Gender-Specific Suicide Risk Factors: A Case-Control Study of Individuals With Major Depressive Disorder

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ABSTRACT

Objective: Available information on risk for suicide completion in females is limited and often extrapolated from studies conducted in males. However, the validity of extending to females risk factors identified among male suicide cases is unclear. In this study, we aimed to investigate clinical and behavioral risk factors for suicide among female depressed patients and compare them to similar factors among male depressed patients.

Method: We identified 201 suicide completers (160 male and 41 female) who died during an episode of major depressive disorder (MDD). Cases were compared to 127 living patients with MDD (88 male and 39 female). All subjects were characterized for Axis I and II diagnoses using the Structured Clinical Interview for *DSM-IV* Axis I Disorders and Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders according to the *DSM-IV*, as well as behavioral and temperament dimensions using proxy-based interviews. The primary outcome was measures of impulsive and impulsive-aggressive behaviors.

Results: Compared to controls, male, but not female suicide cases had higher levels of impulsive aggression ($P < .05$). Nonimpulsive aggression differentiated both female ($P < .05$) and male ($P < .01$) suicide cases from controls. However, nonimpulsive aggression and impulsive aggression were correlated constructs in males ($r = 0.297$; $P < .001$), yet uncorrelated among females ($r = 0.121$; $P = .390$). Established risk factors for suicide, such as alcohol and substance dependence, cluster B disorders, and elevated hostility and aggression, were replicated in the pooled-sex analyses, and, though not statistically significant in discriminating between suicide cases and controls by gender, maintained strong group differences.

Conclusions: Males and females share many risk factors for suicide in MDD, yet alcohol dependence is much more specific though less sensitive among depressed females. Nonimpulsive aggression is part of a diathesis for suicide in females, which is distinct from the well-characterized impulsive aggression that is consistently reported in a portion of male suicide cases.

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Suicide is a major public health problem and a leading cause of death for individuals of all ages.[1] With few notable exceptions,[2,3] men die by suicide at 4–5 times the rate of women.[4] Yet, females attempt suicide 2–3 times more frequently than males[5–13] and are thus more likely to be assessed in clinical settings for risk of recurrence. However, as most studies investigating predictors of suicide completion have focused on males, it is unclear whether established risk factors for suicide are valid among female patients.

While some studies have examined sex-specific predictors of suicide,[14] pooling suicide completion and nonlethal suicidal behavior (suicide attempts that do not result in death), most data concerning risk factors for suicide in females come primarily from samples with overrepresentation of low-lethality attempters. The few studies examining death by suicide as a function of gender have studied youth,[15,16] unrepresentative samples,[17,18] or samples that lacked a nonsuicide control group.[4] Indeed, the literature provides limited guidance with respect to suicide completion among females, as it is unclear how risk factors for suicide attempts in females can be transposed to understand risk for suicide completion among females, and whether findings coming from studies focusing on suicide completion in males can be extended to females.

A large body of evidence now implicates a behavioral vulnerability to suicide characterized by high levels of impulsive-aggressive traits. This heritable pattern of behavior[19] has been strongly implicated in both suicide completion[20–22] and nonlethal suicidal behavior,[23–25] and it is most strongly associated with suicide occurring earlier in life.[26,27] It is unclear how this or other potential behavioral vulnerabilities relate to suicide among females. We have previously reported a bimodal distribution of the "impulsive" component of the impulsive-aggressive diathesis and lower levels of psychopathology associated with impulse dyscontrol in female suicide cases compared to male suicide cases.[4] Accordingly, while a small proportion of female suicide cases evidence high levels of impulsivity, impulsivity may not be characteristic of the female suicide completer. In the absence of properly controlled studies, however, it is impossible to draw conclusions about the role of impulsive aggression as a common vulnerability to suicide in both genders.

While suicide occurs almost exclusively in the context of psychiatric illness,[28] the common pathway to suicide most likely involves unique interactions between different pathologies and underlying vulnerabilities. Depressive disorders, and major depressive disorder (MDD) in particular, are identified in the majority of suicides.[29] As MDD appears to be overrepresented among female suicide cases,[16,28] we aimed to study gender differences in vulnerability to suicide by controlling, through design, for this important risk diagnosis, thereby maximizing homogeneity without compromising clinical relevance.

In sum, in this study we sought to directly assess gender differences in clinical risk of and behavioral vulnerability to suicide.

Clinical Points

- While there are many similarities between risk factors for suicide among male and female depressed patients, there are also differences. Alcohol dependence and type of aggressive behavior are among the most important differences.
- These differences should be taken into account when assessing risk of suicide outcome in males and in female patients affected with major depressive disorder.

We performed a case-control study among representative suicide completers meeting criteria for MDD. Thus, this study involved a 4-group design, with male and female depressed suicide cases compared to male and female depressed never-suicidal controls, allowing decortications of vulnerability to suicide in MDD as a function of sex.

METHOD

Depressed Suicide Cases

Through a partnership with the Montreal Coroner's Office, we identified and recruited consecutive cases of suicide occurring in the greater Montreal area. Included in this study were 201 cases of suicide, identified through psychological autopsy characterization, as persons who died in the context of MDD. This method[26,27,30–32] involves proxy-based interviews with the person best acquainted with the deceased. The suicide sample comprised 160 depressed male suicide cases and 41 depressed female suicide cases. The ratio between male to female suicide cases corresponded to the 4:1 gender ratio observed in suicides from the Canadian population.[33]

Living Depressed Comparison Subjects Without Suicidal Behavior

Comparison subjects diagnosed with recurrent MDD without previous suicide attempts were identified through the Douglas Mental Health University Institute's Depressive Disorders Program, a psychiatric outpatient service clinic affiliated with McGill University, Montreal, Canada. Comparison subjects were eligible for study inclusion following the completion of a proxy-based assessment using the same methodology employed for suicide interviews. Comparison subjects had to meet criteria for MDD and to have a negative history of nonlethal suicidal behavior. This included the absence of ambiguous (ie, unclear if death was desired) or interrupted suicide attempts (ie, stopped by a third party). Using this method, we identified 127 depressed comparison subjects, 88 of whom were males and 39 of whom were females. The clinical profile of probands was similar to other samples of depressed outpatients screened for the absence of nonlethal suicidal behavior.[27]

Assessment

For suicide cases and comparison subjects alike, we employed the psychological autopsy method, allowing proxy-based psychopathological and behavioral characterization. The psychological autopsy involves the identification of an informant best acquainted with the subject (eg, in this study, the spouse, sibling, parent, child, or friend) to undergo the assessment process in the subject's stead. Studies performed by our group[27,34–37] and others[31,32,38] demonstrate the validity of this method to investigate the clinical and behavioral variables measured in this study. Specifically, for observable symptoms and behaviors such as those scored in this study, the relationship between informant and subject does not influence the information obtained,[26,39] and information originating from multiple informants is comparable.[27] Our group has further validated this method for the assessment of behavior and temperament.[26,27]

Sample Characterization

Interviews were carried out by trained investigators who administered the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I)[40,41] and the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID-II).[42,43] All diagnoses were elicited according to the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (*DSM-IV*). Interrater reliability for this study was 0.89 for MDD, 0.80 for alcohol dependence, 1.00 for drug dependence, 0.80 for anxiety disorders, 0.66 for generalized anxiety disorder, 1.00 for PTSD, and 1.00 for cluster B personality disorders.

Suicidal behavior was characterized using the Columbia Mental Health Clinical Research Center Suicide History Form.[44]

Behavioral traits commonly studied under the umbrella of impulsive aggression were examined using informant versions in this study: Brown-Goodwin History of Aggression—adult subscale (BGHA),[45] Barratt Impulsiveness Scale (BIS),[46] Buss-Durkee Hostility Inventory (BDHI).[47] We also studied the temperament domains as assessed by the Temperament and Character Inventory,[48] with the exception of "reward dependence" because of reliability concerns.[26]

Ethical Approval

The project was approved by the Douglas Mental Health University Institute Research Ethics Board, and written informed consent was obtained from all informants and living participants interviewed.

Statistical Analysis

Statistical data analyses were carried out with SPSS Statistical Package version 19.0 (SPSS Inc, Chicago, Illinois). Tests were 2-tailed and significance was set at $P < .05$. For categorical variables, we used χ^2 with odds ratio and 95% CI. For continuous variables, we used Student *t* test when considering suicide case-comparison subject contrasts and analysis of variance when considering 4-group comparisons.

The relationship with age was tested with logistic regressions split according to gender. Regressions predicted suicide status by impulsive aggression or nonimpulsive aggression as a main effect and then the addition of the interaction term with age.

Table 1. Distribution of Comorbid Diagnoses and Behavioral Measures

Variable	Suicide Completers	Control Participants	Statistics	
			χ^2 or t	OR (95% CI)
Sociodemographic				
Age, mean (SD), y	41.39 (12.61)	40.94 (11.25)	−0.32	
Married/common law, n (%)	88 (44.2)	55 (44.4)	0.00	
Completed high school, n (%)	67 (35.3)	55 (47.0)	4.17	0.82 (0.68–0.99)
Axis I disorder: last 6 mo, n (%)				
Alcohol dependence	38 (19.0)	10 (7.9)	7.67**	2.74 (1.31–5.73)
Substance dependence	22 (10.9)	4 (3.1)	6.48*	3.77 (1.27–11.23)
Anxiety disorder	34 (17.0)	18 (14.2)	0.46	1.24 (0.66–2.30)
Eating disorder	3 (1.5)	1 (0.8)	0.32	1.90 (0.19–18.55)
Axis I disorder: lifetime, n (%)				
Alcohol dependence	49 (24.5)	15 (11.8)	7.94**	2.42 (1.29–4.54)
Substance dependence	30 (14.9)	9 (7.1)	4.56*	2.30 (1.05–5.02)
Anxiety disorder	40 (19.9)	21 (16.5)	0.58	1.25 (0.70–2.24)
Axis II personality disorder, n (%)				
Cluster A disorder	19 (9.9)	4 (3.4)	4.63*	3.17 (1.05–9.57)
Cluster B disorder	46 (24.1)	6 (4.2)	21.08***	7.23 (2.78–18.79)
Cluster C disorder	30 (15.7)	18 (15.1)	0.01	1.04 (0.55–1.97)
Behavioral dimensions, mean (SD)				
Barratt Impulsivity Scale score	66.22 (13.65)	65.40 (13.07)	0.48	
Buss-Durkee Hostility Inventory score	37.56 (14.10)	33.97 (13.26)	2.03*	
Brown-Goodwin History of Aggression—adult score	5.11 (5.02)	3.89 (3.55)	2.36*	
Temperament and Character Inventory score, mean (SD)				
Novelty seeking	20.30 (7.58)	20.06 (7.57)	0.25	
Harm avoidance	18.95 (7.53)	19.94 (7.08)	1.06	
Persistence	5.32 (2.29)	4.85 (2.20)	1.62	

*P < .05. **P < .01. ***P < .001.

Analytic Strategy

Our analytic strategy was as follows: First, we performed a case-control study of risk factors for suicide in unselected depressed suicide cases, irrespective of gender. Second, we examined these risk factors utilizing a 4-group design stratified for gender. Third, we constructed a latent variable, "impulsive aggression," as measures of impulsive aggression relate to a superordinate category,[49] and, accordingly, our past experience[19] suggests that individual constituents of the impulsive-aggressive diathesis are less informative than the latent construct indirectly assessed by these items. We therefore performed a theory-driven principal components analysis (loading ≥ 0.40) of the impulsive-aggressive diathesis (BIS, BDHI, BGHA, and cluster B personality disorders) with saved regression scores. Given that we also aimed to potentially identify a vulnerability unique to females, we then repeated the principal components analysis with a data-driven approach including temperament domains. Finally, as several lines of evidence suggest that impulsive aggression is most important early in life,[26,27] we performed logistic regression models in which the constructs were tested in interaction with age, while controlling for their main effects.

RESULTS

Case-Control Comparison of Depressed Suicide Cases

Table 1 shows sociodemographic data and the distribution of comorbid diagnoses and behavioral measures for pooled male and female depressed suicide cases as compared to depressed controls. Concerning Axis I comorbidity, depressed suicide cases were more likely than depressed controls to have been diagnosed with current (OR = 2.74; 95% CI, 1.31–5.73; P < .01) and lifetime (OR = 2.42; 95% CI, 1.29–4.54; P < .01) alcohol dependence, as well as current (OR = 3.77; 95% CI, 1.27–11.23; P < .05) and lifetime (OR = 2.30; 95% CI, 1.05–5.02; P < .05) substance dependence. With respect to Axis II comorbidity, depressed suicide cases were more likely to have met criteria for cluster B disorders (OR = 7.23; 95% CI, 2.78–18.79; P < .001) as well as cluster A disorders (OR = 3.17; 95% CI, 1.05–9.57; P < .05). Furthermore, depressed suicide cases had higher levels of hostility (BDHI, P < .05) and more extensive histories of aggression (BGHA, P < .05).

Suicide and Gender Differences

A comparison of demographic data and clinical and behavioral differences between depressed suicide completers and depressed controls as a function of sex is presented in Table 2. Females in our sample were more likely than males to have completed high school, and female controls were more likely than female suicide cases to have done so. These analyses indicated that depressed female suicide cases were more likely than depressed female controls to meet criteria for lifetime alcohol dependence (OR = 5.20; 95% CI, 1.04–25.86; P < .05), but not for current alcohol dependence. On the other hand, depressed male suicide cases were significantly more likely than depressed male controls to meet criteria for current alcohol dependence (OR = 2.29; 95% CI, 1.04–5.06; P < .05) and showed a trend for significance for lifetime alcohol dependence (OR = 1.93; 95% CI, 0.97–3.86; P = .057). Depressed male suicide cases were significantly more likely than depressed male controls to meet criteria for cluster B disorders (OR = 25.32; 95% CI, 3.40–188.37; P < .001),

Table 2. Comparison of Clinical and Behavioral Differences as a Function of Sex

Variable	Male		Female		Statistics χ^2 or F
	Suicide Completers	Control Participants	Suicide Completers	Control Participants	
Sociodemographic					
Age, mean (SD), y	41.11 (12.77)	41.47 (11.25)	42.29 (12.07)	39.74 (11.31)	0.35
Married/common law, n (%)	72 (45.6)	40 (46.5)	16 (39.0)	15 (39.5)	1.09
Completed high school, n (%)	46 (30.9)	29 (36.3)	21 (51.2)	26 (70.3)	21.95***
Axis I disorder: last 6 mo, n (%)					
Alcohol dependence[a]	33 (20.8)	9 (10.2)	5 (12.2)	1 (2.6)	10.85*
Substance dependence	17 (10.6)	3 (3.4)	5 (12.2)	1 (2.6)	6.61
Anxiety disorder	26 (16.3)	10 (11.4)	8 (19.5)	8 (20.5)	2.39
Eating disorder	1 (0.6)	0 (0.0)	2 (4.9)	1 (2.6)	6.69
Axis I disorder: lifetime, n (%)					
Alcohol dependence[b]	40 (25.2)	13 (14.8)	9 (22.0)	2 (5.1)	9.75*
Substance dependence	23 (14.4)	8 (9.1)	7 (17.1)	1 (2.6)	6.03
Anxiety disorder	28 (17.6)	11 (12.5)	12 (29.3)	10 (25.6)	6.60
Axis II personality disorder, n (%)					
Cluster A disorder	15 (9.7)	2 (2.4)	4 (10.8)	2 (5.7)	5.08
Cluster B disorder[c]	36 (23.4)	1 (1.2)	10 (27.0)	4 (11.4)	23.25***
Cluster C disorder	24 (15.6)	10 (11.9)	6 (16.2)	8 (22.9)	2.29
Behavioral dimensions, mean (SD)					
Barratt Impulsivity Scale score	67.24 (13.32)	65.98 (12.83)	62.38 (14.42)	64.00 (13.73)	1.32
Buss-Durkee Hostility Inventory score	37.08 (14.08)	35.05 (12.96)	39.39 (14.28)	31.44 (13.80)	2.14
Brown-Goodwin History of Aggression—adult score	5.21 (5.18)	4.00 (3.66)	4.82 (4.53)	3.66 (3.33)	1.81
Temperament and Character Inventory score, mean (SD)					
Novelty seeking	20.80 (7.73)	19.18 (7.45)	18.28 (6.70)	22.12 (7.56)	2.05
Harm avoidance	18.50 (7.76)	19.83 (7.16)	20.70 (6.42)	20.20 (7.00)	1.04
Persistence	5.21 (2.31)	4.86 (2.14)	5.74 (2.22)	4.83 (2.37)	1.28

[a]Male suicide cases vs male controls: OR = 2.29 (95% CI, 1.04–5.06), $P < .05$; female suicide cases vs female controls: OR = 5.27 (95% CI, 0.58–47.38), $P = .109$.
[b]Male suicide cases vs male controls: OR = 1.93 (95% CI, 0.97–3.86), $P = .057$; female suicide cases vs female controls: OR = 5.20 (95% CI, 1.04–25.86), $P < .05$.
[c]Male suicide cases vs male controls: OR = 25.32 (95% CI, 3.40–188.37), $P < .001$; female suicide cases vs female controls: OR = 2.87 (95% CI, 0.80–10.21), $P = .106$.
*$P < .05$. **$P < .01$. ***$P < .001$.

while this was not significant for depressed female suicide cases. Depressed male suicide cases, but not depressed female suicide cases, were more likely than controls to be characterized as "highly impulsive," representing a BIS score ≥ 75 (male suicide completers, 51.9% vs male controls, 25.8%; $\chi^2 = 4.27$, $P < .05$; female, $P = .592$).

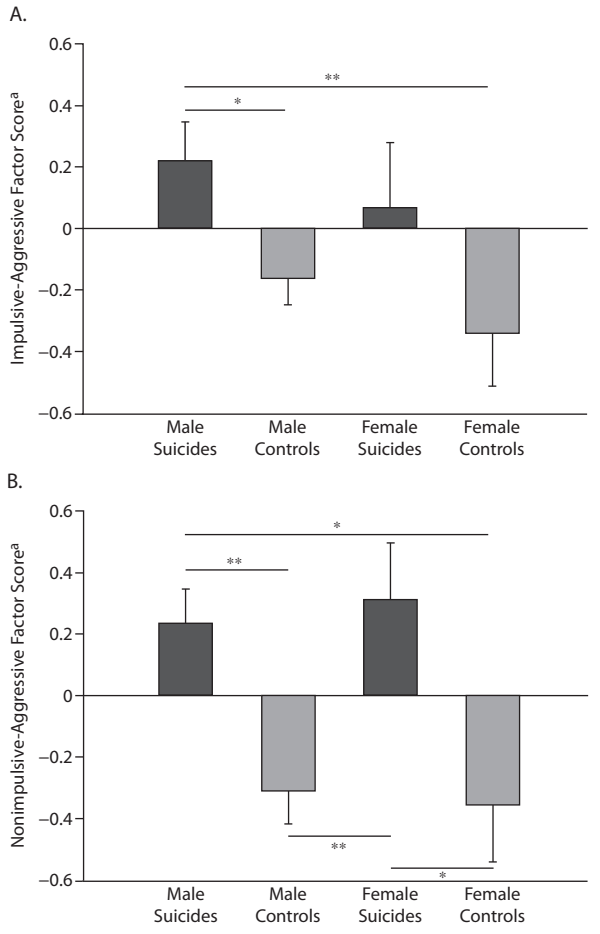
Behavioral Diatheses for Suicide

As previous work[19] suggests that individual measures of the impulsive-aggressive diathesis are less informative than latent constructs assessed by several instruments, we used principal components analyses to assess the superordinate impulsive-aggressive category latently assessed by the BIS, the BDHI, the BGHA, and cluster B personality disorders. This revealed a factor, here referred to as "impulsive aggression," with an eigenvalue of 2.35 accounting for 58% of the variance, with loadings from BIS (0.706), BDHI (0.773), BGHA (0.846), and cluster B personality disorders (0.740). Impulsive aggression significantly discriminated male suicide completers from both male and female comparison subjects, but female suicide completers could not be differentiated from any group ($F_{3,205} = 3.19$, $P < .05$) (Figure 1A).

After we included the temperament dimensions harm avoidance, novelty seeking, and persistence, principal components analyses maintained the impulsive aggression component, in addition to a new component with an eigenvalue of 1.21 accounting for 17.38% of the variance. This latent vulnerability was characterized by aggression (0.40), cluster B personality disorders (0.43), persistence (0.69), low harm avoidance scores (−0.50) and low BIS scores (−0.28). This "nonimpulsive aggression" phenotype significantly differentiated female suicides from both female and male comparison subjects, as it did for male suicide cases, without differentiating suicide completers of either sex ($F_{3,200} = 6.73$, $P < .001$) (Figure 1B).

In addition, impulsive aggression and nonimpulsive aggression revealed significant overlap among male subjects ($r = 0.297$, $P < .001$) but were distinct among female subjects ($r = 0.121$, $P = .390$). Among females, a sample size of 578 females would be required to achieve 90% power at $\alpha \leq .05$ to detect a difference given the observed relationship in this sample between impulsive aggression and nonimpulsive aggression. Conversely, if the relationship observed among males also existed among females, our sample of females would have 86.7% power to detect this difference. Further supporting a phenomenological distinction between impulsive and nonimpulsive aggression, there was no difference in nonimpulsive aggression among male suicide completers in comparison to prior suicide attempts (mean [SD] = 0.23 [0.97] vs 0.23 [1.03]); however, there was a large, nonsignificant difference among female suicide completers (prior attempters: −0.16 [0.76] vs death by suicide on first attempt: 0.46 [0.94]; $P = .207$).

Figure 1. Sex Specificity of Impulsive-Aggressive and Nonimpulsive-Aggressive Diatheses



[a]Factor loading score (arbitrary unit).
*$P < .05$. **$P < .01$.

Impulsive and Nonimpulsive Aggression Across the Life Cycle

We have previously demonstrated, among predominantly male samples, that the impulsive-aggressive phenotype is most strongly related to suicide in younger individuals.[26,27] We therefore wished to test the relationship of the impulsive and nonimpulsive aggressive phenotypes according to age in both males and females.

Among females, a logistic regression indicated the inability of impulsive aggression to discriminate female suicide cases from controls ($\beta = 0.43$, Wald = 2.20, $P = .138$). Including the interaction term with impulsive aggression and age was nonsignificant as well ($\beta = -0.01$, Wald = 0.53, $P = .464$). With respect to nonimpulsive aggression, logistic regression indicated that this variable discriminates female depressed suicide cases from depressed controls ($\beta = 0.76$, Wald = 5.28, $P < .05$). Adding the interaction term to the model did not suggest a contribution of age to the relationship among female suicide cases ($\beta = -0.02$, Wald = 0.37, $P = .542$).

Among males, consistent with our group's previous analyses, both impulsive aggression ($\beta = 0.41$, Wald = 5.52, $P < .05$) and nonimpulsive aggression ($\beta = 0.61$, Wald = 10.81, $P < .001$) discriminated between male depressed suicide completers and controls. Further, the addition of an interaction term with age in these models suggested that age played an important modulating role in the relationship between both impulsive aggression ($\beta = -0.04$, Wald = 5.63, $P < .05$) and suicide in males as well as nonimpulsive aggression ($\beta = -0.04$, Wald = 7.24, $P < .01$) and suicide in depressed males.

DISCUSSION

Epidemiologic data suggest that it is predominantly males who die by suicide, yet females are more likely to attempt. However, the clinician assessing suicide risk more frequently encounters female patients. Most of the inferences made on risk factors for suicide completion are extensions of findings observed in predominantly male samples, and these may not properly apply to suicide in females. Moreover, the abundant literature on suicide attempts among females provides results of dubious validity with respect to suicide completion because it is clear that the majority of female suicide attempters will not die by suicide. In this study, we attempted to address the lacuna in the literature with respect to risk for suicide among females by using a case-control design controlling for major depressive psychopathology. To this end, we characterized a representative sample of suicide completers who died during an episode of major depression and matched them to living depressed subjects.

Our analyses revealed several commonalities in clinical risk factors for suicide between male and female suicide cases, notably with respect to alcohol and substance dependence. Male and female suicide cases, however, appeared to differ with respect to other risk factors related to impulse dyscontrol, specifically a prominent role for cluster B personality disorders, and high levels of impulsivity were observed among male suicide completers but not female suicide completers. Accordingly, the latent construct impulsive aggression did not differentiate female suicide completers from female comparison subjects, while a second construct, nonimpulsive aggression, discriminated depressed female suicide completers from depressed female comparison subjects.

Impulse Dyscontrol, Aggression, and Suicide Among Females

The findings from our study confirm what we had previously proposed, namely, that risk for suicide among females, unlike males, is not strongly related to impulsivity. We had initially hypothesized that this was the case based on a comparison between male and female suicide completers, in which female suicide completers demonstrated lower prevalence of alcohol use disorders as well as lower impulsivity scores, indicating a clear bimodal distribution.[4] However, this was indirect evidence obtained from uncontrolled comparisons between genders and thus subject to several limitations.

Impulsive aggression has been defined as the tendency to react with animosity or hostility when faced with stress,

without consideration of the consequences of this behavior. This heritable vulnerability[19] has been strongly implicated in both suicide completion[20–22] and nonlethal suicidal behavior.[23–25] Impulsive-aggressive behaviors have been strongly associated with suicide occurring earlier in life.[26,27] Among representative (predominantly male) suicide cases specifically, impulsive-aggressive behaviors discriminate suicide completers from controls matched for major psychopathology,[27,34] differentiate those who will die by suicide early as opposed to late during the course of their illness,[37] and predict the use of violent means of suicide attempt.[50]

Our data suggest that the phenomenology of behavioral vulnerability to suicide among females is not adequately described by the impulsive-aggression diathesis. The ability of impulsive aggression to discriminate depressed suicide completers from depressed comparison subjects was insufficient among females. Instead, a data-driven item reduction identified a second construct, which we termed *nonimpulsive aggression*, that was orthogonal to impulsive aggression among females. Specifically, this phenotype was characterized by aggression and cluster B personality disorders, yet low levels of impulsivity as indicated by lower scores on the BIS and elevated persistence scores, in addition to low levels of harm avoidance. This nonimpulsive aggression phenotype discriminated depressed female suicide completers from depressed female comparison subjects, while the impulsive-aggressive phenotype could not. Further, while both impulsive aggression and nonimpulsive aggression were most important among younger males, nonimpulsive aggression did not demonstrate a significant relationship with age when predicting suicide in females.

Clearly, the nonimpulsive aggression vulnerability is not specific to females and also predicts suicide among males. However, impulsive aggression and nonimpulsive aggression were largely overlapping among males yet distinct, in part at least, among females. A legitimate criticism of our analyses pertains to the sample size discrepancy between males (n = 248) and females (n = 80) when testing the relationship between these constructs. Our post hoc power analyses, however, suggest that the female sample would have sufficient power to detect an association of the same magnitude observed in males and that a sample size of 578 females would be required to support the association at the strength observed in this sample. Although this does not demonstrate that the domains are independent in females, it does support a distinction between the constructs to a degree that is not observed in males.

The impulsive-aggressive phenotype represents a spectrum of behaviors that have typically been assessed in suicide research primarily by 3 commonly used instruments: the BIS, the BDHI, and the BGHA, in conjunction with associated psychopathology. While impulsivity, hostility, and aggression do relate to a superordinate category[49] and together characterize a heritable vulnerability to suicide,[19] they nevertheless assess independent constructs that are neither sufficient nor necessary for the others. Our work explicitly states what has been previously suggested by other studies, in which it was shown that aggression, but not impulsivity, discriminates suicide attempters,[51] and hostility has been identified in female suicide attempters specifically.[14]

Clinical Risk Factors for Suicide

Cluster B personality disorders were similarly prevalent among male and female suicide completers, yet their presence was only associated with increased risk for suicide among males. This finding was in part explained by an expected lower prevalence of cluster B personality disorders among depressed male controls than among depressed female controls[52,53] and decreased statistical power among female subjects. Further, our methodological requirement that control subjects must never have engaged in suicidal behavior may have biased the recruitment of depressed control participants to the exclusion of those with cluster B disorders. The clinical importance of cluster B personality disorders in suicide risk assessment, therefore, should not be discounted in either males or females, as the prevalence of cluster B personality disorders was elevated among both depressed male and female suicides compared to controls, and, further, it contributed to both the impulsive-aggressive and nonimpulsive-aggressive factors.

Alcohol and substance dependence disorders were associated with an increased risk for suicide in the larger sample, and this increased risk was also observed when performing sex-specific comparisons. Thus, while of lower sensitivity than among male suicide cases, the specificity of alcohol as a risk factor of suicide in female subjects is much higher. We had previously highlighted this point in our comparison of male and female suicide completers, as female suicide cases who met criteria for alcohol abuse were less likely than their male counterparts to concurrently meet criteria for a depressive disorder.[4] Although this may seem at odds with our findings relating to lower impulsivity and nonimpulsive aggression in females, it should be interpreted in light of the multifaceted and complex etiology of suicide.

Our data did not reveal an increased risk for suicide in either the pooled or sex-split analyses with respect to anxiety disorders, anxiety traits, or for cluster C diagnoses. Among suicide attempters, our group and others have reported an association between suicide attempts and anxiety disorders[54–58] as well as cluster C traits,[59] yet this association occurs most consistently in the presence of comorbid depressive disorders. However, in suicide completers, our data suggest that anxiety disorders do not result in an increased risk for suicide[27] but instead anxiety disorders and traits influence the reversibility of the method of suicide chosen (ie, violent vs nonviolent[4]) and therefore, the associated degree of lethality.

Strengths and Limitations

One of the major strengths of this study is the extensive characterization of a representative sample of consecutive depressed suicide completers. Moreover, suicide

cases and controls were matched for major depressive psychopathology.

The limitations associated with the psychological autopsy method are inherent to postmortem studies involving proxy-based interviews. Nevertheless, we sought to minimize confounds relating to this methodology by employing proxy-based assessments for both cases and controls. We are also aware that an asymmetry of information may exist between proxies of living and deceased individuals, or family members in grief may exaggerate certain symptoms.

Another limitation relates to the statistical power among female suicide cases. Our analyses were limited in their ability to detect statistically significant differences among females using the 4-group design. However, this is a limitation inherent to studying completed suicide among a representative population and the gender paradox of suicide. A specific note of caution, however, is warranted given the increased likelihood of type II error in this setting, and, therefore, we encourage skepticism when concluding lack of clinical significance from the lack of statistical significance for important risk predictors, including cluster B personality disorders.

CONCLUSION

Depressed males and females share many clinical risk factors for suicide. Impulsive aggression does not confer risk to suicide among females to the same degree as among males. A diathesis representing nonimpulsive aggression has greater predictive value in suicide among depressed females throughout the life cycle, while it is more important among younger males. This diathesis has significant overlap among males; however, it represents a distinct vulnerability among females. The specificity of alcohol dependence as a risk factor for suicide in females and the identification of nonimpulsive aggression may prove useful in assessing suicide risk among depressed women.

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