

## Suicidal Behaviour in Young Adults: A Literature Overview on Neurobiological, Epidemiological and Psychosocial Aspects

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### Abstract

Suicidal behavior is considered a very serious public health problem. The World Health Organization has estimated a yearly total of 800,000 deaths by suicide worldwide.

Several recent studies have focused on suicidal behavior in young adults as, in this population, suicide represents the second cause of mortality after road-accident induced deaths. Neurobiological findings on suicidal behavior in young adults have highlighted pathological alterations of various physiological systems, such as the hypothalamic-pituitary-adrenal axis, the serotonergic and noradrenergic pathways. Dysfunctions of neurotrophin production as well as genetic factors are also considered key players in this context. Among risk factors associated with suicidal behavior in young adults, specific socio-demographic, cultural and social characteristics, as well as the presence of psychiatric comorbidities, have been identified as crucial components. In particular, the role of the familial entourage and of possible conflicting relationships experienced with relatives has been largely investigated.

In this review, we will provide an overview of the main neuropsychiatric, epidemiological and psychosocial aspects of the suicidal behavior in young adults. Actual knowledge on prevention strategies together with psychosocial and pharmacological approaches will be also discussed.

**Keywords:** Suicide; Young Adults; Neurobiological Alterations; Psychiatric Comorbidities; Prevention Strategies; Family

### Introduction

Definitions for suicide and suicidal behavior have been the topic of a lively scientific debate [1,2]. Thus, suicide is normally defined as an act of intentionally terminating one's own life. However, this definition cannot be considered exhaustive, given the complexity of this phenomenon. Moreover, the nomenclature of suicidal behaviors without fatal outcome may also significantly differ [3,4]. Globally speaking, a suicidal behavior is characterized by the fact to be self-initiated and potentially injurious, with the intent to die. The outcome of a suicidal behavior might be nonfatal or fatal [5].

If suicidal behavior has made the object of deep philosophical and moral considerations since ancient times, it is currently considered a serious public health problem, being the cause of a considerable number of deaths, in particular in young adults. Indeed, in this population, suicidal behavior has been shown to be the second mortality cause, after deaths by road-accidents [6]. The World Health Organization has estimated a yearly total of 800,000 deaths by suicide worldwide, with a possible underestimation of 20%. Recently, suicidal behavior in young adults has stimulated a lively scientific debate, aimed at better defining associated risk factors and identifying specific prevention strategies

together with psychosocial and pharmacological approaches for this population. This review will provide an overview of neurobiological and epidemiological aspects of suicidal behaviour in young adults. Recent findings on the impact of co-existing psychiatric disorders and associated risk factors, with a focus on the role of the familial entourage, will be also summarized. Prevention strategies targeting psychosocial interventions and pharmacological approaches will be also discussed.

In particular, we reviewed a total number of 79 studies on the subject, published between July 2005 and September 2015 on PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), combining for the searching two or more of the following keywords: suicide, young adults, neurobiological alterations, psychiatric comorbidities, prevention strategies, family.

### Neurobiology of suicidal behavior in young adults

Recent neurobiological findings on the development of suicidal behavior in young adults have focused on dysfunctions of three main physiological systems: the hypothalamic-pituitary-adrenal (HPA)-axis, the noradrenergic pathway (both in the sense of a hyperactivity) and the serotonergic system (in the sense of impairment) [7]. While alterations of the HPA-axis and noradrenergic system seem to be mainly involved in the stress-induced suicidal behavior in young adults [8], dysfunctions of the serotonergic pathway have been shown to be associated with suicidal behavior induced by dysregulations of anxiety, impulsivity or aggressivity. A few studies point towards a possible role of the dopaminergic system in the development of the suicidal behavior in young adults. In particular, a hypo-activity of striatal dopaminergic systems has been identified as a potentially crucial neurobiological correlate [9]. An impairment of GABAergic and glutamatergic neurotransmission, together with specific genetic variants in a subset of glutamatergic and polyaminergic neurosystem genes, have been identified as key players in certain young suicidal subjects [10].

Recently, the hypothesis that the pathogenesis of the suicidal behavior in young adults might be associated with alterations of neuronal plasticity has also been proposed, positing a resulting brain disability to develop adapted responses to exterior stressful events [11]. This hypothesis is sustained by studies showing structural brain alterations in depressed young adults dead by suicide, such as reduction of neuronal body sizes coupled with a decrease in the neuronal and glial density in specific brain areas (prefrontal cortex and hippocampus). Alterations of the synaptic network have been also identified as a potentially crucial pathological element, causing a decrease in the global neuronal activity in the prefrontal and dorsolateral cortexes, together with a reduction of synaptic functioning in the frontal lobe of the brain [12].

Investigations on post-mortem brain samples have identified

the implication of Brain Derived Neurotrophic Factor (BDNF), in particular at the level of the prefrontal cortex, in the suicidal behavior in young adults. Decreased BDNF levels (at mRNA and protein levels) have been found in the prefrontal cortex and hippocampus of young suicidal subjects. Of interest, suicidal subjects who received an anti-depressant medication did not show such a decrease, pointing toward an effect of the pharmacotherapy on BDNF levels [13].

In a 2008 study of adolescents and young adults with suicidal behavior [14], the levels of BDNF mRNA were decreased in the prefrontal cortex and the hippocampus, while BDNF protein levels were found diminished only in the prefrontal cortex and not in the hippocampus. The hypothesis of DNA methylation alterations (specifically hyper-methylation) was also proposed to explain the dysregulation of BDNF gene expression in different brain areas [15].

Results from a number of neuroimaging studies revealed that the orbitofrontal cortex, involved in emotional and cognitive processes, was the most frequently identified altered brain region in studies of suicidal behavior in young adult depressed patients [16-19]. Several studies have focused on the relationship between alterations in the orbitofrontal cortex and impairments in decision-making in suicidal behavior [20,21] as well as reduced grey matter volume in the orbitofrontal cortex [22]. Another considerable cluster is the anterior cingulate cortex [23] which is responsible for conflict detection and the emotional evaluation of errors and connected to brain structures that regulate mood, emotional valence of thought and autonomic and visceral responses [24]. One neuroimaging study has shown that decreased grey matter density in the anterior cingulate cortex is related to suicide [25]. Abnormal activity in the anterior cingulate cortex has been also detected in adolescent suicidal individuals [20,26,27]. These findings appear to be consistent with *postmortem* studies on suicide. One study by Hercher et al. reported that, compared to controls, depressed suicide completers had reduced number and length of dendritic branchings in the anterior cingulate cortex [28]. Alterations in striatum have been increasingly reported in studies on depression and suicide [29,30]. In a fMRI study of suicidal ideation, Marchand et al. found that the striatal network was associated with depression severity and current suicidal ideation [31]. In a voxel-based morphometry study, Hwang et al. reported grey matter reductions in widespread brain regions in suicidal depressed patients compared with non-suicidal depressed patients, including the lentiform nucleus [32]. Alterations of other brain regions have also been reported in studies of young suicide attempters. In a PET study, major depressed suicide attempters showed reduced 5-HTT binding in the midbrain compared to non-suicidal subjects [33,34].

Alterations in immunological pathways have been also detected mainly in peripheral blood and cerebrospinal fluid and, less

frequently, in the brains of young adult patients with positive anamnesis for psychiatric disorders, such as schizophrenia or affective disorders and history of suicide attempts or commitments. In particular, it has been demonstrated that microglial activation as well as specific cytokines, released from microglial cells, could modulate noradrenergic or serotonergic neurotransmission, finally triggering suicidality [35].

Suicidal behavior has been also defined as an inherited factor. Thus, relatives of young adults with clear suicidal behavior or repetitive suicide attempts showed an increased rate of suicidal acts. Also, these behaviors appear to be more strongly correlated between monozygotic twins than dizygotic ones [36]. In a recent review, Zalsman summarized data from several studies showing that family members of children or adolescents who attempt or succeed in suicide presented increased risk of suicidal behavior independently from psychiatric comorbidities, in particular depression, with respect to control subjects. These results could be read in the light of the genetic inheritance of the underlying psychiatric disorders as well as non-genetic factors, such as familial imitation or exposure to violence in the familial entourage [37]. Although genes which contribute to the vulnerability of suicidal behavior in young adults are still unknown, several candidates have been proposed by genetic studies of association, such as genes involved in the regulation of the serotonergic system. In particular, polymorphisms of the serotonin transporter linked polymorphic region (5-HTTLPR) have been shown to play a key role in the neurobiological pathways leading to suicidal behavior in young adults [38].

### **Epidemiology of suicidal behavior in young adults**

Suicide rates in young adults could be underestimated because of the fact that deaths by suicide in this population are often wrongly attributed to casual accidents. International literature on this subject shows that death by suicide is the second cause of mortality in young adults (males and females) after deaths by road accidents and the third cause in male young adults after deaths caused by violence or aggressions [39]. Suicide is not common before the age of 15 years old (1.2 deaths/ 100,000 for boys 5-14 years old). However, its prevalence dramatically increases during adolescence and young adulthood (19.2 death/ 100.000 for male adolescents 15-24 years old) as well as adult age (28.3 deaths/ 100,000 for male adults 25-34 years old). Officially, there are at least 164,000 suicides every year in subjects under 25 years old. The prevalence of suicide in young adult populations varies also according to geographical distribution. In particular, Russia, Ukraine, Japan, Lithuania, Finland and Hungary are the most affected countries. In China, suicide rates are particularly elevated in rural regions with respect to urban zones of the country. Of note, young women (15-24 years old) appear to be the most affected Chinese subpopulation. Conversely, in Europe, the U.S.A., Asia, Australia and

some regions of the South America, suicidal behavior is more prevalent in 15-29 years old males [40]. From a general point of view, between the 1960s-1980s, suicide rates significantly increased. From 1980s to 1990s, a decrease in the rate of the suicidal attempts was observed, specifically among the 15-24 years old males [41]. Evidence related to the period after 1990s reports a significant, constant and progressive increase of suicide rate, with a peak of incidence in the last 6 years.

Available data on the international variations of suicide methods are mainly due to the different access to local archives and database. Suicide by hanging is actually considered the main suicide method used by male young adults in Europe and Australia [42]. Also, Japanese studies showed that hanging is the method used by 63% of 20-39 years old males [43]. In the U.S.A., suicide by firearms appears to be the most common among 15-24 years old males, representing also the 55% of the suicides in the 20-39 years old male population (in this same age class, suicide by hanging represents the 26% of the total suicide rate). In South Africa, suicide by hanging and by firearms has been shown to be the most common method used in 15-34 years old males [44]. In China, 82% of deaths by suicide are attributed to poisoning but this percentage appears to be valid for the general population, without distinction between male and female young adults [45]. In India, poisoning by pesticides is considered the most used suicidal method in male young adults (58% of suicides in 21-30 years old males with respect to 25% of suicides in female of the same class of age) [46].

New methods of suicide (highly lethal) are emerging in the east regions of Asia. These methods include, for example, the use of the hydrogen sulphide or the charcoal-burning. This last compound is especially used in Taiwan and Hong-Kong by 24-39 years old males and females and represented the 34% of total suicides in the year 2006 in these two areas [47].

### **Risk factors for suicidal behavior in young adults**

A theoretical distinction exists between risk factors associated with the development of thoughts of self-harm or suicide and those that increase the possibility that such thought will be translated into suicidal behavior [48]. Table 1. summarizes the sociodemographic, cultural, familial as well as psychiatric and psychological factors differentially related to attempted or completed suicide.

On the other hand, several metanalyses have focused on the identification of the main risk factors specific for male young adults (reviewed in [6]):

#### *1. Individual factors:*

- Presence of psychiatric comorbidities

**Table 1.** Sociodemographic, cultural, familial as well as psychiatric and psychological factors differentially related to attempted or completed suicide

RISK FACTORS	ATTEMPTED SUICIDE	COMPLETED SUICIDE
<i>Sociodemographic and cultural factors</i>	Sexual orientation: homosexuals and trans-sexuals	Gender: young males Difficult economic conditions Restrictive education
<i>Traumatic life events and familial factors</i>	Sexual abuses	Parents' separation or divorce Death of one parent or both Traumatic events experienced during childhood or adolescence Parents suffering from psychiatric disorders Familiarity for suicidal behaviour: inheritance of aggressivity and impulsivity [49] and genetic transmission of dysfunctions of the serotonergic system [50]
<i>Psychiatric and psychological factors</i>	Impulsivity Low self-esteem Impaired problem-solving mental processes	Psychiatric comorbidities: mood disorders and psychosis Substance abuse Feelings of despair

- Substance abuse

- Specific socio-professional identities: farmers in Australia [51], veterans of the U.S.A., English and French armies [52] and medical doctors in England and Wales [53] are at high risk of suicidal behaviour

- Ethnic aspects: the highest suicide rate is observed among male young adults of South Africa [54], the young Maori of New Zealand, the Canadian Inuit [55] and the native Americans of two specific classes of age : 15-24 and 20-39 years old in the U.S.A. [56].

- Residence in rural regions: this is valid in particular for Australia, China, Denmark, Austria, England and Wales

- Low social and economic status in particular in Australia

- Being unmarried, divorced or widowed

## 2. Social factors:

- Unemployment: in particular, in England, Wales, Ireland and Austria

- Social isolation: in particular, in England and Wales

- Impact of mass-media: such as repetitive contacts with special reports focused on cases of suicides.

## Psychiatric comorbidities for suicidal behavior in young adults

Several topical clinical studies on this subject are nowadays available. In 2005, the group of Houbart published the results of a study conducted at the "Centre Patrick Dewaere" in Belgium, a psychiatric center for 15-35 years old who attempted suicide, created in 1995 [57]. Authors collected data from a cohort of 885 patients, admitted to the Centre from July 1996 to November 2003, following specific inclusion criteria such

as age, absence of concomitant clear addiction to any several substances (alcohol, amphetamine, cannabis, cocaine, hallucinogens, solvents, opioids, sedatives, hypnotic or anxiolytic compounds), the anamnestic presence of suicidal acts or active suicidal ideas. Results showed that the most frequent psychiatric disorders associated with suicidal behavior in this population were adjustment disorders (67.3%) followed by dysthymic disorders (13.3%) and by substance-abuse induced mental disturbances (5.6%) for psychiatric disorders included in axis I; personality disorders (histrionic personality disorder 25.2%), non-specific personality disorders (14.6%), borderline personality disorder (12.7%), dependent personality disorder (7.8%), avoidant personality disorder (5%), antisocial personality disorder (4.8%), schizoid personality disorder (2.9%) and paranoid personality disorder (1.2%) for psychiatric disorders included in axis II. Most of the patients included in this study (80%) were also affected by the presence of psychosocial problems. The conclusions of this study pointed toward the polymorphism of the included population in terms of diagnostic classification, showing that, among young adults, suicidal behavior has to be considered as a part of a more complex clinical evaluation and not only as a complication of a major depressive episode.

Data has also been published on the association between suicidal behavior in young adults and first psychotic episodes in the same populations. A review published in 2011 [58] summarizes a total number of about 100 original articles and book chapters published between 1965 and 2010 on this subject, showing that the risk of committing suicide is relatively high among young adults with a diagnosis of first psychotic episode with some peaks during the post-hospitalization period. In particular, in the first year of the psychiatric and psychotherapeutic treatment after the first psychotic episode, the risk of attempting or committing suicide is double compared to the one observed for other mental disorders, also associated to an increased suicidal behavior risk in young adults. Another study showed that the incidence of suicide attempts or acts is double in young adults with first episode of psychosis with respects to what is observed in older adult psychotic subjects [59]. The role of attention deficit hyperactivity disorder (ADHD) in suicide among adolescents and young adults with bipolar disorder has been very recently elucidated in a study of Lan et al. [60]. 500 adolescents and young adults from 2002 to 2008 aged between 15 and 24 years with bipolar disorder and ADHD were included in the study. The sample was matched according to age and sex with 1500 patients with bipolar disorder only and observed until the end of 2011. The patients who attempted suicide during the follow-up period were identified. Results showed that adolescents and young adults with bipolar disorder and ADHD had a greater incidence of attempted suicide than those with bipolar disorder only. After adjustment for demographic factors and psychiatric comorbidities, authors concluded that ADHD was an independent risk factor for attempted suicide later in life among adolescents and young

adults with bipolar disorder.

### **The role of the familial entourage**

The family entourage and, in particular, the characteristics of family relationships, has been shown to be a crucial risk or protective factor for suicidal behavior in adolescent and young adult populations [61-63]. Actual scientific literature on this subject highlights that poor family environment, as well as absence of family support and cohesion, poor parent-child attachment and dysfunctioning of the parental couple [64] might be considered the main risk factors. Conversely, the existence of a strong cohesion among family members has been described as a protective factor together with non-conflicting relationships with a parent or both [65]. Data suggest also a different impact of family factors on the development of suicidal behavior according to gender, clinical severity and dissimilarities between the affective links with mother and father [66]. In a clinical study of Consoli et al., authors investigated specifically the link between family factors and suicidal behavior in a large community-based sample of 17 year-old adolescents [67]. Results showed that 7.5% of adolescents had clinical characteristics compatible with depression, 16.2% reported suicidal ideations in the past 12 months and 8.2% reported lifetime suicide attempts. Other risk factors associated to suicidal behavior in the population included in the study were repeating a school-year (this was associated to a high grade of severity of the suicide risk) and substance abuse. Moreover, these subjects experienced conflicting relationships with parents as well as within the parental couple.

### **Prevention and psychosocial strategies for suicidal behavior in young adults**

Prevention strategies of suicide in young adults should consider the specific characteristics of this population. Globally speaking, prevention approaches might be divided in strategies applied to the general population of young adults and interventions concerning the young adults at suicide risk. For the general population of young adults, school appears to play a crucial role, assuring psycho-educational interventions by teachers, social workers and psychologists as well as dedicated listening spaces on this subject with the aim of a first screening of young adults to be considered at risk for suicidal behaviour.

Outside school, a decreased access to the means used to attempt or commit suicide might represent a crucial step of prevention strategies (difficult to achieve for the hanging method). The decreased use of co-proxamol in Scotland and of imported pesticides in Sri-Lanka has significantly reduced the suicide rate by poisoning in 17-35 years old young adults [68]. Changes in the legislation concerning the possession of firearms have not reduced the suicide rate by using this method in the U.S.A. but had a significant impact on the suicide rate in Canada in the 15-34 years old population [69]. Crucial inter-

ventions are also represented by the existence of specific help-lines together with a general reduction of the social, individual and familiar stigmatization of mental affections.

Concerning the strategies of prevention for young adults at risk of suicide, the psychotherapeutic approach, if necessary associated with pharmacological treatments, has been shown to be an essential element. However, evidence in favor of a significant effect of antidepressant medication is still controversial [70]. In this context, the Food and Drug Administration has recently published a meta-analysis showing no significant reduction of the suicide rate in young adults (younger than 25 years old) treated with antidepressant compounds [71]. Moreover, it has been shown that the benefits of an antidepressant therapy in young adults is frequently unbalanced by a high risk of sparking a clear suicidal behavior in these populations [72]. Although this appears to be more evident in the first phases of antidepressant treatment, several studies have detected no differences of the effects of this therapy on suicidal behavior between the first month of medication and the following treatment period [73-75]. Other studies detected no differences between the effects of cognitive-behavioral psychotherapy and SSRI antidepressant medication on the reduction of suicide rates in the young adult population [76].

Very recent clinical evidence point towards a possible anti-suicidal effect of the N-methyl-D-aspartic acid (NMDA) receptor antagonist ketamine in depressed young adult patients [77-79]. Price and co-workers showed that a single infusion of ketamine displayed significant anti-suicidal effects through a decrease in depression symptoms [80]. A number of other case reports indicate the beneficial effects of ketamine on young patients with suicidal behavior or ideation in treatment-resistant depression associated to alcohol and benzodiazepine dependence or post-traumatic stress disorders and in severe major depression [81-84].

## Conclusions

Suicidal behavior has to be considered a serious expression of psychological stress and deep despair. This appears to be particularly true in the population of young adults. Although a large quantity of information on this subject is now available, other crucial aspects, such as the clinical management of people who attempted suicide or the psychological and pharmacological approaches to these patients, remain still controversial and requires further clarifications.

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## Conflicts of Interest

The authors declare no biomedical financial interests or potential conflicts of interest relevant to the subject matter of this work.

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