1 and who were remitted again 12 months prior to T_2. The characteristics of this sample are described in Table 2.

The mean (SD) SF-36 mental functioning score was 75.9 (19.2) prior to onset of the anxiety disorder, dropped to 62.9 (22.6) at T_1 when the anxiety disorder was present, and increased to an almost identical level of functioning (74.5 [18.8]) following remission at T_2. Also in the linear mixed models, there appeared not to be a scarring effect with regard to mental functioning; ie, analyses showed no interaction effect with time between T_0 and T_2 ($\beta = -1.40$ [SE = 1.96], $P = .48$ [unadjusted] and $\beta = -1.94$ [SE = 1.93], $P = .32$ [adjusted for gender, age, education, and comorbid mood disorder]). A similar pattern was seen with regard to mean (SD) physical functioning score, which was 73.8 (23.1) at T_0 and 72.1 (23.8) at T_2. Also with respect to physical functioning score, no scarring effect appeared in the linear mixed models ($\beta = -1.70$ [SE = 2.07], $P = .41$ [unadjusted]; $\beta = -0.71$ [SE = 2.06], $P = .73$ [adjusted for gender, age, education, and somatic disorder]).

Figure 3. Mean Scores Over Time on the Mental Health Component (MHC) of the SF-36 for First-Incident Anxiety Disorder Versus Recurrent Anxiety Disorder Adjusted for Gender, Age, Education Level, and Mood Comorbidity[a]



[a]β = –9.23 (SE = 4.22), *P* = .03.
Abbreviations: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey, T_0 = baseline, T_1 = first follow-up, T_2 = second follow-up.

Finally, we examined the presence of a scar effect in specific groups of subjects by adding an interaction with time (first-incident vs recurrent type of disorder) and disorder severity (mild, moderate, severe) to the model. Thus, for example, in studying a scar effect across severity subgroups, we examined whether subgroups differed in the way the level of functioning changed over time. For mental functioning, interaction between time and disorder severity was not significant, indicating that mental scarring did not occur in any of the severity subgroups (results not shown). However, interaction between time and type of incidence disorder (first-incident vs recurrent) showed a trend (*P* = .03) indicating that, in the recurrent subgroup, mental scarring may occur; ie, mental functioning may not return to premorbid levels (see Figure 3). When examining physical functioning, we found no significant interactions between time and type of incident disorder (first-incident vs recurrent) and disorder severity, meaning that physical functioning returned to premorbid levels in all subgroups.

DISCUSSION

Previous clinical studies have found persistent functional limitations in anxiety disorders.[6,11,13,14] These have been labeled as symptoms of an overall anxiety disorder syndrome,[11] or as a psychosocial vulnerability.[13,14] The purpose of our population-based study was to examine whether these limitations reflect a trait effect, a scar effect, or both.

The level of both mental and physical functioning was already significantly impaired in subjects who developed anxiety disorder prior to the onset of the disorder compared to subjects who did not develop a common mental disorder. This effect was most pronounced in those who developed a severe anxiety disorder. To distinguish between a trait effect and a prodromal phase (in which case limitations will be largest in participants who are closest to developing the anxiety disorder), a post hoc analysis was conducted,

Table 2. Baseline Characteristics of the Sample Without an Anxiety Disorder at T_0 Who Developed an Anxiety Disorder at T_1 and That Had Remitted at T_2 (n = 92), as Used to Examine a Scar Effect

Variable	% (n)
Age < 35 y	29.3 (27)
Female	72.8 (67)
High education level	63.0 (58)
Comorbid mood disorder at T_1	40.2 (37)
First incident of disorder	70.7 (65)
Any somatic disorder at T_1	51.1 (47)

Abbreviations: T_0 = baseline, T_1 = first follow-up.

comparing participants with an onset within 1 year after baseline and those with a later onset. This post hoc analysis revealed no significant difference, thereby suggesting that the limited functioning prior to the onset is not simply a prodromal phase but rather a preexisting vulnerability. Our hypothesis regarding the presence of a trait effect in anxiety disorders was thereby confirmed.

As mentioned in the introduction, we hypothesized that scarring would not occur in general. This hypothesis was confirmed. On the basis of the presence of scarring in severe and recurrent disorders like schizophrenia[21] and bipolar disorder,[22,23] and scarring in severe and recurrent forms of MDD,[18] we additionally hypothesized that the occurrence of scarring would depend on the severity and/or recurrence of anxiety disorders, too. This hypothesis was partly confirmed. Severity of anxiety did not have an impact on scarring. However, a trend toward mental scarring was seen in a subgroup with a recurrent anxiety disorder. This finding may suggest that scarring is mainly driven by course, rather than severity.

Our findings further indicate that scarring is present solely in mental domains of functioning. Whether this association is similar for other psychiatric disorders cannot yet be determined, because previous studies assessed functioning in various ways. For example, Ormel et al[18] assessed social disability with the Groningen Social Disability Schedule, including both mentally and physically oriented items. Likewise, studies focusing on schizophrenia used the GAF scores as measurement,[21] and in studies of functioning in bipolar disorder, the focus is on neurocognitive function loss.[22]

It should be noted that other variables might have had an impact on results. For example, negative life events frequently occur prior to the onset of anxiety disorders[40,41] and might have resulted in lower functioning prior to anxiety disorder onset. Likewise, type of treatment or use of antidepressants may influence residual impairment following remission. We examined whether the trait effect and the trend toward scarring in the recurrent subgroup

were driven by negative life events, use of antidepressants, or treatment in mental health care, but adding these variables to the model did not change results.

Likewise, because subthreshold symptoms frequently occur and are associated with limited functioning,[42,43] we examined whether scarring in the recurrent subgroup might be related to higher prevalence of subthreshold symptoms in the recurrent subgroup as compared to the first-incidence group. In this post hoc analysis, presence of subthreshold symptoms was estimated using the K10 questionnaire, which assesses anxiety and depressive symptoms.[44,45] We found no differences in subthreshold symptoms between the first-incident and recurrent subgroups. Therefore, the scar effect could not be explained by subthreshold symptoms.

To our knowledge, this is the first study investigating the origin of functional limitations following remission of anxiety disorders. Other strengths of the study are the use of reliable and valid measures to assess anxiety disorders and level of functioning. A limitation relates to the retrospective, self-reported assessment of functioning. However, because functioning was assessed prior to onset and following remission, it is unlikely that information-processing biases, such as negative interpretations of social events[46,47] or negative memory biases for one's own performance compared to others,[48] are present. In addition, the number of subjects in the severity subgroups was relatively low. Therefore, we cannot rule out the possibility that a larger sample would show a more distinct trait effect for the severe subgroup and possibly also a scar effect, which would be in line with scarring in other severe psychiatric disorders. Finally, because the CIDI does not assess the duration of disorders, impact of duration on regaining level of functioning could not be examined.

Clinical Implications

This study is a first step in understanding how functioning and anxiety are connected. Functional limitations following remission from anxiety disorders largely reflect a trait effect. Given the increased risk for relapse associated with functional limitations, investing in optimizing levels of functioning seems an appropriate goal in treatment, besides symptom reduction. This may be especially true in those with recurrent anxiety disorders. In this subgroup, relapse prevention may decrease scarring, whereas optimizing levels of functioning may prevent relapse. Meeting this goal requires a change in clinical practice, as current treatment mainly focuses on symptom reduction. Further research is needed to assess whether the cycle of chronicity can be broken by an increased focus on relapse prevention and functional outcomes.

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Additional information: The original data set for NEMESIS-2 belongs to the Trimbos Institute, the Netherlands Institute of Mental Health and Addiction (www.trimbos.org). The data on which this manuscript is based are not publicly available. However, data from NEMESIS-2 are available upon request. The Dutch ministry of health financed the data, and the agreement is that these data can be used freely under certain restrictions and always under supervision of the Principal Investigator (PI) of the study. Thus, some access restrictions do apply to the data. The PI of the study is second author of this article (Margreet ten Have, PhD; mhave@trimbos.nl) and can at all times be contacted to request data. At any time, researchers can contact the PI of NEMESIS-2 and submit a research plan describing its background, research questions, variables to be used in the analyses, and an outline of the analyses. If a request for data sharing is approved, a written agreement will be signed stating that the data will be used only for addressing the agreed research questions described and not for other purposes.

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