Severe melancholic depression is more vulnerable than non-melancholic depression to minor precipitating life events

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Abstract

Background: The present study examines the moderating role of global depression severity on the relation of melancholic versus non-melancholic depression to severe and non-severe levels of stress.

Method: A community sample of 50 women with unipolar major depressive disorder, of which 54% met Research Diagnostic Criteria for melancholic depression, were interviewed regarding stressful life events experienced prior to onset. Events were coded as severe or non-severe based on the rigorous Bedford College contextual rating system.

Results: Greater severity of depression was related to a higher likelihood of a severely stressful event prior to onset only for women with non-melancholic major depression. By contrast, greater severity of depression was related to a higher likelihood of a non-severe, more minor, stressful event prior to onset only for women with melancholic major depression.

Limitations: The present study was limited by its use of a female volunteer sample, which might not be entirely representative of the population of individuals with major depression. In addition, the study employed a cross-sectional design, which limits conclusions relating to the causal relation of stress to melancholic versus non-melancholic depression.

Conclusions: Far from being autonomous of stress, individuals with severe melancholic depression may be especially sensitive to stress, such that their episodes are influenced by more minor stressors than those of individuals with non-melancholic depression.

Keywords: Melancholic depression; Stressful life events; Depression severity

1. Introduction

Theorists even before Kraepelin (1921) suggested that the neurovegetative symptoms of melancholia result from an “endogenous,” biogenetic process. By contrast, the non-melancholic subtype was presumed to have a psychosocial etiology (Jackson, 1986). A distinction was made, then, between depression that is autonomous of the environment and depression that develops as a reaction to stress. However, while some studies have reported higher rates of severely stressful events preceding non-melancholic versus melancholic depression (e.g., Brown et al., 1994; Frank et al., 1994; Paykel et al., 1984), other equally rigorous studies have reported null findings (e.g., Bebbington et al., 1988; Benjaminsen, 1981; Brown et al., 1979; Mitchell et al., 2003; Zimmerman et al., 1986).
The goal of the present report is to examine the relation between stress and depression subtype by considering two important issues that are germane to this question. First, controversy exists regarding the validity of melancholic depression, and the weight of the evidence to date suggests an “integrated threshold model” (Leventhal and Rehm, 2005). That is, melancholic depression is both a qualitatively distinct subtype of depression (e.g., Beach and Amir, 2003; Davidson et al., 1988; Grove et al., 1987) and is also more globally severe than non-melancholic depression.

However, applying the integrated threshold model to the results of studies investigating the role of stress in melancholic versus non-melancholic depression is challenging. Significant stress differences between subtypes could mean that stress is less strongly associated with the qualitatively distinct subtype of melancholic depression than with non-melancholic depression. Alternatively, stress may simply be related to a less severe form of depression, regardless of symptom profile. We include a measure of global severity scores in our models, and thus are able to examine differences in life events in relation to depression subtype, depression severity, and their potential interaction.

Second, studies examining the relation of stress to depression subtypes typically focus on severely stressful life events. A lower likelihood of such an event prior to onset in melancholic versus non-melancholic depression has suggested that stress is less important in the etiology of melancholic depression. However, a biogenetic distal etiology (e.g., strong genetic loading) is not incompatible with the need for proximal environmental triggers of episode onset. Indeed, recent studies have shown that individuals with a strong genetic liability to depression are especially sensitive to the depressogenic effects of stress (Caspi et al., 2003; Kendler et al., 1995). Therefore, perhaps individuals with melancholic depression are less likely to experience severe events prior to onset because they more frequently break down in the face of more common minor stressors due to their strong biological diathesis (see Monroe and Harkness, 2005; Monroe and Simons, 1991).

We address this possibility by assessing both severe and non-severe events in our models. If a purely endogenous process is operating in melancholic depression, then these individuals should be less likely than those with non-melancholic depression to experience both severe and non-severe events. However, if individuals with melancholic depression possess heightened sensitivity to life event triggers, then an increase in rates of non-severe events should be evident prior to onset.

2. Method

2.1. Participants

Women were recruited from a community in the Pacific Northwest by way of media advertisements. Participants all met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994) criteria for a current episode of nonpsychotic, nonchronic, unipolar major depressive disorder with a Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) score of greater than or equal to 15 (M=19.78, SD=3.14). Exclusion criteria included psychosis, substance abuse or dependence, concurrent medical disorder that could cause depression, or acute suicidality. Of the 245 women who responded to the advertisements, 90 women met initial criteria for the study based on a telephone screening. Nine women failed to attend the full interview and 31 participants failed to meet study criteria based on the complete diagnostic interview, leaving a final sample of 50.

Participants ranged in age from 18 to 70 (M=37.24, SD=11.64), 44% (n=22) were married, 34% (n=17) had a college education, 22% (n=16) were employed outside the home, 34% (n=17) worked in the home, and 34% (n=17) were unemployed. Consistent with the ethnic distribution of this small city, 90% (n=45) were White.

2.2. Procedure and measures

After complete description of the study, written informed consent was obtained. Following the study, all participants were paid $20 for their time and were provided with treatment referrals.

2.2.1. Diagnostic and symptom measures

Psychiatric diagnoses according to DSM-IV criteria were derived through a SCID-I/P (First et al., 1994) interview administered by the first author or an advanced graduate student who had been trained to gold standard reliability status (Grove et al., 1981). Research Diagnostic Criteria (RDC; Spitzer et al., 1978) for definite “endogenous” (melancholic) depression were also assessed, and the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) was administered. The reliability and validity of these instruments have been well documented in the study of depression (e.g., Rehm and O’Hara, 1985; Williams et al., 1992).
2.2.2. Life event measure

The Life Events and Difficulties Schedule (LEDS-II; Bifulco et al., 1989) is a semi-structured interview that involves questions regarding health, housing, employment, marital issues, and crises. Based on the audi-taped interview, a panel of 2–3 master’s-level raters rated all events based on Bedford College LEDS procedures (see Brown and Harris, 1978). Raters were unaware of the participants’ subtype diagnosis, date of episode onset, or subjective response to the events. Events were rated on a 5-point threat scale (1—marked, 2a—high moderate, 2b—low moderate, 3—some, 4—little/none). Severe events were coded as 1 or 2a on threat (e.g., loss of job in a financially strained household, revelation of spouse’s extra-marital affair). Non-severe events were coded as 2b, 3, or 4 on threat (e.g., friend moves away, loss of a job with little to no financial strain). Contextual information surrounding each event was used to inform the ratings, and the LEDS manual, containing over 5000 case vignettes, was used to ensure standardization. Inter-rater reliabilities ranged from .76 to .81 (M=.78, corrected for chance by Cohen’s kappa).

2.3. Data analysis

Two logistic regression models examined the likelihood of having a severe or non-severe stressful life event prior to onset versus having an episode that was independent of stress, based on depression subtype (melancholic versus non-melancholic) and severity (HRSD scores). The dependent variables were either the presence or absence of a severe event, or the presence or absence of a non-severe event in the 3 months prior to onset. Depression subtype and severity were entered as main effects on the first step. Their interaction was entered on the second step.

3. Results

3.1. Descriptive characteristics and preliminary analyses

Descriptive statistics of events by depression subtype are presented in Table 1. Women with a non-severe event in the 0–3 months prior to onset were significantly younger than those without, Ms=34.59, 44.77; SDs=9.47, 14.17; t(48)=2.91, p<.005. The same relation held for non-severe events in the 3–6-month period, Ms=31.93, 45.20; SDs=9.24, 10.38; t(48)=4.74, p<.005. Depression subtype and depression severity were not significantly associated with any demographic covariate. As expected, those with melancholic depression had significantly higher HRSD scores than those with non-melanchoic depression, Ms=21.07, 18.26; SDs=2.81, 2.86; t(48)=3.50, p<.005.

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<tr>
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<tr>
<td></td>
<td>(n=23)</td>
<td>(n=27)</td>
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<tr>
<td>3-month severe event: No</td>
<td>16 70</td>
<td>20 74</td>
</tr>
<tr>
<td></td>
<td>7 31</td>
<td>7 26</td>
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<tr>
<td>3-month non-severe event: No</td>
<td>8 35</td>
<td>5 19</td>
</tr>
<tr>
<td></td>
<td>15 65</td>
<td>22 81</td>
</tr>
<tr>
<td>6-month severe event: No</td>
<td>19 83</td>
<td>21 78</td>
</tr>
<tr>
<td></td>
<td>4 17</td>
<td>6 22</td>
</tr>
<tr>
<td>6-month non-severe event: No</td>
<td>10 43</td>
<td>10 37</td>
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<td>13 57</td>
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3.2. Severe life events and melancholic depression

The model containing the main effects of depression subtype and depression severity approached significance, χ² (2)=5.08, p=.08. No significant difference emerged between depression subtypes in the likelihood of experiencing a severe event (OR=1.27, p=.20). However, those with higher depression severity were more likely to have experienced a severe event (OR=2.17, p<.05). This main effect was qualified by a significant interaction with depression subtype, χ² (1)=4.22, p<.05, OR=1.83 (see Fig. 1a). As predicted, a significant positive relation emerged between depression severity and the likelihood of a severe event among those with non-melancholic, χ² (1)=9.11, p<.005, OR=2.33, but not melancholic, χ² (1)=.05, p=.81, OR=.23, depression.

3.3. Non-severe life events and melancholic depression

The effect of age was significant, χ² (1)=7.80, p<.005, OR=3.00. The entry of the two main effects was not significant, χ² (2)=4.00, p=.14: Neither depression severity (OR=1.57, p=.12) nor depression subtype (OR=.29, p=.77) was significantly associated with a non-severe event. The interaction term was significant, χ² (1)=7.41, p<.01, OR=1.78 (see Fig. 1b). A significant positive relation emerged between depression severity and likelihood of a non-severe event among those with melancholic, χ² (1)=14.37,
3.4. Control analyses: 6-month events

To make claims about a differential etiologic relation of severe and non-severe life events to depression, we should ensure that the events are specifically linked in

$p < .001$, OR $= 2.10$, but not non-melancholic, $\chi^2 (1) = .20$, $p = .65$, OR $= .45$, depression. That is, the significant relation between depression severity and risk for a non-severe event prior to onset was accounted for only by those with melancholic depression.

Fig. 1. Regression lines indicating interaction between depression subtype and depression severity on the risk for (a) a severe event and (b) a non-severe event in the 3 months prior to depression episode onset.
time to onset. We thus examined the relation of depression subtype to events in the more distal 3–6 months prior to onset.

3.4.1. Severe life events

The main effect of depression severity and depression subtype was not significant, $\chi^2 (2) = .86, p = .65$. The interaction effect improved the model only at a trend level, $\chi^2 (1) = 3.27, p = .07$, OR = 1.63. Therefore, our results regarding the relation of depression subtype and severity to severe events were not replicated in the more distal 3–6-month period.

3.4.2. Non-severe life events

The age covariate was significant, $\chi^2 (1) = 18.37, p < .001$, OR = 3.42. The second step including the main effects was not significant, $\chi^2 (2) = .44, p = .83$. However, the interaction effect significantly improved the model, $\chi^2 (1) = 7.77, p < .005$, OR = 2.44. As in the case of the 0–3-month events, a significant positive relation emerged between HRSD score and odds of experiencing a non-severe event for those with melancholic depression, $\chi^2 (1) = 5.80, p < .05$, OR = 2.05, but not among those with non-melancholic depression, $\chi^2 (1) = 3.04, p = .08$, OR = 1.60.

These results suggest that rates of non-severe events may be chronically elevated in melancholic depression and not specifically linked to onset. To examine this issue, we performed within-group comparisons of the likelihood of experiencing a non-severe event in the 3–6- versus the 0–3-month periods prior to onset. An increase in the likelihood of a non-severe event from the 3–6-month period to the 0–3-month period would provide evidence that episode onset follows a period of increased stress. Wilcoxon Signed Ranks tests revealed a near-significant increase in the likelihood of experiencing a non-severe event across the two time periods in those with melancholic depression, $Z = 1.89, p = .06$, but not in those with non-melancholic depression, $Z = .82, p = .41$.

4. Discussion

Consistent with hypotheses, a differential relation emerged between melancholic and non-melancholic depression and stressful life events. As predicted, the likelihood of having a severe event prior to onset was significantly related to depression severity in women with non-melancholic depression only. By contrast, the likelihood of having a non-severe event prior to onset was significantly related to depression severity in women with melancholic depression only. These novel results highlight the importance of defining depression by both its qualitative and quantitative aspects. In particular, the distinction between melancholic and non-melancholic depression only emerged in individuals at the upper end of the global severity continuum.

The finding that those with severe melancholic depression were more likely to have a non-severe event prior to onset than those with non-melancholic depression forces a reinterpretation of traditional etiological models. One compelling interpretation is that those with severe melancholic depression require a lower threshold of stress to precipitate their episodes because they are sensitive to stress. Individuals with melancholic depression have a stronger genetic diathesis for depression (Kendler, 1997) and are more likely to report a history of childhood trauma (Harkness and Monroe, 2002) than those with non-melancholic depression. Both of these risk factors have been shown to increase individuals' sensitivity to future stress (Hammen et al., 2000; Harkness et al., 2005; Kendler et al., 1995). Indeed, increased sensitivity to stress may be mediated by a specific polymorphism in the serotonin transporter gene (Caspi et al., 2003; Kendler et al., 2005). Research is now needed to determine whether these risks increase stress sensitivity in melancholic depression, in particular.

As predicted, the strong pattern of association between non-melancholic depression and severe events immediately preceding onset (0–3 months) was not replicated in a more distal control period (3–6 months). Therefore, this significant pattern does not reflect simply stable long-term trends in rates of severe events. Instead, it may represent a distinct manifestation of events that have a direct etiological role in severe non-melancholic depression.

However, the significant relation of depression severity to non-severe events in the women with melancholic depression held for events experienced in both the 0–3-month period and the more distal 3–6-month period. Therefore, one alternative interpretation of our results is that women with melancholic depression experience high rates of minor stressors in their lives, in general, perhaps due to particular temperamental diatheses that render them especially likely to generate stress (e.g., Akiskal, 1995). However, we found that these women experienced an increase in non-severe events leading up to the most etiologically central period preceding onset, whereas women with non-melancholic depression did not. This result suggests that the non-severe events in the 0–3-month period likely played an etiological role for the women with melancholic depression.
Nevertheless, to further address the above alternative explanation, we compared the likelihood of experiencing a non-severe event in the 0–3 and 3–6 months prior to onset in our depressed women to a matched sample of 33 women with no psychiatric history that we had recruited at the same time as the present depressed sample. Logistic regressions revealed that women with melancholic depression differed significantly from controls in the likelihood of a non-severe event in the 0–3 months prior to onset (or a matched comparison time in controls), $OR=2.54$, $p<.05$, but not in the 3–6 months prior to onset, $OR=.42$, $p=.67$. By contrast, women with non-melancholic depression did not differ from controls in non-severe events in either period: 0–3 months ($OR=1.17$, $p=.24$); 3–6 months ($OR=.12$, $p=.90$). These analyses provide further evidence that melancholic depression is preceded by an increased likelihood of minor events, thus supporting our suggestion that those with severe melancholia may be sensitized to stress.

The present study was limited in the following ways. First, participants were community volunteers and, thus may not be representative of the full spectrum of severity present in patient samples. Therefore, we may not have indexed “true” melancholic depression in all cases, and replication of this study is needed with more severe groups. Second, the present sample comprised women exclusively, thus the generalizability of our findings to men is unclear. Third, we employed a cross-sectional design. Previous studies have found that subtype diagnosis does not remain consistent from episode to episode across recurrence (e.g., Young et al., 1987). Longitudinal studies that chart within-subject variations in the relation between stress to subtypes over time are now needed.

Finally, because of the retrospective design, there is the potential for mood-biased recall of life events. The LEDS addresses this concern in a much better way than do traditional self-report stress measures (McQuaid et al., 1992) by querying in detail about the facts surrounding each event. These details, and not the respondents’ emotional reaction to the events are used to guide the threat ratings. The raters were also unaware of the participants’ subtype diagnosis and any other features of the participants’ depression that could bias their rating.

The present project had a number of strengths, including the use of structured diagnostic interviews and a rigorous contextual interview to assess life events. From a theoretical perspective, this study posited a new way to investigate the relation of stress to depression that considers quantitative and qualitative differences in depression phenomenology, as well as a more fine-grained investigation of stress severity. The present findings have important implications as they suggest that even individuals with severe melancholic depression may be vulnerable to the effects of stress.

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**References**


