Chapter **4**

**Trajectories of recovery of
social and physical functioning in
Major Depression, Dysthymic Disorder
and Double Depression:
a 3-year follow-up**

ABSTRACT

Background Depressive disorders have a large impact on psychosocial functioning. Since lower functioning predicts recurrence of a depressive episode, insight into the post-morbid course of psychosocial functioning of persons with different depressive disorders may facilitate recurrence prevention.

Methods Data were derived from NEMESIS, an epidemiologic survey in the adult population in the Netherlands. Respondents, who met the CIDI criteria of Major Depression (MDD; n=102), Dysthymic Disorder (n=66) or Double Depression (n=73) at baseline and recovered during three year follow-up were included; as was a control group without any diagnosis (NoDiag, n=4140). Functioning was assessed using the Groningen Social Disability Schedule (GSDS) and the SF-36 physical health summary-scale. Linear Mixed Models were conducted to compare 3-year trajectories of functioning across depressive groups and with NoDiag group.

Results Compared to NoDiag, all depressed groups were significantly impaired on social and physical functioning. Dysthymic Disorder and Double Depression had a lower level of post-morbid physical functioning compared to MDD (after 1 and 3 years respectively: Dysthymic Disorder: B=-13.8, p=.002 and B=-8.1, p=.09; Double Depression: B=-8.9, p=.03 and B=-9.1, p=.05). Determinants for impaired social functioning (neuroticism) and for impaired physical functioning (age, comorbid somatic disorders and neuroticism) were identified.

Limitations Attrition was higher among persons with a depression. Inclusion of the drop outs would most likely have resulted in stronger associations, since we expect lower functioning among the drop-outs.

Conclusion This study indicates the long-term debilitating effects of psychopathology, even after recovery of depressive disorders. Duration of the index symptoms appears to be associated with impaired functioning, since especially those with Dysthymia (either with or without a MDD) showed slower and less recovery of functioning.

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INTRODUCTION

Depressive disorders have a large impact on both social as well as physical domains of functioning (Coryell et al., 1993; Judd et al., 1996; Rapaport et al., 2005; Wells et al., 1992) similar to or even exceeding the impact noted in common medical illnesses (Buist-Bouwman et al., 2004, 2006; Merikangas et al., 2007; Ormel et al., 1994; Schonfeld et al., 1997; Wells et al., 1989, 1992). The level of functional impairment is positively associated with the severity of depressive disorders (Judd and Akiskal, 2000; Kruijshaar et al., 2003; Ormel et al., 1994, 2004; Rapaport et al., 2005; Spijker et al., 2004a). Additionally, chronicity of the depressive disorder might affect the level of functioning of persons with depressive disorders (Rytsala et al., 2006). However, literature on this issue is not conclusive. Some studies have demonstrated that chronic depressive disorders, such as Dysthymic Disorder and Double Depression, have a larger impact on social and physical functioning than non-chronic depressive disorders (Yang and Dunner, 2001), but others did not (Spijker et al., 2004b).

After remission of the depressive symptoms, social and physical functioning returns to levels found among healthy subjects, although some functional impairment may persist after recovery (Buist-Bouwman et al., 2004; Coryell et al., 1993; Hirschfeld et al., 2002; Judd et al., 2000; Ormel et al., 2004). This postmorbid impaired functioning may be a trait, state or scar effect (Ormel et al., 2004), or a consequence of a so-called "trajectory of recovery", in which recovery of functioning parallels, but lags considerably behind the curve of depressive symptoms recovery (Bijl and Ravelli, 2000a; Mintz et al., 1992). However, long-term follow-up comparisons of post-morbid functioning across different depressive subtypes are lacking. To what extent severity and/or chronicity of the various depressive subtypes predict post-morbid functioning is unclear. In addition, improvement in depressive disorders has been especially associated with improvements in the social domain of functioning, and to a lesser extent in the physical domain (Simon et al., 2005), illustrating the need to differentiate between social and physical domains of functioning.

Since persistence of a lower level of functioning predicts recurrence of a depressive episode, even after the symptoms of depression are alleviated (Faravelli et al., 1986; Judd et al., 2000; Judd and Akiskal, 2000; Solomon et al., 2004; Spijker et al., 2004b), insight into the course of social and physical functioning of persons with depressive disorders, and into the determinants of an impaired recovery of functioning may facilitate recurrence prevention and limit the burden of disease.

Most studies on functional impairment have a cross-sectional study design and focus on outpatients with depressive disorders, in particular non-chronic Major Depressive Disorder, lacking comparison across different depressive subtypes in the general population. In the present paper, we compare the 3-year "recovery trajectories" of social and physical functioning of persons who reach remission of a baseline diagnosis of Major Depressive

Disorder (MDD), pure Dysthymic Disorder, Dysthymic Disorder with a superimposed MDD (Double Depression) and persons without any diagnoses (NoDiag). By comparing both non-chronic and chronic, as assessed by the absence or presence of Dysthymic Disorder, as well as mild and severe depressive disorders, as assessed by the absence or presence of MDD, the interplay between these two factors on functioning can be tested. First, we hypothesized that at baseline, persons with a current chronic and severe depressive disorder (Double Depression) have a lower level of social and physical functioning than persons with a current chronic, but mild depressive disorder (Dysthymic Disorder), who in turn have a lower level of functioning than persons with a current non-chronic, but severe depressive disorder (MDD) (Bijl and Ravelli, 2000a; Wells et al., 1992). Second, we compare the 3-year follow-up of social and physical functioning between persons with depressive disorders and persons without any diagnosis. We hypothesized that post-morbid functioning of all depressive disorders gradually returns to the level of persons without any diagnosis, but some functional impairment, as compared to persons without any diagnosis will prevail (Friedman et al., 1999; Ormel et al., 2004). Furthermore, we hypothesized that the recovery of social and physical functioning of persons with chronic depressive disorders lags behind the recovery of social and physical functioning of persons with MDD (Hays et al., 1995; Rytsala et al., 2006). Third, besides chronicity and severity, other possible determinants of recovery trajectories of social and physical functioning (demographic, clinical and personality characteristics) will be explored.

METHODS

Study sample and depression groups

Data of the current study are derived from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). This is a naturalistic, prospective, epidemiological survey among a representative sample (n=7076) of the general adult (aged 18 to 64 years) population in the Netherlands. Data were gathered in three waves: at baseline in 1996 (T0), after 12-month follow-up (T1, 1997) and after 3 years (T2, 1999). The sampling procedure consisted of a multistage, stratified, random sample. The method of recruitment was extensively described elsewhere (Bijl et al., 1998). Procedures were approved by the ethics committee of the Netherlands Institute of Mental Health and Addiction and informed consent was obtained according to the prevailing Dutch law of 1996. At T0, 7076 (69.7%) respondents could be included. At the T1 and T2 waves, 1458 (20.6%) and 822 (14.6%) respondents respectively were lost to attrition (Bijl et al., 1998). After adjustment for demographic factors, a 12-month disorder at T0 only slightly increased the probability of loss to follow-up between T0 and T1, as well as between T0 and T2 (Graaf et al., 2000a,b).

For the present study, we included NEMESIS respondents with a one-month prevalence of MDD and/or Dysthymia at baseline, based on the Composite International Diagnostic Interview (CIDI), version 1.1 (Smeets and Dingemans, 1993). The CIDI, developed by the

WHO (World Health Organization, 1990), is a structured interview with acceptable reliability and validity (Wittchen, 1994). Organic exclusion rules were used in making diagnoses, and hierarchy-free diagnoses were made to allow for research into comorbid depressive disorders, and hence Double Depression. Persons, who fulfilled the CIDI-criteria of a bipolar disorder, were not included. Since we were interested in the trajectories of social and physical functioning during remission of a depressive disorder, only those depressed persons were included who had achieved remission at follow up, both after one and three years of follow up (n=241). Remission was defined as the absence of a depressive disorder (MDD and Dysthymic Disorder) after one and three years of follow up according to the CIDI (Smeets and Dingemans, 1993). Based on the presence of last-month MDD and Dysthymia diagnoses at baseline, different depressive disorder groups were defined. MDD only (n=102) consisted of those fulfilling a MDD but not a Dysthymic Disorder diagnosis, indicating a non-chronic and severe depressive disorder, whereas Dysthymia only (n=66) consisted of those with a Dysthymic Disorder but not a MDD diagnosis, indicating a mild, but chronic disorder. Double Depression (n=73) was defined as Dysthymia with a comorbid MDD, ignoring the sequence of onset of Dysthymia and MDD, indicating a severe and chronic disorder. A comparison group of healthy controls was selected and consisted of all subjects without a CIDI psychiatric diagnosis at baseline and any of the follow-up waves (n=4140). Attrition rates, adjusted for sociodemographic factors (age, gender, level of education, marital status, number of somatic illnesses), were significantly higher for the depressed groups compared to the group without any diagnosis (No diagnosis as reference, MDD (OR 3.31 [95% CI 1.98-5.55]), Dysthymic Disorder (OR 1.58 [95% CI 0.88-2.84]), Double Depression (OR 1.89 [95% CI 1.22-2.92])). Between depressive disorder subgroups, attrition rates did not differ significantly.

Measurements

Social and physical functioning

At all waves, two domains of functioning were measured: social and physical functioning, using the Groningen Social Disability Schedule (GSDS) and the Short-Form-36 Health Survey-physical health domain, respectively. The Groningen Social Disability Score (GSDS) measures social functioning in different domains of life (or social roles). It has good reliability and validity properties in the Dutch population (De Jong and Van der Lubbe, 1995; Wiersma et al., 1988). At each wave we administered three GSDS subscales, consisting of 21 items in total, covering domains of social role functioning (Cronbach's α=0.63), housekeeping (Cronbach's α=0.69) and leisure time functioning (Cronbach's α=0.80). Total GSDS scores were constructed by summarizing the three scale scores and standardizing the overall score on a scale ranging from 0 to 100. The physical health domain of the Short-Form 36 Health Survey (SF-36) (Ware and Sherbourne, 1992) is a widely applied questionnaire involving 4 subscales and consisting of 21 items, all with sufficient internal reliability in the present study, covering physical functioning (Cronbach's α=0.90), role limitations due to physical

health (Cronbach's α=0.88), bodily pain (Cronbach's α=0.86), and general health (Cronbach's α=0.75). Scoring was performed on a 0-100 scale, with 100 defined as maximum functioning. A total SF-physical health summary score was constructed by adding the four scale scores and dividing by four. Good reliability and validity of this instrument has been shown elsewhere (Aaronson et al., 1998; Burke et al., 1995; McHorney et al., 1993, 1994), and there is no substantial loss of information when summary scales are used (Ware et al., 1995).

Demographic and clinical characteristics

Characteristics of the participants were recorded during the baseline interview. We included the following possible predictors of functioning: Gender, age, level of education, marital status, a comorbid anxiety disorder, number of comorbid somatic disorders, childhood adversity and neuroticism. Age was included as a continuous variable. Level of education was included to assess socio-economic status and dichotomized into low (≤ 10 years of education) and high level (> 10 years of education). Marital status was dichotomized into living with a partner or not. Comorbid anxiety disorder was assessed by means of the CIDI (Smeets and Dingemans, 1993). Last-month diagnoses were applied, covering all anxiety diagnoses as recorded by the CIDI (Panic Disorder (with or without Agoraphobia); Agoraphobia without history of Panic Disorder; Social Phobia; Simple Phobia; Generalized Anxiety Disorder and Obsessive Compulsive Disorder). Somatic health was defined as the number of self-reported somatic disorders out of a 32-item list (Berg and Bos, 1989) that were treated or monitored by a doctor. Childhood adversity was assessed using a structured interview in which respondents were asked to retrospectively recall whether they had experienced emotional neglect, psychological abuse, physical abuse or sexual abuse before the age of 16. Neuroticism was assessed using the Groningen Neuroticism Questionnaire (Ormel, 1983; Ormel et al., 2001; Ormel and Wohlfarth, 1991), a 14-item, 3 point scale with sufficient internal reliability in the present study (Cronbach's α=0.80). An inversed scale was computed, resulting in high scores reflecting high levels of neuroticism.

Statistical analyses

Statistical analyses were undertaken using SPSS version 15 (SPSS, 2006). First, the distribution of the characteristics of participants across the depressive disorder groups and the group with no disorder were compared using two-tailed chi-square statistics (for categorical variables) and one-way-analysis of variance statistics (ANOVA; for continuous variables). Next, Linear Mixed Models (LMM) were used to examine the association of the type of depressive disorder at baseline (no disorder, MDD, Dysthymia, Double Depression) and functioning during three years of follow-up. Mixed Models analyses were applied since this method can handle repeated measures data with correlated measures and non-constant variability. In addition, missing values and unequal time intervals do not hamper analyses in LMM. All variables were entered in the model as fixed factors. The only random

factor entered in the model was the subject. An unstructured covariance structure was used. Dependent variables were the GSDS-total score and SF-physical summary score during three years of follow up (T0, T1, T2). In order to examine whether the depression groups show differential change in functioning over time, we tested an interaction term between depressive disorder group* time. Estimated mean scores (unadjusted and adjusted) were calculated for the GSDS total score and the SF-physical summary scale. Additional analyses were performed to test the impact of the other putative determinants of functioning: gender, age, education, marital status, a comorbid anxiety disorder, number of comorbid somatic disorders, childhood adversity and neuroticism, on the association between depression groups and social and physical functioning, and their interactions with time.

RESULTS

Characteristics
As expected, the depressed groups differed significantly from subjects without any diagnosis (NoDiag) on all baseline characteristics, except for age (Table 1). Across depressive groups, some significant differences were found. Subjects with Double Depression were less educated and reported more comorbid anxiety disorders and a higher level of neuroticism than persons with MDD at T0. In addition, persons with Double Depression reported a higher level of neuroticism than persons with Dysthymic Disorder.

Trajectory of recovery of social functioning
A graphical display of the trajectories of recovery of all depressive disorders, as compared to NoDiag is presented in Figure 1. At baseline, the level of social functioning was lowest for Double Depression (B=-15.2; p<.001) followed by MDD (B=-13.3; p=<.001) and Dysthymia (B=-13.2; p<.001) with NoDiag as the reference category. After one year of follow-up, significant interaction with time was found for all depressive disorder groups, indicating larger improvement in functioning over time as compared to NoDiag (MDD*Time1: t=6.0; p<.001; Dysthymia*Time1: t=2.3, p=.02; Double Depression*Time1: t=2.8; p=.005). Considering the overall 3-year follow up, MDD improved most (MDD*time: t=7.1; p=<.001, see Figure 1) followed by Double Depression (Double Depression*time: t=2.3; p=.02). Persons with Dysthymic Disorder only mildly improved (Dysthymia*time: t=1.9; p=.05). Despite the improvement over time, the level of social functioning of MDD, Dysthymic Disorder and Double Depression remained significantly lower than NoDiag at all waves.

Table 1. Characteristics of persons with no depressive disorder, Major Depressive Disorder (MDD), Dysthymic Disorder and Double Depression at baseline.

		No disorder n=4140	MDD n= 102	Dysthymia n=66	Double Depression n= 73	Statistical analyses			
		%	%	%	%	X^2/ F	Df	p- depressive groups versus NoDiag	p- between groups (presented if significant)
Gender	*% Female*	53.6	68.6	72.7	57.5	X^2= 18.5	3	<.001	
Age (mean ± SD)		42.0 (± 12.4)	40.0 (± 11.6)	43.0 (± 11.3)	42.8 (± 10.5)	F= 1.1	3	0.34	
Education	*% High*	56.0	50.0	36.4	32.9	X^2= 26.5	3	<.001	MDD vs Double Depression: .02
Partner	*% Yes*	74.1	52.0	57.6	50.7	X^2= 52.0	3	<.001	
Comorbid anxiety	*% Yes*	0	52.9	56.1	68.5	X^2= 2537.5	3	<.001	MDD vs Double Depression: .004
No. somatic disorders (mean ± SD)		0.8 (± 1.1)	1.3 (± 2.0)	1.6 (± 1.8)	1.6 (± 1.6)	F= 29.9	3	<.001	
Childhood adversity	*% Yes*	23.0	57.8	60.6	64.4	X^2= 172.6	3	<.001	
Neuroticism (mean ± SD)		60.6 (± 3.0)	70.1 (± 5.9)	70.4 (± 5.7)	73.3 (± 6.1)	F= 813.3	3	<.001	MDD vs Double Depression: 0.001 Dysthymia vs Double Depression: 0.004

Figure 1. Social functioning trajectories over 3 years across depression groups and a no disorder group (n=4381).
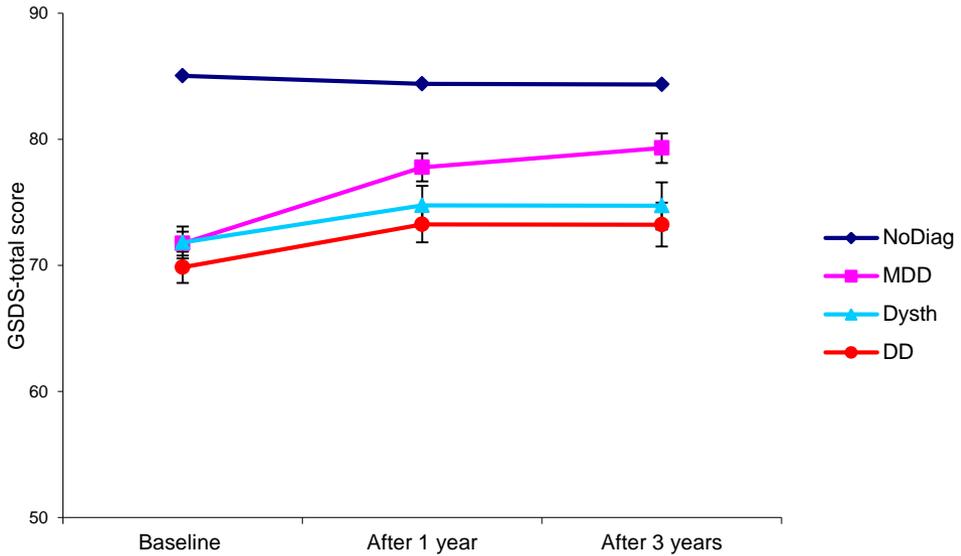
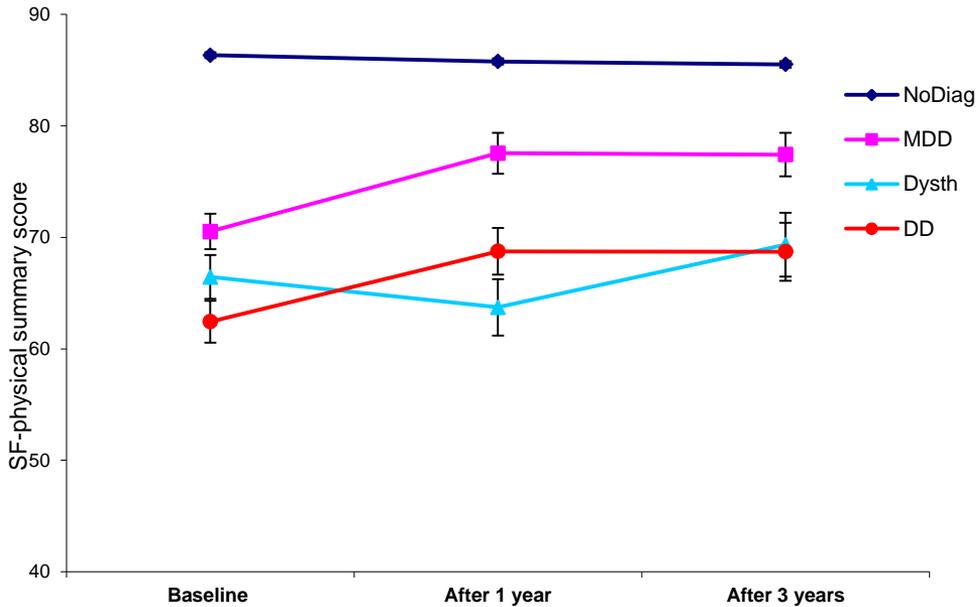|	Estimate	Std. Error	t	Sig.
No disorder	ref	ref		
MDD	-13.29	0.96	-13.88	<.001
Dyst	-13.21	1.27	-10.44	<.001
DD	-15.18	1.25	-12.18	<.001
Time	-0.68	0.18	-3.76	<.001
NoDiaig*Time	ref	ref		
MDD*Time	8.24	1.16	7.09	<.001
Dysth*Time	3.59	1.86	1.93	0.05
DD*Time	4.06	1.76	2.31	0.02

NoDiag= No diagnosis, MDD= Major Depressive Disorder, Dysth= Dysthymic Disorder, DD= Double Depression; All depression groups differed significantly from the no diagnosis group at all waves.

Table 2. 3-Year course trajectories of social functioning across depressive subtypes- with and without adjustment for putative predictors (n=241).

Parameter	Estimate	SE	t	Sig.	Estimate	SE	t	Sig.
Intercept	71.77	1.32	54.54	0.00	71.41	3.90	18.31	0.00
Depression group								
MDD	ref	ref			ref	ref		
Dysthymia	0.07	2.19	0.03	0.97	-0.61	2.06	-0.30	0.77
Double Depression	-1.95	2.17	-0.90	0.37	0.86	2.11	0.41	0.68
Time								
T0	ref	ref			ref	ref		
T0-T1	5.79	1.66	3.49	0.00	6.27	1.63	3.86	0.00
T0-T2	7.33	1.74	4.21	0.00	7.66	1.72	4.44	0.00
Interaction: Depression*Time								
MDD	ref	ref			ref	ref		
Dysthymia*T0	ref	ref			ref	ref		
Dysthymia*T1	-2.74	2.84	-0.96	0.34	-2.55	2.79	-0.91	0.36
Dysthymia*T2	-4.06	3.30	-1.23	0.22	-3.63	3.22	-1.13	0.26
Double Depression*T0	ref	ref			ref	ref		
Double Depression*T1	-2.24	2.72	-0.82	0.41	-3.91	2.72	-1.44	0.15
Double Depression*T2	-3.38	3.16	-1.07	0.29	-4.84	3.11	-1.56	0.12
Covariates								
Female					-0.86	1.64	-0.52	0.60
Age (mean)					0.05	0.07	0.67	0.50
Low education					-2.41	1.59	-1.52	0.13
Partner					1.41	1.45	0.97	0.33
Anxiety disorder					-2.29	1.54	-1.48	0.14
No. somatic illnesses (mean)					-0.23	0.41	-0.57	0.57
Childhood adversity					0.03	1.49	0.02	0.98
Neuroticism (mean)					-0.95	0.16	-5.92	0.00
Interaction								
Neuroticism*Time (T0-T2)					0.40	0.23	1.72	0.01

Comparing depressed subjects at baseline did not yield significant differences in social functioning across MDD/Dysthymia/Double Depression groups (Table 2). The difference between MDD and Dysthymia enlarged over time (after one year: B=-2.7; p=.34; after 3 years: B=-4.0 p=.22), however, without reaching significance. Similarly, the difference between MDD and Double Depression enlarged, both after one year of follow up (Double Depression: B=-4.2; p=.11) and after 3-year follow-up (B=-5.3; p=.08), reaching borderline significance. None of the interactions of depressive disorder*time was significant (Table 2).

Figure 2. Physical functioning trajectories over 3 years across depression groups and a no disorder group (n=4381).

	Estimate	Std. Error	t	Sig.
No disorder	ref	ref		
MDD	-15.83	1.61	-9.83	<.001
Dyst	-19.90	1.99	-9.98	<.001
DD	-23.92	1.90	-12.61	<.001
Time	-0.83	0.28	-3.00	<.001
NoDiag*Time	ref	ref		
MDD*Time	7.74	1.94	4.00	<.001
Dysth*Time	3.72	2.84	1.31	0.19
DD*Time	7.11	2.58	2.75	0.01

Abbreviations: NoDiag= No diagnosis, MDD= Major Depressive Disorder, Dysth= Dysthymic Disorder, DD= Double Depression; All depression groups differed significantly from the no diagnosis group at all waves.

Trajectory of recovery of physical functioning

As shown in Figure 2, at baseline, the level of physical functioning was lowest for Double Depression (B=-23.9; p<.001), followed by Dysthymic Disorder (B=-19.9; p=<.001) and MDD (B=-15.8; p<.001) (NoDiag=reference). After one year of follow-up both MDD (MDD*time: t=4.2; p=<.001) as well as Double Depression (Double Depression*time: t=3.4; p=.001) showed significant interaction with time, indicating larger improvement in functioning over time as compared to NoDiag. Persons with Dysthymia did not show any significant improvement of physical functioning during the first year of follow up. Considering the total of 3-year follow up, both MDD (MDD*time: t=4.0; p=<.001, see Figure 2) as well as Double Depression (Double Depression*time: t=2.8; p=.01) showed significant improvement over

time, whereas Dysthymic Disorder (Dysthymia*time: t=1.3; p=.19) failed to reach a significantly higher level of physical functioning. Despite the larger improvement over time, the level of physical functioning of MDD, Dysthymic Disorder and Double Depression remained significantly lower than NoDiag at all time points.

Comparisons at baseline across depressive disorder subtypes only (n=241), revealed that physical functioning of persons with Double Depression was significantly lower (B=-8.1; p=.02) than that of persons with MDD, persisting after one year (B=-8.9; p=.03), and three years of follow-up (B=-9.1; p=.05). Persons with Dysthymia did not significantly differ in level of physical functioning at baseline (B=-4.1; p=.27), but had a lower level of functioning compared to MDD after one year of follow-up (B=-13.8; p=.002), and after 3 years (Dysthymia: B=-8.1; borderline significant p=.09). The greater difference between Dysthymic Disorder and MDD after one year of follow-up is illustrated in Table 3. We found a significant interaction between Dysthymia*time (B=-9.7; t=-2.3; p=.02) between T0 and T1. Considering the total follow-up period of 3 years, the difference between Dysthymic Disorder en MDD enlarged, but not significantly (Dysthymia*time (T0-T2): B=-4.1; t=-0.9; p=.38).

Table 3. 3-Year course trajectories of physical functioning across depressive subtypes- with and without adjustment for putative predictors (n=241).

Parameter	Estimate	SE	t	Sig.	Estimate	SE	t	Sig.
Intercept	70.51	2.29	30.78	<.001	83.77	5.99	13.99	<.001
Depression group								
Major Depression	ref	ref			ref	ref		
Dystymia	-4.06	3.66	-1.11	0.27	-1.80	3.17	-0.57	0.57
Double Depression	-8.08	3.55	-2.28	0.02	-1.83	3.19	-0.57	0.57
Time:								
T0	ref	ref			ref	ref		
T0-T1	6.92	2.42	2.86	0.00	7.40	2.41	3.07	<.001
T0-T2	6.79	2.60	2.61	0.01	7.41	2.60	2.85	0.01
Interaction: Depression* Time								
MDD	ref	ref			ref	ref		
Dysthymia*T0	ref	ref			ref	ref		
Dysthymia*T0-T1	-9.70	4.14	-2.34	0.02	-9.57	4.07	-2.35	0.02
Dysthymia*T0-T2	-4.05	4.63	-0.87	0.38	-4.31	4.55	-0.95	0.34
Double Depression*T0	ref	ref			ref	Ref		
Double Depression*T0-T1	-0.83	3.67	-0.23	0.82	-2.63	3.75	-0.70	0.48
Double Depression*T0-T2	-1.02	4.35	-0.23	0.82	-2.60	4.31	-0.60	0.55
Female					-0.88	2.45	-0.36	0.72
Age (mean)					-0.22	0.11	-1.96	0.05
Low education					0.77	2.44	0.31	0.75
Partner					2.10	2.28	0.92	0.36
Anxiety dis					-3.70	2.40	-1.55	0.12
Number of somatic illnesses (mean)					-4.43	0.67	-6.63	<.001
Childhood adversity					2.01	2.37	0.85	0.40
Neuroticism (mean)					-1.17	0.24	-4.94	<.001

Possible determinants of social and physical functioning across depressive subtypes

Table 2 and 3 show the estimates of effects of several possible predictors on trajectories of social and physical functioning across depressive subtypes: gender, age, education, marital status, a comorbid anxiety disorder, number of comorbid somatic disorders, childhood adversity and neuroticism. Neuroticism (B=-0.95; p<.001) was the only significant determinant of the 3-year trajectory of social functioning (Table 2). In addition, the interaction between neuroticism*time was significant over three years of follow-up (B=0.4; t=1.7; p=.01). These findings for neuroticism illustrate that subjects with high neuroticism have a generally lower social functioning over time. However, the significant interaction between neuroticism and time with a positive B indicates, that this difference of social functioning between persons with high and neuroticism levels diminishes over time. All other interactions between putative predictors*time were examined, but not significant.

Considering physical functioning, older age (B=-0.2; p=.05), somatic comorbidity (B=-4.4; p<.001) and high neuroticism (B=-1.2; p<.001) were significantly associated with a lower level of physical functioning over 3 years of time (Table 3). No significant time interactions were observed for the putative determinants (all p>.10). After inclusion of these determinants, Double Depression failed to be significantly associated with more physical impairment as compared to MDD (Table 3). The disappearance of this effect appeared to be mainly due to an effect of neuroticism, since the single inclusion of neuroticism- but not the single inclusion of age or somatic comorbidity - already reduced the physical functioning difference between subjects with Double Depression and MDD to non-significance.

DISCUSSION

Our primary aim was to examine differences in the 3-year trajectories of social and physical functioning after remission in a community sample of people with MDD, Dysthymic Disorder or Double Depression, thereby comparing their functioning with persons without any diagnosis. The results clearly indicate the long-term debilitating effects of psychopathology, even after depressive disorders are absent over 3 years of time. Duration of the index symptoms appears to be associated with impaired recovery of functioning, since especially those with Dysthymia (either with or without a superimposed MDD) showed slower and less recovery of functioning.

Studies on functioning comparing different subtypes of depressive disorders are inconclusive. In general, most studies agree that people with a current Double Depression are more impaired than persons with a current Dysthymia or MDD (Goldney and Fisher, 2004; Leader and Klein, 1996; Rapaport et al., 2005), but results on the ranking of Dysthymic Disorder and MDD differ. Some report a higher level of functioning of people with Dysthymia, compared to MDD (Broadhead et al., 1990; Goldney and Fisher, 2004; Judd et al., 2000; Rapaport et al., 2005). Others, however, found higher levels of psychosocial

functioning of MDD as compared to Dysthymia/Double Depression (Bijl and Ravelli, 2000a; Buist-Bouwman et al., 2006; Wells et al., 1992), or equivalent levels of psychosocial functioning between Dysthymic Disorder and (recurrent) MDD (Leader and Klein, 1996; Subodh et al., 2008), which is in accordance with our baseline results.

In addition, we demonstrated the persistence of impaired functioning after recovery of the depressive disorders. Comparisons across depressive subtypes revealed that Dysthymic Disorder and Double Depression improved to a lesser extent than persons with MDD. Even after three years of recovery, the level of functioning remains considerably lower for persons with Dysthymia and Double Depression than that of persons with MDD. To our knowledge, this is the first study that examined a long-term follow-up of functioning during remission of MDD/Dysthymic Disorder/Double Depression in the general population. It was previously shown that after remission of depressive symptoms of subjects with MDD, some functional impairment persisted (Buist-Bouwman et al., 2004; Coryell et al., 1993; Hirschfeld et al., 2002; Judd et al., 2000; Ormel et al., 2004). Furthermore, Friedman et al. (1999) previously showed comparable trajectories of social functioning of outpatients with Dysthymic Disorder and Double Depression after 6-month continuation treatment, suggesting that the MDD component may add little to social impairment and that chronic Dysthymic Disorder is the main determinant of social functioning.

Comparison of trajectories of functioning across subtypes of depressive disorders, varying in level of severity and chronicity, may illustrate the impact of either severity or chronicity on levels of functioning. Our results both at baseline as well as during 3-year follow-up indicate that chronicity may have a larger impact on trajectories of functioning than severity. Literature on this issue is not conclusive. There is some evidence that duration of a depressive episode exceeding 2 years leads to more functional disability (Hays et al., 1995), thus, chronicity is a predictor of the level of functioning (Rytsala et al., 2006; Subodh et al., 2008). However, others did not find an association between duration of depressive disorders and social functioning (Spijker et al., 2004b). In this study among persons with MDD only, Spijker et al. (2004b) found the severity of the depressive disorder and a comorbid anxiety disorder to be the strongest predictors of dysfunctioning. Since incident MDD between T1 and T2 were included, the study population greatly differs from the study population in the present study, which hampers comparisons. However, in a study of Rapaport et al. (2005) both acute as well as chronic depressive disorders were examined. They also found only 1% of the variance explained by duration of the disorder versus 9% by symptom severity.

How could it be explained that more chronic types of depressive disorders are associated with lower functioning and less improvement over time? Part of this effect may be due to residual depressive symptoms, possibly more apparent in persons with chronic depressive disorders, that might alter the level of social and physical functioning (Broadhead et al., 1990; Judd et al., 1996, 2000) and cause a lagging behind in recovery of functioning. In

addition, we found some evidence that chronic types of depression were present among persons with higher neuroticism scores which appeared to be the most important predictor for both poorer physical as well as social functioning over time.

Possible predictors

As mentioned above, we demonstrated that neuroticism predicted impaired recovery of social functioning, while determinants for impaired recovery of physical functioning included age, number of comorbid somatic disorders and neuroticism. Literature on predictors of social and physical functioning, comparing Dysthymia/Double Depression/MDD, is sparse, generally limited to outpatients, mostly limited to brief follow-up periods and lacking comparisons with pure Dysthymic Disorder. Age was previously identified as a predictor of impaired recovery of physical functioning (Klein et al., 2008; Schonfeld et al., 1997). Also, psychiatric as well as somatic comorbidity has been previously found to be associated with functioning (Baune et al., 2007; Bijl and Ravelli, 2000b; Klein et al., 2008; McDermut et al., 2001; Rytsala et al., 2006; Spijker et al., 2004b). For somatic comorbidity this is in line with our findings, since the number of comorbid somatic illnesses was associated with a poorer physical functioning trajectory over time. However, we did not find an effect of comorbid anxiety disorder on functioning trajectories in our study, maybe because a potential effect of this variable was supplanted by effects of neuroticism and somatic comorbidity, as shown before (McDermut et al., 2001, Baune et al., 2007). Finally, neuroticism proved to be a significant predictor of both social functioning, as well as physical functioning. Seivewright et al. (2004) showed, that personality pathology significantly predicted a lower level of social functioning after 12 years. Since social dysfunction is a major manifestation of personality disorder, Seivewright et al. (2004) questioned, whether a long-term lower level of social functioning after treatment of depressive disorders, might be a consequence of personality rather than mental state pathology.

Strengths and limitations

A strength of this study is its prospective design of three years of follow-up with evaluations blind to diagnosis at baseline. In addition, the study is population-based which allows generalization to the general population. This study also has some limitations. First, we were faced with attrition. Whereas the numbers included at baseline were considerable, attrition limited the power to detect small effects at follow up. Attrition was more likely among the depressed, when compared to persons without depression. Inclusion of the dropouts would most likely have resulted in stronger associations, since we expect lower social or physical functioning among the drop-outs. Attrition across the three depressive subtypes was non-differential. Therefore, the results comparing depressive subtypes are unlikely to be influenced by attrition. Also, our study lacks pre-morbid assessment of functioning. Consequently, we cannot differentiate whether a post-morbid lower level of social and physical functioning might be a state, trait or scar effect, or a consequence of a so-called

"trajectory of recovery". Finally, we have no information on comorbid personality disorder, which has been shown to be associated to functioning in depressive disorders (Kennedy et al., 2007; Klein, Shankman and Rose, 2008; Mulder, 2002). Since the prevalence of personality disorders is higher among the early-onset Dysthymics (Klein et al., 1988), the age of onset might be of importance for the level of functioning as well. However, age of onset is difficult to assess (Simon and Korff, 1995). Due to the high risk of recall bias and the limited power we have for such subgroup analyses, the impact of early versus late-onset Dysthymic Disorder was not examined.

To conclude, this study provides a clear indication that depression can have long-term debilitating effects, persisting even after remission of the depressive disorder: social and physical functioning is substantially lower even after depressive disorders are absent over three years of time. Furthermore, chronicity of symptoms appears to be associated with impaired recovery of functioning to a greater extent than severity of symptoms, since especially those with Dysthymia (either with or without a superimposed MDD) showed slower and less complete recovery of functioning. Specific attention should be addressed in clinical practice to social and physical functioning of persons with chronic depressive disorders. As Solomon et al. (2004) demonstrated, psychosocial impairment (of euthymic patients) is a risk factor for recurrence of a depressive disorder. In addition, attention should be paid to neuroticism as a significant predictor of both social and physical functioning. Thus, treatment focused on depressive symptoms only will not suffice to reduce risk of recurrence and enhance functioning of depressed individuals. In accordance with Rapaport et al. (2005), we conclude that successful treatment must go beyond ameliorating signs and symptoms to address the broader issue of restoration of health.

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