

Danger and loss events and the incidence of anxiety and depressive disorders: a prospective-longitudinal community study of adolescents and young adults

E. Asselmann^{1,2*}, H.-U. Wittchen^{1,3}, R. Lieb^{3,4}, M. Höfler¹ and K. Beesdo-Baum^{1,2}

¹Institute of Clinical Psychology and Psychotherapy, Technische Universität Dresden, Germany

²Behavioral Epidemiology, Technische Universität Dresden, Germany

³Max Planck Institute of Psychiatry, Munich, Germany

⁴Department of Psychology, Division of Clinical Psychology and Epidemiology, University of Basel, Switzerland

Background. There are inconclusive findings regarding whether danger and loss events differentially predict the onset of anxiety and depression.

Method. A community sample of adolescents and young adults ($n=2304$, age 14–24 years at baseline) was prospectively followed up in up to four assessments over 10 years. Incident anxiety and depressive disorders were assessed at each wave using the DSM-IV/M-CIDI. Life events (including danger, loss and respectively mixed events) were assessed at baseline using the Munich Event List (MEL). Logistic regressions were used to reveal associations between event types at baseline and incident disorders at follow-up.

Results. Loss events merely predicted incident ‘pure’ depression [odds ratio (OR) 2.4 per standard deviation, 95% confidence interval (CI) 1.5–3.9, $p<0.001$] whereas danger events predicted incident ‘pure’ anxiety (OR 2.3, 95% CI 1.1–4.6, $p=0.023$) and ‘pure’ depression (OR 2.5, 95% CI 1.7–3.5, $p<0.001$). Mixed events predicted incident ‘pure’ anxiety (OR 2.9, 95% CI 1.5–5.7, $p=0.002$), ‘pure’ depression (OR 2.4, 95% CI 1.6–3.4, $p<0.001$) and their co-morbidity (OR 3.6, 95% CI 1.8–7.0, $p<0.001$).

Conclusions. Our results provide further evidence for differential effects of danger, loss and respectively mixed events on incident anxiety, depression and their co-morbidity. Since most loss events referred to death/separation from significant others, particularly interpersonal loss appears to be highly specific in predicting depression.

Received 18 October 2013; Revised 14 April 2014; Accepted 25 April 2014; First published online 5 June 2014

Key words: Anxiety, danger, depression, epidemiology, loss, prospective-longitudinal, psychopathology, stressful life events.

Introduction

Although anxiety and depressive disorders have been shown to be associated with stressful life events (Newman & Bland, 1994; Kessler, 1997; Kendler *et al.* 1998, 1999; Gillespie *et al.* 2005; Hammen, 2011), few studies have examined whether both disorders are associated with different types of events. In their pioneering work, Finlay-Jones & Brown (1981) hypothesized that depressive disorders arise specifically from loss events whereas anxiety disorders arise specifically from danger events. According to these authors, loss events typically refer to events including death or separation from a valued person, in addition to loss of health, jobs, career opportunities or material

possessions. By contrast, danger events typically refer to events that have the potential to trigger a specific future crisis. Although the extent of a loss event’s unpleasantness is immediately evident, the extent of a danger event’s unpleasantness is initially uncertain as it may or may not entail specific negative consequences. This suggests that exposure to loss events may primarily trigger grief or depression whereas exposure to danger/threat events may primarily trigger fear or anxiety.

Finlay-Jones & Brown (1981) investigated 164 women attending a general practitioner (GP) in London and found that, consistent with their hypotheses, the report of a recent severe loss was associated with the onset of depression whereas the report of a recent severe danger was associated with the onset of anxiety. In addition, more cases of depression than of anxiety reported a severe loss event whereas more cases of anxiety than of depression reported a severe danger event. However, the link between danger and anxiety was only specific within 3 months before

* Address for correspondence: E. Asselmann, Dipl.-Psych., Institute of Clinical Psychology and Psychotherapy, Behavioral Epidemiology, Technische Universität Dresden, Chemnitz Str. 45, 01187 Dresden, Germany.
(Email: eva.asselmann@tu-dresden.de)

onset, and both danger and loss events were associated with the onset of co-morbid depression and anxiety. Eley & Stevenson (2000) came to similar conclusions by showing that loss events were linked to depression but not anxiety whereas threat events were linked to anxiety but not depression. Kendler *et al.* (2003) found that 'pure' anxiety was predicted by danger and loss whereas 'pure' depression and co-morbid anxiety and depression were predicted by loss and humiliation.

However, these findings were partially inconclusive and marked by methodological difficulties (e.g. selective samples and retrospective designs), which impede the generalization of findings and inferences on differential effects of event types (Kraemer *et al.* 1997). Moreover, previous studies were mostly based on principles of the Life Events and Difficulties Schedule (LEDS; Brown & Harris, 1989) and additional studies using alternative life event measures might be useful to clarify whether danger and loss events are linked differently to anxiety and depression. Resolving this question would contribute to an improved understanding of etiological similarities and differences between anxiety and depression (Brown *et al.* 1993; Roy *et al.* 1995; Kendler, 1996; Watson, 2005; Beesdo *et al.* 2010) and help to identify high-risk groups for targeted preventive interventions. Given that especially frequent and severe stressful life events were found to be linked to psychopathology (Kessler, 1997; Kendler *et al.* 1998), we strived to further examine whether associations of danger and loss events with anxiety and depression increase with higher number and severity of event types.

Aims and hypotheses

In the current study we aimed to examine prospective longitudinal associations between different life event types and subsequent onset of anxiety and depressive disorders in a representative community sample of adolescents and young adults. We hypothesized that loss events would specifically predict incident depression, danger events would specifically predict incident anxiety, and respectively mixed events would specifically predict incident co-morbid anxiety and depression. A higher number and severity of danger, loss and mixed events should increase the hypothesized associations between event types and psychopathology.

Method

Sample

Data came from the Early Developmental Stages of Psychopathology Study (EDSP), a 10-year prospective-longitudinal study with one baseline (T0, 1995,

$n=3021$, response rate 70.8%) and three follow-up investigations (T1, 1996–1997, $n=1228$, response rate 88.0%; T2, 1998–1999, $n=2548$, response rate 84.3%; T3, 2003, $n=2210$, response rate 73.2%). The sample was drawn randomly from the Munich area (Germany), participants were aged 14–24 years at baseline and 21–34 years at last follow-up. As the EDSP focuses on early developmental stages of psychopathology, 14–15-year-olds were sampled at twice the probability of individuals aged 16–21 years, and 22–24-year-olds were sampled at half this probability. Details on sampling and sample weights have been reported previously (Wittchen *et al.* 1998b; Lieb *et al.* 2000). The EDSP has been approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (No: EK-13811). All participants aged ≥ 18 years provided written informed consent; for respondents younger than 18 years, parental consent was provided.

Because the current study focused on incident anxiety and depression as the diagnostic outcome, the present analyses are based on a subsample of individuals with no baseline anxiety and/or depressive disorder, who participated in at least one follow-up assessment ($n=2304$). Cases with anxiety and/or depression at baseline ($n=542$; 19.6%) were excluded. Sample characteristics are presented in Table 1.

Diagnostic assessment

Diagnostic information was assessed repeatedly using the lifetime (baseline) and interval version (follow-up assessments) of the Computer-Assisted Personal Interview (CAPI) version of the Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI; Wittchen & Pfister, 1997). The M-CIDI is an updated version of the World Health Organization's CIDI version 1.2 (WHO, 1990) with additional questions to cover DSM-IV and ICD-10 criteria. The M-CIDI can be used to assess symptoms, syndromes and diagnoses of 48 mental disorders along with additional information on onset, duration, and clinical and psychosocial severity. Detailed descriptions of psychometric properties have been presented elsewhere (Reed *et al.* 1998; Wittchen *et al.* 1998a).

The current study focused on follow-up incidences of depression (comprising major depressive disorder and dysthymia) and anxiety (comprising social phobia, panic disorder, agoraphobia and generalized anxiety disorder, GAD) (see Table 1). For social phobia, the impairment criterion was only applied to participants aged ≥ 18 years (Wittchen *et al.* 1999). Specific phobias were disregarded because of the early age of onset, which had occurred mostly prior to baseline (Beesdo *et al.* 2010). Obsessive-compulsive disorder,

Table 1. Sample characteristics of the total sample, males and females

| Sample characteristics | Sample | | | Associations with sex ^b | |
|--|----------------|----------------|------------------|------------------------------------|----------------------|
| | Total (n=2304) | Males (n=1259) | Females (n=1045) | OR (95% CI) | p |
| Age (years) | | | | | |
| Mean (s.d.) | 19.33 (3.33) | 19.35 (3.34) | 19.31 (3.31) | 1.0 (1.0–1.0) | 0.759 |
| Education, n (%) | | | | | |
| Eighth grade | 309 (12.5) | 202 (14.8) | 107 (9.9) | | |
| Tenth grade | 551 (23.3) | 270 (20.7) | 281 (26.3) | 1.9 (1.4–2.6) | < 0.001 ^c |
| High school | 1379 (61.7) | 752 (61.8) | 627 (61.6) | 1.5 (1.1–2.0) | 0.007 ^c |
| Other | 65 (2.5) | 35 (2.7) | 30 (2.3) | 1.3 (0.7–2.3) | 0.441 ^c |
| Any loss event, n (%) | | | | | |
| No | 1954 (84.5) | 1079 (85.4) | 875 (83.5) | | |
| Yes | 350 (15.5) | 180 (14.6) | 170 (16.5) | 1.2 (0.9–1.5) | 0.268 |
| Any danger event, n (%) | | | | | |
| No | 1652 (72.3) | 914 (72.8) | 738 (71.7) | | |
| Yes | 652 (27.8) | 345 (27.2) | 307 (28.3) | 1.1 (0.9–1.3) | 0.601 |
| Any mixed event, n (%) | | | | | |
| No | 2086 (89.4) | 1125 (88.8) | 961 (91.2) | | |
| Yes | 218 (10.6) | 134 (12.2) | 84 (8.8) | 0.7 (0.5–1.0) | 0.023 |
| Number of event types among those with any danger/loss/mixed event, mean (s.d.) | | | | | |
| Loss events | 1.12 (0.37) | 1.14 (0.40) | 1.11 (0.35) | 0.8 (0.4–1.6) | 0.545 |
| Danger events | 1.38 (0.71) | 1.37 (0.74) | 1.40 (0.68) | 1.1 (0.8–1.3) | 0.695 |
| Mixed events | 1.16 (0.45) | 1.15 (0.38) | 1.18 (0.55) | 1.2 (0.6–2.2) | 0.629 |
| Incident anxiety disorder, n (%) | | | | | |
| No | 2175 (94.4) | 1210 (96.2) | 965 (93.1) | | |
| Yes | 129 (5.6) | 49 (3.8) | 80 (6.9) | 1.9 (1.2–2.8) | 0.003 |
| Incident depressive disorder, n (%) | | | | | |
| No | 1947 (85.1) | 1103 (88.1) | 844 (81.6) | | |
| Yes | 357 (14.9) | 156 (11.9) | 201 (18.4) | 1.7 (1.3–2.2) | <0.001 |
| Years between loss event and incident anxiety disorder among those with loss event ^d | | | | | |
| Mean (s.d.) | 1.33 (1.87) | 0.50 (0.75) | 1.78 (2.15) | 1.7 (1.0–2.9) | 0.055 |
| Range | 0–5 | 0–2 | 0–5 | | |
| Years between loss event and incident depressive disorder among those with loss event ^d | | | | | |
| Mean (s.d.) | 2.80 (2.68) | 3.16 (2.80) | 2.63 (2.63) | 0.9 (0.8–1.1) | 0.455 |
| Range | 0–10 | 0–8 | 0–10 | | |
| Years between danger event and incident anxiety disorder among those with danger event ^d | | | | | |
| Mean (s.d.) | 1.72 (2.37) | 1.03 (1.81) | 1.99 (2.53) | 1.2 (0.9–1.7) | 0.209 |
| Range | 0–8 | 0–5 | 0–8 | | |
| Years between danger event and incident depressive disorder among those with danger event ^d | | | | | |
| Mean (s.d.) | 2.82 (2.71) | 3.43 (2.61) | 2.43 (2.72) | 0.9 (0.8–1.0) | 0.059 |
| Range | 0–9 | 0–9 | 0–9 | | |
| Years between mixed event and incident anxiety disorder among those with mixed event ^d | | | | | |
| Mean (s.d.) | 1.84 (2.42) | 1.93 (2.44) | 1.75 (2.49) | 1.0 (0.7–1.4) | 0.852 |
| Range | 0–8 | 0–8 | 0–8 | | |
| Years between mixed event and incident depressive disorder among those with mixed event ^d | | | | | |
| Mean (s.d.) | 3.13 (3.06) | 3.44 (3.35) | 2.73 (2.70) | 0.9 (0.7–1.2) | 0.488 |
| Range | 0–10 | 0–10 | 0–7 | | |

OR, odds ratio; CI, confidence interval; s.d., standard deviation.

^a Unweighted number of participants (weighted percentages, means and standard deviations).

^b 0= male, 1= female.

^c Reference group: eighth grade.

^d Slightly smaller numbers of participants because of missing age of onset information.

post-traumatic stress disorder and bipolar disorder were disregarded because of inconsistent findings in structural models (Cox *et al.* 2002; Kessler *et al.* 2005; Watson, 2005; Slade & Watson, 2006).

Assessment of life events

Life events were assessed at baseline using the Munich Event List (MEL; Maier-Diewald *et al.* 1983), a questionnaire-like procedure for the assessment of positive and negative short-term events and chronic conditions in 11 areas of life. The MEL contains 83 items (74 specific event categories and nine open categories) that ask about the occurrence of specific life events within a particular time interval. In the EDSP, participants were asked to indicate the presence of each life event in yearly intervals from 1995 to 1999, the year of interview. Detailed descriptions and psychometric properties of the MEL have been presented previously (Wittchen *et al.* 1989; Friis *et al.* 2002).

For the present study, 21 psychologists rated each MEL event category on the dimensions danger and loss. This is different from the rating procedure for danger and loss events used by Finlay-Jones & Brown (1981). Our expert rating differs conceptually from the original rating procedure because no contextual information was collected or was available to our raters. Raters were instructed to mark event categories as loss if they referred to death or separation of a valued person, loss of physical health or loss of jobs, career opportunities or material possessions[†]. Subsequently, raters were asked to rate the severity of event categories marked as loss on a scale from 1 (little loss) to 6 (extreme loss). Raters were instructed to mark event categories as danger if they were likely to trigger specific future problems. To prevent raters from marking all event categories judged as loss additionally as danger (because a loss event may entail an emotional crisis for the affected individual), raters were instructed to not mark event categories as danger if the respective event was merely likely to trigger an emotional crisis because of its loss character. Subsequently, raters were asked to indicate the severity of event categories marked as danger on a scale from 1 (little danger) to 6 (extreme danger) by judging how severe the most likely future problem would be. Each event category was rated on both dimensions. Inter-rater reliability was 0.86 for loss ratings and 0.71 for danger ratings.

In a second step, each event category was classified as loss, danger or mixed event category type. To be consistent with previous studies (Finlay-Jones &

Brown, 1981; Eley & Stevenson, 2000; Kendler *et al.* 2003), event categories scoring low on both dimensions (mean rating score < 2.5 on both loss and danger) were excluded and only event categories with mean rating scores of 2.5 or higher on at least one dimension were considered. Paired *t* tests were conducted to reveal whether ratings on both dimensions for individual event categories differed from each other [95% confidence interval (CI)]. Event categories with significantly differing means on both dimensions were classified as loss or danger event types whereas event categories not differing on both dimensions were classified as mixed event types. That is, danger, loss and mixed event types were mutually exclusive and no event category could be classified as more than one event type. Table 2 presents event categories classified as loss, danger and respectively mixed event types along with their mean severity scores. For 'pure' loss event types and 'pure' danger event types, the mean loss rating score or mean danger rating score was used to indicate severity, whereas for mixed event types, the mean of both loss and danger rating score was used. To determine the test-retest reliability of danger, loss and mixed event types, a 1-year follow-up rating was conducted among a subsample of the original raters (*n*=15). Test-retest reliability was 0.71 for loss, 0.65 for danger and 0.61 for mixed event types.

The current analyses considered three binary variables (any loss event, any danger event and any mixed event) and six dimensional variables (number of loss events, number of danger events and number of mixed events along with weighted number of loss events, weighted number of danger events and weighted number of mixed events) (see Table 1). The variables weighted number of loss, danger or mixed event consider number and severity of event types (each event category was weighted with its main event score of the expert rating). Consistent with Finlay-Jones & Brown (1981) and Eley & Stevenson (2000), information on the year prior to baseline was used for the current work.

Statistical analyses

The software package Stata version 12.1 (StataCorp, 2011) was used for all analyses. Data [percentages, odds ratios (ORs)] are weighted to match the original distribution of the sampling frame; frequencies are unweighted.

Analyses refer to associations (ORs) between life event types during the year prior to baseline and incident anxiety and depression at follow-up (cumulated information from T1, T2 and T3). Only participants with no lifetime history of anxiety or depression at

[†] The notes appear after the main text.

Table 2. Outline of all MEL event categories classified as danger, loss or mixed event types

| No. | Original MEL no. | Event type | Mean event score |
|----------------------|------------------|--|------------------|
| <i>Loss events</i> | | | |
| 1 | 7 | You were not able to move to an intended higher school or did not get a desired place at the university/vocational school | 2.55 |
| 2 | 20 | A long friendship (at least 3 months) ended | 3.45 |
| 3 | 29 | You (or your partner) finished/discontinued the relationship (that lasted for at least 3 months) | 3.70 |
| 4 | 31 | You divorced from your partner | 4.20 |
| 5 | 50 | Your partner (husband/wife) died | 5.50 |
| 6 | 51 | Your child died | 5.80 |
| 7 | 52 | Your mother/father died | 5.00 |
| 8 | 53 | A close friend or relative you had a close relationship and frequent contact with died | 4.95 |
| <i>Danger events</i> | | | |
| 1 | 11 | You had serious conflicts/tensions with your parents for a longer period of time (living, school, university, training, friends, not felt understood) | 2.90 |
| 2 | 15 | You had serious conflicts/tensions with relatives living with you for a longer period of time (at least 3 months) | 2.90 |
| 3 | 16 | Your parents had serious conflicts for a longer period of time (at least 3 months) that you were suffering from | 2.80 |
| 4 | 17 | You had serious conflicts/tensions with your siblings for a longer period of time (e.g. feeling of disadvantage) | 2.50 |
| 5 | 21 | You did not have any close friend you could share personal problems with for a longer period of time | 2.75 |
| 6 | 24 | You were burdened with difficulties with your friends for a longer period of time (at least 3 months) | 2.70 |
| 7 | 42 | You/your partner gave birth to a mentally or physically disabled child | 3.90 |
| 8 | 47 | You were heavily burdened by problems/conflicts with your child/children for a longer period of time (at least 3 months) (e.g. education, school) | 3.20 |
| 9 | 65 | You had serious tensions/conflicts with your colleagues/superiors at your workplace for a longer period of time (at least 3 months) | 2.70 |
| 10 | 74 | You had great financial difficulties for a longer period of time (at least 3 months) (e.g. insufficient pocket money, income too low, repayment of debts) | 3.60 |
| 11 | 78 | You were burdened with your living conditions for a longer period of time (at least 1 year) | 2.65 |
| 12 | 87 | A close relative (child, partner, parent, sibling) had to stay in hospital because of a very serious physical or mental illness or an accident | 3.55 |
| 13 | 89 | A close relative (child, partner, parent, sibling) received medical treatment for a longer period of time (at least 3 months) because of a very serious physical or mental illness | 2.95 |
| 14 | 90 | The care of a close relative (child, partner, parent, sibling) required much of your time | 3.15 |
| <i>Mixed events</i> | | | |
| 1 | 4 | You canceled a training scheme or failed a final examination (apprenticeship examination, high school entrance examination, high school, university) | 3.10 |
| 2 | 14 | Your parents divorced | 2.53 |
| 3 | 33 | You were living separately from your partner for a while because of partnership conflicts (at least 3 months) | 2.50 |
| 4 | 35 | You found out that your partner had a second sexual relationship (is cheating on you) | 2.70 |
| 5 | 43 | You/your partner had a stillbirth | 3.88 |
| 6 | 44 | You/your partner had to undergo a pregnancy termination | 3.48 |
| 7 | 46 | You had to separate from your child (at least 1 year or permanently) (e.g. because of illness or divorce) | 3.75 |
| 8 | 54 | You lost/quit your job | 3.58 |
| 9 | 59 | You were demoted in your job or suffered career failure | 2.78 |
| 10 | 62 | You were unemployed for at least 3 months | 2.75 |
| 11 | 63 | You were disabled to work (for at least 3 months) (e.g. because of illness) | 2.50 |
| 12 | 73 | Your financial situation worsened substantially (e.g. job change, change of profession, financial demotion, commercial failure) | 2.85 |
| 13 | 86 | You had to stay in hospital because of a very serious physical illness or an accident | 3.63 |
| 14 | 88 | You received medical treatment because of a very serious, enduring (at least 3 months) physical illness | 3.05 |

MEL, Munich Event List.

Table 3. Associations between type of event and follow-up incidence of anxiety or depression (n=2304)

| Type of event | Incidence of anxiety disorder | | | | Incidence of depressive disorder | | | |
|---------------|-------------------------------|-------------|---------------|--------|----------------------------------|-------------|---------------|--------|
| | No (n=2175) | Yes (n=129) | OR (95% CI) | p | No (n=1947) | Yes (n=357) | OR (95% CI) | p |
| Loss event | | | | | | | | |
| No | 1848 (84.6) | 106 (82.3) | | | 1680 (86.0) | 274 (76.1) | | |
| Yes | 327 (15.4) | 23 (17.7) | 1.2 (0.7–1.9) | 0.553 | 267 (14.0) | 83 (23.9) | 1.9 (1.4–2.6) | <0.001 |
| Danger event | | | | | | | | |
| No | 1574 (72.8) | 78 (63.1) | | | 1439 (74.7) | 213 (58.0) | | |
| Yes | 601 (27.2) | 51 (36.9) | 1.6 (1.1–2.3) | 0.028 | 508 (25.3) | 144 (42.0) | 2.1 (1.7–2.8) | <0.001 |
| Mixed event | | | | | | | | |
| No | 1985 (90.1) | 101 (77.3) | | | 1771 (90.0) | 315 (86.0) | | |
| Yes | 190 (9.9) | 28 (22.7) | 2.8 (1.7–4.6) | <0.001 | 176 (10.0) | 42 (14.0) | 1.5 (1.0–2.3) | 0.029 |

OR, Odds ratio; CI, confidence interval.

^aUnweighted number of participants (weighted percentages, means and standard deviations).

Simple logistic regressions with any loss, danger or mixed event as predictors, adjusted for sex and age.

baseline and at least one follow-up assessment (n=2304) were included into analyses.

First, associations between any event types (any loss event, any danger event and any mixed event) and incident anxiety and depression were tested using simple logistic regressions. In addition, we graphically assessed intervals between event types at baseline and incident disorders at follow-up. Whenever age of reported onset at follow-up was lower than age at baseline, age of onset was recoded to age of baseline.

Second, analyses were repeated using numbers of events types (number of loss events, number of danger events and number of mixed events) and weighted numbers of event types (weighted number of loss events, weighted number of danger events and weighted number of mixed events) as predictors. To assess whether (weighted) numbers of event types were non-monotonically related to incident disorders, outcomes were regressed on both the linear and the squared term of (weighted) numbers (because this is sensitive for identifying non-linear associations).

Third, to assess whether the hypothesized associations between event types and anxiety/depression were specific, multinomial logistic regressions were fit using the following mutually exclusive predictor and outcome groups: predictor group: (0) no danger, loss or mixed event, (1) 'pure' loss event (excludes cases with danger or mixed events), (2) 'pure' danger event (excludes cases with loss or mixed events), (3) loss/danger/mixed event (includes cases with mixed events or more than one event type); outcome group: (0) no anxiety and no depression (no incident anxiety disorder and no incident depressive disorder at follow-up), (1) anxiety but no depression

(incident anxiety disorder but no incident depressive disorder at follow-up; that is 'pure' anxiety), (2) depression but no anxiety (incident depressive disorder but no incident anxiety disorder at follow-up; that is 'pure' depression), (3) anxiety and depression (incident anxiety disorder and incident depressive disorder at follow-up; that is co-morbid anxiety and depression).

Scores for any event types, numbers of event types and weighted numbers of event types were standardized (mean=0, standard deviation=1). All analyses were adjusted for sex and age (age at last completed assessment).

Ethical standards

The authors assert that all procedures contributing to this work have been approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (No. EK-13811) and comply with the Helsinki Declaration of 1975, as revised in 2013.

Results

Associations between event types and incident anxiety and depression

Table 3 presents associations between any event types and incident anxiety and depression: any loss event predicted incident depression only (OR 1.9), any danger event predicted incident anxiety (OR 1.6) and depression (OR 2.1), and any mixed event predicted incident anxiety (OR 2.8) and depression (OR 1.5).

Figure 1 shows time intervals between any event types at baseline and incident disorders at follow-up.

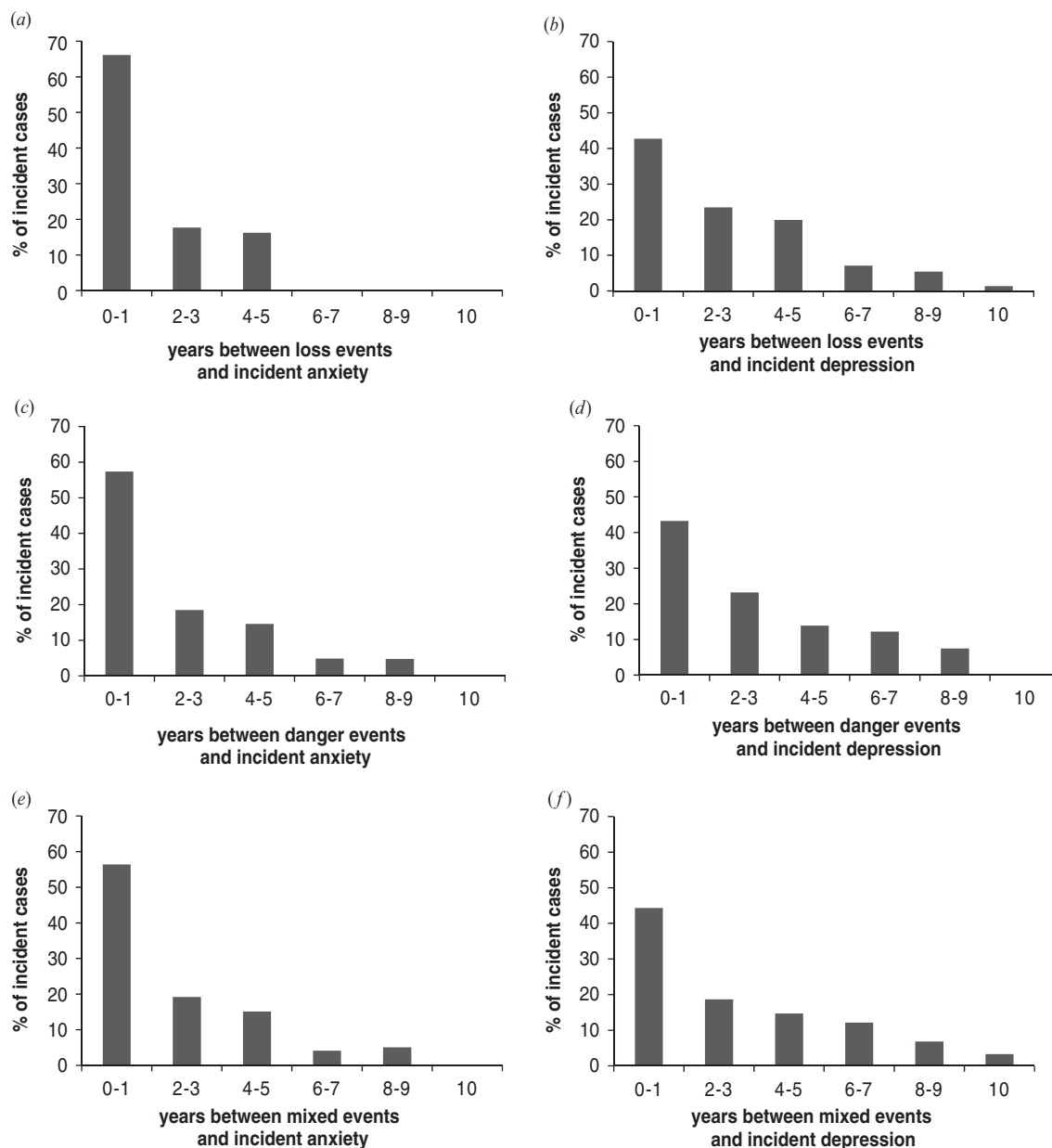


Fig. 1. Time intervals between (a) loss events and incident anxiety, (b) loss events and incident depression, (c) danger events and incident anxiety, (d) danger events and incident depression, (e) mixed events and incident anxiety and (f) mixed events and incident depression in those with respective events at baseline and incident disorder at follow-up.

In those with danger, loss or mixed events at baseline, incidence rates for anxiety and depression at follow-up were highest shortly after baseline and decreased with time.

Table 4 presents means and standard deviations for numbers and weighted numbers of event types by incident anxiety and depression.

Examining associations between linear numbers (LN)/linear weighted numbers (LWN) of event types and incident anxiety and depression revealed the

following results: LN and LWN of loss events only predicted incident depression (LN, OR 1.2 per standard deviation, 95% CI 1.1–1.4, $p < 0.001$; LWN, OR 1.2, 95% CI 1.1–1.4, $p < 0.001$). LN and LWN of danger events predicted incident anxiety (LN, OR 1.2, 95% CI 1.0–1.5, $p = 0.030$; LWN, OR 1.2, 95% CI 1.0–1.4, $p = 0.034$) and incident depression (LN, OR 1.4, 95% CI 1.2–1.6, $p < 0.001$; LWN, OR 1.4, 95% CI 1.2–1.6, $p < 0.001$). LN and LWN of mixed events predicted incident anxiety (LN, OR 1.4, 95% CI 1.3–1.7, $p < 0.001$;

Table 4. Numbers and weighted numbers of type of event by follow-up incidence of anxiety or depression (n=2304)

| Type of event | Incidence of anxiety disorder | | Incidence of depressive disorder | |
|---|-------------------------------|-------------|----------------------------------|-------------|
| | No (n=2175) | Yes (n=129) | No (n=1947) | Yes (n=357) |
| Number of type of event, mean (s.d.) | | | | |
| Loss event | 0.17 (0.43) | 0.20 (0.47) | 0.16 (0.41) | 0.27 (0.52) |
| Danger event | 0.38 (0.71) | 0.53 (0.90) | 0.34 (0.69) | 0.61 (0.86) |
| Mixed event | 0.11 (0.36) | 0.32 (0.70) | 0.12 (0.37) | 0.17 (0.47) |
| Weighted number of type of event, mean (s.d.) | | | | |
| Loss event | 0.68 (1.69) | 0.78 (1.79) | 0.62 (1.62) | 1.05 (2.06) |
| Danger event | 1.15 (2.17) | 1.60 (2.70) | 1.05 (2.11) | 1.85 (2.60) |
| Mixed event | 0.34 (1.10) | 0.98 (2.16) | 0.35 (1.13) | 0.52 (1.44) |

LWN, OR 1.4, 95% CI 1.3–1.7, $p < 0.001$) and incident depression (LN, OR 1.2, 95% CI 1.0–1.3, $p = 0.019$; LWN, OR 1.2, 95% CI 1.0–1.3, $p = 0.016$).

Only for the associations between squared numbers (SN) and squared weighted numbers (SWN) of danger events and incident depression did the squared term predict the outcome beyond the linear term (SN, OR 0.9, 95% CI 0.9–1.0, $p = 0.018$; SWN, OR 0.9, 95% CI 0.8–1.0, $p = 0.016$). In particular, danger events predicted an increased risk of depression for zero to three danger events (danger severity scores from 0 to 8) and a decreased risk for four or more danger events (danger severity scores > 8). All other associations of event types with anxiety and/or depression were found to increase monotonically with a higher number and greater severity of the respective event types.

Specificity between event types and incident anxiety and depression

To assess whether associations between event types and incident anxiety and depression were specific, we used mutually exclusive groups, that is ‘pure’ danger events, ‘pure’ loss events and respectively mixed events as predictors and no anxiety and depression, ‘pure’ anxiety, ‘pure’ depression and co-morbid anxiety and depression as outcome. As shown in Table 5, ‘pure’ loss events only predicted incident ‘pure’ depression (OR 2.4 per standard deviation). ‘Pure’ danger events predicted incident ‘pure’ anxiety (OR 2.3) and ‘pure’ depression (OR 2.5). Mixed events predicted incident ‘pure’ anxiety (OR 2.9), ‘pure’ depression (OR 2.4) and co-morbid anxiety and depression (OR 3.6).

Discussion

This study revealed the following core findings: (1) loss events predicted incident depression only, (2) danger events predicted incident anxiety and depression,

and (3) mixed events predicted incident anxiety, depression and co-morbid anxiety and depression.

Loss events and depression

We found that loss events only predicted incident depression and that a higher number and greater severity of loss events increased this association monotonically. This suggests that loss events specifically increase the risk for depression but not the risk for anxiety, probably because loss events primarily trigger immediate distress but hold no (or little) potential for specific future problems. It is further noteworthy that (with one exception) all event categories classified as loss in our study were related to death of or separation from significant others, and it seems that this form of interpersonal loss is highly specific in predicting depression.

Our finding that loss events are associated with incident depression complies with previous research (Finlay-Jones & Brown, 1981; Eley & Stevenson, 2000; Kendler *et al.* 2003). However, Finlay-Jones & Brown (1981) found that loss events were associated with both depression and co-morbid anxiety and depression, and Kendler *et al.* (2003) showed that loss events were linked to depression, anxiety and co-morbid anxiety and depression although, in their study, the link was strongest for depression, intermediate for co-morbid disorders and weakest for anxiety.

These differences in findings may lie in the fact that earlier studies distinguished between (non-mutually exclusive) danger and loss events whereas the present study distinguished between ‘pure’ danger events, ‘pure’ loss events and respectively mixed events. Moreover, assessment of life events differed considerably between our and previous studies: in previous studies, life events were assessed along with contextual data that were fundamental for the categorization of event types. By contrast, life events in our study were assessed using a checklist with specified events

Table 5. Associations^a of 'pure' loss events, 'pure' danger events and mixed events with follow-up incidence of no anxiety disorder (AD) and no depression disorder (DD), AD but no DD, DD but no AD, and co-morbid AD and DD (n=2304)

| Type of event | No AD and no DD (n=1881) | | AD but no DD (n=66) | | DD but no AD (n=294) | | AD and DD (n=63) | |
|--|--------------------------|-----------|---------------------|---------------|----------------------|-----------|------------------|--------|
| | n (%) | n (%) | n (%) | OR (95% CI) | p | n (%) | OR (95% CI) | p |
| No event (n=1342) | 1166 (61.9) | 26 (42.6) | 127 (40.6) | | | 25 (40.9) | | |
| 'Pure' loss event ^b (n=176) | 133 (7.3) | 4 (5.4) | 35 (11.8) | 1.1 (0.4-3.2) | 0.903 | 4 (5.7) | 1.2 (0.4-3.5) | 0.803 |
| 'Pure' danger event ^c (n=440) | 332 (16.5) | 18 (24.4) | 75 (26.2) | 2.3 (1.1-4.6) | 0.023 | 15 (20.8) | 1.9 (0.9-3.8) | 0.074 |
| Mixed event ^d (n=344) | 250 (14.3) | 18 (27.6) | 57 (21.5) | 2.9 (1.5-5.7) | 0.002 | 19 (32.7) | 3.6 (1.8-7.0) | <0.001 |

OR, Odds ratio; CI, confidence interval.

^a Multinomial logistic regression, adjusted for sex and age. Reference group: no danger, loss and mixed event.

^b Excludes cases with danger or mixed events.

^c Excludes cases with loss or mixed events.

^d Includes cases with mixed events or more than one event type.

classified as danger, loss or mixed events independent of contextual data.

Danger events and anxiety

We further found that danger events predicted both incident anxiety and depression. Although the association with anxiety increased monotonically for a higher number and greater severity of danger events, the association with depression increased for zero to three danger events (event severity scores between 0 and 8) and decreased for four or more danger events (event severity scores higher than 8). These results suggest that danger events are non-specifically related to anxiety and depression when considering a lower number and severity of danger events, but specifically related to anxiety when considering a higher number and severity of danger events, possibly because high levels of danger especially indicate an increased likelihood of unfavorable future consequences.

Our finding for any danger event to predict both anxiety and depression complies with Finlay-Jones & Brown (1981), who found that danger events were linked to anxiety and depression. However, in contrast to our findings, Finlay-Jones & Brown (1981) revealed that danger events were additionally associated with co-morbid anxiety and depression, whereas Eley & Stevenson (2000) and Kendler *et al.* (2003) found that danger events were associated with anxiety but not with either depression or co-morbid anxiety and depression.

These differences may be explained partially by the fact that, in our study, a higher number and a greater severity of danger events were associated with incident anxiety only. In addition, event types in our study were established without using contextual information, which may have resulted in fewer specific event categories and contributed to broader associations of danger events with both anxiety and depression. However, further research is needed to examine more closely the associations of danger events with depression and co-morbid anxiety and depression.

Mixed events and co-morbid anxiety and depression

We also found that mixed events predicted all outcome patterns, namely incident anxiety, depression and co-morbid anxiety and depression. A higher number and greater severity of mixed events increased these associations. It is particularly noteworthy that, in the multinomial model, only mixed events and neither 'pure' danger nor 'pure' loss events predicted co-morbid anxiety and depression, probably because mixed events indicate both immediate distress

and potential unfavorable long-term consequences. These findings are in accordance with Finlay-Jones & Brown (1981), who found that more co-morbid cases than anxiety cases or non-cases reported both danger and loss events at any period of time.

Strengths and limitations

This study firstly examined prospective-longitudinal associations of danger and loss events with incident anxiety and depression in a representative sample of adolescents and young adults.

However, the following limitations need to be considered: first, life events at baseline and psychopathology at each wave were assessed retrospectively and recall may have been biased (Andrews et al. 1999). Second, only moderate/severe danger and loss events were included in the analyses and hence dissimilar associations may exist between milder life events and anxiety and/or depression. Third, no contextual information was used for the categorization of danger, loss and mixed events, although contextual data might have influenced how participants perceived and responded to specific types of life events. Fourth, our study focused on considerably longer time intervals between event types and incident disorders than previous studies, although we did find that, consistent with previous research (Surtees & Ingham, 1980; Kendler et al. 1998; Wainwright & Surtees, 2002), incidence rates for anxiety and depression in those with any danger, loss or mixed event at baseline were highest shortly after baseline and decreased with time. Nevertheless, we were unable to assess systematically the duration of risk periods of danger, loss and mixed events for incident anxiety and depression. Fifth, the study sample contained adolescents and young adults from a relatively wealthy area in Germany, and hence the generalizability of findings, especially to other age groups, may be limited.

Conclusions

We found loss events to specifically predict incident depression, danger events to predict incident anxiety and depression, and mixed events to predict incident anxiety, depression and their co-morbidity. Thus, although associations between danger events and anxiety and also mixed events and co-morbid disorders were non-specific, our findings suggest partly distinct etiologies for anxiety and depression. Future research is required to replicate our findings and focus on temporal associations between exposure to different event types and incidence of anxiety and depression.

Note

- 1 In contrast to Finlay-Jones & Brown (1981), we did not include 'loss of a valued idea' as an indicator/criterion for loss because it seemed relatively broad/vague to us and conflicted with our idea of a preferably explicit rating instruction.

Acknowledgments

This work is part of the EDSP and is funded by the German Federal Ministry of Education and Research (BMBF) project nos 01EB9405/6, 01EB 9901/6, EB01016200, 01EB0140 and 01EB0440. Some of the fieldwork and analyses was also supported by grants from the Deutsche Forschungsgemeinschaft (DFG; LA1148/1-1, WI2246/1-1, WI 709/7-1 and WI 709/8-1). The first author (Eva Asselmann) was funded by a doctoral stipend of the German National Academic Foundation (Studienstiftung des Deutschen Volkes).

Principal Investigators were H.-U. Wittchen and R. Lieb. Core staff members of the EDSP group are: K. von Sydow, G. Lachner, A. Perkonig, P. Schuster, M. Höfler, H. Sonntag, T. Brückl, E. Garczynski, B. Isensee, A. Nocon, C. Nelson, H. Pfister, V. Reed, B. Spiegel, A. Schreier, U. Wunderlich, P. Zimmermann, K. Beesdo-Baum, A. Bittner, S. Behrendt and S. Knappe. Scientific advisors were J. Angst (Zurich), J. Margraf (Basel), G. Esser (Potsdam), K. Merikangas (National Institute of Mental Health, Bethesda), R. Kessler (Harvard, Boston) and J. van Os (Maastricht).

Declaration of Interest

Dr Wittchen is on the advisory board and has received grant support to his institution from Servier, Novartis, Lundbeck, Pfizer, Sanofi, and Hoffmann-La Roche.

References

- Andrews G, Anstey K, Brodaty H, Issakidis C, Luscombe G (1999). Recall of depressive episode 25 years previously. *Psychological Medicine* **29**, 787–791.
- Beesdo K, Pine DS, Lieb R, Wittchen HU (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Archives of General Psychiatry* **67**, 47–57.
- Brown GW, Harris TO (1989). *Life Events and Illness*. Guilford Press: New York.
- Brown GW, Harris TO, Eales MJ (1993). Etiology of anxiety and depressive disorders in an inner-city population. 2. Comorbidity and adversity. *Psychological Medicine* **23**, 155–165.

- Cox BJ, Clara IP, Enns MW (2002). Posttraumatic stress disorder and the structure of common mental disorders. *Depression and Anxiety* **15**, 168–171.
- Eley TC, Stevenson J (2000). Specific life events and chronic experiences differentially associated with depression and anxiety in young twins. *Journal of Abnormal Child Psychology* **28**, 383–394.
- Finlay-Jones R, Brown GW (1981). Types of stressful life event and the onset of anxiety and depressive disorders. *Psychological Medicine* **11**, 803–815.
- Friis RH, Wittchen HU, Pfister H, Lieb R (2002). Life events and changes in the course of depression in young adults. *European Psychiatry* **17**, 241–253.
- Gillespie NA, Whitfield JB, Williams B, Heath AC, Martin NG (2005). The relationship between stressful life events, the serotonin transporter (5-HTTLPR) genotype and major depression. *Psychological Medicine* **35**, 101–111.
- Hammen C (2011). Association between recent stressful life events and prevalence of depression, anxiety and PTSD differs according to exposure to childhood adversity. *Evidence-Based Mental Health* **14**, 9.
- Kendler KS (1996). Major depression and generalised anxiety disorder – same genes, (partly) different environments – revisited. *British Journal of Psychiatry* **168**, 68–75.
- Kendler KS, Hettema JM, Butera F, Gardner CO, Prescott CA (2003). Life event dimensions of loss, humiliation, entrapment, and danger in the prediction of onsets of major depression and generalized anxiety. *Archives of General Psychiatry* **60**, 789–796.
- Kendler KS, Karkowski LM, Prescott CA (1998). Stressful life events and major depression: risk period, long-term contextual threat, and diagnostic specificity. *Journal of Nervous and Mental Disease* **186**, 661–669.
- Kendler KS, Karkowski LM, Prescott CA (1999). Causal relationship between stressful life events and the onset of major depression. *American Journal of Psychiatry* **156**, 837–841.
- Kessler RC (1997). The effects of stressful life events on depression. *Annual Review of Psychology* **48**, 191–214.
- Kessler RC, Chiu WT, Demler O, Walters EE (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry* **62**, 617–627.
- Kraemer HC, Kazdin AE, Offord DR, Kessler RC, Jensen PS, Kupfer DJ (1997). Coming to terms with the terms of risk. *Archives of General Psychiatry* **54**, 337–343.
- Lieb R, Isensee B, von Sydow K, Wittchen HU (2000). The Early Developmental Stages of Psychopathology Study (EDSP): a methodological update. *European Addiction Research* **6**, 170–182.
- Maier-Diewald W, Wittchen HU, Hecht H, Werner-Eilert K (1983). *The Munich Event List (MEL) – Manual* [in German]. Max Planck Institute of Psychiatry: Munich.
- Newman SC, Bland RC (1994). Life events and the 1-year prevalence of major depressive episode, generalized anxiety disorder, and panic disorder in a community sample. *Comprehensive Psychiatry* **35**, 76–82.
- Reed V, Gander F, Pfister H, Steiger A, Sonntag H, Trenkwalder C, Sonntag A, Hundt W, Wittchen HU (1998). To what degree does the Composite International Diagnostic Interview (CIDI) correctly identify DSM-IV disorders? Testing validity issues in a clinical sample. *International Journal of Methods in Psychiatric Research* **7**, 142–155.
- Roy MA, Neale MC, Pedersen NL, Mathe AA, Kendler KS (1995). A twin study of generalized anxiety disorder and major depression. *Psychological Medicine* **25**, 1037–1049.
- Slade T, Watson D (2006). The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. *Psychological Medicine* **36**, 1593–1600.
- StataCorp (2011). *STATA Statistical Software: Release 12*. Stata Corporation: College Station, TX.
- Surtees PG, Ingham J (1980). Life stress and depressive outcome: application of a dissipation model to life events. *Social Psychiatry* **15**, 21–31.
- Wainwright NW, Surtees PG (2002). Time-varying exposure and the impact of stressful life events on onset of affective disorder. *Statistics in Medicine* **21**, 2077–2091.
- Watson D (2005). Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology* **114**, 522–536.
- WHO (1990). *Composite International Diagnostic Interview (CIDI): (a) CIDI version 1.0, (b) CIDI user manual, (c) CIDI training manual, (d) CIDI computer programs*. World Health Organization: Geneva.
- Wittchen HU, Essau CA, Hecht H, Teder W, Pfister H (1989). Reliability of life event assessments: test-retest reliability and fall-off effects of the Munich Interview for the Assessment of Life Events and Conditions. *Journal of Affective Disorders* **16**, 77–91.
- Wittchen HU, Lachner G, Wunderlich U, Pfister H (1998a). Test-retest reliability of the computerized DSM-IV version of the Munich Composite International Diagnostic Interview (M-CIDI). *Social Psychiatry and Psychiatric Epidemiology* **33**, 568–578.
- Wittchen H-U, Lieb R, Schuster P, Oldehinkel AJ (1999). When is onset? Investigations into early developmental stages of anxiety and depressive disorders. In *Childhood Onset of 'Adult' Psychopathology: Clinical and Research Advances* (ed. J. L. Rapoport), pp. 259–302. American Psychiatric Publishing: Washington, DC.
- Wittchen HU, Perkonig A, Lachner G, Nelson CB (1998b). Early Developmental Stages of Psychopathology Study (EDSP): objectives and design. *European Addiction Research* **4**, 18–27.
- Wittchen HU, Pfister H (1997). *DIA-X-Interviews: Manual für Screening-Verfahren und Interview; Interviewheft Längsschnittuntersuchung (DIA-X-Lifetime); Ergänzungsheft (DIA-X-Lifetime); Interviewheft Querschnittuntersuchung (DIA-X-12 Monate); Ergänzungsheft (DIA-X-12 Monate), pC-Programm zur Durchführung des Interviews (Längs- und Querschnittuntersuchung); Auswertungsprogramm*. Swets & Zeitlinger: Frankfurt.