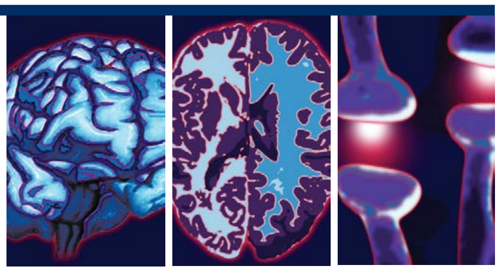
Research



Psychopathology and Patterns of Sensory Processing In Non-suicidal Self-Injured Adolescents: Insights from Neuropsychological and Neurophysiological Studies

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ABSTRACT

Background and objectives

Nonsuicidal self-injury (NSSI) is most common in adolescent populations whose prevalence is continuously increasing. The underlying neurobiology of NSSI and pain processing has not yet sufficiently understood. Alterations of the sensory processing and modulation could explain the emotional dysregulation. We investigated the clinical usefulness of short and long-latency somatosensory evoked potentials (Sh and LL-SSEPs) as indirect evaluation of sensory processing characteristics, compared to psychological, sensory and behavioural measures in adolescents with NSSI.

Methods

A group of 12 patients with NSSI and a control group comprised 9 patients with other psychopathological disorders without NSSI were investigated with the Self Harm subscale of the Risk-Taking and Self-Harm Inventory for Adolescents, the Italian form of assessment of self-injurious behaviour, the Adult/Adolescent the Sensory Profile (SP), an Italian a self-report psychiatric scale for children and adolescents (SAFA), Theory of Mind and Affect Recognition subscale of NEPSY II. All data tests were compare to median nerve Sh-LL SEP. We adopted a Bayesian approach to the statistical analyses.

Results

The two groups substantially differed in some scales of the SAFA with higher scores in the subscale of inadequacy, anorexic conduct and body acceptance, and in lower scores in the Emotional/social response of SP in the NSSI group.

Conclusion

Prolonged latency of N140 LL-SEPs could be considered a marker for the altered ability to modulate the incoming sensory responses in a group of adolescents with NSSI. This could be the basis of the emotional dysregulation found in the NSSI subjects, with the consequent impossibility to put in place adequate behavioral responses and predilection of deactivated coping strategies. These hypotheses should be confirmed by future studies on larger samples.

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Keywords

Nonsuicidal self-Injury, Adolescent, NEPSY-II, RITSHIA, Italian SRCA, AASP, Short latency somatosensory Evoked potentials, Long latency somatosensory evoked potentials, Sensory processing

Introduction

Nonsuicidal self-injury (NSSI) is the intentional damaging (e.g., by cutting, burning, or scratching, or a combination of these) of one's own body tissue to induce bleeding, bruising, or pain without suicidal intent and for purposes not socially sanctioned. Injuries are usually shallow, yet painful, and are inflicted with the purpose of reducing negative emotions or to cope with interpersonal difficulty. This process provides an immediate sensation of relief that might lead to a sense of urgency and craving that, in its turn, can yield an addiction-like behavioral pattern [1].

NSSI is most common in adolescent populations (7-47%) [2] With a typical onset at age 12-14 [3], while it is less observed in adults (3%-6%), [4,5], but its prevalence can rise as high as 60% in adolescent psychiatric populations [6]. Although not formally recognized as a disorder in diagnostic manuals, the NSSI has been included as a condition requiring further study in Section III, Emerging Measures and Models of the most recent edition of the Diagnostic and Statistical Manual of Mental disorders (DSM-5) [7].

The underlying neurobiology of NSSI and pain processing has not yet sufficiently understood, but many studies have shown that adolescents engaged in NSSI have a higher pain tolerance and threshold than the general population [8-11]. Other studies suggest a possible role of a generalized deficit in the somatosensory information processing [12]. Alterations of the sensory processing and modulation could explain the emotional dysregulation and the reduced problem-solving skills of adolescents that engage in impulsive and maladaptive behaviours as NSSI [13-15].

At the physiological level, somatization and sensory processing can be investigated by short and long-latency somatosensory evoked potentials (Sh and LL-SSEPs), which assess function of the dorsal column–medial lemniscal system, ventroposterior thalamus, and reflect brain activity related to the processing of somatosensory stimuli (the primary somatosensory cortex (SI) in the postcentral gyrus, secondary somatosensory cortex (SII) in the parietal operculum and into the insula with bilateral input, in the posterior parietal cortex) [16,17]. SEP is electroencephalographic components occurring time-locked to somatosensory stimuli. Their late components appear to indicate psychological processes of perception and appraisal [18]. LL-SEPs have been suggested as possible vulnerability markers for affective disorders [19,20] found significant differences between a group with major depressive disorder and a control group in the 170–370 ms range. Relevant to this study, Schmahl et al. [11] compared women meeting criteria for Borderline Personality Disorder (in which NSSI has a prevalence of 70-80%) with healthy female control participants, but did not find any significant differences in laser-evoked potentials amplitudes. They Authors argued that a disturbance of the affective-motivational or cognitive-evaluative pain components were the most likely mechanisms of the analgesic state.

Since NSSI in adolescents usually occurs without association to any other overt psychopathology [21] or related to depression [22], in the present study we investigated the clinical usefulness of short (latency<40 msec) and long-latency somatosensory evoked potentials (Sh and LL-SSEPs) (latency>40 msec) as indirect evaluation of sensory processing characteristics, compared to psychological, sensory and behavioural measures in adolescents with NSSI.

Materials and Methods

■ Participants

A group of 12 patients (11 females, mean age 13.70 ± 0.97 years) with self-harm was recruited from out and in-patients referred to the Infantile Neuropsychiatry Unit of Gaslini Children's Research Hospital of Genoa. All patients presented with at least one episode of confirmed self-harm within the past year. The control group comprised 9 patients (7 females, mean age 13.56 ± 1.73 years) with other psychopathological disorders without a lifetime history of self-injury.

Inclusion criteria for all participants were age between 10 and 18 years and being right handed. Exclusion criteria included a history of intellectual disability, clinical diagnosis of Psychotic Disorders, Autism Spectrum Disorders or epilepsy, head injury, neurological disorders, current substances abuse. Written informed consent was obtained from all participants.

Experimental procedure

Neuropsycological tests: We evaluated the presence and severity of self-injurious behaviours using the Italian version [23] of the Self Harm subscale of the Risk-Taking and Self-Harm Inventory for Adolescents (RITSHIA) [24]. The clinician also filled in the Italian form of assessment of self-injurious behaviour (Scheda di Rilevamento dei Comportamenti Autolesivi - SRCA [25] to obtain a complementary measure of self-harm features, as frequency, localization, and typology of self-injury.

Furthermore, participants were administered the Adult/Adolescent Sensory Profile (AASP) [26] in order to assess the patterns of sensory processing preferences and they parents were asked to complete Sensory Profile (SP) [27]as a secondary measure of youth sensory preferences. In particular,we focused on some subcategories of SP: touch processing, modulation of sensory input related to emotional response, modulation of visual input affecting emotional responses and activity level, emotional/social responses, and behavioural outcomes of sensory processing.

In order to assess the psychological functioning of the participants, we administered an Italian a self-report psychiatric scale for children and adolescents (Scale Psichiatriche di Autosomministrazione per Fanciulli e Adolescenti [Psychiatric Self-Report Scales for Children and Adolescents] [28], that assesses the presence of anxiety (SAFA A), depression (SAFA D), obsessions (SAFA O), somatic symptoms (SAFA S) and eating disorders (SAFA P). Finally, we administered the Theory of Mind and Affect Recognition subtests of the Italian version [29] of the NEPSY-II battery [30] with the purpose to evaluate participants' social perception and mentalizing abilities.

Short and long latency somatosensory evoked potentials acquisition and signal analysis: Short and long latency somatosensory evoked potentials (Sh–LL SEPs) were recorded on an 8-channel system (Viking on Nicolet EDX Electrodiagnostic System; Natus Medical Incorporated, Middleton, WI, USA). Electrical constant current square wave impulses, with a duration of 0.2 ms and delivered at a rate of 1 Hz, were used to stimulate separately left and right median nerves. The stimulating skin electrodes were placed at the wrist. The sensory threshold was determined individually and the experimental stimuli were set to 1.5 times the individual threshold in order to control for individual differences in somatosensory perception. The bandpass filter was 1-1000 Hz.

To confirm reproducibility, at least two average recordings of 300 responses were superimposed. The analysis time was 300 ms. SEPs were recorded with Ag/AgCl disk electrodes placed on the scalp at Fz, Cz, Pz, Oz, C3, C4, P3 and P4 according to the International 10-20 System referenced to linked earlobes. The impedance was maintained at less than 5 kohm.

The peaks were labelled according to their polarity and latencies in adults: we recorded and analysed temporal and topographical distribution across the cortex of N20-N30-P45-N60-N70-N90-P100-N140.

Statistical analyses

The statistical analyses had two main aims: (i) investigating differences in neuropsychological and behavioral measures and in SEPs across groups and (ii) investigating the association of SEPs with test scores in the NSSI group.

Given the small sample sizes, we used a Bayesian approach. Group comparisons were performed using the *BESTmcmc* function in the BEST package [31], while correlations were computed using the *jzs_cor* function in the BayesMed package [32] in R [33]. In order to control the potentially biasing effect of outlying observations, we first converted observed values in ranks and then translated them into z-scores using the inverse-normal cumulative distribution function, as suggested by Gelman [34].

A detailed description of Bayesian inference methods is beyond the scope of this paper [35], but, in general, they use the Bayes' theorem to update the probability for a hypothesis as more evidence or information becomes available. Parameters of an underlying distribution are estimated grounding on the observed distribution. The likelihood of the observed distribution is then computed as a function of parameter values, multiplied by the prior distribution, and normalized to obtain a unit probability over all possible values. This is called the posterior distribution. A central location index (e.g., the mean, the median, or the mode) of the distribution is then chosen as the parameter estimate, and the bounds of highest posterior density intervals (HPDIs, the Bayesian analog of frequentist confidence intervals) can be determined. As we estimated mean group differences and correlation coefficients, we considered HPDI not including zero as evidence of the presence of a difference or of an association, respectively. As a measure of evidential strength and support for rejecting the null hypothesis of no group differences or no linear associations between variables, we used the Bayes Factor (BF), which is a comparison of how well two competing hypotheses predict the data. Following Lee and Wagenmakers [36], we interpreted BFs as follows: BF<1: no evidence of an effect; 1 ≤ BF<3: anedoctal evidence (barely worth mentioning); 3 ≤ BF<10: moderate (substantial) evidence; 10 ≤ BF < 30: strong evidence; 30 ≤ BF<100: very strong evidence; BF ≥ 100 extreme (decisive) evidence.

Having adopted a Bayesian approach to the analyses, and thus not relying on *p*-values as in the traditional Null Hypothesis Significance Testing approach, no adjustment for multiple comparisons or false discovery rate was needed [37].

Results

In the group with NSSI, 62% engaged in low-intensity NSSI, 38% in mild intensity NSSI. The frequency of self-injurious behaviors was continuous (self-injury that occurred daily) in 15% of cases, frequent (several times a week) in 23% of cases, episodic (more than once a month) or rare (once or more times a year) in 31% of cases each.

The most frequent form of self-injury at the time of evaluation was cutting (100% of patients), followed by scratching and interference with wound healing in 77% of cases, biting and banging the head in 31% of cases, and burning in 23% of cases. The most frequent localization of the self-injurious conduct results in the arms (100% of the subjects), in the tummy and the legs in 38% of cases, in the face in 15% and in the groin in 8% of cases. No significant differences between the two groups were found about the sensory quadrants of A/ASP or SP and the subtests Theory of the Mind and Recognition of Emotions of the NEPSY II.

In the Self-Harm subscale of the RITSHIA questionnaire, patients with self-injurious behaviors obtained, as was expected, markedly higher scores (*M*=19.42, *SD*=8.46) than controls (*M*=1.78, *SD*=2.28, BF=1380.56, HPDI:11.47-23.62).

The two groups substantially differed in some scales of the SAFA-P. The NSSI group showed higher scores in the subscale of inadequacy (*M*=63.38; *SD*=11.69) than the controls (*M*=48.55; *SD*=11.25; BF=5.41, HPDI: 2.87-27.43) and a higher level of symptomatology in the subscale anorexic conduct and body acceptance (*M*=62.00, *SD*=9.96 vs. *M*=51.44, *SD*=11.20, BF=4.50, HPDI: 0.98-22.13). Finally, the NSSI group obtained lower scores than the control group in the Emotional/social response scale of SP (*M*=50.50, *SD*=13.49 vs. *M*=64.78, *SD*=11.05, BF=3.33, HPDI: -26.95- -1.57), suggesting a lower ability of these patients in managing emotional responses.

Substantial differences were found also in the cortical components registered to LL-SEP. The NSSI group showed an increased latency of N140 in C4 from left stimulation (*M*=165.39; *SD*=20.45) compared to the control group (*M*=138.33, *SD*=9.75; BF=236.00, HPDI: 7.93-41.12).

A very strong BF value, with larger values in the NSSI group, was also found for latency of N140 in P3 (*M*=163.25, *SD*=19.10 vs. *M*=135.64, *SD*=9.54, BF=94.91, HPDI: 11.88-42.38) and in P4 (*M*=165.31, *SD*=19.21 vs. *M*=140.67, *SD*=9.64, BF=33.89, HPDI: 9.05-39.70) from right stimulation, as well as of N30 from left stimulation (*M*=31.44, *SD*=1.63 vs. *M*=28.11, *SD*=1.53, BF=98.47, HPDI: 1.68-5.05); strong BF values were also found in the increased latency of N140 in Pz (*M*=164.31, *SD*=19.72 vs. *M*=141.56, *SD*=9.42, BF=10.04, HPDI: 7.62-37.94) and in P4 (*M*=159.67, *SD*=16.29 vs. *M*=139.89, *SD*=8.92, BF=18.01, HPDI: 7.21-32.76) from left stimulation **(Figure 1)**.

Correlations between neurophysiological results and administered questionnaires

We then tested the association between the latency of the N140 with the scores on the SAFA battery, on the SP, and on the subtests Affect Recognition and Theory of Mind of the NEPSY II in the NSSI-engaging group.

The results showed the presence of a strong positive correlation (*r*>0.50) between the increased latency of the N140 from stimulation to the left median nerve in C4, Pz, and P4, as well as from the right stimulus in P3 and P4 with the ability to recognize the emotions evaluated at the NEPSY-II. For a complete view of the results, see **Table 1**.

A correlation between the latency of the N140 in P4 from stimulus on the left median nerve and the scores obtained on Touch Processing of the Sensory Profile (*r*=0.60, BF=3.35, HPDI: 0.09-1.00) was also found **(Figure 2)**.

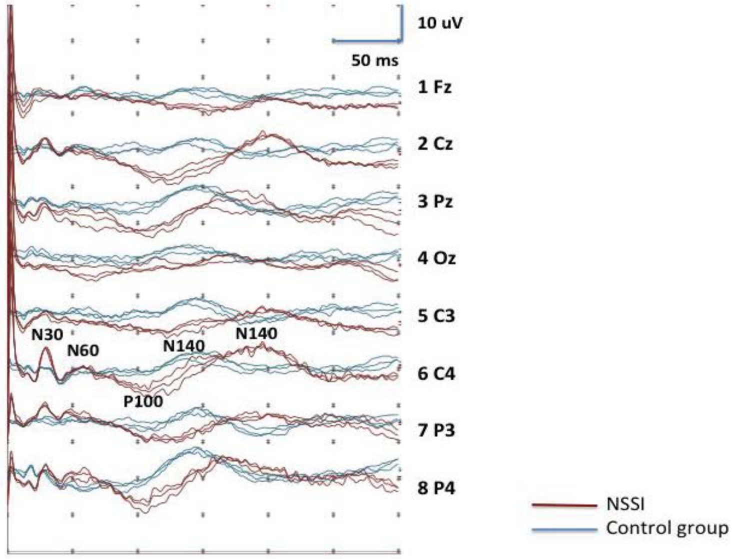

Figure 1: Left median nerve - LLSEP cortical components for NSSI group (red traces) and control group (blue traces): Significant increase of N140 latency in NSSI compare to control group, mainly in C4 electrode.

Table 1: Correlations (Pearson's r) (between latency N140 and the ability to recognize emotions at the NEPSY – II.			
N140 latency	***r* Estimate**	**HPDI**	**BF**
Left median nerve stimulation			
C4	0.72	0.28-1.00	18.44
Pz	0.59	0.09-1.00	3.07
P4	0.67	0.20-1.00	7.60
Right median nerve stimulation			
P3	0.73	0.30-1.00	21.62
P4	0.66	0.19-1.00	7.18

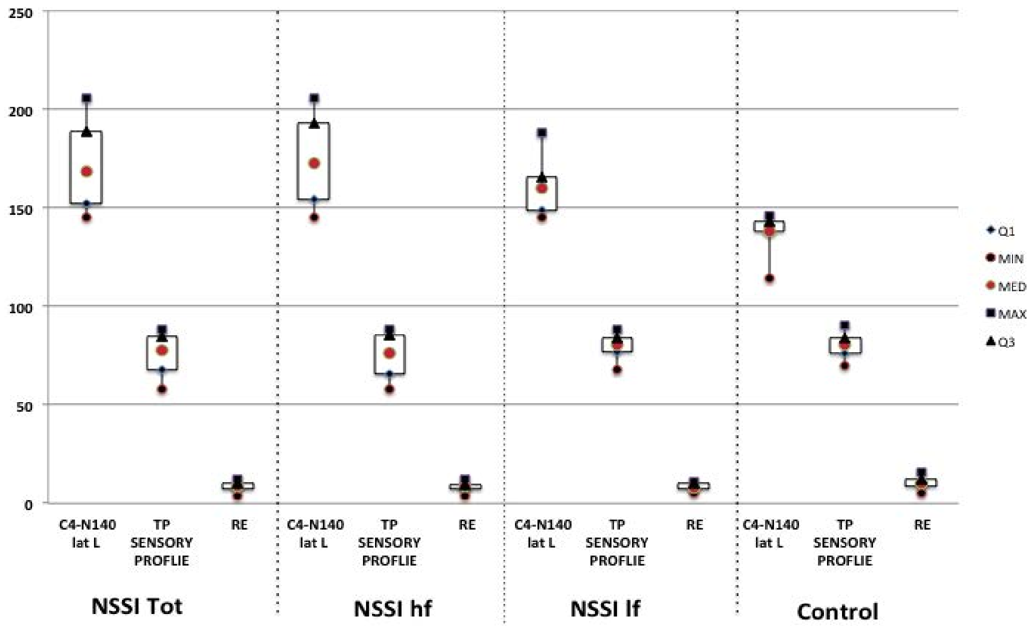

Figure 2: Boxplot representation (average, minimum, maximum, first and third quantile) N140 latency in C4 from left median nerve stimulation (C4-N140 Lat L), score in Touch Processing in Sensory Profile (TP Sensory Profile) and the ability to recognize emotions at the NEPSY - II score (RE) in NSSI group (NSSI Tot - first column), high frequency NSSI (NSSI hf - second column) , low frequency NSSI (NSSI lf - third column) and control group (Control - fourth column): noticed as the trend is very similar between NSSI tot and NSSI hf from one side, and in the NSSI lf and Control in the other side.

Discussion

The present study was designed to address several gaps in the understanding of the sensory functions and neuopsychology of adolescent NSSI. Our sample has characteristics similar to those reported in the literature. In our study the average age of our sample is in progress with the most recent data in the literature according to the onset of self-injurious behaviors most frequently in early adolescence between 12 and 14 years [38-40]. The age is more than 12 years [41] in the clinical reviews, where they are considered with an average of 50 episodes per year [42]. With regard to the intensity of the self-injurious behaviors, the data that emerged from our study (low or moderate intensity) do not agree with what has been described in the literature, that many subjects with self-harm report moderate to severe tissue damage due to their behavior [43,44]. This discrepancy could be due to the fact that, because of the young age of enrolled the subjects, hospital access had occurred following the first episodes of self-harm. The main types of self-injurious performed in our sample, self-cutting and scratching, are similar to those reported in the literature [45-47]. Also with regard to the location of the self-injurious conduct, the data emerged in the proposed study agree with the literature, finding that the most frequently affected body regions are the arms, followed by the legs and abdomen [48,49].

The underlying neurobiology of NSSI and pain processing has not yet sufficiently understood and the different threshold for pain clinically supposed [11] doesn't expalin self-injurious conduct but alterations of the sensory processing and modulation could explain the emotional dysregulation. Regarding the neuropsychological profile, the analysis of the results of the sensory profile obtained in the SP and the A/ASP doesn't support the hypothesis that adolescents with self-injurious behaviors have different sensory preferences in comparison with controls [50]. The subjects with NSSI show lower scores in the sensory quadrant of the sensation seeking, presenting less sensory research behaviors with respect to the controls but without significant differences. The results obtained at the SAFA P scales agree with the literature that highlighted the presence of a greater negative attitude towards the body in those with NSSI compared to controls [51]. Studies have shown that patients with Eating Disorder and self-injurious behaviors have higher levels of body dissatisfaction and self-loathing than patients with DCA without NSSI [52]. Body dissatisfaction plays a critical role in the determination of self-injurious behavior. The vision of the body as a "hated object" facilitates the implementation of self-mutilation behaviors [53,54]. The presence of feelings of inadequacy also agrees with what is reported by numerous studies, which have shown in the NSSI subjects a greater tendency to self-criticism and self-denigration as well as lower self-esteem compared to peers [55]. In this sense, the NSSI behaviours could represent a strategy of self-regulation of emotions mediated by the body and put in place by subjects with negative representations of self and poor adaptive regulation strategies.

The main data that emerges from our study regarding LL-SEP is the increase in latency of N140 in subjects with NSSI. The N140 component is considered the most sensitive marker for the processing capacity of the sensory stimulus. The P100-N140 temporal sequence through the stimuli is modulated in the time interval 120-220 ms for N140, with an initial lateralization of the component generator on the contralateral somatosensory cortex and a subsequent ipsilateral, and therefore bilateral, representation [56]. In particular, the N140 component reflects the activation of area 46 at the mid-frontal level that regulates cognitive behavior, recalling and maintaining as important the representations of objects or relations in space. Furthermore, the interactions of area 46 with the posterior parietal cortex and the formation of the hippocampus allow the association of a cognitive meaning to sensory stimuli [57]. In NSSI subjects, this component which presents important cognitive and affective characteristics, results in latency increased above all contralateral to the stimulus, already in the first phase of its formation, before becoming also ipsilateral. The corresponding behavioral correlation could manifest itself with a low relevance of the stimulus for the subject: the subject with NSSI would not be able, in fact, to consider the delivered stimulus relevant, although there is no alteration of the stimulus arrival in the primary cortex (N20), therefore in the early phase of the processing of the sensory stimulus.

This increase in latency of main component of LL-SEP could find its physiopathological justification in the results of functional MR studies [58], which showed that there are no differences, between subjects with NSSI and controls, in the neuronal response to electrical stimuli of increasing intensity of the posterior insula, commonly associated with the discriminative perception of stimuli of intensity deemed not pleasant. The same pattern was observed at the level of the primary somatosensory cortex (SI) while there was a significant reduction in intensity-modulated neuronal activation in the anterior insula bilaterally in NSSI subjects compared to controls.

Thus, the NSSI subjects seem unable to modulate the neuronal response of the anterior amygdala based on the intensity of the stimulus. In fact, the anterior amygdala is responsible for processing cognitive aspects as well as emotional aspects and their regulation.

The NSSI subject seems to have lost the ability to modulate the response to the sensory stimulus by the anterior amygdala and the neurophysiological correlation could be the increase in latency of the N140 (correlated with the ability to recognize the emotions evaluated at the NEPSY-II and the scorees obtained on Touch Processing of the Sensory Profile).

Furthermore, the lack of alterations in the ability to process tactile stimuli, demonstrated by the scores in the SP touch processing standard and by the no differences in latency and amplitude of Sh-SEP components in the NSSI group, could underline how in these subjects there is no deficit in the stimulus-discrimination processes; this agrees with what emerges from the few existing studies in the literature that described a generalized deficit of somatosensory processing in these subjects. Pavony and Lenzeweger [59], examining the exteroceptive and proprioceptive abilities compared to controls in subjects with characteristics of Borderline Personality Disorder and NSSI through tactile discrimination tests of a two-point stimulation and weight discrimination, have shown that these subjects do not they have generalized somatosensory deficits, but greater precision in detecting tactile stimuli and greater impulsivity, with a tendency to respond even in the absence of the stimulus.

The altered ability to decode the salience of stimuli would therefore make the subject with NSSI an error of emotional-cognitive evaluation regarding the processing of received and self-inflicted exogenous stimuli.

In particular, the increased latency of medium and late latency components (N30, N140) could underlie to a distortion in the processes of stimulus processing.

For their ability to explore the somatosensitive pathway and the processing of the sensory stimulus, LL-SEPs have been used in the last thirty years to try to understand the mechanisms of alteration of the processing of the sensory stimulus that underlie and sometimes unite the main psychiatric pathologies such as depression [60-62,19,20], psychosis [63], Borderline Personality Disorder [64], obsessive-compulsive disorder [65], schizophrenia, and suicidal behavior [61,66]. with results that are not always consistent.

Limits: The proposed study has some limitations. In the first place, the reduced number of the recruited sample imposes limits in statistical processing and therefore also in their interpretation and applicability on large numbers.

It would therefore be desirable to expand the sample in the study to eventually confirm the data obtained and to deepen some aspects that emerged of the distinction between the two groups without achieving statistical significance.

In addition, the control group, recruited by a clinical population belonging to the U.O. of Neuropsychiatry, it was found to consist of subjects affected by different psychopathological frameworks. The psychiatric diagnoses, highlighted in the control group, although not homogeneous, have nevertheless allowed to hypothesize that the latency changes of the cortical components of LL-SEP are closely linked to self-injurious behavior and not to the presence of psychopathology in and of itself.

As for the LL-SEP, moreover, the cortical components were registered on an 8-channel system, thus not allowing to evaluate any changes in the topographic distribution of the late components on the scalp.

Conclusions

This study is one of the few studies that has proposed to examine the presence of an alteration of the sensory processing process in adolescents with NSSI.

The data obtained therefore demonstrate the actual presence of an alteration of the sensory processing and modulation in subjects with NSSI. The finding of increased latencies of the N140 could in fact be related to an altered ability of the amygdala to modulate the incoming sensory responses. This could be the basis of the emotional dysregulation found in the same subjects, with the consequent impossibility to put in place adequate behavioral responses and predilection of maladaptive coping strategies. All this, together with the response of a negative attitude towards one's own body, could be the basis of the mechanism that pushes adolescents to engage in NSSI.

These hypotheses should be confirmed by future studies on larger samples.

To our knowledge, it's the first time that LL-SEPs have been used to investigate the ability to process sensory stimulation in a group of adolescents with NSSI. The N140 component may in our opinion be proposed as one of the neurophysiological markers of the alteration of the sensory stimulation processing capacity in adolescents with NSSI irrespective of the presence or absence of another associated neuopsychiatric pathology. The significant increase in latency of the N140 both hypsi and contralateral to the stimulus seems to support the hypothesis that NSSI is a pathological condition in itself that can be associated with other psychopathological conditions.

Conflict of Interest

The authors declare no conflict of interest. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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