A COMPARISON OF MELANCHOLIC AND NONMELANCHOLIC RECURRENT MAJOR DEPRESSION IN HAN CHINESE WOMEN

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Background: Although the diagnosis of melancholia has had a long history, the validity of the current DSM-IV definition remains contentious. We report here

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The authors report the following financial relationships within the past 3 years: Contract grant sponsor: Wellcome Trust.

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Received for publication 10 May 2011; Revised 27 June 2011; Accepted 5 July 2011

DOI 10.1002/da.20875
Published online in Wiley Online Library (wileyonlinelibrary.com).

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the first detailed comparison of melancholic and nonmelancholic major depression (MD) in a Chinese population examining in particular whether these two forms of MD differ quantitatively or qualitatively. Methods: DSM-IV criteria for melancholia were applied to 1,970 Han Chinese women with recurrent MD recruited from 53 provincial mental health centers and psychiatric departments of general medical hospitals in 41 cities. Statistical analyses, utilizing Student’s $t$-tests and Pearson’s $\chi^2$, were calculated using SPSS 13.0. Results: Melancholic patients with MD were distinguished from nonmelancholic by being older, having a later age at onset, more episodes of illness and meeting more A criteria. They also had higher levels of neuroticism and rates of lifetime generalized anxiety disorder, panic disorder, and social and agoraphobia. They had significantly lower rates of childhood sexual abuse but did not differ on other stressful life events or rates of MD in their families. Discussion: Consistent with most prior findings in European and US populations, we find that melancholia is a more clinically severe syndrome than nonmelancholic depression with higher rates of comorbidity. The evidence that it is a more “biological” or qualitatively distinct syndrome, however, is mixed. Depression and Anxiety 29:4–9, 2012. © 2011 Wiley Periodicals, Inc.

Key words: major depression; melancholia; symptom; stressful life events

INTRODUCTION

Melancholia is one of the oldest and most frequently studied subtypes of major depression (MD). Its symptoms according to DSM-IV include anhedonia, nonreactivity, psychomotor disturbance, cognitive slowing, diurnal variation of mood, terminal insomnia, appetite, and weight loss. Some have argued that melancholia is an etiologically distinct form of MD that should be included in DSM-V as a separate mood disorder and that it possesses a distinctive biological etiology with characteristic laboratory test markers.

Several studies have identified characteristic features that distinguish melancholia from MD, including overall severity, a later age of onset, and higher rates of comorbidity. For example, Kendler et al. found that patients with melancholia had higher rates of comorbidity, a larger number of episodes, lower levels of neuroticism, and an increased risk of MD in co-twins. However, from a familial perspective, the differences between melancholic and nonmelancholic MD was quantitative rather than qualitative. In other words, their results were most consistent with the hypothesis that melancholic MD is more severe than, but not etiologically distinct from, nonmelancholic MD.

All the major studies comparing melancholic and nonmelancholic depression have been carried out in European populations. It is not known to what extent current findings will apply to patients in Asia. The aim of this study is to investigate, for the first time to our knowledge, whether features reported to characterize melancholia in the United States and European studies are to be found in China. These features are differences in the clinical symptoms of MD, comorbidity, personality, family history, and environment sensitivity. We set out to test not only whether melancholia has characteristic clinical features but also whether it has the same relationship to two known environmental precipitants of MD: stressful life events (SLEs) and childhood sexual abuse (CSA). We carried out our study in a large clinically acquired cohort of women with recurrent MD, all of whom are from the largest ethnic group in China, the Han Chinese. Our major goal is to clarify in this population the degree to which melancholia is quantitatively more severe than, or qualitatively distinct from, nonmelancholic depression.

SUBJECTS AND METHODS

STUDY SUBJECTS

The data for this study were drawn from the ongoing China, Oxford, and VCU Experimental Research on Genetic Epidemiology (CONVERGE) study of MD (MD). These analyses were based on a total of 1,970 cases recruited from 53 provincial mental health centers and psychiatric departments of general medical hospitals in 41 cities in 19 provinces and four central cities: Beijing, Shanghai, Tianjin, and Chongqing. All cases were female and had four Han Chinese grandparents. Cases were excluded if they had a pre-existing history of bipolar disorder, any type of psychosis, or mental retardation. Cases were aged between 30 and 60 years, had two or more episodes of MD, with the first episode occurring between 14 and 50 and had not abused drug or alcohol before the first episode of MD. The mean age (and SD) of cases in the data set was 45.1 (8.8).
Cases were interviewed using a computerized assessment system. All interviewers were trained by the CONVERGE team for a minimum of 1 week in the use of the interview. The interview includes assessment of psychopathology, demographic and personal characteristics, and psychosocial functioning. The study protocol was approved centrally by the Ethical Review Board of Oxford University and the ethics committee in participating hospitals in China.

MEASURES

The diagnoses of depressive (dysthymia and major depressive disorder, melancholic and nonmelancholic depression) and anxiety disorders (generalized anxiety disorder (GAD), panic disorder (PD) with or without agoraphobia) were established with the Composite International Diagnostic Interview, which classifies diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. The interview was originally translated into Mandarin by a team of psychiatrists in Shanghai Mental Health Centre with the translation reviewed and modified by members of the CONVERGE team. Phobias, divided into five subtypes (animal, situational, social, blood-injury, and agoraphobia) were diagnosed using an adaptation of DSM-III criteria requiring one or more unreasonable fears, including fears of different animals, social phobia, and agoraphobia that objectively interfered with the respondent's life. The section on the assessment of phobias was translated by the CONVERGE team from the interview used in the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD). All conditions were assessed by asking about lifetime episodes.

SLEs were assessed by asking about 16 traumatic lifetime events and the age at their occurrence. The CSA was a shortened version of the detailed module used in the VATSPSUD study, which was in turn based on the instrument developed by Martin et al. and included three factors that were nongenital, genital, and intercourse.

The case interview was fully computerized into a bilingual system of Mandarin and English developed in house in Oxford, and called SysQ. Skip patterns were built into SysQ. Interviews were administered by trained interviewers and entered offline in real time onto SysQ, which is installed in the laptops. Once an interview is completed, a backup file containing all the previously entered interview data can be generated with database compatible format. The backup file together with an audio recording of the entire interview is uploaded to a designated server currently maintained in Beijing by a service provider. All the uploaded files in the Beijing server are then transferred to an Oxford server quarterly.

STATISTICAL ANALYSIS

Sociodemographic and clinical characteristics of the sample were analyzed. For continuous variables, independent Student's t-tests were performed; for categorical variables, Pearson's \( \chi^2 \) were calculated. All the characteristics of individuals with melancholic versus nonmelancholic MD were assessed by logistic regression, with melancholia as the dependent variable (0 = absence and 1 = presence). Associations between variables were expressed as odds ratios (OR) and 95% confidence intervals (95% CI). SPSS 13.0 for Windows was used in data analysis.

RESULTS

We obtained 1,970 cases of recurrent MD from 53 hospitals in China. 81.3% of our cases (\( n = 1,602 \)) met DSM-IV criteria for melancholia during their worst lifetime episode. In this, and subsequent analyses, we carried out a within-case study to determine if there are any characteristics that differentiate those with melancholic MD from those with nonmelancholic MD.

Clinical characteristics of MD cases with and without melancholia are shown in Table 1. Compared with individuals with nonmelancholic MD, the melancholic group was significantly older, and had a later age of onset. Those with melancholia met a significantly higher number of DSM-IV criteria for MD; during the worst depressive episode, the melancholic group were significantly more likely to report feeling hopeless, crying, helpless, nervous and to have experienced functional impairment than nonmelancholic depressives. In addition, the melancholic group had significantly higher neuroticism scores and a more recurrent course than nonmelancholic patients. However, the two groups did not differ in the length of the longest episodes or in the risk of having a positive family.

Comorbid rates for other psychiatric disorders in the nonmelancholic and melancholic groups are shown in Table 2. A diagnosis of dysthymia was not associated with a melancholic subtype nor with a diagnosis of animal, situational or blood-injury phobia. Cases of MD with melancholia had significantly higher rates of comorbidity with GAD, PD, social phobia, and agoraphobia.

We assessed three groups of environmental risk factors for MD in our sample: lifetime SLEs, parenting and CSA. As depicted in Table 3, while we found no differences in the number of reported SLEs or history of parenting, melancholic patients were highly significantly less likely to report a history of CSA.

DISCUSSION

There has been a resurgence of interest in the validity of melancholia as a defined mood disorder, with participants at a recent conference on melancholia arguing that it is a distinctive syndrome. Taylor and Fink want to divide depressive disorders into two categories (melancholia and nonmelancholia), but the lack of clear qualitative differences (including
### TABLE 1. Clinical characteristics in female with melancholic versus nonmelancholic patients with MD

| Characteristics                  | Melancholic | Nonmelancholic | OR    | 95% CI          | P-value |
|----------------------------------|-------------|----------------|-------|-----------------|---------|
| Age                              | 45.5 ± 8.8  | 43.4 ± 8.7     | 1.03  | 1.01–1.01       | .003    |
| Age of onset, years              | 36.2 ± 10.0 | 34.3 ± 9.5     | 1.02  | 1.01–1.03       | .003    |
| Number of episode                | 4.4 ± 5.4   | 3.5 ± 3.1      | 1.06  | 1.02–1.09       | .005    |
| Length of longest episode        | 46.7 ± 91.2 | 49.5 ± 93.5    | 1.00  | 0.99–1.00       | .60     |
| No. of DSM-IV A criteria         | 8.5 ± 0.8   | 7.2 ± 1.4      | 2.75  | 2.43–3.10       | <.001   |
| Feeling irritable                | 1,172 (71.3)| 244 (73.5)     | 0.99  | 0.76–1.30       | .96     |
| Feeling hopeless                 | 1,326 (83.0)| 213 (64.2)     | 2.72  | 2.10–3.53       | <.001   |
| Crying                           | 1,060 (66.4)| 202 (60.8)     | 1.27  | 0.99–1.62       | .06     |
| Feeling helpless                 | 1,437 (89.9)| 266 (80.1)     | 2.22  | 1.62–3.03       | <.001   |
| Feeling nervous                  | 1,451 (90.8)| 279 (84.0)     | 1.88  | 1.34–2.63       | <.001   |
| No known precipitant             | 1,054 (66.0)| 229 (69.0)     | 0.87  | 0.67–1.12       | .30     |
| Functional impairment            | 1,386 (87.0)| 230 (69.5)     | 2.93  | 2.22–3.86       | <.001   |
| Neuroticism                      | 12.7 ± 6.1  | 11.0 ± 5.9     | 1.05  | 1.03–1.07       | <.001   |
| Feeling irritable                | 1,172 (71.3)| 244 (73.5)     | 0.99  | 0.76–1.30       | .96     |
| Feeling hopeless                 | 1,326 (83.0)| 213 (64.2)     | 2.72  | 2.10–3.53       | <.001   |
| Crying                           | 1,060 (66.4)| 202 (60.8)     | 1.27  | 0.99–1.62       | .06     |
| Feeling helpless                 | 1,437 (89.9)| 266 (80.1)     | 2.22  | 1.62–3.03       | <.001   |
| Feeling nervous                  | 1,451 (90.8)| 279 (84.0)     | 1.88  | 1.34–2.63       | <.001   |
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Odds ratios (OR), P-values, and 95% confidence intervals (95% CI) are shown for clinical features of MD. ORs greater than one indicate that the clinical feature or symptom is more common in patients with melancholia. ORs less than one indicate that the clinical feature or symptom is less common in melancholic patients. MD, major depression.

### TABLE 2. Pattern of comorbidity in female with melancholic versus nonmelancholic MD

| Disorder                | Melancholic | Nonmelancholic | OR    | 95% CI          | P-value |
|-------------------------|-------------|----------------|-------|-----------------|---------|
| Dysthymia               | 286 (17.9)  | 68 (19.0)      | 0.93  | 0.70–1.25       | .64     |
| Generalized anxiety disorder | 518 (32.7)  | 63 (17.7)      | 2.26  | 1.69–3.03       | <.001   |
| Panic disorder          | 176 (11.1)  | 19 (5.3)       | 2.22  | 1.37–3.63       | <.001   |
| Social phobia           | 520 (33.4)  | 88 (24.4)      | 1.50  | 1.156–1.96      | .002    |
| Agoraphobia             | 437 (28.0)  | 74 (21.0)      | 1.46  | 1.11–1.94       | .007    |
| Animal phobia           | 878 (56.3)  | 186 (52.7)     | 1.15  | 0.92–1.46       | .22     |
| Situational phobia      | 629 (40.4)  | 128 (36.2)     | 1.19  | 0.94–1.32       | .14     |
| Blood phobia            | 634 (40.7)  | 133 (37.6)     | 1.14  | 0.89–1.45       | .30     |

Odds ratios (OR), P-values and and 95% confidence intervals (95% CI) are shown for comorbid disorders. ORs greater than one indicate that the clinical feature or symptom is more common in patients with melancholia. ORs less than one indicate that the clinical feature or symptom is less common in melancholic patients. MD, major depression.

### TABLE 3. Environment sensitivity in female with melancholic versus nonmelancholic MD

| Environment sensitivity | Melancholic | Nonmelancholic | OR    | 95% CI          | P-value |
|-------------------------|-------------|----------------|-------|-----------------|---------|
| Stressful life events   | 1.7 ± 1.7   | 1.6 ± 1.6      | 1.04  | 0.97–1.12       | .30     |
| Parental bonding        |             |                |       |                 |         |
| Warmth of mother        | 18.2 ± 8.3  | 18.3 ± 8.3     | 0.99  | 0.96–1.01       | .80     |
| Authoritarianism of mother | 7.7 ± 4.7   | 7.9 ± 4.5      | 0.99  | 0.97–1.02       | .53     |
| Authoritarianism of father | 7.8 ± 4.8   | 7.8 ± 4.5      | 0.99  | 0.97–1.02       | .94     |
| Protectiveness of mother | 8.0 ± 4.4   | 7.8 ± 4.2      | 1.01  | 0.98–1.03       | .55     |
| Protectiveness of father | 7.4 ± 4.3   | 7.4 ± 4.1      | 0.99  | 0.97–1.03       | .87     |
| Childhood sexual abuse  | 134 (8.6)   | 55 (15.4)      | 0.52  | 0.37–0.72       | <.001   |
| Nongenital              | 50 (3.2)    | 17 (4.8)       | 0.66  | 0.38–1.16       | .15     |
| Genital                 | 54 (3.5)    | 22 (6.2)       | 0.55  | 0.33–0.91       | .02     |
| Intercourse             | 30 (1.9)    | 16 (4.5)       | 0.42  | 0.23–0.77       | .006    |

Odds ratios (OR), P-values and and 95% confidence intervals (95% CI) are shown for life events (including childhood sexual abuse) and for three measures of parenting, taken from the parental bonding instrument (warmth, authoritarianism and protectiveness), in each cases assessed in the mother and father. ORs greater than one indicate that the clinical feature or symptom is more common in patients with melancholia. ORs less than one indicate that the clinical feature or symptom is less common in melancholic patients. MD, major depression.
abnormal dexamethasone suppression test and treatment response) lead Parker to propose a hierarchical model that distinguishes psychotic, melancholic, and nonmelancholic subtypes. Evidence from twin studies supports the existence of melancholia as a quantitatively more severe form of depression, with increased comorbidity, greater number of episodes, lower levels of neuroticism, and an increased genetic loading. Validation of melancholia’s independent status in a different ethnic group would lend further support to its diagnostic validity and might help to resolve whether it is quantitatively or qualitatively different from MD.

Our results from a large clinical population of Chinese women with recurrent depression consistently support the view that melancholia is a more severe form of MD. The pattern of symptom severity, episode duration and comorbidity echoes that previously reported. Furthermore, our finding that childhood sexual abuse is more common in nonmelancholic depression is consistent with the idea that melancholia has more biological features and approximates to an endogenous depression. However, our findings are not entirely consistent with this hypothesis. CSA was the only life event showing the expected pattern; other SLEs were not significantly different between the two categories. Furthermore, two further predictions from the hypothesis that melancholia reflects a more “biological” and less “environmental/neurotic” form of MD were not supported in our sample. That is, we did not find the predicted increased familial loading for depression nor did we replicate findings of decreased neuroticism in patients with melancholia.

These discrepancies may be due to the greater severity of the features of MD in our sample, rather than reflecting characteristics of MD in Chinese patients. Our cases differ from those used in other studies of melancholia in a number of ways: they were ascertained through hospital in- and outpatient services, required to be aged between 30 and 60 years, with two or more episodes of MD, the first of which had to occur when the patient was older than 14 and younger than 50. Our sample is therefore enriched for melancholia or melancholia increasing the risk for MD in families as might be predicted if melancholia were a more “biological/genetic” syndrome. Such a perspective would also predict that melancholic patients should have fewer environmental risk factors. This is seen for childhood sexual abuse but not for overall stressful life events or disturbed parent–child relationships. Finally, melancholic MD with its “biological” roots is sometimes contrasted with “neurotic” depression that is often seen as based in personality disturbances. Our results are clearly inconsistent with this hypothesis. Contrary to what might be expected from this viewpoint, cases of melancholic MD had higher levels of the personality trait of neuroticism than nonmelancholic depressives.

Our study has a number of limitations. First, we used a DSM-IV diagnosis of melancholia, many of whose features overlap with MD. We chose this approach because it remains the most widely used, and, as we pointed out earlier, has been used to identify qualitative, as well as quantitative differences from MD. Second, we relied on a cohort that consists entirely of women with recurrent MD in a treatment setting. We cannot be certain that our conclusions will apply to men, or to those with MD outside of hospital. Third, our assessment is based on a single clinical interview, which, while detailed, is subject to the vagaries of remembrance. Fourth, our assessment of SLRs cannot distinguish the degree to which the observed associations between SLRs and melancholia are a result of SLE exposure increasing risk for melancholia or melancholia increasing the risk for SLRs. Fifth, we assessed all conditions for lifetime occurrence, so that they may not always be coterminal with an episode of MD. Consequently, we cannot be certain that conditions are always comorbid. Finally, we do not have estimates of inter-rater reliability of diagnoses; thus, we caution that there is an unspecified degree of error in estimates of the effect sizes that we observe.

Acknowledgments. All authors declare themselves free from financial involvement or affiliation with any organization whose financial interests may be affected by material in the manuscript. All authors are part of the CONVERGE consortium (China, Oxford, and VCU Experimental Research on Genetic Epidemiology) and gratefully acknowledge the support of all partners in China.
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