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

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Abstract

Background—Clinicians routinely ask patients with non-psychotic major depressive disorder (MDD) about their family history of suicide. It is unknown, however, whether patients with a family member who committed suicide differ from those without such a history.

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Conflict of interest

No conflict declared.

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Methods—Patients were recruited for the STAR*D multicenter trial. At baseline, patients were asked to report first-degree relatives who had died from suicide. Differences in demographic and clinical features for patients with and without a family history of suicide were assessed.

Results—Patients with a family history of suicide ($n = 142/4001$; 3.5%) were more likely to have a family history of MDD, bipolar disorder, or any mood disorder, and familial substance abuse disorder, but not suicidal thoughts as compared to those without such a history. The group with familial suicide had a more pessimistic view of the future and an earlier age of onset of MDD. No other meaningful differences were found in depressive symptoms, severity, recurrence, depressive subtype, or daily function.

Conclusions—A history of completed suicide in a family member was associated with minimal clinical differences in the cross-sectional presentation of outpatients with MDD. Limitations of the study include lack of information about family members who had attempted suicide and the age of the probands when their family member died. STAR*D assessments were limited to those needed to ascertain diagnosis and treatment response and did not include a broader range of psychological measures.

Keywords

Family history; Suicide; Major depressive disorder

1. Introduction

Major depressive disorder (MDD) is a risk factor for completed suicide and those who complete suicide frequently have MDD. Yet, MDD and suicide have distinct heritable components (Brent and Mann, 2005; Mann et al., 1999; Roy, 1983). Those with MDD with familial suicidal ideation, suicidal behavior, or completed suicide (which, for brevity, can be referred to as familial suicidality) may or may not have distinct clinical characteristics such as greater severity of MDD or greater probability of suicidality.

Suicidality results from a complex and heterogeneous mix of impulsivity, intolerance of negative affect, low frustration tolerance, stereotypical dysfunctional thoughts and cognitive distortions, substance abuse, and intolerable psychic pain, each of which is not necessarily part of the MDD syndrome (Brent et al., 2002; Goodwin et al., 2004). Suicidality may have a heritable component independent of psychiatric diagnosis (Brent et al., 2004; Qin et al., 2002, 2003). For example, tryptophan hydroxylase (Pooley et al., 2003) and brain derived neurotrophic factor genes are associated with suicidality (Dwivedi et al., 2002). Suicidality has also been associated with distinct specific neurotransmitter and receptor profiles (e.g., Asberg, 1997; Correa et al., 2000).

Because clinicians ask patients about suicide in family members as part of routine evaluations, it would be important to assess if such a history has any clinical relevance. 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 completed suicide for 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). STAR*D was designed to define prospectively which of several treatments are most effective for outpatients with nonpsychotic MDD who have had an unsatisfactory clinical outcome to an initial and, if necessary, subsequent treatment(s). Eligible and consenting STAR*D enrollees were treated initially with a selective serotonin reuptake inhibitor (citalopram). Participants who did not achieve symptom remission could enter one or more subsequent randomized trials of medications or cognitive therapy. Those that achieved an adequate clinical response could enter a 12-month naturalistic follow-up phase.

The STAR*D infrastructure included the National Coordinating Center in Dallas, the Data Coordinating Center in Pittsburgh, and 14 regional centers across the United States. Each regional center oversaw implementation of the protocol at two to four clinical sites that were identified based on the availability of outpatients with depression, clinicians, administrative support, and minority populations. The clinical sites included 18 primary care and 21 psychiatric care settings. Clinical Research Coordinators (CRCs) located at the clinical sites were trained and certified in implementing treatment and research procedures. 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 a telephone-based interactive voice response system (Kobak et al., 1999).

2.2. Study population

Between July 2001 and April 2004, STAR*D enrolled self-declared outpatients 18–75 years of age (inclusive) who presented at participating clinics and were diagnosed by their clinician as having single or recurrent nonpsychotic MDD by DSM-IV criteria (American Psychiatric Association, 1994) that required treatment. STAR*D enrolled participants with a score > 14 (moderate severity) on the 17-item Hamilton Rating Scale for Depression (HRSD₁₇) (Hamilton, 1960) as rated by the CRC, to ensure sufficient symptom severity that symptom change could be measured during the trial. All potential benefits and risks (including possible adverse events) associated with the trial were explained to potential participants prior to obtaining written informed consent.

Exclusion criteria included a diagnosis of bipolar disorder or the presence of psychotic symptoms (life-time), a current primary diagnosis of obsessive compulsive or eating disorder, suicidal risk or substance abuse/dependence that required inpatient care, or a seizure disorder or other general medical condition that contraindicated medications used in the first two levels of the study. All other psychiatric and medical comorbidities were allowed. Women who were pregnant, breastfeeding or planning to conceive in the nine months subsequent to study entry were also excluded, as were patients who had not responded (during their current episode of depression) to an adequate treatment trial of any

study treatment used in the first two levels of the study. Exclusion criteria were kept to a minimum to ensure that findings were generalizable to clinical practice in applied settings.

2.3. Assessments

CRCs collected standard demographic information and self-reported psychiatric history at baseline and rated the severity of participants' depressive symptoms using the HRSD₁₇. The self-report Psychiatric Diagnostic Screening Questionnaire (PDSQ) (Zimmerman and Mattia, 2001a,b) was collected at baseline to assess the burden of psychiatric comorbidities. The ROA used a telephone interview at baseline to collect a second HRSD₁₇ and the 30-item Inventory of Depressive Symptomatology – Clinician-rated (IDS-C₃₀) (Rush et al., 1996, 2000; Trivedi et al., 2004), a well-studied tool that uses unconfounded items to measure both core criterion diagnostic symptoms and associated symptoms. On the IDS-C₃₀, suicidal ideation was classified into one of four categories: (1) does not think of suicide or death, (2) feels life is empty or is not worth living, (3) thinks of suicide/death several times a week for several minutes and (4) thinks of suicide/death several times a day in depth, or has made specific plans, or attempted suicide.

2.4. Family history

Participants were asked for information regarding the psychiatric history of their immediate biological family members (parents, siblings, half-siblings, and/or children). They were specifically asked if any family member (s) had been diagnosed or treated for depression, bipolar disorder, alcohol or drug abuse. The family history of mood disorder was recorded as positive if the participant reported that at least one first-degree relative had been diagnosed with or treated for MDD or bipolar disorder. Similarly, family history of substance use disorder was recorded as positive if the participant reported at least one first-degree relative with alcohol or drug abuse. In addition, participants were asked if a parent, sibling, or child had committed suicide.

2.5. Statistics

Descriptive statistics are presented as percentages for discrete variables and as means (standard deviation) for continuous variables. A chi-square statistic was used to compare the distribution of discrete characteristics between participants with and without a family history of suicide. Comparisons of continuous characteristics by family history were completed using the *t*-test. A *p*-value<.05 indicated a statistically significant association. No adjustments of *p*-values for multiple comparisons were performed, so results must be interpreted accordingly.

3. Results

Of the 4041 patients enrolled in STAR*D, 4001 had evaluable family history of suicide data. Of these 4001 patients, 142 (3.5%) reported a family member had committed suicide. Participants with MDD and a family history of suicide were more likely to have a family history of depression, bipolar disorder, or any mood disorder, or familial substance abuse, and age of onset of MDD prior to 18 years of age with a longer time since the onset of illness (Table 1). Of the 142 patients with a family history of suicide $34/142 = 23.9\%$ had a

family history of bipolar disorder compared to $316/3851 = 8.2\%$ of those without a family history of suicide ($p=.0001$). No other demographic or clinical variables differentiated the two groups (Table 2). There were no differences in the rate of history of suicide attempt between groups (16.3% with no family history of suicide, 19.9% with family history of suicide, $p=.27$). Those with a family history of suicide were more likely to have a pessimistic view of the future (87.8% and 76.5%, $p=.0027$), but no other depressive symptoms differed significantly between the groups, including decreased pleasure and presence of suicidal ideation. No differences were found in symptoms of comorbid psychiatric conditions (Table 3).

4. Discussion

In this large cohort of treatment-seeking outpatients, less than 4% reported that a first-degree relative committed suicide. Those who reported a familial suicide were more likely to have a family history of mood disorder and substance use disorder (SUD), a pessimistic view of the future, and early age of onset. Of particular note, a family history of suicide was strongly associated with a family history of bipolar disorder. No other meaningful differences were found. Overall, familial suicide did not appear to differentiate a specific subgroup of MDD by cross-sectional assessment.

Previous studies that examined the relationship between familial suicide and major depressive disorder focused on divergent aspects such as patients with mood disorders who had made suicide attempts (Brent et al., 2002; Hawton et al., 2002), the transmission of mood disorders and suicidal behavior (Brent et al., 2002, 2004), and the prediction of suicide in family members of suicidal completers (Runeson and Asberg, 2003). While studies consistently found that impulsive aggression and sexual abuse are associated with familial suicide, no studies have examined the specific symptoms and comorbid psychiatric disorders in individuals with MDD. In the current study, we found that remarkably few characteristics of patients with MDD who had reported a completed suicide by a first-degree family member differed from those who had no family history of suicide.

This study has several limitations. Patients were asked about first degree relatives who had committed suicide but not about those who had attempted suicide but had not died by their own hands. No information was gathered about family members who had attempted suicide and the age of the probands when their family member died. In addition, STAR*D assessments were limited to those needed to ascertain diagnosis and treatment response and did not include a broader range of psychological measures that might be needed to fully characterize the nature of the psychological scar inflicted by a family member's suicide. Future studies could focus on these other potential sequelae of suicide of a family member. Patients were excluded at baseline if they were at imminent risk of suicide, unable to be managed as outpatients or required immediate hospitalization. While a family history of completed suicide did not identify distinct groups at baseline, subsequent analyses of the STAR*D dataset can determine if such a history predicts course of illness.

In summary, a familial history of completed suicide was associated with a familial history of mood disorder, especially bipolar disorder, and a few cross-sectional clinical differences.

Overall, those patients with major depressive disorder who had such a history were more similar than distinct at baseline compared to those without a history of family members who had completed suicide.

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Table 1

Association with family history of completed suicide

	Absence of family member with completed suicide	Presence of family member with completed suicide	Unadjusted <i>p</i> -value
	%	%	
<i>Race</i>			
White	75.5	81.0	0.3195
Black or African American	17.6	14.1	
Other	6.9	4.9	
<i>Ethnicity—Hispanic</i>			
Yes	12.8	9.2	0.1992
No	87.2	90.8	
<i>Sex</i>			
Male	37.5	32.4	0.2192
Female	62.5	67.6	
<i>Employment status</i>			
Employed	57.3	58.9	0.4689
Unemployed	37.0	33.3	
Retired	5.8	7.8	
<i>Attempted suicide</i>			
Yes	16.3	19.9	0.2662
No	83.7	80.1	
<i>Clinic type</i>			
Primary care	39.0	38.7	0.8336
Specialty	61.0	61.3	
<i>Marital status</i>			
Married	41.2	40.9	0.5022
Never	30.0	25.4	
Divorced	25.6	29.6	
Widowed	3.1	4.2	
<i>Family history of depression</i>			
Yes	53.8	71.1	<.0001
No	46.2	28.9	
<i>Family history of mood disorder</i>			
Yes	55.8	76.8	<.0001
No	44.2	23.2	
<i>Family history of substance use disorder</i>			
Yes	45.3	66.9	<.0001
No	54.7	33.1	
<i>Age of onset</i>			

	Absence of family member with completed suicide	Presence of family member with completed suicide	Unadjusted <i>p</i> -value
	%	%	
<18 years of age	36.8	48.2	.0057
18 years of age	54.7	33.1	

Table 2

Association with family history of completed suicide

Characteristics	Absence of family member with completed suicide		Presence of family member with completed suicide		Unadjusted <i>p</i> -value
	mean	sd	mean	sd	
Age	40.4	13.3	42.8	12.8	0.0324
Education (years)	13.4	3.2	13.3	3.5	0.5766
Number of MDE episodes	5.7	11.2	7.7	11.3	0.0542
Length of episode (Months)	24.9	53.6	19.7	37.4	0.2592
Length of illness	14.8	13.1	19.3	13.8	<.0001
HRSD ₁₇ (ROA)	19.9	6.5	20.4	6.7	0.4042
IDS-C ₃₀	35.5	11.5	36.3	11.5	0.4865
QIDS-SR ₁₆	15.4	4.3	15.5	4.4	0.9247

HRSD₁₇, 17-item Hamilton Rating Scale for Depression; IDS-C₃₀, 30-item Inventory of Depressive Symptomatology — Clinician-rated; MDE, major depressive episode; QIDS-SR₁₆, 16-item Quick Inventory of Depressive Symptomatology — Self-report (Rush et al., 2000, 2003, 2005a; Trivedi et al., 2004); ROA, Research Outcome Assessor.

Table 3

Psychiatric comorbid conditions (PDSQ) by family history of suicide completers

	Absence of family member with completed suicide	Presence of family member with completed suicide	Unadjusted <i>p</i> -value
	%	%	
<i>Obsessive-compulsive disorder</i>			
Present	144.0	12.1	0.5212
Absent	86.0	87.9	
<i>Panic</i>			
Present	12.1	9.9	0.4422
Absent	87.9	90.1	
<i>Social phobia</i>			
Present	29.3	24.8	0.2521
Absent	70.7	75.2	
<i>Post-traumatic stress disorder</i>			
Present	17.9	15.6	0.4887
Absent	82.1	84.4	
<i>Agoraphobia</i>			
Present	11.0	10.0	0.7130
Absent	89.0	90.0	
<i>Alcohol abuse</i>			
Present	11.7	14.9	0.2400
Absent	88.4	85.1	
<i>Drug abuse</i>			
Present	7.5	7.1	0.8435
Absent	92.5	92.9	
<i>Somatoform</i>			
Present	2.3	3.5	0.3557
Absent	97.78	96.5	
<i>Hypochondriasis</i>			
Present	4.4	2.1	0.1984
Absent	95.6	97.9	
<i>Bulimia</i>			
Present	12.3	10.6	0.5492
Absent	87.7	89.4	
<i>Anxious</i>			
Present	79.2	76.6	0.4605
Absent	20.8	23.4	
<i>Number of psychiatric comorbid conditions</i>			
0	38.1	44.3	0.2939
1	26.1	20.7	
2	15.5	12.9	

	Absence of family member with completed suicide	Presence of family member with completed suicide	Unadjusted <i>p</i> -value
	%	%	
3	8.5	11.4	
4	11.8	10.7	

Notes to Table

PDSQ, Psychiatric Diagnostic Screening Questionnaire (Zimmerman et al., 2001a,b).

Diagnoses established by the Psychiatric Diagnostic Screening Questionnaire (PDSQ) set at a threshold of 90% specificity for each Axis I disorder (Rush et al., 2005b).