REVIEW

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Concept of Suicide: Neurophysiological/Genetic Theories and Possible Oxytocin Relevance

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The suicidal behavior is regarded as the act by which a person seeks to take his life, being aware of the consequences of his action. In our review, besides describing the main introductory aspects for the concept of suicide, we focus our attention on the main neurophysiological and genetical mechanisms relevant for this extremely difficult to manage and controversial behavior. Moreover, considering the latest interests in the current literature on the relevance of central oxytocin to various superior cognitive behaviors, we will also make a short description on how important effects of oxytocin could be in the context of suicidal behavior.

Keywords: suicide, neurophysiological and genetic mechanisms, oxytocin.

INTRODUCTION

THE CONCEPT OF SUICIDE

The suicidal behavior is regarded as the act by which a person seeks to take his/her life, being aware of the consequences of this action [1]. Thus, suicide can be regarded as a rationally executed act, based on moral, social, religious, philosophical and/or personal reasons. Conversely, suicide may be seen as a pathological act, which occurs during the development of various mental disorders (e.g., depression, persistent delirium, dementia, confusion, etc.), or in the context of an acute existential crisis in which the manifestations may take the form of an auto-aggressive anxious raptus. These raptuses are spontaneous, unpredictable, and are manifested extremely rapidly, as compared with the premeditated suicide of patients with melancholic depression or in the context of systematized deliria [2]. Overall, regardless of motivations and context (e.g., social, family, or personal), the concept of suicidal ideation refers to a person's thoughts to take his/her own life.

The World Health Organization defines suicide as an act by which an individual seeks for his/her physical self-destroy, with the more or less authentic intention to waste his/her life or being more or less conscious of the rationale of the gesture [3]. Interpreted more broadly, the concept of suicide can also refer to any action, tendency, or behavior of self harm (including the so-called "chronic suicide " of drug addicts, alcoholics, or individuals with mental anorexia) that by certain self-destructive behaviors of repetitive cyclical-nature attempts to finish the personal life. Also, in a narrow interpretation, suicide is the act of global self-destruction, of sudden suppression of one's own life, intentionally, willfully, knowingly, and considering death as a total and inexorable ending.

In fact, suicide is the expression of an acute crisis of conscience that expresses a subjective-affective tension between the individual and the group, favored by situational factors, with the ability to precipitate the autolytic gesture in a fragile and vulnerable personality [4]. In this way, Douglas [5] defines suicide from a double perspective, both psychological and sociological, addressing rather a concept than an operational definition. Douglas reveals the five dimensions of the suicidal

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act, namely initiative, motivation, intention, will, and desire. According to Scripcaru et al. [6], the suicide definition would represent a tempted or actual behavior expressing a psycho-emotional tension between the individual and the social group, triggered or precipitated by circumstantial factors with a consciously designed self-destruction idea. In addition, other theorists consider suicide a disruption of homeostasis in the individual/environmental relation and deciphering its code depending on the visibility and understandability of its forms of expression. Thus, in some individuals a death will is certain, while in others it is uncertain, in some it is impulsive, in some it can be cyclical, in some it is chronic, persistent, and in others the wish to die is acute, transient, with or without a repeatability trend.

The concept of suicidal behavior refers to the technical support, consisting of the preparatory work for staging the suicidal act, the steps and settling the suicidal plan. Choosing the manner of ending one's own life is determined by many factors, such as effectiveness, speed, ease of execution, imitation, keeping physical appearance and bodily integrity, availability of the suicidal method, and sometimes also by limiting as much as possible the beforehand suffering and anguish. To ensure the success of the method, the most efficient approach will be adopted in accordance with the availability and access to certain types of methods. But ultimately, the choice of the suicidal means is determined by the significance of the act and the mental condition of the person at the time when committing suicide. The effectiveness of the chosen means is regarded as revealing the authenticity of the suicide attempt. Traditionally, it is considered that the main autolytic means are traumatic (defenestration and shooting), asphyxia (gas inhalation, submersion, strangulation), and toxic (ingestion of the respective substances) [7].

Also, certain aspects due to cultural differences should be mentioned when choosing other variants of self harm. Thus, while in China the poisoning with opium and salts of arsenic is frequent, in Japan the traditional seppuku was replaced by the use of firearms, while in France the order of the most commonly used methods is hanging, drowning, and using firearms [8].

Below, we will briefly review the main methods used in suicidal behavior. One such method involves exsanguination by damaging the easy to access arteries (radial, ulnar, carotid, or femoral), wich causes hypovolemia below the critical level leading to a circulatory collapse. Chronic suicide attempts, parasuicide, or self-mutilation attained in the same manner can be assessed by looking for traumatic marks (scars) at the level of these arteries. Also typical of this type of conduct is a large number of injuries [9]. In addition, suicide by hanging involves two types of mechanisms, depending on the length of the drop. Thus, one of the mechanisms that occurs in the short drop achieves death by hypoxia through the compression of the carotid artery and jugular vein. For the longer drops, vertebral fractures can occur, often in the C5-C6 vertebrae, which cause death or paralysis in the survivors [10].

Another autolytic method used by suicidal persons is by jumping from high buildings, through windows (defenestration), from bridges or cliffs. This is frequent especially in the areas with increased accessibility to these kind of methods. For example, in Hong Kong, where there are a large number of high buildings, more than half of the deaths by suicide are executed through this method [11]. This autolytic approach is associated with a high risk of severe consequences in the case of a failed suicide, such as paresis, paralyses, bone fractures, and severe damages to internal organs.

Another method of suicide used relatively frequently involves the use of firearms. The use of such arms in suicide attempts is more common in people who routinely possess firearms, but also in countries with permissive legislation on firearms possession [12]. However, it is doubtful to believe that the legislative restrictions concerning the firearms possession would lead to lower overall rates of suicide. The decrease of certain methods of suicide by reducing the access possibilities could lead to increased rates of other types of methods as a compensatory mechanism.

Suicide produced by asphyxia is often achieved by exposure to certain toxic gases, such as carbon monoxide. This produces a quick death as it rapidly induces the unconsciousness state preventing an eventual change of mind of the suicidal person [13].

Suicide by drowning is relatively rare, as compared to other autolytic methods. A study conducted on the US population reported less than 2% of suicide deaths as caused by drowning. The mechanism of death consists in the acute oxygen deprivation of the brain by immersion in water that impedes the breathing process.

Other common suicidal methods include drug overdose, traffic accidents, electrocution, or

poisoning. Also, as previously mentioned, the modern trend concerning the growing use of hallucinogens suggests that drug addiction can be a passive form of self-distructive behavior. The chronic use of hallucinogens, naturally, has strong negative consequences on health.

Very interestingly, a research on the places selected for accomplishing the suicide reported that about 44% of suicidal acts are performed at home; public places, hotels, and working places are less preferred [14]. In this way, such aspects could represent an important lead when intending to oversee and prevent a person known with a high risk of suicide.

According to Stengel [15], the genuine suicidal act unfolds as follows: the occurrence of one's decision to end his/her life or the impulsive action to self-kill, using for this the most efficient methods, and taking all the safety measures that nobody will interfere. If death occurs, it is considered a successful suicide attempt; if the person survives, the act would be considered a failed suicide one. As death is the only purpose of the act, it should be considered the criterion for success. The failure may be caused by any of the following: motivation is not strong enough; the act has not been well prepared (either due to lack of total conviction on completing the act, or because of lack of knowledge on the limits of the chosen method, lack of judgment, and determination because of a mental illness). According to these criteria, only a part of the accomplished suicidal acts and only a small part of those unfinished can be considered genuine acts of suicide. However, even in the suicidal acts where the person is not fully committed to end his life, a significant number of cases come to completion, while the rest remain as unclear trends or insufficient efforts, ending rather by accident than by determination in action.

In this way, it could be stated that suicide is actually the action of taking one's own life, while a suicide attempt or non-fatal suicidal behavior refers to self-harming in order to take one's own life, but that does not lead to death. The differences between assisted suicide and euthanasia, types of suicide that require another person in order to be completed, should also be mentioned. The assisted suicide occurs when a person indirectly helps another to end his/her life, by providing advices or means for the suicidal act, and it differs from euthanasia, in which the other person is playing a more active role in causing someone's death.

In most cases, the completed suicide follows repeated suicide attempts. A large number of patients who died by suicide have a history of autolytic suicide attempts or even suicidal ideation. Sometimes, the suicidal people have in their family relatives with suicide attempts or completed suicide, which may account for models in their autolytic behavior. Attempted suicide is actually the missed (failed) suicidal act. The attempts may be the expression of a compulsion, can have a demonstrative value, or embody the expression of a punitive act. In fact, clinical studies have shown that suicidal attempts are 8-10 times more common in young people than in adults and about 5-10 times more often in women than in men, the ratio decreasing with age [16].

In general, the suicidal tendencies are explained by self-aggression, and the suicidal impulse explains the suicide as an expression of an irresistible trend. The irresistible suicidal impulse drives the individual to make use of the first means he/she comes across, in opposition to the former suicide plan. Often, the suicide attempts leave long-term physical consequences, which can be very different depending on the autolytic method. Thus, some serious physical sequelae may occur following autolytic attempts, such as mutilation, fractures, severe locomotor, psycho-sensorial, or mental disabilities (e.g., dementia after oxygen deprivation), or functional disabilities (paralysis).

In this way, Biberi [17] considers the suicide as a bio-psycho-social dimensional phenomenon representing an act requiring the deviation for one of the most deeply rooted instincts of the biological structure. In a dramatic situation in which the vital instinct is denied (out of which the subject does not see any escape), suicide becomes the only solution to avoid its unbearable conditions.

Also, according to Menninger [18], suicide encompasses the three desires that could foster a suicidal act, namely the desire to kill, the desire to be killed, and the desire to die. The desire to kill may be directed not only against an object of love, but also against the internal space. In fact, the conclusions of some long-term clinical trials showed that suicide is sometimes intended to destroy the lives of survivors, as an act of revenge against the others. For example, depressed patients often feel that suicide is the only satisfactory revenge. Sometimes, this act is directed against the parents, relatives, or the partner, and the act is intended to produce suffering of the latter.

In other cases, aggression plays a much more

modest role in terms of motivating the suicide. Thus, Fenichel [19] noted that suicide could mean the fulfillment of a desire to reunite. Losing a loved one is often behind suicidal behavior, and many suicidal patients exhibit strong desires of dependence on the lost person. From this point of view, suicide may be a regressive desire to reunite with a lost figure. Sometimes, a pathological process of mourning is involved, especially in attempts to commemorate the death of a loved one. In this way, there are some ideas that it could be a correlation between suicide and the commemoration for the death of a parent.

EPIDEMIOLOGICAL ASPECTS

The suicidal behavior is considered a psychiatric emergency. Virtually, all psychiatric disorders can sometimes generate either spontaneous auto-aggressive and hetero-aggressive outbursts on a background of high psychoemotional tension or, by contrary, those planned and idealized previously of the act. The demographic analysis of the completed suicide shows that, generally, the chosen suicide method depends on the geographical area and availability of the method, but also on certain personal factors. Among the chosen suicide methods, the most commonly used seems to be hanging, probably due to the easy access to material, as compared to other methods. A study conducted in 56 countries found hanging as the prevailing method of suicide in most countries [20]. This method was employed by 53% of men and 39% of women [21].

Also, a relatively high number of suicides have been recorded as a result of drug overdose, the cause of about 60% of the suicide cases in women and 30% in men [22]. Frequently, the suicide by overdose is not previously planned, or it occurs during a period of acute ambivalence. The difference between sexes regarding this method supports the idea of a higher frequency of planned suicide in men. The most often tried methods differ from the most often successful methods; up to 85% of suicide attempts in the developed countries consist in ingesting an overdose of drugs [23].

Moreover, the studies are generally indicating different percentages regarding the type of suicidal methods. A meta-analysis concerning the most frequent suicide methods identified shooting in 80-90% cases, drowning 65-80%, inhalation of an exhaust gas 40-60%, jumping from height 35-60%, and pesticides 6-75% [24].

Also, a regional analysis of the methods and frequency of suicide methods showed that 57% of suicides in the United States involve the use of a firearm, the percentage being distinctly higher in men than in women. A second cause of suicide in men is hanging, while in women this is poisoning. In Switzerland, the most common suicidal method is suicide by hanging [25], while in Hong Kong and Singapore suicide by jumping from height is very common, with rates ranging from 50% in Hong Kong to 80% in Singapore [24]. Moreover, in Japan, suicide by hanging is the most common method [26], but also the traditional suicide by disembowelment known as seppuku, or harakiri, is still used nowadays.

NEUROPHYSIOLOGICAL MECHANISMS AND THEORIES OF SUICIDE

In this way, among the most investigated neuro-chemcal systems related to the suicidal behavior is the serotonergic system. The researches focused on the levels of serotonin, its metabolite (5-hydroxy-indoleacetic acid, 5HIAA), its receptors (5HT2A), and its carrier (5HTT) in platelets. There are also several studies that have compared the whole blood- or platelet- levels of 5HT in patients with mood disorders and a suicide risk. Thus, Roggenbach et al. and the group led by Mann [35, 36] reported decreased serotonin levels in blood platelets in suicidal patients with real suicide attempts, as compared to patients with suicidal ideation only or without autolytic attempts and also non-suicidal patients.

Also, Almeida-Montes et al. [37] reported significantly decreased serum levels of 5HT in depressed patients who attempted suicide, when compared with depressed patients without suicide attempts. Moreover, in a meta-analysis by Lester [38] on a CSF serotonin metabolite, the authors found significantly lower levels of 5HIAA in the patients with previous suicide attempts, as well as in those who subsequently committed suicide or attempted this. In addition to low CSF 5-HIAA levels, the persons who committed suicide showed also an increased number of binding sites for serotonin. In terms of the autolytic ideation intensity, Tyano et al. [39] also found a negative correlation between plasma levels of 5HT and the severity of suicidal behavior in patients.

In addition, determining the 5HT receptors in

suicidal patients or those with affective disorders led to the extensive study of the 5HT2A receptor. This receptor type seems more likely to be modified in patients with depressive disorders and suicidal ideation. In general, the 5HT2A receptors were examined in blood platelets by radioligand binding techniques, and the pharmacological profile of the 5HT2A receptors in the platelets appears to be very similar to that observed in the brain [39].

Even more, Pandey and his collaborators [40] studied the platelet levels of 5HT2A receptors in patients with affective disorders with and without autolytic ideation. In the first instance, the level of 5HT2A receptors was found to be higher in depressed patients, as compared with control subjects. Also, the 5HT2A receptor density was even higher in depressed patients with suicidal behavior, when compared to depressed patients without suicidal ideation. When analyzing whether the increase of the 5HT2A receptors in the depressed suicidal patients is independent or not diagnostic and by examining the 5HT2A receptor levels in patients with various psychiatric diagnoses (such as depression, bipolar depression, manias, schizoaffective disorder, or schizophrenia), the authors also noted that the average receptor density in the total group of suicidal patients was significantly higher than that in non-suicidal patients or in the control group. Also, the receptor density was significantly higher in the patients with psychiatric disorders and autolytic ideation, as compared with control subjects. In addition, this study [40] suggested the increase of the platelet 5HT2A receptor density in suicidal patients, irrespective of the diagnosis.

In addition, numerous evidences supported the involvement of the 5-HT1A receptor in the formation of suicidal behavior. The important role of 5-HT1A receptors in suicidal behavior was in this way assayed by studying the changes of these receptors in the *postmortem* brains of the suicide victims. In this way, the results showed that binding to the 5-HT1A receptors was found to increase in the cortex of suicidal patients with major depression, but no change in binding to these receptors was observed in the frontal lobes, occipital cortex, hippocampus, and amygdala of depressed suicidal patients [41, 42]. These discrepancies could be explained by the intervention of other factors, such as gender, presence or absence of affective disorders, or ethanol consumption (as we would like to insist immediately on this important factor).

Also, the involvement of the serotonergic system in suicidal behavior seems to correlate with specific nervous areas, such as the forebrain, medial prefrontal cortex, orbitofrontal cortex, amygdala, and *nucl. accumbens* [43]. In this way, the *postmortem* studies of suicidal persons reported fewer serotonin transporters in the prefrontal cortex, hippocampus, occipital cortex, and brainstem [44].

We should also mention that the relationship between serotonin and aggressiveness [45] is an important aspect in studying the neurobiological underpinnings of suicide, especially in violent suicide cases. In fact, suicidal behavior is influenced by many biological variables that modify the serotonergic neurotransmission, including the psychosocial stress, traumatic experiences, pathological personality traits, disorders, or the alcohol abuse [46, 47].

Regarding the latter mentioned aspect, it is well known that alcoholism can be found in most psychiatric disorders and is often having an etiopathogenic role. Thus, affective disorders, anxiety, psychosis, dementia, and personality disorders frequently are accompanied by alcoholism as a co-morbidity. Moreover, some mental disorders are caused by prolonged or abusive alcohol consumption; other disorders appear as withdrawal phenomena, while in many cases alcoholism aggravates a preexisting psychiatric conditions. In some cases, alcohol consumption is intended to improve the psychiatric symptoms, such as anxiety, depression, psychosis, hypnic disorders, or side effects of medications [48]. Among the psychiatric disorders, depression and mood disorders are particularly associated with alcohol abuse. Of course, patients suffering from a major depressive disorder are at increased risk of suicide. What is important in the present context, is that studies on patients who died by suicide showed that in 30% of cases the blood alcohol level was close to or over the legal limit at the time of suicide, and half of them suffered from major depression [49]. Moreover, alcohol abuse is also suspected to dramatically (by an order of magnitude) increase the risk of suicidal behavior [50].

Still, the relationship between alcoholism, depression, and suicidal behavior is complex and clearly supported on the biochemical level. Some CSF analysis showed abnormalities of serotonin metabolism, through the dosing of the 5-hydroxyindoleacetic (5HIA) metabolite in depression and particularly in suicidal behavior. Moreover, low levels of this serotonergic metabolite

are encountered in impulsivity and aggressive excesses, which are manifested especially during the consumption of ethanol. As was many times mentioned, the elements of impulsivity and aggression are known to correlate with suicidal behavior [51].

Moreover, the risk of suicide for the patients addicted to alcohol is 60 to 120 times higher than that in the general population [52]. The gender distribution shows also a much higher frequency in men, in relation to the use of alcohol before committing the suicidal act [53]. Also, alcohol consumption can cause disinhibition and increased impulsivity, which could favor mobilization to complete the suicidal act.

GENETIC STUDIES

With regard to suicidal behavior, the research on families, twins, and adoptions provided evidence on the significant heritability of suicide and suicide attempts, independent of the family transmission for the major psychiatric disorders. Thus, for twins the estimated heritability for suicidal risk ranges between 21-50%, while for the broader phenotype of suicidal behavior (attempts, suicidal thoughts, and plans) it is 30-55%, depending on the type of study [27]. Also, some genetic researches have attempted to identify the genes involved in suicide and suicidal behavior by studies of genetic association or following specific single nucleotide polymorphisms for studies of association.

Candidate genes for association studies were generally selected on the basis of evidence from neurobiological studies in suicidal patients. Therefore, the serotonergic system has been extensively investigated in relation with other target systems, including the dopaminergic and noradrenergic ones, derived neurotrophic factor, and, more recently, the genes related to hypothalamic-pituitary-adrenal (HPA) axis. Apparently, the environment could be also very influential in this matter, especially during the development.

Moreover, the neurobiological evidences indicated a considerable serotonergic dysfunction in suicide cases, while the genetic research has been mainly focused on genes related to the serotonin system. At the molecular level, serotonin appears to be one of the key neurotransmitters involved in the formation and control of suicidal behavior. Thus, among the genes encoding proteins involved in the serotonergic neurotransmission in suicidal persons, the most consistent scientific evidences are referring to the tryptophan hydroxylase gene, especially in the case of violent suicidal behavior [28]. In addition, promising studies have examined the serotonin receptors, monoamin oxidase receptors, serotonin 2a and 2c receptors, and tyrosine hydroxylase.

Thus, the genetic factors seem to be a significant risk factor, apart from the environmental aspects of suicidal behavior. Moreover, epidemiological and genetic studies indicated a familial aggregation of suicidal behavior, with a fivefold greater risk for relatives of persons with suicidal behavior [29, 30]. In this way, Voracek et al. [27] reported a significantly higher rate of concordance for suicidal behavior in monozygotic twins (24.1%), as compared to dizygotic ones (2.8%).

Also, the neurobiological and genetic studies have suggested that, generally, the suicidal behavior results from a complex interaction of multiple genes and environmental factors. The suicide attempts in this suicidal model are considered a combination of stressors and personality traits. Basically, for this model, the innate genotypic and phenotypic profile of the individuals determines their inability to cope with stressors [31]. Also, many specific genetic variants may exert additive effects on suicidal behavior by intensifying the impact of a stressor.

The researchers who analyzed the importance of genes in suicide have primarily focused on the genes involved in the serotonergic, adrenergic, noradrenergic, and dopaminergic neurotransmitter systems by the analysis of the samples taken from *postmortem* brain tissues of persons who completed suicide. Thus, a strong evidence supporting the association with suicidal attempts was identified for one of the most commonly studied suicide-related gene, the S allele of the serotonin transporter, but this was not found with respect to completed suicide [31]. Moreover, a study published in 2007 on bipolar patients highlighted the importance of the 2p12 locus in the patients with suicidal attempts, supporting previous studies on the relevance of this locus to suicidal behavior [32].

Also, the results of some studies have suggested the involvement of the dopaminergic system, in particular of the D2 receptor, in the expression of suicidal behavior. Thus, a study on 120 patients with suicidal attempts assessed the association between these attempts and two types of functional polymorphisms of the dopamine D2 receptor gene (*DRD2*), *TaqIA,* and *141C*, as compared with the

control group. It was demonstrated [33] that there are significant differences in the frequency of the allele-*141C Ins/Del* and *TaqIA* polymorphisms between patients and the healthy control group, suggesting that *DRD2* gene polymorphisms might be involved in the biological susceptibility to suicidal behavior.

Also, cholecystokinin (CCK) could play a significant role in the suicidal behavior. In this way, Shindo et al. [34] found a strong association between the gene for CCK (the latter as a central nervous system neurotransmitter found inside certain dopaminergic neurons and also modulating dopamine release) and suicidal behavior, by analyzing the DNA of 154 suicide victims, as compared with 328 control subjects. The statistical analysis demonstrated an association between the polymorphism of *CCK -196G/A* and suicide occurance only in men of the studied group, and not in women.

OXYTOCIN RELEVANCE

As we mentioned at different other occasions [45], within the last few years there was an increase in the number of research groups and general interest for better understanding of the possible beneficial effects exerted especially by oxytocin on the main neuropsychiatric diseases, with a focus on schizophrenia [54], depression [55], frontotemporal dementia [56], autism [57], or anxiety-related behavior [58].

In relation to suicidal behavior, there are also some interesting and controversial aspects to be mentioned for the possible influence exerted by oxytocin.

These possible correlations basically started in a study performed in 2009 by the group of Lee et al. [59], who mainly focused on the relations between CSF oxytocin, aggression, and personality disorder, but also did manage to increase awareness on possible relations between oxytocin and suicidal behavior through only 4 patients with suicide attempts *vs.* 54 controls (non-suicidal attempters) by using the specific LHA scale.

One of the most important studies in this research area regarding the interactions between oxytocin and suicide was performed in 2012 by the Swedish group of Jokinen et al. [60], who clearly demonstrated decreased levels of oxytocin in the CSF obtained by lumbar punctures of 28 medication-free suicide attempters *vs.* healthy controls [60]. Moreover, the aforementioned group did manage to find some important correlations between most of the specific scales they have used to asses suicidal behavior (e.g., the Beck Suicide Intent Scale, the Freeman scale, or the Karolinska Interpersonal Violence Scale) and both CSF and plasma oxytocin levels, but only in men and not in women. However, the authors also found correlations between aggressive/violent behavior and oxytocin levels only in female suicide attempters (we would like to insist immediately on the relevance of this aspect). In fact, our research group also described earlier the complex interaction between aggressive behavior and oxytocin activities [45].

On the other hand, there are still controversies in this area of research, since some research groups failed to find any correlations between the oxytocin levels and psychiatric patients with and without recent suicide attempts. For example, this was the Deisenhammer et al. group [61], who found no differences in terms of plasma oxytocin concentrations between people with affective disorders and suicide attempts within the last 12 months *vs.* people with affective disorders but no suicide attempts.

Dissimilar results obtained by various research groups could be explained by differences in the established research protocol (e.g., oxytocin levels could be quite different in the CSF *vs.* plasma, as was in the two studies mentioned above), different medication, or the fact that suicidal behavior can exhibit extremely important gender differences [60, 62].

Mechanistically speaking, the implications of oxytocin in suicidal behavior could also be explained through the important effects exerted by oxytocin in stress modulation, e.g., by decreasing cortisol levels. This could be done by inhibiting the HPA axis [63].

Important correlative results between the decreased levels of plasma oxytocin and borderline personality disorder were also observed only in women patients [65]. This could be quite relevant in the present context, especially considering that certain behaviors, such as self-injury, suicidal, or parasuicidal one, are for a long time accepted in patients suffering from borderline personality disorder [65]. In addition, the aforementioned Bertsch group [64] showed correlations between traumatic childhood experiences (e.g., emotional neglect or abuse and aggressive behavior) and

oxytocin concentrations in the plasma.

In fact, in direct relation to the traumatic childhood experiences, the group of Chatzittofis [66] quite recently (in 2014) showed that there is also an interesting relationship between the CSF/plasma oxytocin concentrations in suicide attempters and the role of a childhood trauma and revictimization. These authors, using evaluation scales (such as the Karolinska Interpersonal Violence Scale), showed important correlations between revictimized suicide attempters and plasma oxytocin levels in 28 medication-free suicide attempters. Still, the authors failed to find any correlation between interpersonal violence exposure as a child *vs.* CSF and/or plasma oxytocin [66]. However, it is generally accepted in the literature that a strong correlation between childhood abuse and oxytocin concentration should exist [67].

Recent studies also described important interactions between CSF oxytocin concentrations and the schizophrenic pathology, especially in men [68]. This could be extremely relevant, especially considering the very well known and extensively accepted relationship between schizophrenia and suicidal behavior [69]. Anyway, the schizophrenic pathology has attracted an increased interest from the most important worldwide names in the effects of intranasal oxytocin studies, as, e.g., from the group of Guastella et al. [72]. These authors showed that only one dose of oxytocin nasal spray could facilitate social cognition in schizophrenia [54]. Still, there are controversies also in this area of research with previous reports stating significant correlations [70] or no correlations at all [71] between the CSF levels of oxytocin and schizophrenic pathology. One of the explanations for this aspect could be represented by a complex nature of the relations existing between administration of antipsychotics in schizophrenia and the oxytocin concentration (e.g., they might actually decrease the levels of oxytocin [72]).

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In our paper we, besides describing the main introductory aspects for the concept of suicide, focused our attention on the main biological and genetical mechanisms relevant for the suicidal behavior. Moreover, considering the latest interests in the current literature on the relevance of central oxytocin in various superior cognitive behaviors, we also desribed how important oxytocin could be in the context of suicidal behavior.

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