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Title: Syndromes versus symptoms : towards validation of a dimensional approach of depression and anxiety
Date: 2012-10-04

Chapter 6:

Change in Symptom Dimensions of Depression and Anxiety in Response to Life Events

Abstract

Background: Results on the association between life-events and depression and anxiety have been inconsistent. This could be due to heterogeneity of DSM diagnoses, which does not allow the detection of symptom-specific effects of life events. Therefore, the current longitudinal study was aimed to close in on more specific associations between different types of life-events and change in different symptom dimensions over time.

Methods: Data from 2267 participants with or without psychiatric diagnoses were included. Dimensions of the tripartite model (general distress, anhedonic depression and anxious arousal) were assessed at three times (baseline, 1-year, 2-year), to model change over time. The positive and negative life-events that occurred between the measurement points were assessed retrospectively at 1-year and 2-year follow-up. The data were analysed with linear mixed models to adjust for repeated measures and several covariates.

Results: Negative life-events (e.g. financial problems, getting ill or wounded) were associated with increased general distress and anxious arousal. Positive life events (e.g. making new friends, going on holiday) were associated with decreased anhedonic depression. These associations were independent for both types of life-events and persisted when adjusted for demographic covariates and DSM-based course-trajectories.

Conclusions: Different types of life-events lead to specific symptomatology. Negative life events affect both general distress and anxiety symptomatology, whereas positive life events specifically affected depression-specific symptomatology. These findings illustrated the added value of using specific symptom dimensions in etiological research.

Submitted as:

Wardenaar, KJ, Van Veen, T, Giltay, EJ, Zitman, FG , Penninx, BWJH. Change in Symptom Dimensions of Depression and Anxiety in Response to Life Events

6.1 Introduction

Many authors have suggested a relationship between life events and the onset (e.g. Kendler et al., 1995; 2000; Kessler, 1997) and course of depression (e.g. Mundt et al., 2000; Friis et al., 2002) and anxiety (e.g. Lteif & Mavissakalian, 1985; Roy-Byrne, 1986; Blazer et al., 1987). Unfortunately, findings on the association between life events and psychopathology have been inconsistent with studies that reported varying (reviewed by Mundt et al., 2000) or no associations between life events and depression and/or anxiety (e.g. Spinhoven et al., 2010). These inconsistent results could be explained by the use of different samples, definitions, instruments, and analyses across studies (reviewed by Mundt et al., 2000; Kessler, 1997). However, the heterogeneity and arbitrary boundaries of the used DSM-diagnoses are also likely contributors to the inconsistent results found so far (Widiger & Samuel, 2005). From this perspective, it could pay off to use better-specified and more homogeneous outcome measures in life event research.

Several studies have shown that different types of life-events are associated with specific types of symptoms. Keller and Nesse (2005; 2006) showed that in healthy participants, social loss (e.g. death of a loved one, romantic breakup) led to increased crying, desire for social support, and decreased appetite, and that chronic stress and failure led to increased feelings of guilt, hopelessness, and fatigue. In a later longitudinal study in participants with previous depressive symptoms, Keller et al (2007) showed that social loss was followed by symptom patterns with increased sadness, anhedonia and decreased appetite, and that chronic stress and failure were followed by symptom patterns with increased fatigue and hypersomnia. Although they did not include all types of life events (e.g. positive events) and symptoms (e.g. anxiety symptoms), the results of these studies strongly suggest that life events affect specific symptoms rather than complete syndromes.

A good way to define and measure symptoms more specifically, is through the assessment of symptom dimensions with reliable psychometric instruments. Dimensions cover distinct symptom domains and follow a severity-continuum from healthy to severely pathological (Goldberg, 2000). In addition to being homogeneous, dimensions conveniently circumvent the DSM-related problems of comorbidity and arbitrary dichotomous boundaries between ill and non-ill (Widiger & Clark, 2000; Widiger & Samuel, 2005). Moreover, dimensions provide more statistical power in etiological research because they are continuous, which makes them more sensitive to variation between and within patients (MacCallum et al., 2005).

The *tripartite model* is a well-known dimensional approach, which assumes the existence of three basic symptom dimensions of depressive and anxiety symptomatology (Clark & Watson, 1991). The dimension of *general distress* covers symptoms of psychological distress (e.g. feeling guilty, worry), which are common in both depression and anxiety. The more specific dimension of *anhedonic depression* covers symptoms that involve decreased positive affect and energy, which are specific features of a depressed state. The dimension of *anxious arousal* covers symptoms of somatic hyperarousal, which

are specific for anxiety, and panic disorder in particular. The tripartite model has been thoroughly validated through the years; studies have shown its structure to be valid (e.g. Watson et al., 1995; Keogh & Reidy, 2000) and its dimensions to be associated with different biological mechanisms, such as the stress system (Wardenaar et al., 2011) and metabolic factors (Luppino et al., 2010). In line with this, studies in healthy subjects have shown the tripartite dimensions to be associated with different life events: negative life-events were associated with increased general distress and positive life events with increased positive affect/decreased anhedonic depression (e.g. Reich *&* Zautra, 1981; Zautra & Reich, 1988; Suh et al., 1996). However, these studies were limited to healthy subjects and did not include anxious arousal. Therefore, it is still unclear to what extent the tripartite dimensions can help to clarify the link between life events and symptomatology when looking at a broader spectrum of symptoms. Also, previous studies have been cross-sectional, comparing dimensional scores between those that did and those that did not experience a certain event. However, to optimally benefit from the dimensions' sensitivity to change, a prospective design should be used to evaluate the effects of life-events on the development of symptoms *within* individuals. Previous work has shown that such change is clearly detected in response to daily hassles on a day-to-day 'micro' timescale (e.g. Peeters et al., 2003; Gable et al., 2000; Suls et al., 1998). So far, this approach has not been used to investigate the associations between major life-events and symptom-dimensions on a 'macro' time-scale of months or years.

A final issue is that studies should ideally address whether the employed dimensions actually help to uncover associations that would go undetected when only using categorical measures of psychopathology. Research could do this by checking whether dimensional results hold when adjusted for DSM-based clinical features. Likewise, analyses of longitudinal course of dimensional scores could be adjusted for DSM-based course trajectories to see if and how much variation in symptomatology is uniquely captured by the dimensions.

We aimed to investigate the associations between, on the one hand, negative and positive life-events, and on the other hand, change on the tripartite dimensions in a large group of subjects from the Netherlands Study of Depression and Anxiety (NESDA; n=2981). We used a 2-year longitudinal design with three measurements (baseline, 1 year, 2 years) and we analysed the data with multilevel regression analyses to account for repeated measures. These analyses were adjusted for demographic covariates, but also for DSM-based course trajectories to evaluate whether the dimensions captured unique temporal variation in symptomatology.

6.2 Methods

Participants

Participants came from the NESDA study, a large longitudinal study to investigate the course of depressive and anxiety disorders (N=2981), who were recruited from

community, primary care and specialized mental health care organizations. At baseline, the mean age was 41.9 years (range 18-65), there were 1002 men and 1979 women, and 2329 participants had a lifetime diagnosis of major depressive disorder (MDD) and/or an anxiety disorder. Six hundred fifty two participants had no lifetime psychiatric diagnosis. Exclusion criteria were not being fluent in Dutch and a primary diagnosis of psychotic, obsessive-compulsive, bipolar or severe addiction disorder because these latter low prevalent disorders would largely affect the course trajectories in NESDA. Detailed objectives and rationales of NESDA can be found elsewhere (Penninx et al., 2008). The Ethical Review Boards of all participating universities approved the research protocol. All participants signed informed consent.

All participants were seen for a baseline assessment (T0), which consisted of a face-to-face structured psychiatric interview by a trained research-assistant, administration of self-report questionnaires, biological measurements and a blood-draw. After 1 year (T1), all participants were sent a booklet of self-report questionnaires to complete at home and return by post. Two years after baseline (T2), participants were assessed again in a face-to face session, similar to the one at baseline. The used dimensional scores were collected at T0, T1 and T2 and all participants were included, who provided all dimensional scores on these time-points and information about life-event occurrence (independent variable) for at least one of the two covered years. In total, 2267 participants (76.0%) provided sufficient data to be included in the study. The included participants were older ($t=-5.8$; $p<0.001$), had more years of education ($t=-7.5$; $p<0.001$), and were less probable to be male ($\chi^2=5.58$; $p=0.02$) than excluded subjects.

Study design

The study design is illustrated in Figure 6.1. To investigate if change on symptom-dimensions was associated with the occurrence of life-events, change in dimensional score between T0 and T1 was associated with life-events between T0 and T1 and change between T1 and T2 was associated with life-events between T1 and T2 and T0 and T1. By clustering repeated measurements within persons in LMM analyses, an effect-estimation (β) could be calculated, while accounting for interdependence between repeated measures. To evaluate whether the dimensions actually captured unique specific symptom variation in response to life events, very strict multivariable adjustment was used: all variation that was also explained by DSM-based course-trajectory variables (confounding) and their interactions with life events (effect-modification), was covaried out.

The main analyses were done with negative and positive life events clustered in two respective variables. Additional exploratory analyses were done to investigate the patterns of more specific effects of individual life events.

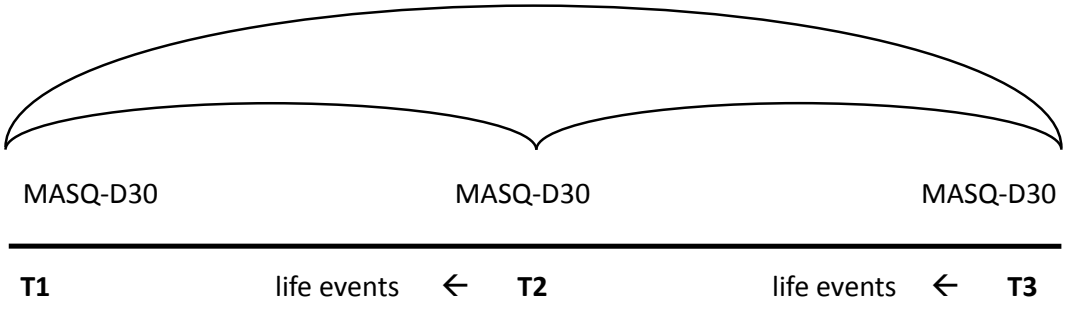

Figure 6.1: the used study design: change in the dimensions of the Dutch 30-item adaptation of the Mood and Anxiety Symptoms Questionnaire (MASQ-D30) was modelled over 2 years. Life events that occurred in the meantime were assessed retrospectively at T1 and T2.

Instruments

Dimensions: MASQ-D30

To measure the tripartite dimensions at T0, T1 and T2, the 30-item Dutch adaptation of the Mood and Anxiety Symptoms Questionnaire: the MASQ-D30 was used (Wardenaar et al., 2010; original MASQ by Watson et al., 1995a, 1995b). On the MASQ-D30, participants are asked to rate to what extent in the past week they have experienced "feelings, sensations, problems and experiences that people sometimes have" on a 5-point scale, with 1 being "not at all" and 5 being "extremely". The MASQ-D30 consists of three 10-item subscales: 'general distress', 'anhedonic depression' and 'anxious arousal'. The anhedonic depression scale items are reverse-keyed and are rescored before subscale computation. The MASQ-D30 scales have been shown to have adequate psychometric characteristics (Wardenaar et al., 2010).

Life-events

To assess the occurrence of negative life-events between respectively T0 and T1 and T1 and T2, the List of Threatening Events Questionnaire (LTE-Q; Brugha et al., 1985) was (retrospectively) administered at T1 and T2. The LTE-Q has been shown to have good test–retest reliability, high agreement between participant and informant ratings and good agreement with interview-based ratings (Brugha and Cragg, 1990). Examples of the assessed negative life events were: 'financial problems', 'the death of a close friend or family-member', and 'getting fired'. Positive life-events were also assessed at T1 and T2 with an additional list of seven positive life-events. Examples of the assessed positive life events were: 'making new friends', 'getting a new job or an important promotion', and 'finding a new partner'. For each listed event, participants were asked to indicate if it

happened in the period before the assessment and - if yes – when the event occurred or started (in case of long-lasting events). The complete lists of assessed individual life events are displayed in Figure 6.2. Positive and negative life-events were clustered to investigate the effects of the *occurrence* of any (yes/no) and the *number* of negative or positive life-events. As outlined above, the individual life events were also used in additional analyses.

Course-trajectory variables

The DSM-based course-trajectory variables were computed on the basis of two data-sources. At To and T2, the presence of DSM-IV diagnoses (MDD, Dysthymia, Panic disorder, Social Phobia, GAD, and Agoraphobia) was established with the Composite Interview Diagnostic Instrument (CIDI, WHO version 2.1). The organic exclusion rules were used and diagnoses were hierarchy-free. If at T2 participants met the criteria for any diagnosis since T0, the Life Chart Interview (LCI) was also administered to assess the course of this disorder. The presence (yes/no) of symptoms was evaluated for each month during follow-up by use of a calendar method (Lyketsos et al., 1994). Participants rated the symptom-severity for each symptomatic month on a 5-point scale (no/minimal, mild, moderate, severe, very severe). Symptomatology was only considered to be present if at least mildly severe. Remission was considered present after at least 3 consecutive months without symptoms.

The CIDI and LCI data were combined to define three course-trajectory groups: (a) the *stable healthy* group (no disorder between T0 and T2), (b) the *stable chronic* group (persistent disorder between T0 and T2), and (c) the *unstable course* group (onset of a new disorder/remission from a disorder/remission and recurrence of a disorder). Membership of each group (0=no, 1=yes) was used as a dummy variable in the analyses.

Statistical Analyses

Both the dependent variables (dimensions) and the independent variables (life events) were standardized to enable effect-size comparisons across different event types and dimensions. Several LMM analyses were conducted, each with a MASQ-D30 scale as dependent variable and one of the investigated life-event-variables as independent variable. 'Time' was used as a repeated measures factor in all analyses and an *unstructured* covariance structure was used to account for the dependence between repeated measures. The T0 value of the MASQ-D30 dimension under investigation was always added as a covariate to model all dimensional change across T0, T1 and T2. The main analyses were run with two different independent variables: between change on dimensions and (1) the *occurrence* of any negative or positive life-event, and between dimensions and (2) the *number* of negative and/or positive life-events. The analyses were adjusted for several covariates. Age and gender were added as covariates in Model 1 to adjust for potential confounding and to increase the general precision of model-estimations. In model 2, the course-group membership dummies and their interactions

with life events (e.g. positive life event occurrence*stable chronic) were added to covary out all dimensional variation that was explained by the course-trajectory groups. Additional exploratory LMM analyses, each with an individual life event as independent variable and one of the dimensions as dependent variable, were done to explore the patterns of effects of the individual life-events on symptomatology. All analyses were done with SPSS 17.0 and $p<0.05$ was taken to indicate statistical significance.

6.3 Results

Demographic and psychiatric characteristics

The sample characteristics are listed in Table 6.1. In the complete sample, there were 1531 (67.5%) women and the mean age at baseline was 42.6 years (SD=13.1). Of the group, 949 (41.9%) had a stable healthy course, 431 (19.0%) had a stable chronic course, and 887 (39.1%) had an unstable course between T0 and T2. Anhedonic depression and anxious arousal were only moderately correlated ($\rho=0.43$), in line with their distinct symptom coverage. General distress was moderate-strongly correlated with anhedonic depression ($\rho=0.60$) and anxious arousal ($\rho=0.61$), in line with its general role in the tripartite model.

The occurrence of life events

The results of the LMM analyses of the association between the occurrence of any (1,0) negative or positive life-event and the MASQ-D30 scores are shown in Table 6.2. In model 1, negative life-event occurrence was associated with increased general distress ($\beta=0.19$) and with increased anxious arousal ($\beta=0.12$). Negative life-events were not associated with change in anhedonic depression. The significant effects both increased after additional adjustment for course trajectories in model 2. Positive life-event occurrence was most strongly associated with decreases in anhedonic depression ($\beta=-0.22$), but also with anxious arousal ($\beta=-0.18$), and general distress ($\beta=-0.15$). When adjusted for course-trajectories in model 2, the effect on anhedonic depression was much less decreased ($\Delta\beta=0.01$ [4.5%]), compared to general distress ($\Delta\beta=0.04$ [26.7%]) and anxious arousal ($\Delta\beta=0.06$ [33.3%]).

These results indicated that general distress and anxious arousal showed the strongest and most consistent increase in reaction to the occurrence of a negative life event, and that anhedonic depression consistently decreased in reaction to the occurrence of a positive life event.

Table 6.1: Baseline descriptive characteristics of the used study samples

N	2267
Mean Age at baseline (SD)	42.6 (13.1)
Number of women (%)	1531 (67.5%)
Mean years of education (SD)	12.4 (3.2)
MASQ-D30 scores, mean (SD)	
General Distress	19.8 (8.4)
Anhedonic Depression	33.2 (9.6)
Anxious Arousal	15.5 (5.8)
DSM-IV diagnoses	
No disorder	1240 (54.7%)
Depressive disorders	225 (9.9%)
Anxiety disorders	418 (18.4%)
Depression and Anxiety	384 (16.9%)
Course-trajectory groups	
Stable Healthy	949 (41.9%)
Stable Chronic	431 (19.0%)
Unstable course	887 (39.1%)

MASQ-D30 = Dutch short adaptation of the Mood and Anxiety Symptoms Questionnaire; DSM-IV= Diagnostic and Statistical Manual of Mental Disorders Fourth Edition

Table 6.2: Multivariate longitudinal Linear Mixed Models analyses of the change in the tripartite model dimensions in reaction to the occurrence any life-event

N=2267	Model	General Distress	Anhedonic Depression	Anxious Arousal
		β (p-value)	β (p-value)	β (p-value)
Negative life event	Model 1	0.19 (<0.001)	0.05 (0.12)	0.12 (<0.001)
(yes/no)	Model 2	0.20 (<0.001)	0.01 (0.84)	0.18 (<0.001)
Positive life event	Model 1	-0.15 (0.001)	-0.22 (<0.001)	-0.18 (<0.001)
(yes/no)	Model 2	-0.11 (0.04)	-0.21 (<0.001)	-0.12 (0.03)

Data based on Linear Mixed Models analyses: an unstructured covariance matrix was used to account for repeated measures

Model 1: adjusted for age, gender and MASQ scale-score at T1.

Model 2: additional variables: stable chronic (1,0); stable healthy course (1,0) unstable course (1,0), and six interactions between the course variables and life event variables.

Table 6.3: Multivariate longitudinal Linear Mixed Models analyses of the change in the tripartite model dimensions in reaction to the number of life-events

N=2267		General Distress β (p-value)	Anhedonic Depression β (p-value)	Anxious Arousal β (p-value)
Number of Negative life events	Model 1	0.11 (<0.001)	0.05 (<0.001)	0.08 (<0.001)
	Model 2	0.11 (<0.001)	0.03 (0.07)	0.10 (<0.001)
Number of Positive life events	Model 1	-0.06 (<0.001)	-0.12 (<0.001)	-0.05 (<0.001)
	Model 2	-0.04 (0.05)	-0.11 (<0.001)	-0.04 (0.10)

Data based on Linear Mixed Models analyses: an unstructured covariance matrix was used to account for repeated measures
Model 1: adjusted for age, gender and MASQ scale-score at T1.
Model 2: additional variables: stable chronic (1,0); stable healthy course (1,0) unstable course (1,0), and six interactions between the course variables and life event variables.

The number of life events

The results of the LMM analyses of the association between the number of negative and positive life events and MASQ-D30 scores are shown in Table 6.3. In model 1, the number of negative life-events was associated with increased anhedonic depression (β=0.05), but more strongly with general distress (β=0.11) and anxious arousal (β=0.08). When adjusted for course trajectories in model 2, the associations remained significant and unchanged with general distress (Δβ=0) and increased with anxious arousal (Δβ=0.2). The association with anhedonic depression was no longer significant in model 2. The number of positive life-events was associated with general distress (β=-0.06) and Anxious Arousal (β =-0.05), but most strongly with anhedonic depression (β=-0.12). When adjusted for the course trajectories in model 2, the associations with general distress and anxious arousal decreased and were no longer significant (p=0.05-0.10). The association with anhedonic depression only decreased with 8.3% (Δβ=0.01).

These results indicated that general distress and anxious arousal were consistently associated with the number of negative life events, and that anhedonic depression was associated with the number of positive life events.

Individual life-events

The associations of the individual life-events with each of the tripartite dimensions are illustrated in Figure 6.2. The results showed that most life events had effects on one or

more dimensions. Only four events were not associated with any dimension (e.g. 'contact with police or justice system' and 'completion of education').

Figure 6.2 clearly shows that negative life events were primarily associated with general distress and/or anxious arousal. 'Financial problems', 'being seriously ill or wounded' and 'becoming unemployed' led to increases in all dimensions, but strongest in general distress. This indicated that events with a broad and long-lasting impact on quality of life had a general effect on symptomatology. 'Death of a parent, child, brother or sister' and 'death of a friend or other family member' specifically led to increased general distress, 'Getting fired' led to increased anxious arousal, and 'a serious problem with a friend, family member or neighbour', 'the ending of a friendship with a friend, family member or neighbour' and 'a close family member getting ill or wounded' led to increases on both dimensions. Only 'separation from a partner' was associated with increased general distress and anhedonic depression. These results indicated that general distress was mainly affected by events that involved social loss. Figure 6.2 clearly illustrates that positive life events had most effect on anhedonic depression. 'Making new friends' and 'going on holiday' led to decreases on all dimensions, but most strongly on anhedonic depression. 'Meeting a new partner', 'being better off financially', and 'a new job or promotion' specifically decreased anhedonic depression.

6.4 Discussion

The current longitudinal study investigated the association between life-events and change on the dimensions of the tripartite model over a 2-year period. The results showed that different types of life-events led to change in different symptom dimensions. Negative life-events led to increases in general distress and anxious arousal and positive life-events led to a decrease in anhedonic depression. These associations were not affected by the adjustment for (confounding and effect-modification by) DSM-based course trajectories, indicating that the dimensions captured unique symptom variation in response to life events. Additional analyses of the individual life events showed that some life events had larger effects than others. Several high-impact events (e.g. 'financial problems', 'being seriously ill or wounded') led to increases on all dimensions. However, most negative life events (e.g. 'death of a parent, child, brother or sister') primarily led to increases in general distress and/or anxious arousal. Positive life events (e.g. 'making new friends') primarily led to decreased anhedonic depression. Taken together, these findings indicated that dimensions can be used to detect specific effects of life events on psychiatric symptomatology.

The current results had several interesting implications. The findings of consistent effects of negative and positive life-events on respectively general distress and anhedonic depression, was in line with previous research in healthy subjects (e.g. Reich & Zautra, 1981; Zautra & Reich, 1988; Suh et al., 1996). The present findings suggested that the specificity of the effects of negative and positive life events to different symptom-dimensions is a phenomenon that is generalizable across both healthy and diseased

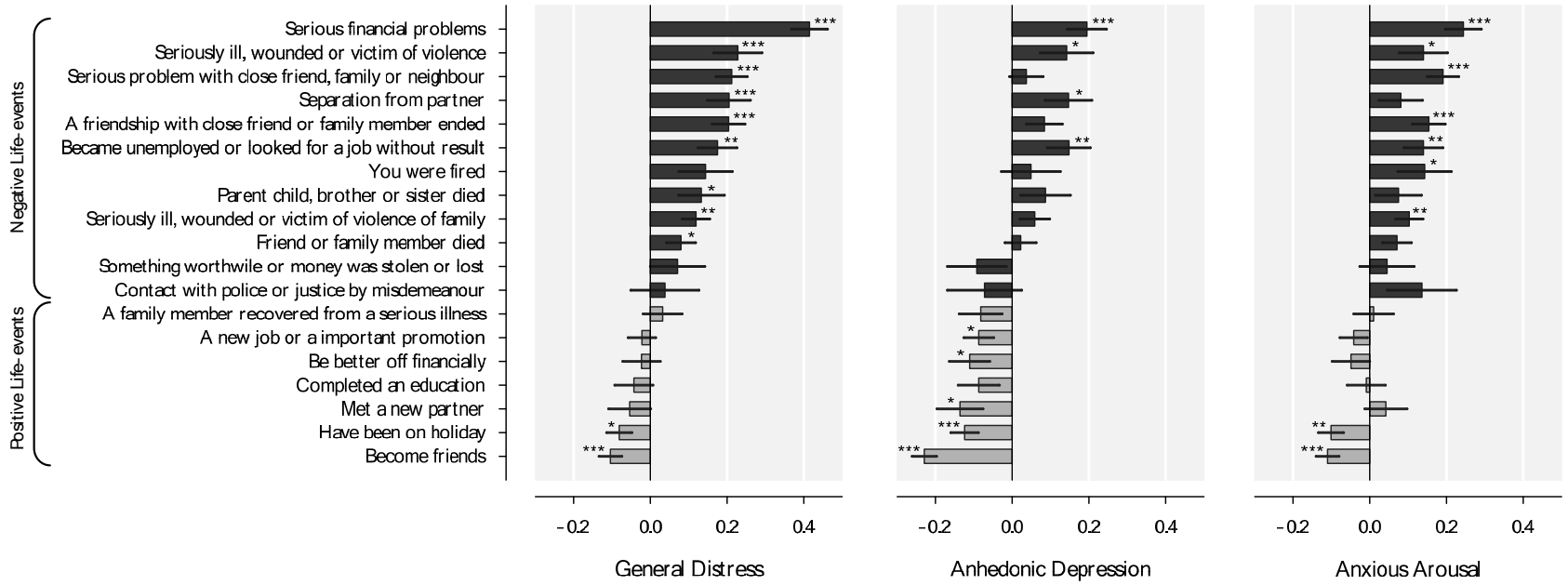

Figure 6.2: β 's (on x-axis) and standard errors for the associations between individual negative and positive life-events (on y-axis) and change on the three dimensions of the tripartite model over time (T1, T2 and T3) in a large group of subjects with or without depression and/or anxiety (n=2267). Results based on Linear Mixed Models analyses with an unstructured covariance matrix to account for repeated measures. All associations adjusted for age, gender, MASQ scale-score at T1 and time (as repeated measures factor).

*) p<0.05; **) p<0.01; ***) p<0.001

individuals. Also, the results were largely in line with the expectation of the tripartite model that the dimensions of general distress and anhedonic depression represent separate constructs with separate etiology. In line with their previously reported moderate interrelatedness (e.g. Wardenaar et al., 2010), some life events (e.g. 'serious financial problems', 'being seriously ill or wounded' or 'making new friends') were found to significantly affect both general distress and anhedonic depression. However, in all cases the effects of these events were still stronger on one of the two dimensions. Thus, on the one hand, these results indicated that some etiological mechanisms are shared between the dimensions (based on significance alone). On the other hand, the results also showed that there is still differentiation between the dimensions (based on effect-sizes), supporting the validity of the tripartite model assumptions.

Change in anxious arousal was primarily associated with negative life-events, although the effects were slightly smaller than for general distress. In addition, analyses of the individual events showed anxious arousal was associated with several negative life events and specifically with 'being fired' and 'becoming unemployed'. Although not previously investigated in a similar fashion, these findings were in line with the idea that negative life events play a role in the onset of anxiety and panic disorders in particular (Klauke et al., 2010). The above described findings that anhedonic depression changed in response to positive life events is also in line with previous work, which showed that positive life events predicted future depressive disorders and do not predict anxiety disorders (Spinhoven et al., in press).

The current results illustrate the ability of dimensions to detect temporal variations in mental state in reaction to external triggers. Even within groups of patients with a supposedly stable course (e.g. chronic over 2 years), there was notable variation in dimensional scores. The pattern of symptoms could differ across persons but the development of each symptom dimension could also change within each person over time. All this variation is not captured by categorical classifications and likely to reflect the complex effects of many etiological mechanisms. In the current study, part of the variation turned out to be explained by the occurrence of particular types of life-events. This was in line with previous work on a much smaller time-scale, which found that emotional responsivity to particular daily hassles was also captured very effectively with repeated dimensional assessments (Peeters et al., 2003; Gable et al., 2000; Suls et al., 1998). Expanding this previous work, our results indicate that dimensions can be used in a comparable fashion to detect emotional reactivity across a much larger time-span.

The effects of life events on change in symptom dimensions were only minimally affected by the inclusion of DSM-based course trajectories and their interactions with life events. This indicated that the dimensions picked up life event-induced changes in mental state that were not also explained by the more traditionally defined course trajectories. The fact that dimensions are specific and continuous probably made them sensitive to

specific effects of life-events that cannot be picked up by changes in heterogeneous syndrome classifications. The reason that life-events have often been observed not to cause the onset of full-fledged depression might be due to the fact that all individuals, irrespective of diagnosis, react differently to environmental stimuli. These differences in emotional reactivity might reflect the widely observed variation in susceptibility to depression in reaction to life-events (e.g. Kessler, 1997). The mechanisms underlying this variation are still unclear, but might involve coping mechanisms (Billings & Moos, 1981; Kraaij et al., 2003), the amount and quality of social support (Cohen & Wills, 1985) but also genetic predisposition (Wichers et al., 2007) and early life adversity (Heim & Nemeroff, 2001).

Different life events were found to be associated with different dimensions. As described above, the most consistent differential associations were found between negative and positive life event types. However, the additional analyses of the individual life events also provided some further hints about more event-specific effects. For instance, life events that lead to deterioration on all dimensions seemed to mainly deal with the loss of aspects like good health and a steady income, which are first requirements for a good quality of life. Events that specifically affected general distress all involved some amount of social loss, ranging from 'losing a friend' to 'the death of a close family member'. Although we should be careful not to overinterpret these explorative results, which involved a large number of statistical tests, the observed associations at least indicate that it is likely that specific types of psychopathology can be linked to specific types of life events, in line with previous findings (Keller et al., 2007; Keller & Nesse, 2005; 2006).

Although the current study had several strong characteristics, including large sample-size, a longitudinal approach, sophisticated statistical analyses and the possibility to look at both patients and healthy participants, some study-limitations should be kept in mind. First, the results apply to a mixed group of healthy persons and psychiatric outpatients, but cannot be directly generalized to more severely affected inpatients. Second, only three dimensions were used as outcome variables, whereas in reality much more relevant symptom-dimensions will exist (e.g. Den Hollander-Gijsman et al., 2011). Third, the LMM analyses of the individual events could not be used to account for clustering of events because this resulted in an overly complex (19 independent variables, without covariates) and unstable model. Fourth, it is known that pre-existent psychopathology increases the chance of life-event occurrence, which often leads to an overestimation of the causal effect of life-events that precede measured psychopathology (e.g. Kessler, 1997). Although we adjusted for the severity of baseline symptomatology in our longitudinal analyses, it is possible that the incidence of certain events was associated with preexistent psychopathology not included in our models. This should be kept in mind when interpreting our results. Future studies could investigate the mediating roles of protective factors (e.g. coping, social support) and susceptibility factors (e.g. genetic predisposition) in the association between life-events and symptoms over time.

In conclusion, the current study showed that dimensions capture life-event induced changes in mood/emotionality. Moreover, the results indicated that these changes transcended the traditional DSM-based course-trajectory distinctions and might thus be useful as alternative or additional outcome characteristic in the etiological research of psychopathology.