Association of Four Medication Classes and Non-suicidal Self-injury in Adolescents with Affective Disorders – A Retrospective Chart Review

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ABSTRACT

Background Non-suicidal self-injury (NSSI) behaviour is frequently observed in children and adolescents with psychiatric conditions. Affected individuals are regularly treated with psychotropic drugs, although the impact of these agents on NSSI behaviour remains elusive.

Methods We performed a retrospective chart review from clinical routine data in a large cohort (N = 1140) of adolescent inpatients with primary affective and non-affective psychiatric disorders according to ICD-10 (mean age = 15.3 ± 1.3 years; 72.6 % female). Four separate mixed regression models compared the frequency of NSSI between treatment periods without any medication and four medication categories (benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), high- and low-potency antipsychotics).

Results In those individuals with affective disorders as the primary diagnosis, periods without medication were associated with significantly lower NSSI/day compared to all four other medication conditions (benzodiazepines $p < 10^{-8}$, antidepressants/SSRIs $p = 0.0004$, high-potency antipsychotics $p = 0.0009$, low-potency antipsychotics $p < 10^{-4}$). In individuals with a primary diagnosis other than an affective disorder, NSSI was significantly lower during the period without medication compared to the treatment periods with benzodiazepines ($p = 0.005$) and antidepressants/SSRIs ($p = 0.01$). However, NSSI rates in the no-medication condition were comparable to NSSI rates under high-potency ($p = 0.89$) and low-potency antipsychotics ($p = 0.53$).

Conclusions The occurrence of NSSI correlates with the treatment with a psychotropic drug in children and adolescents with psychiatric disorders. Due to the retrospective design, it remains elusive to what extent psychotropic drugs might alter the frequency of NSSI in adolescents or if NSSI might indicate a transdiagnostic feature of more pronounced disease severity.

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Introduction

Self-harm (SH) is defined as intentional self-poisoning or self-injury regardless of the degree of suicidal intent or other motivational factors [1]. Non-suicidal self-injury (NSSI) refers to "the intentional destruction of one's own body tissue without suicidal intent and for purposes not socially sanctioned" [2]. NSSI is thought to be a maladaptive emotion regulation strategy and often co-occurs with affective disorders in adolescence [3]. According to recent findings from community samples, NSSI occurs with a lifetime prevalence of 6.2 % in preadolescents (age < 11 years) and increases to an average of 18.0 % in adolescents (age 11–18 years) [4]. NSSI behaviour is described to peak around mid-adolescence (around 15–16 years) and decreases significantly in late adolescence [5]. While NSSI and suicidality differ in many ways, both conditions may co-occur and NSSI is considered a major risk factor for suicidality[2]. Nevertheless, NSSI is a transdiagnostic phenomenon and a marker of psychopathology and suicide risk [6].

Since the early 2000s, research has contributed to a better understanding of risk factors [7, 8] and the origin of NSSI, which is, e. g., reflected in the current German guideline on NSSI [9]. Self-harm (and NSSI) appear to be associated with past experiences of childhood maltreatment and adverse experiences during childhood, with interpersonal problems including bullying and emotional dysregulation [10]. The NICE guideline on self-harm recommends performing a psychosocial assessment in children and young people who have self-harmed to ask about their social, peer group, education, home situations, and any child protection or safeguarding issues [11]. Especially childhood maltreatment – except for emotional neglect - is associated with NSSI [12]. Adolescents and young adults with major depressive symptoms and NSSI experienced more childhood adversity than adolescents and young adults with a major depressive disorder alone [13, 14]. Of note, stressful life events within the family are more common in early (11–15 years) than in mid (15–17 years) adolescence [15].

Limited evidence is available regarding effective treatment interventions for NSSI (or SH) in children and underage adolescents [9, 11]. A recent Cochrane review on SH (including NSSI) in adolescents mostly diagnosed with major depression, found sparse evidence regarding the efficacy of psychosocial individual or group-based psychological interventions [1]. Four randomized controlled trials (RCTs) investigated dialectical behaviour therapy for adolescents (DBT-A), which was the only intervention with a lower post-intervention self-harm repetition rate compared to treatment as usual, enhanced usual care, or alternative psychotherapy [1]. Of note, none of the included RCTs evaluated the effectiveness of pharmacological agents [1], which illustrates the limited available evidence in child and adolescent psychiatry for effective pharmacologic treatment options for NSSI [16].

The German national guideline for suicidality in childhood and adolescence recommends the use of benzodiazepines for an acute suicidal crisis independently of the underlying psychiatric disorder [17]. In comparison, the recent German guideline for NSSI in childhood and adolescence recommends not to use benzodiazepines but rather low-potency antipsychotics for a medication "pro re nata" [9]. The reasoning for this recommendation is a secondary analysis of a non-randomized, open-label trial in a small cohort of adolescents (N = 10) where increased rates of NSSI were observed during treatment with add-on benzodiazepines [18]. The recent NICE guideline on SH states that there is no supporting evidence regarding the benefit of pharmacological interventions in children and young people who engage in SH. Thus, the NICE guidelines recommend not to offer pharmacological treatment specifically for the purpose of reducing SH [11]. In clinical practice, hypnotics, sedatives, or benzodiazepines are prescribed frequently in children and adolescents and even more frequently than antidepressants [19]. A large-scale Swedish register study showed that around 30 % of benzodiazepine prescriptions in children and adolescents extended a period of six months[20]. In 2.6 % of the cases, a high dose (1.5 DDD/day) of benzodiazepine was prescribed [20]. Previous case reports point to a a possible disinhibition of behavioural control in some cases of children and adolescents due to benzodiazepines [21–23]. Neuronal disinhibition due to the GABAnergic effects of benzodiazepines might be a possible pathophysiological explanation for the association between increased NSSI rates and the use of benzodiazepines [24–28].

In general, combined psychotherapeutic and pharmacological treatment is recommended as a first-line treatment for moderately to severely ill depressive adolescents [29], but the impact of psychoactive drugs on NSSI rates in this population remains elusive [30]. Thus, we aimed to investigate the impact of different medication classes on the occurrence of NSSI in the context of established NSSI risk factors in a large retrospective cohort of adolescent inpatients with both affective and non-affective disorders. Based on the evidence described above and the clinical impression of the authors, we expected an accumulation of NSSI in times of medication with benzodiazepines, and based on our metanalyses published ahead [30], no association of SSRIs and NSSI in adolescents.

Methods

We performed a monocentric, anonymized, retrospective data collection of existing routine clinical data from patient records at a community hospital for children and adolescents. We included all inpatients (mean age = 15.3 ± 1.3 years; 72.6 % female; see ▶ **Table 1**) that were discharged from inpatient treatment between 01/01/2015 and 31/07/2020 (N = 1140) independent of diagnostic criteria, age, or other factors. Patients who attempted (N = 8) or completed (N = 1) suicide during the inpatient treatment were excluded. The project was approved by the local ethics committee (Nr.: 20–0804).

Treatment periods were defined as the number of days in which the patients were treated with either a fixed psychotropic medication (with benzodiazepines, antidepressants, low- and high-potency antipsychotics defined according to dopamine D_2-receptor-blocking properties [31]) or with no fixed psychotropic medication. Data was extracted manually, mainly from digital records for every patient individually, along with demographic and relevant diagnostic information (i. e., main/secondary diagnosis). If available, risk factors - as described in the German guideline for NSSI [9] - were extracted: psychiatric illness of a parent (2.0 in axis 5 of the multiaxial classification scheme (MAS) [32], separation of the parents (5.1 in axis 5 of the MAS), unemployment, abuse and childhood maltreatment (1.3 or 6.4 in axis 5 of the MAS), somatic complaints/comorbidity, aggressiveness, anxiety disorder or dissociative dis-

▶ **Table 1** Description of main demographics for all subjects as well as for a sub-group of subjects with affective disorders as the main diagnosis

	All Subjects (N = 1140; 100 %)		**Subjects with affective disorders as the main diagnosis (N = 715; 62.7 %)**	
	N	**Range / Mean (SD)**	**N**	**Range / Mean (SD)**
Female/Male	828 (72.6 %)/312(27.4 %)		538(75.3 %)/177(24.7 %)	
Age (years)		12–18 years/15.34 (1.27)		12–18 years/15.38 (1.2)
Length of hospital stay (days)		1–367 days/72.85 (42.56)		1–256 days/70.75 (36.05)
Depression as main diagnosis*: yes/no	662 (58.2 %)/475(41,8 %)		658(92.0 %)/57(8.0 %)	
Parents with psychiatric disorders: yes/no	437 (38.3 %)/703(61.7 %)		295(41.3 %)/420(58.7 %)	
NSSI before treatment: yes/no	574 (50.3 %)/566(49.7 %)		457(63.9 %)/258(36.1 %)	
Notes: (*) ICD-10 diagnosis codes F32.0 to F32.3.				

order as secondary diagnosis and neglect in the family (1.0 or 4.1 in axis 5 of the MAS). Information on NSSI was extracted from non-medical and medical documentation (assessed with weekly body check-ups). In these body check-ups, two same-sex employees carried out a visual examination of the skin (in a partially undressed state of the patient) accompanied by an interview about NSSI that had taken place in the last week. All visible wounds inflicted according to the criteria of NSSI were documented. Since routine clinical data were extracted, no information can be given about the reliability of the detection of NSSI. To improve reliability, data were partially extracted independently by two authors (VE and LB) and anonymized for analyses. Conflicts were resolved by consultation with a third person (AH).

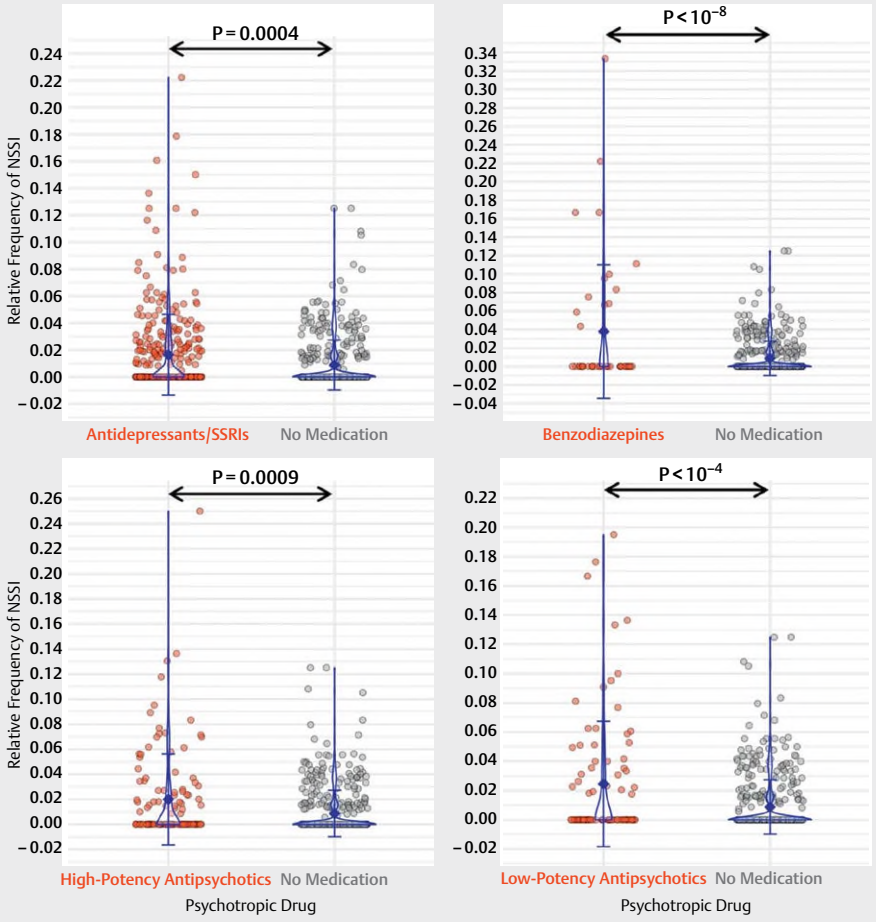
Statistical analyses

A simple between-subject design comparing NSSI between subjects receiving no psychotropic medication to those receiving one specific psychotropic medication was not possible in this retrospective dataset. That is because many subjects were treated with at least two combined medication classes, meaning that many subjects received no medication in a certain time period and later received a psychotropic medication for another time period and possibly even another medication for the next time period. Therefore, our analysis does not compare NSSI between subjects in different medication conditions, but rather compares NSSI between time periods in which different medication conditions were administered. Time periods were defined as the number of days between the beginning and the end of administration of a certain psychotropic medication or no medication in a patient. Linear mixed-effects regression models were chosen for the analyses since they allow comparing NSSI between different medications beyond between-subjects conditions and also incorporate various random effects, which need to be taken into account from our retrospective clinical dataset.

Five different medication conditions were defined: 1) no medication (N = 455): time periods in which no medication was administered; all other four categories (2–5) were compared to this condition to disentangle their effect on NSSI; this included time periods of treatment with 2) benzodiazepines (N = 42), 3) antidepressants/selective serotonin reuptake inhibitors (SSRIs; N = 351), 4) low-potency antipsychotics (N = 122), or 5) high-potency antipsychotics (N = 88). Four separate mixed-regression models compared NSSI between no medication and the other four medication categories. NSSI was the dependent variable in all models and was operationalized as the relative frequency of NSSI attempts during the application of a certain medication condition, calculated by dividing the number of NSSI attempts by the length of the time period (number of days) being treated in that medication condition. Medication condition was added to the model as a fixed effect (no medication vs. the aforementioned medication conditions 2–5 separately in the four models). The model included the following random effects: sex, age, length of hospital stay in days, depression as the primary diagnosis (ICD-10 diagnosis codes F32.0 to F32.3: yes or no), psychiatric disorders in parents (yes or no), separation of parents (yes or no), and NSSI before treatment (yes or no).

Our main analyses focused on subjects with affective disorders (ICD-10 codes: F3x); further analyses, as detailed below, were performed on subjects without an affective disorder as the primary ICD-10 diagnosis. To investigate if the association between NSSI and different medications is modulated by age in subjects with affective disorders as primary diagnosis, the median age of the affective sample (= 15 years old) was used to create two sub-groups with subjects in their early (≤ 15 years old, N = 375, mean age = 14.4 ± 0.04) and mid-adolescence (> 15 years old, N = 340, mean age = 16.45 ± 0.03). In subsequent analyses, we ran the models in subgroups of subjects in their early or mid-adolescence (≤ 15 and > 15 years old, respectively) and because adolescents with a documented history of family abuse are presumed to have a higher risk for NSSI [12], as well as sub-groups of subjects with or without a history of family abuse (subjects with affective disorders as primary diagnosis). This category applies when an individual reported any physical or emotional abuse or neglect by their families.

The threshold for statistical significance was set at p-value < 0.05. Descriptive statistics are shown as mean ± standard error of the mean. This study is retrospective in nature; thus, no power calculation was performed prior to data collection. However, considering the number of parameters included in the mixed models (= 8), the sample size in all medication conditions is appropriate, except for benzodiazepines (= 42, all other conditions > 80), for which findings must be interpreted with caution. The R language in the Rstudio environment was used for all statistical analyses and visualizations.



▶ **Fig. 1** Violin plots comparing the relative frequency of NSSI between periods of "no medication" and periods in which a psychotropic drug was administered in individuals with affective disorders as the primary diagnosis. Points represent individual subjects. The error bar shows mean ± standard error. The "no medication" condition showed a significantly lower relative frequency of NSSI than all four psychotropic drugs (ps < 0.001). NSSI: Non-suicidal self-injury.

Results

Our cohort of children and adolescents with psychiatric disorders (n = 1140, 828 female and 312 male, mean age 15.34 years, SD = 1.27). In 38.3 % of individuals (N = 437/1140), at least one parent was diagnosed with a psychiatric disorder, and a majority of 50.4 % (N = 574/1140) showed NSSI behavior before treatment (see ▶ **Table 1**). Overall, 364 patients presented NSSI during inpatient treatment (31.9 %). Nearly half of the patients who showed NSSI before treatment did not show NSSI during inpatient treatment (N = 265/574, 46.2 %). Fifty-five patients commenced NSSI during inpatient treatment (4.8 %).

For our analyses, the cohort was divided into individuals with primary affective (N = 715) and non-affective disorders (N = 425).

Non-suicidal self-injury and psychotropic drugs in affective disorders

In those individuals with affective disorders as the primary diagnosis (N = 715, 538 females, age range = 12–18, mean age = 15.38 ± 0.04 years, see ▶ **Table 1**), periods without medication (0.01 ± 0.0 NSSI/day) were associated with significantly lower NSSI compared to all four other medication conditions (see ▶ **Fig. 1**). A significant model ($F_{(8, 488)} = 13.11$, $p < 10^{-16}$) showed lower NSSI ($p < 10^{-8}$) with no medication compared to administration of benzodiazepines (0.04 ± 0.01 NSSI/day). Similarly, patients in periods without medication showed lower NSSI (p = 0.0004) when contrasted to treatment periods with antidepressants/SSRIs (0.02 ± 0.0 NSSI/day; $F_{(8, 797)} = 13.76$, $p < 10^{-16}$). Less NSSI occurred in periods without medication (p = 0.0009), compared to periods with high potency antipsychotics (0.02 ± 0.0 NSSI/day; $F_{(8, 568)} = 9.9$, $p < 10^{-12}$) and with low-potency antipsychotics (0.02 ± 0.0 NSSI/day; $F_{(8, 534)} = 12.93$, $p < 10^{-15}$). Among the co-variates, the occurrence of NSSI before treatment was significantly associated with higher NSSI ($ps < 10^{-4}$) in all models and longer days of hospital stay showed a tendential association with higher NSSI (ps < 0.06). ▶ **Table 2** provides a descriptive summary of NSSI in different medication conditions and Supplementary Table 1 summarizes the statistical details of all factors in the four models.

▶ **Table 2** Descriptive summary of the relative frequency of NSSI in the five medication conditions in individuals with affective disorders as main diagnosis.

Medication condition	N	Mean (SD)	SE	Range (Min – Max)
No medication	455	0.01 (0.02)	0.0	0–0.12
Benzodiazepines	42	0.04 (0.07)	0.01	0–0.33
Antidepressants/SSRIs	351	0.02 (0.03)	0.0	0–0.22
High-potency Neuroleptics	122	0.02 (0.04)	0.0	0–0.25
Low-potency Neuroleptics	88	0.02 (0.04)	0.0	0–0.2

Notes: "N" shows the number of periods in which a medication condition is applied. NSSI: nonsuicidal self-injury; SSRI: selective serotonin reuptake inhibitors

Non-suicidal self-injury and psychotropic drugs in non-affective disorders

The same four models were applied to the data from individuals without affective disorders as their primary diagnosis, comprising a heterogeneous sample of subjects with various diagnosis categories (mainly eating disorders but also anxiety disorders, somatoform disorders, psychosis, obsessive-compulsive disorders, N = 421, 281 females, age range = 12–18, mean age = 15.34 ± 1.37 years old, see Table 3). NSSI in the period without medication (0.0 ± 0.0 NSSI/day) was significantly lower in the treatment period with benzodiazepines (0.03 ± 0.02 NSSI/day, p = 0.005) and antidepressants/SSRIs (0.01 ± 0.0 NSSI/day, p = 0.01). However, NSSI in no medication condition was comparable to NSSI when applying high-potency (0.01 ± .0 NSSI/day, p = 0.89) as well as low-potency (0.01 ± 0 NSSI/day, p = 0.53) antipsychotics. The occurrence of NSSI before treatment was shown to be significantly associated with higher NSSI in all models (ps < 10^{-5}).

Early vs. mid-adolescence

The treatment periods without medication were significantly associated with lower NSSI compared to treatment periods with antidepressants/SSRIs and high-potency antipsychotics in both early and mid-adolescence groups (ps < 0.03). Compared to benzodiazepine (p < 10^{-7}) and low-potency antipsychotics (p < 10^{-5}) conditions, however, significantly lower NSSIs with no medication were only found in the early adolescence and not in the mid-adolescence group (ps > 0.05; see ▶ **Fig. 2**). Higher NSSI was found to be associated with the occurrence of NSSI before treatment in all models for both early- and mid-adolescence subjects (ps < 0.001).

Non-suicidal self-injury in the context of family abuse

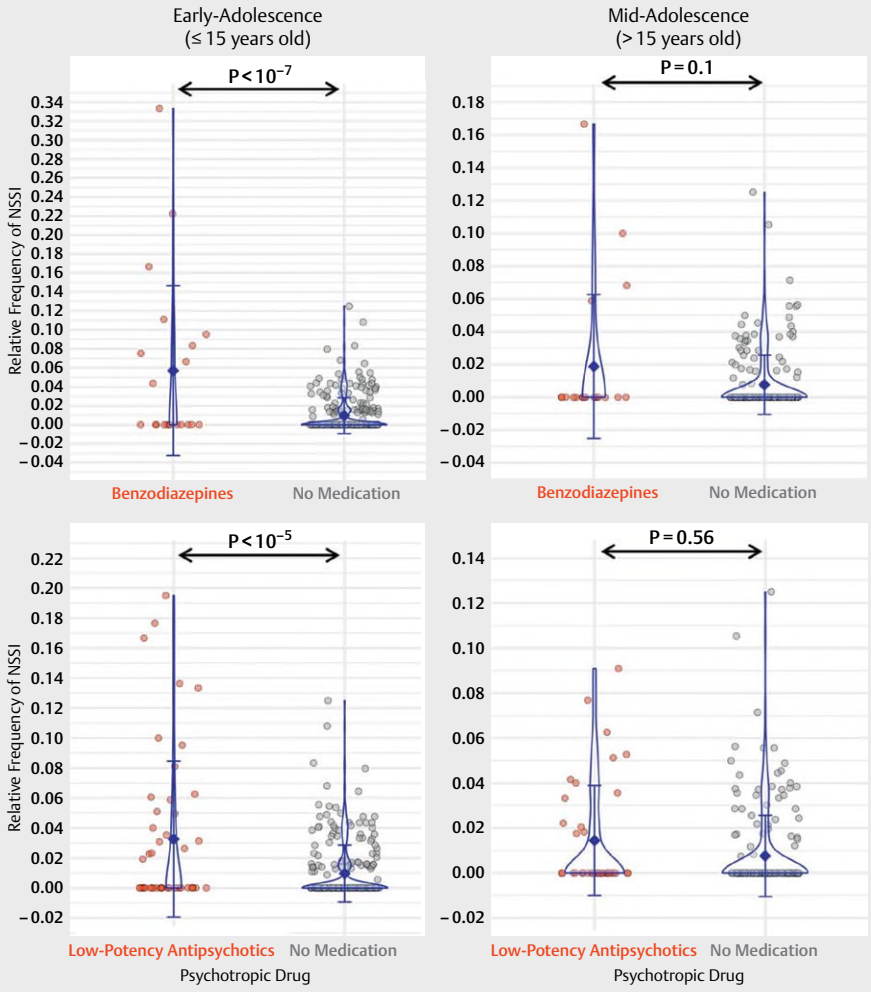
In this group (N = 160), significantly less NSSI occurred in periods without medication than in treatment periods with benzodiazepines (p < 10^{-8}), antidepressants/SSRIs (p = 0.03), and low-potency antipsychotics (p = 0.002). A comparable number of NSSI was found in treatment periods between without medication and with high-potency antipsychotics (p = 0.27; see ▶ **Fig. 3**). The occurrence of NSSI prior to treatment was significantly associated with higher NSSI (ps < 0.001).

Discussion

Our aim was to elucidate the relationship between the use of four different classes of psychotropic drugs and the frequency of NSSI in a large retrospective cohort of adolescent inpatients with affective and non-affective disorders.

Among individuals with affective disorders, treatment periods without medication were significantly associated with less frequent NSSI than treatment periods with benzodiazepines, antidepressants, or high- and low-potency antipsychotics. A possible explanation of the increased frequency of NSSI associated with psychotropic medication could be that individuals with affective disorders presenting NSSI during inpatient treatment might have a more pronounced disease severity compared to individuals without NSSI and were therefore treated more frequently with any psychotropic drug. This clinical decision-making would be in line with the official treatment guidelines, which recommend medication as the first-line treatment for severe depression [33–35]. In all analyses, NSSI before treatment was the only co-variate showing a stable trend which means being significantly associated with higher NSSI rates and thus, this risk factor should be taken into consideration in the clinical decision-making process among adolescents challenged with any psychotropic agent. Furthermore, the length of a stay correlated positively with the frequency of NSSI. Our study failed to show any beneficial effects of medication on the frequency of NSSI in adolescents with primary affective disorders. This is in line with the recommendation from the current NICE guideline on SH not to offer psychopharmacological treatment to reduce self-harming behavior as a target symptom [11]. Since SSRIs are generally recommended for the treatment of depressive disorders in adolescents in international guidelines [33–35], NSSI should be regularly monitored in adolescents with affective disorders and a history of NSSI or any other major risk factor for NSSI during treatment with an SSRI.

To investigate the impact of different developmental stages on the risk of NSSI in adolescents with affective disorders, the population was divided into groups of early- and mid-adolescence since NSSI is presumed to peak around mid-adolescence [5]. We detected an increased frequency of NSSI behaviour on days with psychopharmacological treatment, including benzodiazepines and low-potency antipsychotics, in younger adolescents compared to medication-free days. This result is in keeping with the warning in the German guideline for NSSI in adolescents [9] regarding the use of benzodiazepines as an on-demand medication and might specifically affect early-adolescence. Furthermore, our results suggest

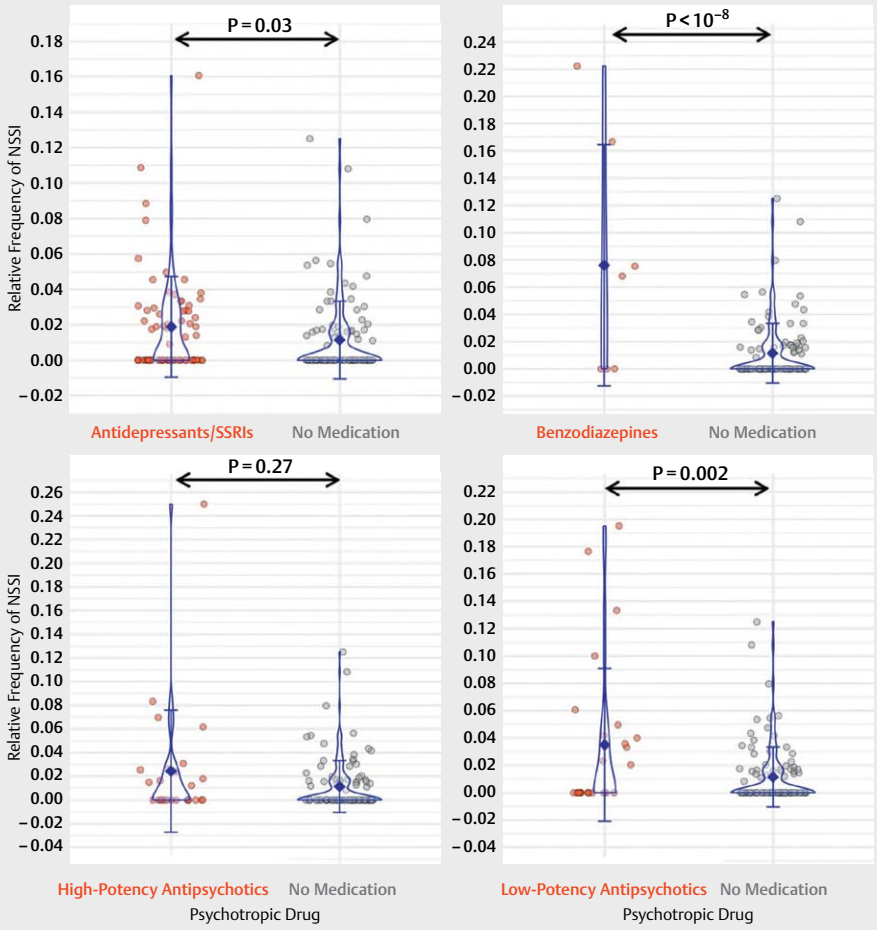


▶ **Fig. 2** Violin plots comparing the relative frequency of NSSI between periods of "no medication" and periods in which "benzodiazepines" or "low-potency antipsychotics" were applied, separately for subjects in early adolescence (left panel: ≤ 15 years old) and mid-adolescence (right panel: > 15 years old). Points represent individual subjects. The error bar shows mean ± standard error. "Benzodiazepines" and "low-potency antipsychotics" showed significantly higher relative frequency of NSSI than "no medication" condition only for subjects in early adolescence (ps < 10^{-5}). This distinction between the two age groups was not found in the comparison between "no medication" and "antidepressants/SSRIs" or "high-potency antipsychotics" (not shown here), where both age groups showed significantly lower NSSI in "no medication" condition than both of these psychotropic drugs. NSSI: Non-suicidal self-injury.

that the use of low-potency antipsychotics as an on-demand medication for NSSI [9] in patients under 16 years of age and in patients with affective disorders, in general, should only be performed after a close risk-benefit evaluation.

In the group of individuals with affective disorders and a history of family abuse, NSSI was less frequently observed during medication-free periods, and only treatment periods with high-potency antipsychotics showed no significant difference compared to medication-free periods. In the heterogeneous group of individuals with a primary ICD-10 diagnosis other than an affective disorder (mainly eating disorders but also anxiety disorders, somatic symptom disorders, psychosis, and obsessive-compulsive disorders, as shown in Supplementary Table 1), NSSI was significantly less frequently observed on medication-free days compared to treatment periods with benzodiazepines or antidepressants/SSRIs. However, there were no significant differences in NSSI rates between medication-free periods and treatment periods with high-potency (0.01 ± 0, p = 0.89) as well as low-potency (0.01 ± 0, p = 0.53) antipsychotics. (▶ **Table 3**).

As a limitation of this study, it must be mentioned that this is a monocentric, retrospective data analysis. Furthermore, due to our retrospective design, it remains unclear to which extent psychotropic drugs can aggravate NSSI in adolescents since no conclusions can be drawn about a possible causality. In addition, the reliability of our data could not be examined since the data was collected during the clinical routine. In the context of the complex treatment of adolescents, all patients received behavioural therapy-oriented interventions in individual and group settings, and we have no information about the chronological sequence of medication administration and NSSI within one day or the information whether treat-



▶ **Fig. 3** Violin plots comparing the relative frequency of NSSI between periods of "no medication" and periods in which a psychotropic drug was administered in individuals with a history of family abuse (i. e., self-reported history of physical or emotional abuse or neglect). Points represent individual subjects. The error bar shows mean ± standard error. The "no medication" condition showed a significantly lower relative frequency of NSSI than "antidepressants/SSRIs", "Benzodiazepines", and "low-potency antipsychotics" (ps < 0.05). The relative frequency of NSSI was comparable between "no medication" condition and "high-potency antipsychotics" (p = 0.27). NSSI: Non-suicidal self-injury.

ment days without medication occurred mainly at the beginning of inpatient treatments.

Furthermore, we also aimed to investigate the impact of benzodiazepine use on NSSI rates to elucidate the sparse evidence in NSSI guidelines [9], where the warning is based almost exclusively on a small study from Brent et al. (N = 10) [18]; yet due to the retrospective design of our study, it must be stated that our sample is composed with an insufficient number of patients with a fixed medication with benzodiazepines (N = 42) with at the same time many other parameters in our mixed model (N = 8). Therefore, the impact of benzodiazepines on NSSI rates in adolescents remains elusive. Furthermore, meaningful comparisons between individual psychotropic drugs were not feasible. Nevertheless, we systematically investigated the widespread clinical phenomenon of NSSI in a large representative sample of adolescent inpatients in relation to psychotropic medication vs. no medication to foster the evidence and inform future clinical trials. In summary, we conclude that NSSI appears to indicate a more pronounced disease severity in adolescents and therefore makes it more likely that these adolescents are treated with a psychotropic drug. Nevertheless, according to our results, psychotropic drugs should be administered only under close medical supervision to adolescents in the presence of risk factors for NSSI since our data suggests an increased probability of NSSI in periods with psychotropic drug treatment, especially in adolescents under the age of 16 and in adolescents with affective disorders. Our results do not suggest any indication for the use of effective psychopharmacological treatment to decrease NSSI. Considering that individuals with non-affective disorders presenting NSSI are treated more frequently with any psychotropic drug and that a comparable number of NSSI was found in treatment periods between without medication and with high-potency antipsychotics, high- (and low-) potency antipsychotics should be further investigated for their effectiveness in reducing NSSI among children and adolescents.

▶ **Table 3** Description of main demographics for the sub-group of subjects without affective disorders as the main diagnosis

	N (Total: 421 * (36.9 %))	Range/Mean (SD)
Female/male	281 (66.7 %)/ 135 (32.0 %)	
Age (years)		12–18 years/ 15.34 (1.37)
Length of hospital stay (days)		1–367 days/ 77.26 (51.49)
Parents with psychiatric disorders: yes/no	140 (33.3 %)/ 256 (60.8 %)	
NSSI before treatment: yes/no	109 (25.9 %)/ 307 (72.9 %)	
ICD-10 categories/codes:		
-F2x: Schizophrenia	52 (12.4 %)	
-F4x: Neurotic, stress-related, and somatoform disorders	153 (36.3 %)	
-F5x: Eating disorders	95 (22.6 %)	
-F60: Personality disorders	2 (0.5 %)	
-F8x/F9x: developmental disorders and behavioral and emotional disorders	107 (25.4 %)	
-Others**	12 (2.9 %)	

Notes: (*) sample size of the entire sub-group of subjects without affective disorders, including five individuals with suicide attempts during inpatient treatment, who were excluded from consecutive analyses; (**) ICD-10 codes include F1x, F63, F64, and F66. NSSI: nonsuicidal self-injury

Conflict of Interest

VE, MM, and LB report no conflict of interest. SKK is the scientific advisor of the GOLDKIND Stiftung. AH has been invited to scientific meetings by Lundbeck, Janssen, and Pfizer, and he received paid speakerships from AbbVie, Advanz, Recordati, Rovi, Janssen, Otsuka, and Lundbeck. He was member of Recordati, Rovi, Otsuka, Lundbeck, and Janssen advisory boards. EW has been invited to advisory boards from Recordati.

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