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Family history of mood disorder and characteristics of major depressive disorder: A STAR*D (sequenced treatment alternatives to relieve depression) study

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Abstract

Introduction—Clinicians routinely ask patients with major depressive disorder (MDD) about their family history. It is unknown, however, if patients who report a positive family history differ from those who do not. This study compared the demographic and clinical features of a large cohort of treatment-seeking outpatients with non-psychotic MDD who reported that they did or did not have at least one first-degree relative who had either MDD or bipolar disorder.

Methods—Subjects were recruited for the STAR*D multicenter trial. Differences in demographic and clinical features for patients with and without a family history of mood disorders were assessed after correcting for age, sex, race, and ethnicity.

Results—Patients with a family history of mood disorder (n = 2265; 56.5%) were more frequently women and had an earlier age of onset of depression, as compared to those without such a history (n = 1740; 43.5%). No meaningful differences were found in depressive symptoms, severity, recurrence, depressive subtype, or daily function.

Conclusions—Women were twice as likely as men to report a positive family history of mood disorder, and a positive family history was associated with younger age of onset of MDD in the proband. Consistent with prior research, early age of onset appears to define a familial and, by extension, genetic subtype of major depressive disorder.

Keywords

Family; History; Major depressive disorder

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1. Introduction

Clinicians have long obtained and used patient reported family history to confirm diagnoses. Clinicians believe that patients who present with depressive symptoms are considered more likely to have a true diagnosis of major depressive disorder (MDD) if they report of at least one first-degree relative with a mood disorder. Genetic epidemiological data support this clinical practice, because, compared to the general population, people with a family member with a mood disorder are about 2.8 times more likely to have depression (Sullivan et al., 2000).

Researchers use family history to identify homogeneous subtypes for investigations into pathophysiology and genetics, but require more rigorous assessment of family psychopathology since the validity of patient report can be limited (Orvashel et al., 1982; Chapman et al., 1994). A positive family history has been used to categorize patients who are more likely to have neurophysiological or functional neuroimaging abnormalities (Lewis and McChesney, 1985; Kupfer et al., 1992; Drevets et al., 2002) or to find associations between genes and the diagnosis of MDD (e.g., Maher et al., 2002).

Much of the work on the clinical and research significance of family history of mood disorders was pioneered by Winokur and colleagues (Winokur et al., 1978, 1995; Winokur, 1982; Winokur and Coryell, 1992). They postulated that a familial pure depressive disorder (FPDD) was a specific subtype of major depressive disorder characterized by early age of onset of depressive disorder (before the age of 40), without a family history of alcoholism or antisocial personality disorder. In contrast, depression spectrum disease (DSD) included those with FPDD but who had family members with either alcoholism or antisocial personality. Those depressed patients without a family history of depression, alcoholism, or antisocial personality disorder were considered to have sporadic depressive disorder (SDS). FPDD inpatients were initially found to have a worse course of depression, but subsequent studies showed that FPDD patients had a better course in the hospital and a better 6-month course compared to DSD patients (Zimmerman et al., 1998). FPDD patients were found in another study to have an earlier age of onset and more episodes of depression, but without any major biological differences with the DSD group (Rush et al., 1995).

Other studies have focused on the clinical implications of having family members with mood disorders (i.e., characteristics of outpatients with MDD who have a positive family history of mood disorders compared to those without a family history of mood disorders). A study of twins found that those with depression whose co-twin also had depression had longer depressive episodes, were more impaired, and had more thoughts of death or suicide (Kendler et al., 1999). As for clinical presentation, sibling pairs who were both depressed were found to have slightly or moderately similar depressive symptoms (Korszun et al., 2004). A meta-analysis found that familial depression was associated with earlier onset, more depressive recurrence, greater impairment, longer duration of longest depressive episode, but without any clear pattern of specific depression symptoms or comorbid conditions (Sullivan et al., 2000). Studies that focus on depressed offspring of proband parents with MDD show that these high risk children have an earlier age of onset compared to depressed children without such a family history (Wickramaratne et al., 2000; Kaufman et

al., 2001), and conversely the parents with early onset MDD have more depressed children compared to parents with later onset MDD (Klein et al., 2005). Having a parent and a grandparent with MDD conferred even greater risk on offspring (Weissman et al., 2005).

The purpose of this paper is to assess the clinical implications of the presence of at least one first-degree relative with a history of mood disorder in a large group of outpatients with non-psychotic MDD who participated in the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (Fava et al., 2003; Rush et al., 2004).

2. Methods

2.1. Study description and organization

The rationale and design of STAR*D are detailed elsewhere (Fava et al., 2003; Lavori et al., 2001; Rush et al., 2004). In brief, STAR*D will define prospectively which of several treatments are most effective for outpatients with nonpsychotic MDD with an unsatisfactory clinical outcome to an initial and, if necessary, subsequent treat-ment(s). Eligible and consenting STAR*D enrollees were treated initially with a selective serotonin reuptake inhibitor (citalopram). Those not achieving symptom remission may enter one or more subsequent randomized trials of medications or cognitive therapy. Patients with an adequate clinical response to treatment at any treatment level may enter a 12-month naturalistic follow-up phase.

Clinical sites were identified based on multiple factors including the availability of depressed outpatients, clinicians, administrative support, and minority populations. Nearly half of the clinical sites are primary care settings.

Clinical Research Coordinators (CRCs) located at the clinical sites were trained and certified in implementing the treatment protocol and in data collection methods (e.g., screening procedures, inclusion and exclusion criteria, data collection). CRCs worked closely with participants and clinicians, administered some of the clinician-rated instruments, ensured that all self-rated instruments were completed, and functioned as study coordinators. Research outcome data were collected via telephone interviews with trained Research Outcomes Assessors (ROAs), masked to treatment and to treatment settings, and by telephone-based interactive voice response system (Kobak et al., 1999).

2.2. Study population

Self-declared outpatients presenting at participating clinics and identified by their clinician as having MDD requiring treatment were approached to consider participating in STAR*D. All potential benefits and risks (including possible adverse events) associated with the trial were explained to potential participants prior to obtaining written informed consent. All subjects, 18-75 (inclusive) years of age, who met DSM-IV criteria for single or recurrent non-psychotic MDD, were required to score ≥14 (moderate severity) on the 17-item version of the Hamilton Rating Scale for Depression ($HRS\text{-}D_{17}$) as rated by the CRC to ensure sufficient symptom severity that symptom change could be measured during the trial (Hamilton, 1960).

Patients were excluded who met criteria for bipolar disorder or exhibited psychotic symptoms (lifetime), had a current primary diagnosis of obsessive compulsive or eating disorders, suicidal risk or substance abuse/dependence that required inpatient care, or a seizure disorder or other general medical condition contraindicating medications used in the first two levels of the study. All other psychiatric and medical comorbidities were allowed. Women who were pregnant or breastfeeding were also excluded, as were patients who had not responded to an adequate treatment trial of any study treatment (during their current episode of depression) used in the first two treatment levels. Exclusion criteria were kept to a minimum to ensure that the findings generalized to clinical practice in applied settings.

2.3. Assessments

CRCs collected standard demographic information and self-reported psychiatric history at baseline and rated patients' severity of depressive symptoms on the $HRSD_{17}$. They also evaluated current general medical conditions on the Cumulative Illness Rating Scale (CIRS), a 14-item interview that gauges the severity/morbidity of general medical conditions relevant to different organ systems (Linn et al., 1968). Psychiatric Diagnostic Scale (PDSQ) (Zimmerman and Mattia, 1999) was also used to screen for psychiatric mental disorders. The ROA used a telephone interview at baseline to collect a second $HAMD_{17}$ and the 30-item Inventory of Depressive Symptomatology ($IDS\text{-}C_{30}$)(Rush et al., 1996), a well-studied tool that uses unconfounded items to measure both core criterion diagnostic symptoms and associated symptoms.

Subtypes of depression were defined as endogenous, atypical, and anxious by using selected items from the IDS-C to be consistent with DSM-IV criteria (Novick et al., 2005). For the purpose of this analysis, the STAR*D research group developed a specific definition based on items of the 30-Item Inventory of Depressive Symptom-atology-Clinician-Rated (IDS-C30) (Rush et al., 1986, 1996).

For endogenous depression, the patient must have an IDS-C30 item score of mood reactivity greater than one and at least two of the following criteria: IDS-C30 items quality of mood item score = 3, time of the day mood worsens item score = 1, mood variation item score >1, early morning insomnia item score = 3, psychomotor slowing item score >1 or psychomotor agitation >1, appetite (decreased) item score >1 or weight (decreased) = 3, or outlook (self) item score >1.

For atypical depression, the patient had to have a IDSC30 score of 0, 1, or 2 for mood reactivity, 2 or 3 for leaden paralysis, 2 or 3 for weight gain or increased appetite, 2 or 3 for hypersomnia, and 3 for interpersonal sensitivity. Of note, the IDS mood reactivity item scores 0 for a highly mood reactive individual, and 3 for someone considered to be highly non-reactive. To qualify as having atypical depression, the patients had to be rated as having mood reactivity, and they had to qualify as having at least two of the other four symptoms.

As per previous studies from our group (Fava et al., 2000) and the preliminary report from the STAR*D study (Fava et al., 2004), anxious depression was defined as MDD with high levels of anxiety symptoms (HRSD anxiety/somatization factor score ⩾7). The anxiety/somatization factor, derived from a factor analysis of the $HRSD_{17}$ scale conducted by Cleary

and Guy (1977), includes 6 items from the original 17-item version: (10) anxiety (psychic); (11) anxiety (somatic); (12) somatic symptoms (GI); (13) somatic symptoms (general); (15) hypochondriasis; and (17) insight. The $HRSD_{17}$ obtained at baseline by the ROAs was used to define anxious depression.

2.4. Family history

The patients were asked by the CRCs about psychiatric history of immediate biological family (parent, sibling, half-sibling, or child). They were specifically asked if family members have been diagnosed or treated for depression, bipolar disorder, alcohol or drug abuse. They are also asked if a family member committed suicide. The family history was said to be positive if the subject reported that at least one first-degree relative had been diagnosed with or treated for MDD or bipolar disorder.

2.5. Statistics

Descriptive statistics are presented as percentages for discrete variables and as means (standard deviation) for continuous variables. A χ^2 statistic was used to compare the distribution of discrete characteristics between those with and without a family history of mood disorder. Comparisons of continuous characteristics by family history were completed using the appropriate parametric (*t*-test) or non-parametric (Wilcoxon). Analysis of covariance, logistic, and multinomial regression models was used to determine the independent association of family history, after adjusting for the effects of race, sex, ethnicity and age, with continuous, binary and discrete characteristics. *P*-values less than 0.05 were considered to indicate a statistically significant association. Because these analyses were intended to be exploratory, no adjustments were made for multiple comparisons.

3. Results

With 3891 available subjects, variables associated with a positive family history of mood disorder were female sex, white race, and non-Hispanic ethnicity (Table 1). Prior to adjustments, those with a positive family history were more likely white, less likely black, more likely female, more likely employed, less likely married, and more likely to be seen in psychiatric treatment settings. They were also more likely to have their initial major depressive episode before age 18 (and before age 25).

After adjusting for sex, race, ethnicity, and age, the only characteristic that distinguished those with and without a family history of mood disorders was earlier age of onset in those with a family history (see Table 1).

Those with a family history of mood disorder were younger and were ill for a longer time. Otherwise, both groups had similar years of education, similar levels of general medical conditions, length of current episode, severity of depression, quality of life, and functioning (Table 2).

Those with positive family history were significantly more likely to meet PDSQ criteria for generalized anxiety disorder, though adjusted odds ratios were low, ranging from 1.2 to 1.4

(Table 3). No differences were found in the proportion with anxious, endogenous or atypical depressive subtypes for those with a family history of mood disorder. When the results were examined separately for those patients with a family history of bipolar disorder (351/4005; 8.8% of the overall group and of those with a family history of mood disorder 351/2265; 15.5%), none of the findings changed.

While no clinically useful presenting symptoms differentiated those with a positive family history (Table 4), a few symptoms were significantly more frequent in those with a family history of depression, but the odds ratios for these differences were small.

4. Discussion

This study assessed the demographic and clinical features associated with a patient report of a positive family history (in first-degree relatives) of a mood disorder in a large cohort of highly representative outpatients with non-psychotic MDD who enrolled in STAR*D. The main findings were that a positive family history was reported by over half of the patients. Those who reported a family history of mood disorders were more frequently women, and, after correcting for age, sex, race and ethnicity, family history was more likely associated with an earlier age of onset of the first major depressive episode (about 5.7 years earlier). Otherwise, no substantial symptomatic or functional differences were found between the two groups. These results strongly suggest that clinical presentation of MDD is not related to patient report of first-degree family history.

Why would women more frequently report that their family members have a mood disorder? Genetic epidemio-logical studies strongly suggest the lack of any sex relationship to heritability (Sullivan et al., 2000). But these conclusions arise from controlled, population-based studies. The current study is from a treatment-seeking cohort, a cohort that introduces a different set of biases. Since those with a positive family history are more likely to seek treatment than those without (Kendler, 1995; Sullivan et al., 1996), one possible cause of the sex difference is that women with a family history of mood disorder may be more likely to seek treatment than men with a similar family history. Another possibility is that men may be less aware of mood disorders in family members. That half of this treatment-seeking cohort reported a family history of mood disorder is consistent with other studies (e.g., Sullivan et al., 1996).

Why would earlier age of onset be related to family history? Out of six studies included in a meta-analysis, four found an association between family aggregation of MDD and early age of onset of depression in the proband (Sullivan et al., 2000). As Sullivan and colleagues point out, it is essential to control for the cohort effect, i.e., since the 1940s, the age of onset of depression has been decreasing (Klerman and Weissman, 1989; Kessler et al., 2003). We found an earlier age of onset by about 6 years, and more frequent age of onset <18 or <25 after correcting for current age in those who reported that a first-degree relative had a mood disorder. This correction should be sufficient to correct for the cohort effect. As reviewed by Levinson (2005), previous studies that explored the relative risk of depression given the early age of onset defined an early age of onset at the age of 30 or earlier. Our results refine this distinction further by showing that the age of onset of this treatment-seeking cohort was

below 30 and that those who report a family history of mood disorder had an onset of depression in their early 1920s, while those who did not report family members with a mood disorder had an onset in their late 1920s. In a population-based study, Kendler and colleagues (2005b) found that female twins with a co-twin with major depression were at higher risk for major depression. Early age of onset of major depression was associated with increased risk in the co-twin, with a complex relationship that decreased in a non-linear pattern between the ages of 15 and 35 and flattened out thereafter.

Overall, we did not find any substantial difference between those with and without a reported family history of mood disorders in terms of severity of depression, specific depressive symptoms or subtypes, comorbid conditions, functioning, or course (recurrence). While a few of these variables achieved statistical significance, the absolute differences and odds ratios were quite small. Thus, the few differences that were found were not of clinical significance. Since patients with a positive family history had slightly higher number of depressive episodes that were not statistically significant after adjusting for sex, age, race and ethnicity, it is possible that the number of episodes, age, and age of onset are all closely related. In contrast, a genetic segregation analysis found a familial relationship between those with a combination of early age of onset (<age 25) and recurrent depression (>2 episodes) (Maher et al., 2002). Additionally, a study of adolescents and young adults with major depression in the community found that recurrence and impairment were associated with higher rates of major depression in the probands' parents (Lieb et al., 2002). Appetite disturbance and excessive guilt were previously found to distinguish those with family members with major depression (Leckman et al., 1984). It is possible that in the treatment-seeking cohort that we studied, those with early age of onset, greater impairment, and specific symptoms had more depressive episodes, such that, after correction for the age of onset, the no statistical effect was found between these variables and positive family history of mood disorder.

The major limitation of this study was that study personnel asked patients about first-degree family history of mood disorder without directly interviewing family members — this limitation could explain differences from studies that used structured interviews for family history. Note that the purpose of this study was not to assess the rates of family members with depression, but instead to compare those who reported that their family members were affected with those who did not. Nevertheless, recent studies that used more sensitive, validated, direct interviews of family members have found that the rates of depression in first-degree family members of probands with major depression range from 23.3% to 26.2% (Klein et al., 2001) of a young adult community sample to 39.3% and 24.5% case-wise concordance in a community sample of monozygotic and dizygotic twins, respectively (Kendler et al., 2005). While non-structured inquiry of family history from probands may have insufficient specificity (Orvashel et al., 1982; Chapman et al., 1994; Kendler and Roy, 1995; Duggan et al., 1998), the strength of this approach is that this method is used clinically and has ecological validity. In addition, it is well known that patient reports of family history typically underestimate the actual incidence (Andreasen et al., 1986; Weissman et al., 2000). As such, the few differences that we found can be considered to be robust. On the other hand, our failure to find additional differences may, in theory, be attributed to the method (patient report) used to designate the family history of each subject.

5. Conclusions

Patient report of positive family history of mood disorder appears associated with younger age of onset probands with major depressive disorder and twice as frequent among women compared to men, but not associated with a distinct and homogeneous phenotype. Consistent with prior research, early age of onset appears to define a familial and, by extension, genetic subtype of major depressive disorder. Future genetic studies should consider a heritable phenotype that includes family history, early age of onset and recurrence along with gene-environment interactions (Caspi et al., 2003; Kendler et al., 2005a,).

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Table 1

Association of family history of mood disorder and categorical baseline demographic variables and age of onset of MDD

Characteristics	Mood disorder		*P*-value	Adjusted *P*-value
	No (%) *n* = 1740 (43.5%)	Yes (%) *n* = 2265 (56.5%)		
Setting			0.0411	0.5938
Primary	40.8	37.6		
Specialty	59.2	62.4		
Race			<0.0001	–
White	69.7	80.3		
Black	23.1	13.3		
Others	7.3	6.4		
Ethnicity – Hispanic			0.0003	–
No	85.2	89.1		
Yes	14.8	10.9		
Sex			<0.0001	–
Male	42.5	33.3		
Female	67.5	66.7		
Marital status			0.0120	0.8632
Never married	27.5	31.6		
Married	42.4	40.3		
Divorced	26.2	25.4		
Widowed	3.9	2.7		
Employment status			0.0016	0.4141
Employed	54.7	59.3		
Unemployed	38.3	35.8		
Retired	7.0	4.9		
Age at onset of 1st MDE			<0.0001	<0.0001
<18 years	27.3	44.7		
⩾18 years	72.7	55.3		
Age at onset of 1st MDE			<0.0001	<0.0001
<25 years	48.0	65.6		
⩾25 years	52.0	34.4		

Adjusted for race, sex, ethnicity and age.

Table 2

Association of family history of mood disorder and continuous demographic and clinical variables

Characteristics	Mood disorder				Unadjusted *P*-value	Adjusted *P*-value
	No *n* = 1740 (43.5%)		Yes *n* = 2265 (56.5%)			
	Mean	SD	Mean	SD		
Age (years)	41.9	13.4	39.4	13.1	<0.0001	–
Education (years)	13.3	3.4	13.6	3.1	0.0053	0.2843
General medical conditions						
Categories endorsed	2.9	2.2	3.0	2.3	0.3355	<0.0001
Total score	4.3	3.8	4.1	3.6	0.0555	0.0591
Severity index	1.3	0.7	1.2	0.6	<0.0001	0.2371
Age at onset of 1st MDE	28.7	15.1	23.1	13.4	<0.0001	<0.0001
Number of episodes	5.7	11.3	6.0	11.3	<0.0001	<0.0001
Length of current episodes (months)	23.8	47.5	25.1	55.1	0.6771	0.1795
Length of illness (years)	13.3	12.6	16.4	13.3	<0.0001	<0.0001
Severity of depression						
$HRSD_{17}$ (ROA)	19.9	6.6	20.0	6.5	0.3645	0.0597
$IDSC_{30}$ (ROA)	35.3	11.6	35.8	11.4	0.2444	0.1066
Quality of life						
WSAS	23.3	9.6	23.7	9.0	0.2826	0.1305
Q-LES-Q	42.0	15.4	41.6	15.2	0.4339	0.1170
SF-12						
Physical	48.3	12.3	50.1	11.7	<0.0001	0.2715
Mental	27.4	8.9	26.2	8.5	<0.0001	0.1344

0 means health problems had no effect on work. 10 means health problems completely prevented from work. MDE, Major Depressive Episode; HRSD, Hamilton Rating Scale for Depression; ROA, Research Outcomes Assessor; IDSC, Inventory of Depression Symptomatology – Clinician Rated; WSAS, Work and Social Adjustment Scale; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire; SF-12, Short-Form Health Survey. Adjusted for race, sex, ethnicity and age.

Table 3

Association of family history of mood disorder with PDSQ diagnoses of comorbid axis I disorders (using 90% specificity)

PDSQ	Mood disorder		Unadjusted		Adjusted	
	No (%) *n* = 1740 (43.5%)	Yes (%) *n* = 2265 (56.5%)	OR	*P*-value	OR	*P*-value
GAD	18.7	22.6	1.3	0.0029	1.3	0.0029
OCD	15.1	13.0	0.8	0.0561	1.0	0.8554
Panic	12.4	11.7	0.9	0.5117	1.0	0.9976
Social phobia	26.9	30.9	1.2	0.0059	1.2	0.0301
PTSD	19.8	16.3	0.8	0.0042	0.8	0.0823
Agoraphobia	11.2	10.7	0.9	0.6116	1.1	0.5205
Alcohol abuse	10.4	12.9	1.3	0.0167	1.4	0.0010
Drug abuse	6.8	8.2	1.2	0.0851	1.3	0.0688
Somatoform	2.5	2.3	0.9	0.7139	0.9	0.8177
Hypochondriasis	4.8	3.8	0.8	0.1099	0.9	0.6599
Bulimia	10.8	13.4	1.3	0.0149	1.1	0.2457

Adjusted for race, sex, ethnicity and age.

Table 4

Baseline $IDSC_{30}$ (ROA) – absence/presence of mood disorder

$IDSC_{30}$	Mood disorder				Unadjusted		Adjusted	
	No *n* = 1740 (43.5%)		Yes *n* = 2265 (56.5%)					
	Absent (%)	Present (%)	Absent (%)	Present (%)	OR	*P*-value	OR	*P*-value
Sleep onset insomnia	30.8	69.2	32.8	67.2	0.9	0.1861	0.9	0.4548
Mid-nocturnal insomnia	18.6	81.4	19.3	80.7	0.9	0.5546	1.1	0.5081
Early morning insomnia	45.5	54.5	48.4	51.6	0.9	0.0741	1.0	0.9166
Hypersomnia	77.1	22.9	73.9	26.1	1.2	0.0306	1.0	0.7479
Mood – sad	3.2	96.8	2.4	97.6	1.4	0.1355	1.3	0.2150
Mood – irritable	19.9	80.1	17.5	82.5	1.2	0.0688	1.1	0.1886
Mood – anxious	19.7	80.3	17.0	83.0	1.2	0.0365	1.2	0.0218
Reactivity of mood	29.2	70.8	24.8	75.2	1.3	0.0028	1.2	0.0072
Mood variation	80.0	20.0	75.8	24.2	1.3	0.0025	1.3	0.0059
Quality of mood	26.4	73.6	24.3	75.7	1.1	0.1367	1.1	0.3085
Appetite – decreased	54.6	45.4	55.5	44.5	0.9	0.5945	1.0	0.9421
Appetite – increased	80.1	19.9	76.7	23.3	1.2	0.0125	1.2	0.0476
Weight – decrease	68.4	31.6	69.9	30.1	0.9	0.3093	1.0	0.7855
Weight – increase	78.3	21.7	76.0	24.0	1.1	0.1040	1.1	0.1446
Concentration/decision making	10.2	89.8	9.3	90.7	1.1	0.3671	1.1	0.4576
Outlook – self	21.0	79.0	17.9	82.1	1.2	0.0170	1.1	0.1982
Outlook – future	24.3	75.7	22.3	77.7	1.1	0.1526	1.2	0.2264
Suicidal ideation	52.7	47.3	51.4	48.6	1.1	0.4176	1.1	0.2707
Involvement	14.1	85.9	15.1	84.9	0.9	0.3872	0.9	0.2703
Energy/fatigability	10.6	89.4	9.8	90.2	1.1	0.4283	1.1	0.7329
Pleasure/enjoyment	28.4	71.6	28.9	71.1	1.0	0.7684	1.0	0.8502
Sexual interest	37.4	62.6	34.8	65.2	1.1	0.1029	1.1	0.0715
Psychomotor slowing	37.1	62.9	37.1	62.9	1.0	0.9695	1.1	0.3521
Psychomotor agitation	38.3	61.7	37.0	63.0	1.1	0.4131	1.1	0.4255
Somatic (pain) complaints	23.3	76.7	23.5	76.5	1.0	0.9252	1.0	0.7105
Sympathetic arousal	32.1	67.9	31.6	68.4	1.0	0.7452	1.1	0.1710

IDSC$_{30}$	Mood disorder				Unadjusted		Adjusted	
	No *n* = 1740 (43.5%)		Yes *n* = 2265 (56.5%)					
	Absent (%)	Present (%)	Absent (%)	Present (%)	OR	*P*-value	OR	*P*-value
Panic/phobic symptoms	60.9	39.1	62.5	37.5	0.9	0.3139	1.0	0.7663
Gastrointestinal	58.8	41.2	57.0	43.0	1.1	0.2711	1.1	0.1584
Interpersonal sensitivity	41.0	59.0	37.5	62.5	1.2	0.0296	1.1	0.3594
Leaden paralysis/physical energy	55.2	44.8	55.5	44.5	1.0	0.8734	1.1	0.3084

Adjusted for race, sex, ethnicity and age.