Archives of Psychiatry and Psychotherapy, 2020; 2: 25–35

DOI: 10.12740/APP/117705

Neurobiology of the association between non-suicidal self-injury, suicidal behavior and emotional intelligence: A review

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Summary

Non-suicidal self-injuries (NSSI) and suicidal behaviours (SB) are common causes of serious medical problems leading to hospitalization or death in adolescents and young adults. The prevalence of NSSI in adolescents is estimated at 17-18% in general population and in 40% of psychiatric hospitalized patients. Nearly one million people worldwide die from suicide each year. The epidemiological data show that suicide is the fourth cause of death among children between 10 and 14 years old, the third cause among people aged 15-19 years old, the first or second among people 14-25 years old and the second among people 25-34 years old. Many psychological, psychiatric, genetic and demographic factors have been previously studied in order to assess risk factors leading to NSSI and SB. One of psychological factors influencing the engagement in NSSI and SB is emotional intelligence (EI), which is defined as collection of social skills. More frequent NSSI and SB have been found in individuals with low EI in previous studies. The relationship between SB, NSSI and underlaying neurotransmission and brain structures have been also extensively studied. Studies applying neuroimaging techniques show correlation between alterations of brain areas which are responsible for involving in self-injourous acts and suicidal behaviours and regions key to EI levels. Thus we aimed to review the neurobiological background of emotional intelligence and self-harm and discuss the current state of knowledge on its relationship

emotional intelligence, suicide, adolescence, suicide attempt, non-suicidal self-injury

BASIC DEFINITIONS AND EPIDEMIOLOGICAL ISSUES

In order to describe self-injury behaviours, researchers usually use the following terms: suicidal behaviour (SB) and non-suicidal self-injury (NSSI). The first one includes thoughts of suicide, suicidal attempt (SA) and committed suicide (suicide, S). NSSI is a deliberate self-harm behaviour without intent of death.

Suicide traits include: purposefulness, intentionality, independence, voluntary, consciousness and planned [1]. According to current WHO data, suicides are among the twenty most common causes of death among the general population, the third leading cause of death among adolescents aged 15-19 years and the fourth leading cause of death in children aged 10-14 years [2]. In 2001, the number of people who died as a result of suicide was about one

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million, exceeding the number of murder and war victims (500.000 and 230.000 respectively). According to current estimates, the number of suicide victims may reach as much as 1.5 million in 2020. The suicide rate varies from country to country per year, ranging from 0.1 (Egypt) to over 40 (Hungary, Russia, Lithuania) per 100.000 inhabitants [2]. In Poland, this indicator has oscillated around 15 per 100.000 people in recent years [3].

Due to the epidemiological importance of the problem, research is underway into the identification of risk factors for suicide acts. Despite the fact, that in DSM-5 the following criteria for SBD have been established, this diagnostic construct is still included in the section "conditions for further study".

Suicidal behavior disorder (SBD) can be diagnosed when:

1. at least one suicide attempt occurred in the last two years,
2. suicide attempt does not meet the criteria for self-mutilation,
3. diagnosis does not apply to suicidal thoughts, suicidal plans or preparation for suicide,
4. suicidal behaviour is not related to disturbances of consciousness,
5. the suicide act is not connected with political or religious motivation [4].

NSSI is a specific form of self-injury connected with the destruction of the body tissue occurring without the intention of death. These are activities in which the individual aims at causing immediate damage to himself, which has no effect and no suicidal intent. These behaviours are undertaken in order to damage the body, induce bleeding, bruising or physical pain. NSSI is most commonly performed as a result of cutting the skin continuity – cutting and incision (70-90%), as well as striking (21-44%), burning (15-35%), biting, bruising or scratching the skin, interfering with wound healing (e.g. scratching wounds and scabs), sticking, sticking needles, sticking objects under the nails, pulling hair out [5]. NSSI coexists with emotional and developmental disorders of different etiologies or personality disorders. According to DSM-5, these behaviours are pereceived as a separate nosological entity. The ICD-10 and DSM-IV classifications include self-mutilations as one of the symptoms of borderline personality disorders.

The DSM-5 non-suicidal self-injury disorder diagnostic criteria include [4]:

A. Intentionally committed physical damage, but without suicidal intent, on five or more days in the last year;
B. These acts should be made for at least one of the following reasons:
   1. to free oneself from negative thoughts or feelings,
   2. to solve an interpersonal problem,
   3. in order to evoke positive feelings or emotions;
C. Such behaviour is associated with one or more of the following factors:
   1. negative thoughts, feelings or interpersonal problems that immediately precede the self-mutilations,
   2. absorbing self-mutilations, which is hard to resist,
   3. frequent coercion to perform self-mutilations;
D. Behaviour is not socially sanctioned and is more significant than biting nails or scratching wounds (scabs);
E. It causes clinically significant suffering or damage;
F. This behaviour does not only occur in the context of another disorder and cannot be explained by another mental disorder or condition.

The NSSI is being undertaken by 17-18% of adolescents in the world. After the adolescent period, the prevalence of these behaviors decreases, reaching 6% in adults [6]. In adolescents staying in care and educational centres, this behaviour occurs in 30-40% of cases [7, 8]. The intensity of NSSI is related to developmental stage. The onset of NSSI appears around 12-15 years of age. [5]. These behaviours become particularly intense in the middle of puberty. The highest prevalence of self-mutilations is observed among 15-year-old adolescents (12.7%) [9]. Among younger teenagers (13-15 years of age), NSSI is chronic (12-month period) in 2.5% – 7.5% [10].

It should be noted that the are certain differences in prevalence rates of NSSI acts between girls and boys. The prevalence of NSSI among girls ranges from 13.5% to 24.3% and among boys from 4.3% to 8.5% [10]. Zetterqvist et. al. [11] describe that DSM-5 self-mutilations frequency criterion among girls (11.1%) than among boys (2.3%).

The risk factors of self-injury include: co-occurrence of mental disorders or psychopathological symptoms (especially affective disorders or borderline personality disorder), substance use, post-traumatic stress disorder, impulsiveness, externalizing disorders, attention deficit disorder with or without hyperactivity and behavioural disorders [1, 5-11]. One of the factors not related to psychopathology, influencing SB and NSSI, is the level of emotional intelligence (EI).

What is EI and how is it related to self-injuring?

EI is a clustering of social skills, and according to Goleman [12], it is the ability to understand, direct, control, and empathize with oneself and one's own emotions. There are two main models describing EI: Trait Emotional Intelligence (TEI) and Abilities Emotional Intelligence (AEI). TEI – capturing EI as a permanent personality trait [13] and is evaluated by questionnaires, e.g. The Trait Meta-Mood Scale [14]. AEI that captures EI as ability [14] and is assessed in objective tests, e.g. The Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) [15].

One of the variables influencing self-injurious behaviour is the level of EI. The results of many studies indicate a correlation between low EI level and more frequent self-destructive actions: both self-injuries and suicide attempts [16-18]. Studies using different brain imaging methods show that differences in the structure and function of similar brain areas are responsible for differences in self-injurious responses as well as differences in EI levels.

Search strategy

The aim of this research is to discuss the neurobiological background of EI, NSSI and SB on the structural, functional and molecular levels and to present the current knowledge on the relationship between EI and suicide risk and deliberate self-harm. Reviewed brain-imaging modalities included structural magnetic resonance imaging, diffusion tensor imaging, positron-emission tomography, single-photon emission computed tomography, resting-state functional imaging, and functional magnetic resonance imaging. Studying these brain-imaging modalities of suicide behaviour have provided crucial information on the neural circuitry associated with EI, NSSI and SB.

For this purpose, from February to April 2019 a review of the latest literature from the years 2015-2019 was carried out, to included only the latest data.

The following data bases were used to review the literature: Scopus, PubMed, Web of Science and Google Scholar. Initially, the combination of keywords was: "emotional intelligence" AND "suicide" OR "suicide attempt" OR "suicidal behavior" OR "suicidality" OR "non-suicidal self-injury", to ensure that the review covers a wide range of research issues related to the problem of co-existence of NSSI and SB with EI. To found neurobiological background in the next searches were added keywords like: "brain structure" OR "structural neuroimaging" OR "functional neuroimaging" OR "molecular neuroimaging" OR "magnetic resonance imaging" OR "neuroimaging" OR "diffusion tensor imaging" OR "positron emission tomography"OR "positron-emission tomography" OR "single-photon emission computed tomography". Then these keywords were added in various combinations to select the articles that are focused on the theme of the brain imaging: Another criterion of selection were the years of publication: 2015-2019. The language of the publication was not a criterion.

Brain structure and its functioning of the self-harming people

The first reports on neurobiological changes concerning people after suicide attempts have their origin in the middle of 1960's. One of the first such studies was conducted by Bunney and Fawcett. They observed elevated levels of 17-hydroxycorticosteroid (a cortisol breakdown product) in urine samples of the suicidal attempters, before suicide [19]. So far, several neurobiological models have been developed to explain the etiology of suicide. The most common explanation is a model explaining stress-diathesis. It advocates interaction between life stressors and biological susceptibility to suicide. According to this model, susceptible individuals show abnormal or exaggerated reactions to neutral stimuli [20]. There is now more neurobiological data explaining the phenomenon of NSSI and SB that includes the structural, functional and molecular changes in the brain [21-30].

Among methods used to study suicidal brain we can mention: structural imaging, functional imaging and molecular imaging. These methods allowed researchers to explore the relationship between the cognitive, emotional and behavioral components of suicide and the altered neuroanatomy and neural function. The majority of data comes from the results of the magnetic resonance imaging (MRI).

Structural changes mainly concern the areas of the limbic system and are associated with a reduction in the volume of some anterior and temporal parts of the brain [23, 24]. In suicide attempters, a reduction in the volume of brain structures has been demonstrated: the brain cortex (CC, *cerebral cortex*) – mainly *prefrontal cortex* (PFC) and *orbitofrontal cortex* (OFC) [31],*insula*, *hippocampus*, grey matter (GM, *substantia grisea*), white matter (WM, *substantia alba*), *lentiform nucleus* and *corpus callosum*. Neuroanatomical changes in such individuals are also associated with reducing the volume of the left *angular gyrus* and the right *gyrus rectus* [32]. Some studies have also shown reduction the *anterior cingulate cortex* (ACC), *nucleus caudatus* and reduced volume of the *globus pallidus* on both sides [31-33]. These structural changes appear to be in general particularly involved in the processing of the relevant aspect of the event and can therefore mediate behavioral planning on the basis of negative stimuli [32]. OFC is involved as a key area of the brain for the regulation of emotions and impulses. Studies applying neuroimaging techniques in patients with suicidal behavior demonstrate an increased activity in the *temporal gyrus*, *nucleus caudatus* and *gyrus cinguli* [34], however lower activity is observed in the right *anterior cingulate cortex* (ACC) [30]. Structural changes are present even on the cellular level: the decrease of dendritic branches, decrease in the number of glial cells, especially astrocytes and dendrocytes [31, 32] and the dysfunction of astrocytes [33]. Neurotrophins such as brain-derived neurotrophic factor (BDNF) and fibroblast growth factor (FGF) play a regenerative role and are involved in neuroplastic processes. Among the self-injurious patients, a decrease in the number of these molecules is observed.

Therefore, self-injurious acts seems to be associated as well with neuroanatomical dysfunctions of the brain on a structural level, as with its hyperactivity in some areas and low activity in others. The results of the study indicate that the frontostriatal circuitry is a part of SA etiology. This network regulates emotional stimulation between grey matter and prefrontal cortex. GM and WM are part of the frontostriatal circuitry, which is up to eight times more common among the SA patients than these without SA [30].

Reisch and others [35] have demonstrated, in addition to the aforementioned activation of some areas responsible for emotional control, increased work in the hippocampus area while recalling experiences of suicide attempts with simultaneously cortical inhibition. This suggests deactivation of the frontal areas during the most severe mental pain, inhibiting the emotional control system, leading to suicide attempts or NSSI, and thus to the relief of a mental pain. PFC and ACC are areas activated not only during self-harming behaviour, but also during target-oriented activities. However, focusing on goals can protect from SA, as mental pain is one of the factors of self-mutilation [36,37]. Therefore, this finding can be useful in the therapy of suicidal patients.

The majority of changes in the brain structures of the self-injuring individuals are related to dopamine and serotonergic systems. Suicide etiopathogenesis is associated with a lower level of 5-HT (5-hydroxytryptophan) and 5-HIAA (5-hydroxyindoloacetic acid) in the brainstem [38] and a higher level of TPH2 (tryptophanic hydroxylase 2, an enzyme limiting the rate of serotonin synthesis) among the suicidal attempters. Considering the evidence indicating a general decrease in 5-HT neurotransmission in both cortical and subcortical regions of the individuals after SA, an increase in the amount of TPH2, TPH proteins and mRNA levels can be attributed to the compensation of 5-HT central transmission mitigation mechanism and stress response [38]. A low level of noradrenaline in the *locus coeruleus* was also found in suicide victims [39].

Brain structures related to EI

The key role in the process of regulation of emotional impulses, processing of emotional information, emotional perception and emotional decision making [19] is played by the limbic system and cerebral cortex (CC, *cerebral cortex*). The limbic system consists mainly of the following brain structures: cingulate cortex, entorhinal cortex (EC, *cortex entorhinalis*) and perirhinal cortex, thalamus, hypothalamus, hippocampus, fornix, mammillary body (*corpus mamillare)* and amygdala.

Due to the complexity and diverse nature of emotional processes, the integration of AEI and TEI constructs is necessary to understand their creation. In persons with higher AEI rates, low activation of aMPFC (*anterior medial prefrontal cortex*) in the context of social understanding is observed [21]. A similar relationship of TEI is observed in adolescents in the context of emotional understanding [22], which suggests the involvement of common nervous pathways for both EI models. On the other hand, it has been demonstrated that only high AEI results are associated with increased activation of vmPFC (*ventromedial prefrontal cortex*), amygdala and insula during emotional responses [23, 24]. High TEI patients were characterized by increased activity of mFC (medial frontal cortex), ACC [25] and default mode network (DMN). Moreover, persons with high TEI results show low correlation between DMN and TPN (dorsal-lateral areas of PCF) [26]. The relationship between the height of TEI and activation of these areas increases during developmental changes – from childhood to early adulthood [27]. Among the patients with high AEI level, increased activity of RSN (resting state network) and decreased activity of DMN and the main emotional processing areas (e.g. insular cortex and orbitofrontal cortex, abdominal corpus striatum, amygdala) are observed [21]. Patients with low Ability EI show a strong basal ganglia network BGN activation [23]. Due to strong connections between the areas responsible for emotional regulation and BGN, people with low AEI have difficulties with emotional self-regulation [11]. Therefore, one of the neurobiological mechanisms underlying the low AEI is ineffective BGN modulation by prefrontal control areas. Moreover, Li et al. [26] have discovered less functional connections between the regions involved in emotion regulation and the antero-medial region of the brain in people with severe depression. They also found a significant correlation between MSCEIT results and functional connectivity in the abdominal prefrontal cortex. The results indicate that people with severe depressive disorder have difficulty in perceiving, understanding and managing emotions.

It was found that the volume of grey matter (GM, *substantia grisea*) in the right upper temporal gyrus, another important region of social emotion processing, decreased in the group of people attempting suicide with major depressive disorder (MDD). It was considered as evidence to support the suggestion that emotional and impulse dysregulation may be associated with suicidal behavior [20]. Several lines of evidence obtained from MRI studies indicated that the frontostriatal network was involved in the etiology of suicide. This network includes a pathway for regulating emotions between subcortical GM areas (e.g. basal ganglia) and PFC. Another area where dysfunction is observed in both self-injurious patients and these with low EI level is ACC. Deficiency in the antero-ACC-striatum system may contribute to impaired decision-making and dysfunctional patterns of emotional regulation [42]. ACC is associated with control of impulsive behaviour and the caudate nucleus is also involved in dopamine rewarding processes [43]. Structural changes in the frontostriatal pathway may lead to impaired behavioral and emotional control, leading to suicidal behavior.

The latest data on the analysis of brain structures related to SB and EI

Study on emotional intelligence and suicidal behaviour is becoming increasingly popular among scientists, but there is still little known about the neurobiological mechanisms of these behaviors. There are also few meta-analyses of this studies – one of them was created by Balcioglu [21], which reviewed articles studies of suicide behavior published from 1990 to 2017. Analyzed brain-imaging data included structural magnetic resonance imaging, diffusion tensor imaging, positron-emission tomography, single-photon emission computed tomography, resting-state functional imaging, and functional magnetic resonance imaging. This review concerned only neuroimaging studies of suicide behavior, not including NSSI and EI. The effect of this review was to describe the nerve circuits associated with the SB risk: the frontostriatal network, frontal-limbic structures and serotonergic system.

The highest number of data in SB literature is related to studies utilizing neuroimaging techniques which allow to indicate abnormalities in brain morphology and neuronal activity. These studies, however, are often conducted on patients with additional psychopathologies: with diagnosed MDD, BD, SCZ, BPD, which makes the identification of biomarkers specific for SB more difficult. Cox Lippard et al. have performed a review of 57 original studies utilizing diverse neuroimaging methods in the context of the aspects of suicidial behavior. According to the results, there is a noticeable decrease in the volume of gray matter (GM) in the orbitofrontal cortex (OFC) area in the case of MRI attempters in the patient population with MDD, BD, schizophrenia, BPD, as well as white matter hyperintensities in young/mid-adult MDD and BD attempters [44].

In a literature review from 2018 [45] the authors summarize the results of 33 studies related to identifying brain regions associated with SB in patients with various mental disorders. The phenomena with the largest amount of coverage involve volume loss or cortical thinning, especially in the temporal cortex area of suicidal patients in MDD, schizophrenia, BPD. Other areas where cortical reduction has been observed include the frontal, limbic, orbitofronal, and insular lobes.

An interesting meta-analysis of molecular studies on the functioning of the serotonergic system, as the one most strongly involved in the etiopathogenesis of suicide, was carried out by Wang et al. [46] The findings provide an indication of connection between pathological functioning of this system with some subtypes of 5-HT receptors and suicidal behaviours. The authors conclude that the decreased binding of the 5-HT1A receptor was associated with depression pathology in various regions of the brain, which may be associated with suicidal behaviour.

There is a smaller number of reports dealing with changes in the noradrenergic system and dopaminergic system (reduction in the dopamine turnover). These involve dysfunctions at the level of receptors and enzymes [47]. Noradrenergic studies in the postmortem brains of suicide victims indicate increased protein expression of tyrosine hydroxylase (TH) as well as a rise in the amount of α_2 – and β_2-adrenergic receptors [48].

The table below shows the results of the latest reports on brain structures associated with EI and SB (SA and NSSI). It presents the most important publications of oryginal research carried out on N>50 groups of recent years (2015-2019) concerning neurobiological determinants of EI and self-injury/suicidal bahaviour.

Table 1. The table presents the most important publications of oryginal research from 2015-2019 regarding the analysis of brain structural and cellular changes among the self-injurious and suicidal patients.

Author(s)	The aim of the study	Sample characteristics	Measures	Results
Quarto et al. [33].	Analysis of brain structures associated with AEI.	N = 63; age 29.4 (6.3) the number of women 34; Hollingshead 41.8 (16.7); Handedness0.8 (0.4); IQ=112 (12.3).	fMRI; AEI behavioral test.	High AEI results are associated with increased activation of vmPFC, amygdala and insula in emotional reactions; low AEI results are associated with strong BGN activation [26].

Killgore et al. [34].	Analysis of brain structures associated with EI (TEI and AEI).	N=70; women32; age 18-45 years(average age = 30,9 years; SD = 8,4 years).	fMRI; Bar-On Emotional Quotient Inventory (EQ-i); MSCEIT.	High AEI results are associated with insula activity and vmPFC and deactivation of BGN and DMN.
Linget al. [43].	Analysis of brain structures associated with EI.	N=105.	resting-state functional magnetic resonance imaging (rs-fMRI); MSCEIT.	The region strongly associated with EI is the superior left parietal lobe (SPL).
Oliveira et al. [49].	Analysis of brain structures associated with cognitive and emotional intelligence.	N=50; age 24-37years (average for women (SD) = 29,4 (4,5), average for men (SD) = 30,2 (4.6); 50% women).	fMRI; Empathy self report measure.	High activity of DMN in cognitive processing, low activity in emotional processing.
Duarte et al. [27].	Analysis of brain structures associated with SB and ChAD.	N=59.	fMRI.	In persons with SB an increased activation of PFC and ACC is observed.
Zhang et al [40].	Search differences in DMN activity which could be related to SB.	N=100.	rs-fMRI.	Depressive adolescents involved in SA are characterized by abnormal functional connectivity in some DMN regions, and abnormal connectivity in the PCC/precuneus and left cerebellum.
Groschwitz et al. [50].	Analysis of brain structures associated with NSSI.	N=53; average age u15,2 years (SD = 1,8).	fMRI.	In persons with NSSI an increased activation of mPFC, vrPFC, right *ventrolateral prefrontal cortex*) and vlPFC, *left ventrolateral prefrontal cortex*) is observed.
Pu et al. [51].	Association between prefrontal function and suicidal ideation in MDD.	N= 134; 67 MDD patients (31 suicidal ideators) vs. 67 healthy controls.	Near-infrared spectroscopy with verbal fluency task: regional cerebral oxy-hemoglobin measurement.	Smaller hemodynamic changes during the task in the right dorsolateral PFC, the OFC, and the frontopolar cortex in the MDD patients with suicidal thoughts.
Tsujii et al. [52].	Fontotemporal hemodynamic responses in depressed patients with a history of suicide attempts using 52-channel NIRS.	N=108; 68 MDD patients (30 attempters) vs. 40 healthy controls.	Near-infrared spectroscopy with verbal fluency task: regional cerebral oxy-hemoglobin measurement.	Smaller hemodynamic changes during the task in the left precentral gyrus in the attempters.

Cao et al. [53].	The relationship between abnormalities involving local brain function and suicidal attempts in depressed youths.	N=100; 53 MDD patients (35 attempters) vs. 47 health controls (young adults).	fMRI: Resting-state activity.	Increased activity in the right superior temporal, left middle temporal, and left middle occipital gyri; decreased activity.
Cyprien et al. [24].	The impact of suicidal behavior on CC integrity in mood disorders.	N=121; 91 patients with mood disorders (45 attempters) vs. 30 healthy controls.	MRI: DTI.	Significantly lower FA value of the splenium part of the corpus callosum in attempters.
Colle et al. [54].	The association between hippocampal volumes and suicide attempts in MDD.	N=63 MDD patients (24 attempters).	MRI: volumetric analysis of the hippocampus.	Smaller hippocampal volumes in the attempter group.
Lee et al. [55].	The relationship between alterations in brain white matter (WM) and suicidal behavior in people with schizophrenia or schizophreniform disorder.	N=56 patients with schizophrenia/ schizophreniform disorder (15 attempters).	MRI: DTI.	Higher FA values in various parts of the fronto-temporolimbic circuits in attempters.
Baek et al. [56].	Tested the hypothesis that suicidal behavior is associated with heightened aversion to risk and loss, which might produce negative predictions about uncertain future events.	N=167; 92 MDD patients (45 attempters) vs. 75 healthy controls.	fMRI: Monetary risk and loss aversion tasks.	Disrupted neural responses to potential gains and losses in the subgenual ACC, insular cortex and left amygdala.
Sullivan et al. [57].	To determine the relationships between brain serotonin(1A) binding and suicidal behavior in vivo in major depressive disorder (MDD).	N=91 MDD patients (29 with a history of suicide attempt).	PET ([11C]-WAY-100635): 5-HT1A binding potential.	Greater serotonin 1A binding potential in the raphe nuclei predicted higher suicidal ideation and more lethal suicidal behavio

SUMMARY

The aim of this paper was to give a clear indication of the association between the EI level and NSSI/SB but also presenting the findings on the structural, functional and molecular levels. NSSI/SB associated with the different functioning of limbic system and CC [e.g. 25, 27, 30, 42, 54]. Reviewed data support the conclusion that dysregulation of emotional states underlies NSSI and SB in many individuals [21-30]. Many data indicate that individuals with high EI are less involved in NSSI and SB compared to those with low EI [16, 18]. Alterations in the brain structures are related to the modified neurotransmission of dopamine, serotonin and noradrenaline[40, 42, 45-47].

Our ability to predict NSSI and SB is still not much better than a chance, although, there has been a welcome focus on suicide prevention interventions (both at the public health and clinical level), many gaps in our knowledge remain. Better knowledge about the brain areas activated during emotional processes and NSSI and SB will allow a better understanding of these phenomena and facilitate the development of more effective pharmacologic interventions as well as preventive and therapeutic programs. Future research should seek to better understand NSSI and SB risk factors, taking into account gender differences. We assume that more detailed information about biological markers associated with NSSI and SB will allow to reduce this behaviour.

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