A History of Major Depressive Disorder Influences Intent to Die in Violent Suicide Attempters

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Background: The inconsistency of the results obtained in biological studies of suicidal behavior may be due to the use of broad categories lacking validity. In previous genetic studies, in which we identified an association between a serotonin-related gene and violent suicide attempts, we suggested that a history of major depressive disorder (MDD) might influence this association. In this study, we aimed to clarify the relationships between the violence of suicide attempts, intent to die, and depression in a large sample of suicide attempters.

Method: We investigated intent to die, according to history of violent suicide attempts and MDD, in 502 consecutively admitted suicide attempters. We characterized patients in terms of lifetime DSM-IV Axis I diagnoses, suicidal intent (Beck Suicide Intent Scale), and history of violent suicide attempts.

Results: Suicidal intent, for both the last suicide attempt before admission and the most lethal suicide attempt, was higher in those with history of MDD (p = .03 and p = .04, respectively) but was not affected by history of violent suicide attempt. In violent suicide attempters, suicidal intent was higher in patients with a history of MDD than in patients with no such history (p = .04 for last suicide attempt and p = .02 for most lethal attempt), whereas MDD had no effect on suicidal intent in nonviolent suicide attempters.

Conclusion: Violent suicide attempters constitute a heterogeneous group in terms of suicidal intent. Our results suggest that biological and genetic studies should take into account the method used to attempt suicide, intent to die, and history of MDD.

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B iological and molecular genetic studies have suggested that dysfunction of the serotoperaic system. gested that dysfunction of the serotonergic system is associated with susceptibility to suicidal behavior, regardless of psychiatric diagnosis.^{1,2} Since Asberg et al.³ first reported that low levels of 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF) were associated with the use of violent means in suicide attempts, this relationship has been extensively explored in biological studies of suicidal behavior. As a result of the consistently reproducible correlation between low CSF 5-HIAA levels and violent suicidal behavior, 4,5 low levels of serotonergic activity are seen as an external validation of the dichotomy between violent and nonviolent gestures. There is also compelling evidence that impaired serotonergic function constitutes a fundamental predisposition to impulsive behavior, whether directed at oneself or at others. Thus, after almost 30 years of biological research into suicide, it is now widely accepted that impulsive personality traits are associated with the impulsivity and violence of suicidal acts.

However, as recently pointed out by Müller-Oerlinghausen and Roggenbach,⁶ the inconsistency of results in this field may be due to a lack of validity of certain conceptual views of suicide. First, biological studies have shown that the greater the deficiency in the serotonin system, the more serious the suicide attempt is likely to be, with seriousness defined in terms of behavioral dimensions as diverse as high level of planning, serious injury involved, violence of the suicide attempt, and strong intent to die. ^{2,3,7,8} Second, impulsivity, both as a personality trait and in the suicide attempt, has been shown to be negatively correlated with the lethality of the attempt.8-10 Thus, conflicting results have been obtained, with serotonergic dysfunction associated with both impulsive aggression and high lethality of the suicide attempt, i.e., high degree of planning and intent to die.⁶

In previous genetic studies, we reported an association between the serotonin transporter gene and violent suicide attempts and a lack of association between this gene and nonviolent suicide attempts.^{2,11} These results, apparently consistent with the literature,¹² suggested that violent suicidal behavior might be a homogeneous phenomenon, at least in terms of genetic susceptibility. However, we also

observed a difference in genotype frequencies between violent suicide attempters with and without a history of major depressive disorder (MDD). No such difference was observed in groups of subjects who had not attempted suicide or in groups of nonviolent suicide attempters. This finding led us to suggest that the serotonin transporter gene may be associated with a psychobiological trait that is more common in subjects with a history of both violent suicide attempt and MDD.² Together with biochemical findings, we formed the hypothesis that violent suicidal behavior should be considered a heterogeneous phenomenon.

When trying to identify the traits associated with genetic susceptibility to suicidal behavior, clinicians need to understand the complex relationships between the intention and the act within a biological and psychological context. In 1991, van Praag13 reported that low CSF 5-HIAA levels were correlated not with the seriousness of the attempt, but with the degree of intent, defined as "the intensity of the wish to die at the time of the act" 14(p127) or more commonly as the seriousness or intensity of the wish to die at any time. 15 These results suggest that disturbances in the serotonergic system are most likely to be correlated with disturbances in the regulation of aggression, in turn affecting the strength of the will to die. In a recent neuroimaging study, Oquendo et al. 10 reported that suicidal intent could be used to distinguish between low- and high-lethality suicide attempters and that lowand high-lethality suicide attempters may display different patterns of serotonergic activity in various areas of the brain. Conflicting results have been obtained concerning the specific relationship between suicidal intent and the use of violent means for the suicidal act: some authors 16-18 have claimed that such a relationship exists whereas, according to van Praag et al., 19 "suicide method is an imperfect indicator of the wish to die."(p159) These studies were subject to several limitations: few data were available and sample sizes were generally small, particularly for violent suicide attempters.

Van Praag thought that a lack of inquiry into previous episodes of depression might account for negative findings in biological studies of suicide. Several studies have investigated the relationship between depression and suicidal intent. Suicidal intent was found to be higher in patients suffering from MDD and in patients with the most severe depressive symptoms. Little is known about the relationship between intent to die and lifetime history of MDD, but it has been suggested that suicidal intent may be influenced by chronic or recurrent affective illness. 22,23

In clinical practice, the assessment of suicide attempters requires the investigation of a large number of psychiatric, psychosocial, and psychological factors. Improvements in our understanding of the interactions between these factors would enable clinicians to construct comprehensive models incorporating many variables and would make it possible to develop a more focused therapeutic approach.

In this study, we tested the hypothesis that a psychobiological trait, associated with past psychological experience of mood disturbances, may affect intent to die differently in violent and nonviolent suicide attempters. In a new sample of consecutively admitted suicide attempters, we investigated whether intent to die was influenced by the violence of the means used and history of MDD.

METHOD

Subjects

This study included 502 patients (377 women and 125 men) with a mean (SD) age of 38.1 (14.3) years consecutively admitted following a suicide attempt to the Psychiatric Department of the Academic Hospital of Montpellier, France. The genotypes of serotonin-related genes were known for only a few of these patients at the time of writing. All patients who were willing to participate were eligible for the study, with the exception of those patients under 18 years of age or those with a history of neurologic illness, serious or unstable medical illness, organic mental disorder, schizophrenia, or delusional disorder. Evaluations were carried out during the last few days before discharge, with a view to minimizing the influence of current depressive symptoms, as assessed with the 17-item Hamilton Rating Scale for Depression (HAM-D).²⁴ The study was approved by the institutional ethics committee, and written informed consent was obtained from all subjects.

Lifetime DSM-IV Axis I diagnoses were assessed based on the Mini-International Neuropsychiatric Interview, French Version 5.0.0.25-27 Suicide attempts were characterized on the basis of clinical assessment and personal and family history (first- and second-degree relatives) of suicidal behavior. Almost a quarter (23.1%) of the attempts were classified as violent according to the criteria proposed by Asberg et al.³ (hanging, use of firearms, jumping from heights, several deep cuts, car crash, burning, gas poisoning, drowning, electrocution, and jumping under a train). The other attempts (76.9%) were considered to be nonviolent (drug overdose and superficial wrist cutting). We used the Beck Suicide Intent Scale (SIS) to assess the last suicide attempt before admission and the most lethal or violent suicide attempt.²⁸ A higher score on the SIS indicated greater intent to die.

Statistical Analyses

Analyses were carried out using SAS, version 8.0 (SAS Institute, Cary, N.C.). Differences between violent and nonviolent suicide attempters and between patients with and without a history of MDD were assessed by χ^2 tests or by Mantel-Haenszel χ^2 tests if expected counts

	With	Without			df
Characteristic	History of MDD	History of MDD	p	χ^2	
Sex					
Male, N	84	17	.19	1.66	1
Female, N	289	39			
Age, y, mean (SD)	38.9 (14.1)	34.4 (16.3)	.03		
Age at first suicide attempt, y, mean (SD)	31.9 (13.5)	28.2 (13.4)	.07		
Total no. of suicide attempts, mean (SD)	3.1 (4.0)	2.4 (2.1)	.08		
Family history of suicide attempts			.08	2.91	1
Yes	84	8			
No	189	36			
Family history of completed suicide			.31	0.31	1
Yes	53	6			
No	222	40			

^aComplete data were not available for the whole population. Abbreviation: MDD = major depressive disorder.

were too low. Differences in the characteristics of suicide attempters (sex, age, age at first suicide attempt, total number of suicide attempts, family history of attempted or completed suicide, and SIS scores) between groups were assessed by pooled t tests if variances were found to be equal or by Satterthwaite t test if this was not the case. Analysis of variance (ANOVA) was used to assess differences in SIS scores between groups. All statistical tests were carried out using 5% as the level of significance.

RESULTS

According to DSM-IV criteria, 87% of the patients presented with a lifetime diagnosis of MDD; 11.9% had diagnoses of dysthymia; 9.7%, eating disorders; 27.3%, alcohol abuse; 9.7%, substance abuse; 29.9%, generalized anxiety disorder; 15.9%, agoraphobia; 15.3%, social phobia; 13.7%, panic attacks; and 6%, obsessive-compulsive disorder. The mean HAM-D score at inclusion was 9.0 (SD = 6.6). Mean age of the patients at first suicide attempt was 31.1 years (SD = 14.3), and mean number of suicide attempts was 2.9 (SD = 3.9) per patient. A family history of suicide attempt was found in 29.3% of the patients, and a family history of completed suicide was found in 18.1%.

Patients with and without a history of MDD were similar in terms of sex ratio, age at first suicide attempt, total number of suicide attempts, family history of attempted or completed suicide (Table 1), and comorbid psychiatric disorders. The only significant difference observed between these 2 groups was that patients with a history of MDD were older at the time of examination.

Patients with a history of violent suicide attempt were more likely to be older and to have a family history of completed suicide than patients without a history of violent suicide attempt. The proportion of men was higher for violent suicide attempters than for nonviolent suicide attempters. The number of suicide attempts was significantly higher in violent suicide attempters than in nonviolent suicide attempters (mean \pm SD = 4.0 \pm 6.3 and 2.6 \pm 2.9, respectively, z = 2.21, p = .04) (Table 2).

SIS total scores for both the last suicide attempt before admission and for the most lethal suicide attempt differed significantly between patients with and without a history of MDD (z = 2.24, p = .03; and z = 2.08, p = .04, respectively) (Table 3). Violent and nonviolent suicide attempters did not differ for the 2 measures of suicidal intent (z = 0.38, p = .70; and z = 0.27, p = .79). SIS total score for the last suicide attempt before admission was higher in violent suicide attempters with a history of MDD than in violent suicide attempters without a history of MDD (z = 2.96, p = .04). SIS total score for the most lethal suicide attempt was higher in violent suicide attempters with a history of MDD than in violent suicide attempters without a history of MDD (z = 2.01, p = .02). No such difference was found for nonviolent suicide attempters (z = 0.67, p = .37; and z = 0.81, p = .30, respectively).Moreover, patients with a history of both violent suicide attempt and MDD differed significantly from the other groups in intent scores for both the last (z = 2.99, p = .04)and the most lethal (z = 3.71, p = .03) suicide attempt. We were unable to perform regression analysis of SIS scores because some of the samples were too small. However, our analyses revealed no effect of either sex or age on intent scores.

DISCUSSION

The major finding of this study is that suicidal intent, as measured by the SIS, is affected by history of MDD only in violent suicide attempters. A history of violent suicide attempt alone cannot account for a stronger intent to die but may contribute to a stronger suicidal intent in patients who also have a history of MDD. Indeed, the group of patients with a history of both MDD and violent suicidal behavior had the highest SIS scores, whereas the lowest SIS scores were obtained for violent suicide attempters with no history of MDD. Our results, suggesting that violent

Table 2. Clinical Characteristics of Enrolled Subjects According to History of Violent Suicide Attempt^a With Without History of Violent History of Violent Suicide Attempt Suicide Attempt Characteristic < .0001 30.38 Sex Male, N 48 67 Female, N 57 284 40.7 (14.1) 37.3 (14.3) .04 Age, y, mean (SD) Age at first suicide attempt, y, mean (SD) 31.2 (14.3) 31.1 (14.4) .95 4.0 (6.3) 2.6 (2.9) .04 Total no. of suicide attempts, mean (SD) Family history of suicide attempts .91 0.0127 1 23 73 54 177 No Family history of completed suicide .02 6.1637 22 38 Yes 58 212

Table 3. Differences in Beck Suicide Intent Scale	(SIS) Scores for the Various Categories ^a
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Category	Last Suicide Attempt			Most Lethal Attempt		npt
		Total Score			Total Score	
	N	Mean	(SD)	N	Mean	(SD)
History of violent suicide attempt	34	15.26	(6.45)	40	16.55	(5.21)
No history of violent suicide attempt	90	15.72	(5.81)	86	16.26	(5.86)
History of MDD						
Yes	120	15.89 ^b	(5.81)	120	16.66 ^c	(5.46)
No	8	11.13	(5.99)	6	11.83	(6.79)
History of violent suicide attempt						
History of MDD	30	16.20 ^c	(6.21)	37	17.19 ^d	(4.79)
No history of MDD	3	8.33	(4.16)	2	9.00	(5.66)
No history of violent suicide attempt						
History of MDD	86	15.89	(5.74)	82	16.40	(5.78)
No history of MDD	4	13.25	(7.63)	4	13.25	(7.63)

^aComplete data were not available for the whole population.

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suicidal behavior is a heterogeneous entity, are consistent with the conclusions of van Praag: first, the violence of the method used does not reflect the strength of suicidal intent, ¹³ and second, depression influences suicidal intent. ¹⁹ Our findings are consistent with the initial hypothesis that a psychobiological trait that is more common in subjects with a history of both MDD and violent suicide attempt may affect intent to die. Further genotypic analyses should investigate the effect of genotype on the violence of suicidal acts and intent to die.

Most studies on the relationship between suicidal intent and depressive disorders have been designed on the basis of current diagnoses of mood disorders. 4,10,16,21,29,30 We used a different approach, based on the existence of a hypothetical common psychobiological trait, presumably controlled by low levels of serotonergic activity, responsible for both violent behavior and mood disorders and with possible effects on suicidal intent. Our observation is consistent with reports that recurrent or chronic depression increases suicidal intent. 22,23 Suicidal intent may be affected by a trait associated with recurrent depression,

such as hopelessness. Indeed, hopelessness has been put forward as a "missing link" between depression and suicide¹⁴ and has been shown to be stronger in suicide attempters than in those who do not attempt suicide both during and outside episodes of acute depression.^{31–33} Thus, these data suggest that history of past depressive disorders should be taken into account in the evaluation of the suicidal risk in clinical practice.

Two groups of patients with violent suicidal behavior were identified in this study: a group with low intent to die and with no history of MDD (group 1) and a group with a high intent to die and a history of MDD (group 2). According to the clinical model purposed by Mann et al.,³⁴ the patients in group 1 would display high impulsivity. This group may correspond with studies reported by Baca-García et al.⁹ and Oquendo et al.¹⁰ in which impulsive aggression was inversely correlated with lethality. The patients in group 2 share a number of characteristics with the survivors of serious suicide attempts described by O'Donnel et al.³⁵ In this study, patients who attempted suicide by jumping in front of a railway train were more

 $^{^{}b}p = .03$ for MDD vs no MDD.

 $_{d}^{c}p = .04 \text{ for MDD vs no MDD.}$

 $^{^{}d}p = .02$ for MDD vs no MDD.

Abbreviation: MDD = major depressive disorder.

likely to suffer from severe mental disorders and to carry out impulsive and high-intent-to-die acts.³⁵

At the biological level, we can hypothesize that the patients in group 1 probably have a mild serotonergic dysfunction, whereas those in group 2 probably have a moderate to severe serotonergic dysfunction and are susceptible to both violent suicidal behavior and MDD. This model is also consistent with that proposed by Depue and Spoont, who suggested that "suicidal behavior and impulsive aggression may represent 2 different indicators of a central (behavioral and biochemical) trait, such as a low threshold of emotional facilitation." 36(p364) This hypothesis is supported by the finding that the cooccurrence of these 2 indicators is associated with the lowest 5-HIAA concentrations in cerebrospinal fluid.³⁶ However, low levels of central serotonergic activity would be associated with the frequency of depressive episodes, rather than with the depressive disorder per se, contributing to the appearance of "neurotic depression" in some subjects with personality disorders.³⁷

In this study, we evaluated patients in the last few days before discharge, about 1 week after the suicide attempt. In this way, we tried to minimize the effect of depressive symptoms on the evaluation (mean HAM-D score was only 9.0) and to take into account the moderating effect of elapsed time on the SIS score, as reported by Salter and Platt.³⁰ We also tried to minimize bias by reporting lifetime data from both the last and the most lethal suicide attempt, considering susceptibility to suicidal behavior to be a trait rather than a state. The data for the last and the most lethal suicide attempt were similar in this study.

Patients with a history of violent suicide attempt tended to be older and were more likely to be male, to have attempted suicide a greater number of times, and to have a family history of completed suicide than those patients without a history of violent suicide attempt. These findings are consistent with those of previous studies. ^{16,29,34} SIS scores were not higher in older patients, in contrast to the results reported in other studies, ^{16,38} but we included few adolescents in our sample.

The difference accounting for the lowest SIS scores was not statistically significant due to a lack of power, as our sample included very few patients with no history of MDD but violent suicidal behavior. A sample of at least 200 such patients (i.e., a total sample of about 2000 suicide attempters) would be required to obtain significant results with a significance threshold of p=.05 and a power of 80%.

If these results are to be generalized, then further studies are required including patients with antisocial personality disorders, compulsory admissions, and psychotic disorders. Indeed, patients with highly aggressive behavior might be expected to display antisocial personality disorders and to have undergone compulsory ad-

mission to the hospital. A larger sample is also required to replicate these results.

In conclusion, this study suggests that the violence of the suicide attempt, suicidal intent, and history of depression are independently significant variables that also interact and may be useful for the constitution of a more homogeneous group of suicide attempters. Thus, in clinical practice, suicidal intent, the violence of the means used, and the lethality of suicidal acts should be assessed independently. The use of such an approach, together with molecular genetics studies, would provide a useful way of refining the definition of the suicidal phenotype associated with genetic variants.

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