Psychoneuroendocrinology 110 (2019) 104460

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Adolescent nonsuicidal self-injury and cortisol response to the retrieval of adversity: A sibling study

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ARTICLE INFO

Keywords:
Non-suicidal self-injury
Hypothalamus-pituitary-adrenal axis
Childhood adversity
Cortisol
Sibling study

ABSTRACT

Background: There is evidence for alterations in hypothalamus-pituitary-adrenal (HPA) axis response to the retrieval of traumatic events among individuals with Posttraumatic Stress Disorder. However, no study has so far investigated HPA response to trauma retrieval among individuals engaging in non-suicidal self-injury (NSSI). In the present study, we compared reports of childhood adversity (CA) between adolescents engaging in NSSI and their siblings and tested for differences in the cortisol response to the retrieval of CA.

Methods: The sample consisted of 32 adolescents engaging in NSSI (M_{age} = 15.8 years) and their siblings (M_{age} = 15.6 years). Standardized interviews were used for the assessment of CA, NSSI, and axis I diagnoses. Salivary cortisol was measured before and after the trauma interview. Basal HPA axis activity was measured in hair.

Results: Reports of CA were moderately interrelated between siblings. Adolescents engaging in NSSI reported more severe CA. A significant decrease of salivary cortisol during the trauma interview was found only in the NSSI group. The NSSI group had significantly higher hair cortisol levels.

Conclusions: Moderate relations in siblings' reports of CA point to non-shared experiences that may play a role in the development of NSSI. In the NSSI group, the decrease of salivary cortisol during the interview may be explained by a downregulation of the HPA axis subsequent to the retrieval of former experience of CA.

1. Introduction

Nonsuicidal self-injury (NSSI) is defined as the repeated infliction of injuries to the surface of the body, mostly with the purpose of reducing negative emotions or the resolution of interpersonal difficulties, without suicidal intent (American Psychiatric Association, 2013, p. 803f). The worldwide prevalence rate of NSSI among adolescents has been estimated to be around 17% (Swannell et al., 2014). Biological factors as well as experiences during childhood and adolescence can be expected to contribute to the development of NSSI (Plener et al., 2017).

In this sense, alterations in biological systems such as the hypothalamus-pituitary adrenal (HPA) axis (Plener et al., 2017) have been observed in the context of NSSI. The HPA axis constitutes one of the core stress response systems of the human body (de Kloet et al., 2008). Experiences of stress result in the release of corticotropin-releasing hormones (CRH) and arginine vasopressin (AVP) from the hypothalamus and subsequently of adrenocorticotropic hormones (ACTH) from the pituitary gland. Finally, in the sense of a negative feedback loop, the glucocorticoid cortisol is released from the adrenal cortex binding to receptors in the brain and inhibiting the release of additional CRH and AVP (Lupien et al., 2009). Previous studies further found young adults and adolescents engaging in NSSI to show decreased salivary cortisol (Kaess et al., 2012) and blood cortisol levels (Plener et al., 2017) in response to a psychosocial stressor, but an increased salivary cortisol secretion in response to pain stimulation (Koenig et al., 2017b). In a previous study from our group, an increased cortisol awakening response was found in adolescents engaging in NSSI compared to a healthy control group (Reichl et al., 2016). With regard to basal cortisol, meta-analytical results provided evidence for hair cortisol levels being increased in stress-exposed groups (Stalder et al., 2017). Given that engagement in NSSI has been associated with experiences of psychological distress (Richmond et al., 2017), it might be suggested that adolescents engaging in NSSI show elevated hair cortisol levels. In contrast, no significant difference in hair cortisol levels was found

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https://doi.org/10.1016/j.psyneuen.2019.104460
Received 7 May 2019; Received in revised form 16 September 2019; Accepted 18 September 2019

between adolescents engaging in NSSI and a healthy control group in a previous study from our working group (Reichl et al., 2016).

Whereas empirical evidence suggests a dysregulation of the HPA axis and specifically a decreased responsiveness to psychosocial stress among adolescents engaging in NSSI, future research is needed to understand the mechanisms that might contribute to alterations in HPA axis functioning. The investigation of childhood adversity (CA) in the context of stress regulation and NSSI might constitute one promising approach. Experiences of CA may result in alterations of the HPA axis that, in the short term, represent biological adjustment processes but, in the long term, are supposed to enhance stress vulnerability and promote the onset of mental disorders (Kuhlman et al., 2017). Specifically, the repeated activation of the HPA axis by chronic stress experiences could lead to a habituation process over time (Kaess et al., 2018), which results in a downregulation of the stress system. A less adaptive functioning of the HPA axis in turn impedes with other physiological functions such as sleep or the immune system (Kuhlman et al., 2017). Numerous studies examined relations between experiences of different forms of CA and alterations in HPA axis functioning, pointing to heightened cortisol secretion with respect to short-term experiences of CA and a downregulation of the stress system as a result of chronic experiences of CA (Koss and Gunnar, 2018).

Moreover, an increasing body of research reported experiences of childhood adversity (CA), such as physical or sexual abuse, neglect or antipathy, to constitute major risk factors for the development of NSSI (Kaess et al., 2013; Serafini et al., 2017). It has further been shown that increased cortisol levels after pain stimulation (Rinnewitz et al., 2018) and the slope of cortisol during the day (Reichl et al., 2016) were reinforced in the context of CA among adolescents engaging in NSSI. However, given the high prevalence rates of experiences of CA among adolescents engaging in NSSI, there is a lack of knowledge about the specific effects of NSSI on alterations in HPA axis functioning. Comparing groups who have experienced comparable adversities might contribute to closing this knowledge gap.

When investigating the role of HPA axis functioning and CA in the development of NSSI, the reliance on previous findings derived from research on suicidal ideation or behavior could give helpful insights into potential mechanisms. NSSI and suicide attempts are closely related phenomena (Groschwitz et al., 2015; Koenig et al., 2017a), and both show a strong link to past experiences of CA (Evans et al., 2005; Serafini et al., 2017). A number of previous studies found a blunted HPA axis reactivity to be related to suicidal ideation and behavior. Particularly, lower baseline cortisol levels in expectancy of a psychosocial stressor were found among adults who had attempted suicide compared to non-attempters (Keilp et al., 2016; Melhem et al., 2016). Moreover, previous studies revealed individuals with past suicidal behavior to show blunted cortisol reactivity during a psychosocial stress test compared to those with suicidal ideation or non-suicidal control groups (Eisenlohr-Moul et al., 2018; O'Connor et al., 2017). Interestingly, in the study conducted by Eisenlohr-Moul et al. (2018), peer stress was related to suicidal behavior only among those adolescents with blunted cortisol responses. O'Connor et al. (2018) found blunted cortisol reactivity to physiological and psychosocial stress among individuals with a suicidal history to be related to childhood trauma. Finally, a less pronounced cortisol reactivity to dexamethasone administration was related to suicidal ideation and NSSI among female adolescents with a history of depression (Beauchaine et al., 2015). With regard to cortisol levels selected at single time points without stress induction, meta-analytic findings (O'Connor et al., 2016) found positive relations between suicide attempts and cortisol levels in studies with young samples (mean age < 40 years) and negative relations in studies with older samples (mean age > 40 years). Melhem et al. (2017) further found lower hair cortisol levels among adolescents and young adults who attempted suicide shortly before the assessment compared to inpatients with suicidal ideation or healthy controls, indicating that blunted cortisol secretion preceded suicide attempts.

In the present study, we specifically investigated the stress reactivity of adolescents engaging in NSSI and their siblings during the retrieval of traumatic experiences. Theories of trauma memory suggest that the encoding of emotions and sensations is enhanced under traumatic experiences (e.g., Ehlers and Clark, 2000; Hardy, 2017). When the episodic memory, the contextual representation of the adverse event, is later retrieved, these emotions should be intensively re-experienced. It can consequently be hypothesized that the recall of CA in trauma-related clinical interviews might activate a memorial network associated to these adverse experiences which induces emotional responses and is supposed to activate the stress system. Thus far, only few studies have investigated cortisol secretion in the context of trauma retrieval and found rather mixed results. An increased salivary cortisol secretion has been observed among individuals with post-traumatic stress disorder (PTSD) during clinical interviews assessing traumatic events experienced through rape (Gola et al., 2012) or during the escape after the World Trade Center Attacks (Dekel et al., 2017). In a sample of female refugees with stress-related disorders, however, Schalinski et al. (2015) found an attenuated salivary cortisol reactivity of sexually abused women during a trauma interview compared to those women without sexual abuse. Furthermore, male refugees with PTSD showed decreases of salivary cortisol when being neutrally interviewed about absorption behavior or being interviewed about traumatic experiences (Kolassa et al., 2007). These mixed findings of increased versus attenuated cortisol reactivity to trauma retrieval may occur due to the complex interplay between the nature of experienced adversity and associated psychopathology that may both influence HPA axis reactivity and have not yet been disentangled.

To sum up, the outlined theoretical considerations and some previous findings suggest that the retrieval of traumatic experiences should generally result in an increased salivary secretion among individuals with compared to those without past trauma experiences. However, given that NSSI had been shown to be linked to blunted cortisol responses to psychosocial stress, we assumed that individuals with past trauma experiences and NSSI should show a less steep increase in cortisol levels during the trauma interview compared to their siblings.

The sibling design has strong advantages over traditional between-family or case-control designs. First, reports of childhood adversity should be more comparable between siblings, who grew up in the same family environment, than between unrelated individuals. For example, there are many different behaviors which can be subsumed under specific forms of adversity such as physical abuse (e.g., hitting at different parts of the body with or without objects) or neglect (e.g., not providing enough food or clothes; verbal abuse; withdrawal of affection). Parents showing abusive behaviors from a specific category might rather tend to show comparable behaviors towards their children than completely different ones. Except for experiences of sexual abuse, previous studies found substantial agreements in reports of various forms of CA between children and adolescents and their siblings (Hines et al., 2006) and between adult siblings (Bifulco et al., 1997; Laporte et al., 2012). Second, siblings have shared a family environment which, besides adverse experiences, includes additional risk and protective factors for the onset of later NSSI such as familial communication patterns (Michelson and Bhugra, 2012). Third, the investigation of siblings, who share on average about 50% of their genes, allows for the reduction of genetic variance compared to studies relying on unrelated individuals.

To summarize, we tested for the validity of the following hypotheses in our study: First, we hypothesized that siblings show moderate to high agreements in reports of CA, relying on the fact that they grew up in the same family environment and referring to previous findings derived from samples of adolescent and adult siblings (Bifulco et al., 1997; Hines et al., 2006; Laporte et al., 2012). Second, we assumed adolescents of both groups (NSSI; siblings) to show an increase of cortisol secretion during the retrieval of traumatic experiences with less pronounced cortisol responses in the NSSI group. Theories of trauma

memory (Ehlers and Clark, 2000) suggest that strong negative emotions and stress might be induced during the retrieval of adversity. However, previous findings suggest an attenuated HPA axis reactivity in both NSSI (Kaess et al., 2012; Plener et al., 2017) and suicidal behavior (Eisenlohr-Moul et al., 2018; O'Connor et al., 2017). Third, we assumed that salivary cortisol secretion during the trauma interview should be positively related to the severity of CA in both groups. Again, we based this hypothesis on theories of trauma memory and the assumption of trauma retrieval reactivating stress experiences (Ehlers and Clark, 2000). And fourth, we hypothesized that adolescents engaging in NSSI show increased basal (hair) cortisol levels compared to their siblings because engagement in NSSI comes along with generally higher distress (Richmond et al., 2017), and recent research suggests that suicidal behavior is related to increased cortisol levels when no stress induction has been performed (O'Connor et al., 2016).

2. Method

2.1. Participants and procedure

Our study was approved by the institutional ethics committee of the Medical Faculty, University of Heidelberg and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Adolescents engaging in NSSI (NSSI group) were consecutively recruited from the specialized outpatient clinic for adolescent risk-taking and self-harm behavior (AtR!Sk; "Ambulanz für Risikoverhalten & Selbstschädigung") as well as the inpatient units at the Clinic of Child and Adolescent Psychiatry, University Hospital Heidelberg, Germany. They were included in the study if they were between 12 and 17 years old, had engaged in NSSI on at least 5 days during the last year, and had a sibling who was between 12 and 19 years old ($\leq$ 4 years age difference). Gender was not an inclusion criterion. Siblings were invited to separate appointments for examination after detailed information about the study procedure. Dyads were not included in case of acute psychotic symptoms, acute suicidality, poor knowledge of the German language, pregnancy, the intake of glucocorticoid medication or endocrine disorders (Stalder et al., 2016) of at least one sibling.

The study procedures were equivalent for the group of adolescents engaging in NSSI and their siblings. After a short assessment of general information ($<$ 5 min), we conducted a structured clinical interview for the assessment of adversity during childhood and adolescence. Saliva samples were taken immediately before and after the interview. Consequently, we took two strands of hair samples and conducted the additional clinical interviews that are described below. In both groups, the majority of interviews were conducted in the afternoon between 1 and 5 pm. Only three adolescents from the NSSI group (9.4%) and two adolescents from the sibling group (6.3%) were interviewed in the morning between 9 and 10 a.m. The interviews were scheduled according to the availability of the adolescents. For 6 dyads (18.75%) interviews took place on the same day, for 8 dyads (25%) the adolescent engaging in NSSI and for 18 dyads the sibling was interviewed on a preceding day. On average, there were 8.9 days between the interviews. All interviews were performed by a trained clinician in the field of child and adolescent psychiatry and a student assistant who was supporting the collection of biological samples. All interviews took place in the same room in the research department of the Clinic for Child and Adolescent Psychiatry of the University Hospital Heidelberg. Adolescents were instructed not to eat food, have drinks or chew gums for one hour and not to smoke or engage in sport activities for at least two hours prior to the assessment. Informed and written consent was obtained from participants and their parents/caregivers. The present study is part of a more comprehensive study procedure that has been described in detail elsewhere (Reichl et al., 2016).

2.2. Measures

The interviews assessed basic socio-demographic variables along with variables that may influence HPA-axis functioning, such as height, weight, days since the last menstrual cycle, regular use of medication, smoking behavior, and substance abuse. Use of medication and smoking behavior during the last three months were measured by dichotomous variables and drug abuse by a 3-point scale ranging from 1 (never) to 3 (at least 20 days per month).

Childhood adversities were measured with the German version (Kaess et al., 2011) of the Childhood Experiences of Care and Abuse Interview (CECA; Bifulco et al., 1994). The CECA is a standardized interview assessing different forms of experiences of adversities during childhood or adolescence (antipathy, neglect, psychological abuse, physical abuse, sexual abuse) within the family environment. Specifically, participants are asked to report about experiences of care and abuse with both parents (or alternatively a mother or father figure). Throughout the interview, the interviewee is asked to provide concrete examples of typical processes within daily family life during childhood and adolescence and, if applicable, of incidents of abuse or maltreatment in the family. The subscale of sexual abuse is the only one allowing for ratings of abusive experiences induced by individuals from outside the family environment. The subscales are rated on a 4-point scale ranging from 0 (no adversity/abuse) to 3 (severe adversity/abuse). We consequently calculated a total score of CA ranging from 0 (no adversity/abuse) to 15 (severe adversity/abuse on all dimensions). The subscales have been shown to be highly interrelated (Reichl et al., 2016; Cronbach's $\alpha = 0.81$), so we calculated a general score of CA.

Non-suicidal self-injury was assessed using the German version (SITBI-G; Fischer et al., 2014) of the Self-Injurious Thoughts and Behavior Interview (Nock et al., 2007). The semi-structured interview assesses the presence, frequency, and characteristics of a variety of thoughts and behaviors of NSSI as well as suicidal thoughts, gestures, plans, and attempts. Previous research reported good reliability for the German version (SITBI-G) and good convergent validity in relation to an established questionnaire of self-harming behavior (Fischer et al., 2014).

Psychiatric diagnoses were assessed by means of the Mini-International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I.-KID; Sheehan et al., 2010), a structured interview for the assessment of axis I psychiatric disorders according to DSM-IV and ICD-10. Moreover, adolescent borderline-personality disorder (BPD) traits were assessed with the respective module of the German version of the Structured Clinical Interview for DSM-IV Personality Disorders (SKID II; Fydrich et al., 1997).

We assessed *saliva cortisol* for the analysis of acute cortisol levels immediately before and after the CECA interview using salivettes (Sarstedt) collection devices. Previous research revealed saliva cortisol to constitute a good proxy for the assessment of HPA axis activity (Kirschbaum and Hellhammer, 1994). Saliva samples were frozen and stored at $-20\,^{\circ}C$ until assay. After thawing, salivettes were centrifuged at 3000 rpm for 5 min, which resulted in a clear supernatant of low viscosity. Salivary concentrations were measured using commercially available chemiluminescence immunoassay with high sensitivity (IBL International, Hamburg, Germany). Sample and reagent handling was semi-automated using a liquid handling robot (Genesis, Tecan, Switzerland) and quality control samples of low, medium, and high cortisol concentrations were run on each microtiter plate assayed. The intra and interassay coefficients for cortisol were both below 8%. Moreover, we took *hair samples* for the analysis of basal cortisol levels of the past three months. Procedures for the analysis of hair cortisol are described in Gao et al. (2013). The analysis of cortisol in hair has been shown to be a reliable and valid method for the retrospective assessment of cumulative cortisol up to several months (Stalder and Kirschbaum, 2012). Data were excluded if hair samples were shorter than 3 cm, which was the case for 1 out of 64 samples. Biochemical assays for the analyses of

saliva and hair samples were performed at the Laboratory of the Department of Biological Psychology at the Technical University of Dresden (Prof. Clemens Kirschbaum).

2.3. Analytic strategy

Statistical analyses were performed using the statistical software STATA 15.0. We took account of the dependence of samples in all our analyses comparing sibling dyads. First, we tested for significant differences between the dyads regarding variables that might potentially be confounded with cortisol levels using multi-level mixed effects linear regression for continuous variables (body mass index; days since the last menstrual cycle) and conditional fixed-effects logistic regression for categorical variables (regular use of medication; smoking behavior; substance abuse). Second, differences between siblings regarding the total score of CA were analyzed using multi-level mixed effects linear regression. Third, to test for the correspondence of reports of CA between siblings, we computed intraclass correlation coefficients (ICC) for two-way mixed-effects models for the total score of CA. Fourth, we performed a multi-level mixed-effects linear regression testing for main effects of group (NSSI; siblings), time of sampling (before and after the trauma [CECA] interview) and for interactions between group and time of sampling in the prediction of saliva cortisol levels and for differences in hair cortisol levels. For results of mixed-effects models, we report standardized β-coefficients as indicators of effect sizes. Finally, we tested for relations between the total score of CA and the slope of cortisol levels during the trauma interview for adolescents engaging in NSSI and their siblings. Given that cortisol data were skewed, we log-transformed salivary cortisol data and used the Huber-White sandwich estimator. Regarding hair cortisol, we applied a multilevel mixed-effects generalized linear model with a log-link, which resulted in normally distributed residuals.

We tested whether the results differed depending on the adjustment for gender (for analyses including CA and/or salivary or hair cortisol levels), smoking behavior (for analyses including salivary or hair cortisol levels), the time of day at the beginning of the assessment and the duration of the assessment (for analyses including salivary cortisol levels). The overall results of our models did not differ in dependence of the inclusion or exclusion of covariates. Results are consequently reported only for analyses with covariates. Moreover, we tested whether results changed if dyads with siblings with past or present NSSI or dyads with adolescents who had experienced sexual abuse occurring outside the family environment were excluded from the analyses. Results did not change, so we relied our analyses on the whole sample.

3. Results

3.1. Descriptive statistics

Overall, 32 sibling dyads were included in our study; among them were 4 dyads of dizygotic twins. Twenty-eight (87.5%) dyads were grown up together and still living in the same household(s), 4 (12.5) dyads were living in separate households for 1 to 3 years (e.g., due to moving out of the older sibling). Adolescents engaging in NSSI were on average 15.82 years (SD = 1.33) and the siblings 15.61 years old (SD = 2.35), with 14 (50.0%) adolescents engaging in NSSI being older and 14 being younger than their sibling. There was an average age difference of M = 2.34 years (SD = 1.21) between siblings. We included 23 (71.9%) same-sex and 9 (28.1%) opposite-sex dyads in our sample, whereby adolescents of the NSSI group were all female. Adolescents were visiting comparable school types in both groups: 20 adolescents engaging in NSSI and 18 siblings attended the *Gymnasium* (terminating with the general qualification for university entrance), 7 from each group attended the *Realschule* (terminating with a secondary school level-I certificate) and 5 or respectively 7 adolescents attended a *Hauptschule* (9 years of elementary school) or another school type.

Table 1
Number of axis I diagnoses and BPD diagnostic criteria (DSM-IV) for adolescents engaging in NSSI and their siblings.

	NSSI group (n = 32)		siblings (n = 32)	
	n	%	n	%
Axis I diagnoses				
Mental and behavioural disorders due to psychoactive substance use	8	25.00	3	9.38
Schizophrenia, schizotypal and delusional disorders	0	0	0	0
Affective disorders	27	84.38	9	28.13
Neurotic, stress-related and somatoform disorders	18	56.25	8	25.00
Behavioral syndromes associated with physiological disturbances and physical factors	5	15.63	0	0
Disorders of psychological development	0	0	0	0
Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	6	18.75	4	12.50
BPD diagnostic criteria				
Fear of abandonment	2	6.25	1	3.13
Unstable relationships	12	37.50	2	6.25
Identity disturbances	11	34.38	1	3.13
Impulsivity	9	28.13	3	9.38
Self-harm / Suicidality	32	100	5	15.63
Affective instability	19	59.38	8	25
Inner emptiness	18	56.25	1	3.13
Inappropriate anger	6	18.75	2	6.25
Paranoia / Dissociation	14	43.75	4	12.50

Notes: NSSI = non-suicidal self-injury; BPD = Borderline Personality Disorder; n = number of participants.

Adolescents engaging in NSSI and siblings fulfilled on average the criteria for 2 (SD = .88) and 0.75 (SD = 1.02) groups of axis I diagnoses and 3.81 (SD = 2.07) and 0.81 (SD = 1.51) diagnostic criteria of BPD, respectively (see Table 1). In the NSSI group, frequency of NSSI was on average 63.22 times during the last year (SD = 68.62; Median = 50; IQR = 70) and 5.13 times during the last month (SD = 8.45; Median = 2; IQR = 6). The most common forms of NSSI were deliberate cutting (100%), followed by manipulating wounds (68.8%), hitting one's body (65.6%), scratching (59.4%), biting (53.13%) and burning one's body (43.75%). In the sibling group, 6 out of 32 adolescents (18.75%) reported that they had ever engaged in NSSI with a frequency of M = 5.83 during the last year (SD = 7.83; Median = 2; IQR = 9) and 0.40 during the last month (SD = .55; Median = 0; IQR = 1). Twenty-two adolescents (68.8%) in the NSSI group and one in the sibling group (3.13) reported that they had already attempted suicide at least once during lifetime.

No significant differences were found between siblings regarding their body mass index (NSSI: M = 21.64, SD = 2.62; siblings: M = 20.77; SD = 3.24; $\chi^2_{(1)}$ = 1.92; p = .17; 95% CI_{MD} = -2.10 - 0.36; β = -0.15), days since last menstrual cycle (NSSI: M = 15.15, SD = 10.34; siblings: M = 18.32; SD = 13.47; $\chi^2_{(1)}$ = .94; p = .33; CI_{MD} = -2.80 - 8.28; β = .12), the regular use of medication (OR = .33, p = .18; 95% CI = .07–1.65) or substance abuse (OR = .29, p = .12; 95% CI = .06–1.38). A significant higher proportion of adolescents engaging in NSSI (14 out of 32) reported regular smoking behavior compared to their siblings (5 out of 32) (OR = -2.15, p = .03; 95% CI = .07–.89).

3.2. Experiences of childhood adversities

Adolescents engaging in NSSI reported significantly more severe experiences of CA with respect to the total score of CA (β = -0.29; see Table 2). In the NSSI group, 11 (34.4%) adolescents reported moderate to severe experiences of antipathy, 4 (12.5%) of neglect, 5 (15.6%) of

Table 2
Means and standard deviations of experiences of CA and cortisol levels for adolescents engaging in NSSI and their siblings.

	NSSI group (n = 32)		siblings (n = 32)		Group differences		
	M	*SD*	*M*	*SD*	*z*	*p*	95% CI_{MD}
Total score of CA	2.69	2.35	1.41	1.56	−2.73	< .01	−2.05 – −.34
Salivary cortisol before the CECA	5.59	4.69	4.42	3.77	−.89	.37	−.56 – .21
Salivary cortisol after the CECA	3.26	2.11	4.68	5.40	.50	.62	−.31 – .53
Hair cortisol	3.16	1.97	3.04	2.40	−2.57	.01	−.41 – −.06

Notes: NSSI = non-suicidal self-injury; CA = childhood adversity; CECA = Childhood experiences of care and abuse interview; *M* = mean; *SD* = standard deviation; 95% CI MD = 95% confidence interval for the mean difference between groups. *n* = number of participants. The total score of CA ranges from 0 (no adversity) to 15 (severe adversity on all subscales). Salivary cortisol is indicated in nmol/l. Hair cortisol is indicated in pg/mg. * Covariates included the following variables: gender for analyses regarding the total score of CA; gender and smoking behavior for analyses regarding hair cortisol; gender, smoking behavior and time of assessment for analyses regarding salivary cortisol before the CECA; gender, smoking behavior, time of assessment and duration of the interview for analyses regarding salivary cortisol after the CECA.
Mean values and standard deviations are based on unstandardized values. Statistics on group differences in salivary cortisol are based on log-transformed values and on hair cortisol on results from a general linear model with log-link.

physical abuse, 4 (12.5%) of sexual abuse (all occurring outside the family environment), and 2 (6.3%) of psychological abuse. In the sibling group, 5 (15.6%) adolescents reported severe experiences of antipathy, 3 (9.4%) of neglect, and 1 (3.1%) of psychological abuse. Overall, 17 (53.1%) adolescents from the NSSI group and 14 (43.8%) adolescents from the sibling group reported experiences of at least one form of a severe adversity or abuse. Our findings revealed a moderate intercorrelation between siblings for the total score of CA (ICC = .32, p = .01; 95% CI = -0.0003 – .59).

3.3. Cortisol reactivity to the retrieval of adverse experiences and basal cortisol levels

Regarding salivary cortisol levels during the appointment, we did not find significant main effects for the comparison between groups (NSSI and siblings; $\chi^2_{(1)}$ = .13, p = .72, β = -0.13) but for the time of sampling (before and after the trauma interview; $\chi^2_{(1)}$ = 18.25, p < .01, β = -0.28) and a significant interaction between the group affiliation and the time of sampling ($\chi^2_{(1)}$ = 5.72, p = .02, β = .16) (see Fig. 1). A significant decrease of salivary cortisol was found only in the NSSI group ($\chi^2_{(1)}$ = 40.56, p < .01). There was no significant group difference in the time of day at the beginning of the assessment (NSSI: M = 14:29; SD = 1 h, 59 min; siblings: M = 14:32; SD = 1 h, 49 min; χ^2 = 0.02, p = .90. CI_{MD} = 39.04–44.66 min, β = 0.01). Moreover, the duration of the trauma interview did not vary significantly (χ^2 = 2.23, p = .14; CI_{MD} = - 10.46 – 1.41 min, β = -0.16) between adolescents engaging in NSSI (M = 52.00 min; SD = 16.58) and their siblings (M = 47.29 min; SD = 12.17). We did not find group differences in basal cortisol levels retrieved from hair samples between adolescents engaging in NSSI and their siblings in the model not taking account of covariates. However, adolescents from the NSSI group exhibited significantly higher hair cortisol levels when controlling for smoking behavior and gender (see Table 2).

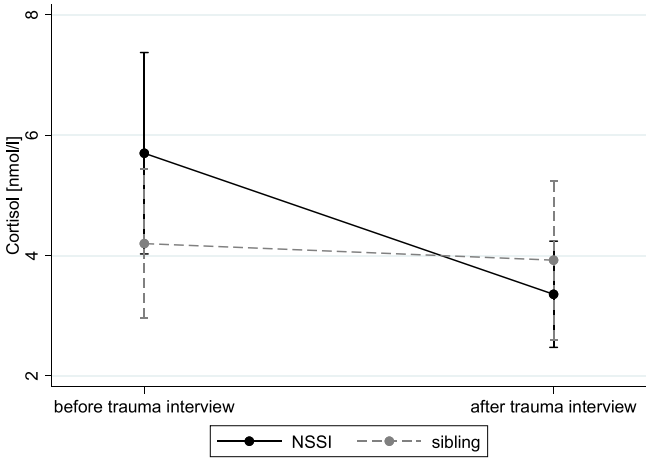

Fig. 1. Salivary cortisol levels in adolescents engaging in NSSI and their siblings before and after the assessment of a trauma interview (CECA).
Notes: NSSI = non-suicidal self-injury; Vertical lines indicate the 95% confidence intervals. For a more comprehensible presentation, unstandardized values are depicted.

We did not find any significant relations between the slope of cortisol during the trauma interview and the severity of CA among adolescents engaging in NSSI (r < -0.01, p > .99; 95% CI = -.07 –.07) or among siblings (r = -0.03, p = .76; 95% CI = -.19 – .14) and regression coefficients did not vary significantly between groups (χ^2 = 0.09, p = .77). Moreover, the total score of CA was not related to hair cortisol levels in the group of adolescents engaging in NSSI (r = .04, p = .67, 95% CI = -0.13 – .20) or the sibling group (r = -0.04, p = .81, 95°% CI = -.34 – .26).

4. Discussion

The present study sought to investigate HPA axis responsivity to the retrieval of CA in adolescents engaging in NSSI and their siblings. In general, adolescents engaging in NSSI reported more severe experiences of CA compared to their siblings. Moderate agreements in reports of CA were found in our study. We did not find differences between adolescents engaging in NSSI and their siblings regarding salivary cortisol before or after a trauma interview. However, a significant slope of cortisol during the interview was found only for the NSSI group. Changes in cortisol levels during the interview were not related to the severity of CA. Adolescents from the NSSI group had significantly higher hair cortisol levels when controlling for smoking behavior and gender.

Although the use of a sibling design comes along with several advantages, it has not received a lot of attention in psychiatric research yet. Rather it is often assumed that familial risk for neglect of abusive behavior is equivalent for children or adolescents growing up in the same family environment (Hines et al., 2006). Findings from our study revealed moderate agreements between siblings' reports of CA. In general, our results correspond well to those from previous research (Bifulco et al., 1997; Laporte et al., 2012). Substantially higher agreements were found by Hines et al. (2006) for neglectful behaviors in children drawn from clinical and community samples. The authors argued that a higher correspondence between siblings regarding neglectful behaviors might be explained by neglect being less child- and more family-specific than other forms of maltreatment.

Despite the substantial agreements between siblings, it needs to be mentioned that an important part of variance in adolescents' reports of

CA could not be explained by their siblings reports of adversity. Several reasons might explain differences in siblings' reports of CA. On the one hand, parents might behave differentially towards siblings (Dunn and Plomin, 1991) putting one child in greater risk for poor parenting behavior, abuse or neglect than the other. On the other hand, siblings might differentially perceive (Neiderhiser et al., 1998), memorize (Bifulco et al., 1997) or react to (Plomin et al., 2001) shared familial experiences. Differential parental treatment as well as interindividual differences in the perception of and reaction to shared experiences could have moderated effects of CA on the development of NSSI, corresponding to our finding of significantly more severe reports of CA in the NSSI group compared to their siblings.

In the present study, NSSI moderated cortisol responses to the retrieval of CA during a clinical interview. A significant slope of salivary cortisol during the interview was found among adolescents engaging in NSSI but not among their siblings. Referring to the cognitive model of posttraumatic stress disorder proposed by Ehlers and Clark (2000), we assumed that the retrieval of adverse experiences during the CECA interview might trigger negative emotions (e.g. fear, feelings of powerlessness) that have been stored during the adverse event in the perceptual memory which consequently results in increased HPA axis functioning in both groups. Referring to previous work regarding cortisol responses of adolescents engaging in NSSI (Kaess et al., 2012; Plener et al., 2017) and individuals with suicidal behavior (Eisenlohr-Moul et al., 2018; O'Connor et al., 2017) to psychosocial stress, we further hypothesized a less pronounced cortisol response in the NSSI compared to the sibling group. In case that negative emotions might have been triggered in the interview, this did not result in an increased cortisol secretion in none of the two groups. It could be hypothesized that the retrieval of CA evokes stress among adolescents engaging in NSSI but that the use of dissociative coping styles results in a shutdown of the stress system. The literature on the relationship between dissociative symptoms and cortisol reactivity to acute stress experiences is still inconsistent with previous studies reporting that dissociative symptoms are positively (e.g., Simeon et al., 2007) or negatively (e.g., Powers et al., 2006) related to cortisol secretion. However, all these studies focused on psychosocial stressors. To our knowledge, only one study has thus far investigated correlations between dissociative symptoms and HPA axis reactivity to the retrieval of traumatic experiences: Koopman et al. (2003) did not find immediate changes in plasma cortisol after a trauma-related interview among sexually abused women but an increase of plasma cortisol after a delayed period of 24 h which was increased for women with acute dissociative symptoms. With respect to PTSD, a dissociative subtype has been proposed that contrasts to the non-dissociative subtype by a decrease in heart rate and amygdala activation in response to traumatic reminders (van Huijstee and Vermetten, 2017). Further studies are needed to investigate whether dissociative symptoms might lead to an attenuated cortisol secretion among adolescents engaging in NSSI during trauma retrieval. Given that our study design did not include measures of acute dissociative symptoms before, during and after the interview, we can only give an idea of what might be promising directions for future research.

Our findings might alternatively be explained by CA having generally resulted in a long-term downregulation of the HPA axis (Strüber et al., 2014) among adolescents engaging in NSSI, which could also appear in the context of trauma retrieval. This is in line with previous studies showing decreased cortisol responses to psychosocial stress among adolescents engaging in NSSI (Kaess et al., 2012; Plener et al., 2017). Moreover, it might be explained by the theoretical assumptions of Lovallo (2013). Specifically, he formulated a conceptual model describing different pathways by which experiences of CA might lead to risk-taking and impulsive behaviors and subsequently to poor health and addiction behaviors. Mechanisms such as alterations in frontolimbic functions, a blunted reactivity of the HPA axis, an altered cognition and an associated orientation on short term goals, as well as an unstable affect regulation are proposed as mechanisms mediating relations between CA and impulsive and risk-taking behaviors. However, our findings of hair cortisol being significantly increased among adolescents engaging in NSSI contradicts the assumption of the HPA axis being generally downregulated among adolescents engaging in NSSI.

Finally, we cannot rule out the possibility that the decrease in salivary cortisol concentration in the NSSI group may be a function of personal interaction irrespective of the content of the interview. In this sense, Kolassa et al. (2007) found a decrease in salivary cortisol among male refugees who were interviewed about experiences during torture and those who were neutrally interrogated about their absorption behavior. In general, it need to be mentioned that the salivary cortisol levels (mean of levels before and after the interview) for adolescents in the NSSI and the sibling group correspond well to the mean salivary cortisol levels during the day that have been reported for healthy female adolescents (Oskis et al., 2009).

Moreover, our results do not correspond to previous studies who found blunted baseline cortisol levels in expectancy of a psychosocial stressor among individuals who had attempted suicide compared to non-attempters (Keilp et al., 2016; Melhem et al., 2016). Even though, baseline cortisol levels before the interview did not differ significantly between groups, adolescents from the NSSI group showed in tendency higher salivary cortisol levels in expectancy of the trauma interview.

Contrary to our expectation, the severity of CA was not related to changes in cortisol secretion during the interview. This finding contradicts those reported by O'Connor et al. (2018), who found relations between the severity of experiences of CA and blunted cortisol responses to a stress test among young adults with a history of suicide attempts. The use of different inventories for the assessment of CA could give one possible explanation for these divergent findings. While O'Connor et al. (2018) made use of a self-report questionnaire, we assessed CA by clinical interviews. The CECA interview aims at giving an as objective rating of the severity of CA as possible. Ratings refer to concrete examples of adversities rather than to the severity perceived by the interviewee. It is possible that HPA axis functioning might be more related to the subjectively perceived severity of CA than to objective ratings of CA. Alternatively, the retrieval of even severe forms of CA during a clinical interview might not have induced distress among the interviewees which consequently did not result in an increased cortisol secretion. It needs to be mentioned that adolescents from the NSSI group were all seeking help in our department and have for the majority already received therapeutic treatment. It could be assumed that they have already get used to talking about personal issues and adverse life experiences.

Our investigation of HPA axis activity further revealed significant differences between siblings on basal (hair) cortisol levels. It might be expected that self-harming behavior is associated with a set of psychological variables known to increase basal cortisol levels among adolescents engaging in NSSI. For example, NSSI has been shown to be associated with increased levels of distress (Richmond et al., 2017) or poorer sleep quality (Liu et al., 2017). Referring to our finding of the NSSI group showing a significantly steeper decline in salivary cortisol levels during the interview, it could be hypothesized that adolescents engaging in NSSI in general show increased HPA axis functioning whereas the stress system is downregulated in specific stressful situations. However, our finding contradicts those of a previous study (Reichl et al., 2016) that did not find significant differences in hair cortisol between adolescents engaging in NSSI and a healthy control group and those of Melhem et al. (2017) who found lower hair cortisol levels among young people who attempted suicide compared to a healthy control group. However, referring to previous results from twin studies, it may be argued that basal cortisol should be more strongly influenced by genetic factors than diurnal cortisol (Tucker-Drob et al., 2017; Van Hulle et al., 2012), reducing differences between siblings irrespective of experiences gained within the family environment or through the effects of psychopathology.

4.1. Limitations and directions for future research

This study investigated HPA axis reactivity to the retrieval of CA in the context of NSSI making use of an innovative sibling design and reliable clinical interviews. However, our results should be considered in the light of some limitations. First, the sibling group was heterogeneous with regard to the position in birth order, gender and psychopathology. Whereas gender was unrelated to experiences of CA or cortisol levels, we could not account for potential effects of birth order due to the small sample size. Moreover, we do not know whether siblings being younger might start engaging in NSSI in the future. However, the mean age of NSSI onset in the NSSI group was at 12.34 years (SD = 1.47). Only two participants from the sibling group were under this age. Second, the sibling group cannot entirely be considered a healthy control group. However, our results did not change if dyads with siblings who have ever attempted suicide or engaged in NSSI were excluded from our study. Moreover, the lifetime prevalence of NSSI in the sibling group was below the rate reported for a representative community sample of German pupils (Brunner et al., 2014). Third, our study did not control for the duration of sleep during the last night and the time of awakening, which might affect cortisol levels during the day. Fourth, we only applied single measures of salivary cortisol before and after the trauma interview. Future research would benefit from using multiple measures throughout the interview to detect the course of cortisol secretion during trauma retrieval. Fifth, we did not assess stress perception before and after the trauma interview. However, it would be important for the interpretation of our results to understand whether the retrieval of CA was perceived as stressful by the participants and whether this potential stress induction is associated with changes in cortisol secretion. Sixth, the assessment of CA allowed for the assessment of sexual abuse occurring outside the family environment affecting comparability between siblings. Whereas four individuals from the NSSI group reported experiences of sexual abuse (all occurring outside the family environment), no sibling reported any experience of sexual abuse. However, the exclusion of those four dyads with one adolescent reporting sexual abuse did not change our results. Seventh, our study relied on a small sample size, which comes along with an increased risk for sampling errors and a limited power to detect true effect sizes.

Another critical point concerns the fact that siblings reported significantly less severe experiences of CA than adolescents engaging in NSSI. One main objective of the present study was to test for specific effects of NSSI on alterations in HPA axis functioning by comparing dyads of siblings who were supposed to have experienced comparable adversities. Although we found moderate agreements between siblings with regard to ratings of CA, the reported differences in the severity of CA limit the interpretation of our results. Future research could examine HPA axis functioning during stress exposure of adolescents engaging in NSSI by comparing groups of adolescents with and without experiences of CA.

4.2. Summary and conclusions

In our study, siblings' reports of CA experienced within the family environment were moderately correlated. On the one hand, practitioners should be aware of an increased risk for siblings experiencing comparable CA than those reported by patients. On the other hand, the moderate interrelations in reports of CA also underline the importance of considering interindividual differences for example through differential treatment of siblings by parents or through differences in perception or memorization. We further found group (NSSI; siblings) and time of sampling (before and after an announced interview about CA) to interact in the prediction of salivary cortisol concentration. We found a significant slope of cortisol during the interview only among adolescents engaging in NSSI. This finding might carefully be interpreted by a downregulation of the HPA axis in stressful situations subsequent to the experience of CA among adolescents engaging in NSSI. Changes in cortisol secretion during the trauma interview were unrelated to the severity of CA. We further found slightly increased hair cortisol levels in the NSSI group compared to the sibling group. This points to a generally increased HPA axis activity among adolescents engaging in NSSI that might not be related to stress stimulation in specific demanding situations.

Declaration of Competing Interest

None.

Acknowledgements

We thank the Dres. Majic/Majic-Schelz-Foundation that financially supported this study.

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