Research report

Family study of subthreshold depressive symptoms: risk factor for MDD?

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Received 30 January 2002; accepted 3 April 2002

Abstract

Background: Family study data from a large community sample of young adults and their first-degree relatives were used to examine three questions regarding the relation between subthreshold depression (SubD) and major depressive disorder (MDD): (a) is there an elevated rate of MDD in the relatives of probands with SubD? (b) does SubD aggregate in the families of probands with MDD and SubD? (c) is the relationship between SubD and familial psychopathology specific to MDD? Methods: A total of 941 probands were assessed twice during adolescence and then at age 24. Direct and informant information was obtained on 2750 first-degree relatives of 840 probands. Results: The rate of MDD in the relatives of probands with SubD (24.3%) was significantly lower than the relatives of probands with MDD (31.9%) but was significantly higher than the relatives of probands with no history of mood disorder (NMD; 20.2%). Relatives of MDD, SubD and NMD probands did not differ on rates of SubD (9.0, 9.4 and 9.0%, respectively). Familial aggregation of psychopathology in SubD probands was specific to MDD. Limitations: The primary limitation may be the absence of a standardized definition and assessment procedure for the SubD category. In addition, the sample size, although large, may have been inadequate to detect smaller associations or the moderating effects of sex. Conclusion: The results data support the view that SubD occupies a milder position on a continuum with MDD.

1. Introduction

In recent years there has been considerable interest in 'subthreshold' forms of psychopathology, and particularly in subthreshold depression (SubD) (Akiskal et al., 1997; Judd and Akiskal, 2000; Judd et al., 1994; Pincus et al., 1999). A number of conflicting classification systems have been proposed, which has stymied progress in this area (Judd and Akiskal, 2000). This term has generally been used to refer to individuals with depressive symptomatology that falls short of the criteria for a diagnosis of Major Depressive Disorder (MDD). It is closely related to the categories of Minor Depressive Disorder (Beck and Koenig,
1996; Spitzer et al., 1978), Recurrent Brief Depressive Disorder (Angst et al., 1990), and Mixed Anxiety-Depressive Disorder, all of which are included in the DSM-IV Appendix of Criteria Sets and Axes Provided for Further Study (American Psychiatric Association, 1994). SubD has also been defined by elevated scores on self-report symptom inventories in individuals who fail to meet full criteria for MDD (Coyne, 1994; Gotlib et al., 1995; Lewinsohn et al., 2000).

Numerous studies have reported that SubD is associated with significant functional impairment (Gotlib et al., 1995; Hays et al., 1995; Judd et al., 2000). While these data provide compelling evidence that SubD is a significant clinical and public health problem, they do not directly address the question of the nosological relationship between SubD and MDD. Specifically, is SubD best conceptualized as lying on the milder end of a continuum with MDD, is it a qualitatively distinct condition, or does it have a non-specific association with a variety of forms of psychopathology?

Two of the most widely-used approaches to addressing the nosological relationship between psychopathological conditions are follow-up and family studies. Several studies have demonstrated that persons with SubD are at increased risk for developing MDD over time (Brown et al., 1986; Horwath et al., 1992; Lewinsohn et al., 2000).

Data from research using the family history method (in which diagnostic information about a family member is obtained from an informant) and the family study method (in which diagnostic information about a family member is obtained by direct interview with the family member) also suggest that there may not be a discontinuity between SubD and MDD. Although the family history method has good specificity (i.e. very few ‘false positive’ reports by informants), sensitivity is only moderate (i.e. relatively high rates of ‘false negatives’) and the informant’s report can be biased by his or her history of psychopathology (Chapman et al., 1994; Cohen, 1988).

To our knowledge, five studies employing the family history method have addressed these issues. Remick et al. (1996) reported that the relatives of patients with minor depression had similar rates of mood disorders as the relatives of patients with MDD. In contrast, in a sample drawn from both general medical and psychiatric settings, Sherbourne et al. (1994) found that a significantly greater proportion of patients with MDD had a family history of depression compared to patients with minor depression. In two studies using large community samples, Kessler et al. (1997) and Chen et al. (2000) reported that probands with MDD and probands with minor depression were both significantly more likely than control probands to have family histories of depression. In both cases, the odds ratios for MDD in relatives were substantially higher for probands with MDD than probands with minor depression, but the magnitude of the associations was not directly compared. Finally, in a longitudinal study of a community sample of young adults, Angst et al. (1990) reported that, compared to nondepressed controls, significantly greater proportions of probands with MDD and Recurrent Brief Depression had a family history of depression (defined as receiving treatment for depression), however the two groups of depressed probands did not differ from each other. We are aware of only one study that has used the more rigorous family study method: Kendler and Gardner (1998) reported that the co-twins of index twins with SubD had a significantly higher rate of MDD than the co-twins of nondepressed index twins, but a lower rate of MDD than the co-twins of index twins with MDD.

In the only study that examined the specificity of the familial relationship between SubD and MDD, Kessler et al. (1997) reported that probands with minor depression were significantly more likely than controls to have family histories of generalized anxiety and substance use disorders, but did not differ on family history of antisocial personality disorder. To our knowledge, no studies have examined whether SubD itself aggregates in families.

In this paper, we report the results of a family study of the relationship between SubD and MDD in a large community sample of young adults and their first-degree relatives. We address three questions. First, is there an elevated rate of MDD in the relatives of probands with SubD? If SubD occupies a milder position on a continuum with MDD, the rate of MDD in the relatives of SubD probands should be significantly greater than the rate of MDD in the relatives of probands with no history of mood disorders (NMD), but significantly lower than in the relatives of MDD probands.
Second, does SubD aggregate in the families of probands with MDD and SubD? If SubD is a milder form of MDD, the elevated rate of MDD in the relatives of probands with SubD should be paralleled by an elevated rate of SubD in the relatives of probands with MDD. On the other hand, if SubD is a distinct condition in its own right, we would expect to find a significantly higher rate of SubD in the relatives of probands with SubD than in the relatives of MDD and NMD probands.

Third, is the relationship between SubD and familial psychopathology specific to MDD or is the rate of non-mood disorders in the relatives of SubD probands also elevated? Given that mild depressive symptoms are common in the persons with non-mood disorders (Fechner-Bates et al., 1994), it is important to determine whether SubD is associated with a broad range of psychiatric disorders in relatives.

2. Method

2.1. Participants

2.1.1. Probands

Probands were randomly selected from nine senior high schools in western Oregon. After a thorough description of the study, written informed consent was obtained from the probands and family members. A total of 1709 adolescents (ages 14–18; mean age 16.6, S.D. = 1.2) completed the initial (T1) assessments between 1987 and 1989. The participation rate at T1 was 61%. Approximately 1 year later, 1507 of the adolescents (88%) returned for a second evaluation (T2). Differences between the sample and the larger population from which it was selected, and between participants and those who declined to participate or dropped out of the study before T2, were small (Lewinsohn et al., 1993).

At age 24, all probands with a history of MDD by T2 (n = 360) or a history of non-mood disorders (n = 284), and a random sample of adolescents with no history of psychopathology by T2 (n = 457) were invited to participate in a T3 evaluation. Of the 1101 T2 participants selected for a T3 interview, 941 (85%) completed the age 24 evaluation. The T2 diagnostic groups did not differ on the rate of participation at T3.

2.1.2. Relatives

We assessed lifetime psychopathology in the first-degree relatives (over the age of 13) of the OADP participants in the T3 evaluation. To ensure that at least some data were available even for relatives who could not be directly interviewed, and to supplement the direct interviews, informant data on first-degree relatives were collected from the proband and/or another relative. Our goal was to collect at least two sources of diagnostic data regarding each family member. Of the 1101 probands selected for a T3 interview, family diagnostic information was available for 840 (76%). Of the 941 probands with T3 data, family diagnostic data were available for 802 (85%). There were an additional 38 probands with family diagnostic information who completed the T2 but not the T3 evaluation. For these participants, proband data were only available through T2. Of the 2750 first-degree relatives for whom diagnostic information was collected, direct interviews were obtained from 1744 (63%). At least two sources of data were available for all but 440 (16%) of the family members.

All probands with data on at least one first-degree relative were included in this report except for probands with a history of a nonaffective psychotic disorder, bipolar disorder, or dysthymic disorder with no history of MDD (n = 38 probands and 120 relatives). In addition, to ensure that probands were not in the prodromal phase of an incipient MDD episode, one proband who met criteria for SubD (with three relatives) at the time of the T3 assessment was excluded. The final sample included 387 probands with a history of MDD through age 24 and their 1241 first-degree relatives; 193 probands with a history of SubD (but no lifetime mood disorder diagnoses) and their 650 first-degree relatives; and 221 probands with no history of a mood or psychotic disorder (NMD) through age 24, and their 736 first-degree relatives. The NMD group was comprised of probands with no mental disorder (n = 141) and those who met criteria for non-mood psychopathology (n = 80).

2.2. Definition of SubD

SubD was defined as an episode of depressed mood or loss of interest or pleasure lasting at least 1 week, accompanied by at least two of the seven
DSM-IV associated symptoms of MDD (only one associated symptom was required if both depressed mood and loss of interest/pleasure were present). These criteria are similar to the criteria for Minor Depressive Disorder in the Research Diagnostic Criteria (Spitzer et al., 1978) and DSM-IV (American Psychiatric Association, 1994), differing in that we required more symptoms (three instead of two) but a shorter minimum duration (1 week instead of 2). The lifetime diagnosis of SubD in probands was based on information obtained at the three diagnostic evaluations conducted between entry into the study and age 24. SubD in relatives was assessed in a single diagnostic interview. As the validity of informants’ reports of SubD is unknown, diagnoses of SubD in the relatives were based solely on data from direct interviews. It is important to note that probands and relatives who had ever been diagnosed with MDD were not eligible for a diagnosis of SubD. In other words, the diagnoses of MDD and SubD were mutually exclusive hierarchical categories based on lifetime diagnostic information.

2.3. Diagnostic interviews

2.3.1. Probands

At T1, probands were interviewed with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (Orvaschel et al., 1982), which combined features of the Epidemiologic and Present Episode versions to derive DSM-III-R diagnoses. At T2 and T3, probands were interviewed using the Longitudinal Interval Follow-up Evaluation (LIFE) (Keller et al., 1987), which elicited detailed information about the onset and course of psychiatric disorders since the previous evaluation. To assess interrater reliability, independent raters reviewed audiotapes of a random sample of interviews. The reliability of lifetime diagnoses of MDD was excellent (T1, $k=0.86, n=233$; T1–T2, $k=0.75, n=166$; T2–T3, $k=0.86, n=178$). Mean interrater reliability at the level of individual MDD symptoms (evaluated at T1) also was excellent, $k=0.85$ (range = 0.79–0.90).

2.3.2. Relatives

Parents and siblings over the age of 18 were interviewed using the Structured Clinical Interview for DSM-IV (SCID), Nonpatient version (First et al., 1997b) and the antisocial and borderline personality disorder sections of the SCID for Axis II Personality Disorders (First et al., 1997a). Siblings between the ages of 14 and 18 were interviewed with the K-SADS, modified for DSM-IV. All interviews were conducted without knowledge of proband diagnoses. To reduce the chances of interviewers being biased by patterns of psychopathology within a family, no interviewer evaluated more than two members of the same family. Independent raters reviewed audiotapes of interviews with a random sample of 184 relatives. Interrater reliability was excellent for lifetime diagnoses of MDD ($k=0.94$), anxiety disorders ($k=0.90$), alcohol abuse or dependence ($k=0.86$), and drug abuse or dependence ($k=0.89$). There were too few cases to calculate interrater reliability for antisocial and borderline personality disorder. Mean interrater reliability at the level of individual MDD symptoms was $k=0.92$ (range = 0.58–1.00). Rates of some disorders (e.g. eating disorders, somatization disorders) were too low to examine as separate categories.

Family history data were collected using the Family Informant Schedule and Criteria (FISC) (Mannuzza and Fyer, 1990) supplemented with all items necessary to derive DSM-IV diagnoses. Independent raters reviewed audiotapes of 242 randomly selected informant interviews. Interrater reliability ranged from fair to excellent for lifetime diagnoses of MDD ($k=0.90$), anxiety disorders ($k=0.77$), alcohol abuse or dependence ($k=0.90$), drug abuse or dependence ($k=0.82$), antisocial personality disorder ($k=0.56$), and borderline personality disorder ($k=1.00$).

Proband interviews at T3 and interviews with relatives and informants were conducted by telephone, which generally yields comparable results to face-to-face interviews (Rohde et al., 1997; Sabin et al., 1993; Wells et al., 1988). Most of the interviewers had advanced degrees in clinical or counseling psychology or social work, and several years of clinical experience. All interviewers were trained in the use of the SCID and FISC and completed a minimum of two supervised training interviews, achieving $k>0.80$ for concordance between their symptom ratings and those of the supervisor.

Lifetime best-estimate diagnoses (Leckman et al., 1982) were independently derived for all relatives.
using DSM-IV criteria by the four senior diagnosticians on the project. Two diagnosticians, blind to proband diagnoses, reviewed all available data for each participant. Disagreements were resolved by consensus following the guidelines in Klein et al. (1994). Interrater reliability, based on the independently derived best-estimate diagnoses prior to the resolution of any discrepancies, was good to excellent for MDD ($k = 0.91$), anxiety disorders ($k = 0.94$), alcohol abuse or dependence ($k = 0.97$), drug abuse or dependence ($k = 0.96$), antisocial personality disorder ($k = 0.80$), and borderline personality disorder ($k = 0.72$).

2.4. Data analysis

Probands with no history of psychopathology were undersampled in the T3 follow-up, therefore we weighted relatives as a function of the probability of the probands’ selection for the T3 follow-up. Descriptive features were compared between groups using $\chi^2$ tests for categorical variables and analysis of variance for continuous variables. Rates of MDD in relatives were analyzed using Cox proportional hazards (PH) models. Rates of SubD in relatives were analyzed using multiple logistic regression (LR) models, as we did not have data on the age of onset of the first SubD in relatives. LR, rather than PH, models were also used to compare rates of non-mood disorders in relatives because we focused on higher order, aggregate categories (e.g. any anxiety disorder, any substance use disorder). As many relatives had several specific diagnoses with different ages of onset within each higher order category, any decision rule to select which age of onset to employ would have been arbitrary.

Two sets of comparisons were conducted to examine each issue: (1) relatives of SubD probands versus relatives of MDD probands; and (2) relatives of SubD probands versus relatives of NMD probands.

Relatives were clustered within families rather than comprising independent observations, hence the use of standard PH and LR models would underestimate the standard errors, increasing the chance of Type 1 errors. Therefore, we estimated the PH and LR models using Taylor series linearization (or generalized estimating equations), which take the clustered structure of the data into account (King et al., 1996). The models were adjusted for proband sex, relative sex, relative generation (parent versus sibling), and for analyses based on best-estimate diagnoses, whether the relative was directly interviewed. As all probands were in the same age range and recruited during the same period, relative generation also serves as a close approximation to birth cohort, with parents representing the older, and siblings the younger, cohort. N values varied slightly between analyses due to missing data.

We ran a series of preliminary models that included terms for the interactions between group and proband sex and between group and relative sex. The number of significant interactions was no more than would be expected by chance, hence these data are not reported.

3. Results

3.1. Descriptive characteristics

Demographic characteristics of the probands and their relatives are shown in Table 1. The proband groups differed significantly on gender, $\chi^2 (2) = 47.40$, $P < 0.001$, with a greater proportion of females in the MDD than the NMD groups, and the SubD group

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Descriptive characteristics of the probands and their relatives</th>
</tr>
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<tbody>
<tr>
<td>Variable</td>
<td>Proband group</td>
</tr>
<tr>
<td></td>
<td>MDD</td>
</tr>
<tr>
<td>Probands</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>387</td>
</tr>
<tr>
<td>Age at T1, M (S.D.)</td>
<td>16.7 (1.1)</td>
</tr>
<tr>
<td>Female*** (%)</td>
<td>69.4a</td>
</tr>
<tr>
<td>White (%)</td>
<td>90.7</td>
</tr>
<tr>
<td>Relatives</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>1,241</td>
</tr>
<tr>
<td>Direct interview** (%)</td>
<td>59.9a</td>
</tr>
<tr>
<td>Age, M (S.D.)</td>
<td>40.3 (13.5)</td>
</tr>
<tr>
<td>Mothers (%)</td>
<td>31.2</td>
</tr>
<tr>
<td>Fathers (%)</td>
<td>30.5</td>
</tr>
<tr>
<td>Sisters (%)</td>
<td>19.0</td>
</tr>
<tr>
<td>Brothers (%)</td>
<td>19.3</td>
</tr>
</tbody>
</table>

Abbreviations: MDD, Major Depressive Disorder; SubD, Sub-threshold Depression; NMD, No history of mood disorder. Means or percentages with different superscripts differ significantly at $P < 0.05$. **, $P < 0.01$; ***, $P < 0.001$. 
falling in between; all three groups differed significantly from each other. The proband groups did not differ on age or race.

The relative groups differed significantly on the proportion who received direct interviews, \( \chi^2(2) = 14.69, P < 0.01 \). The proportion of relatives with direct interviews was greatest among the relatives of NMD probands, lowest among relatives of MDD probands, and intermediate for relatives of SubD probands; the MDD group differed significantly from the other two groups, but the NMD and SubD groups did not differ significantly from each other. The three groups of relatives did not differ on age, gender, or relationship to the proband.

3.2. Rates of MDD in relatives

Cox PH models were used to compare rates of MDD in the relatives of the SubD and MDD probands, and between the relatives of the SubD and NMD probands. The results are shown in Table 2. Controlling for proband sex and relative sex, generation, and interview status, the relatives of MDD probands had a significantly higher rate of MDD than the relatives of SubD probands, hazard ratio (HR) = 1.39, 95% confidence interval (CI) = 1.11–1.75, \( P < 0.005 \). In addition, the rate of MDD in the relatives of the SubD probands was significantly higher than the MDD rate in relatives of the NMD probands, HR = 1.33, CI = 1.01–1.76, \( P = 0.04 \).

Table 2
Rates of lifetime diagnoses in relatives of MDD, SubD and NMD probands

<table>
<thead>
<tr>
<th>Diagnosis in relative</th>
<th>Proband group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MDD ((n=387))</td>
</tr>
<tr>
<td>MDD^a</td>
<td>31.9</td>
</tr>
<tr>
<td>SubD</td>
<td>9.0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>13.3</td>
</tr>
<tr>
<td>Substance use^b</td>
<td>39.6</td>
</tr>
<tr>
<td>Antisocial/borderline personality</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Abbreviations: MDD, Major Depressive Disorder; SubD, Sub-threshold Depression; NMD, No History of Mood Disorder.

^a MDD vs. SubD, \( P < 0.005 \); SubD vs. NMD, \( P < 0.05 \).

^b MDD vs. SubD, \( P < 0.05 \).

3.3. Rates of SubD in relatives

LR models using only relatives with direct interviews were used to compare rates of SubD between relative groups. Proband gender and relative gender and generation were included as covariates in the model. As shown in Table 2, the relatives of SubD probands did not differ significantly on rates of SubD from either the relatives of the MDD probands, odds ratio (OR) = 1.01, CI = 0.69–1.49, \( P = 0.94 \), or the relatives of the NMD probands, OR = 0.90, CI = 0.60–1.35, \( P = 0.62 \).

3.4. Rates of non-mood disorders in relatives

LR models were used to compare rates of three categories of non-mood disorders between relative groups, with proband gender and relative gender, generation, and interview status included as covariates. Rates are shown in Table 2. The relatives of probands with MDD had a significantly higher rate of substance use disorders than the relatives of SubD probands, OR = 1.39, CI = 1.01–1.91, \( P = 0.04 \). The relatives of MDD and SubD probands did not, however, differ on rates of anxiety disorders (OR = 1.13, CI = 0.77–1.64, \( P = 0.63 \)) or borderline and/or antisocial personality disorder (OR = 1.63, CI = 0.79–3.36, \( P = 0.18 \)). Similarly, the relatives of SubD and NMD probands did not differ on rates of anxiety (OR = 1.32, CI = 0.88–1.98, \( P = 0.18 \)), substance use disorders (OR = 1.27, CI = 0.92–1.76, \( P = 0.14 \)), or antisocial or borderline personality disorders (OR = 1.25, CI = 0.47–3.33, \( P = 0.68 \)).

4. Discussion

We conducted a family study examining the relationship between SubD and MDD and nonaffective disorders using a large community sample of young adults. Three major findings were obtained. First, the rate of MDD in the first-degree relatives of probands with SubD was significantly lower than MDD rates in the relatives of probands with MDD, but were significantly higher than the relatives of NMD probands. These findings are consistent with most previous family (Kendler and Gardner, 1998) and family history (Chen et al., 2000; Kessler et al.,
1997; Sherbourne et al., 1994) studies of SubD, as well as with studies reporting an elevated rate of minor depression in the relatives of probands with MDD (Maier et al., 1992; Weissman et al., 1984). Taken together with studies finding that SubD predicts the subsequent onset of a first lifetime MDD episode (Horwath et al., 1992), these data provide strong support for the view that SubD occupies a milder position on a continuum with MDD.

Second, an unexpected finding of the present study is that the relatives of MDD, SubD, and NMD probands did not differ on rates of SubD. In other words, an episode of MDD in the probands was not associated with an increased rate of SubD in the relatives. Does this mean that MDD in the probands does not create a vulnerability for SubD in the relative? Our data suggest an affirmative answer to this question but with the important caveat that our operational definition of SubD differs from what has been used in other studies in this area (e.g. Judd and Akiskal, 2000), in which the subthreshold diagnostic category has been applied to individuals with MDD who continue to experience depressive symptoms a significant proportion of the time, even when no longer meeting full criteria for MDD diagnosis. We maintain that, for the specific purposes of the present study, our operational definitions of MDD and SubD as mutually exclusive disorders was warranted. This important negative finding, if replicated, qualifies support for the continuum perspective, which predicts an increased rate of SubD in the relatives of MDD probands. However, our findings are also inconsistent with the view that SubD and MDD are qualitatively distinct disorders.

Third, the familial aggregation of psychopathology in relatives of SubD probands was specific to MDD. That is, the relatives of SubD probands did not have elevated rates of anxiety, substance use, and antisocial and borderline personality disorders compared to the relatives of MDD and NMD probands. Thus, contrary to the family history data reported by Kessler et al. (1997), subthreshold depressive symptoms were not associated with a familial liability for psychopathology in general or for particular non-mood disorders. It should be noted, however, that our findings were in the same direction as results reported in the study by Kessler et al. which was based on a sample that was several times larger than the present study. A lack of diagnostic specificity might have been detected given a much larger sample size.

In evaluating our findings, several limitations should be considered. First, data were not available on the interrater reliability of our diagnoses of SubD (although interrater agreement at the level of MDD symptoms was very good). Second, onset age data for the SubD episodes were not consistently obtained in either proband or relatives samples. Unlike MDD, which tends to first occur in adolescence and young adulthood (Burke et al., 1990), we do not know the period of greatest risk for SubD. It is possible that the probands are relatively early in the period of risk for SubD and that the familial aggregation of SubD might become clearer as our probands get older.

Third, although the group sizes were large for the primary analyses, statistical power may have been too small to detect significant gender interactions. Fourth, given that (a) we had a priori hypotheses for the comparisons on the family member rates of MDD and SubD, and (b) the comparisons for the three non-mood disorder aggregates in the relatives were exploratory, no adjustments to $\alpha$ were made. Thus, the finding of a significant difference between the MDD and SubD probands on the family member rates of substance use disorders was not predicted and needs to be replicated. Lastly, although not a limitation, two design aspects of the study need to be remembered: (a) MDD and SubD were mutually exclusive hierarchical lifetime categories (i.e. if the proband or relative ever had MDD, they were excluded from the SubD category), and (b) the three diagnostic groups did not take comorbid conditions into account. Regarding the first caveat, Judd and Akiskal (2000) have documented the fluctuating, often persistent, course of symptoms after an individual experiences MDD. Regarding the second caveat, future research needs to examine the degree of comorbidity between different categories of subthreshold diagnostic groups (e.g. individuals with SubD and subthreshold alcoholism) and between SubD and other Axis I disorders. To the extent that individuals with SubD have elevated rates of other Axis I psychopathology (at either subthreshold or threshold levels), the clinical importance of the SubD classification will be further enhanced.
In conclusion, these findings support the view that SubD has a strong and specific relationship to MDD from the standpoint of familial aggregation. The present results add to a growing literature suggesting that milder forms of depression are not discrete diagnostic categories but instead are part of a broader spectrum of depression conditions that vary in terms of symptom severity and chronicity. In addition to family studies and epidemiologic research, sleep studies indicate that subthreshold depression conditions share neurophysiological similarities to major affective disorders (Akiskal et al., 1997). The present findings may contribute to empirically-based decisions for depression nomenclature. Taken together with previous epidemiologic, longitudinal, and polysomnographic studies, these data indicate that SubD occupies a milder position on the continuum with MDD, and its occurrence has important clinical implications.

**Acknowledgements**

This work was partially supported by National Institute of Mental Health Grants MH40501, MH50522, and MH52858 (Dr. Lewinsohn).

**References**


