

# VULNERABILITY TO SUICIDAL BEHAVIOURS: RISK AND PROTECTIVE FACTORS

Sarchiapone M., Carli V., Cuomo C., Babore A.

## *Summary*

Aggressive and suicidal behaviours are one of the most common psychiatric emergencies and, as every psychiatric disorder or human behaviour, have a multifactorial origin in which biological, psychological and social factors act together. These factors may have a protective value or may be risk factors and both concur in determining the individual's vulnerability to suicidal behaviour. With the aim of evaluating impact of some psychopathological dimensions on suicidal acting, we conducted a study on a sample of psychiatric patients with a history of suicide attempt, comparing it with a sample of psychiatric patients without suicidal tendencies, homogeneous for age, sex and psychiatric diagnosis. 203 adults outpatients consecutively enrolled, were the study subjects (mean age:  $39.47 \pm 13.15$ ; M:F 89/114), whose diagnoses were heterogeneous and assessed according to DSM-IV-TR criteria. 112 patients (54.6%) had a lifetime suicide attempt in psychiatric history. Among suicide attempters, a significantly higher number of subjects were female sex, not married and unemployed. Results also showed that patients with a suicide attempt had higher Childhood Trauma Questionnaire (CTQ) total scores and Brown Goodwin Life History of Aggression (BGLHA) scores in comparison to the control group and lower scores on the resilience scale.

## *Key words:*

suicide, risk factors, protective factors, psychopathology

## *For Correspondence:*

Department of Health Sciences, University of Molise, Campobasso, Italy

## **Introduction**

Suicidal and violent behaviours represent one of the most common psychiatric emergencies, and their prediction and prevention constitutes a relevant and complex issue.

Both completed and attempted suicide, likewise all psychiatric disorders and human behaviours, have a multifactorial basis, in which biologic, psychologic and social factors combine, and are currently considered multi-determined and complex traits, characterized by a phenomenology in which diverse components synergically act. Those components build a network of risk factors classically differentiated in predisposing and potentiating factors. Predisposing factors are also referred to as distal factors, while potentiating factors as proximal factors and both concur in determining a so-called "suicidal threshold".

The main predisposing factor for suicidal behaviours is undoubtedly the presence of a psychiatric disorder. Recent data show that more than 90% of suicide attempters are affected by a psychiatric illness, mainly a mood or psychotic disorder. Substance abuse, a family history of suicide or other psychiatric disorder, familial risk factors (disrupted family environment indicated by separation, divorce, family conflict, parental legal troubles, etc.) are also important predisposing factors. Among them we should also include some peculiar personality traits such as impulsivity, aggressiveness and tendency to violent and antisocial behaviours. Prominent indeed as predisposing risk factor for suicidal behaviour is childhood trauma. In the last two decades several studies described a strong association between traumatic experience during infancy and psychopathological traits developed in adulthood such as depression, anxiety, dissociative symptoms, substance abuse, personality disorders and self-destructive behaviours. It has been estimated that childhood abuse victims, as adults, are 5-fold more frequently affected by an affective disorder, and 12-fold more frequently affected by a personality or conduct disorder,

become 5-6-fold more frequently substance addicted and are at a 5-fold risk for the development of suicidal behaviours. Therefore childhood trauma is deemed to be an important vulnerability factor for suicide, since it has varied and relevant psychological or behavioural effects such as a low self-esteem and destructured forms of attachment, which are also associated to suicidal behaviours. Childhood trauma can also affect brain functioning in a period of intense development. In this regard, victims of childhood abuse were found having abnormalities in physiological mechanisms of stress response and neurotransmitter systems. For instance significant associations between childhood trauma and 5-HIAA and HVA CSF levels were observed; an association was also reported between sexual abuse during infancy and Urinary Free Cortisol excretion.

On the other hand the availability of lethal means, life stressors such as affective, familiar and job-related stressors, medical illnesses and grief are the most frequent triggering events. It should furthermore be noted psychopathological traits can also interact, and a single vulnerability factor can initiate a cascade of events culminating in the development of suicidal behaviours. Impulsivity for instance could be directly implied in the predisposition to suicidal behaviours, and at the same time to psychiatric disorders or substance abuse, which are in turn predisposing factors for suicidal behaviours.

Among predisposing factors we should also include neurobiological risk factors. Several studies demonstrated that neurotransmitter abnormalities were associated to violent and suicidal behaviours: functional impairment of serotonergic transmission appear to be correlated to self-destructive behaviours, and among them an absolute reduction in serotonin and its metabolite 5-HIAA in CSF (Asberg M, 1976), an altered response to challenge tests (Sarchiapone M, 2001), and receptorial abnormalities (Mann, 2000) appear to stand out.

Many reports also described a significant correlation between some biochemical variables (inflammatory cytokines, plasmatic cholesterol, etc.), depression and suicidal risk, specifically demonstrating an important association between low plasmatic levels of cholesterol and impulsive behaviours (Sarchiapone et al, 2000). Among the most accessible markers, in the recent years attention has been paid to inflammatory cytokines both for their involvement in stress processes and for their role in neural transmission: several studies have already clarified an involvement of these proteins in certain conditions such as major depression, schizophrenia, Alzheimer Disease and other psychiatric disorders (Kronfol et al., 2000), but never extensively investigated the possible correlations to violent and suicidal behaviours.

Mounting evidence in literature prove the existence of a genetic susceptibility to violent behaviour (Roy et al, 1997), which in a clinical context is considered to be the inability to control an impulsive drive. Molecular biology studies have reported significant associations between suicidal behaviours and gene polymorphisms involved in the serotonin metabolism (specifically TPH and 5-HTT), emphasizing that some allelic forms significantly correlated to violent modalities of self-destructive behaviours.

Genetic risk factors could play a key role in determining a suicidal behaviours, and this role is still debated among researchers. Genes could be implied in a predisposition to suicidal behaviours, but could also have a direct role in the development of a psychopathology or personality traits associated to suicide such as impulsivity, aggressiveness or hopelessness. In any case, it is possible that many genes with a limited effect concurred in determining a genetic vulnerability to a complex phenomenon as a suicidal behaviour. The involvement of genetic factors in predisposing to suicidal events is also supported by cumulative experimental evidence. Firstly, the result of epidemiological studies on families indicate that suicidal behaviours runs in families. A strong evidence on the presence of a genetic component comes also from twin studies on monozygotic and adoptees. Roy and Segal described an increase in concordance for suicide in monozygotic twins in comparison to dizygotic twins (18% vs. 0.7%). Schulsinger et al. reported

a suicide frequency 6-fold greater among biological relatives of adoptees with suicidal behaviours without suicidal behaviours in families of adoptive parents. Many studies thus provide evidence for a genetic susceptibility which is also shared among attempters and completers. The presence of a genetic susceptibility is then sufficiently ascertained by the above described studies. These last, however, do not provide information on which genes could be actually transmitted.

With the aim of individuating these gene, similarly to what happened in other biomedical research fields, an approach through candidate genes was frequently attempted, beginning from biological mechanisms possibly implied in suicidal behaviours. Vast majority of studies examined the genes involved in the serotonergic neurotransmission, and enzymes implied in the serotonin metabolism such as TPH, MAO, COMT, 5-HTT and various subtypes of serotonergic receptors, chiefly 5HT2A.

Other studies analyzed also other genes not directly involved with serotonin, such as DRD2, DRD4, BDNF and CCK. However methodologies are often heterogeneous, thus making impossible, or at least difficult, a comparison of the findings described by different research groups. Majority of studies on candidate genes provided inconsistent or inconclusive results, producing both positive and negative data for the same candidate genes. The only genes upon which researchers seem to concur are the TPH and 5HTT genes.

As said before we can thus conceive a model characterized by a suicidal threshold determined by the sum of predisposing factors (including the biologic o genetic ones), and in which potentiating factors determine the transition from a suicidal ideation to a suicidal act. This threshold could be influenced also by protective factors, and also these factors could be genetically determined.

A potential protective factor for suicidal behaviours, which has recently taken into consideration and is being currently evaluated, is the so-called “resilience”. Resilience can be defined as the ability to bounce back from an adverse life event and successfully adjust to it, involving the capacity for escaping an awkward situation with greater strength and resources deriving from acquired experience. Since suicide is often regarded to as the only possible “way out” by patients, and hopelessness is one of the major drives to acting, it is well understood that resilience can represent a key protective factor for suicidal behaviours.

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At the mean time, looking at the suicidal act as the ultimate solution to overwhelming difficulties suggests the presence of a further dimension of psychological vulnerability to suicide, that is the possible existence of a peculiar neurocognitive attitude. A recent review took into consideration the present neuropsychological studies on suicide attempts, and tried to compare them with the literature on such alterations in patients with BPD, who are typically impulsive and self-destructive, and have suicidal tendencies. Actually BPD is one of the most frequent diagnoses in cases of attempted suicide. Despite being scarce, studies on suicide attempters point out the presence of several aspects of behavioural dysregulation, which reflect an abnormal pattern of complex functioning both at an executive and a motivational level. In spite of some inconsistencies, literature outlines a profile of *cognitive vulnerability* to suicidal behaviours, beginning from the works by Neringer and collaborators in 1964, and by Durbstein and collaborators in 1994, in which rigid thinking was observed as characterising feature of suicidal subjects, together with a reduced ability in problem solving. Neuropsychological abnormalities

obviously reflect a biological correlate of dysfunctioning of whole brain areas. Specifically for attempted suicide, strong evidence for an impairment of *verbal fluency* relates to a dysfunction of the frontal lobe. Verbal fluency is a measure of response initiation, which may contribute to the lack of initiative and self-direction, to a poor *problem solving*, as well as to an excessive interpersonal dependence. Bartfai and coworkers in 1990 found this abnormality being present, together with a reduction in the design fluency and intellectual reasoning, until 3 weeks after a suicide attempt, and implied a reduced ability of generating alternative solutions to problems. Audenart and collaborators in 2002 associated a neuropsychological study to an fMRI protocol, and described a reduced perfusion in certain areas of the prefrontal cortex; in 1995 the same group added the finding of a reduced serotonin binding in recent suicide attempts, with serotonin levels even lower in those who carried out self-injurious behaviours. From the whole studies it is nonetheless possible to assume that the executive impairment in suicide attempters is independent of comorbidity with a co-occurring psychopathology, which may act as confounding factor, for instance with depression or substance abuse. Jollant and colleagues in 2005 also showed an impairment in the *decision-making* process among both violent and non-violent suicide attempters, which thus resulted largely independent from the underlying affective disorder and from other variables such as age, intelligence, education, features of the attempt. Conversely, this kind of abnormality was positively correlated with affective lability for all suicide attempts, and an additional association was found between the group of non-violent attempters and hostility expression. It has been suggested that qualitative differences exist between self-injurious behaviours without an intent of taking one's life, and suicide attempts, which could relate to distinct underlying cognitive processes and other inhibitory control processes. These features would partly differentiate BPD from suicide attempters without BPD: automatic and repetitive self-injurious behaviours would provide a sort of prompt emotional relief to an individual whose inability to tolerate a transient but intense negative emotional state could reflect the propensity to immediate rewards and anxiety avoidance, regardless of future consequences and in spite of past experience. The cognitive circuitry towards a deliberate suicide attempt would be rather different, and would imply inhibition impairments in both arousal and execution, with a higher risk of acting as a result of an inability to express and repress an inappropriate choice. Such impairments would show through the perseverative non-suppression of a thought, and a deliberate action in order to end one's life. An impaired ability of originating and verbalizing more creative solutions to problems would then bring to feelings of entrapment, by virtue of which paradoxically suicide would represent a way of reducing anxiety. With the aim of evaluating impact of some of the vulnerability factors we described above on suicidal acting, we conducted a study on a sample of psychiatric patients with a history of suicide attempt, comparing it with a sample of psychiatric patients without suicidal tendencies, homogeneous for age, sex and psychiatric diagnosis. Our main intent was thus to test the hypothesis by which patients with a history of suicide attempts were provided with certain psychopathological correlates and a set of risk and protective factors which included childhood trauma, aggressiveness, severity of depressive symptom, resilience. Our secondary aim was also to identify significant correlations between those psychopathological dimensions and some feature of suicide attempts such as intent, lethality, number of repetitions and age of the first attempt.

### **Materials and Methods**

203 adults outpatients consecutively enrolled were the study subjects (mean age:  $39.47 \pm 13.15$ ; M:F 89/114), whose diagnoses were heterogeneous and assessed according to DSM-IV-TR criteria.

168 subjects had a diagnosis of mood disorder (47 with major depressive episode, first episode; 91 recurrent major depression; 21 bipolar disorder, 2 dysthymic disorder), 12 had a diagnosis of schizophrenia, 11 subjects a diagnosis of anxiety disorder and 12 a diagnosis of substance dependence. Sample is accurately described in table 1.

137 patients were consecutively enrolled at the Day Clinic of Psychiatry of the University Hospital A. Gemelli of Rome, and 67 patients were enrolled at the Department of Emergency of the same hospital, were they had been admitted for suicidal behaviours.

Inclusion criteria were the presence of an Axis I psychiatric diagnosis according to DSM-IV-TR criteria, and the signature of the informed consent. Exclusion criteria were the presence of mental retardation or cognitive impairment which could affect psychometric evaluation, and refusal of participation to the study.

All patients were subject to a medical and psychiatric examination. A structured psychiatric interview (MINI interview) was administered in order to formulate a diagnosis according to DSM-IV criteria. Another structured interview was administered also to collect details about recent or past suicidal behaviours, number of attempts, modality, intent, lethality, age of the first attempt and the presence of predisposing and potentiating risk factors.

By the same interview data were collected about the most common socio-demographic variables, and a pharmacologic history. Severity of depressive symptoms was measured through the Hamilton Depression Rating Scale. Brown Goodwin Lifetime Aggression Interview evaluated aggressive tendencies among patients; patients were also administered the Childhood Trauma Questionnaire (CTQ), 34 items-version, and the Connor-Davidson Resilience Scale (CD-RISC). Patients were then divided into 2 groups according whether they had a history of suicidal behaviours. Collected data were then compared in order to highlight possible differences between suicide attempters (TS) and non-attempters (NTS). Consequently, by examining only the TS group, correlations were searched for among the psychopathological variables examined and the features of suicide attempts.

Statistical analysis was performed using the Student t-test and Pearson's correlation coefficient through SPSS software for Windows, version 14.

**Table 1. Description of sample**

	Number of subjects		
	Total	TS	Controls
<b>Major Depression</b>	151	95	56
<b>Disorder Bipolar</b>	18	7	11
<b>Schizophrenia</b>	20	6	14
<b>Opioid Dependence</b>	7	3	4
<b>Anxiety Disorder</b>	9	1	8
<b>Total</b>	205	112	93

## Results

112 patients (54.6%) had a lifetime suicide attempt in psychiatric history. Among suicide attempters, a significantly higher number than the non-attempter group was female sex, not

married and unemployed. No differences were found between groups for age, education and psychiatric diagnosis.

According to the psychometric evaluation, HDRS scores were not significantly different among groups, while attempters showed significantly higher scores on BGLHA ( $p < 0.01$ ) and CTQ ( $p < 0.01$ ). This last scale, a significant difference was found between the weighted total score and also for some subscales (emotional abuse, physical abuse, emotional neglect). Patient with a history of suicide attempt had furthermore lower mean scores on CD-RISC, and difference between the 2 groups was statistically significant.

In the attempters group, statistically significant correlations were found between scores and CTQ scores for emotional abuse and physical neglect, in addition to the weighted total score.

No significant correlations were found between psychometric variables and features of suicidal acts pertaining to lethality, intent and number of suicide attempts.

Study results are shown in tables 2 and 3

**Table 2. Socio-demographic variables and patients clinical data**

	TS (N=112)	Controls (N=93)	Significance
<b>Females</b>	67 (68,4%)	50 (58,1%)	P<0.01
<b>Married</b>	29 (29,6%)	41 (47,7%)	P<0.01
<b>Single</b>	46 (46,9%)	30 (34,9%)	P<0.01
<b>Divorced</b>	15 (15,3%)	11 (12,8%)	NS
<b>Unemployed</b>	36 (36,7%)	19 (22,1%)	P<0.01
<b>Age</b>	42,1±13,8	43,6±13,8	NS
<b>HDRS</b>	21,5±6,7	20,2±6,6	NS
<b>BGLHA</b>	33,3±7,6	29,3±8,3	P<0.01
<b>CD-RISC</b>	52,9±14,8	59,28±15,3	P<0.01

**Table 3. Childhood Trauma Questionnaire Scores**

	TS	Controls	Significance
<b>Emotional Abuse</b>	11,3±4,9	8,5±4,7	P<0.01
<b>Physical Abuse</b>	8,9±4,2	7,1±3,9	P<0.01
<b>Sexual Abuse</b>	9,0±4,6	7,1±2,5	P<0.01
<b>Emotional Neglect</b>	28,9±8,5	28,5±10,4	P<0.01
<b>Physical Neglect</b>	11,9±4,4	11,3±3,8	P=NS
<b>Weighted sum</b>	10,0±2,1	8,6±2,2	P<0.01

### Discussion and Conclusions

For more than one half of the sample one or more suicide attempts could be found in psychiatric history. This data emphasizes the importance of a psychiatric diagnosis as predisposing factor to suicidal behaviour.

Subjects with suicidal behaviours were more frequently female, unemployed and single in comparison to the control group, and this data further support the construct that suicide is a multi-determined act in which also socio-demographic variables play an important role.

Results also showed that patients with a suicide attempt had higher CTQ total score in comparison to the control group and in addition significantly higher scores at the subscales for emotional abuse, physical abuse, sexual abuse and emotional neglect. These data are noteworthy since they are consistent with ample evidence - based both on general population studies and psychiatric patients studies - which identified childhood trauma as distal factor for the subsequent development of suicidal behaviours as adults.

Another relevant finding is that patients with a suicide attempt also showed higher BGLHA scores for aggressiveness than patients without a suicide attempt. Malone et al. (1995) similarly reported higher BGLHA scores in depressed patients with suicidal behaviours, and an analogue finding was also described for bipolar patients (Oquendo et al. 2000). More recently Dumais et al. (2005) observed that personality disorders characterized by impulsivity and aggressiveness are an independent risk factor for the development of suicidal behaviours in depressed patients. The data from these 4 studies suggest that impulsive and aggressive traits play a role in the development of suicidal behaviours.

In our study correlations between BGLHA scores and CTQ scores were also examined. Statistically significant correlations were found between BGLHA scores and CTQ subscales scores of emotional abuse and physical neglect. Likewise Garino et al. (2005) reported that in a sample of bipolar patients cluster B personality disorders were significantly associated to CTQ scores for emotional abuse, physical abuse and emotional abuse, while Roy et al. (2004) in a study on 500 alcoholics found statistically significant correlations between BGLHA scores and all the CTQ subscales. Brodski et al. (2001) reported that child abuse, aggressiveness and impulsivity were associated with the presence of suicidal behaviours in depressed patients, inferring that childhood trauma could be an environmental risk factor for the onset of suicidal behaviours and impulsivity or aggressiveness.

As a support for a role of protective factors for the onset of suicidal behaviours, in our sample patient with a suicide attempt had lower scores at the CD-RISC for resilience. Furthermore, patients without suicide attempt were more frequently married. It is thus possible to suggest that risk factors and protective factors interact in determining the suicidal risk for each individual. The concept of vulnerability to suicide, and the knowledge on both risk and protective factors can be used with the aim of individuating high risk groups, and providing a valid instrument for determining selection criteria for the identification of individuals on whom prevention program for suicidal behaviours should be addressed; because of the wide number of vulnerability factors and their hardly predictable interactions, such a validity fades as long as the estimate of risk for a single subject is required. The instruments which we currently master, albeit sophisticated, hardly allow to measure to which extent an individual is vulnerable to suicide, or to estimate the risk level, while they resulted useful in establishing the presence or absence of the same vulnerability. Further elements which could serve as support could come in the next future from genetic and neuroimaging studies, which could allow for the identification of other specific markers associated to high risk for suicide.

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